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Histopathologic prognostic factors for alopecia areata treated by intralesional corticosteroid

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Introduction: Alopecia areata (AA) is a common distress skin condition. Successful treatments are associated with several factors. Although clinical prognostic factors have been reported, histopathologic prognostic factors have not been revealed in alopecia areata.

Objectives: The objectives of this study were to evaluate histopathologic prognosis factors in intralesional corticosteroid treatment for alopecia areata.

Material and methods: In a nested case-control study, all patients with less than 50% area involvement of AA were diagnosed as alopecia areata by clinical presentation and histopathologic study before they received monthly intralesional corticosteroid injection for 6 months. Several histopathologic findings were compared between partial/complete responders and non-responders from intralesional corticosteroid treatments. The response at 3 and 6 months were assessed using the Severity of Alopecia Tool (SALT score) and categorized into three groups: non response (<50% regrowth), partial response (50-89% regrowth) and complete response (≥90% regrowth). Wilcoxon-rank sum test was performed to compare histopathologic prognostic factors between partial/complete responsive and non-responsive groups.

Results: Ninety-seven of 113 patients clinically diagnosed with alopecia areata were confirmed the diagnosis by histopathologic study. Only 73 patients could continue with the treatment until 6 month due to time constraint. At the end of the study, 65 of 73 patients were classified to be partial/full responsive group and 8 patients were in nonresponsive group. The number of vellus hairs ($P = .028$), follicular streamers ($P = .018$), catagen hairs ($P = .006$), telogen hairs ($P = .008$) and terminal:vellus ratio ($P = .019$) were significantly higher in partial/full responsive group at 3-month period than those in non-responder group. The number of lymphocyte infiltration around muscle ($P = .004$) and polytrichia ($P = .004$) were significantly higher in nonresponsive group at the 6-month period than those in partial/complete responsive group.

Conclusion: The presence of vellus hairs, follicular streamers, catagen and telogen hairs are associated with favorable results at early treatment of intralesional corticosteroid. Lymphocyte infiltration around muscle and polytrichia indicates poor prognosis of intralesional corticosteroid treatments.

Commercial support: None identified.

2597

Interest of a vitamin and mineral supplement in the management of telogen effluvium: Clinical study on Brazilian women

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Introduction and objective: Telogen effluvium (TE) is a common scalp disorder, characterized by an increased transient shedding of telogen hairs by early entry of hair in the telogen phase. It mainly concerns women, mostly on the frontal-parietal area of the scalp and can have psychological effects by impairing self-esteem. Regrowth is spontaneous, can require one year for the hair's volume to be restored. Vitamin or sulfur amino acid treatments can help faster regrowth, thus help patients feel better psychologically. We evaluated the effect of an oral supplement containing 12 active ingredients that may act synergistically to protect hair and stimulate hair growth in the management of TE, by clinical methods and self-assessment.

Materials and methods: Nonmenopausal women with TE and positive pull test were included in this open label noncomparative study conducted in Brazil. The oral supplement V0433 containing vitamins (E, B, C) and mineral salts (Fe, Se, Mo, Zn), was taken once daily for 12 weeks. Evaluations were performed at baseline (W0) and weeks 4, 8 and 12. Efficacy was assessed by: clinical scoring by dermatologist from standardized photographs of frontoparietal area of the scalp taken at W0 and W12 -pull test performed at all visits and self-perceived efficacy (SPE) by subjects through questionnaires with questions related to hair density, strength, volume at every visit from W4. Adverse events and product's tolerance were assessed throughout the study. Statistical analysis was made with a confidence level of 95%, the time-points compared with ANOVA and Dunnett test or Wilcoxon signed rank test.

Results: 39 subjects aged 38 ± 10.4 years completed the study. A highly significant reduction ($P < .001$) of telogen hair collected with pull test was found after 4, 8 and 12 weeks, increasing with time. After 12 weeks, the clinical scoring of the TE condition was improved in 89,8% of the cases. The SPE improved significantly overtime for all the items at 8 and 12 weeks compared to 4 weeks. At W12, the % of subjects with improvement on density, strength and volume was 91.9%, 94.6%, and 86.5%, respectively. Only one subject (2.6%), presented discomfort sensation possibly related to the product use.

Conclusion: This study demonstrated the interest of the vitamin and mineral supplement in the management of TE in women, by a progressive and significant improvement over 12 weeks on clinical improvement observed by the dermatologist, reduction in telogen hair.

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3815

Investigating the effectiveness of treatments used in trichotillomania

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Background: Trichotillomania (TTM) affects between 4-10% of the general population. It is a hair pulling disorder usually preceded by an increasing sense of tension around affected areas of the scalp which is relieved by the act of hair pulling. In childhood the prevalence in males and females is equal however as age increases, TTM becomes more common in females. TTM can have major physical, emotional and social complications yet there are no clear guidelines as to the management of this condition. Current treatments strategies include cognitive behavioral therapy (CBT) and psychotropic medications.

Aim: To investigate the effectiveness of treatments used in TTM.

Method: Notes belonging to 9 adult patients (ages 24-65 years old) seen in a London psychodermatology clinic between the years 2011-2014 were reviewed retrospectively. There were 8 females and 1 male in this study. All were between the age of 24 and 65 years old. Effectiveness of treatments was measured collecting subjective and objective data. Subjective data was documented commentary made by patients during clinic about the treatment they were on. Objective data were collected using formal assessment tool scores (S-16, DLQI, HADS, DAS-29) documented in patients notes to assess severity of TTM symptoms.

Results: All 4 patients who had tried (CBT) reported improvement in their symptoms. 6 out of 7 patients on psychotropic medication reported improvements in their TTM. There was one patient with a complex psychiatric history treated with quetiapine. Her TTM was treated with both CBT and light therapy which she responded well to.

Conclusion: This is the first study to suggest that light therapy can be an effective treatment for TTM. Our study shows that CBT is an effective form of treatment for TTM. Despite inconclusive results from previous studies regarding the effectiveness of anti-psychotic therapy for TTM, this study shows these medications are helpful. Patients with associated complex psychiatric disorders are more difficult to treat and require a continued multidisciplinary approach.

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Lipedematous scalp: A rare illness

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Described for the first time in 1935 by Cornbleet et al, lipedematous scalp has few cases reported in literature. Nowadays, it is considered that lipedematous scalp and alopecia are two spectra of the same disease. Despite still having an unknown pathogenesis, they present distinctive clinical and histopathologic findings which are presented in the following case. A female, aging 65, healthy patient has presented diffuse edema on the scalp and pain when dealing with her own hair for two years. When examined, she showed diffuse edema on the scalp without alopecia sites. Ultrasonogram has showed subcutaneous cell tissue diffusely swollen in the frontoparietal, temporal and occipital regions, with thickness of 7 mm (common up to 3 mm). Skin biopsy has presented paucity of hair follicles with intradermal adipocytes, compatible with lipedematous scalp. Lipedematous scalp is the thickening of the subcutaneous tissue of the scalp, which can be diffuse or localized, in the absence of hair loss. The presence of nonscarring alopecia on the thickened areas is called lipedematous alopecia. Both conditions present higher prevalence amongst African American women. The sites primarily involved are the vertex and occipital areas, and it may spread over the rest of the scalp. There may be pain and itching in the involved areas. Some authors suggest that lymphatic vessel dilation could be responsible for alopecia, as this finding is absent in cases of lipedematous scalp. Hormonal factors could also be involved in its pathogenesis, due to the greater female prevalence. The diagnosis is based on anatomopathologic examination and clinic, presenting soft edema of the scalp and the thickening of subcutaneous tissue, respectively. Imaging exams, such as ultrasonogram and nuclear magnetic resonance are auxiliary diagnosis methods and show increased scalp thickness, about two to three times thicker than unaffected individuals. Piraccini et al have described the presence of vascular malformations, such as linear telangiectasias, restricted to the thick areas of the scalp in the dermatoscopy and videodermatoscopy of two patients. Their differential diagnoses include cutis verticis gyrata and encephalocraniocutaneous lipomatosis. There is still no known definite treatment for these conditions.

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3044

Longitudinal erythronychia: Retrospective single center study

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Longitudinal erythronychia (LE) is characterized by a linear red band that extends from the proximal nail fold or lunula to the distal tip of the nail. Accurate diagnosis often requires biopsy and clinicopathologic correlation. Most cases of LE feature a shared pathogenesis that affects the distal matrix, resulting in a nail plate that is grooved on the ventral surface. The nail bed swells into this space as the nail plate grows out, compressing the bed on the narrow sides of the groove and intensifying the normal pink-red erythema of the underlying nail bed. The differential diagnosis for LE is based on whether the presentation is limited to one nail ("localized") or on multiple nails ("polydactylous" or "generalized"). Most cases of localized longitudinal erythronychia (LLE) represent local processes, while polydactylous longitudinal erythronychia (PLE) cases are usually caused by inflammatory processes, or simply idiopathic. Despite the well-established diagnostic criteria, large studies evaluating patients with erythronychia are lacking. Our study evaluated the prevalence of biopsy-proven diagnoses in patients presenting with nails with the predominant clinical sign of erythronychia.

Methods: This was a single center retrospective study over six years. All patients presenting with longitudinal erythronychia, either LLE or PLE, that had a nail biopsy of the band of erythronychia, were included. Patients were identified in the nail surgery log and pathology reports evaluated. In cases with descriptive histologic diagnoses, clinicopathologic correlation through examination of the medical record was undertaken.

Results: 65 patients were identified who had biopsies of erythronychia. Overall, by far the most common diagnosis was onychopapilloma (63%), followed by lichenoid inflammation (8%), glomus tumor (6%), wart (5%), and squamous cell carcinoma in situ (3%). Single cases of invasive melanoma and nevus with moderate to severe atypia were identified.

Conclusions: This study, the largest to date of which we are aware, demonstrates that most cases of LE represent benign diagnoses. Onychopapilloma was the most common diagnosis (63%), with only 5% of biopsied cases malignancies.

Limitations: This study was limited by its retrospective nature, the bias of including only those cases biopsied, and taking place over only a six-year period.

Commercial support: None identified.

2676

Paclitaxel-induced onycholysis: A case study

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Chemotherapeutic drugs are associated with a wide array of adverse effects. Nail changes occur commonly and can affect the nail matrix, nail plate, or surrounding soft tissues. The taxane family of drugs, including docetaxel and paclitaxel, is known to cause such nail changes. These occur much more commonly with docetaxel, however, and are only rarely seen with paclitaxel (11%-41% vs 2%). Changes seen with paclitaxel include hyperpigmentation, Beau's lines, onycholysis, subungual hemorrhages, and subungual abscesses. Although uncommon, the nail changes range in severity and may warrant discontinuation from the drug. We describe the case of a 55-year-old women treated with paclitaxel for breast carcinoma. After three weeks of therapy, she developed a severe peripheral neuropathy and subsequent hemorrhagic onycholysis. After discontinuation of the drug, she experienced complete remission and healing.

Commercial support: None identified.

2782

Phase-2 controlled study to assess the efficacy of two new nail solutions in the treatment of nail psoriasis

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At present there is no cure for nail psoriasis. No pharmaceutical product is approved for the treatment of this particular disorder. The objective of this study was the screening between two different antipsoriatic drugs formulated in nail solutions based on the patented chitosan technology. The study design was randomized, double blind, vehicle controlled, parallel groups. The two nail solutions contained as sole active ingredients cyclosporine 5% (P-3072) and calcipotriene 0.005% (P-3073), respectively. Placebo was the vehicle of P-3073. Randomization was 2:2:1. Main inclusion criteria were patients of both genders, aged ≥18 and ≤80 years with mild to moderate psoriasis (BSA ≤10% or PASI ≤10) with fingernail psoriasis of the nail matrix and/or the nail bed. P-3072, P-3073 or vehicle were randomly applied once daily for 24 weeks and were followed up for 12 weeks. The primary endpoint was the evaluation at end of treatment of total NAPSI score. Secondary endpoints included total NAPSI at different time points, as well as NAPSI matrix and NAPSI bed. Safety was assessed by standard methods. Full Analysis Set (FAS) for primary efficacy analysis included 30 patients in the P-3072 group, 34 in the P-3073 group and 14 in the vehicle group. NAPSI total was at baseline 23.9 ± SD 17.8 in P-3072, 20.3 ± 14.3 in P-3073 and 22.3 ± 14.5 in vehicle group (no significant differences). At end of treatment, primary endpoint was statistical significant ($P = .0395$) comparing P-3073 group (-6.78, -32% from baseline) to vehicle group (-1.11) while P-3072 group (-2.42) was not significantly superior to vehicle. At the same time point, both NAPSI of nail bed signs (-3.5) and NAPSI of nail matrix signs (-3.3) decreased in P-3073 group while P-3072 decreased NAPSI bed (-4.0) but not NAPSI matrix (+1.6). The secondary analyses showed that the significantly superior efficacy of P-3073 versus vehicle in NAPSI total was already evident at the week 12 and was maintained for all following time points, including end of follow up. Interestingly, the scores were even lower 12 weeks after end of treatment with P-3073 (-7.43, -3.6, -3.8,). In conclusion, P-3073, applied once daily to fingernails, was able to reduce both signs of nail bed and nail matrix psoriasis, leading P-3073 to be a candidate for further development in pivotal trials. Cyclosporine had effect only on nail bed and no effect on nail matrix.

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Relapsing nail fibrokeratoma: A case report on a teenager

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We report a case of a 14-year-old female patient, presenting with a painless lesion, which has evolved with progressive growth in the first right finger over the last two years. There is no known history of previous trauma or manipulation with clippers. There is no relevant medical information on medical history, family history and social history. On dermatologic exam, a keratotic lesion with stony consistency was observed, in addition to onycholysis and partial destruction of the distal edge of the right toe nail. The following diseases were considered as a possible diagnosis: pyogenic granuloma, köenen tumor, nails keratoacanthoma, squamous cells carcinoma, onychomatricoma, cutaneous horn and neuroma. Surgical excision was performed and subsequent histopathologic exam showed hyperkeratosis with acanthosis, thick collagen in the dermis arranged perpendicular to the epidermis, consistent with the diagnosis of fibrokeratoma. After 30 days of surgical treatment, the patient developed new lesions with characteristics similar to those described above, but smaller. Surgical excision was performed and the histopathologic exam showed compatible with fibrokeratoma. Fibrokeratomas are benign epithelial tumors, generally asymptomatic that preferentially affect the digits, but may also occur on the lower lip, nose, nail bed and heels. The fibrokeratoma is almost always solitary, painless, usually small (<1 cm), and has no spontaneous regression. These features were seen in our patient. Its etiology is still unknown, and trauma considered the most important predisposing factor. The diagnosis is confirmed by histopathologic examination in all cases. Surgical treatment leads to healing in most cases and recurrences are rare. We report a case of a teenager presenting with fibrokeratoma showing an atypical course, since it recurred after surgical removal. This case report intend to show the importance of considering fibrokeratoma on the differential diagnosis of squamous cells carcinoma and other lesions that can also be keratotic affecting the finger.

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3601

Scalp ulceration in a pediatric patient after hair weave placement

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The use of sewn-in weaves (hair extensions, either artificial or real) is a common cosmetic practice in the United States, particularly among African American women. This hairstyle has been implicated as a risk factor for traction alopecia, hair loss due to prolonged tension on the hair. Less commonly, hair weaves and the tension that is placed on the hair follicles are concerning as a nidus for infection. In this case report, we describe a case of an adolescent patient who presented with significant open, purulent, and draining wounds on the scalp 3 weeks after her first weave placement. The patient was treated with antibiotics to cover MRSA and Pseudomonas infection as well as collagenase for wound care with narrowing to coverage of MRSA alone when culture results returned. Two weeks after the initial presentation and four days after discontinuation of levofloxacin, the patient was readmitted in the setting of high fever and cervical lymphadenopathy, despite evidence of clean granulation tissue and refollicularization at the wound sites. These symptoms resolved after additional treatment with ampicillin-sulbactam. The etiology of this patient's scalp ulcerations was ultimately determined to be traumatic from hair weave placement, allowing for inoculation of cutaneous tissue, superimposed polymicrobial bacterial infection, and subsequent lymphadenitis. This case highlights a serious complication to consider as hair weaves increase in prevalence. Finally, it is important to note that the use of hair weaves is often in conjunction with other hair care practices such as the use of chemical relaxers. This may contribute to the development of infection or other hair and scalp disorders, such as contact dermatitis and fungal infection, that must be ruled out by careful dermatologic evaluation.

Commercial support: None identified.

3228

Topical minoxidil solution in stimulating nail growth: A pilot study

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Background: Topical minoxidil solution is widely used for stimulating hair growth. The solutions' effectiveness appears to stem from its vasodilatory property. As hair and nail structures are similar, and periungual blood flow is one of the factors affecting nail growth, our assumption is that minoxidil can help nails grow faster.

Objective: A pilot study to measure nail growth, comparing nails that have had a 5% topical minoxidil solution applied to them and those that have not.

Methods: Thirty-two Thai subjects were randomized into two groups, each characterized by the pattern of nails. A 5% topical minoxidil solution was applied twice daily. The first group was instructed to apply the solution on the right index and left ring fingernails and the second group to apply the solution on the left index and right ring fingernails. All subjects were followed weekly for a month and then every two weeks during the second month. On each visit, we measured the nail length of the 2nd, 3rd and 4th fingers of both hands with a digital caliper. The subjects' blood pressure, pulse, and cutaneous complications were recorded as well.

Results: In our preliminary analysis of the twelve female subjects, the nail growth rate difference between nails that had been treated with the 5% topical minoxidil solution and those that had not was statistically significant within the first two weeks of the treatment. After the first week, the mean nail length of the nails that had been treated with the solution was 1.54 mm, compared to 1.21 mm on nails that had not been treated, with a P of .001. After the second week, the mean nail length of the treated nails and untreated nails were 0.94 mm and 0.69 mm, respectively, with a P of .046. The nail growth rate difference between the two groups after one month was also statistically significant, (with the mean length of 4.12 mm on treated nails and 3.44 mm on untreated nails with a P <.001). None of the subjects experienced cutaneous or systemic complications.

Conclusion: Nails grow faster with the application of 5% topical minoxidil solution in healthy Thai subjects. This information can be useful for determining treatment of a number of nail diseases as well as for stimulating nail growth thereby leading to better outcomes, such as onychomycosis. However, further studies should be conducted.

Commercial support: None identified.

3351

Randomized controlled evaluator blinded study of dutasteride versus finasteride in men with androgenetic alopecia

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Background: Dihydrotestosterone plays a key role in the causation of androgenetic alopecia(AGA). Finasteride, a type II 5-alpha reductase inhibitor, and dutasteride, a dual inhibitor of both type I and type II 5 alpha-reductase, inhibit the conversion of testosterone to dihydrotestosterone.

Objective: To evaluate and compare the efficacy, safety and tolerability of dutasteride versus finasteride in men with AGA.

Methods: Men with AGA (18-40 years) were randomized to receive 0.5 mg dutasteride or 1 mg finasteride for 24 weeks. Baseline and 24 weeks evaluation was done on the basis of hair count, global photographs and subjective assessment. Total, thin and thick hair count over 1 cm^2 area was done manually from the prints of phototrichogram captured using Heine delta 20 dermatoscope. Global photographs, taken on a specially designed stereotactic device, were assessed by a blinded and nonblinded investigator. Subjective assessment was done using a preset questionnaire. Patients were assessed at regular intervals for development of any side effects.

Results: Ninety men with AGA were recruited. Dutasteride showed a significantly greater increase in total and thick hair count, a decrease in the thin hair count over the target area at the end of 24 weeks. Global photographs assessed by the investigators also showed better improvement in the dutasteride group compared to finasteride group. Both the groups showed similar side effect profile with sexual dysfunction being the most common and reversible side effect. Inter investigator assessment was significant as per Kappa coefficient.

Conclusions: Dutasteride when compared to finasteride has proven to be more efficacious and have comparable have comparable adverse events.

Limitations: The study was limited to 6 months.

Commercial support: None identified.

3299

Safety and efficacy of a topical treatment (SM04554) for androgenetic alopecia (AGA): Results from a phase 1 Trial

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Introduction: AGA, a form of hair loss impacting approximately 35 million men in the US, has received only two US drug approvals in the last 15 years. SM04554 is a novel small molecule, topical scalp treatment for AGA targeting the Wnt pathway, a pathway known to regulate hair growth. This abstract summarizes the analysis of a randomized, double-blind, placebo-controlled, single-center trial assessing safety and efficacy of SM04554 in treating AGA.

Methods: Male subjects were treated topically once daily for 14 days with either 0.05%, 0.15% or 0.45% SM04554 solution or vehicle; subjects returned 14 days posttreatment for final evaluation. Safety data, including pharmacokinetics (PK), electrocardiogram (ECG), laboratory parameters, application site assessments and vital signs, were collected throughout treatment, with subject-reported efficacy outcomes collected at end of study.

Results: 29 subjects (0.05% n = 7, 0.15% n = 8, 0.25% n = 8, vehicle n = 6; average age 44.6) were enrolled; 13 (45%) had a Norwood-Hamilton score of 5 (range 4–7). 15 treatment-emergent adverse events (TEAEs) were reported by 11 (38%) subjects, 4 (67%) of the vehicle group reported TEAEs, compared to 1 (14%) in the 0.05% group, 4 (50%) in the 0.15% group, and 2 (25%) in the 0.45% group. The most frequently reported TEAE was eye irritation/hyperemia (N = 2 [7%]). ECGs, labs and vital signs were unremarkable with no clinically significant changes from baseline reported in any subject. One vehicle subject presented with minimal scalp erythema, no other subject reported application site irritation. No serious adverse events were reported. Day 14 PK was dose dependent. No subjects had detectable SM04554 concentration in the 0.05% group; 3 (38%) subjects had systemic exposure in 0.15% group (Tmax = 9 hours) and 7 (88%) had systemic exposure in 0.45% group (Tmax = 15 hours). In the 0.05% group, 4 (57%) reported slowing of hair loss and 2 (29%) reported hair growth; in the 0.15% group, 6 (75%) subjects reported slowing of hair loss and 3 (37%) reported hair growth; in the 0.45% group, 2 (25%) reported slowing of hair loss and 3 (37%) reported hair growth, compared to zero (P = .01 for 0.15% group) and 1 (17%) of vehicle subjects, respectively, at end of study.

Conclusions: SM04554 appears to be safe, well-tolerated, and potentially efficacious. These results will help guide future AGA trials using this treatment.

Several authors are employees of Samumed LLC.

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Trachyonychia as first presentation in myeloma-associated amyloidosis

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Amyloid light chain amyloidosis is the most common type of systemic amyloidosis caused by extracellular deposition of insoluble amyloid fibrils derived from monoclonal immunoglobulin light chains. Systemic amyloidosis presents with variable and nonspecific symptoms such as weight loss, fatigue, dyspnea, and edema, which are rarely helpful for the diagnosis. Mucocutaneous lesions, observed in 29% to 40% of the cases, can be the initial presenting signs of systemic amyloidosis and provide key clues for the diagnosis. Nail changes are rarely seen in systemic amyloidosis. To our knowledge, there are 9 patients who presented nail dystrophy as a first manifestation of systemic amyloidosis prior to diagnosis. Herein, we present a 64-year-old man who came to our clinic with trachyonychia of fingernails and toenails. Amyloid deposits were found in the nail matrix biopsy specimen. Further evaluation such as serum electrophoresis, immunofixation and bone marrow examination revealed the diagnosis of amyloid light-chain amyloidosis. We suggest that clinicians should consider systemic amyloidosis as one of differential diagnosis when facing any patient with nail dystrophy who are refractory to recurrent therapy and perform nail biopsy to exclude this life-threatening disease.

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Trichoscopic and clinical characteristics of temporal triangular alopecia. A multicenter study

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Temporal triangular alopecia (TTA) is an asymptomatic permanent circumscribed noncicatricial alopecia. It is usually confined to one frontotemporal region of the scalp without any underlying cutaneous alterations. TTA has been related to Down syndrome, leukonychia, sectorial hyperpigmentation of the iris and other malformations.

Method: Observational descriptive multicenter study including 31 patients with TTA attended at 6 hospitals from Spain during 2014. The variables collected were: demographics, clinical characteristics, comorbidities, trichoscopic features and treatment.

Results: 17 females and 14 males were included. Diagnostic mean age was 2.8 years of age for females and 0.9 for males making for an average of 1.9 for the total. More than half (19) were diagnosed at birth (mode). Triangular shape was the most prevalent (48.4%), followed by oval (38.7%) and lancet-shape (12.9%).21 of 28 cases were on the left side. The rate of bilateral occurrence was 6.5% (2 cases). We measured 26 lesions and its maximum diameter mean was 3.67 cms. For the patients older than 16 years old was 3.9 cm. Only 5 cases presented nondermatologic comorbidities being prematurity at birth, Down syndrome and bronchial asthma. Trichoscopy was performed in 19 cases (61.3%).white hairs and diversity of diameter were the most frequent features found (18), followed by vellus hair (16), empty follicles (12), and white dots (10). We found pityriasis in 3 cases, broken hairs in 2, black dots in one case with frontal fibrosing alopecia (FFA), cadaveric hairs in a 84-year-old woman with FFA and no one, exclamation hairs. The three patients with yellow dots also presented white dots and including those 4 with arboriform pattern were more than 30 years old and had androgenetic alopecia (AGA). The 19.4 % presented other type of alopecia (3 with AFF, 2 with AGA and 1 with chronic effluvium telogen). No family history of TTA was referred. There were not any improvements with expectant treatment noticed with a mean of 81.96 months.

Conclusion: There is a slight predominance of female sex. Left side is the most prevalent but it can be bilateral. Most cases are sporadic and have a triangular shape of 3.6 cm, without any malformation associated. It is diagnosed during the two first years of life. Trichoscopy is a useful tool for diagnosis dubious cases and it shows white hairs, diversity of diameter and vellus hair. There are not any effective treatments except surgery.

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2726

Trichoscopic features of folliculitis decalvans: A multicenter review

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Introduction: Folliculitis decalvans (FD) of Quinquaud is a rare form of neutrophilic scarring alopecia that presents with scarring alopecic patches with follicular pustules, crusts and tufted hairs.

Methods: We performed a descriptive, retrospective, observational and multicenter study, including the digital trichoscopic images of 58 patients diagnosed with FD between 2001 and 2014 in 12 Spanish centers. The diagnosis of FD was established based on typical clinical and dermoscopic findings together with histopathologic confirmation. Two different dermatologists expert on dermoscopy evaluated all the cases. Clinical aspects and severity variables included were: FD severity (I-II: < 4.99 cm of maximum diameter of the scarring patch and III: 5 cm or more) and years of evolution, previous trauma, pruritus, trichodynia, tufted hairs, pustules, seborrhea and facial papules.

Results: The most frequent trichoscopic features were: tufted hairs (54 = 93.1%), perifollicular erythema (51 cases = 87.9%), follicular hyperkeratosis (42 patients = 72.4%), hair diameter diversity (24 = 41.4%), cicatricial white patches (31 = 53.4%) and yellow dots (9 = 15.5%). A bivariate analysis and a multivariate logistic regression were carried out. We found that 95.3 % of patients with mild severity presented tufted hairs, 86% perifollicular erythema and 69.8% follicular hyperkeratosis. On the other hand, 92.3 % of patients with severe FD presented perifollicular erythema, followed by tufted hairs in 86% of cases and follicular hyperkeratosis in 80%. No statistical association was found between the disease severity and trichoscopic findings but was positive with the presence of pustules (confirmed in multivariated analysis. We also evidenced association with statistical significance ($P < .05$) between pruritus and patients with a history of FD of more than 25 years of evolution ($P = .01$).Remarkably, we found that the presence of follicular hyperkeratosis and hair diameter diversity was statistically associated to trichodynia in multivariate test. The presence of yellow dots was related with statistical significance ($P < .05$) with pruritus and those patients with tufted hairs presented more frequently facial papules.

Conclusions: Tufted hairs, perifollicular erythema and follicular hyperkeratosis are the hallmarks trichoscopic features of FD. Patients with trichodynia presented follicular hyperkeratosis and hair diameter diversity while the presence of pustules could be a marker of severity and activity of FD.

Commercial support: None identified.

3838

Using automated microneedling with platelet rich plasma for treating cicatricial alopecia, recalcitrant alopecia areata and traction alopecia, case report

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Introduction: Alopecia due to different causes especially traction and cicatricial are recalcitrant to treatment. Also scalp alopecia areata may be resistant to treatment when affecting large areas and ignored by patients for months. Microneedling is an effective methods for treating telogen effluvium whether alone or when combined with platelet rich plasma or mesotherapy. It is thought to act by induction of neovascularization.

Aim of the study: Creation of a new method for scalp hair follicles stimulation and regrowth in cases of cicatricial alopecia, traction alopecia and alopecia areata.

Patients and methods: One case of cicatricial alopecia, another with traction alopecia and third with alopecia areata were treated by twenty sessions of automated microneedling combined with platelet rich plasma. Sessions were done every two weeks. Clinical improvement was done by a blind dermatologist and patient satisfactory scale at the end of sessions.

Results: The three cases showed marked clinical improvement with variable degrees of patient satisfaction.

Conclusion: Automated microneedling may provide a successful future procedure for treating cicatricial alopecia, traction alopecia and recalcitrant alopecia areata.

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IMMUNODERMATOLOGY AND BLISTERING DISORDERS

3549

A case of Senear-Usher syndrome treated with rituximab

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When present in conjunction with other autoimmune diseases, pemphigus foliaceus (PF) is more commonly associated with rheumatoid arthritis or autoimmune thyroid disease. Senear-Usher syndrome, or comorbid PF and systemic lupus erythematosus (SLE), is relatively uncommon. We describe a case of treatment-resistant pemphigus/SLE overlap whose blistering condition improved dramatically with rituximab. A 47-year-old African American male presented with blisters that started on the face and progressed to the chest, upper back and scalp. On exam, erosions and crust were present in a seborrheic distribution, including the malar region, with no apparent mucosal involvement at that time. The patient demonstrated objective lower extremity weakness but no joint changes despite a history of arthralgia. Labs revealed positive desmoglein 1 and desmoglein 3 antibodies as well as positive ANA, anti-Smith, and anti-DS DNA antibodies and low C3 level. Scalp biopsy showed superficial acantholysis and a perivascular dermal infiltrate with granular immune complex deposition at the dermoepidermal junction. The patient was worked up extensively by rheumatology for lupus and thought to have only cutaneous involvement. The patient's condition failed to remit with a prolonged oral prednisone taper, mycophenolate mofetil, and hydroxychloroquine, prompting a trial course of rituximab. After two infusions two weeks apart, >90% of the skin lesions resolved with continued remission at 3 month follow-up. Although reports of successful treatment of pemphigus vulgaris with rituximab are prevalent in the literature, specific examples of Senear-Usher syndrome treated with rituximab could not be found. Thus our patient is notable for his unique clinical scenario, including strongly positive SLE serology and immunopathology with skin-predominant exam findings along with the presence of both desmoglein 1 and 3 antibodies with clinical PF. It will be interesting to monitor the evolution of his disease and important to assess for new systemic manifestations of his underlying autoimmune dysfunction.

Commercial support: None identified.

2996

A clinical and serological study of linear IgA bullous dermatosis

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Linear IgA bullous dermatosis (LABD) is a rare autoimmune bullous disease that was first reported in children in 1901. For the past 30 years or more, childhood-onset LABD and adult-onset LABD were recognized as separate entities but are currently known as a single entity. LABD is characterized by subepidermal blisters with linear IgA deposition along the basement membrane zone (BMZ) in direct immunofluorescence (DIF) of perilesional skin. Although there has been no consensus on diagnostic criteria for LABD, some investigators believe that concurrent weak IgG deposition at the BMZ in DIF can occur. To date, no large-scale studies have been conducted on LABD patients with sole IgA deposition at the BMZ in DIF. Here, we defined LABD as subepidermal blisters with linear IgA deposition with or without C3 deposition at the BMZ in DIF. We excluded patients with additional IgG deposition at the BMZ in DIF from the test group. We recruited 101 patients who fulfilled our criteria of LABD, most of whom were referred for serological evaluation. The number of male and female patients in the study was almost equal. Mean age at LABD onset was 53.0 years. In 69.7% of the patients, only the skin was affected; in 6.1%, only the mucosa was affected. Remaining patients had both cutaneous and mucosal lesions. Twenty-seven patients had erythema with peripheral vesicles, and five had prurigo-like lesions. The oral mucosa was the most affected mucosal site. Approximately 90% of the patients suffered from pruritus. Six patients had been administered vancomycin before LABD onset. Malignant neoplasm reported in 12.1% of the patients was the most frequent comorbidity. Effective treatments included dapsone, corticosteroid, and dapsone with corticosteroid in 8, 15, and 20 patients, respectively. Neutrophils were predominant within the subepidermal bulla, but eosinophils were also seen. Indirect immunofluorescence of normal human skin sections revealed IgA and IgG antibodies to BMZ of human skin in approximately 50% and 10% of the patients, respectively. Immunoblotting detected not only IgA autoantibodies but also IgG autoantibodies. The results of this study may contribute to establish both the criteria and definition of LABD.

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3530

A new treatment for autoimmune blistering diseases - the efficacy of the Bruton's tyrosine kinase inhibitor PRN473 in canine pemphigus foliaceus

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Bruton's tyrosine kinase (BTK) inhibition has the potential to target multiple pathways and cell types involved in inflammation and autoimmunity. These include modulation of B-cell receptor-mediated B-cell pathways, as well as inhibition of FcR-induced cytokine release from monocytes and macrophages. FcεR-induced mast cell degranulation and granulocyte migration and mediator release. As human pemphigus foliaceus (PF) is very similar to PF in dogs we explored the efficacy of the reversible, covalent, oral, small molecule BTK inhibitor, PRN473, in client owned, pet dogs presenting with a skin biopsy-confirmed diagnosis of PF. Dogs were seen at the University of California School Veterinary Medical Teaching Hospital in a 16 week clinical trial. PRN473 was administered orally once a day at a dose of 15 mg/kg as monotherapy, while withholding the usual treatment of high dose corticosteroids. BTK target engagement by PRN473 or "occupancy" was measured 24 hours after the first dose and two to six hours after dosing on various days during subsequent outpatient follow up. Clinical response was measured by a canine pemphigus disease activity index (cPDAI) modified from the validated, human PDAI. Each of the first four dogs treated responded to PRN473 monotherapy with greater than 50% reduction in cPDAI score within two weeks (mean at baseline, 59; mean at two weeks, 25). Three dogs continued to improve and achieved complete and sustained remission of their disease within four weeks. One dog failed to improve beyond the benefits seen in the initial two weeks of therapy and was switched to a rescue protocol of prednisolone and azathioprine. BTK occupancy 24 hours after the first dose ranged from 64% to 77%, with the dog that failed to achieve remission having an initial BTK occupancy of 77%. Subsequent BTK occupancies at follow up visits ranged from 43% to 91%. Given that canine PF, human PF and human pemphigus vulgaris (PV) are autoimmune skin diseases driven by inflammation resulting from autoantibody binding to epidermal antigens, the results of this study suggest that BTK inhibition has the potential to induce and maintain clinical remission in human PF and PV. BTK inhibition may be a viable alternative to corticosteroids for the induction and maintenance of remission in autoimmune blistering diseases.

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A novel approach to pretibial epidermolysis bullosa: A case report and literature review

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Pretibial epidermolysis bullosa (PEB) is a rare localized variant of dystrophic epidermolysis bullosa (DEB). Clinically, PEB presents as recurrent blistering and scarring largely confined to the pretibial surface of the legs. The most common extrapretibial sites of involvement include the dorsal hands and feet. Other distinguishing features include lichenoid papules, milia, nail dystrophy and delayed onset. Despite the classic clinical findings the diagnosis of PEB can be a challenge. Patients often experience pruritus at the site of disease thereby making clinical distinction from DEB-prurigino sa challenge; although patients with DEB-prurigino sa often experience an increased severity of pruritus and disease may be more widespread. Treatment for all forms of epidermolysis bullosa remains challenging. Most importantly, patients should take careful measures to minimize trauma. Multiple treatment options have been described. There are two published reports of successful treatment with various skin grafting techniques. In addition, Thalidomide has also proved successful in the management of DEB-prurigino sa. Of note, topical, intralesional and oral steroids have not demonstrated utility in this disease. Here we present a case of PEB, review the literature, and describe our findings of a novel treatment method consisting of triamcinolone 0.1% ointment used in combination with daily ACE Bandage wrappings.

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2753
A retrospective medical chart review of the use of omalizumab in chronic idiopathic urticaria

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Chronic idiopathic urticaria (CIU) affects up to 1% of the population and is defined as transient hives occurring for longer than six weeks without an identifiable etiology. Omalizumab is FDA approved for CIU at 150 mg and 300 mg dosing every 4 weeks. Our clinical experience suggests that dosing at 300 mg every 2 weeks (Q2W) provides greater efficacy in CIU than 300 mg every 4 weeks (Q4W). We herein present data from a retrospective chart review investigating the efficacy and clinical features of CIU patients treated with omalizumab at different doses Q2W vs. Q4W. We reviewed charts from all patients treated with omalizumab for any cutaneous indication at a university-based dermatology and immunology practice. A total of 48 patients with chronic urticarial dermatoses were identified: 43 with CIU, 2 with urticarial vasculitis, and 3 with urticarial bullous pemphigoid. Only patients with CIU were included in the analysis. Between January 2006 and March 2015, 31 CIU patients (mean age, 43.2 years, female, 79.1%, white, 90.7%) were treated with omalizumab; one patient was lost to follow-up. Nearly one-third of patients had a history of angioedema. Overall 90.5% (38/42) patients responded to omalizumab with at least 50% improvement within 3 months. Failure rates for other treatments are as follows: antihistamines, 100%, prednisone, 74.4%; cyclosporine, 48.8%; methotrexate, 34.9%; mycophenolate mofetil, 25.6%; dapsone, 20.9%; colchicine, 14.0%, etanercept, 2.3%. In CIU patients receiving either 300 mg Q2W or 300 mg Q4W of omalizumab (n = 36), ≥50% response rates were achieved in 100.0% (24/24) of patients treated Q2W compared to 66.7% (8/12) of patients treated Q4W ($P = .008$). Adverse events were mild, including headaches, alopecia, nausea, and arthralgias, and none of the patients stopped the medication due to adverse events. In conclusion, in our retrospective cohort, higher response rates were obtained by treating CIU with 300 mg every 2 weeks instead of every 4 weeks.

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3553
Asymptomatic esophageal and ENT findings in a patient with pemphigus vulgaris

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Pemphigus vulgaris is an autoimmune blistering disease that involves the skin and mucous membranes, especially the oral mucosa. The frequency of ear, nose, and throat involvement is high, though many cases are underdiagnosed because patients are often asymptomatic and no ENT examination is taken. Hale and Bystryn reported 55 patients with PV, in which laryngeal and nasal lesions were found, and only 11 underwent ENT examination. In the Mexican population, it predominates in young women, with a median age of 32 ± 16 years. Clinically it presents with flaccid blisters, cutaneous and mucosal erosions. Histologically it is characterized by intraepidermal (suprabasilar) blister formation due to acantholysis. The immunopathology is characterized by circulating IgG autoantibodies directed against the cell surface of keratinocytes. The immunofluorescence reports intercellular deposition against desmoglein 3 in the mucosal-dominant type and desmoglein 1 and 3 in the mucocutaneous type. The diagnosis is made with the clinical findings, histopathology and direct immunofluorescence. We report a 31-year-old woman that presented to our dermatology clinic with a 4-month history of cutaneous erosions and blisters following multiple symptomatic oral lesions without treatment. She referred dysphagia, and denied odynophagia, hoarseness or dysphonia. She has a 1 year medical history of bulimia nervosa. On physical examination, she presented flaccid blisters, erosions and hemorrhagic crusts on the scalp, trunk, and proximal extremities associated with erythematous and edematous oral erosions. Because of the history of bulimia, the ENT department was consulted, finding new lesions on posterior pharynx and larynx. The panendoscopy reported multiple erosions on the esophagus with fibrin on the surface. Esophageal and skin biopsies were performed reporting a suprabasilar bullae with acantholytic cells and eosinophils in the interior, consistent with pemphigus vulgaris. The direct immunofluorescence showed intercellular deposition of IgG. Treatment was started with prednisone 1 mg/kg and azathioprine 50 mg per day, followed by mouthwash with mometasone. The purpose of this article is to demonstrate the importance of a multidisciplinary approach in the management of patients with pemphigus vulgaris since the majority of patients may present with asymptomatic lesions either on the esophageal or ENT mucosa.

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2719
Association between HLA-DRB1 and HLA-DQB1 alleles and pemphigus vulgaris in Indian patients: A case-control study

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Background: Pemphigus vulgaris (PV) is a chronic and occasionally fatal autoimmune blistering disease. HLA-DRB1*04, DRB1*08, DRB1*14, DQB1*05 and DQB1*05 are reported to have significant association with PV; however this is partially dependent on ethnicity. This study was done to determine the HLA-DRB1 and DQB1 alleles prevalent in Indian patients with PV.

Method: A prospective case-control study was done in a University affiliated hospital in India from November 2013-Aug 2014. The diagnosis of PV was based on clinical and histologic features, direct immunofluorescence test and desmoglein levels. The sample size was calculated to be 45 patients. Low resolution HLA-DRB1 and DQB1 typing was done by PCR using sequence specific oligonucleotide probes for patients and healthy controls. The HLA antigen level allele frequencies in cases and controls were compared and odds ratios with 95% CI were calculated.

Results: 54 (32 females, 22 males) patients with PV and 50 controls (36 males, 14 females) were enrolled into the study. The mean age of the patients was 42.01 ± 14.20 years (range, 12-70 years) and that at onset of disease was 39.25 ± 13.33 years (range, 12-68 years). The mean age of the controls was 35.42 ± 11.09 years (range, 20-59 years). HLA typing was done in 50/54 patients and 50 controls. It was not done in 4 patients because consent was not given. DRB1*14 was present in 47 patients and 18 controls (OR, 27.85; 95% CI, 7.57- 102.42). 9 patients and 1 control were homozygous for the same. HLA-DQB1*05 was present in 47 patients and 24 controls (OR, 16.97; 95% CI, 4.66- 61.80). 10 patients showed DQB1*05 homozygosity. Haplotype analysis revealed that the haplotype HLA-DRB1*14-DQB1*05 was present in 44 patients and 14 controls (OR, 18.86; 95% CI, 6.58- 54.05). DRB1*15 was present in 7 patients and 16 controls (OR, 0.35; 95% CI, 0.14-0.94) and DQB1*06 was present in 8 patients and 19 controls (OR, 0.31; 95% CI, 0.12- 0.80). There was no significant association between DRB1*04, DRB1*08 and DQB1*03 and PV.

Conclusion: In Indian patients, the presence of HLA-DRB1*14 and HLA-DQB1*05 was significantly associated with PV. A negative association was seen with DRB1*15 and DQB1*06. This study provides further insight into the association between HLA-DR and DQ types and PV from India where the data available in published literature is limited.

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3654
Atypical presentation of lichen planus pemphigoides

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Background: Lichen planus pemphigoides (LPP) is a rare disease usually affecting adults, with less than 100 cases of LPP reported in the literature over the past 50 years. It is thought to be a combination of lichen planus (LP) and bullous pemphigoid (BP) however its pathogenesis is incompletely elucidated. The diagnosis of LPP is made by a combination of clinical, histopathologic, and immunologic features.

Case 1: A 2"-year-old African American female presented with a long-standing history of recurrent painful oral erosions and ulcers since age " as well as vulvovaginal ulcers which began 2 months prior to presentation. She had previously been diagnosed with oral and vulvovaginal erosive LP. Vulvar biopsy demonstrated lichenoid mucositis with eosinophils; no evidence of immune deposits. She was found to have elevated titers for IgG autoantibodies to both BP180 and BP230 via ELISA.

Case 2: A 50-year-old African American female presented with a skin eruption for 4 months that began shortly after being hospitalized for a COPD exacerbation. She first noticed pruritic, tender blisters on her palms, which progressively worsened and generalized including her genital and oral mucosa. Initial biopsy showed polymorphic infiltrate and dermal edema consistent with drug eruption. A later biopsy was consistent with BP, LPP variant.

Discussion: Clinically, lichen planus pemphigoides is characterized by the development of blisters on lichenoid lesions and/or on normal skin. Bullae predominantly occur on the upper and lower extremities; involvement of palms and soles occurs more frequently in children. Oral mucosa may be involved, but involvement of other mucosal sites (conjunctiva, esophagus, vulva, vagina), or nails is rare. The mean age at diagnosis of LPP is 52 years, and most patients have no family history of immunobullous disorders. It is generally viewed that LPP is a variant of BP or that there is a strong association between the two entities. The presented cases are unique in terms of their atypical clinical presentations that overlapped with other mucosal ulcerative conditions and drug eruptions. Increased awareness of LPP is important in order that dermatologists readily recognize this underdiagnosed condition, minimize delay in diagnosis, and reduce patient morbidity.

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3412
Autoimmune diseases of the innate and adaptive immune system including atopic dermatitis, psoriasis, and tertiary treponematosis

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In atopic dermatitis, we have recently shown the innate immune system is activated by biofilm-forming staphylococci that occlude sweat ducts. Toll-like receptor 2 (TLR 2) is activated and moves from its epidermal control location in the basal zone to the proximal stratum corneum (surrounding the occluded duct). There it likely initiates the MyD88 and the PAR 2 pathways in an effort to inactivate the staphylococci; these efforts are fruitless because of the biofilms and lead to the prime pathological finding of spongiosis and to the prime symptom of pruritus which leads to the disease. If the pruritus is intense enough to cause excoriations severe enough to disrupt the epidermis, the involvement of the dermis likely causes the activation of the adaptive immune system leading to the documented appearance of IL 31, another even more potent pruritogen. We have also shown that the innate system is involved in psoriasis, again with TLR 2. This time it was present in the dilated upper dermal capillaries; TLR 2 has been shown to lead to TNFα, IL 12/23, and IL 17, which have all been shown to be involved in the production of psoriatic lesions. In this instance, the streptococcus is most likely the organism involved; it is not recoverable because it internalizes or makes biofilms, so TLR 2 instead of combating the bacterium attacks host cells. Antistreptococcal IgG is markedly elevated in plaque psoriasis in one half the patients; it is of interest to postulate these patients were those who would develop the systemic findings of arthritis, uveitis, and the metabolic syndrome which develop in 40% of patients. In arthritis and tertiary spirochetal neurologic disease where the disease has been shown to be caused by Borrelia and dental treponemes, TLR 2 is activated and leads to the chronic course noted in osteoarthritis and Alzheimer disease. When the adaptive immune system is involved, as in rheumatoid arthritis and after a stroke, it is curious that the disease occurs more rapidly and is much more destructive.

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3019
Bullous pemphigoid and neurodegenerative disease: A retrospective study of postmortem neuropathological, immunohistochemical, and molecular genetics findings

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Background: An epidemiologic association has been reported between neurodegenerative disease (ND) and bullous pemphigoid (BP). Prior reports have proposed that collagen XVII is unmasked with neuronal damage, as occurs in ND, thus leading to generation of autoantibodies that cross-react with the basement membrane zone of the skin, resulting in BP.

Objective: We aimed to investigate the presence of collagen XVII gene (BP180) expression in hippocampal brain tissue and to evaluate detectable differences in histopathologic features between brain tissue from patients with BP and ND.

Methods: This study was approved by the internal review board. We selected 2 positive skin controls and 20 FFPE (formalin fixed, paraffin-embedded) patient-derived hippocampal biospecimens. RNA was extracted from FFPE tissue sections and reverse transcribed into cDNA using commercially available kits. Quantitative reverse transcription PCR was performed and RNA copy number was determined by running standards of diluted and linearized DNA containing the desired amplicon, ranging from 5 to 5 million in copy number. BP180/AGRN copy number was normalized to 25 000 copies of housekeeping genes (ACTB, RPL8, RPLP0). For immunohistochemistry (IHC), tissue recuts were processed and stained with a Leica Bond-Max autostainer, using EPR14758 rabbit monoclonal BP180 antibody (Abcam) in combination with an alkaline phosphatase-based red detection kit. Lesions were categorized as IHC positive if cell surface staining was detected in any part of the tissue specimen. All existing hematoxylin and eosin—stained FFPE sections of autopsy brains in patients with BP and ND were retrieved and reviewed.

Results: All brain specimens reviewed were devoid of collagen XVII gene expression despite immunoreactivity in skin controls. Collagen XVII immunoreactivity was absent in the corresponding autopsy brain tissue. Postmortem neuropathological review did not disclose specific neurodegenerative-related findings in patients with BP and ND.

Limitations: This was a retrospective, single-site study with a small sample size. Brain tissue evaluation was limited to the hippocampus.

Conclusions: Our neuropathological, immunohistochemical and molecular genetics findings cast doubt on the previously proposed pathogenic mechanism underlying the epidemiologic association between BP and ND.

Commercial support: None identified.

3493
Bullous pemphigoid induced by dipeptidyl peptidase-IV inhibitors. Five cases with documented sustained remission after discontinuation

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Introduction: Bullous pemphigoid (BP) is the most common autoimmune blistering disease. In some cases, its development has been linked with the intake of certain drugs. Recently, dipeptidyl peptidase-IV inhibitors (DPP-IVi), a new generation of antihyperglycemic drugs, have been increasingly related as causative agents of BP. In our country, the most commonly used DPP-IVi are vildagliptin and sitagliptin, which are mainly used in combination with metformin on fixed-dose oral formulations.

Objectives: To identify and report cases in which the use of DPP-IVi (4 vildagliptin, 1 sitagliptin) was likely to be involved in the pathogenesis of BP.

Material and methods: We reviewed clinical, histopathologic, and laboratory findings of all patients with BP probably induced by DPP-IVi, from the dermatology departments of 5 university hospitals with specialized units in bullous skin diseases, from 2013 to 2015. The relationship between DPP-IVi and BP was evaluated by the World Health Organization causality assessment system.

Results: A total of 5 patients met these criteria (3 female and 2 male), with a mean age of 76 years old. The mean period before the onset of BP after the introduction of DPP-IVi was of 13 months (range 6 to 33). Clinical and histopathologic findings were identical to those observed in idiopathic BP. In all patients the DPP-IV were suspended shortly after the diagnosis of BP. Two patients were treated with topical clobetasol propionate alone, while 3 patients received systemic treatment at low doses (2 dapsone and 1 oral cyclophosphamide, along with low doses of oral corticosteroids on a tapering-off regimen). All patients achieved rapid clinical remission. The withdrawal of the treatment for BP was possible in all patients in a mean time of 6 months (range 1.5 to 8), without subsequent clinical relapses during a mean follow-up period of 9.5 months (range 1 to 25).

Conclusions: Since 2011, when the first cases of BP induced by DPP-IVi plus metformin were published, a total of 14 cases have been described in the literature. Follow-up data after complete clinical remission were not available in all these cases. The documented sustained clinical remission in our patients, during a long period and without any treatment, supports the role of DPP-IVi in the etiology of BP. In conclusion, this fact highlights the importance of an early detection and discontinuation of these drugs, given the good prognosis of the disease after its withdrawal.

Commercial support: None identified.

2363
Brunsting–Perry cicatricial pemphigoid secondary to radiation therapy

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Brunsting–Perry cicatricial pemphigoid is a rare subepidermal blistering skin condition of the head and neck that can result in significant scarring. Previously reported cases have occurred spontaneously or subsequent to cutaneous trauma involving the affected skin. We present the unusual case of a 71-year-old male who was treated with percutaneous radiotherapy to the head and neck for a parotid tumor and subsequently developed Brunsting–Perry cicatricial pemphigoid over the previously irradiated skin. This reaction could be caused by radiation-induced changes in the basement membrane zone leading to bullae formation. In an effort to avoid potential permanent scarring, we recommend early referral for a dermatological opinion in patients who have a treatment resistant bullous skin condition in the context of previous radiotherapy.

Commercial support: None identified.

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2365

Characterization of circulating autoantibodies by immunoblotting in patients with immunobullous diseases

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Background: Routine investigations such as histology, direct immunofluorescence studies (DIF), indirect immunofluorescence studies (IIF) and enzyme-linked immunosorbent antibody assays (ELISA) used in the diagnosis of immunobullous diseases might be inadequate. This study aimed to determine the usefulness of immunoblotting in the diagnosis of suspected immunobullous diseases where routine investigations were negative, inconclusive, or discordant.

Methods: Subjects were recruited at the National Skin Centre from January 2008 to May 2015. Patients were included if they had undifferentiated blistering disorders with negative findings on standard investigations (histology, DIF, IIF, ELISA) or inconsistent clinical, pathological or serological findings. Immunoblotting studies were performed at the Department of Dermatology, University of Lubeck, Germany.

Results: Thirty-seven patients were recruited, of which 19 (51.4%) were men and 18 (48.6%) were women. Mean age of presentation was 57.6 years. Thirty-three (89.2%) had subepidermal and 4 (10.8%) had intraepidermal blistering diseases. Immunoblotting was useful in establishing the diagnosis in 29 patients (78.4%), namely 14 (48.3%) patients with anti laminin I pemphigoid, 4 (13.8%) with mucous membrane pemphigoid (MMP), 3 (10.3%) with bullous pemphigoid (BP), 3 (10.3%) with epidermolysis bullosa acquisita (EBA), 2 (6.9%) with exclusion of paraneoplastic pemphigus (PNP), 1 (3.4%) with PNP, 1 (3.4%) with linear IgA bullous disease (LABD) and 1 (3.4%) with bullous SLE. Of the remaining 8/37 (21.6%) patients with inconclusive immunoblot results, 3/8 (37.5%) had the diagnosis established via repeating standard investigations (histology, DIF, IIF) during periods of disease activity and 1/8 (12.5%) had the diagnosis confirmed with immunomapping. The remaining 4 out of 8 patients (50%) had blistering disorders that remain uncharacterized.

Discussion and conclusions: This study was limited by the small sample size, which made subgroup analysis difficult. Immunoblotting was a useful adjunct in 78.4% of subjects with negative or inconclusive results on standard investigations. Most of these patients were found to have subepidermal blistering disorders; particularly antilaminin 1 pemphigoid, BP, MMP and EBA. In patients with blistering disorders that remain uncharacterized after immunoblotting, repeating standard investigations during periods of disease activity appeared to be useful in 50% of cases.

Commercial support: None identified.

2679

Clinicopathologic correlation of 282 leukocytoclastic vasculitis cases in a tertiary hospital

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Introduction: Leukocytoclastic vasculitis (LCV) is an inflammatory vasculopathy of small vessels, which is often idiopathic, but may be secondary to an underlying cause. Its pathophysiology relates to deposition of immune complexes at the wall of postcapillary venules, leading to an inflammatory process. Therefore, we aimed to explore the direct immunofluorescence (DIF) findings in patients with LCV from a tertiary hospital.

Methods: We performed a retrospective study of 282 biopsy-proven LCV cases with DIF diagnosed at the Department of Dermatology, University of São Paulo Medical School, from January 2007 to December 2014.

Results: Ages ranged from five to 87 years old (yo), median age of 45 and 191/282 (67.73%) were female individuals. DIF analysis showed positivity in 70.21% of the samples, and C3 was the most frequent immunoreactant. Immunoglobulin A (IgA) deposition at the blood vessel wall related to age and absence of autoimmune/inflammatory diseases. Immunoglobulin M (IgM) deposition at the blood vessel wall related to females and autoimmune/inflammatory disorders. C3 and C4 consumption, antinuclear antibody and anti SSA/SSB positivity. Immunoglobulin G (IgG) deposition at the blood vessel wall was associated to age and positive ANCA; finally, C3 deposition at the blood vessel wall associated to hematuria and renal involvement. Systemic involvement was present in 12.5% cases of LCV patients.

Conclusions: To our knowledge, this is the largest DIF analysis of patients with histology-proven cutaneous LCV. DIF seems to be an important method to establish the prognosis and underlying etiology of LCV. Characterization of the immune complex at the blood vessel wall by DIF is relevant to determine underlying conditions related to LCV. C3 deposits, the most frequent finding of this study, related to renal involvement; IgA deposits related to absence of autoimmune or inflammatory diseases; IgM deposition related to the presence of autoimmune or inflammatory diseases, and IgG deposits were associated to positive ANCA.

Commercial support: None identified.

3046

Characterization of glycosylation profiles in psoriasis

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Alterations in glycosylation have been identified in multiple autoimmune diseases, including rheumatoid arthritis, vasculitis, and myasthenia gravis, but their utilization as biomarkers have yet to be investigated. We fought to determine if site-specific glycosylations can be used as biomarkers for autoimmunity. This study utilized multiple reaction monitoring (MRM) to successfully characterize glycome alterations associated with autoimmune diseases. This was initially done in two gastrointestinal autoimmune conditions, primary biliary cirrhosis (PBC, n = 74) and primary sclerosing cholangitis (PSC, n = 36), by using healthy controls (n = 104) as comparison. This demonstrated 30 unique glycoconjugates differentially expressed between PBC and controls, 27 between PSC and controls and 20 between PBC and PSC. This method was then utilized to characterize the site-specific glycosylation profile of 32 patients with psoriasis compared to 10 healthy controls. A total of 75 glycoconjugates that are differentially expressed in psoriasis compared to healthy controls were identified. These findings support the field of glycoscience as having the potential to find new and unique biomarkers for diseases of autoimmunity. We anticipate that glycan biomarkers may be used in the future for stratification of psoriasis subtypes in order to identify which patients are more likely to respond to a particular therapy.

Commercial support: None identified.

3045

Concurrent pemphigus foliaceus and Graves' disease

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A 15-year-old Hispanic female presented with a scaly eruption on her scalp and breasts for 7 weeks, and diarrhea, fatigue and weight loss for one month. Initial evaluation by the ED revealed a low TSH, normal CBC and she was given a presumptive diagnosis of tinea capitis and was empirically treated with griseofulvin. Exam in the dermatology clinic revealed diffuse pink plaques on the scalp and forehead with thick yellow malodorous crust, and pink papules and plaques with yellow crust on the chest, upper arms and bilateral breasts. She complained of pruritus and continued diarrhea, fatigue, and cold intolerance. Bacterial culture of her chest grew pan-sensitive *Staphylococcus aureus*. A provisional diagnosis of psoriasiform dermatitis with impetiginization was made, and she was started on an oral antibiotic and topical steroids. She was also urgently referred to endocrinology who diagnosed her with Graves' disease due to a low TSH and markedly elevated thyroid antibodies, and was started on methimazole and atenolol. Four week later at her follow-up dermatology visit, flaccid vesicles on the inner upper arms and axilla, and superficial erosions with crust on her buttocks, back, chest, face and scalp were noted. Biopsy of a vesicle was performed for routine histology and perilesional skin was sent for direct immunofluorescence. Histopathology showed a subcorneal split with eosinophilic spongiosis and positive direct immunofluorescence for intercellular IgG and C3 in the epidermis consistent with pemphigus foliaceus. She was subsequently started on prednisone and mycophenolate mofetil. She was slowly tapered down on prednisone. At 6 months status post–thyroid ablation, she was nearly clear on 10 mg QOD of prednisone. Pemphigus foliaceus (PF) is an autoimmune blistering disorder which targets the desmosomal protein desmoglein 1. It is more common in adults in the 4th-6th decades of life. Patients typically present with scaly, crusted erosions in a seborrheic distribution. Sporadic PF is rare in children, with fewer than 50 cases reported. Only one other case of Graves' disease and PF in childhood has been reported in the literature, in this case, Graves' disease developed after the diagnosis of PF was made. There have been other autoimmune mediated diseases diagnosed in children with PF, such as neuromyelitis optica in a 16-year-old female with biopsy proven PF. However, since PF is such a rare disease, the true incidence of concurrent autoimmune disease is unclear.

Commercial support: None identified.

3304

Dietary and smoking habits in patients with pemphigus vulgaris and bullous pemphigoid

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Background: Pemphigus vulgaris (PV) and bullous pemphigoid (BP) are rare autoimmune skin blistering disorders that can involve the mucous membranes. Several genetic and environmental etiologic factors have been postulated. Food could be a potential environmental trigger. Previous studies have shown possible association of diet containing allyl compounds and tannic acid with acantholysis in in vitro models. Nicotine on the other hand has been known to have antiacantholytic effects.

Methods: We performed a retrospective survey study to analyze the dietary difference and smoking patterns prior and post diagnosis of PV or BP. We hypothesized – (1) No dietary difference exists between PV and BP patients, (2) Patients with PV and BP do not change their diet after diagnosis, (3) Smoking habits of PV and BP patients are the same. Using the patient registration software at our institution, 241 patients with the search terms "pemphigus," "pemphigoid," "pemphigus vulgaris," and/or "bullous pemphigoid" were identified of which 61 qualified and 20 from which responded. Exclusion criteria included other diagnosis, Nursing home patients, and patients with dementia or with no confirmatory diagnosis with biopsy. Statistical analysis was carried out using Vassar Stats, significance was considered at $P < .05$.

Results: Based on the survey population, PV patients ate diet containing tannic acid significantly more frequently compared to BP patients prior to diagnosis ($P = .0082$). We also saw, significantly decreased intake of allyl compounds in PV patients postdiagnosis when compared to prediagnosis ($P = .0336$). No statistically significant difference in willingness to change dietary lifestyle was seen between PV or BP patients ($P = .4513$). Smoking information was limited and difficult to analyze primarily because of recall bias, timeline associated with smoking as well as modes of smoking and using tobacco.

Conclusion: Our study points to importance of possible dietary triggers in PV or BP. Limitations in our study included population bias and recall bias as previously mentioned. Future prospective studies including blood and or patch allergen testing are needed to provide additional information about the roles of dietary triggers in these rare, but severe blistering disorders.

Commercial support: None identified.

3536

Epidermolysis bullosa with pyloric atresia and significant urologic involvement

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Epidermolysis bullosa (EB) is comprised of a variety of rare, inherited diseases that cause epidermal fragility, blistering, and erosions. EB results from a variety of mutations in proteins of the skin and mucous membranes of the body. Mutations in the gene encoding plectin, a protein involved in hemidesmosome functioning, are associated with subtypes of EB, including EB with pyloric atresia (EB-PA) and EB with muscular dystrophy (EB-MD). We present a unique case of hemidesmosomal EBS with two novel plectin mutations resulting in pyloric atresia and significant urologic involvement. Our case also demonstrated extensive involvement of the respiratory tract requiring tracheostomy as well as esophageal involvement. While our patient has had no clinical signs of muscular dystrophy by 5 years of age, elevated levels of creatinine kinase may suggest possible muscular dysfunction in the future. It is highly rare to have EBS with such extensive involvement of multiple organ systems. An awareness of the potential clinical manifestations of EB will help clinicians to manage this complex and extensive disorder.

Commercial support: None identified.

3404

Erythrodermic pemphigus foliaceus: A rare refractory variant

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A 53-year-old woman presented with erythroderma, generalized exfoliation and ectropion. She had a history of erythematous papules and micropustules on the trunk, about 9 months ago, which progressively lead to erythroderma. She was hospitalized, 5 months ago, with a diagnosis of staphylococcal scalded skin syndrome and treated with systemic intravenous antibiotics. She was released without the achievement of full remission of erythroderma. The patient had a long journey with antibiotics and low doses of systemic prednisone and cyclosporine in the time period between the first and the second hospitalization. At that point, histology revealed acantholysis just underneath the granular layer of the epidermis. Direct and indirect immunofluorescence showed intercellular deposition of IgG and C3. Anti-DSG-1 antibodies with ELISA techniques were detected in extremely high titers. Western blot analysis in extract of human epidermis confirmed the molecular weight of the causative antigen. Diagnosis of pemphigus foliaceus (PF) was established with all diagnostic procedures. Treatment decisions were made after a multidisciplinary collaboration. Plasmapheresis and pulses of intravenous prednisolone were combined. Patient was released with significant improvement after 7 weeks of hospitalization and under systemic prednisone and azathioprine. Due to the refractory course of PF, the treatment plan is not completed yet, as an approval of health authorities is anticipated, in order to continue with rituximab. Pemphigus foliaceus is an autoimmune bullous disease, with the target antigen being in most cases desmoglein-1. It has two forms, the sporadic and the endemic one (fogo selvagem). Progression to erythroderma is unusual. It has been estimated to occur in about 6% of PF cases. Differential diagnosis in these generalized cases from staphylococcal scalded skin syndrome is difficult, based only on clinical picture and histology. Immunofluorescence and molecular studies are essential to define the disease. Therapeutic procedures (systemic steroids, immunoapheresis, immunomodulatory adjuvants, rituximab) show accordingly slow response and hospitalization of such cases is usually prolonged.

Commercial support: None identified.

3511

Esophagitis dissecans superficialis in a patient with mucosal pemphigus vulgaris and multiple gastrointestinal symptoms: A case report

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Introduction: Pemphigus vulgaris is a rare, immune-mediated blistering disorder characterized by acantholysis and intraepithelial blister formation involving the skin and mucous membranes. The binding of autoantibodies to keratinocyte adhesion molecules induced blister formation. While mucosal disease in pemphigus is common, esophageal involvement is reported in only 5% of patients and may cause significant morbidity, including gastrointestinal bleeding or pain. Pemphigus patients also are commonly treated with oral steroids, which can further exacerbate peptic ulcer disease and/or increase bleeding risk. Therefore, a high index of suspicion for esophageal involvement in these patients is required by dermatologists and gastroenterologists in order to improve clinical outcomes. We report a case of mucosal pemphigus vulgaris in a patient who presented with multiple gastrointestinal symptoms in the absence of cutaneous disease.

Case report: A 50-year-old female was evaluated for a constellation of gastrointestinal symptoms, including early satiety, bloating, nausea, hoarseness, dysphagia, and heartburn. Physical examination revealed two small oral erosions with no cutaneous involvement. The patient was referred for upper gastrointestinal endoscopy, which revealed bulla and erosions along the esophagus. Epithelial shearing also was noted from minor endoscopy instrument pressure—a finding consistent with a positive Nikolsky sign or esophagitis dissecans superficialis. Biopsy of the esophagus for direct immunofluorescence demonstrated prominent IgG cell surface antibody and C3 cell surface reactivity. Indirect immunofluorescence revealed positive IgG cell surface antibody staining, an increased IgG desmoglein 3 antibody level, and a normal IgG desmoglein 1 antibody level. These findings were consistent with a diagnosis of mucosal-limited pemphigus vulgaris.

Discussion: Mucosal involvement in pemphigus vulgaris may involve the esophagus resulting in odynophagia, dysphagia, or nonspecific gastrointestinal symptoms. Although rare, a positive endoscopic Nikolsky sign of the esophagus or esophagitis dissecans superficialis has a strong relationship to immunobullous diseases, including mucosal-limited pemphigus vulgaris. Direct and indirect immunofluorescence testing reveals typical findings of pemphigus vulgaris. This case highlights the importance of considering pemphigus in the differential when patients present with esophageal or gastrointestinal symptoms.

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Evaluation of ELISA testing for BP180 and BP230 as a diagnostic modality for bullous pemphigoid: A clinical experience

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Bullous pemphigoid (BP) is a common autoimmune blistering disorder of the elderly. Several diagnostic modalities are available, including clinical impression, histopathology, direct and indirect immunofluorescence, and enzyme-linked immunosorbent assay (ELISA) detection of pathogenic antibodies. In this study, we aim to examine the utility of the newest test, ELISA, in comparison to the constellation of other tests. We describe our clinical experience in which 170 patients diagnosed with bullous pemphigoid had multiple tests performed. BP180 alone showed a sensitivity of 54% and specificity of 94%. The positive predictive value (PPV) is 95% while the negative predictive value (NPV) is 52%. BP230 alone yielded a sensitivity of 48% and specificity of 94%. The PPV is 94% and the NPV is 49%. Using both tests in combination yielded a sensitivity of 66% and specificity of 89%. The PPV of at least one of two tests returning positive is 92% while the NPV of dual negative tests is 58%. Use of ELISAs for suspected cases of BP are an inadequate standalone test, and are only helpful in making the diagnosis should they return positive. However, they would appear to miss about one-third of cases.

Commercial support: None identified.

3788

Evaluation of HBD-1, HBD-2 and LL-37 levels in patients with psoriasis vulgaris after phototherapy

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Antimicrobial peptides are small molecular weight proteins which role on as a member of native immune system with a broad spectrum antimicrobial activity against to bacteria, viruses, fungi. Role of these peptides in dermatologic diseases are shown in different inflammatory diseases, especially in etiopathogenesis of atopic dermatitis and psoriasis. Overproduction of these peptides are shown in etiopathogenesis of psoriasis vulgaris, such as cathelicidin, b-defensins, S100 proteins, RNase 7, lysozyme, elafin, neutrophil gelatinase associated lipocalin recently. Today many studies have focused on the association between psoriasis and cathelicidin, b-defensins or S100 proteins. In this study we aimed to search the effect of phototherapy on levels of b-defensins (HBD1-2) and LL37 in patients with psoriasis vulgaris. We included 17 psoriasis patients who was treated with phototherapy. At baseline and at the end of therapy immunohistochemistry from lesional skin was performed for human b-defensin-1,human defensin-2 and LL-37. After 4 months, the modified psoriasis area and severity index significantly decreased 8.93 ± 7.51 points. We did not detect a significant decrease in lesional immunoreactivity scores of hBD-1, HBD-2 and LL-37 after phototherapy in our study ($P > .05$). These findings suggest that phototherapy treatment does not affect on hBD-1, hBD-2 and LL-37 expressions in psoriasis vulgaris. We think phototherapy may use another pathway for immunomodulation in psoriasis etiopathogenesis other than decreasing the highly inducted levels of antimicrobial peptides. Further studies are needed for better understanding this point.

Commercial support: None identified.

3881

Increased relapse and complications in pemphigus patients treated by the same doctors in a public safety net hospital versus a private university hospital

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Pemphigus is a potentially life-threatening and incurable autoimmune bullous disease. The mainstay of pemphigus treatment is potent, systemic immunosuppressive agents that can have significant side effects. The management of pemphigus requires frequent clinical evaluations, laboratory testing, and medication adjustments. At the Keck School of Medicine, the same doctors treat patients at two different medical center systems on campus, ie the private university hospital (Private Hospital) for patients with healthcare insurance and the public safety net LA County hospital (Safety Net Hospital) for patients with minimal or no health care insurance. Spanish speaking patients of Mexican origin with or without US citizenship are overrepresented in the latter cohort. We took this unique opportunity to assess potential health care disparities between seriously ill patients with pemphigus vulgaris and foliaceus treated by the same doctors within these two very different systems. We found that access to care (doctors, tests, and medications) and achievement of remission was roughly equivalent between these two populations. The Safety Net Hospital patients (n = 34), however, experienced more relapses (59% vs. 30%, $P = .03$) and adverse events, such as infections (79% vs 37%, $P = .001$) than those seen in the Private Hospital system (N = 27). The precise etiologe(s) of the observed outcome disparities is unknown, but may include differences in medication noncompliance, ethnic culture, genetics (Hispanics vs non-Hispanics), language barriers, and transportation issues. Dissecting these possibilities may lead to insights to improving the care of pemphigus patients in a Safety Net Hospital system.

Commercial support: None identified.

2453

Increased vascular endothelial growth factor expression in erythrodermic pemphigus foliaceus patients

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Introduction: Pemphigus foliaceus (PF), an autoimmune blistering disease against desmoglein (Dsg) 1, may disseminate and evolve to erythroderma. Erythroderma occurs in many dermatosis due to the secretion of cytokines, chemokines, and adhesion molecules, such as vascular endothelial growth factor (VEGF). Keratinocytes produce VEGF after skin damage, causing vasodilation, angiogenesis and endothelial cell proliferation. VEGF plays a role in physiological tissue repair, but its unbalanced expression in psoriasis (PSO) and eczema increases keratinocyte proliferation and chemotaxis, leading to chronicity. VEGF is up-regulated in erythrodermic PSO, eczema, bullous pemphigoid and pemphigus vulgaris (PV) patients. However, there is scarce information on VEGF expression and PF.

Methods: We performed a chart review of all PF patients from our clinic (January 1991-December 2014). We included 30 PF patients with erythroderma, and collected serum samples during erythroderma and at nonerythrodermic phase. As positive controls, we included 10 PSO and 10 PV patients, and 10 individuals as healthy controls (HC). We measured circulating VEGF, soluble VEGF receptor 1 (sVEGFR1, R&D Systems, US), and anti-Dsg1 (Euroimmun, Germany) by ELISA. Statistical analysis was conducted with GraphPadPrism 5.0; significance was considered to be $P < .05$.

Results: In PF patients, higher anti-Dsg1 ($P = .0026$) and VEGF levels ($P = .02$) were detected in erythrodermic vs. nonerythrodermic phase, and there was no difference in serum levels of VEGF of PF and controls. No difference of sVEGFR1 was detected in PF in all phases. Interestingly, sVEGFR1 in PF with erythroderma was higher than the controls. In PF, sVEGFR1 correlated with anti-Dsg1 only during nonerythrodermic phase ($r = 0.5443$; $P = .004$). In PF, circulating anti-Dsg1 usually correlates with disease severity. Since our PF patients showed enhanced VEGF with erythroderma, the correlation between sVEGFR1 and anti-Dsg1 suggest a down regulating response to the VEGF increase.

Conclusion: Serum VEGF is increased in PF patients with erythroderma, and may contribute to vasodilation. Erythroderma may lead to protein loss, lack of thermal regulation, facilitating infection; therefore, VEGF may represent a potential prognostic factor.

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Laryngeal involvement in paraneoplastic pemphigus associated with benign Brenner tumor

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Introduction: Paraneoplastic pemphigus (PNP), a distinct autoimmune blistering disorder with underlying neoplasia, was first described in 1990 by Anhalt et al. PNP is usually associated with hematologic malignancy, although correlated solid tumors were described in nearly 15% of the cases. Polymorphic cutaneous lesions may resemble pemphigus vulgaris, erythema multiforme, bullous pemphigoid, lichen planus and graft versus host disease. Oral, ocular and genital mucosa are predominantly affected, and laryngeal manifestation is exceptional. We report a PNP case with exuberant laryngeal involvement associated with benign Brenner tumor.

Case report: A 55-year-old female patient presented a 2-year history of brownish keratotic plaques on the trunk and limbs and violaceous papules on the face and neck. She also had conjunctival hyperemia and oral erosions with intense hoarseness. Ophthalmologic evaluation reported conjunctival erosions; nasofibroscopy revealed blisters at the laryngeal face of epiglottis. Due to benign Brenner tumor diagnosis, bilateral adnexectomy had been performed 6 months before referral to our clinic. A biopsy from left arm was obtained: histopathologic analysis showed apoptotic keratinocytes and lichenoid interface dermatitis. As she developed blisters on the face and palate with dysphagia and odynophagia, a biopsy from the palate was performed. Histopathologic evaluation exhibited apoptotic keratinocytes and a lymphoplasmacytic infiltrate at the lamina propria; direct immunofluorescence (IF) demonstrated IgG intercellular deposits at the epidermis, and IgG and C3 bound to the basement membrane zone. Indirect IF with rat bladder epithelium as substrate is under analysis. These findings suggested the diagnosis of PNP. She was submitted to a complete neoplasia screening, and no other tumor was found. Treatment with prednisone 1 mg/kg/day and azathioprine 150 mg/day was introduced with improvement of the lesions.

Discussion: In our case, PNP onset preceded the diagnosis of the neoplasia, and persisted despite of complete surgical removal of the tumor. Besides, mucosal involvement may contribute to morbidity related to PNP and require sustained immunosuppressive therapy for adequate control.

Conclusion: To our knowledge, this is the first case of PNP in association with benign Brenner tumor. Multidisciplinary evaluation and follow-up is recommended to determine the degree of mucosal involvement, and adjust therapy.

Commercial support: None identified.

3325

Muckle–Wells syndrome: A rare cryopyrinopathy

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Muckle–Wells syndrome (MWS) is a rare autosomal dominant disease caused by a heterozygous mutation on chromosome 1q44 affecting the NLRP3 (CIAS1) gene responsible for cryopyrin encodement. The NALP3 inflammasome complex utilizes cryopyrin as scaffolding for the promotion, activation and amplification of proinflammatory cytokines IL-1β and IL-18 responsible for the induction and maintenance of inflammation. Cryopyrin hyperactivity produces the classic clinical triad of urticaria, episodic fevers and sensorineural deafness, as displayed in MWS. Additionally, renal amyloidosis resulting in proteinuria and chronic renal insufficiency will occur in 25% of patients. We present a case of a female in her mid-30s with a transient urticarial eruption on her bilateral upper extremities, chest and back with associated recurrent low-grade fevers, eye redness and arthralgia present for approximately 20 years. Cold temperatures and stress exacerbated these symptoms. The patient also complained of new onset hearing loss with associated tinnitus. A family history of similar symptoms was present in her brother, mother and maternal grandmother. Laboratory examination revealed an elevated CRP. Protein electrophoresis demonstrated beta-gamma bridging with an increased IgA and polyclonal gamma globulins. Further examination findings were within normal limits. Genetic evaluation confirmed a diagnosis of MWS. Treatment with an IL-1 receptor antagonist has demonstrated vast improvement of her clinical symptoms. Early identification and treatment of MWS is key to delaying disease progression.

Commercial support: None identified.

3314

Mucocutaneous involvement in newborn with congenital epidermolysis bullosa acquisita

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Background: Epidermolysis bullosa acquisita (EBA) is a rare subepidermal bullous dermatosis with autoantibodies against type VII collagen, the main component of anchoring fibrils. EBA onset commonly occurs between 40 and 60 years of age, although cases during childhood have been described. Only one case of congenital EBA has been reported. We describe a second newborn with congenital EBA mucocutaneous lesions.

Case report: A 25-year-old patient with EBA, receiving low dose prednisone, delivered a white female newborn with erosions on the scalp, nose, upper lip, tongue and limbs. A skin biopsy was performed at the right thigh; histopathologic analysis showed a subepidermal blister with neutrophils; direct immunofluorescence microscopy of perilesional skin exhibited IgG, IgM, and C3 deposits at the basement membrane zone. Serum IgG antibodies were bound to the dermal side of the cleavage in indirect immunofluorescence microscopy on salt-split skin; detection of serum antibodies against noncollagenous domain 1 of type VII collagen by ELISA is under analysis. These findings corroborated the hypothesis of congenital EBA and after approximately 3 months of supportive care, lesions completely healed with multiple milia. No recurrence was observed.

Discussion: Neonatal autoimmune bullous disease may be attributed to placental transfer of maternal autoantibodies influenced by hormonal changes during pregnancy. In experimental EBA mice models, serum levels of pathogenic type VII collagen antibodies were comparable in neonatal offspring and maternal mouse immediately after birth. On the previous report of congenital EBA, no new lesions developed after 10 days of life, earlier than the patient described on our case, who presented new erosions until 45 days of age. Although plasmatic IgG half-life is approximately 14 days in human adult, skin-bound IgG against type VII collagen may still be detectable after 8 weeks in neonatal offspring of maternal mice with EBA.

Conclusion: To the best of our knowledge, our patient is the first case of congenital EBA with mucocutaneous lesions. Similar to the previous case, she improved without systemic treatment, and no complications were observed. Prolonged supportive care and follow-up may be recommended as delayed clinical remission might occur due to persistence of tissue-bound maternal autoantibodies.

Commercial support: None identified.

3603

Neutrophilic dermatosis of the hands: Case report

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Neutrophilic dermatosis of the hands (NDH) is a rare disease with about 60 cases being described in literature. The exclusive involvement of hands is characteristic, which differentiates from Sweet syndrome and pyoderma gangrenosum. Having been described by Stratton et al in 1995 as pustular vasculitis of the dorsal hands (considered a variant of Sweet syndrome) it received its current denomination in 2000 by Galaria et al, and in the last few years it has been considered a distinct entity. A case report is presented below. A 49-year-old female of African descent diagnosed with rheumatoid arthritis five years ago (in use of 15 mg of methotrexate a week) came to us complaining about having asymptomatic lesions in her hands for two months. On examination there was a noninfiltrated erythematous plaques with undefined papulous edge on the dorsal of the hands. Biopsy was compatible with neutrophilic dermatosis. After topic application of corticotherapy with betamethasone for 10 days there was full remission of lesions. NDH manifests itself with papules, plaques, pustules, blisters and ulcerations, usually limited to the dorsal of hands and it can less often involve the palm area. It mostly attacks female patients (69%), and the average age is 62. There may be association with hematologic neoplasia (27% of cases) and inflammatory bowel disease (15%). Most of them present fever, leukocytosis and/or HSV increase and C-reactive protein. It is seldom associated with rheumatoid arthritis and other neoplasias. There were also demonstrations of associations with hepatitis C and sarcoidosis, and it does not seem to be inducted by drugs. In the histopathologic examination, there were infiltrated neutrophils in the reticular and papillary dermis, together with spongiosis, with the possibility of having intraepidermal pustules. Vasculitis is found in 22.28% of older injuries, which is a result of the release of toxic products by the neutrophils, with no immunological ground. In almost all cases described, there was a good response to the use of systemic corticosteroids with a dose of 1 mg per kilogram per day. Rarely, and in less extensive cases, topical corticosteroids or tacrolimus can be used. Spontaneous remission is rare. In case of relapse, dapsone and colchicine can be associated. Cyclosporin, azathioprine, methotrexate, indomethacin, and minocycline are cited less frequently.

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Rituximab as first line therapy for Juvenile pemphigus vulgaris

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Juvenile pemphigus vulgaris (JPV) is a rare autoimmune epidermal blistering disease that represents a clinical entity of the spectrum on pemphigus vulgaris (PV) that affects adolescents between the ages of 13-18 years of age. PV is further classified as a childhood variant if occurring in children less than 12 years of age and adults greater than 18 years of age. Pathologic autoantibodies directed at keratinocytes cytoplasmic proteins desmoglein 1 (dsg 1) and desmoglein (dsg 3) results in intraepidermal vesicles with acantholysis. Clinically this manifests as flaccid blisters and erosions with oral or cutaneous involvement. Optimal treatment regimens have not been established for JPV and generally treatment for JPV follows adult PV regimens. Systemic corticosteroids are the most common initial therapeutic option for active disease. Systemic corticosteroids can be effective but can lead to severe side effects. Other therapeutic options include immunosuppressive (azathioprine, cyclophosphamide, mycophenolate mofetil), intravenous immunoglobulins, and rituximab. The latter has been typically reserved for refractory lesions. Rituximab is a monoclonal chimeric antibody directed towards CD20+ antigen, which is normally used for B cell activation and proliferation. Targeting this cell surface protein results in B cells depletion. Rituximab was initially approved for B cell lymphomas but it has been utilized in various autoimmune diseases. Since there is no conventional dosing of Rituximab for pemphigus vulgaris administration generally falls under the B cell lymphoma or rheumatoid arthritis dosing schedules, which are 375 mg/m^2 once a week for four consecutive weeks or two 1000 mg infusions separated by a 2-week interval. Recently, there have been several reports of recalcitrant JPV being successfully treated with rituximab. Here we present a 17-year-old male with JPV who was successfully treated with high-dose corticosteroids and rituximab as first line therapy.

Commercial support: None identified.

3409

Rituximab combined with conventional therapy vs conventional therapy alone for the treatment of mucous membrane pemphigoid: A retrospective review

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Background: The anti-CD20 monoclonal antibody rituximab (RTX) is becoming increasingly accepted as a safe and effective treatment for autoimmune blistering diseases, including pemphigus and bullous pemphigoid. However, data utilizing RTX for the treatment of patients with mucous membrane pemphigoid (MMP) is limited. Several case series have demonstrated increased rates of clinical remission in MMP patients refractive to conventional immunosuppressive therapy; however, they have been constrained by small sample sizes and limited follow up time.

Objective: To compare the efficacy of adding RTX to traditional immunosuppressive therapies in the treatment of MMP in terms of both time to disease control and cessation of corticosteroids, and to compare the safety profile following addition of RTX.

Methods: Patients with a diagnosis of MMP commencing immunosuppression at Emory University between August 2001 and June 2015 were identified. To be included in this retrospective analysis, patients had at least 6 months of follow-up data after initiating therapy. In total, 49 patients fit these criteria. All patients treated with RTX had already been treated with at least one systemic immunosuppressive agent, and all remained on concomitant immunosuppressive therapy throughout the study period. Outcome measures included both achievement of and time to disease control, time to relapse, withdrawal of corticosteroids, and number of adverse events.

Results: Twenty-four patients were treated with RTX and 25 were treated with conventional immunosuppression only, with a mean follow-up period of 28.5 months for the RTX group and 44.46 months in the conventional group. 100% of patients in the RTX group achieved disease control compared to 40% in the conventional group ($P < .01$), with a mean time to disease control of 10.17 months and 39.11 months, respectively ($P < .01$). Ten patients who had achieved disease control following RTX experienced a relapse after a mean time of 9.6 months, compared to 3 in the conventional group after a mean time of 2.33 months ($P = .11$). 75% of patients in the RTX group were able to come off of steroids completely, compared to 52% in the conventional group ($P = .15$). Adverse events were seen in 29% of patients following RTX, compared to 48% of patients in the conventional group ($P = .17$).

Limitations: This is a retrospective review at a single academic center. There were limitations in matching by disease severity in the absence of defined clinical severity indices. Additionally, the two groups were not randomized to specific immunosuppressive regimens or fixed doses.

Conclusions: A review of the recent MMP literature suggests a favorable clinical response to RTX, but no studies have directly compared RTX to conventional immunosuppressive therapy in this disease. Our study indicates that the addition of RTX to conventional therapy in patients with MMP results in more rapid and sustained disease control, a steroid-sparing effect, and a favorable side effect profile.

Commercial support: None identified.

2785

The isomorphic response in vancomycin-induced linear IgA bullous dermatosis

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Background: Linear IgA bullous dermatosis (LABD) is a subepidermal vesiculobullous eruption occurring most often with vancomycin in drug-induced cases. We describe a case of vancomycin-induced LABD presenting with an atypical isomorphic response.

Case report: An 88-year-old woman who underwent hip replacement surgery following femoral neck fracture developed prosthetic joint infection and *C difficile* colitis for which she was receiving intravenous and oral vancomycin. She developed localized vesicles and bullae around the surgical wound, the left brachial peripherally inserted central catheter (PICC), the vulva and inner thighs. Due to the localized nature of the eruption, contact dermatitis to a no-rinse perineal and body cleanser and/or adhesive strip placement was initially suspected. New lesions continued to appear and spread despite the discontinuation of no-rinse soap and adhesives. Examination revealed tense vesicles and bullae on an inflammatory base at the surgical wound, PICC-line site, and sites of previous adhesive contact. We observed annular, sausage-shaped vesicles and vesicles with the specific "string of pearls" morphology, both of which were suggestive of LABD. Skin biopsy revealed subepidermal vesicles and a superficial inflammatory infiltrate in the dermis, containing neutrophils and eosinophils. Direct immunofluorescence studies revealed a linear IgA band at the dermoepidermal junction. These findings confirmed the diagnosis of LABD. The lesions resolved after discontinuation of vancomycin and a short course of oral prednisone.

Discussion: A small number of recent cases describe vancomycin-induced LABD (VI-LABD) presenting with an isomorphic response. In one patient with multiple dressings, VI-LABD appeared at all sites of previous adhesive strip placement and removal. Contact dermatitis to adhesive strips was initially suspected. VI-LABD with koebnerization at the site of an old surgical scar has also been reported. We observed VI-LABD both at fresh wound margins and sites of previous adhesive placement, which suggests a possible role of epidermal trauma in inducing these lesions. Clinicians should be aware that LABD can present with an isomorphic response that may initially be difficult to distinguish from contact dermatitis.

Commercial support: None identified.

3353

The sensitivity and specificity of mosaic-based indirect immunofluorescence biochip method in the diagnosis of pemphigus and bullous pemphigoid

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Autoimmune bullous diseases are characterized by autoantibodies against structural proteins of the epidermis or the dermoepidermal junction, clinically presented with cutaneous and/or mucosal bulla or erosions. Pemphigus and bullous pemphigoid are the major groups of autoimmune bullous diseases. The diagnosis of these rare diseases are based on a combination of clinical features, histologic and direct immunofluorescence (DIF) findings and serology with indirect immunofluorescence (IIF) and enzyme-linked immunosorbent assay (ELISA) tests. In recent years, a new mosaic-based indirect immunofluorescence biochip method has been developed as a cheaper, practical and a less time consuming test. In this study, we aimed to state the value of this new method in the diagnosis of pemphigus and bullous pemphigoid. We analyzed sera from pemphigus patients (n = 45) and bullous pemphigoid patients (n = 18) in whom the clinical diagnosis had been confirmed by histopathologic and immunofluorescence findings and/or ELISA tests. The control group included 35 patients with other skin diseases. The sensitivity and specificity of mosaic-based IIF biochip method in the diagnosis of pemphigus and bullous pemphigoid was considerably high; in the diagnosis of pemphigus was found %91 and %97; respectively and in the diagnosis of bullous pemphigoid was found %94 for both of them. Our findings showed that the mosaic-based IIF biochip method has highest diagnostic sensitivity in detecting the autoantibodies against Dsg3 in pemphigus patients and the autoantibodies against BP180-NC16A in bullous pemphigoid patients, a good rate of agreement was observed among mosaic-based IIF biochip method and ELISA test ($P < .01$). In conclusion, mosaic-based IIF biochip method has value as a cheaper, practical, less time consuming and minimally invasive test which can be used as an initial screening test in the diagnosis and differential diagnosis of autoimmune bullous diseases.

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INFECTION—BACTERIAL AND PARASITIC

3522

A case of New World cutaneous leishmaniasis in Danville, PA

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Background: New World cutaneous leishmaniasis is a protozoal infectious disease transmitted by a bite from the Lutzomyia sandfly that is not commonly seen in the U.S. outside of South-Central Texas. It is most commonly seen in those who have traveled to endemic areas such as Central or South America, and is most commonly caused by the subspecies *Leishmania mexicana* or *L braziliensis*.

Case report: A 21-year-old woman presented to the clinic with a 5-month history of a slowly progressive, nonhealing erythematous 2-cm crusted plaque on the left cheek that had initially appeared as a "pimple-like bump" while studying abroad in Costa Rica. The lesion had been previously biopsied by an outside physician, but pathology showed nonspecific inflammation and she was subsequently treated with topical antibiotics. She had developed no other mucocutaneous findings or systemic symptoms despite enlargement of the lesion and thickened crust formation. Her previous slides from the left cheek were requested and read within the Geisinger system, revealing multiple amastigotes in small clusters within the papillary dermis and within the cytoplasm of the dermal histiocytes. An additional biopsy was sent to the CDC for PCR and DNA sequencing and came back positive for the subspecies *L panamensis*. After consulting with the CDC, she was started on oral ketoconazole 600 mg daily for 30 days. She responded well to the treatment with resolution of the lesion and residual scar formation.

Discussion: Cutaneous leishmaniasis due to *L panamensis*, a subgroup of the species *L braziliensis*, is a common cause of New World protozoal infections endemic to Central and South America. Infections begin as a papule at the site of inoculation from the bite of a sandfly that slowly grows into an ulcerated plaque or nodule, leading to scar. Histopathology commonly shows amastigotes within dermal macrophages with a mixed inflammatory infiltrate. Lesions can be cultured using specialized Nicolle-Novy-MacNeal media available from the CDC. Cultures are positive in approximately 40% of cases. PCR is the most sensitive and specific diagnostic test. Real-time PCR assay is available at the CDC. Ketoconazole at a dose of 600 mg/day for 28 days has been shown to be more effective than sodium stibogluconate in small studies. Side effects include transient aminitis and reversible decrease in serum testosterone.

Conclusion: New World cutaneous leishmaniasis may go unrecognized without high clinical suspicion and history of travel to endemic areas. Diagnosis can be confirmed by pathology, culture, and real-time PCR.

Commercial support: None identified.

3740

A protean master mimic: Secondary syphilis presenting as psoriasiform balanitis

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Case Description: The patient is a 47-year-old white male who presented to our facility complaining of a 1-month history of a pruritic erythematous, scaly, psoriasiform rash of the penis. He was referred to dermatology by his primary care provider (PCP) after self-treatment with over-the-counter (OTC) clonitrazole and emollients had failed to improve his symptoms. A few weeks prior, the patient had an episode of penile discharge, tested negative for gonorrhea and chlamydia, was treated with azithromycin, and had complete resolution of symptoms. He was found to have reactive RPR and FTA-ABS titers. Punch biopsy revealed *T pallidum* on Warthin-Starry and immunohistochemical staining. Based on this information he was given a diagnosis of secondary syphilis. A sexual history revealed that the patient had unprotected intercourse with a known male partner who tested positive for syphilis. He was successfully treated with 3 doses of IM penicillin G with improvement of his rash and pruritus and no complications.

Discussion: This patient's case illustrates the importance of recognizing the diverse presentations of syphilis and the threat it poses to vulnerable populations. Syphilis is known as "the great imitator" due to its myriad diverse manifestations that can be difficult to distinguish from other diseases. The erythematous scaly psoriasiform patches on this patient represent a rare and unusual presentation of secondary syphilis, which, although very polymorphic, is much more often macular or maculopapular. Syphilis has shown a rising incidence in the United States and men who have sex with men (MSM) are at higher risk than other populations. Diagnosing and treating syphilis is vital, because if unrecognized it can lead to highly destructive and often irreversible cardiac and neurologic effects. Improved provider awareness as well as patient education and safe practices may combat this trend and prevent these unfortunate sequelae.

Commercial support: None identified.

3301

An unusual presentation of primary cutaneous nocardiosis

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Introduction: Nocardiosis is an uncommon cause of infection seen in 500-1000 people annually in the United States. The primary cutaneous form of the disease is the least common and is seen in just 5-7% of these cases. Direct inoculation of the immunocompromised host by means of trauma or surgery is the usual route of infection. However, we present a case of infection without history of skin barrier compromise.

Case Presentation: A 71-year-old man with a history of non-Hodgkin lymphoma presented with a one-week history of a painful abscess on the right hip. He was otherwise well with no systemic symptoms or fever. He denied any local trauma to the area, but did note he had placed a food wrapper in his waistband around the area that was subsequently affected. The lesion was cultured and grew Nocardia. Treatment with trimethoprim-sulfamethoxazole was initiated and within one week the lesions showed much improvement.

Discussion: To our knowledge, this is the first case of primary cutaneous nocardiosis to cause infection of the skin without preceding trauma. We hypothesize that infection may have been caused by contact with a contaminated material. Although primary cutaneous infection caused by Nocardia is uncommon, it should be suspected for soft tissue infections occurring in the immunocompromised host.

Commercial support: None identified.

2682

Atypical cutaneous mycobacteriosis by *M mucogenicum* mimicking squamous cell carcinoma in immunocompetent patient

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Introduction: Different mycobacterial species from *Mycobacterium tuberculosis* and *Mycobacterium leprae* have been called as environmental, opportunistic or atypical mycobacteria, although the term of nontuberculous mycobacteria (NTM) is one of the most accepted today. We report an interesting clinical case of a cutaneous infection produced by *M mucogenicum* mimicking a squamous cell carcinoma in an immunocompetent patient.

Case report: A 59-year-old male was attended in our dermatology unit complaining about an excrescent cutaneous tumor of rapid growth, which had developed for the previous three months. He denied contact with animals, though regarding his occupation, he admitted an occasional prick with a rose thorn. On clinical examination, an infiltrated erythematous tumor with markedly hyperkeratosis in the central part could be appreciated on the dorsal aspect of his right hand. No locoregional lymph nodes and hepatosplenomegaly were observed. Histologic examination showed the existence of pseudoepithelioma hyperplasia with presence of acute inflammatory reaction. Ziehl Nielsen, Fite Faraco and periodic acid–Schiff (PAS) status, as well as the smear, were all negative. However, the culture showed the presence of nonpigmented mucoid colonies of alcohol-resistant bacilli (AFB). Species identification based on 16S rRNA was consistent with *M mucogenicum*. The patient was started on clarithromycin 500 mg twice daily, in association to rifampicin 300 mg, twice daily, with resolution of symptoms at 3 months.

Discussion: *M mucogenicum* is a fast-growing NTM, formerly known as *M chelonae*-like. Infections due to *M mucogenicum* are extremely rare, but often involve skin and soft tissues. Immunocompetent patients rarely develop severe infections. It can also induce a granulomatous hepatitis, pneumonia in AIDS patients and skin infections in patients treated with TNF blockers. From a clinical point of view, the presentation of cutaneous infections caused by NTM may be highly variable. Differential diagnosis includes common warts, verrucous tuberculosis, aquarium granuloma, sporotrichosis, and squamous cell carcinoma, as in the present case. DNA sequencing may be used to identify the exact subtype isolated from culture. There is no defined therapeutic regimen for its treatment due to the existence of multiple bacterial resistances. A combination of two or more agents should be considered in immunocompromised patients.

Commercial support: None identified.

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Bacillary angiomatosis from *Bartonella quintana* in a cardiac transplant patient

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Bacillary angiomatosis (BA) is a vasoproliferative disorder caused by *Bartonella henselae*, or less frequently *B quintana*, and often associated with exposure to cat bites, scratches, cat fleas and body lice. If left untreated it can affect the liver, spleen, heart, and gastrointestinal tract and lead to death. While it was previously thought to be an AIDS-defining illness, it has also rarely been described in other immunocompromised states, such as organ transplant recipients. A 68-year-old female with PMH of peripheral neuropathy, foot drop, and dilated cardiomyopathy s/p cardiac transplant on mycophenolate mofetil, cyclosporine, and prednisone presented for right heart catheterization. She was found to be febrile and admitted for monitoring. Dermatology was consulted for an acute onset of bright red, nonblanching papules in her right antecubital fossa, bilateral forearms, chest, and abdomen. The lesions erupted simultaneously three weeks prior. She denied chills, recent travel, sick contacts, chest pains, worsening shortness of breath, weight loss, and abdominal pain. She was started empirically on doxycycline. A punch biopsy was performed and showed a vascular proliferation; however, a Warthin–Starry stain was negative. HIV and CMV were negative. Serology for *B henselae* (titer 1:256) and *B quintana* (titer ≥1:1024) suggested recent infection. The patient completed a four-month course of doxycycline with full resolution of these lesions. BA is a vasoproliferative form of infection with *B henselae* or *B quintana* that occurs in immunocompromised patients such as those with HIV or leukemia, on chemotherapy, or on immunosuppression after organ transplantation. Clinical and histologic features are used to make the diagnosis. Histology reveals vascular proliferation with the presence of neutrophils adjacent to blood vessels. While Bartonella species can be demonstrated by Warthin-Starry stain, up to 30% of cases do not stain positively. Culture and PCR-based methods can also be used to identify the organisms. Clinicians must have a high index of suspicion and low threshold for empiric treatment of new vascular lesions in immunocompromised patients. To our knowledge, there is only one other case in peer-reviewed literature of BA in a cardiac transplant patient.

Commercial support: None identified.

3760

Fosfomycin therapy in a case of mycetomatoid granulomatous mastitis by *N brasiliensis* in pregnancy

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Nocardia is a genus of Gram-positive bacteria. *N brasiliensis* and *N asteroides* complex are the most notable. Fosfomycin is an antibiotic that inhibits peptidoglycan synthesis. It is a pregnancy category B drug that has been effective against actinomycetes. To our knowledge there are no reports of a Nocardia infection treated with fosfomycin. A 19-year-old otherwise healthy woman presented with a dermatosis on the left breast of 3 weeks evolution, characterized by erythema, induration and pain. A soft tissue infection was diagnosed and surgical debridement was performed, together with a biopsy and cultures. The patient was treated with several antibiotics without improvement. Biopsy revealed a chronic granulomatous inflammation with a negative Ziehl–Nielsen (ZN) stain, bacterial and mycobacterial cultures, PPD, coccidioidin, HIV by ELISA and imaging studies were normal. The patient was referred to our dermatology clinic for diagnosis and treatment. Physical examination revealed increased volume on her left breast and presence of multiple fistulae draining a seropurulent secretion. Biopsy and cultures were negative for fungi and bacteria. A granulomatous chronic inflammation with negative stains (PAS, Grocott, ZN) was observed. *N brasiliensis* IgG antibodies were positive with a titer of 0.64 (cut-off = <0.3). A presumptive diagnosis of mycetomatoid granulomatous mastitis associated to *N brasiliensis* was made. Treatment with trimethoprim/sulfamethoxazole (TMP/SX) 160/800 mg every 12 hours and amoxicillin/clavulanate 87.5 mg/12.5 mg every 12 hours was started but there was no improvement after 2 weeks. Amoxicillin was discontinued and fosfomycin 4 grams/day orally was added with TMP/SMX for 2 weeks with clinical improvement. Three weeks later, the patient got pregnant, and TMP/SMX was halted and fosfomycin was continued 2 g per day for 3 weeks, achieving complete resolution. At 6 months follow-up, the patient was asymptomatic and the *N brasiliensis* antibody titer decreased (0.438). In this case *Nocardia brasiliensis* infection was detected indirectly by positive serology. Although TMP/SMX was primarily initiated, the patient did not show improvement until fosfomycin was administered. During pregnancy, fosfomycin achieved clinical cure and decreased antibody titer. Fosfomycin can be an alternative treatment in some Nocardia infections and could be used during pregnancy.

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3440

Crusted scabies in a patient with lepromatous leprosy

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Crusted scabies (CS) is a very contagious rare skin infestation caused by *Sarcoptes scabiei* var *hominis*, an obligate human parasite, transmitted by skin-to-skin contact. Clinically, it can present with psoriasiform skin lesions in acral distribution with variable whitish scaling. It usually involves the subungueal area with nail hyperkeratosis and dystrophy. A 56-year-old man presented with a seven month history of pruritus (with nocturnal exacerbation), weight loss and muscle weakness. The patient was diagnosed with lepromatous leprosy (LL) 22 years ago, abandoned treatment several times and developed neurologic damage and deformities. On examination, hyperkeratosis with crusted lesions were seen on hands and feet, with severe nail dystrophy. We also noted an erythematous scaling eruption in the face, and on neck, scalp, trunk and arms. Laboratory results included a negative HIV test and skin scraping revealed the mite. The patient was treated with oral antihistamines, topical antipruritics, keratolytics, topical permethrin (5%) and repeated doses of ivermectin (200 μg/kg) on the 1st, 2nd, 8th, 9th and 15th day. The usual method for scabies diagnosis is skin scraping with microscopic examination or dermatoscopy. CS is frequently found in immunocompromised patients (such as HIV or HTLV-1 patients), and mentally retarded or physically incapacitated individuals. Infested individuals and their close contacts should be treated at the same time, even if asymptomatic. There are few reported cases showing the association between CS and LL in non-HIV infected individuals. In Brazil, due to the high number of leprosy, physicians should be aware of the possibility of CS in leprosy patients who develop widespread hyperkeratotic eruptions.

Commercial support: None identified.

3846

High relapse rate on completion of who recommended multidrug therapy in patients of leprosy

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Aim: To study the relapse rate and change in bacillary index (BI) and morphological index (MI) after completing the multidrug therapy by WHO guidelines in lepromatous (LL), borderline (BT, BB, BL), and tuberculoid leprosy (TT).

Materials and methods: 32 patients with leprosy (slit smears (BI) and histopathology confirmed) were included. Paucibacillary category were given 600 mg rifampin monthly, 100 mg dapsone daily for 6 months and for multibacillary 600 mg rifampin, 300 mg clofazimine monthly, 100 mg dapsone, 50 mg clofazimine daily for 12months. Follow up was done monthly and after 6 months of completion of MDT.

Results: Out of 32, 6 patients of lepromatous, 4 of borderline and 5 of tuberculoid leprosy had relapse even after completion of the MDT. Decrease in bacillary and morphological index in case of lepromatous leprosy also was not significant. So, all were given ofloxacin tablets 400 mg once daily for 6 months before they were declared fit for "release from treatment".

Conclusion: Even after treatment, skin lesions may be present with WHO short duration treatment in patients with high bacillary load. It is difficult to distinguish clinical relapses (failure of treatment) from late type 1 lepra reaction causing skin lesions to reappear. Failure may also result from drug resistance. There are insufficient data to evaluate efficacy of shorter treatment regimens by WHO (12 months) for multibacillary leprosy and this area has vast scope of improvement and modifications in order to make this world free from "leprosy".

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2334

Leprosy presenting as a reversal reaction requiring urgent treatment

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Introduction: Leprosy usually presents insidiously with cutaneous lesions and variable loss of sensation in the tuberculoid form and with extensive skin and peripheral nerve manifestations in the lepromatous form. Most cases of leprosy, however, do not strictly fall into either extreme. A reversal reaction is a form of cell-mediated immune response involving a delayed hypersensitivity reaction and an acute upregulation of the immune response to *Mycobacterium leprae* antigens. Reversal reactions usually present gradually over a few weeks as erythema, swelling, and edema in previously flat and asymptomatic cutaneous lesions in patients who have been receiving antileprosy therapy for several months. We present an unusual case in which a patient with no prior diagnosis of leprosy presented acutely with new-onset skin lesions and a severe and rapidly progressive peripheral neuritis clinically consistent with a reversal reaction as the first manifestation of her indolent infection.

Case: A 43 year-old woman was admitted to the hospital with an 8-day history of an eruption beginning on her right leg and eventually appearing on her left leg, bilateral earlobes and helices, left nose, left cheek, and left elbow. The rash appeared as large nonpruritic, erythematous, anesthetic patches and plaques that progressively increased in size and coalesced. She also developed pain in her right distal leg accompanied by motor weakness, including a foot drop. She had a spontaneous ulceration and ecchymosis on her right lateral malleolus and a palpable branch of the dorsal cutaneous nerve on her right foot. A clinical diagnosis of leprosy with associated neuritis was made, and the patient was started on prednisone (1 mg/kg), dapsone, and rifampin. Clofazimine would be added outpatient. All of her sensorimotor neuritis symptoms responded dramatically to therapy over the subsequent 48 hours. She was able to bear weight on her right foot again and regained significant range of motion.

Conclusion: The current case is noteworthy since it illustrates an unusual presentation of a reversal reaction that was severe, rapidly progressive, and required urgent empiric corticosteroid treatment in a patient with previously asymptomatic borderline tuberculoid leprosy. Early clinical recognition of reversal reactions followed by immediate initiation of corticosteroid therapy is crucial since these reactions can quickly result in severe and potentially permanent sensorimotor nerve damage.

Commercial support: None identified.

2805

Lucio phenomenon (necrotizing erythema) in patients with Lucio leprosy: A case report

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The phenomenon of Lucio (LP) or necrotizing erythema, described in 1852 by Lucio and Alvarado, is a rare event that occurs in patients with Lucio leprosy (LL) or near the pole Virchowian. This is a reaction type III mediated by inflammatory cytokines that produce prostaglandins, IL-6, and factor III, actually triggering the coagulation cascade. It can be triggered by recurrent infections, drugs, and pregnancy. The clinical picture is characterized by purpuric plates, aspect livedoid and star, and little painful injuries. In general there are no lumps or fever and lesions progress to skin necrosis. Histopathology observed skin ulceration, vascular thrombosis and invasion of the blood vessel wall by Hansen bacillus. Patients who have never been treated and with low immune defense are more likely to start LP. Treatment is based in multibacillary multidrug therapy (MDT/MB), corticosteroids and thalidomide. We report the case of a male patient, a 67-year-old, white, born and raised in São Paulo - Brazil without a previous diagnosis of LL and presented LP. The clinical examination showed ulcer in right ankle with tendon exposure Achilles and other ulcerated lesions in the left ear, upper limbs, abdomen and legs and also madarosis eyelashes and distal third of eyebrows and signs of vasculitis in palmar and plantar region. The smear of the elbows and earlobes was positive 2+/1+. Pathological anatomic examination showed: extensive areas of skin necrosis, microthrombi blocking small- and medium-sized vessels in the superficial and deep dermis and numerous bacillus intact and fragmented in the dermis within the thrombus. Differential diagnosis of vasculitis were excluded such as an autoimmune disease. The patient remained hospitalized for 18 days, received rifampicin 600 mg single dose, dapsone 100 mg daily, clofazimine 50 mg daily, oxacillin intravenous for 7 days, prednisone 30 mg per kilo, hydrogel slab and debridement of necrotic lesions. Evolving with hemodynamic stability and improvement of lesions was discharged for treatment completion in domicile for another 24 months. Although LP it is rare, it should be aware of the risk of death from cachexia, disseminated intravascular coagulation or septicemia.

Commercial support: None identified.

2807

Lucio's phenomenon and antiphospholipid syndrome in a leprosy patient

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Lucio's phenomenon is an uncommon cutaneous reaction caused by necrotizing vasculitis in multibacillary leprosy patients. Antiphospholipid syndrome (APS) is a syndrome featured by recurrent venous or arterial thrombosis. It usually presents with persistently elevated levels of antibodies against phospholipids and often occurs in association with systemic lupus erythematosus or other rheumatic or autoimmune disorder. Although autoimmune profile abnormalities, such as elevated antinuclear factor, rheumatoid factor, antithyroid antibody, have been documented in lepromatous leprosy; however, the concurrent occurrence of Lucio's phenomenon and APS is rare and makes the diagnosis more difficult. Herein, we present a female Indonesia patient without any medical history who suffered from sudden onset of fever, chills, and painful erythematous swelling and hemorrhagic bullae on her bilateral lower legs for several days. She was admitted in the impression of cellulites, vasculitis, or unknown autoimmune disease. The blood tests showed normal white blood cell count, normal liver and renal function test, but elevated CRP and ESR. The antinuclear factor was 40X positive and the C3 and C4 level were decreased. Both c-ANCA and p-ANCA were negative. There were positive lupus anticoagulant and very high levels of anticardiolipin IgM and anti-β2 glycoprotein IgM. Rheumatologist made the diagnosis of APS and systemic corticosteroid was given. Unfortunately, the fever persisted and skin biopsy was arranged. The pathological findings showed epidermal necrosis and necrotizing vasculitis. Moreover, many dermal vessels were occluded by periodic acid–Schiff positive and diastase-resistant thrombi. There was a lobular panniculitis and multiple globi were noted. The acid fast stain showed numerous bacilli within these globi and within the endothelial cells. Leprosy with Lucio's phenomenon was confirmed. Antileprosy therapy was started with continuing the oral steroid. Her general condition and skin lesion improved gradually and she was able to be discharged. Leprosy-related APS has the different immunoglobulin isotype in antiphospholipid antibodies, which IgM is much more prevalent, such as in this patient. The concurrent Lucio's phenomenon and APS were rare and only three cases were reported. Antileprosy medications are the most important therapy and systemic steroid may also help to control the reaction. Skin pathology is essential to make the diagnosis.

Commercial support: None identified.

2958

Lues maligna: Report of three cases in HIV-infected patients

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Introduction and objectives: Lues maligna is a rare ulceronodular form of syphilis associated with significant morbidity and mostly observed in patients with HIV. The objective is to report the clinical manifestations of three cases of lues maligna, with emphasis on the importance of early diagnosis.

Material and methods: We report three HIV-infected heterosexual male: white patients, all former intravenous drug users, with ulceronodular skin lesions, nataise and palpable lymphadenopathies. The patients had a median age of 42 years, median CD4 cell count of 435/mm^3 and were all on antiretroviral therapy, although two were noncompliant. The skin lesions were present in the trunk and upper limbs and in one patients the head was also involved, and had a minimum of two weeks and a maximum of 8 weeks evolution. The patients had been observed before in the emergency department of our and others hospitals but were treated as furunculosis, without being tested for syphilis. Our differential diagnosis, beside syphilis, included skin bacterial infections, lymphoma, leishmaniasis and mycobacterial or fungal infections. All patients tested positive for two treponemal tests, one being TPHA, and their nontreponemal tests (VDRL) had titers higher than 1:256. The patients, and their sexual partners, were treated with 2.4 million units of intramuscular benzathine penicillin, with good response, although one patient had recurrence one month later, due to exposure to an untreated partner. The lesions healed leaving atrophic scars, being cribriform in one patient and leaving a patch of cicatricial alopecia in other. At one year follow up, recurrences were not observed, the VDRL titers were all lower than 1:4 but the patient that had the longest delay in the diagnosis still complained of itch and sporadic pain on his scars.

Conclusions: Lues maligna should be considered in the differential diagnosis of ulceronodular skin lesions in HIV-infected patients and early diagnosis is important to lessen morbidity and avoid unnecessary tests.

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3273
Lyme disease: Beyond erythema migrans

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With 300,000 new cases (CDC) in the USA each year, many challenges arise in each stage of this disease; with erythema migrans, the rash is present only 60-80% of the time, and often is a circular red patch/plaque rather than a "bulls-eye." The Ixodes tick that transmits the disease is tiny and may be overlooked if not recovered. If Lyme disease is suspected, the serology (using CDC guidelines utilizing ELISA and immunoblot staining) is confirmatory in only 29-40% cases. The recommended treatment is problematic in that 34% of patients have long-term sequelae 6 years after recommended treatment. In comparison, untreated syphilis leads to tertiary findings in 30-40% of patients, leading to the consideration that treatment with doxycycline is similar to no treatment at all. Animal studies have shown the persistence of spirochetes despite the recommended treatment. Further, 25% of the organisms discovered in the brains of Alzheimer disease patients were Borrelial spirochetes on PCR examination. The DNA of these organisms has also been found in the synovial fluid of Lyme disease arthritis. (Montauk knee was Lyme arthritis before *Borrelia burgdorferi* was discovered.) Persistence of these organisms in both brain and joints is highly likely related to biofilms which have been shown to be present in the arthritic joints. The treatment with doxycycline, a bacteriostatic antibiotic, is thus imperfect, as persistence of organisms is present in a significant number of patients. Vaccine development is limited by the organism producing "false signaling." Insurance payments are limited by both these diagnostic and treatment pitfalls.

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3757
Mycobacterias in aesthetic tattoos as a late complication

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Reports of secondary infections in tattoos due to mycobacteria are on the rise since 2003, not many cases have been reported since then. We present a patient with evidence of mycobacteria in tattoos she had acquired 9 years ago. A 63-year-old woman with eyebrow and lip tattoos presented to our dermatology clinic because of edema, pruritus, and an increase in size of eyebrows and lip contour 2 months earlier. She had first acquired the tattoos 10 years before clinical presentation and had had a touch-up of the tattoos 3 years before the visit to our clinic. Her general practitioner had prescribed topical hydrocortisone, betamethasone, and oral loratidine, acyclovir, with no improvement. A skin biopsy was performed and revealed a granulomatous infiltrate with a positive Ziehl–Neelsen stain. Chest radiography did not show any anomalies. Skin prick testing for PPD and Coccidioidin were performed and both resulted negative. Treatment with clarithromycin was started at 500 mg every 12 hours and after completing three months, new biopsies were taken without evidence of mycobacterias as well as negative skin cultures and an improvement of the lesions was observed. We suspected that the tattoo ink or any of the instruments used, were contaminated with mycobacterias which lead to the clinical presentation of this patient. This is a potential complication of tattooing without the appropriate hygiene standards. Another etiology may be contamination of premixed tattoo inks before their distribution. The actual incidence of mycobacterial infections may be due to underreporting, and this case may help raise awareness of this differential diagnosis when encountering a patient with these type of lesions.

Commercial support: None identified.

3769
Malignant syphilis and neurosyphilis in an immunocompetent patient

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Background: Syphilis is a sexually transmitted disease that, if left untreated, can progress chronically with periods of activity and latency. Neurological manifestations of neurosyphilis occur more commonly in the tertiary form. Malignant syphilis is a rare form of secondary syphilis manifested most commonly in patients with AIDS and can be the first manifestation of the viral infection. It is also associated with malnutrition, abuse of alcohol and illicit drugs, and rarely commits immunocompetent individuals. It is characterized by destructive ulcerated papules covered with hemorrhagic or thick crusts, rupia-like ulcerative lesions and frequent mucosal involvement; histopathologic study compatible with syphilis; high titles of VDRL; Jarish-Herxheimer reaction and rapid resolution of lesions after appropriate therapy.

Case report: A 50-year-old female, alcoholic and user of illicit drugs, presented with pruritic diffuse nodules of 4 months duration. Dermatological examination revealed erythematous scaly infiltrated papules in the face, sometimes isolated sometimes confluent, forming plaques. Trunk, back, upper and lower limbs presented popular, nodular erythematous scaly lesions, some in annular disposal. Lymphadenopathy in more than one chain was detected. Two biopsies were performed, compatible with secondary syphilis, and laboratory tests revealed VDRL reagent 1: 512, FTA-ABS IgG and IgM positive, anti-HIV 1 and 2 negative. The patient lost follow-up and returned two months later with significant worsening of the skin condition and appearance of thicker and psoriasis-like lesions in the face. Treatment was initiated with benzathine penicillin 2,400,000 IU. After 36 hours, she returned with exacerbation of the lesions, characterized by bleeding and ulcerations of some injuries, headache and myalgia, compatible with Jarisch-Herxheimer reaction, and a recent complaint of loss of visual acuity. Suggested the hypothesis of neurosyphilis, the patient was admitted in a secondary hospital for the examination of cerebrospinal fluid which confirmed the diagnosis. She was treated with ceftriaxone for 14 days due to unavailability of penicillin in the hospital, and evolved with clinical and laboratory improvement.

Discussion: Although malignant syphilis is characteristic of secondary syphilis, it may appear as a concomitant clinical manifestation or preceding neurosyphilis. Despite the high titers of VDRL, malnutrition and the use of illicit drugs, the patient was not HIV positive, one of the main risk factors for the development of both entities. In this case, we chose to treat her with ceftriaxone which, although not the drug of first choice, was the drug available in the hospital able to cross the blood–brain barrier. The case therefore is relevant to illustrate the concurrence between two rare clinical entities and the satisfactory response to treatment with ceftriaxone.

Commercial support: None identified.

3124
***Mycobacterium haemophilum* in a renal/pancreas transplant patient: A case report demonstrating multiple manifestations of the disease**

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Introduction: *Mycobacterium haemophilum* is a fastidious nontuberculosis mycobacterium (NTM) that must be considered in the differential diagnosis of infections in immunocompromised patients. *M haemophilum* infections are most commonly found in patients with AIDS or those who have undergone solid organ transplant and typically occur in the cutaneous or subcutaneous tissue. *M haemophilum* can also present as septic arthritis, osteomyelitis, pulmonary disease, lymphadenitis, and more. The incidence of all NTM infections in renal transplant patients is estimated to be between 0.16 and 0.38%, and *M haemophilum* is the most common cause of NTM cutaneous infections in this group.

Case report: A 51-year-old white man two years post cadaveric renal/pancreas transplant on oral immunosuppressive therapy presented with a 1 month history of arthralgia that initially involved the left ankle but progressed to involve bilateral elbows, wrists, knees, and ankles. During the same time frame, he developed painful skin lesions on his mandible (2.4 x 1.9cm violaceous nodule with small, central crust) and back (1.9 x 1.3 cm pink, shiny plaque with central ulceration). Biopsy of both skin lesions demonstrated granulomatous inflammation with numerous acid-fast bacilli. PCR testing identified the organism as *M haemophilum*. The patient began treatment with azithromycin and ciprofloxacin as well as isoniazid for latent tuberculosis. While initial skin lesions resolved, new lesions occurred as nodules on the extremities despite treatment. Joint pain persisted and tenosynovitis of the right wrist occurred. Although he continued treatment for over one year, the patient developed patellar osteomyelitis due to *M haemophilum*. He underwent two rounds of irrigation and debridement, and has now been asymptomatic for six months.

Comment: This case illustrates multiple manifestations of *M haemophilum* and emphasizes that even with treatment, the disease may have a protracted course. There is no standard therapeutic regimen against the organism, yet current guidelines suggest dual or triple therapy for 1 to 2 years. While the patient's lesions initially presented on the trunk and face, cutaneous manifestations most commonly occur on the extremities do to the organism's affinity for cooler temperatures. Physicians must have a low threshold for suspecting this organism in immunocompromised patients presenting with any skin or joint complaint.

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2745
***Mycobacterium haemophilum* infection in a renal transplant patient**

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A 61-year-old woman with a history of Crohn's disease and renal transplantation on immunosuppressive medication presented with skin lesions and intermittent fevers. She reported tender pink nodules on her left breast and right wrist for 5 months and a similar eruption on her arms, legs, and abdomen for 1 week. She was treated with intravenous vancomycin and oral amoxicillin for presumed cellulitis, which did not completely resolve her lesions. Physical examination revealed generalized extremity edema. There were several firm, edematous, and erythematous nodules on her left upper extremity with a peau d'orange appearance. On her left breast and upper and lower extremities were scattered well-circumscribed, indurated erythematous plaques. A biopsy was taken, showing mixed inflammation with panniculitis thought to be secondary to Crohn's disease. AFB and other microbial stains were negative. Due to ongoing lesions, a second biopsy at a different site was performed and revealed a dense perivascular lymphocytic and interstitial granulomatous infiltrate with scattered nuclear dusts and focal microabscesses. AFB and Fite stains showed many mycobacteria within and outside granulomas. PCR and culture indicated *M haemophilum* was present in the lesion. Given the diagnosis of disseminated cutaneous *M haemophilum*, the patient was started on ciprofloxacin, azithromycin, and rifabutin. Within several weeks of treatment, her nodules became less swollen and tender. To date, she reports no new lesions. *M haemophilum* has been reported to cause disseminated skin infections in severely immunocompromised individuals. The growth of *M haemophilum* requires incubation at 30 degrees Celsius and addition of iron to the culture medium. Due to its rarity and unique growth characteristics, infection with *M haemophilum* is often difficult to diagnose. Our case highlights the importance of considering *M haemophilum* infection in the differential diagnosis in immunosuppressed patients who present with chronic tender nodules and plaques, even if the initial biopsy is not indicative of infection. Not only may early treatment of these patients' skin lesions help to reduce their symptoms, but it can also prevent contiguous or hematogenous spread to other areas.

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3123
Persistent cutaneous nocardiosis in a patient with catastrophic antiphospholipid antibody syndrome

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A 43-year-old female, chronically immunosuppressed for treatment of catastrophic antiphospholipid antibody syndrome was admitted to the hospital for left upper extremity skin lesions suspicious for cellulitis. History was significant for a cat scratch approximately four months earlier with subsequent development of the initial lesion on her left forearm a week later. These lesions improved during two unrelated hospitalizations, at which time she was treated with clindamycin, meropenem, and vancomycin. However, she later noted reappearance and spread of these lesions from her left forearm to her upper arm with associated drainage. She was treated with two weeks of doxycycline for suspected cat scratch disease without improvement and was subsequently admitted. She had been on chronic trimethoprim sulfamethoxazole (TMP-SMX), fluconazole, and acyclovir for prophylaxis against opportunistic infections. She denied any similar lesions elsewhere on the body and reported no fevers or chills. She denied any specific hobbies, travel outside of United States, or contact with other animals. On physical examination, several 5 to 10 mm ulcers, eschars, and erythematous papules and plaques were noted on left proximal forearm and distal arm. The lesions were distributed in a sporotrichoid pattern. An approximately 8 cm x 4 cm erythematous indurated patch surrounded the lesions on her arm. Left axillary lymphadenopathy was noted. Laboratory studies revealed white blood cell count of 1.4 with associated neutropenia and lymphopenia. Two punch biopsies of a pustule were performed for histopathologic evaluation as well as bacterial, fungal, and mycobacterial cultures. Histopathologic evaluation with the aid of different stains revealed a dermal abscess with filamentous bacteria. The overall findings were most consistent with Nocardia-like organisms. Warthin-Starry silver stain did not demonstrate findings consistent with Bartonella. Bartonella PCR of blood was negative. Tissue and wound bacterial cultures showed gram positive rods possibly Nocardia species. DNA sequencing was unable to further speciate the organism. Fungus and AFB cultures were negative. She was subsequently treated with high dose TMP-SMX for cutaneous nocardiosis with improvement of these lesions.

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3405
Penicillin: The new/old wonder drug: New treatments include psoriasis and tertiary treponematosis

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The "old" wonder drug has been effective in a wide spectrum of diseases caused by Beta hemolytic *Streptococcus pyogenes*, *Diplococcus pneumoniae*, *Neisseria gonorrhea* and *meningitides*, *Treponema pallidum*, and many others. The "new" wonder drug has been shown to treat psoriasis effectively and be curative in many cases. Streptococcus is the organism responsible for beginning the process and has previously escaped detection by moving intracellularly or by forming biofilms. The treatment is low dose for many months and thus is similar to rheumatic fever. Arthritis has been shown to be caused by biofilm-forming dental and Lyme treponemes, and these organisms, like the streptococcus in psoriasis, have escaped detection. Penicillin plus a biofilm-dispersing agent is effective in treating arthritis in which tissue destruction has not already occurred. Seven of ten patients with arthritis took the above protocol and responded with clearing of their arthritis. The three who nonresponders needed joint replacement within three months. Alzheimer disease has been shown to be caused by those same treponemes (dental and Lyme) involved in arthritis, and, is in every way, similar to the dementia of neurosyphilis caused by *Treponema pallidum*. These organisms make biofilms that induce B amyloid and a Toll-like receptor 2 response leading to tissue destruction. Penicillin given prior to the organisms arrival in the brain (or before they create biofilms) would likely prevent dementia in Alzheimer as it does in syphilis. Treatment with PCN in psoriasis, arthritis, and syphilis, has thus far not led to resistance and may actually prevent resistance by killing organisms before they make biofilms and share resistance genes.

Commercial support: None identified.

2932
Rapidly progressive soft tissue infection caused by *Aeromonas sobria* in an immunosuppressed patient

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Introduction: We report a rare case of *Aeromonas sobria* (*A sobria*) occlusive vasculopathy with sepsis in an immunosuppressed patient. When patients present with a rapid onset of skin necrosis and progressive sepsis, an *A sobria* or *A ichrio* infections should be considered in the differential diagnosis.

Case: A 41-year-old woman with a medical history of renal transplant was referred to our department for severe pain on right leg. On the initial physical examination, her right leg was swollen and painful, with no changes in temperature or color, and there was no clinical evidence of inflammatory response. After few hours a change in color was observed on the distal portion of the leg with purpuric irregular patches and two bullae on the center of the lesion. We proceeded to perform a skin biopsy and tissue was sent for microbiologic analysis. The patient was admitted with systemic inflammatory response syndrome. Piperacillin/tazobactam and vancomycin were started and multiple surgical debridements were needed in order to achieve control of the infection. The biopsy revealed an occlusive vasculopathy and multiple gram-negative bacilli. The isolated agent from the skin culture was *A sobria*. The patient was discharged after 3 weeks with a negative pressure wound therapy device.

Discussion and conclusions: *A sobria* is a facultative anaerobic Gram-negative rod that is ubiquitous in aquatic environments and is considered an opportunistic pathogen for humans. Aeromonas spp. release factors which contribute to its virulence, such as hemolysins, enterotoxins and proteinases. It initially presents as severe pain with no apparent skin changes followed by progressive purpuric patches, bullae, ulcers and necrosis. Impairment of the host immune system increases the incidence of septic shock. The mortality rates range from 25% to 50% and without rapid treatment mortality rate is above 90%. An aggressive antibiotic therapy and surgical debridement must be performed to achieve a positive outcome. In conclusion, this clinical entity is uncommon, but its incidence is increasing due to immunosuppressive therapies and conditions such as AIDS, diabetes mellitus and solid organ transplantation. Dermatologists should have a high index of suspicion for an Aeromonas spp. infection while dealing with an immunosuppressed patient with a rapidly progressive soft tissue infection.

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3322

Reactive erythema resulting from *Capnocytophaga canimorsus* bacteremia

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Herein we describe a case of reactive erythema occurring in the setting of *Capnocytophaga canimorsus* bacteremia. While the pathogen is known to cause a myriad of cutaneous manifestations, reactive erythema is not typical. A 59-year-old male with history of right total knee arthroplasty and alcoholism was admitted for right knee pain and swelling, fever, night sweats, leukocytosis, and a diffuse skin rash. He was bitten by his dog on his right hand 8 days prior to the onset of symptoms. His skin exam was significant for an edematous, erythematous right knee. There were numerous small, crusted erosions without surrounding erythema or induration on the right dorsal hand, as well as several large pink to erythematous annular edematous plaques distributed symmetrically on the abdomen, lower extremities, and back. The patient subsequently underwent surgical irrigation and debridement of the right knee. A 4 mm punch biopsy of an annular lesion on the left thigh demonstrated nonspecific superficial and mid neutrophilic and eosinophilic dermatitis without vasculitis. The direct immunofluorescence performed on lesional skin was negative. While cultures taken from the right knee were negative, the patient's initial blood cultures grew *Capnocytophaga canimorsus* after an eight-day incubation period. His rash completely resolved after 48 hours of intravenous antibiotics. *Capnocytophaga canimorsus* is a slow growing Gram-negative rod found as part of the normal gingival flora of canine and feline species. There have been reports of severe systemic illness associated with this bacterium, including meningitis, septicemia, endocarditis, and septic arthritis. Approximately 50% of affected individuals also experience cutaneous manifestations, such as petechiae, purpura, cellulitis, or gangrene but there has not been a documented case of associated reactive erythema. This case aims to highlight *Capnocytophagi canimorsus* as an important human pathogen and a potential cause of reactive erythema.

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3028

Rosacea blepharitis treated with a novel preparation of dilute povidone iodine and dimethylsulfoxide

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Background: Povidone iodine (PVP-I) 10% aqueous solution is a commonly utilized antiseptic employed for sterilization of the ocular surface prior to interventional procedures. We have been utilizing a low dose formulation of 1% PVP-I (w/w) in a gel containing dimethylsulfoxide (DMSO) for a variety of skin indications. Described here is the first case report of its use in the setting of recalcitrant rosacea blepharitis.

Findings: A 78-year-old male presented with chronic, long-standing blepharitis involving both the anterior and posterior lid margins. Posterior lid and skin inflammatory changes were consistent with ocular rosacea. Previous oral and topical therapies had been ineffective at controlling his condition.

Conclusion: The topical PVP-I/DMSO system was effective in eliminating the signs and symptoms of rosacea blepharitis. Further investigation of this novel agent is warranted.

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3567

Syphilis presenting with paraphimosis: Painless no longer

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Paraphimosis is a painful urologic emergency that occurs when the prepuce becomes trapped behind the glans penis. If the foreskin is left retracted long enough, venous and lymphatic flow to and from the glans penis and the prepuce itself can ensue; untreated, this can result in ischemia, edema, and eventual penile gangrene and autoamputation within days to weeks. A 24-yo M with PMH of depression presented to dermatology with two weeks of a progressively worsening red rash of the penis, edema of the prepuce and glans penis, penile pain, and dysuria. On physical examination, the prepuce, distal shaft and glans penis were significantly edematous, tender, and erythematous, with some crusting. A superficial round ulcer was noted on the distal penile shaft, suspicious of a chancre. Bilateral inguinal lymphadenopathy was noted. The patient was treated with intramuscular kenalog and betamethasone in an attempt to reduce swelling, and started empirically on 100 mg doxycycline twice daily. Upon evaluation by urology, the patient was diagnosed with paraphimosis. A manual reduction was performed, bringing the patient considerable pain relief. Rapid plasma reagin (RPR) (titer 1:256) and reactive serum fluorescent treponemal antibody absorption (FTA-ABS) testing confirmed syphilis. The rest of the patient's sexually transmitted disease workup was negative, including HIV 1/2, gonococcus, and chlamydia. Upon further questioning, the patient admitted to having received oral sex two months prior to onset of symptoms. He received definitive treatment of syphilis with 2.4 million units intramuscular benzathine penicillin G. On follow-up, the paraphimosis and penile edema had resolved. Paraphimosis is an uncommon complication of primary syphilis. One published case report from 1969 was found of primary syphilis presenting with paraphimosis, which was complicated by eventual perforation of the anterior wall of the prepuce. Clinicians should keep syphilis on the differential diagnosis of penile pain and edema, despite the notion that primary syphilis presents with a painless chancre.

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3292

The ABCs of perineal streptococcal dermatitis: Case series and review of the literature

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Perineal streptococcal dermatitis (PSD) is a localized bacterial infection involving the perianal, perivulvar, or penile skin. It is classically a superficial, sharply demarcated patch of erythema that can be associated with pruritus, pain, constipation, incontinence, and blood-streaked or mucoid discharge. PSD is traditionally thought to be exclusively caused by group A β-hemolytic Streptococcus (GAS). We report three cases of PSD: one caused by GAS in a 4-year-old male who presented with guttate psoriasis, one caused by group B β-hemolytic Streptococcus (GBS) in a 4-year-old male who also presented with guttate psoriasis, and one associated with group C β-hemolytic Streptococcus (GCS) in a 3-year-old female who presented with vulvar erythema and yellowish discharge. The first two cases cleared with oral cefuroxime 200 mg BID for seven days, although the third had persistent vulvar erythema. GBS and GCS are very rarely reported in pediatric cases of PSD. These cases add to the limited described cases of GBS and GCS PSD, as well as instances of PSD caused by group G β-hemolytic Streptococcus (GGS) and *Staphylococcus aureus* revealed in the literature. Notably, the case of GBS PSD presented with guttate psoriasis. GBS is generally not associated with superantigenic exotoxins and has never previously been reported to trigger guttate psoriasis. This may be explained by horizontal gene transfer of virulence factors between GBS strains. Any patient with acute guttate psoriasis should be investigated for streptococcal infection of the pharynx and perineum. GBS, GCS, GGS, and *S aureus* are significant causes of PSD to consider, particularly among adult patients, based on our cases and the literature. Although some authors recommend rapid streptococcal antigen tests to accelerate the diagnosis of PSD, we caution against this practice as it would fail to detect cases of non-GAS PSD, and could result in misdiagnosis and ineffective treatment. Lesional swab for bacterial culture is still the best diagnostic test. Therapy should be tailored to the microbiologic cause. In particular, GBS has an average minimum inhibitory concentration two to nine times higher than that of GAS. Therefore, a longer duration of therapy may be appropriate.

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2813

The efficacy of pentamidine in comparison to pentavalent antimonial in American tegumentary leishmaniasis: An open label, randomized, controlled trial

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Introduction: N-Methyl-glucamine antimoniate SbV (N-MA) is considered the standard treatment of American tegumentary leishmaniasis (ATL) in most endemic countries; nevertheless, its use is limited by the necessity of parenteral administration and by the already reported side effect profile. These factors justify the urgent need of alternative drugs with the aim of reducing costs, improving safety of the treatment and reducing cases of resistance. Pentamidine is an antimicrobial medication considered as a second-line treatment for ATL. The purpose of the present study consists in comparing the efficacy of a pentamidine cycle versus the standard treatment performed by the use of N-MA in patients suffering from the cutaneous form of ATL.

Methodology: This open-label, randomized, controlled trial compared two parallel groups that consisted in the intramuscular use of 3 pentamidine doses, 4 mg/kg/per day (intervention group), each 3 days versus the standard treatment that consisted in the use of intravenous N-Methyl-glucamine 20 mg SbV/kg/per day during 20 days (control group) in patients suffering from ATL. Seventy CL patients without any previous treatment were included. Allocation was made following a random assignment in fixed block sizes of 4 patients. Thirty four patients were included in the intervention group and 36 patients were included in the control group. The diagnosis was constituted by clinical history, epidemiological and physical examination compatible with ATL, and it has been confirmed by positive results of the following diagnostic methods: Montenegro skin test (MST), histopathology and smear (with presence of amastigotes forms) and culture, indirect immunofluorescence test (IFI) and PCR (polymerase chain reaction). The main endpoint was defined as the clinical cure (complete ulcer healing without any sign of inflammation) 180 days after the end of each treatment. Clinical assessments for secondary endpoints were carried out 1, 2, 3, 6, and 12 months after treatment. We perform analytical statistics for categorical and continuous variables. Relative risks were estimated by an univariate analysis, considering a last-observation-carried forward method as an intention-to-treat strategy, using OpenEpi Version 3.01. Statistical significance was defined as $P < .05$, and confidence intervals (CIs) were set at 95%. This study was approved by the ethics committee of all departments involved and all patients have signed the informed consent form.

Results: The statistical analysis has demonstrated homogeneity between groups regarding gender, age, number of lesions, location of all lesions and evolution time. MST was positive in 31 (91.2%) patients in the intervention group, and in 33 (91.7%) in the control group. IFI, smear, culture, histopathology and PCR, were positive in 7/10 (70.0%), 5/15 (33.3%), 7/15 (46.6%), 8/19 (42.1%) and 15/15 (100%) patients of the intervention group; and 15/15 (100%), 3/11 (27.2%), 3/12 (25%), 7/20 (35%) and 14/14 (100%) in the control group, respectively. In the PCR exams, Leishmania (Viannia) braziliensis was identified in 15/15 (100%) patients of the intervention group and in 14/14 (100%) patients of the control group. The relative risk (RR) for cure was 0.8319 (95% confidence interval 0.6142-1.127) considering that 22/34 (64.7%) patients in the intervention group and 28/36 (77.7%) patients in the control group presented clinical cure, without significant differences ($P = .12$). The variables, time of disease, number and size of lesions didn't show any difference were not different between groups. Side effects were observed in 14/34 (41.1%) patients in group I and in 14/36 (38.8%) in group II ($P = .42$). The most common side effects observed in the intervention group were pain in the injection site, paresthesias in both legs and increase of CPK. In the control group, arthralgia, pain the local application, myalgia, increase of amylase, headache and ECG alterations.

Discussion: Patients treated in the control group achieved cure in 77.7% (28/36) of cases and patients treated in the pentamidine group achieved cure in 64.7% (22/34) of patients. Nine (26.4%) patients were considered cured previously to the main endpoint in the intervention group and 7 (19.4%) patients in the control group were cured before 180 days after treatment. Side effects in patients treated with N-MA were clinically more serious and side effects profile of pentamidine although, despite the absence of statistical difference between groups, seems to be more easily handled by assistant physicians.

Conclusions: We can conclude that the scheme with pentamidine is comparable to the use of N-MA in ATL. The tested intervention also showed less serious side-effects in comparison to the standard treatment. New phase III and IV studies are necessary to evaluate the real role of pentamidine in the treatment of ATL.

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3188

Topical imiquimod for cutaneous leishmania in the face of a child: Is it a useful treatment?

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Introduction: Localized cutaneous leishmaniasis is a common infection in the Mediterranean countries that can affect children. The exact incidence rate is unknown and today there are not established clinical guidelines of treatment. Recently, there have been reported some cases of cutaneous leishmania with good results using topical treatment with imiquimod.

Materials and methods: We report the case of a 4-year-old boy with localized cutaneous leishmaniasis on the right cheek that was confirmed by histological examination of a skin smear. He was treated with topical imiquimod.

Results: We used three treatment cycles, in the first one three times a week and in the rest five times a week. The improvement was gradual until it was completely healed.

Conclusions: The lesions of localized cutaneous leishmania usually are on exposed areas, especially on the face. There are no established clinical guidelines of treatment, but the most used is the infiltration of pentavalent antimonials because of their effectiveness and low rate of side effects. There are other possible treatments: systemic antimonials, liposomal amphotericin B, cryotherapy, photodynamic therapy, oral imidazoles, topical paromomycin, zinc sulfate, amiodarone, azithromycin, pentoxifylline, allopurinol, dapsone and miltefosine. The immunomodulatory effect of imiquimod stimulates the remission of the cutaneous lesions of leishmania. It has been demonstrated in animal models and in the cases reported in humans, in which the cosmetic results are excellent. The aesthetic result is important because the facial lesions are frequent. The effects of imiquimod are considered to be short-lived and it may explain why it was necessary to extend the treatment for three cycles. We must consider the possibility of spontaneous healing without any treatment therefore we cannot establish if the healing was completely due to imiquimod. In our opinion, comparative studies versus placebo with more number of patients are required.

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3684

Treatment of interdigital foot erythrasma with ozonated olive oil

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Erythrasma is caused by *Corinebaterium minutissimum* producing a porphyrin that with Wood's light emits a coral red fluorescence. It is the most common bacterial infection of the feet. It affects intertriginous areas of the skin, proliferates under conditions such as humidity and heat, invades the upper third of the stratum corneum and dissolve keratin fibrils. The incidence is around 4% and is more frequently in tropical and subtropical areas. Interdigital erythrasma is more common in women. Treatment is with oral erythromycin and there is no consensus regarding the topical therapy of choice. Ozonated olive oil decreases the cytoplasm and damages bacterial proteins and lipids. The effects of ozone are mediated through free radical reactions, although O_3 is not a radical species per se. The ozonation of vegetable oils leads to the formation of trioxolanc that generates compounds, like polyunsaturated fatty acids, responsible for wound healing when applied on skin. It normalizes levels of organic peroxides and activates superoxide dismutase which plays an important role in the antimicrobial properties. It has antiinflammatory effects, inducing COX-2 inhibitors and promoting metalloproteinases. The objective of the study was to evaluate the therapeutic efficacy of ozonated olive oil in a pilot trial for erythrasma. We performed an experimental, open, observational, descriptive, longitudinal clinical trial in the Section of Mycology, Division of Dermatology, General Hospital "Dr Manuel Gea González." We included 10 individuals with interdigital feet erythrasma who were given ozonated olive oil every 12 hours for 10 days. Direct exam with KOH was performed to exclude tinea pedis. At the end of the study the coral red fluorescence, erythema, fissures, pruritus, and maceration had disappeared from all patients; two patients persisted with scaling. There are few studies that describe the efficacy of topical and oral agents in the treatment of erythrasma. Oral erythromycin has cure rates (clinical and bacteriological) of about 100%. We found that the ozonated olive oil efficacy is similar to that of oral erythromycin. According to our results ozonated olive oil is a good topical treatment option for interdigital erythrasma without additional oral medications. However larger studies are required.

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2942

What's lurking in the sand? A case of bullous cutaneous larva migrans acquired on the Connecticut shoreline

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Background: Cutaneous larva migrans (CLM) is an infestation typically caused by hookworms, most commonly *Ancylostoma caninum* or *Ancylostoma braziliense*. CLM is most commonly seen in tropical and subtropical areas and is uncommonly acquired in temperate climates. Clinical manifestations are typically characterized by erythematous, linear or serpiginous tracts that are intensely pruritic. Rarely, they can manifest as vesiculobullous eruptions in the skin.

Case description: We present a case of bullous CLM acquired on the Connecticut shoreline. The patient is a healthy 22-year-old woman with no significant medical history. She presented to our clinic with multiple (>70) pruritic, tense, fluid-filled vesicles and bullae with erythematous, serpiginous, elevated tracts radiating outward, located on her forearms, thighs and lower legs bilaterally. She was digging for clams 5 days earlier on the Connecticut shoreline with her boyfriend. The boyfriend developed a mild cutaneous eruption consistent with CLM, but without vesicles or bullae. The patient and her boyfriend have not traveled outside of Connecticut over the past 3 months. One week after a course of ivermectin, the patient's lesions showed signs of healing. She was given an additional dose of ivermectin and will follow-up in clinic later this month for further assessment of treatment response.

Discussion: There have been few reports of bullous CLM. However, reported cases had a lesser amount of cutaneous involvement than our patient and reported cases were acquired in tropical or subtropical settings. The pathogenesis of blister formation is unclear. It has been proposed that vesicles and bullae may be a result of lytic enzymes released by larvae or may be a result of a delayed hypersensitivity reaction. Physicians should be aware of this rare form of CLM that can be acquired on the Northeast shoreline.

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3858

WITHDRAWN

INFECTION—FUNGAL

3638

Acute invasive fungal sinusitis with Zygomycetes

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A 54-year-old African American female with history of acute myelogenous leukemia (AML), status post 5th cycle of chemotherapy combination of cladribine, idarubicin, and cytarabine on protocol was admitted with *Clostridium difficile* pancolitis. Her hospitalization was complicated by a transfer to the intensive care unit (ICU) for refractory *C. difficile* colitis, pneumonia, septic shock, respiratory failure, acute kidney injury due to acute tubular necrosis, and altered mental status. After transfer out of the ICU it was noted that the patient had developed orbital edema and indurated purple patches on the left side of her nose, left cheek, and the left upper palate and gingival margin of uncertain duration. A CT of the head revealed findings concerning for invasive fungal infection. She was started on amphotericin and caspofungin and taken to the operating room where she underwent aggressive debridement with total maxillectomy, septectomy, subtotal palatectomy, and subtotal rhinotomy. Her fungal infection was confirmed as mucormycosis with fungal culture growing Zygomycetes isolates. This patient continued to deteriorate despite debridement and antifungal therapy and died six days later. Fungal infections with Zygomycetes, even in high-risk patients, are rare ranging from 8.3-13% of all fungal infections. Advancements in treatment for cancer have led to an increase in both the number of immunocompromised patients and incidence of invasive fungal infection. At MD Anderson Cancer Center in Houston, the incidence of hematological cancer patients with mucormycosis increased from 0.7 % in 1989-1998 to 1.9% in 1994-1998. Mortality rates for mucormycosis range from 20-80%. This case illustrates how acute invasive fungal sinusitis is a dangerous condition that can rapidly progress and cause death despite treatment. This patient's clinical presentation, diagnosis, and resulting death are reminders for clinicians to maintain vigilance for invasive fungal infection, as early detection may decrease mortality.

Commercial support: None identified.

3135

Cutaneous alternariasis with suspected dissemination in a patient with sarcoidosis on immunosuppression

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A 60-year-old male with a history of pulmonary sarcoidosis on chronic immunosuppression including prednisone, infliximab, and mycophenolate mofetil, presented to the hospital for further work-up of a six month history of fevers, myalgias, skin lesions, weight loss, and general functional decline. The patient had undergone an unrevealing, extensive outpatient work-up including bronchoscopy, transesophageal echocardiogram, and skin biopsy from his left lower extremity. Per family reports, the skin biopsy showed venous stasis changes. Dermatology was consulted during his hospital stay to further elucidate the etiology of his skin lesions. On exam, tender, reticulated, violaceous patches and plaques with central eschar formation were noted on circumferentially on his left leg. Purpuric patches with central eschar were noted on his bilateral arms and forearms, and small hemorrhagic vesicles on an erythematous base were noted on his right palm and flexor wrist. Skin biopsy was performed on his left leg and demonstrated suppurative ulceration with dermal and fat necrosis, with an associated giant cell reaction. GMS and PAS stains demonstrated fungal hyphae within the dermis and subcutaneous tissue. Fungal tissue culture was also completed and showed few Alternaria spp. The patient was started on amphotericin B when initial biopsy results became available. Of note, the patient was found to have infectious discitis/osteomyelitis of his thoracic spine and new pulmonary infiltrates on imaging during his stay. Unfortunately, three days later, the patient became unresponsive, required emergent intubation, and later expired. Alternaria spp. are dematiaceous hyphomycetes that rarely cause disease in immunocompetent individuals despite being ubiquitous in nature. In immunocompromised hosts, they most commonly cause skin and soft tissue infections, however dissemination has been reported. In our patient, we suspect that his thoracic discitis/osteomyelitis and pulmonary infiltrates, as well as overall clinical decline were representative of a disseminated Alternaria spp. infection. It is important to recognize that Alternaria spp. may be a potential culprit for chronic skin lesions in the immunocompromised host and should be considered as potential a source for disseminated infection and clinical decline.

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Cutaneous *Chaetomium globosum* infection in a vedolizumab-treated patient

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In the expanding landscape of targeted biologic therapies for chronic inflammatory disease, dermatologists increasingly encounter novel cutaneous side effects, including skin and soft tissue infections with unusual pathogens. Chaetomium spp., a dematiaceous mold associated with cellulose containing materials, has been found in indoor environments such as moldy rugs, mattresses and environmental air in a transplant ward. Recently, it has been identified in cases of onychomycosis in immunocompetent patients and as an opportunistic pathogen in immunocompromised patients with hematologic malignancies, organ transplant and catheters. We report a case of *Chaetomium globosum* skin infection in a patient with inflammatory bowel disease on vedolizumab, a gut-specific integrin inhibitor. The skin manifestations and course of treatment for Chaetomium spp. infections in immunocompromised patients are reviewed. Dermatologists must retain a high index of suspicion for unusual infections in patients treated with new biologics.

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3794

Dematiaceous fungi: A rare case of longitudinal melanonychia

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The patient is a 41-year-old white man with a 2-year history of longitudinal melanonychia associated with linear onychodystrophy of the left great toenail following minor nail trauma. Examination of the nail revealed a faint grey-to-brown thin longitudinal groove, originating at the proximal nail fold and extending to the distal edge where there was jet-black pigmentation and accumulation of dark subungual debris. The cuticle was uninvolved. The patient had failed an 18-month trial of topical ciclopirox. Nail clipping was performed and histopathology revealed PAS positive clusters of numerous pigmented fungal organisms composed of hyphae and chains of yeast, consistent with dematiaceous fungi. Speciation is being performed by the CDC. Fungal melanonychia can result from both dematiaceous and nondematiaceous fungi. The term "dematiaceous" is used to classify a group of nondermatophyte fungi that appear pigmented when cultured due to production of melanin, which is excreted extracellularly or incorporated into the fungal cell wall. Dematiaceous fungi are common environmental pathogens found in soil, plants, and decaying debris. At least 21 species have been implicated in fungal melanonychia. Although disseminated and deep disease can occur in immunocompromised patients, dematiaceous nail infection typically occurs in healthy patients and remains localized. Notably, many species of fungi can produce melanin and cause clinical hyperpigmentation (ie. the well-known dermatophyte *Trichophyton rubrum*) but do not appear pigmented in vitro, distinguishing them from true dematiaceous fungi. Identification of dematiaceous fungi is critical as they are resistant to most antifungals. This is likely due to melanin's protective role (ie, protection from environmental stresses, UV radiation, free radicals, and extreme temperatures). Diagnosis is made by routine histology and speciation requires fungal cultures. As cases like ours are exceedingly rare, treatment options, which range from itraconazole to nail avulsion, are limited to isolated case reports and small case series. Our case is unique in that longitudinal melanonychia is typically seen in dermatophyte strains. Dematiaceous infection is an important diagnosis to consider in the differential for any brown-to-black discoloration of the nail, especially in patients unresponsive to common antifungal agents.

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3611

Cutaneous cryptococcosis mimicking spinocellular carcinoma

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Cryptococcosis is an infection caused by the yeast-like fungus Cryptococcus spp., which is isolated from pigeon droppings, soil and vegetables. Cutaneous cryptococcosis is classified as primary when there is direct inoculation, a rare condition, and as secondary when it occurs by hematogenic dissemination. The infection is generally acquired by inhalation and it can disseminate in the occurrence of immune suppression. The skin involvement may produce a wide variety of lesions and can be similar to other dermatoses. This case reports a 56-year-old man, HIV infected, who had a erythematosus, keratotic and infiltrated plaque in the left dorsal hand for a year, which mimicked a spinocellular carcinoma, a condition that hasn't been reported until this date. The patient used to have constant contact with grains during his daily work, but denied a local trauma. The anatomopathologic examination presented yeast elements suggesting Cryptococcus spp., which were confirmed in the direct and cultural mycological examination. The species *Cryptococcus neoformans* was identified by flow spectrometry (MALDI-TOF) and latex particle agglutination test was negative. The patient did not present any alterations in the chest radiography (other systemic investigation exams are still in progress), which led us to start a treatment with fluconazole. The Cryptococcus species is related to the immunity state of the host. The infection caused by *C neoformans* is generally associated with immunosuppressed patients and tends to produce cutaneous lesions without systemic involvement, such as the patient described above, who presents evidences of localized lesion. The clinical spectrum of lesions has a wide variety, and it can resemble other illnesses such as molluscum contagiosum, Kaposi sarcoma, basal cell carcinoma and pyoderma gangrenosum. Spinocellular carcinoma has not yet been described as a pathology mimicked by Cryptococcus. However, this case shows the importance of valuing this distinguished diagnosis. In general, the identification of skin lesion indicates the presence of disseminated disease and an intensive and persistent search for systemic involvement must be conducted. Tests are important, not only to reach some specific diagnosis, but also to allow the early detection and the treatment of a potentially fatal disease.

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3742

Diagnosing cutaneous *Mycobacterium haemophilum* by PCR

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Mycobacterium haemophilum is a slowly growing, nontuberculous acid-fast bacillus (AFB) that causes ulcerating skin infections in the immunocompromised patient. A 52-year-old man from Ghana presented to the NIH for evaluation of multidrug resistant HIV (CD4 10 cells/mm^3, viral load 600,000 copies/mL). He had a 5-month history of multiple scattered, pruritic eroded papules. He denied any primary skin lesions, and reported frequent picking at the affected sites. On the right thigh were two 1.0 cm keratotic papules with dark brown hyperpigmented edges and pink centers with yellow crusting. On the left forearm was a 2.5 cm keratotic plaque with hyperpigmented edges and a pink scar-like center. Histologic analysis of a biopsy from the thigh revealed a predominantly neutrophilic infiltration with inflamed granulation tissue and abscess in the superficial dermis. Dermal scar was also evident. AFB-Fite stain was positive for abundant AFB within the superficial dermis. Microbiologic analysis of the biopsy smear demonstrated multiple AFB using auramine-rhodamine stain. DNA from the biopsy was processed for SecA1 Real-Time PCR, an assay that can differentiate 29 mycobacterial species by sequence variants in the secA1 gene. The SecA1 ATPase is important in bacterial protein secretion. The PCR assay amplifies a 700-bp fragment of secA1 coding for a 233 amino acid residue in the N-terminal region of the protein. A hypervariable region between nucleotides 7 and 70 of the PCR amplicon codes for amino acid sequences unique to each nontuberculous Mycobacterium species. Direct sequencing of the PCR product from our patient was positive for *M haemophilum* DNA. Cultures from the biopsy were grown on sheep blood agar at 30°C for confirmation. The patient was treated with antiretroviral therapy using emtricitabine/tenofovir, dolutegravir, darunavir, and ritonavir based on his HIV resistance profile. Ciprofloxacin, rifabutin, and azithromycin were initiated for his cutaneous mycobacterial infection.

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3193

Epidemiology, clinical manifestations, and laboratory investigations of fungal nail and foot infections in patients with hallux valgus

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Background: Hallux valgus (HV) is one of foot conditions that cause nail and feet fungal infections. However, the studies on fungal infection in patients with HV were limited.

Objective: This study aimed to identify prevalence, clinical characteristics and laboratory investigations regarding nails and feet fungal infection in patients with HV.

Materials and methods: This study was a cross-sectional study. Patients with HV from foot clinic, department of rehabilitation medicine between January to August 2015 were included. Potassium hydroxide examination and fungal culture were used to distinguish abnormal nails and feet from uninfected ones. If nails and feet were normal, the laboratory was done on right big toe and right sole. Demographic data, clinical presentations including pedographs were recorded. Subclinical presentation was defined as normal clinical appearance but positive for dermatophytes (DMPs).

Results: A total of 81 patients, 77 females (95.1%), with mean age of 65 year-old were enrolled. Out of all patients, 27 (33.3%) were diagnosed with fungal infection; 7 (25.9%) had solely nail infection; 6 (22.2%) had only feet infection and 14 (51.9%) had both nails and feet infection. Among those with only nail infection, 85.7% had clinical presentations of onychomycosis (OM), 14.3% had subclinical OM. Similarly, 66.7% of those with feet infection had obvious lesions (94.4%); 33.3% had subclinical fungal feet infection. From all patients with nails and feet infections, 14.3% had subclinical OM and 7.1% had clinical manifestation of OM with subclinical feet infection. Multivariate analysis revealed HV angle more than 30 degrees was significantly associated with fungal infection (adj. OR = 3.33, $P = .042$). Of all infected nails from 81 patients, 68% were infected with DMPs (*Trichophyton mentagrophytes* 40 % and *Trichophyton rubrum* 24 %). One third of patients were infected with nondermatophytes (NDMs) which 16% were *Neoscytalidium dimidiatum*. Likewise, of all infected feet, 88% were infected with DMPs (*T mentagrophytes* 72% and *T rubrum* 8%), 12% were caused from NDMs (*N dimidiatum* 8%).

Conclusion: This study revealed one third of patients with HV having fungal skin and nail infection. The valuable clinical presentation significantly associated with fungal infection was severity of HV. Subclinical presentation was common. Fungal laboratory investigation should be more concerned for holistic approach in patients with HV.

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3264

Fixed sporotrichosis mimicking keratoacanthoma

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Sporotrichosis is a subcutaneous infection caused by the dimorphic fungus *Sporothrix schenckii*. It is prevalent in South America and other tropical/subtropical zones. Keratoacanthoma is a tumor characterized by the proliferation of atypical, highly differentiated squamous epithelium cells. We report a case of sporotrichosis histopathology compatible with keratoacanthoma. A 67-year-old Southern Brazilian male presented with a cutaneous lesion, which developed over 5 months following a cat scratch. Physical examination revealed a well-defined crusted ulcer showing erythematous and rough surface on the back of his left hand. Neither satellite lesions nor lymphangitis were observed. A biopsy was performed to confirm the hypothesis of squamous cell carcinoma, keratoacanthoma or subcutaneous mycosis. Histopathology revealed marked acanthosis, keratosis and dense inflammatory infiltrate, predominantly neutrophilic in the dermis, compatible with keratoacanthoma. However, the culture evidenced *Sporothrix schenckii* growth in mycosel agar at 25°C, and was negative in the KOH exam. The fungal species was confirmed by mass spectrometry MALDI-TOF on a trial basis. Sporotrichosis is the most common subcutaneous mycosis in Latin America. South and Southeastern Brazil hold the highest prevalence of the infection, which usually results from trauma, including animal scratches. The clinical presentations are highly variable, including lymphocutaneous, fixed cutaneous, disseminated cutaneous and systemic sporotrichosis. The lymphocutaneous type—the most common—is characterized by nodule-ulcerative lesion at the site of fungal inoculation and strings of similar lesions along the lymphatics in up to 80% of cases. The fixed cutaneous type described in this report, occurs as infiltrated nodular, ulcerated or erythematosquamous lesions at the inoculation site. The forms that are not considered classical lymphocutaneous injury can mimic other dermatoses such as rosacea, sarcoidosis, basal cell carcinoma, squamous cell carcinoma, keratoacanthoma, sarcoma and pyoderma gangrenosum. In these cases, histopathology and mycology exams are diagnostic. High clinical suspicion is required to yield diagnosis, especially in nonendemic areas, allowing early treatment to prevent chronicity and morbidity. Despite being recognized as a differential diagnosis, sporotrichosis mimicking keratoacanthoma is a rare condition, with few reported cases.

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3226

Giant plantar bulla associated with *Trichophyton rubrum* infection

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Tinea pedis is a fungal infection of the soles and interdigital spaces common to the general population. Clinical presentation varies widely and is commonly caused by the dermatophyte *Trichophyton rubrum*. In this case report, we describe an extensive clinical manifestation of this cutaneous mycosis. A 15-year-old healthy female patient was referred to the dermatology department with an extensive pruriginous bulla on her left foot that had been present for 4 weeks. Physical examination revealed a 7-cm tense bulla with satellite vesicles on her left sole. The KOH exam and culture allowed identification of hyaline hyphae and *Trichophyton rubrum*, respectively. She underwent treatment with oral terbinafine for 4 weeks which resulted in complete resolution of manifestations. Tinea pedis is the most prevalent dermatophytosis and can be transmitted by direct human-to-human contact or through contaminated surfaces and objects. This infection is most often due to *Trichophyton rubrum* and the severity of disease is regulated by the host's immune response and the etiological agent. *T rubrum*, *T mentagrophytes* var. interdigitalis and *E floccosum* are the dermatophyte species that are frequently related to chronic infections. The clinical types of tinea pedis are moccasin, interdigital, inflammatory and ulcerative. The most frequent form is the interdigital, which presents with maceration, fissures and scaling in the web spaces. Vesicles, pustules and bullae are clinical features of the inflammatory type, usually caused by *T mentagrophytes*. Vesiculobullous tinea pedis must be distinguished from dyshidrotic and allergic contact eczemas and is generally diagnosed by KOH examination and culture. Skin biopsy may be required for diagnosis, revealing hyphae within the stratum corneum. Although plantar bullous lesions by dermatophytes are common, a case as extensive as the one described above has not been previously reported to our knowledge.

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2360

Hypersensitivity reaction to *Sporothrix schenkii*: Erythema nodosum associated with sporotrichosis

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Since 1998, Rio de Janeiro undergoes an epidemic of sporotrichosis transmitted by cats and its incidence rates remain high, so far. The disease may evolve with different clinical presentations and, although lymphocutaneous is the most prevalent one, the disease can have unusual manifestations in some patients, fact that makes it harder to be diagnosed. The current paper reports an atypical case of sporotrichosis associated with erythema nodosum diagnosed at the Dermatology Clinic of Santa Casa da Misericórdia of Rio de Janeiro (Prof Rubem David Azulay Dermatology Institute).

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3156

Investigation of the effects of nano- to micro-ampere ranged alternating current stimulation on the growth of *Trichophyton rubrum*: A pilot study

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Background: Fungi are eukaryotic microorganisms including yeast and molds. There have been a lot of researches on modifying the growth of bacterial growth but only few on fungal growth. However, microcurrent electricity could have stimulatory effect on the fungal growth.

Objective: This study aims to investigate the effects of microcurrent electric stimulation on the growth of *Trichophyton rubrum*.

Materials and methods: Standard sized inoculums of *T rubrum* derived from a spore suspension were applied to potato dextrose cornmeal agar (PDACC) plates, which was then gently withdrawn with a sterile pipette and applied to twelve PDACC plates with a sterile spreader. Twelve Petri dishes were divided into 4 groups. The given amperage of electric current was 500nA, 2μA, 4μA in group A, B, C and no electric current was given in group D.

Results: In the firth 48 hours, only 500nA and 2μA exposed fungus appeared colonies, which of 500nA were denser. 4μA exposed plates showed a barely visible film of fungus after 96 hours of incubation. Fungal growth became visible after 144 hours in the control group.

Conclusion: The lower intensity of electric current was supplied, the faster fungal growth was observed in the amperage range used in this study. On the basis of this pilot study, further studies with larger sample size, various fungal species, and various intensities of electric stimulation should be carried out.

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3678

Malassezia infections—Management with pulsed oral ketoconazole

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Malassezia folliculitis, a common mimic of acne and folliculitis, is caused by species of the yeast Malassezia, the cause of tinea versicolor. Present in over 65% of acne papules, Malassezia is a significant part of the microbiome. Immune reaction to this yeast, especially in the scalp, often causes intense itch. Usually undiagnosed, this chronic itch is treated safely and effectively with ketoconazole. We compiled data on a three month cross section (Sept-Nov, 2014) of patients seen in a general dermatology practice treated for Malassezia infections with oral ketoconazole. Of the 151 patients, over half cleared or showed significant improvement, while only 8% reported no change. This inflammatory reaction presents as dozens to hundreds of pinhead to 2-mm folliculopapules and folliculopustules scattered over the acne area (face, chest, shoulders and back), and is often mistaken for acne. Treating acne patients with an antibiotic, ignoring the underlying yeast, creates an opportunistic environment for overgrowth of the Malassezia, similar to the relationship between broad spectrum antibiotics and vulvovaginal "yeast infections." In our cohort, 51% of patients had been on a recent course of antibiotics or corticosteroids. Diagnosis is clinical. Culture and biopsy confirmation are of limited use. Koch postulates are rendered incapable of proof because of the ubiquity of the organism. The best way to confirm the clinical diagnosis is with a trial of therapy. Pulsed oral ketoconazole for this yeast overgrowth is dosed as two 200 mg tablets (400 mg) weekly over an eight week course. The highly lipophilic nature of the ketoconazole dovetails with the yeast's metabolic dependence upon sebum. The Malassezia cell wall becomes unable to 'hold on' to the ductal keratinocytes, the yeast is pushed out onto the skin's surface, and washed away. Patients take the medicine with a swallow of water on an empty stomach, followed by a spoonful of peanut butter (or lipid equivalent) to aid in absorption and to reduce the possibility of GI upset. Oral ketoconazole has proven superior to topical antifungals because the topicals do not penetrate the follicle to the depth required. It is also more cost effective than itraconazole. Oral ketoconazole, never FDA-indicated for use against Malassezia, is not FDA-restricted from 'off label' use. FDA files show no serious adverse events recorded at this dose. Further investigation of this off-label use of ketoconazole is warranted.

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2374

Management of subcutaneous phaeohyphomycosis via Mohs micrographic surgery

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Background: Phaeohyphomycosis (PHM) is a term describing a cohort of infections caused by hyphae-forming dematiaceous fungi. PHM infections can be categorized as superficial, cutaneous, subcutaneous or systemic, and management options include excision and/or prolonged systemic antifungal agents. Treatment of subcutaneous PHM is typically surgical; however, guidelines using prospective data for surgical margin recommendations are lacking and recurrence after excision of clinically involved tissue has been reported. We present a case of subcutaneous PHM managed via Mohs micrographic surgery (MMS).

Case description: A 92-year-old male presented with painful skin changes of the right knee that began two months prior. The patient described a history of repeated trauma to the affected site from recurrent kneeling, as the patient is an active farmer and performs machine repair work. No systemic symptoms concerning for infection were reported. Physical examination of the right knee revealed a large irregular, somewhat fluctuant pink plaque with serosanguinous drainage on gentle pressure. The overall clinical picture was concerning for infection. Punch biopsies were performed. Histopathologic evaluation favored PHM, which was confirmed via fungal tissue culture (*Fonsecaea pedrosoi*). After discussion of management options, the patient elected treatment via MMS. After MMS guided margin control, Mohs blocks were sent for routine histopathologic evaluation confirming surgical cure. The patient, now nearly one year status post MMS in the management of subcutaneous PHM, remains without signs and symptoms concerning for persistent or disseminated infection.

Discussion: Although PHM can be managed with prolonged systemic antifungal agents, this is usually only necessary in systemic disease or those who are concomitantly immunosuppressed. Detailed guidelines for surgical treatment are not clearly defined. Additionally, reports of recurrent subcutaneous PHM after excision of visibly affected tissue have been reported. MMS offers margin analysis at the time of excision and can be useful in sites where preservation of uninvolved tissue is preferred.

Conclusions: MMS provides an alternative surgical option to wide local excision in the management of subcutaneous PHM.

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3576

Prospective, randomized, comparative study of 1064-nm Nd:YAG laser with topical antifungal agent in the treatment of onychomycosis

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Background: Conventional treatment approaches in onychomycosis include the use of topical or systemic oral antifungal agents and surgical treatment. Although Nd:YAG laser has been reported to be clinically effective in treating onychomycosis, conflicting results are shown without clear evidence of efficacy. There were few reports conducting controlled studies combining or comparing with topical treatment.

Objectives: In order to evaluate the efficacy and safety of 1064-nm Nd:YAG laser with onychomycosis and compare these results with the responses by topical antifungal treatment alone and combined therapy.

Materials and methods : The patients were enrolled in the prospective study and randomly distributed into three groups of laser treatment only (L group), laser with topical antifungal therapy (L + T group), and topical antifungal treatment only (T group). The laser treatment consisted of 3 to 4 sessions at 4-week intervals. The effect was assessed at 12 week and 24 week visits based on the standardized photographs and mycological examinations.

Results: Total 229 nails of 59 patients were treated and evaluated. In the groups of laser treatment, 76.3% (L group) and 65.9% (L + T group) showed a clinical response (>50%) and 16.3% (L group) and 20.7% (L + T group) showed a complete response (100%) with a negative mycological result at 24 weeks, respectively. The clinical and complete response rates of the both group were significantly higher than those of the T group at 24 week ($P < .05$). Seven nails of 6 patients in the L group showed reinfection, while 2 nails of 2 patients in the L + T group showed reinfection.

Conclusion: 1064-nm Nd:YAG laser was clinically effective for onychomycosis and could be an alternative method. The combination of the laser and a topical antifungal agent appeared not to be more effective, but possibly having protective effects from reinfection.

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3908

Tinea incognito coexistence with systemic lupus erythematosus undergoing immunosuppressant therapy

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Introduction: Tinea incognito (TI) is a dermatophytic infection that may often be associated with chronic use of corticosteroids, calcineurin inhibitors, or other immunosuppressive therapy. It may therefore mimic several conditions such as rosacea, psoriasis, eczema, pityriasis rosea, folliculitis, lupus erythematosus, and seborrheic dermatitis.

Case report: A 51-year-old Mexican female presented with a 1-year history of erythematous papules, and macules in forehead, cheeks, nose and chin, and with multiple annular and petaloid erythematous scaly patches in neck, anterior and posterior superior thorax, and shoulders, but without pruritus. The rest of the physical examination revealed total dystrophic onychomycosis of bilateral first toenails. Her medical history was relevant for systemic lupus erythematosus (SLE) diagnosed 15 years ago during treatment with dellzacorn 30 mg/day. 3 months before her first clinic visit, an outside dermatologist diagnosed these lesions as subacute cutaneous lupus erythematosus (SCLE) adding to her treatment halobetasol cream daily to the affected skin. Her skin condition had worsened and she requested a second opinion. Upon obtaining a positive KOH direct mycological examination with innumerable filaments and a *Trichophyton rubrum* culture of the face, neck and toenails, a diagnosis of TI was made. She received oral terbinafine 250 mg/day for one month, with complete resolution of the skin lesions, and continued this therapy for 5 additional months resulting in both clinical and mycological cure of the toenails.

Discussion: TI is a relatively common condition, both in immunocompetent and compromised patients, who have been exposed to immunosuppressive treatments. The broad diversity in conditions and agents that predispose to immunosuppression, and therefore TI, presents diagnostic, and even, therapeutic challenges to the physician. Previously, reports have described only 6 patients with lupus erythematosus-like TI and 3 patients with underlying SLE. This extraordinary association of SLE coexistent with lupus erythematosus-like tinea incognito denotes the challenges in recognizing that cutaneous manifestations in patients with SLE may be due immunosuppression that may be related to another condition or to immunosuppressant medications.

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3950

Tinea capitis in a 9-month-old infant

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Tinea capitis is predominantly a disease of preadolescent children, adult cases being rare. It is an infection caused by dermatophyte fungi (usually Microsporium and Trichophyton) of scalp hair follicles and the surrounding skin. The incidence of tinea capitis has been increasing and presents a growing public health concern. Tinea capitis (scalp ringworm) is the most common dermatophyte infection of the scalp affecting mainly children and rarely adults. It is most prevalent between 3 and 7 years of age. Today in Turkey, the clinical forms and the distribution of causative agents of tinea capitis differ from region to region. The most frequent causative agents according to the regions are *M.canis* in Aegean, Central Anatolia and Eastern Anatolia regions, *T.violaceum* in Mediterranean and southeast Anatolia. Prevalence of tinea capitis in primary school children in Turkey ranged from 0.03-0.05%. A 8-month-old male presented to our outpatient clinic with a complaint of hair loss since one month. His mother notified that two other brothers of the patient have already completed antifungal therapy. On physical examination, there was diffuse, erythematous, ill-defined 3 x 5 cm diameter plaque with focal areas of scaling and alopecia on the patient's scalp, predominantly involving the parietal region. Direct microscopic examination of scale samples with 15% KOH was positive. Cultural examination on Sabouraud glucose agar was negative. The hematochemical examinations were within normal ranges. The patient was treated with terbinafine 62.5 mg/day orally, and topical application of imidazole cream once a day. Mycologic examination, carried out 30 days after the end of the therapy, was negative. We present this case to draw attentions of clinical dermatologists to perform mycological examination in every patient, especially in infants who presented with a scaling erythematous plaque on his/her scalp.

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3157

Zoonotic sporotrichosis in Brazil

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Sporotrichosis is a systemic subacute or chronic mycosis, caused by dimorphic fungi belonging to the Sporothrix complex: *S schenkii, S brasiliensis, S mexicana, S globosa* and *S albicans*, normally found in the soil and in decomposition of organic matter. The disease is universal, however it is more common in tropical and subtropical areas like the region of southern Africa, Central America, South America, Japan and India. It generally occurs due to the traumatic inoculation of the fungus on the skin through contact with contaminated material. For this reason, it is peculiar to certain professionals, such as gardeners, farmers and animal keepers. Other forms of transmission are described, such as inhalation of fungi and zoonotic transmission through the scratch or bite of sick animals, especially cats. Zoonotic sporotrichosis is an important form of transmission of the disease currently in Brazil and the cat is the most frequently related animal. It can be divided in different forms: fixed cutaneous, lymphocutaneous, extracutaneous or disseminated forms. The diagnosis in human beings is based on the clinical history and isolation of the fungus through culture. Cutaneous and lymphocutaneous forms should be treated with itraconazole or potassium iodide. In the disseminated cutaneous, relapsing lymphocutaneous and extracutaneous forms, amphotericin B is the most effective drug. Clinically, some conditions may have similar presentations to the sporotrichosis, such as leishmaniasis, infections caused by atypical mycobacteria, nocardiosis, tuberculosis verrucosa and chromomycosis. Thus, it is important to acknowledge the clinical forms of the disease as well as the implementation of appropriate diagnostic methods. Despite the favorable prognosis, the disease results in absence from work and embarrassment due to the unpleasant aspect of the lesions on the skin. We report a case of zoonotic sporotrichosis in a female patient, 56 years of age, presenting 2 months ago an ulcer in the distal third of the left forearm and erythematosus painful nodes following the lymphatic pathway in the same member. *Sporothrix schenckii* was isolated through culture. The histopathologic examination revealed chronic granulomatous dermatitis in current ongoing outbreak. The researches for fungi through the PAS and Grocott (GMS) stains were negative. The patient was submitted to therapy with Itraconazole 200 mg/day with complete resolution of the lesions in 3 months.

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INFECTION—VIRAL

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2688

Atypical clinical cutaneous herpes infections. Report of three cases

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Background: Herpes simplex virus (HSV) and varicella zoster virus (VZV) infections represent highly prevalent conditions in our society resulting, in most cases, in typical cutaneous manifestations. However, their clinical presentation may sometimes be misleading, especially in immunocompromised patients. In these cases, the clinicohistologic correlation can lead us to an accurate diagnosis.

Methods: The clinical and histopathologic features of three atypical cases of cutaneous HSV or VZV infections diagnosed in our department over the year 2014 are described.

Results: Three patients, two men and one woman aged 46-62 years, were considered. Two of them were under biological treatment for Crohn's disease and rheumatoid arthritis, respectively. The third one was a HIV-infected patient who had developed acquired immunodeficiency syndrome. Two patients presented with a 10-day and 30-day history of one pruriginous, infiltrated and crusted plaque of 2-cm width on their faces. The third patient presented several violaceous, firm and round papules grouped on his left knee and right ankle for two weeks. In all cases, the herpetic typical epidermal changes, such us, variable degree of epidermal necrosis, intraepidermal vesicles and cytopathic changes, were found. In addition, herpetic folliculitis was observed in one patient and leukocytoclastic vasculitis on the adjacent superficial dermis was evident in a second one. The subsequent immunohistochemical analysis showed positivity for VZV in these two cases and positivity for HSV in the patient with only epidermal involvement.

Conclusions: Three cases of cutaneous herpes infections with atypical clinical features, long-term evolution and/or widespread lesions were presented. It is worth mentioning a certain degree of immunosuppression in our patients which may be responsible for the unusual clinical presentations. Both hair follicle involvement and leukocytoclastic vasculitis are commonly described histological findings in cutaneous herpes infections and so these should be considered in the differential diagnosis when any of them is present. It seems that involvement of the folliculosebaceous unit without epidermal changes would suggest VZV infections. Both clinicohistologic correlation and immunohistochemistry provide the clue to accurately diagnose atypical cutaneous herpes infections, the latter leading to differentiation between VZV and HSV.

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2663

Cutaneous cytomegalovirus infection mimicking acquired perforating dermatosis

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Cytomegalovirus (CMV) infection is a well-known opportunistic infection in immunocompromised patients, such as transplant recipients and human immunodeficiency virus (HIV)-infected patients. Unlike CMV infection in visceral organs, cutaneous CMV infection is rare and hard to diagnose clinically due to nonspecific and variable manifestations. Herein, we describe a case of cutaneous CMV infection mimicking acquired perforating dermatosis in a HIV-infected man. A 42-year-old man with a history of HIV infection, type 2 diabetes mellitus and psoriasis was admitted to our hospital for CMV viremia with CMV retinitis. He complained of a generalized itchy skin eruption over the face, trunk and upper limbs for 6 months. On examination, multiple erythematous papules and nodules with a central keratotic plug or crust were noted over the face, trunk and extensor aspects of upper limbs in a background of treated psoriatic skin. Some keratotic plugs detached leaving a crater-like central depression. A tentative diagnosis of acquired perforating dermatosis was made. A skin biopsy specimen obtained from the back revealed an ulcer with vertically oriented collagen bundles crossing from the dermis into an epidermal depression containing necrotic debris. In the dermis, in addition to a perivascular lymphohistiocytic infiltrate, some enlarged cells showed purple staining intranuclear inclusions surrounded by a clear halo in the enlarged nucleus. The nucleoplasm was marginated and vacuolated. The cytoplasm of these cells was peripherally darker, and eosinophilic intracytoplasmic granules were also seen in some cells. A diagnosis of cutaneous CMV infection was confirmed by CMV immunohistochemical stain. After 2-week intravenous gancyclovir treatment, the number and size of the skin lesions markedly decreased, and most central keratotic plugs detached. The excellent response to gancyclovir treatment further supports CMV infection is the major cause of the skin lesions.

Commercial support: None identified.

3315

Divergent mechanisms of Merkel cell polyomavirus and trichodysplasia spinulosa-associated polyomavirus small T antigens in cutaneous pathogenesis

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Merkel cell carcinoma (MCC) and trichodysplasia spinulosa (TS) are two cutaneous lesions characterized by cell proliferation. While MCC presents as an aggressive neuroendocrine cancer, TS is characterized clinically by folliculocentric papular eruption and histologically by intense staining for the Ki67 cell proliferation marker. The common association of MCC and TS pathogenesis with immunosuppression strongly suggests a viral etiology; the recent discovery of the Merkel cell polyomavirus (MCPyV) and trichodysplasia spinulosa-associated polyomavirus (TSPyV) has shed light on the potential mechanisms that underlie the development of MCC and TS, respectively. MCPyV and TSPyV share many genomic properties, including the expression of a key regulatory protein known as the small tumor (sT) antigen. While both sT antigens have demonstrated a capacity in regulating cellular pathways, it remains unknown whether MCPyV and TSPyV sTs contribute similarly or differentially to cell proliferation. This study was designed to further document the proliferative potential of MCPyV and TSPyV sT antigens by investigating their regulatory effects on the retinoblastoma protein (pRb) tumor suppressor. Specifically, we asked whether and how MCPyV and TSPyV sT antigens could influence pRb phosphorylation and deactivation. Western blot analysis showed that expression of TSPyV sT markedly enhanced the phosphorylation of pRb. In contrast, expression of MCPyV sT did not alter pRb phosphorylation under the same experimental conditions. Densitometric analysis revealed that TSPyV sT antigen expression nearly doubled the ratio of phosphorylated to total pRb ($P < .001$, Student's T-test), while MCPyV sT antigen expression did not cause significant change in pRb phosphorylation status. Given that hyperphosphorylation of pRb is associated with deregulation of the cell cycle, S-phase induction, and increased cell proliferation, our findings support an important role of TSPyV-mediated pRb deactivation in the development of TS. The observation that the pRb tumor suppressor is inactivated by TSPyV sT but not MCPyV sT provides further insights into the distinct pathobiological mechanisms of MCC and TS, two polyomavirus-associated cutaneous proliferative lesions.

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Efficacy of oral zinc sulphate for molluscum contagiosum

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Background: Molluscum contagiosum (MC) is a common and benign contagious viral infection of the skin and mucous membrane that primarily affects children. Spontaneous resolution may occur, but often it takes a prolonged period of months to years and the infection can take up to 4 years to resolve. Zinc has an important effect on the immune system and it has been used as an immunomodulator to treat a variety of skin disorders.

Objective: To assess whether oral zinc is effective in treating patients with MC.

Methods: Fifty nine MC patients were included at Pusan University Yangsan Hospital between July 2012 and July 2014. Twenty seven (45.8%) patients had past history of atopic disease. The patients were treated with oral zinc sulfate (10 mg/kg to a maximum dose of 600 mg/day) for up to 6 months. Serum zinc and copper level, renal and liver function tests were measured at the beginning (baseline) and completion of the trial.

Results: Complete clearance of MC was observed in 47.5% (28/59) of the patients and partial clearance, defined as clearance of 50-99%, in 25.4% (15/59). The mean duration to reach complete clearance was 15.9 weeks. Patients with atopic disease showed higher complete clearance compared to nonatopic disease (56% vs 43%). The response to treatment was not related to the increment in serum zinc level as only 3 patients showed the increment. No serious side effects were reported apart from nausea (1%), mild abdominal pain (1%) and constipation (3%).

Conclusion: Our findings suggest that oral zinc sulfate is worth considering as a therapeutic option for the treatment of MC, particularly for generalized lesions and uncooperative patients. Oral zinc sulfate is an effective option lacking significant side effects.

Commercial support: None identified.

2930

Herpes zoster oticus (Ramsay Hunt syndrome type 2)—A classical presentation

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Introduction: Ramsay Hunt syndrome (RHS) type 2 also known as herpes zoster oticus is a very rare disorder that is caused by the reactivation of latent varicella zoster virus in the geniculate ganglion, a nerve cell bundle, of the facial nerve. The symptoms and signs include acute facial nerve paralysis, pain in the ear, taste loss in the front two-thirds of the tongue, dry mouth and eyes, and eruption of an erythematous vesicular rash in the ear canal, the tongue, and/or hard palate.

Objective: To present a very rare but classical case of herpes zoster oticus. It is one of the very rare clinical entity where multiple cranial nerves are involved simultaneously.

Report of case: A 35-yrs-old woman presented to me with severe pain and vesicular lesions in the left ear for last 3 days. About 36-48 hrs after the onset of otalgia, patient developed facial weakness along with vesicular eruptions on conchae, in external auditory meatus of left side, anterior 2/3 of left side of tongue and hard palate. Examination revealed lower motor neuron facial palsy on left side which was complete. Bell's phenomenon was present on left side. A neurologic examination revealed a weakness in the marginal mandibular branch of the left facial nerve. Loss of definition in the ipsilateral nasolabial fold and weakness in the temporal branch of the facial nerve was detected. There were painful vesicular lesions on erythematous base seen in left conchae and external auditory meatus, associated with difficulties in hearing of the left ear. On examination of oral cavity revealed lesions over the left side of tongue and hard palate. Ocular examination demonstrated a lateral, left-beating gaze nystagmus with normal conjunctiva and sclera. Blood examinations revealed no abnormalities.

Discussion: Classical presentation of herpes zoster oticus is very rare. The VZV (varicella zoster virus) reactivation in the geniculate ganglia and subsequent neural inflammation, pressure, and possible destruction of the facial nerve in the temporal bone are suspected to cause facial palsy, while VZV migrates from the geniculate ganglia into the skin around the ear or into the oropharynx via the sensory fibers, where it replicates and produces zoster in RHS.

Commercial support: None identified.

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Giannotti–Crosti syndrome-like reaction

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A 10-year-old boy with a medical history of asthma and seasonal allergies developed a new mildly pruritic rash on his hands, feet, posterior legs, elbows, knees, and chest. Four weeks ago, he had been treated for molluscum contagiosum (MC) with cantharadin. Evident on exam were multiple pink to violaceous edematous papules coalescing to plaques involving all extremities with minimal chest involvement. Figure 1 shows symmetrical, erythematous to violaceous edematous flat topped papules coalescing centrally into plaques with secondary excoriations and crusting. Giannotti–Crosti (GC) syndrome, also described as papular acrodermatitis of childhood, presents as an abrupt onset, symmetric, monomorphic papular to papulovesicular eruption on the face, buttocks, and extremities in children between the ages of 6 months to 14 years. The pathogenesis is thought to be immune-mediated, with a viral illness often preceding the eruption. The most common etiology is EBV in the United States and hepatitis B in Europe. Histology is nonspecific and variable; skin biopsy is not indicated to confirm a diagnosis. Lesions are usually asymptomatic, but the most common symptom is pruritis. Treatment is supportive although topical corticosteroids may be prescribed for intolerable pruritis. Spontaneous resolution occurs within 3-4 weeks, though persistence up to 8 weeks should not raise concern. Gianotti–Crosti syndrome-like reactions (GCLRs) present as an inflammatory response to MC. This condition represents a cell-mediated immune response in an "id" reaction-like phenomenon which may often herald the resolution of MC and lead to viral clearance. While resembling GC, GCLR differs in that it may be extremely pruritic in up to 80% of patients and responds well to treatment with midpotency topical corticosteroids. Despite significant pruritis and longer persistence (6 weeks), GCLRs are a good prognostic sign for MC, as a dramatic reduction of MC lesions ensues with complete clearance 5 weeks after onset of GCLR.

Commercial support: None identified.

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Herpes zoster with meningitis in a vaccinated, immunocompetent child

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Neurologic complications from varicella zoster virus (VZV) reactivation are rare and mainly reported in immunocompromised patients after reactivation of wild-type varicella zoster virus. In this report, we describe a previously immunized healthy child who developed herpes zoster with meningitis. A 7-year-old boy visited our clinic with painful, itchy skin rash on left face, fever, headache, and vomiting. After admission, he showed meningeal irritation sign and lumbar puncture was performed. Cerebrospinal fluid examination showed an increased protein concentration (51 mg/dL), white blood cells (200 WBC/mm^3, 98% lymphocytes) and VZV DNA was detected by polymerase chain reaction. A review of his immunization record showed a varicella vaccination at 12 months of age and the results of immunologic screening for HIV, serum immunoglobulin and complement levels were unremarkable. Acyclovir was administered intravenously at a dose of 15 mg/kg every 8 hours for 10 days and the patient's clinical condition rapidly improved. Repeated CSF PCR for VZV converted to negative on hospital day 10, he was discharged and was asymptomatic with a normal physical examination at 3 weeks later. Vaccine strain VZV becomes currently important cause of herpes zoster and meningitis among immunized children, so we should aware varicella zoster vaccine have potential for reactivation and complications in both immunocompetent and immunocompromised hosts.

Commercial support: None identified.

3297

Herpetiform acute graft versus host disease

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Background: Dermatologic manifestations are an important aspect of graft versus host disease (GVHD). Acute GVHD usually starts as mild erythema or papular eruption that may progress into morbiliform exanthem. The presence of vesicles or bullae in hematopoietic stem cell transplant recipients is usually related to potentially life-threatening conditions, such as herpes-virus infection or severe forms of acute GVHD. Herein, we describe two patients who developed sterile "herpetic lesions" as the onset of acute GVHD.

Case reports: Case 1: A 41-year-old man with higher-risk myelodysplastic syndrome was admitted for HLA-identical allogeneic stem cell transplant, 30 days later, while he was receiving cyclosporine 175 mg/day and acyclovir prophylaxis (200 mg bid), umbilicated vesicles and erosions appeared over the inguinal folds and lower abdomen. Histopathology showed epidermal basal vacuolation and individual cell necrosis associated with mononuclear cell infiltration of the upper dermis and lower epidermis. Herpes virus was not detected on skin biopsy. Methylprednisolone was added. After a month, he started extracorporeal photopheresis due to extracutaneous GVHD progression. Case 2: A 39-year-old man underwent HLA-identical allogeneic stem cell transplant for T-cell acute lymphoblastic leukemia. 20 days following the transplant, he was evaluated because of asymptomatic lesions while receiving cyclosporine 175 mg/day and acyclovir prophylaxis (200 mg bid). Clinical examination revealed follicular papules over the inguinal folds and axilla, some of them, showing a central vesicle. Skin biopsy and viral culture ruled out herpes infection. Histopathologic findings were similar to that seen in case 1.

Discussion: GVHD disease is the major cause of posttransplantation morbidity and mortality. Acute GVHD have protean skin manifestations and may pose diagnostic and therapeutic challenges. Development of vesicles in the setting of bone marrow transplantation is usually a matter of concern for clinicians because they are frequently associated to herpes virus reactivation (herpes simplex and varicella zoster). However, delaying appropriate therapy for acute GVHD may cause serious and irreversible inflammatory damage of the liver, gut, and skin. Clinicians should be aware that acute GVHD may present as herpetiform lesions over flexural areas. Complete physical examination and direct immunofluorescence staining for detection of viral antigens in vesicular or erosive lesions help in differential diagnosis allowing for a rapid start on high dose immunosuppressive therapy.

Commercial support: None identified.

3782

High-definition optical coherence tomography as a noninvasive technique in the diagnosis and management of molluscum contagiosum

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Background: Molluscum contagiosum (MC) is a common skin infection, especially in children with atopic dermatitis. We utilized imaging with high-definition optical coherence tomography (HD-OCT) to differentiate papules of molluscum contagiosum from inflammatory papules of atopic dermatitis and direct therapy.

Case report: A child between the ages of 5 and 10 years old presented with a history of atopic dermatitis and the recent development of scattered skin-colored papules. The papules had a predilection for the areas of lichenified atopic dermatitis, including the antecubital and popliteal fossae. Some of the larger papules demonstrated central umbilication characteristic of molluscum contagiosum. Imaging with HD-OCT (Skintell; Agfa Healthcare) was utilized to distinguish papules of molluscum contagiosum from inflammatory papules of atopic dermatitis so destructive therapies were directed only at the proper lesions.

Discussion: Molluscum contagiosum is a common cutaneous infection of the human skin caused by the molluscum contagiosum virus, in the Poxvirus family. It most commonly occurs in children, but is also seen in adults, especially the immunocompromised and in the form of a sexually transmitted disease. The classic clinical appearance is an umbilicated firm papule with a waxy surface. While the ailment is typically self-limited, there are various treatments available to speed resolution. Molluscum contagiosum occurs more commonly in patients with atopic dermatitis and can induce a molluscum dermatitis. It is important to be able to distinguish inflammatory papules from lesions of molluscum to avoid unnecessary and ineffective treatments. High-definition optical coherence tomography is a recently developed method of noninvasive skin imaging that allows in-vitro imaging to the cellular resolution. It grants the physician the ability to image any lesions that aren't readily diagnosed clinically within minutes. The noninvasive and painless nature of HD-OCT provides an advantage over the previously available diagnostic techniques such as biopsy or Tzank smear. Many of the HD-OCT findings of molluscum contagiosum mirror the findings on histopathology. The epidermis displays acanthosis, producing a crateriform papule. In the center are lobulated clusters of keratinocytes containing intracytoplasmic inclusions known as molluscum bodies. While on histology the molluscum bodies appear as glassy basophilic to eosinophilic inclusions, on HD-OCT they appear as dark ovoid structures. The epidermis overlying the molluscum bodies shows marked thinning, making it very apparent. As a note on technique, we found it useful to use the en face view while taking the images to be certain that the papule was centered in the view field. HD-OCT is a useful technique to differentiate lesions of MC from inflammatory papules of atopic dermatitis, which only show inflammation and spongiosis.

Conclusion: HD-OCT is a valuable tool that can rapidly aid in the diagnosis of molluscum contagiosum and help ensure treatments are directed only at the appropriate lesions.

Commercial support: None identified.

3035

Hypertrophic genital herpes simplex successfully treated with intralesional cidofovir

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Introduction: Herpes simplex virus (HSV) genital infection is among the most frequent sexually transmitted infections worldwide. The most common clinical presentation is the development of small grouped vesicles that result in painful superficial ulcers. However, in immunocompromised patients, especially in those infected by human immunodeficiency virus (HIV), HSV infection can present as hypertrophic lesions that may simulate a neoplasia and lead to misdiagnosis. Moreover, in the last decades, the number of strains of HSV resistant to first-line antivirals has increased, mainly among HIV infected patients, which has made treatment more complicated.

Case: A 50-year-old man with HIV infection for 10 years, treated with antiretroviral therapy, presented with a painful lesion on his penis which had grown for more than one year despite the use of oral valacyclovir. Physical examination showed a 20 x 20 mm indurated and ulcerated tumor on the coronal sulcus, which suggested a squamous cell carcinoma. A biopsy was performed and the histopathologic analysis demonstrated epidermis ulceration with pseudoepitheliomatous hyperplasia, without signs of malignancy. In the superficial part of the epidermis multinucleated keratinocytes were detected, suggesting HSV infection. Immunostaining and polymerase chain reaction for HSV were positive for HSV-2, confirming the diagnosis of hypertrophic genital herpes simplex. Tissue culture and viral resistance testing could not be performed.

Discussion: HSV genital infection can be a diagnostic and therapeutic challenge. Hypertrophic genital herpes simplex is often refractory to first-line systemic antiviral agents like acyclovir and derivatives, particularly in HIV positive patients. In such cases, foscarnet, cidofovir, imiquimod or thalidomide have been used with variable effectiveness. In our case, valacyclovir resistance was suspected and intralesional cidofovir was initiated, with dramatic improvement after three injections. However, this form of application was badly tolerated by the patient, so he is currently being treated with topical cidofovir three times a week as maintenance therapy, without recurrence or significant local and/or systemic adverse effect.

Commercial support: None identified.

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Idiopathic CD4+ T cell lymphopenia presenting with generalized verrucosus

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Introduction: Generalized verrucosus (GV) is the clinical presentation of human papillomavirus (HPV) linked to several conditions such as warts, epidermodysplasia verruciformis (EV), HIV and other immunodeficiency syndromes. Lately, there has been description of patients with idiopathic lymphopenias and GV.

Case report: A 62-year-old white female presented to our clinics with multiple asymptomatic 2-3 mm warty papules that were scattered in the thighs, legs and clustered in the groin as verrucous plaques. She has a medical history significant for a stage IV diffuse large B-cell lymphoma of the terminal ileum and liver who was treated with six cycles of R-CHOP in 2006 in remission as of 2015. Three years later, scarce warty papules developed on her left leg and groin, which slowly spread to both lower limbs. A shave biopsy showed mild hyperkeratotic epidermis with acanthosis and keratinocytes with blue-gray pallor. No malignancy was found. These changes were consistent with EV. Laboratory investigations showed a normal CBC, chemistries and immunoglobulins. The patient tested negative for HIV and HTLV. Quantitative T and B cell analysis was reported with a CD3+/CD4+ = 4% (27-57%), absolute CD3+CD4+ = 32 mm^3 (340-1568 mm^3). Flow cytometry immunophenotyping revealed an immunophenotypically abnormal T cell population of CD2-, CD5+, CD7+, CD52+, which were mostly alpha-beta T cells with a CD4:8 ratio of 8:80. Peripheral blood tested positive for clonal T cell receptor gene rearrangement.

Discussion: Recent publications have linked idiopathic lymphopenias with IL-7 and GATA2 deficiencies. The immunophenotype is variable, either presenting as decreased NK, B or T-cell populations. These patients have an increased risk of acquiring opportunistic infections such as cryptococcosis or HPV. GV is a rare entity that has been described in HIV patients with low CD4 count. Interestingly, our patient exhibited a low T-helper population which would explain the similarities between our case and the ones described for other patients with similar cellular depleted immunity. The reason of this patient's low T-helper population is still currently under investigation. There are scarce case reports of patients with active lymphomas who have developed GV. To the best of our knowledge, this is the first case report of a patient with a past history of non-Hodgkin lymphoma and a current idiopathic CD4+ lymphopenia, who subsequently developed GV.

Commercial support: None identified.

2879

Long Dan Xie Gan Tang formula in the management of acute stage herpes zoster: A systematic review of randomized controlled trials

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Background: Herpes zoster (HZ) is a neurocutaneous disease characterized by grouped vesicles and pain. Current pharmaceutical treatment is effective, although there is a gap between patient expectations and the efficacy of treatment. Chinese herbal medicines (CHM) may be beneficial in managing symptoms with fewer side effects.

Objective: This review aims to evaluate systematically the efficacy and safety of Chinese herbal medicine formula Long Dan Xie Gan Tang (LDXGT) for HZ.

Methods: Nine English and Chinese language databases were searched from inceptions to February 2015. Randomized controlled trials using LDXGT for HZ were included. Data were extracted and risk of bias assessment was performed to evaluate the methodological quality of included trials. Primary outcome was evaluation of pain using visual analogue scale. Secondary outcomes were incidence of postherpetic neuralgia (PHN), cutaneous outcomes, health related quality of life (HRQoL), and therapeutic effective rate.

Results: A total of 31,906 citations were identified. Twenty six studies enrolling 2829 participants were included. Methodological quality of included studies was moderate. One study reported on the primary outcome of evaluation of pain, with pain resolving 2.6 days earlier in those who received modified LDXGT compared with pharmacotherapy (95% CI -3.61, -1.59). When LDXGT was combined with topical CHM, scab formation occurred 1.13 days earlier compared with pharmacotherapy (95% CI -1.43, -0.83), and the incidence of PHN was lower (RR 0.14, 95% CI 0.03, 0.74). LDXGT was found to improve the therapeutic effective rate based on reduction of lesion count when used in combination with other oral (RR 1.29, 95% CI 1.13, 1.48) or topical CHMs (RR 1.12, 95% CI 1.06, 1.17). None of the studies reported on HRQoL. Several mild gastrointestinal adverse events were reported in both intervention and pharmacotherapy groups, and two cases of vertigo and fatigue were reported in the pharmacotherapy group.

Conclusions: Modified LDXGT alone may hasten alleviation of pain, and when combined with topical CHM may decrease the incidence of PHN compared to pharmacotherapy. Few adverse events were reported. Validity of the evidence for LDXGT was limited by the methodological quality of the included studies and the variability in both intervention and comparator groups. Further rigorous clinical research is needed.

Commercial support: None identified.

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Immunocryosurgery for multiple therapy-resistant condyloma: An alternative therapy for immunocompetent men

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Multiple therapy-resistant condyloma is a relatively common condition in clinical practice and novel treatments are limited. Immunocryosurgery (combination of topical imiquimod and cryosurgery) was recently introduced for the treatment of basal cell carcinomas with very promising therapeutic results. The aim of the study was to evaluate the efficacy of the immunocryosurgery for multiple therapy-resistant genital condyloma in immunocompetent men. All patients had histopathologically confirmed genital condylomas that were resistant to at least 3 different topical therapies (trichloroacetic acid, podophyllin, 0.5% podofilox, imiquimod 5%, sinecatechins, 0.5% podofilox and/or salicylic acid 20%) and cryosurgery used independently. At day 0, one single cycle of cryosurgery was performed on all lesions which were superficially sprayed with liquid nitrogen approximately 1 to 1.5 inches away for 2 to 3 seconds until slight whitening of the lesion. Each patient was instructed to apply imiquimod 5% three times per week on the affected area. At day 14, patients were evaluated and residual lesions retreated with superficial cryosurgery. Patients continued imiquimod to complete 4 weeks of treatment. A total of 12 patients were recruited (mean age 27.75 ± 5.25 years). All patients finished the treatment. Two weeks after the end of treatment, 10/12 patients had complete clearance of lesions. The most common side effects were mild pruritus (58.3%) and local erythema (83.3%). Local painful ulcers were noted in one patient and severe pruritus in other two patients. During the follow-up period (2-12 months), one patient had a relapse. Immunocryosurgery is an alternative and feasible treatment that can be used in multiple therapy-resistant genital condylomas. The treatment in this group of patients was shorter than the regular regimen with imiquimod 0.5%.

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INTERNAL MEDICINE DERMATOLOGY

3624

A case of a recluse spider bite masquerading as cellulitis

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Loxosceles spiders, also known as recluse spiders, are common to the South, West, and Midwest regions of the United States. Recluse spiders uncommonly bite humans, locally causing a painful erythematous papule or plaque. Most often this is a self-limited phenomenon. The bites of recluse spiders characteristically produce an asymmetric shape and "red, white and blue" sign corresponding to reactive erythema, vasoconstriction and thrombosis. The violaceous center develops a necrotic eschar and subsequently ulcerates. Systemic symptoms such as fever and myalgias may also occur. Rarely, patients will develop systemic complications such as circulatory shock, disseminated intravascular coagulation, Coombs-positive hemolytic anemia and acute renal failure. We present a case of a healthy adult male who presented with two painful erythematous plaques on the right lateral malleolus. A complete metabolic panel and complete blood count were normal. He was initially treated with broad spectrum antibiotics for presumed cellulitis. He subsequently developed pseudovesiculation and a central violaceous hue at each lesion concerning for necrosis 24 hours after initial presentation. While no spider was ever visualized and the patient presented to a hospital in the Northeast U.S., he reported a transcontinental flight from the West Coast during which he experienced a memorable, painful stinging sensation. Antibiotic treatment was stopped after 3 days and the patient's lesions healed with basic wound care. This case highlights the importance of history when diagnosing a suspected spider bite. Discussion will highlight the need to exclude systemic complications as well as review more common conditions that mimic insect bites and require more extensive treatment, such as infection, vasculitis, and vascular disease.

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2775

A case of comedonal Darier disease and intractable Crohn's disease

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Case: A 23-year-old woman with a history of intractable Crohn's disease presented with 4 years of persistent scaly red papules on the nose and chin. Of note, the patient had a 2 year history of severe Crohn's disease resulting in significant micronutrient deficiency and anemia requiring transfusions. Her inflammatory bowel disease was refractory to standard treatment with adalimumab, infliximab, and prednisone; ultimately she required a proctocolectomy and was initiated on certolizumab 2 months prior to presenting to dermatology. On exam she had several erythematous scaly papules and dilated comedones around the nasal ala and chin. Dermoscopically, these had a follicular plug with a raised border and trailing scale. A punch biopsy was obtained of the right nasal ala revealing follicular dyskeratosis with comedones. Two adjacent hair follicles contained prominent parakeratotic plugs with focal clusters of neutrophils. Dyskeratosis was accompanied by mild acantholysis in the follicular epithelium. Histopathologic features are suggestive of comedonal Darier disease.

Discussion: Comedonal Darier disease (CDD) is a rarely reported condition characterized by prominent follicular involvement with formation of large comedones on the face and scalp. Lesions reportedly develop in early adulthood as in our patient's case. CDD is a controversial variant of Darier disease, an autosomal dominant genodermatosis associated with a defect in the ATP2A2 gene encoding SERCA2, an intracellular calcium pump. Genetic analysis is rarely performed; though a causative mutation in ATP2A2 has been identified in one case of CDD. Rare cases of mucosal and gastrointestinal involvement of Darier disease have been reported in esophageal and anorectal mucosa. Darier disease has not previously been linked to inflammatory bowel disease, however, mouse models of induced colitis demonstrate decreased expression of SERCA2 within inflamed colonic muscle and subsequent dysmotility. The association of CDD and Crohn's in this patient remains unclear. This patient's highly refractory IBD to the standard regimen suggests other factors may be playing a role.

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3365

A case of refractory pyoderma gangrenosum treated with intravenous immunoglobulin

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A 52-year-old lady had a 0.5-mm Breslow thickness malignant melanoma excised on her right leg, which was left to heal by secondary intention. 4 weeks postoperatively, the wound began to enlarge and become very painful. Skin biopsy showed ulceration with abundant dermal neutrophils also infiltrating into adjacent blood vessels. These findings were consistent with the suspected clinical diagnosis of pyoderma gangrenosum (PG). Prednisolone was commenced at 60 mg daily and gradually tapered, before a steroid-sparing agent was introduced. A range of agents were trialed although unsuccessfully. Mycophenolate mofetil was discontinued because of nausea and lack of improvement; cyclosporin was also ineffective and stopped due to renal impairment; whilst on methotrexate there were some signs of wound healing, but our patient experienced recurrent episodes of sepsis. Despite compression bandaging, pulsed methylprednisolone then higher doses of prednisolone, the ulcer became circumferential involving much of the lower leg and causing significant morbidity. A treatment challenge arose as biologics were deemed unsuitable because of the history of melanoma and recurrent sepsis. Therefore intravenous immunoglobulin (IVIg) was introduced at a dose of 2 g/Kg each month. After three months, there was clear evidence of wound healing and a dramatic reduction of pain. A monthly maintenance dose of 1 g/Kg was continued. To date, IVIg has been well tolerated and there have been no further hospital admissions for sepsis. Prednisolone is now at a low maintenance dose of 7.5 mg and there continues to be signs of improvement. PG is a rare ulcerating inflammatory dermatosis that can occur with no known underlying cause, but often associated with inflammatory bowel disease, arthritis and hematological malignancy. The mainstay of treatment is high-dose oral corticosteroid, but there is a lack of evidence in the literature demonstrating effective therapies. Recently published is a randomized controlled trial which showed prednisolone and cyclosporin to have similar efficacy, and there has only been one other randomized trial, which looked at response to infliximab over placebo. Success with IVIg is has been reported in the literature, with a recent review showing excellent response in almost all reported cases. Those who relapse respond to further IVIg therapy. This case report adds further support to the idea that IVIg is a valid treatment option for patients with refractory PG.

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2899

A classic triad: Granulomatous dermatitis, arthritis and uveitis

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Introduction: Blau syndrome is a rare autosomal dominant condition affecting the skin, joints and uveal tract. It was reported first by Blau in 1985 and it is characterized by granulomatous deforming arthritis, camptodactyly, synovial cysts, skin eruption and severe uveitis in the absence of lung or other visceral manifestations. The skin eruption is often described as being papular, erythematous, generalized and intermittent, but many other types have been reported. Mutations in the Card15/NOD2 gene on chromosome 16 are responsible for the disease.

Observation: We present the case of a young male patient presenting with perifollicular red-brown papules 1-2 mm and severe arthritis since 18 months of age. His mother was known for a nonpruritic intermittent eruption, a symmetric progressive arthritis from 1 year of age, synovial cysts, bony erosion and severe articular deformations with a good response to corticotherapy. At 20 years old, she developed bilateral chronic uveitis. Skin biopsy showed perifollicular noncaseating granuloma infiltration with multiples epithelioid histiocytes. Genetic testing showed the same mutation for the two patients: His 603 Arg 2 copies IVS8 + 158C/T of the NOD2/CARD15 gene. Methotrexate and infliximab were started for our 5-year-old patient and also for the mother once the diagnosis was established. The maternal grandmother was also known for arthritis and died prematurely. Our patient developed a minor uveitis at 10 years old. The patient and mother are still on infliximab and have started leflunomide. They suffer from deforming arthritis and multiple cysts.

Discussion: Blau syndrome is a monogenic disease presenting in childhood initially with skin findings, followed by arthritis and finally uveitis. The differential diagnosis includes among others early-onset childhood sarcoidosis and juvenile rheumatoid arthritis. Reported treatments include glucocorticoid, methotrexate, cyclosporine, mycophenolate mofetil, anti-TNF, canakinumab and anakinra. In our case, the mother was initially treated as juvenile rheumatoid arthritis unfortunately progressing with severe deformations.

Conclusion: We report two siblings with Blau syndrome with important arthritis. Recognition of this diagnosis is important for early treatment with close follow-up to prevent severe morbidity.

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2703

A study of cutaneous manifestations among febrile neutropenic patients: A five-year retrospective review in a single tertiary university hospital in Southern Thailand

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Background: Febrile neutropenia (FNP) is a condition defined by fever and neutropenia. The febrile neutropenic patients are highly susceptible to infection. However, there are little data about cutaneous manifestations among this group.

Objective: To describe cutaneous manifestations and pathological studies in febrile neutropenic patients.

Methods: We retrospectively reviewed (Nov. 2009 to Oct. 2014) cases of forty-three febrile neutropenic patients with cutaneous lesions in Songklanagarind Hospital, Prince of Songkla University, Thailand. The data, demographics, clinical manifestations, pathological reports and tissue cultures, were collected and analyzed.

Results: The demographic data revealed the mean age to be 59 ± 19 with 24 (55.8%) of the subjects being male and 19 (44.2%) female. Mostly underlying disease was hematologic neoplasm, 41 (95.3%), especially with acute myeloid leukemia, 21 (51.2%). Twenty-one (48.8%) of the patients had contracted FNP within 7.5 ± 8.7 days after presenting with skin lesions. On the other hand, 22 (51.2%) had skin lesions after FNP with approximately duration 9.0 ± 11.1 days. Cutaneous manifestations were mostly multiple lesions, 29 (67.4%) and the most common morphology were nodule, 16 (37.2%) which were on lower extremities, 25 (58.1%). The dermatopathological diagnosis included infections, 14 (32.6%) and almost all were fungus 12 (85.7%) and leukemia cutis, 14 (32.6%). Fungal infections were more frequently found in patients who had developed skin lesions after being diagnosed with FNP than patients who had skin lesions before FNP. There was a statistical significance (10 (45%), 2 (9.5%), respectively; $P = .01$). Unfortunately, there were no diagnostic clues for the leukemia cutis. Twenty-nine (67.4%) patients who were sent for skin cultures tested positive for fungal infections six (20.7%); two Aspergillus spp., two Candida spp., and each one of Fusarium spp. and Cladosporium spp. whereas, four of the six tested positive for fungus both of the culture and pathological sections. There were found the fungal organisms in five pathological sections, despite negative cultures.

Conclusion: A variety of cutaneous manifestations in FNP, which is common in the cutaneous nodules of the lower extremities, present problems in a differential diagnosis. Most frequent is a fungal infection in patients who have skin lesions after the onset of FNP. We recommend both a tissue biopsy for pathological study and culture for more definitive results.

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2563

Acquired acrodermatitis enteropathica in an adult patient as the presenting sign of celiac disease

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Acrodermatitis enteropathica is a rare inherited form of zinc deficiency that occurs in infants and characterizes by periorificial and acral dermatitis, alopecia, and diarrhea. Low zinc levels coupled to the histologic findings of epidermal necrosis point to the diagnosis. In adults, conditions that lead to zinc deficiency, such as anorexia, alcoholism, intestinal malabsorption, and diets high in phytate, may present with similar clinicopathological findings and are described as acquired acrodermatitis enteropathica. Celiac disease (CD) is a chronic disorder that results from gliadin intolerance. Ingestion of gliadin results in an immunologically mediated inflammatory response that leads to damage of the intestinal mucosa. CD presents with diarrhea, abdominal cramps, weight loss, growth delay, and/or fatigue. Electrolyte abnormalities, including zinc deficiency have been reported. The frequency of CD is 1% and it has a bimodal age distribution, with two peaks at 1 and 30 years of age. Diagnosis is often delayed due to the subtle symptoms and it is determined with positive immunoglobulin A anti-tissue transglutaminase and anti-endomysial antibodies. Small bowel biopsy is the gold standard test, however, the enteropathy is usually patchy and requires multiple biopsies to establish diagnosis. The spectrum of intestinal involvement ranges from minimal lymphocytic infiltration of the lamina propria to total villus atrophy of the small intestine. The cutaneous manifestations of CD are diverse and include dermatitis herpetiformis, alopecia areata, oral aphthae, vitiligo, urticaria, and others. To our knowledge, no cases of CD in the adult population presenting with an acrodermatitis-like eruption have been reported. We describe a 49-year-old female who presented with periorificial and acral dermatitis, diffuse alopecia, intermittent diarrhea, and hypoalbuminemia requiring hospitalization. The hospital course was complicated by pneumonia and sepsis, which resolved with antimicrobial therapy. Skin biopsies were consistent with nutritional deficiency. Further studies ruled out necrolytic acral erythema, necrolytic migratory erythema, pellagra, and biotin deficiency. Zinc levels were low and antitransglutaminase and anti-endomysium antibodies were positive, supporting the diagnosis of CD with zinc deficiency. The patient received a gluten-free diet and zinc supplementation, which resulted in resolution of her gastrointestinal and cutaneous symptoms within 4 weeks.

Commercial support: None identified.

3913

Acquired zinc deficiency in parenteral nutrition

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Case summary: A 42-year-old female was admitted for a painful rash. Her history is notable for myopathic dysmotility and recurrent intestinal obstructions requiring multiple abdominal surgeries, resulting in total parenteral nutrition (TPN) dependence. The patient reported a chronic erythematous rash of her hands and feet, with acute worsening and development of painful bullae three weeks prior to presentation. Lesions were unresponsive to prednisone, clindamycin, topical antibiotic, corticosteroid and antifungal ointments. Physical examination revealed symmetric flaccid bullae and shallow erosions with hemorrhagic crusting on the bilateral hands, shins and dorsal feet. Perioral erythema and white patches on the buccal mucosa were also noted. Bullous disorders including epidermolysis bullosa acquisita, pemphigus vulgaris, paraneoplastic pemphigus, and infection were suspected and a skin biopsy was performed. Histopathology revealed psoriasiform hyperplasia with prominent ballooning degeneration and hyperkeratosis/parakeratosis with necrotic keratinocytes, suspicious for a nutritional deficiency. Laboratory testing showed reduced serum zinc level of 11 mcg/ml (normal range, 55-150 mcg/ml) and alkaline phosphatase level of 22 U/L (normal range, 31-103 U/L), thus confirming the diagnosis of acrodermatitis enteropathica. Skin lesions improved days after initiation of zinc supplementation.

Discussion: Acrodermatitis enteropathica (AE) may be inherited as a rare autosomal recessive defect in zinc absorption or be acquired secondary to insufficient dietary zinc intake or malabsorption. Vegetarians, alcoholics, premature infants, and the malnourished are at increased risk of dietary zinc deficiency. While less common, patients with a recent history of parenteral alimentation are also vulnerable. AE is classically characterized by alopecia, diarrhea, and skin lesions affecting the extremities, perineal, and periorificial areas. Clinical presentation can vary widely, and bullous lesions may rarely be seen. Early diagnosis of cutaneous lesions with skin biopsy and laboratory testing is essential and can lead to significant reduction in zinc deficiency related morbidity and mortality. Histopathologic features of nutritional deficiencies include cytoplasmic pallor, vacuolization, ballooning degeneration and keratinocyte necrosis. Decreased serum levels of zinc and alkaline phosphatase—a zinc-dependent enzyme—can confirm the diagnosis. Prompt treatment with zinc supplementation leads to rapid clinical improvement, even before significant change in serum zinc levels is seen. When evaluating patients with bullous lesions, dermatologists should suspect zinc deficiency, especially in patients on TPN, to ensure early diagnosis and prevention of deficiency related complications.

Commercial support: None identified.

2404

Acrokeratosis paraneoplastica in the setting of early pancreatic adenocarcinoma

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Importance: Acrokeratosis paraneoplastica, or Bazex syndrome, is a rare cutaneous paraneoplastic syndrome associated with internal malignancy especially squamous cell carcinoma of the upper aerodigestive tract. Nevertheless, atypical malignancies have been reported.

Observations: We report the case of an 82-year-old previously healthy white female who presented with acute desquamation and pruritus of her hands and feet. A biopsy was performed to rule out Bazex syndrome and revealed apoptotic keratinocytes at all levels of the epidermis. Prompted by clinical suspicion for Bazex syndrome and corroborating histology, internal imaging and diagnostic testing revealed a pancreatic adenocarcinoma in situ. Pancreatoduodenectomy was performed without complications, and the patient's skin findings subsequently resolved.

Conclusions and relevance: This report is, to our knowledge, the first case of Bazex syndrome associated with adenocarcinoma of the pancreas. Although there is growing literature on this rare paraneoplastic syndrome, increasing clinical awareness for atypical presentations of malignancy may improve cancer outcomes in patients.

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3066

AIDs patient with one lesion but two problems: Kaposi sarcoma and bacillary angiomatosis

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A 44-year-old white man presented to dermatology clinic for a painful, hemorrhagic lesion on his left foot. Three months prior, he was diagnosed with AIDS after he was admitted to the hospital for cryptococcal meningitis and was found to have a CD4 count of 10. During this hospitalization, the patient was found to have violaceous patches and plaques on his feet and groin suggestive of Kaposi sarcoma. He was started on antiretroviral therapy (ART). The violaceous plaque on his left foot progressed to have a hemorrhagic nodule within it that easily bled. His infectious disease physician started him on cephalexin with no improvement of the lesion. The nodule continued to grow, and the patient was referred to dermatology where a shave biopsy was performed. On one side of the biopsy specimen the histology revealed marked edema in the dermis with an increased number of dilated vessels. Mixed inflammation was present, and rare purple hazy aggregates of bacteria were identified that were characteristic of bacillary angiomatosis. On the other side of the biopsy specimen there was an infiltrative vascular proliferation in the dermis composed of spindled mitotically-active endothelial cells with slit-like and sieve-like spaces filled with blood. These cells expressed human herpesvirus 8 (HHV-8) by immunohistochemistry and represented a component of Kaposi sarcoma. Kaposi sarcoma is a chronic, systemic angioproliferative disorder which is caused by HHV-8. Bacillary angiomatosis is also a vascular disorder that affects HIV infected individuals. Bacillary angiomatosis is caused by the bacteria, Bartonella henselae, and similar to Kaposi sarcoma, usually occurs in HIV patients with low CD4 counts. Most physicians agree that Kaposi sarcoma and bacillary angiomatosis are caused by two distinct disease processes and even though these diseases cause similar looking lesions, they usually present on patients as two separate lesions. Because they are both vascular proliferative disorders caused by infectious processes some researchers have hypothesized that maybe there is some underlying association between these two diseases. However, the majority of the subsequent research has shown that the pathogenesis of Kaposi sarcoma is not related to bacillary angiomatosis. This case is unique in that Kaposi sarcoma and bacillary angiomatosis were found in the same lesion and it reminds physicians to be cognizant of this association when examining their patients.

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3766

An unusual case of tumid lupus mimicking pseudolymphoma in a Kuwaiti man with hyper-IgM syndrome

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A 23-year-old Kuwaiti man with hyper-IgM syndrome presented with an 8-month history of a violaceous facial plaque and a 12-month history of hair loss. Skin biopsy of the facial plaque performed in Kuwait was interpreted as pseudolymphoma. Cutaneous examination at our institution revealed red to purple, arciform soft plaques with sharp borders on the bilateral malar eminences, with less involvement of the nasal bridge and tip. Nonscarring, patchy alopecia was also observed. Twice daily clobetasol 0.05% ointment was started for suspected pseudolymphoma, with mild improvement after several days of therapy. Repeat biopsy was performed which showed a perivascular and periappendageal lymphocytic infiltrate without interface dermatitis. Special stains revealed a predominance of CD3+ T cells, interstitial mucin and basement membrane thickening. Clinical appearance, histopathology and extensive work-up led to a diagnosis of tumid lupus. Lupus tumidus erythematosus (tumid lupus) is a rare form of chronic cutaneous lupus erythematous. It presents as pink to purple, annular, nonscarring plaques without surface change in sun exposed areas. It has been reported in association with nonscarring patches of alopecia. Histopathologic features may mimic other conditions, including pseudolymphoma, lymphoproliferative disorders or infection. There have been reports of collagen vascular disease in the setting of hyper-IgM syndrome, but to the authors' knowledge, this is the first case of tumid lupus. This report highlights the importance for an increased index of suspicion for autoimmune phenomena in patients with primary immunodeficiency disorders, as well as the clinical and histopathologic overlap between tumid lupus and other skin diseases.

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3180

Approach to generalized morphea with pseudoexoftalmos, ectropion, and secondary lagophthalmos

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Introduction: Morphea is an inflammatory skin disease that primarily affects the dermis, but it can also involve subcutis, fascia and bone. Circumscribed and linear subtypes are the most common. Severe forms as generalized (GM) and pansclerotic (PM) correspond to less than 9% of morphea, they affect more than 2 anatomical sites with constitutional symptoms and complications in life style and biopsychosocial field. Ectropion with lagophthalmos is a common complication in PM, however, it is rare that affects patients with MG. We report the approach to a patient with MG with pseudoexoftalmos, ectropion and lagophthalmos.

Clinical case: A 35-year-old male patient with a disseminated skin disease to trunk and upper limbs characterized by well-defined sclerotic patches of 19 years evolution, with joint and muscle pain. Ten years ago the patient developed pseudoexoftalmos and ectropion with exposed tarsal conjunctiva of the four eyelids causing lagophthalmos (beginning with mild ectropion which progressed to a severe form) and causing social and professional repercussions. The patient had also vulgar vitiligo. The skin biopsy was performed and the result was consistent with deep morphea so we decided to put the patient on methotrexate 7.5 mg/week and we performed a surgical treatment of ectropion of the 4 eyelids with skin to improve the conjunctival thickening caused by chronic exposure.

Discussion: GM corresponds to 7% of all subtypes of morphea and is characterized by the presence of more than 4 indurated plaques over 3 cm in at least two or more anatomic sites as trunk and upper limbs. Face is usually not affected and has no circumferential involvement. The association with exophthalmos is very rare and is more common in PM and in the case of this patient was the main reason for surgical correction.

Conclusions: GM is an inflammatory disease that causes sclerosis patches; it has greater extent than circumscribed morphea besides its higher incidence of constitutional symptoms and autoimmune diseases. Nowadays the study of a patient with morphea must be complete ruling out associated diseases in order to begin early treatment to prevent secondary complications such as our patient.

Commercial support: None identified.

2692

Assessment of risk and use of prophylaxis for glucocorticoid-induced osteoporosis among Pacific Northwest dermatologists: A survey study

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Background: There currently exists a wide variation in dermatologists' approach to the assessment and management of glucocorticoid-induced osteoporosis (GIO). Previous studies show that many patients do not receive appropriate GIO prophylaxis despite guidelines for GIO-related fracture prevention. The goals of this study are to characterize Pacific Northwest dermatologists' practices surrounding use of glucocorticoids, GIO risk assessment and GIO prophylaxis.

Methods: A cross-sectional online survey of 22 questions was sent electronically to 392 dermatology providers of the Washington State Dermatology Association and Oregon Dermatology Society registries.

Results: 51 providers (13%) completed the survey. The majority of respondents do not prescribe moderate or high dose, chronic steroids (≥20 mg/day prednisone or equivalent for ≥2 months), with 55% reporting prescribing this fewer than 5 times in the past year and 37% never. Only half prescribe chronic lower dose steroids (>7.5 mg/day prednisone or equivalent for ≥3 months), 53% never/almost never recommend DEXA scanning prior to or after initiating glucocorticoids. For patients on long-term glucocorticoid treatment (>6 mo), 41% follow bone mineral density annually and 24% never. When given clinical scenarios and asked to assess risk of major osteoporotic fracture, respondents frequently overestimated risk (67-71%). The majority (>70%) prescribe/recommend calcium and vitamin D supplementation for patients on glucocorticoid therapy. 80% correctly identify bisphosphonates as appropriate GIO prophylaxis when given a high-risk scenario. However, when asked directly if one would prescribe bisphosphonates as GIO prophylaxis for a high-risk patient on long-term, moderate-high dose glucocorticoid therapy, only 49% responded always/almost always.

Conclusions: Our findings indicate that the majority of dermatologists in this survey region infrequently prescribe chronic, moderate-high dose glucocorticoids and tend to overestimate the risk of GIO when faced with a clinical scenario. Despite the tendency to inflate risk, relatively few providers would consistently recommend appropriate GIO prophylaxis measures. Limitations of our study include small sample size and potential sampling error. Our data suggest that a knowledge deficit exists and dermatology providers may benefit from continuing medical education regarding the GIO risk assessment and prophylaxis.

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2977

Blaschkolinear acute graft versus host disease

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A 30-year-old male with a medical history of multiple myeloma 25 days status post allogeneic bone marrow transplantation presented with a four day history of mildly itchy rash involving his arms, right thigh, and right side of his trunk. Review of systems was significant for profuse diarrhea. Physical exam revealed moderately well demarcated pink-violaceous slightly scaly thin papules coalescing into thin plaques following the lines of Blaschko on the right flank, back, and chest; the right lower extremity and bilateral upper extremities. Punch biopsy of the right upper extremity showed parakeratosis overlying spongiosis and vacuolar alteration of the basal layer with scattered dyskeratotic keratinocytes. There was a superficial perivascular mixed infiltrate of lymphocytes and eosinophils. He was diagnosed with acute graft versus host disease (GVHD) presenting in a Blaschkolinear distribution. The patient was started on 1 mg/kg/day of prednisone with rapid improvement in his rash. However, he then developed elevations in his liver enzymes and worsening diarrhea. He ultimately progressed to grade III acute GVHD necessitating long term inpatient care. Cases of lichenoid chronic GVHD presenting in a Blaschkolinear distribution have been described in the past; however, this is the first case to date of acute GVHD presenting in this distribution. The proposed mechanism for this phenomenon suggests underlying somatic mosaicism. The host's immunocompetent cells tolerate this cell clone until after transplantation when the clone is recognized as foreign by the donor's immune cells.

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3538

Chronic kidney disease associated pruritus impact on dermatological quality of life of patients with chronic renal replacement therapy in hemodialysis from the General Hospital of Mexico

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Introduction: Chronic renal failure affects different dimensions of the quality of life of patients, including physical, social, cognitive and sexual function, emotional well-being and perceptions of health. The presence of complications and morbidities is perhaps the most important factor that affects the quality of life of patients with chronic renal failure. The cutaneous manifestations associated with chronic renal failure are diverse, its prevalence varies between 40-100%, including pruritus defined as a skin sensation when moderate or severe triggers a more or less strong motor response, which is scratching.

Problem: Chronic kidney disease associated pruritus is a common presenting symptom in patients with chronic renal insufficiency replacement therapy in hemodialysis with incidence reported in 58%, it is important to identify its impact on quality of life dermatological to examine barriers and areas for improvement in care and effective management of this symptom from the point of view of patients.

Objective: To establish the relationship between chronic kidney disease associated pruritus and the quality of dermatologic life in adult patients with chronic renal failure in hemodialysis replacement therapy from the Nephrology Service of the General Hospital of Mexico.

Methodology: observational, correlational, cross-sectional study. Pruritus intensity was measured on a 10-point visual analog scale and the Itch severity score. Dermatological quality of life was examined with The Dermatology Life Quality Index (DLQI). Patients who met the criteria of International Forum for the Study of Itch. Chronic kidney disease associated pruritus was considered if they had either of the following conditions: (a) at least 5 episodes of itch during a period of two weeks, with the symptom appearing a few times a day at least a few minutes of duration; or (b) the appearance of an itch in a regular pattern during a period of 6 months, but less frequently than listed above. To ensure that patient's pruritus was associated to chronic kidney disease it had to appear at any time after the beginning of the hemodialysis, without evidence of any other active disease that could explain the symptom. Analysis of results. T test, exact Mann-Whitney U test, χ^2 test, and odds ratios. A value of $P < .05$ considered statistically significant.

Results: A consecutive series of 235 patients undergoing hemodialysis were enrolled. After informed consent, demographic data and data about hemodialysis and the presence and intensity of pruritus were collected. We included 235 patients, 54.8% were female and 45.2% male, with a mean age of 42.03 years (range 18-84 years, standard deviation + 16.54 years). As for the etiology of the renal failure, 42.35% was idiopathic, 32.18% was attributed to diabetic nephropathy, 6.38% to hypertensive disease of pregnancy, 4.68% to polycystic kidney disease, 3.82% to hypertensive nephropathy, lupus nephritis 2.55%, 2.12% to obstructive nephropathy (kidney stones, prostate cancer), renal hypoplasia 2.12%, 1.27% postinfectious glomerulonephritis, 0.8% to autoimmune diseases other than SLE, 1.68% from other causes. 14.88% of the patients had xerosis, 45.95% mild xerosis, 31.5% moderate 7.65% severe. According to visual analogue scale (VAS) the average reported score was 5.24 (SD + 2.51); the Itch Severity Scale average score was 7.97 (+4.23 standard deviation) and the dermatological quality of life was 6.25 (SD + 5.34). The intensity of the pruritus according to VAS in our study had an average of 5.243 ($P = .1114$) was found. According to the Itch Severity Score, the average was 7.97 points ($P = .03$); associated with moderate to severe pruritus, with 21 points the most severe pruritus. The dermatological assessment of the quality of life (DLQI), the average was 6.25. Correlation between the VAS and questionnaire dermatology life quality DLQI ($r = 0.47$, CI 0.36-0.57, $P < .0001$) between VAS and scale Itch Severity scale ($r = 0.61$, CI 0.53-0.69, $P < .001$) between the quality of life questionnaire DLQI and Itch Severity score ($r = 0.65$, CI 0.56-0.72, $P < .0001$). Pruritus intensity was significantly related to poor scores in all sub scales of the DLQI (symptoms, social function).

Conclusions: The presence of pruritus associated with chronic renal disease impairs the quality of life in dermatology adult patients with chronic renal failure in hemodialysis replacement therapy.

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3911

Cantu syndrome: Uncovering a rare gain-of-function ABCC9 gene mutation with possible therapeutic implications for the treatment of hypertrichosis

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A 7-year-old Hispanic girl presented to pediatric dermatology for evaluation of congenital hypertrichosis. Cutaneous examination revealed coarse facies and generalized hypertrichosis with thick dark hairs covering the preauricular cheeks, back, and upper and lower extremities. The patient also had a history of mild learning disability, scoliosis, and asymptomatic structural cardiac abnormalities (aortic root dilation and patent ductus arteriosus), raising suspicion for Cantu syndrome (CS). Therefore, whole exome gene sequencing was performed and revealed a heterozygous de-novo ABCC9 gene mutation (c.3460C > T (p.Arg1154Trp)) (chromosome 12p12.1), a mutation variant previously reported in association with four unrelated CS patients. Cantu syndrome (also known as hypertrichosis-osteochondrodysplasia-cardiomegaly syndrome) is an extremely rare autosomal dominant disorder. Patients typically present with generalized congenital hypertrichosis, macrosomia at birth, macrocephaly, coarse facial features, cardiomegaly, skeletal abnormalities, and developmental delay. Reported cardiac abnormalities include cardiac enlargement, concentric hypertrophy of the ventricles, pulmonary hypertension, pericardial effusion, patent ductus arteriosus, and bicuspid aortic valves. Aortic root dilatation, observed in our patient, has not been previously reported in the literature. Many cases of CS are due to heterozygous ABCC9 gene mutations. These mutations are thought to confer an activating mutation in SUR2, a subunit constituent of the sulfonylurea ATP-regulated potassium channel, leading to over-activation of the channel. Of note, sulfonylureas antagonize SUR2, and in follicular keratinocytes, this activity results in shortening of the anagen phase in cultured hair follicles. Based on this predicted molecular mechanism, topical sulfonylurea has been proposed as a potential novel treatment approach for hypertrichosis. Therefore, we are investigating and developing a compounded topical sulfonylurea as a possible safe, low-cost treatment for this patient's hypertrichosis.

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2754

Cutaneous findings and systemic associations in women with polycystic ovary syndrome

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Importance: There is limited understanding of the relationships between cutaneous findings, systemic abnormalities, and the fulfillment of diagnostic criteria in women suspected of having polycystic ovary syndrome (PCOS).

Objectives: Identify cutaneous and systemic features of PCOS that help distinguish women who do and do not meet diagnostic criteria.

Design: Retrospective cross-sectional study of a racially diverse referred sample of women seen at a multidisciplinary PCOS clinic over a 6-year period.

Setting: University of California San Francisco (UCSF) PCOS Multidisciplinary Clinic.

Participants: 401 women referred for suspected PCOS. 69% (N = 276) met Rotterdam PCOS diagnostic criteria while 12% (N = 48) patients did not. 11% (N = 46) had insufficient data to render a diagnosis. 2% (N = 7) were excluded. 6% (N = 24) refused the study. Main outcomes and measures: Comprehensive skin exam, laboratory testing, and transvaginal ultrasound.

Results: Compared to women who did not meet diagnostic criteria for PCOS, women who met criteria had higher rates of hirsutism (53.3 vs 31.1% [$P = .005$]) – with higher mean modified Ferriman-Gallwey (MFG) scores (8.6 vs 6.3 [$P = .001$]) – acne (61.3 vs 40.4% [$P = .004$]), and acanthosis nigricans (AN) (36.9 vs 20.0% [$P = .028$]). Cutaneous distributions also varied. Women who met PCOS criteria demonstrated more severe truncal hirsutism and higher rates of axillary AN. Among women with PCOS, the presence of hirsutism or AN was associated with higher rates of elevated free testosterone (43.9 vs 30.9% [$P = .041$] and 53.3 vs 27.0% [$P < .0001$], respectively) as well as a number of metabolic abnormalities, including insulin resistance, dyslipidemia, and elevated body mass index (BMI). Though the prevalence of acne was increased in women with PCOS, there were minimal differences in acne types and distribution between the two groups.

Conclusions and relevance: In the high risk population of women referred for suspected PCOS, there is a significant burden of cutaneous, reproductive, and metabolic abnormalities. Hirsutism and AN are the most reliable cutaneous markers of PCOS and require comprehensive skin exam to diagnose; when present, hirsutism and AN should raise clinical concern that warrants further diagnostic evaluation for metabolic comorbidities that may lead to long-term complications. Acne and androgenic alopecia (AGA) are not reliable markers of biochemical hyperandrogenism in this population.

Commercial support: None identified.

2956

Cutaneous xanthomas in homozygous familial hypercholesterolemia: A 12-year follow-up

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Homozygous familial hypercholesterolemia (HFH) is an autosomal dominant disease caused by mutations in the low-density lipoprotein (LDL) receptor. The prevalence is 1 case per 1 million persons. HFH is clinically suspected on the basis of extremely elevated (LDL) serum cholesterol and xanthomas presenting in the first decade of life. A 7-year-old previously healthy boy presented with a 2-year history of multiple asymptomatic yellowish nodules on the extensor surfaces. The examination revealed multiple 5 mm-4 cm coalescing yellow nodules on the elbows and knees (tuberous xanthomas). Skin-colored, 2-5 cm, firm, exuberant nodules were seen along the dorsa of the hands/feet and Achilles tendon (tendinous xanthomas). In addition, the patient had multiple 2-6 mm yellow plaques with a corrugated surface on the web spaces of the hands (intertriginous xanthomas). Skin biopsy from a nodule on the knee showed dermal collections of foamy histiocytes, consistent with xanthoma. Subsequent blood tests revealed elevated total cholesterol of 740 mg/dL and LDL of 650 mg/dL; high-density lipoprotein (HDL) and triglycerides were normal. The patient was referred to a pediatric cardiologist. Parents and sister were heterozygous on screening. The patient was treated with atorvastatin and ezetimibe. However, these measures were insufficient and LDL apheresis was scheduled every 15 days with incomplete decrease on LDL serum cholesterol. After 12 years of follow-up, partial regression of xanthomas was noted. Recently, mipomersen, a novel drug approved by the FDA on 2013 for the treatment of HFH, has been initiated. HFH can present early in life with cutaneous xanthomas of multiple types, including tendinous, tuberous and xanthelasma. Although rare, intertriginous xanthomas of the finger webs are pathognomonic for HFH. Without treatment, most individuals die of atherosclerosis by 30 years of age. Treatment involves diet, lifestyle changes, lipid-lowering drugs, LDL apheresis or liver transplantation. Dermatologists play a key role in the diagnosis and should maintain a high index of suspicion.

Commercial support: None identified.

2798

Dermatology consultations significantly contribute to efficient care of hospitalized patients: A prospective study of dermatology inpatient consults at a tertiary care center

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Background: Cutaneous findings are common in hospitalized patients, but are frequently missed or misdiagnosed by admitting teams. Inpatient dermatology consultations provide an important help in diagnosing and managing these conditions. However, few studies have described dermatology inpatient consultations and their effect on patient care.

Objective: Describe the inpatient dermatology consultations at a large tertiary care center.

Methods: We prospectively collected information of 691 consecutive dermatology consultations from November 2013 to November 2014.

Results: Patients ranged in age from newborns to 97 years old. Dermatology consults were requested on average 3 days (standard deviation = 1.06) after admission or onset of cutaneous complaint. Consults were requested mostly by internal medicine (45%), surgery (12%), hematology/oncology (9%), and pediatrics (7%). Majority of consults were requested for presence of a rash (60%). Other common reasons for consult requests were presence of skin lesions (12%), ulcers (11%), blisters (5%), and cellulitis (3%). Only 6.5% of consultations were requested within 24 hours of appearance of cutaneous findings. Prior to dermatology consultation, 70.3% of patients did not receive treatment for their cutaneous findings. The most common diagnoses were drug rash and contact dermatitis. The majority (59%) of consults were for conditions limited to the skin as seborrheic keratosis, basal cell carcinoma, and squamous cell carcinoma, whereas 41% of consults were requested for complex dermatologic conditions potentially associated with systemic disease as psoriasis and vasculitis. Biopsies confirmed 71.7% of the initial bedside diagnoses by the dermatology consultation team. Overall, dermatology consultations resulted in treatment change in 566 of 691 cases (81.9%). Notably, dermatologic consultations resulted in significantly more ($P < .01$) treatment changes in complex cutaneous conditions potentially associated with systemic disease (97% treatment changes) as compared to simple cutaneous conditions limited to the skin (72% treatment changes).

Conclusion: Common skin diseases were responsible for most dermatology consultations. Most patients were not treated for their cutaneous conditions prior to dermatology consultation. Overall, dermatology consultations resulted in treatment changes in majority of cases.

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2447

Cutaneous metastasis from colonic adenocarcinoma: Mimicker of infectious etiology

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Cutaneous metastasis has been estimated to occur in 0.6% to 10.4% of patients with primary malignancy. Recognition of cutaneous metastasis is of importance due to its clinical and prognostic implications, often requiring a high index of suspicion. Dermatologists and dermatopathologists should maintain this high index of suspicion as cutaneous metastasis may be the first clinical sign of an otherwise unrecognized visceral malignancy, presenting initially in 3% of men and 6% of women. It may also represent recurrence after treatment of a primary tumor. The clinical presentation and appearance of cutaneous metastasis is variable, often causing delay in appropriate diagnosis and proper treatment. Herein, we present a case of cutaneous metastasis from colon adenocarcinoma mimicking an infectious etiology. Below, we highlight the different clinical presentations of cutaneous metastasis from adenocarcicnoma, its characteristic histopathology and immunohistochemical patterns as well as a brief summary of treatment options.

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Dermatomyositis and malignancy: A proposal for evidence-based malignancy screening guidelines

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Background: Recently, metaanalyses confirmed that dermatomyositis (DM) patients have increased risk of ovarian, breast, lung, colorectal, cervical, bladder, pancreatic, nasopharyngeal, and renal cancer. However, there are no guidelines for malignancy screening among newly diagnosed DM patients.

Methods: A Medline search of studies published between May 2000 and April 2015 search was performed using the terms "malignancy," "meta-analysis," "predictors of malignancy," "malignancy imaging," "malignancy detection," and "malignancy screening" in combination with "dermatomyositis." Applicable cancer screening guidelines were also reviewed.

Results: At time of diagnosis, all DM patients should undergo a thorough history, review of systems, and physical examination. Additionally, based on published screening guidelines for malignancies confirmed to occur at increased rates in DM, patients should be screened with low-dose chest CT for lung cancer and by colonoscopy for colorectal cancer. Female patients should be screened with a Pap smear for cervical cancer, with CA-125 blood testing and transvaginal ultrasound for ovarian cancer, and with mammography for breast cancer. Screening for esophageal cancer with upper endoscopy, pancreatic cancer with abdominal MRI/MRCP, renal cancer with abdomen/pelvis CT or abdomen MRI, and bladder cancer with cystoscopy should be performed only in cases of high clinical suspicion or if symptoms consistent with these malignancies are present. Although DM is strongly associated with nasopharyngeal carcinoma, only patients from endemic areas or with associated symptoms should be screened with MRI of the sinuses. Although there are reports of DM associated with numerous other malignancies, these associations were not confirmed in metaanalyses. Thus, we recommend screening for other malignancies only in cases of high clinical suspicion or if associated red flag symptoms are present.

Conclusion: Based on the literature, high priority malignancies for screening newly diagnosed DM patients are lung, ovarian, colorectal, breast, cervical, bladder, pancreatic, esophageal, renal, and nasopharyngeal cancers. Screening for other malignancies may be warranted but should be guided by clinical suspicion and findings. Guidelines for appropriate cancer screening of newly diagnosed DM patients will improve standardization of care, improve resource utilization, and improve identification of potentially treatable cancers in patients with paraneoplastic DM.

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3559

Diffuse papulonodules: A rare presentation of leukemia cutis

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A 42-year-old white female patient with new-onset fatigue and a diagnosis of leukemia of unknown type, presented with a one-month history of largely asymptomatic, scattered, indurated, flesh-colored to violaceous papules and nodules on the bilateral cheeks, forehead, scalp, neck, central upper and lower mid-back, and lower abdomen. The white count was normal with increased metamyelocytes and blasts. A strikingly increased serum lactate dehydrogenase and urine β-2 microglobulin was also detected. Punch biopsy of a lesion on the right lateral mid-back confirmed leukemia cutis. Immunohistochemical stain reaffirmed CD33 positivity consistent with bone marrow biopsy results for acute myeloid leukemia (AML) with complex karyotype, aneuploidy of chromosome 8, myelodysplasia related changes, and 66% blasts. Bone marrow aspirate also showed positivity for HLA-DR, CD33, CD4, CD64, CD123 (partial), CD56 (partial), CD38, CD36 (partial), CD15 (partial), CD184 (partial), CD49b (partial) and myeloperoxidase. Leukemia cutis is a rare manifestation of hematologic malignancies with an estimated incidence of 3% in the population of patients diagnosed with leukemia. This condition usually portends a poor prognosis in the setting of acute leukemia, as it signifies extramedullary involvement. Leukemia cutis has variable clinical presentations; the most common is flesh-colored-to-violaceous papules, nodules, or plaques. Other presentations include those resembling figurate erythema, guttate psoriasis, erythroderma, stasis dermatitis and ulcers. Skin biopsy and immunohistochemical staining are crucial in confirming the diagnosis. Aneuploidy of chromosome 8 has been associated with an increased incidence of leukemia cutis in AML patients, and increased levels of LDH and/or β-2 microglobulin tend to correlate with worsening overall prognosis. Our case is unique in that the patient had numerous papules and nodules diffusely over her head and neck, as well as scattered lesions on the trunk and extremities. This patient's clinical presentation and diagnosis reminds clinicians to keep a high index of suspicion for leukemia cutis in the setting of acute-onset papulonodular eruptions.

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3758

Elastosis perforans serpiginosa: dermoscopic features

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Elastosis perforans serpiginosa (EPS) is a perforating disease characterized by transepidermal elimination of elastic fibers. We present a case of acquired EPS and its dermoscopic features. A 64-year-old female presented with multiple annular, erythematous and keratotic papules with comedo-like structures, arranged in a serpiginous pattern. The lesions were localized on the face, neck, trunk and forearms. Dermoscopy revealed a milky red background, the presence of comedo-like structures within grey structureless linear areas and a peripheral white collarette. Neurologic exploration was normal. Her medical record was positive for systemic hypertension treated with losartan. These papules appeared 6 months before her consult and slowly increased in number. A superficial skin scraping with potassium hydroxide was negative for fungal structures. The differential diagnoses included elastosis perforans serpiginosa, granuloma annulare and sarcoidosis. Histopathology revealed a perforating canal containing elastotic material, keratin, and inflammatory debris, as well as a granulomatous infiltrate. The biopsy confirmed the diagnosis of elastosis perforans serpiginosa. In this case dermoscopy was a very useful tool which aided in the correct diagnosis. We observed dermoscopic structures not reported previously. To our knowledge there is only one case report of dermoscopic features of elastosis perforans serpiginosa, in which the authors described the presence of a central whitish structureless area with a crown of arborizing vessels. In conclusion, we report different dermoscopic features of elastosis perforans serpiginosa, which can aid in the differential diagnoses with granuloma annulare and sarcoidosis.

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3385

Erythematous evanescent morbilliform rash

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Background: Adult-onset Still's disease (AOSD) is a systemic inflammatory disorder that is characterized by fever, arthralgia, evanescent rash, leukocytosis, lymphadenopathy, and liver dysfunction. Histopathology reveals multiple individual or grouped necrotic keratinocytes in the upper epidermis and a dermal infiltrate of neutrophils.

Case report: A 59-year-woman with a history of type II diabetes mellitus, chronic kidney disease stage IV and a previous suspected history of AOSD, was transferred to Geisinger Medical Center from an outside facility for a suspected epidural abscess. Prior to her arrival, she had been empirically treated with vancomycin and cefepime. Upon arrival, she was found to have fever, leukocytosis, liver dysfunction, elevated ferritin, and a prominent eruption of scaly erythematous papules on the upper chest and arms. Blood cultures were negative, and bone marrow biopsy revealed no malignancy. A punch biopsy of one of the papules revealed mild epidermal spongiosis and conspicuous apoptotic/necrotic and dyskeratotic keratinocytes scattered in predominantly the mid to upper epidermis, and a mixed dermal infiltrate of lymphocytes and neutrophils, consistent with the diagnoses of AOSD. Antibiotics were stopped, and after failing a course of glucocorticoids, she was treated successfully with anakinra, with complete resolution of symptoms.

Discussion: AOSD has an estimated prevalence of 1.5 cases per 100,000-1, 000,000 population and has a bimodal age distribution with peak incidences between ages 15-25 and 36-45 years. Diagnosis is made using Yamaguchi's criteria: patients must meet at least 5 features, including at least 2 major criteria. Histopathology of the rash can be very useful in the diagnoses of AOSD, typically showing multiple individual or grouped necrotic keratinocytes in the upper epidermis and a dermal infiltrate of lymphocytes and neutrophils. First line therapies include nonsteroidal antiinflammatory drugs (NSAIDs), glucocorticoids and immunosuppressive drugs, mainly methotrexate. Recent reports demonstrate that anakinra is an option for patients that are resistant to typical therapies.

Conclusion: AOSD can be very challenging to diagnose; however using Yamaguchi's criteria and histological features of the rash one can be more certain of the diagnosis.

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Evaluating the clinical and educational impact of implementing an inpatient dermatology consult service and a dermatology lecture series in a university hospital: A longitudinal 5-year study

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Introduction: Dermatology has increasingly become an outpatient specialty, resulting in potentially complex dermatologic concerns being seen by nondermatologists. There has been a paucity of data regarding the impact of inpatient dermatology consult services. Current data show an exceedingly low concordance rate between the presumptive diagnosis by the referring specialty and the final diagnosis by a dermatologist. Current studies use primarily descriptive data pulled from an already-established program, calling to attention the number and types of consults called. However, extremely few studies follow the effects of a consult program from its inception, and thus cannot comment on the impact of the program in the long-term. Even fewer have analyzed the impact of a dermatologic educational intervention on the referring services. Our study is a retrospective chart review of all consults seen from the implementation of the consult program in 2008 versus 2012, as well as an assessment of the efficacy of a monthly lecture series given to the internal medicine resident team.

Objective: To determine the impact of implementing an inpatient dermatology consult program at a university hospital in combination with the intervention of a dermatology monthly lecture series on concordance rates between presumptive diagnoses by services requesting dermatology consults and final diagnoses by dermatologists.

Methods/design: Retrospective, cross-sectional chart review of all inpatient dermatology consults seen at a single academic university hospital (UCSF) in 2008 and in 2012. 575 patients in 2008 and 395 patients in 2012 were included in the chart review. These were defined as all patients greater than 13 years old admitted into the hospitals or to the emergency department, and for which a dermatology consult was requested and the patient seen by a dermatology attending.

Intervention: A formal teaching program was introduced with the inception of a formal inpatient dermatology consult program in 2008, in which monthly dermatology lectures were given to internal medicine residents. The monthly lecture topics were consistent from year to year.

Main outcomes and measures: Concordance rates between diagnoses made by services requesting dermatology consults and dermatologists. Diagnostic concordance rates were compared between requesting services who received the lectures and those who did not receive the lectures.

Results: Overall diagnostic concordance rates (20-24%; $P = .32$) remained consistent from 2008 to 2012. Concordance rates specifically for diagnoses covered in lecture topics (43%-56%) were significantly higher than for diagnoses not discussed in the lecture series (10%-14%) in both 2008 and 2012 for all consulting services, regardless of their participation in the lecture series ($P < .001$).

Conclusions: There are two main conclusions our study is able to show. First, our inpatient dermatology consult service has shown low concordance rates between the presumptive diagnosis made by the referring team and the final diagnosis made by a dermatologist, in both 2008 (23% concordance) and in 2012 (20% concordance). These results are consistent with the low concordance rates reported in previous studies at other institutions. This suggests a continued need for inpatient dermatology consult services, which is relevant in a time when dermatology is increasingly becoming an outpatient specialty. Second, concordance rates are consistent between both lectured and nonlectured teams in 2008 and in 2012. These data suggest that there is no learning effect from the lectures. One possible explanation could be that the lecture topics are topics that residents already have prior knowledge about. However, interestingly the top misdiagnosed conditions (drug rash, HSV, vasculitis, stasis dermatitis, etc) were topics that were indeed lectured on. This suggests that we are in fact lecturing on the most commonly misdiagnosed conditions, and that perhaps the selection of lecture topics are not the root of the issue. An alternative explanation for the consistent concordance rates between the lectured and nonlectured teams despite the educational intervention is that didactic teaching is not an effective methodology. This suggests that other educational methods should be explored instead, such as quizzes, required online modules, or hands-on engagement. Recent literature suggests that interactive methods could have a more positive impact on professional practice and in some situations, health outcomes. To our knowledge, our study is one of the first to study inpatient dermatology services longitudinally with an educational intervention. The low concordance rates and the lack of a learning effect from monthly lectures suggest a continued need for inpatient dermatology services as well as a need for new, alternative methods to teach dermatology to nondermatologists.

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2464

First report of mesalamine (5-aminosalicylic acid) as the causative agent in a case of acute generalized exanthamous pustulosis

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Acute generalized exanthamous pustulosis (AGEP) is a rare eruption of nonfollicular sterile pustules on a diffuse background of erythema and edema, commonly associated with fever and leukocytosis. Antibiotics are implicated in most cases; however, other drugs have been reported to cause AGEP. We report a case of a 73-year-old man with a history of ulcerative colitis who presented with a diffuse pustular rash, renal failure, transaminitis, and leukocytosis with neutrophilia. A week prior to admission, the patient was started on mesalamine to treat colitis. Upon admission, a workup including a skin biopsy was performed and was consistent with AGEP. Mesalamine was discontinued, and the patient's skin eruption, renal function, transaminitis, and leukocytosis subsequently improved. Mesalamine has an unknown mechanism of action; however, it is thought to be an antiinflammatory agent that blocks the production of leukotrienes and prostaglandins and is an immunosuppressant that increases the release of adenosine, which interferes with leukocyte function. The decrease in prostaglandin synthesis or deregulation of leukocyte function caused by mesalamine may be the etiology in this case. Discontinuation of the offending agent leads to resolution of AGEP, as it did in this patient.

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2975

Graves' hyperpigmentation: an uncommon cutaneous manifestation of autoimmune thyrotoxicosis

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Cutaneous dyspigmentation can cause significant distress in patients, especially in today's image-conscious world. While autoimmune adrenal insufficiency (Addison's disease) remains the commonest cause of hyperpigmentation due to systemic disease, there are sparse reports in the literature of hyperpigmentation associated with hyperthyroidism. A 27-year-old female white patient with Fitzpatrick type 2 skin was referred to our team with a 3-year history of increasing hyperpigmentation affecting the feet. Her medical history included autoimmune thyrotoxicosis (Graves' disease), originally diagnosed in 2009 but poorly controlled due to suboptimal compliance with medical therapy (carbimazole). Examination revealed a striking, symmetrical, well-demarcated, macular hyperpigmentation overlying the dorsal aspect of the feet, extending up to the ankles. There was similar well-demarcated hyperpigmentation involving the periungual region of the fingers and toes. The oral mucosa and palmar creases were spared. She was clearly anxious, with obvious fine bimanual tremor and a diffusely enlarged thyroid gland. Serial thyroid biochemistry over the preceding 30 months confirmed poorly controlled thyrotoxicosis with consistently undetectable TSH [0.30-4.50 mIU/L], fT4 > 90 pmol/L [10.0-22.0 pmol/L] and fT3 > 22 pmol/L [3.1-6.8 pmol/L]. Early morning cortisol (340 [170-540] nmol/L) and ACTH (15.0 [7.2-63.3] ng/L) were normal, effectively ruling out adrenal insufficiency. Skin biopsy of her feet was reported as showing scattered basal melanosis and hemosiderin-containing dermal macrophages (positive Perl's stain). Melanin stain (Masson Fontana) was negative in the dermis. Our patient's rash bears striking similarities to those of two cases of thyrotoxicosis-related rash previously reported by Banba et al (1999). In all cases, dark brown hyperpigmentation was present over the dorsum of the feet with histology showing basal melanosis and dermal hemosiderin deposition as in the current case. Hyperpigmentation responded poorly to thionamide treatment of the underlying condition, unlike the generalized hyperpigmentation of primary adrenal insufficiency, which improves markedly with glucocorticosteroid replacement therapy.

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Mucocutaneous manifestations in systemic amyloidosis at National Institute of Health Sciences and Nutrition, Mexico City. Experience in 13 years

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Background: Amyloidosis refers to the extracellular tissue deposition of fibrils of a variety of normal serum proteins. More than 20 distinct proteins are recognized to form amyloid fibrils, being the two most common causes AL (primary) and AA (secondary). In AL amyloidosis affected patients may have amyloidosis alone or in association with other cell dyscrasias (mainly multiple myeloma MM). AA amyloidosis occurs as a complication of a variety of chronic inflammatory conditions. The clinical presentation depends on organs affected. Skin manifestations are described classically as periorbital purpura, waxy thickening, easy bruising, nodules or plaques.

Objective: To describe skin and mucous membranes involvement in patients with systemic amyloidosis in a tertiary care center.

Design and population: A retrospective was conducted in patients with photographic support and skin biopsy-proved amyloid deposition from January 2003 through July 2015 in our center.

Results: Demographic: A total of 11 patients were included. Of the 11 (100%) patients, 10 (91%) were AL-associated and 1 (9%) was AA-associated. Of the AL amyloidosis subgroup 50% was MM-related. Six patients (55%) were men and 5 (45%) women. Topography: (a) head and neck was involved in all subjects, mainly periorbital (55%), followed by diffuse presentation (45%) and perinasal/perioral regions (9%), (b) trunk was affected in 36%, (c) limbs 18% and (d) mucous membranes in 45% (80% MM-related and 20% AA-associated), oral mucosa in 100% and genital mucosa 20%. Of those with mucosal involvement, tongue was affected in 100%, lips 60% and glans/coronal sulcus 20%. Morphology: Purpuric macules were seen in 73%, followed by papules, plaques and nodules in 18%, ulcers 9% and polymorphous lesions in 27%. Regarding mucous membranes, macroglosia was seen in 60%, nodules and infiltrated-plaques appearance in 40% and atrophy/ulcers in 20%.

Conclusions and discussion: Mucocutaneous involvement in systemic amyloidosis is frequent, and the dermatologist must be aware of the possible clinical presentations. The most frequent topography was head and neck, mainly periorbitally, but diffuse presentations were important too. Concerning to morphology, purpura was mainly observed, followed by polymorphous lesions, papules, plaques, nodules and ulcers. Interestingly, cases with mucosal involvement were almost all MM-related; this datum has not been previously reported in the literature. No cases were observed in subgroup without MM.

Commercial support: None identified.

3308

Necrolytic migratory erythema associated with neuroendocrine tumor

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Necrolytic migratory erythema (NME) is a rare paraneoplastic dermatosis. Its association with neuroendocrine tumors is widely described in the literature, which reinforces the importance of its recognition allowing early diagnosis. We report a case of a 56-year-old male patient presenting a 5-year evolution generalized and pruriginous rash, associated with asthenia and slight weight loss in the last year. Physical examination revealed pellagra-like rash localized on the inferior members, buttocks and abdomen. Investigation exams including biochemical, anatomopathologic and imaging tests were performed. Skin biopsy revealed psoriasiform dermatitis with necrolysis. This finding leaded to the diagnostic hypothesis of NME. Abdomen CT scan evidenced a soft tissue density nodular lesion measuring 5.0 × 4.8cm with calcifications and heterogeneous contrast-enhancement in the pancreatic tail, with no signs of metastatic disease. Patient was submitted to partial pancreatectomy and the histopathology was compatible with neuroendocrine tumor. Immunohistochemistry study was positive for PAX8, CK (AE1/AE3), CK8/18 (5D3), chromogranin, synaptophysin and Ki-67, confirming the diagnosis of neuroendocrine tumor grade 2. After resection, the cutaneous lesions and pruritus were completely resolved within 2 days. NME is frequently associated with neuroendocrine tumors, particularly glucagonoma, being one of the main components of glucagonoma syndrome. However, it may be related to other disorders such as inflammatory bowel disease, celiac disease, liver failure or other neuroendocrine tumors, including insulinoma. It is characterized by recurrent episodes of erythematous maculopapular rash associated with vesicles and flaccid bullae that evolve to erosions and crusting. Classically, these lesions favor the intertriginous areas, thighs and buttocks. Pain and itching are associated clinical features. The typical histologic findings are necrolysis of the upper epidermis with vacuolated keratinocytes. In the absence of metastatic disease, as reported in this case, complete tumor excision can be curative and allows resolution of NME in a short period, with only residual hyperchromia. Nevertheless, the majority of patients have metastatic disease at the time of diagnosis. Recognition of this rare dermatologic sign enables early diagnosis and treatment of neuroendocrine tumors.

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2477

Nonulcerative calciphylaxis: An updated approach

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Calciphylaxis is a potentially fatal derangement of calcium deposition in the intima of blood vessels, triggering vascular injury and occlusion that can result in catastrophic ulcerative disease. It is best known to affect patients with chronic kidney disease (CKD) and is more commonly found in conjunction with females, obesity, diabetes, and peritoneal dialysis. Subcutaneous, or nonulcerative, calciphylaxis is likely an early form of disease in which injury to the subcutaneous vasculature results in tender nodules and plaques commonly located on the lower extremities. Nonulcerative calciphylaxis is increasingly recognized among patients with CKD, and its early detection can lead to significantly decreased morbidity and mortality. Importantly, nonulcerative calciphylaxis carries a lower 6-month mortality rate (33%) than ulcerative calciphylaxis (80%), however, lesions located on the proximal extremities and trunk portend a poor prognosis in either form of disease. We present 3 patients with nonulcerative calciphylaxis, two of whom presented with lesions on the distal lower extremities and improved with IV sodium thiosulfate. One patient who presented with proximal lesions and sepsis died six days after biopsy. Each patient in our series had painful lesions present for months before diagnosis, and each reported improvement of pain with emersion in warm water. Diagnosis of calciphylaxis can be challenging, given the highly morbid condition of patients affected by the disease and the documented risk of necrotic ulcers following biopsy. We present mild alleviation of pain with warm water as a diagnostic clue to help differentiate calciphylaxis from mimickers such as cellulitis and peripheral vascular disease. We review an updated approach to nonulcerative calciphylaxis that acknowledges the hazard of tissue biopsy and examines bone scan as a diagnostic modality of choice.

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2749

Papules and nodules on the knees in an HIV-positive male

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Introduction: Erythema elevatum diutinum (EED) is a rare dermatosis, classified as chronic leukocytoclastic vasculitis, with a varied histopathology dependent on the age of the lesion.

Case report: A 39-year-old HIV infected male, with a CD4 count of 528, was referred for evaluation of skin lesions. The patient presented with periarticular, indurated, erythematous, papules and nodules in knees and elbows, associated with purpuric lesions in ankles. He also gave a history of recurrent fever, arthralgia and mild constitutional symptoms in the last month. The patient was also diagnosed of polyclonal gamma-globulinemia. A punch biopsy was made of the purpuric lesions and showed a leukocytoclastic vasculitis with eosinophilic necrosis of the epithelium. Systemic corticosteroids were initiated, but the lesions no showed improvement. Subsequent late stage lesions biopsies demonstrated characteristic findings of perivascular fibrosis and the diagnosis of nodular EED in a HIV patient was confirmed. Antiretroviral agents were initiated. Intralesional steroids and topical dapsone 5% gel were used, with resolution of the lesions.

Discussion: Histopathologically, features of leukocytoclastic vasculitis are found in early lesions, while a fibrotic replacement of the dermis with small persistent foci of vasculitis is typical of later lesions. The origin of EED is unknown, but is often associated with streptococcal infections, hematologic abnormalities and autoimmune diseases. EED is emerging as a specific HIV-associated dermatosis, 20 cases having so far been reported in the medical literature. The stimulus for EED could be due to immune-complex deposition in blood vessels triggered by the HIV infection itself, or other infections acting as antigenic stimulus. The nodular variant of EED is even rarer, but it evolves most often in HIV-positive individuals. Dapsone is the drug of choice, although it is not very effective in older fibrotic lesions. Intralesional, topical, and oral steroids, topical dapsone 5% gel, colchicine, chloroquine, tetracycline and surgical excision also may be tried.

Conclusions: Physicians should have an awareness of the presence of EED in those infected with HIV, as it may be the first clinical sign of the disease. EED has been considered a clinical simulator of Kaposi sarcoma (KS) and bacillary angiomatosis. This supports the importance of histologic diagnosis for all of assumed KS in patients with HIV.

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3686

Pityriasiform and psoriasiform dermatological toxicities associated with PI3K pathway inhibition in cancer treatment

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The phosphoinositide 3-kinase (PI3K) pathway—which has been found to have key regulatory roles in cell survival, proliferation, and differentiation— is among the most frequently altered pathway in human tumors. PI3K is an attractive target for inhibition as a therapeutic option for a range of cancers and has been an area of intense research, resulting in the first FDA-approved PI3K inhibitor, idelalisib, for leukemia and lymphoma in 2014, with many more being developed or more broadly used. Our aim is to report on a series of oncology patients, treated with novel PI3K inhibitors, who developed cutaneous toxicities that have not been previously reported in the literature. In the longitudinal series of patients evaluated, they were found to primarily develop pityriasiform or psoriasiform drug eruptions. In the majority of these cases, they were effectively treated with topical steroids alone with only one case requiring the addition of acitretin for control. The early identification of these cutaneous eruptions and initiation of treatment by dermatology allowed for the continuation of these critical cancer therapies for these patients with their oncologists. Awareness of these drug toxicities and appropriate management of these cutaneous toxicities is important in not only ensuring that life-sustaining anticancer therapies can be maintained but also improving the quality of life of these patients who are receiving these therapies. Finally, cataloging and classifying drug-induced cutaneous eruptions may potentially provide insight into the molecular mechanisms underpinning skin disorders with a similar clinical appearance to the cutaneous drug toxicities seen with these novel PI3K inhibitors.

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3392

Pustular acrodermatitis enteropathica-like eruptions in the setting of total parenteral nutrition

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Background: Zinc deficiency may be inherited or acquired. We report two cases of acquired zinc deficiency uniquely presenting as pustular eruptions.

Case descriptions: A 55-year-old man presented with a three week history of facial pustules. Six months prior, he was involved in a severe motor vehicle accident, resulting in dependence on total parenteral nutrition (TPN) due to an enterocutaneous fistula. Addition of topical and oral antibiotics did not slow progression. Initial biopsy showed suppurative folliculitis with Pityrosporum yeast; antifungal therapy was added but ineffective. Over days, pustules evolved to markedly crusted plaques in the beard and scalp. Skin graft donor sites developed psoriasiform plaques. Palms showed dusky erythema of the creases and periungual skin with pustules on the digits. Genital erosions developed, however they were confounded by leakage from his fistula to these dependent sites. Subsequent biopsies showed superficial epidermal pallor and broad zones of parakeratosis, suggestive of nutritional deficiency. Serologic zinc level was 7 mcg/dL (normal range 60-130 mcg/dL). Within the same year, a 53-year-old female suffered occlusion of her superior mesenteric artery, leading dependence on TPN for several months. Acute onset yellow crusting developed on her face as did pustules, which spread to her back, palms, and genitals. Zinc level was 13 mcg/dL. Both patients responded rapidly to increased zinc supplementation.

Discussion: Acquired zinc deficiency results from decreased intake, decreased absorption, or increased elimination. Due to national shortage of injectable zinc at the time of diagnosis, these patients' TPN contained 1.3 mg/d of supplemental zinc. The suggested daily intake for patients is 3 mg/d and up to 12 mg/d with diarrhea or fistula losses. Both patients had decreased intake as a result of their TPN, and our first patient had additional losses through his fistula. Manifestations of zinc deficiency include diarrhea, alopecia, and a periorificial and acral cutaneous eruption that begin as eczematous plaques and progress into vesiculobullous, pustular, or erosive dermatitis. Our cases are unique in that they began as pustular eruptions with dermatitis noted later in progression.

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2696

Retrospective review of systemic steroid induced acne in breast cancer patients

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Cutaneous toxicities from chemotherapy are common and are a significant cause of morbidity in cancer patients. With the rapid development of new therapies with significant cutaneous toxicities, it is increasingly important for clinicians to be able to determine the cause of a rash. Although most physicians are aware of steroid-induced acne as a complication of systemic steroid administration in cancer patients, there are no published studies. A literature review demonstrated case reports of steroid-induced acne developing in patients treated for glomerulonephritis, Crohn disease and pseudotumor cerebri. For the retrospective and prospective studies, incidence rates were: 0.62% (8/1276) in surgery patients, 1.11% (2/179) in intralesional steroid knee injections and 3.9% (2/51) in spinal cord injury patients. We performed a retrospective chart review of breast cancer patients treated at the City of Hope National Comprehensive Cancer Center. Of 3848 patients with a diagnosis of breast cancer during the period 2009 to 2015, 1991 (51%) were treated with at least one cycle of chemotherapy. Of these patients 61 were given a diagnosis of "acne" or "steroid acne" by their treating physician based on billing codes. 10 patients were found to have explicit documentation of steroid-induced acne. All patients were female with a median age of 49 (range 36-56). Half of the patients had ER+/PR+ disease and 30% had triple negative breast cancer. Ninety percent of patients had early stage disease (I or II) and 70% developed steroid-induced acne after the first cycle of chemotherapy. Dexamethasone was implicated in all but one case. All regimens contained either docetaxel or paclitaxel. We report an overall incidence of systemic steroid-induced acne of 0.05% among breast cancer patients treated with at least once cycle of chemotherapy. These results suggest that breast cancer patients at highest risk for systemic steroid induced acne are on taxane-based regimens with early stage disease and are most likely to develop the reaction after their first cycle of chemotherapy.

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3810

Rocky Mountain spotted fever from the dermatology consultant's perspective

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Background: Rocky Mountain spotted fever (RMSF), the most lethal tick-borne disease in the US, is endemic to the continental United States, the highest incidence occurs in south central United States where 5 states, including North Carolina, collectively account for over 60% of reported cases. Furthermore, children less than 10 years old suffer the highest risk of fatal outcome from RMSF.

Objective: To review pediatric cases of RMSF seen by the dermatology consult service and evaluate the role of the dermatologists in the diagnosis and management of this disease.

Methods: A retrospective review was performed of all inpatient consults by the dermatology service at a tertiary care center in North Carolina from 2001 to 2011. Data collected included patient demographics, symptoms, pre- and postdermatology consult diagnoses, length of hospital stay, and final clinical outcome.

Results: A total of 3912 consults were made to the dermatology service. There were 6 confirmed pediatric cases of RMSF. Dermatology consults were requested from the general pediatric service and pediatric intensive care unit for patients ranging in age from 22 months to 10 years. There was a predominance of female and white patients. Antecedent tick exposure was identified in 4 of 6 cases. All 6 patients presented with initial symptoms of fever and rash. All consults to dermatology were made within 24 hours of admission and all patients underwent skin biopsies and/or direct immunofluorescence testing. Ultimately, 50% of the pediatric RMSF patients succumbed to infection during the same hospital stay. All fatalities occurred within 3 days of presentation and within 2 weeks of onset of symptoms. Additionally, all fatal cases of RMSF presented to our institution as transfers from local hospitals and 2 of 3 patients received empiric therapy prior to admission.

Conclusion: Despite being a well-understood disease, RMSF continues to induce significant morbidity and mortality. The fatality rate observed in this series was remarkably higher than any reported by the CDC or in any other literature. The extensive differential diagnoses of petechial rash and fever in the pediatric patient contributed to delays in diagnosis and initiation of empiric therapy. Early involvement of the dermatology consultant contributed to the prompt diagnosis of RMSF in pediatric patients presenting with skin findings, especially when differentiating RMSF from other etiologies of petechial rash with fever.

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Subcutaneous nodules with oily discharge

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An 89-year-old female presented with a one month history of skin lesions on her right ankle. She was being investigated for peritoneal carcinomatosis secondary to a metastatic neoplasia of unknown origin. Physical exam revealed three nonspecific violaceous subcutaneous nodules on the right ankle that were painful on palpation. Interestingly, during punch biopsy oily material was discharged from the biopsy site. A punch biopsy was performed which revealed mixed septal and lobular panniculitis with fat necrosis, ghost cells and calcium deposits compatible with pancreatic panniculitis. Amylase and lipase levels were later found to be elevated. The patient's medical condition quickly deteriorated and it was decided to pursue palliative care with no further investigations, she died a few days later. Although the precise nature of the neoplasia remained unknown, it can be assumed that the carcinoma was either of pancreatic origin or metastatic to the pancreas. This case serves as a reminder that pancreatic panniculitis is a rare form of panniculitis, associated with an underlying pancreatic condition with characteristic histologic findings. It can precede the detection of the pancreatic disease and therefore serves as an important marker of an underlying systemic disorder. Although the clinical finding of subcutaneous nodules are nonspecific, the discharge of oily material can serve a clue to the diagnosis even before biopsy results are available. Although the treatment is that of the underlying disease, octreotide can be attempted to inhibit the production of pancreatic enzymes.

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2790

Sun protection knowledge and educational practices of health care professionals involved in the care of organ transplant recipients

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Background: Skin cancers are the most common malignancy among organ transplant recipients (OTRs). It is estimated that within 20 years of transplantation, up to 70% of OTRs develop skin cancer. Of these, nonmelanoma skin cancers (NMSCs) are the most common cutaneous malignancies, and are related to ultraviolet radiation (UVR) exposure. In OTRs, NMSCs tend to be more aggressive and have higher recurrence and metastatic rates. Primary preventative measures are essential in modifying the risk associated with UVR exposure. Sun protection practices include daily application of sunscreen and sun avoidance behaviors. Health care professionals (HCPs) can directly impact lifestyle behaviors of OTRs; however, to date there are no published data on sun protection education practices of HCPs involved in the care of OTRs.

Objective: To evaluate sun protection knowledge and education practices of HCPs involved in the care of OTRs.

Methods: A self-reported online survey using the Survey Monkey questionnaire tool was nationally distributed to members of the Canadian Transplant Society. Data were collected from members who provided informed consent. 40 survey questions assessed knowledge in accordance to the guidelines endorsed by the International Transplant Skin Cancer Collaborative and the Canadian Dermatology Association. Data was collected to evaluate six areas: (1) educational practices, (2) knowledge of skin cancer in OTRs, (3) knowledge of sunscreen, (4) knowledge of tanning beds and UVR, (5) knowledge of screening practices, and (6) knowledge of photosensitivity agents.

Results: Data were obtained from 66 HCPs. 71.2% of respondents reported never having received training regarding skin cancers or sun-protective practices for OTRs. 60.6% of respondents correctly selected squamous cell carcinoma as the most common cutaneous malignancy in OTRs; however, only 31% correctly identified how much more likely OTRs were to develop a SCC compared to nontransplant recipients. 46% correctly responded that sunscreen should be reapplied every 2 hours, while 20% selected every 4 hours. Of nine medications listed, 5 of them were misidentified by more than 40% of participants as not having a risk for inducing photosensitivity.

Conclusions: Our results suggest that there is a role for educating HCPs to improve sun protection counselling for OTRs. Education models could be developed to better provide accurate information that could positively alter lifestyle behaviors among OTRs.

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3346

Sweet syndrome: An epidemiological study of 20 cases in National University Hospital, Singapore

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Background: Acute febrile neutrophilic dermatosis, first described by Robert Douglas Sweet in 1964 has been termed Sweet syndrome. The pathologic hallmark of Sweet syndrome is the involvement of the dermis with mature neutrophilic infiltrates with edema of the dermal papillae and the papillary dermis. There exist many atypical forms of Sweet syndrome.

Objective: To evaluate the clinical associations as well as preponderance of unusual clinical as well as histopathologic features in National University Hospital, Singapore in and compare them with the data found on the literature.

Methods: This is a retrospective study of all the cases of Sweet syndrome over a 5.5-year period from January 2004 to May 2015. Data on their systemic disease was obtained from their medical records.

Results: 21 patients were identified, their ages ranging from 39 to 93. The mean age was 47. The female to male ratio was 1.3:1. 47% of patients had idiopathic Sweet syndrome while 42% had malignancy related Sweet syndrome which was most commonly associated with acute myeloid leukemia and one patient had drug-related Sweet which was secondary to azacytadine and vorinostat. Atypical clinical features occurred in 38% of the patients. 5 patients (23%) had neutrophilic dermatosis of the dorsal hands. 4 of these patients (80%) had an underlying malignancy; 2 had acute myelogenous leukemia, one had T cell lymphoma and one had metastatic non—small cell lung cancer. One patient had what was thought to be nonresolving abscesses which did not improve despite prolonged antibiotics. The painful pustular nodules resolved with steroids. Another patient presented with postauricular nodules associated with nonscarring alopecia. The lower limbs was the most commonly involved area (68%). Atypical histologic features occurred in half of the patients. 28% of the patients had the neutrophilic panniculitis subtype, while 19% had the histiocytoid variant and 4% had Sweet syndrome associated leukemia cutis. The histiocytoid subtype was most commonly associated with malignancy. Vasculitis was concomitantly seen in 3 patients. One patient presented with atypical clinical features with the concomitant presence of vasculitis and nodules with ulceration and vesicles with a varicella zoster–like appearance. 2 patients had neutrophilic infiltrate in the subcutis.

Discussion: The unusual histopathologic features were commonly encountered in our cohort of patients. Despite the female preponderance, the ratio of females to males in reported literature was 4:1 while the ratio in our study was 1.3:1. Previous studies have shown the upper limb to be the commonest site of Sweet syndrome, while this study shows a predominance of it in the lower limbs. This is the first time vorinostat has been implicated as a causative drug for Sweet syndrome. The epidemiology of Sweet syndrome in Singapore is unusual to the ones previously reported in literature.

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3457

The 'knife-cut' sign—Always consider Crohn's

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Background: Cutaneous manifestations occur in approximately 20-40% of Crohn's Disease (CD) patients. There is increasing recognition that CD could represent a multiorgan disorder whose clinical manifestations arise from epithelial barrier dysfunction at different sites.

Case: A 25-year-old Afro-Caribbean female was referred to the dermatology clinic with worsening exudative intertriginous erosions causing debilitating pain and recurrent infections. Past medical history included severe CD, which had necessitated a total colectomy at age 18. She had developed psychosis in response to prior steroid treatment, and displayed significant behavioral problems in addition. Physical examination was challenging, but revealed an obese individual with deep, sloughy linear erosions demonstrating the 'knife-cut' sign beneath the abdominal apron, in the inguinal creases, beneath both breasts, and around the natal cleft, where additional fleshy plaques were noted. Multiple skin swabs were negative for bacterial, candidal, and herpes simplex virus (HSV) infection. A general anesthetic was required to obtain a skin biopsy, which revealed noncaseating granulomatous inflammation. A diagnosis of metastatic CD was made jointly with colleagues in gastroenterology. Treatment with adalimumab was commenced during a prolonged in-patient admission, with a marked improvement in skin status after 6 weeks. She has not had any episodes of infection over the 6 months since commencement.

Discussion: The commonest cutaneous manifestations of CD involve direct extension of intestinal disease, giving features such as perianal skin tags, fistulae or fissures. Also common are nongranulomatous cutaneous reactions to active intestinal disease, such as erythema nodosum and pyoderma gangrenosum. However, the occurrence of noncaseating granulomatous lesions characteristic of CD at sites separate from the gastrointestinal tract is rare, and is termed metastatic CD. It can occur in both active and quiescent intestinal disease. Linear erosions constituting the 'knife-cut' sign is one such presentation, for which the differential diagnosis must always include HSV infection. Case reports have described some success with therapies including topical and systemic steroids, metronidazole, adalimumab and infliximab.

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The most common cutaneous drug reactions and culprit medications encountered on the dermatology consult service: A 5-year experience at a tertiary academic center

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Background: Cutaneous drug reactions are a common reason for inpatient dermatology consults. Few studies have characterized the types and frequencies of drug reactions encountered in the inpatient setting or the most common culprit medications. The purpose of this study is to analyze drug reactions evaluated by the dermatology consult service over 5 years at a tertiary academic institution and describe the most common reactions and etiologic agents.

Methods: Inpatient consults to dermatology from 2008-2012 were reviewed. Data were collected on patient demographics, consulting service, preconsult diagnoses, diagnostic tests, and postconsult diagnosis and management. All consults with a diagnosis of drug reaction were included in the analysis. For each drug reaction, the potential or definitive etiologic agent(s) were identified.

Results: Over 5 years, 2020 consults were made to dermatology. There were 376 (18.6%) consults for drug-related rashes, which were linked to 449 drugs. The mean age of patients was 51.8 years (range 6 months - 94 years), and 51.9% were men. Most drug reactions were seen on internal medicine and subspecialty services (77.5%), with hematology/oncology alone accounting for 27.4%. Biopsies were performed to establish the diagnosis in 52.4%. The overall accuracy of the consulting team was 30.3%. Among specific drug reactions, the most common were Stevens–Johnson syndrome/toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and erythema multiforme. Less common reactions were drug reaction with eosinophilia and systemic symptoms, urticarial drug eruption, bullous pemphigoid, Sweet syndrome, and fixed drug reaction. Nearly half of the drugs identified were antibiotics (47.0%), most commonly penicillins, vancomycin, and cephalosporins. Other classes of medications were antiepileptics and cardiovascular drugs including antiarrhythmic, diuretic, and antihypertensive medications. Etiologic drugs were unknown in 83 cases (18.5%).

Conclusion: In the inpatient setting, almost 1 in 5 consults to dermatology were for drug-related cutaneous eruptions, and most were from general medicine and subspecialty services. The diagnosis was changed by the dermatology consult team in 70% of cases. This large retrospective database allows for the identification and characterization of drug reactions that occur at lower frequencies, such as Sweet syndrome and fixed drug reactions.

Commercial support: None identified.

2806

The use of cyclosporine for Stevens–Johnson syndrome and toxic epidermal necrolysis: The University of Louisville experience

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Background: Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe cutaneous adverse reactions (SCARs) that are most commonly caused by a drug. SJS/TEN are rare and there are few randomized controlled trials regarding treatment. Management is typically supportive care in an ICU or burn unit. The use of systemic agents is controversial and there are only observational data regarding their efficacy. Some investigators have reported success with IVIg, corticosteroids, cyclosporine, etanercept and infliximab. We report four cases of SJS or TEN that were treated with cyclosporine.

Observations: Patient 1: A 23-year-old woman who presented with a one-day history of erythematous papules, vesicles and bullae on her face, conjunctival injection and oral erosions. Patient 2: A 77-year-old woman with a recent diagnosis of endometrial cancer who developed bullae on her face and arms after receiving IV contrast for a staging CT scan. She was initially treated with IV prednisone for 10 days prior to her transfer to our facility. Patient 3: A 62-year-old male who was transferred from another facility with a five-day history of erythematous macules and patches with desquamation on his arms, abdomen, and groin as well as erosions with hemorrhagic crusting on his face and oral mucosa. Patient 4: A 31-year-old male who presented with a tender erythematous plaques on his back erosions in his groin, perioral crusting and conjunctival injection. Respectively, the causes for the four patients were carbamazepine, IV contrast, trimethoprim/sulfamethoxazole and trimethoprim/sulfamethoxazole. The respective SCORTENs were 1, 5, 4 and 1. They were all treated with cyclosporine; the respective doses were 3 mg/kg/day divided twice daily for four days, 3 mg/kg/day divided twice daily with transition to comfort care only on day two, 3 mg/kg/day divided twice daily for four days, and 5 mg/kg/day divided twice daily for five days. Patients 1, 2 and 4 re-epithelialized on days 4, 5 and 4 respectively. Patients 1, 2 and 4 fully recovered.

Comment: Several retrospective studies of SJS/TEN have reported a decreased mortality rate with cyclosporine as compared to IVIg or systemic corticosteroids. The true effectiveness of all of these agents remains unclear, but there have been increasing reports of the efficacy of cyclosporine. We offer four more cases to add to the literature in which cyclosporine appears to have decreased the time to re-epithelialization and mortality.

Commercial support: None identified.

3874

Tofacitinib citrate alleviates alopecia universalis symptoms in recent case study

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Alopecia universalis (AU) is generally considered a variant of alopecia areata (AA). It is characterized as an organ-specific CD8+ T-cell dependent response that results in hair loss as a consequence of autoimmune disease and chronic hair follicle inflammation. Thus far, a reliable treatment has remained elusive, especially in the case of severe occurrences such as AU where whole-body hair loss is observed. To support the ongoing search for improved therapy, the promising small molecule kinase inhibitor tofacitinib was investigated. Tofacitinib is able to specifically target the immune response and avoid pleiotropic effects through the inactivation of the JAK1/3 pathway. Specificity is due to the limited expression of JAK3 to T-, B-, NK and mast cells. To assess the effectiveness of tofacitinib in alleviating AU symptoms, a patient diagnosed with AU was prescribed tofacitinib citrate at a dosage of 5 mg twice daily and observed for eight months. Beard growth was observed by three months of treatment. Hair growth throughout the entire body was established by six months of treatment. Scalp hair continued to grow longer and thicker, with the return of eyelashes and eyebrows by eight months of treatment. Although spontaneous remission of AU is a possibility, in this case, the chronology suggests that tofacitinib was successful in relieving AU symptoms in the absence of adverse side effects. With the accumulation of promising results for the use of tofacitinib in AA therapy, we recommend that further study be required to establish safety and confirm efficacy.

Commercial support: None identified.

3672

Toxic epidermal necrolysis–like presentation of acute cutaneous lupus erythematosus: A report of 2 cases

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Background: Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) can complicate the clinical course of lupus erythematosus. They represent disease flare in the absence of any invoking drugs. We report two previously-diagnosed patients of systemic lupus erythematosus (SLE) who presented with TEN-like acute cutaneous lupus erythematosus (ACLE).

Case reports: Patient 1 was a 36-year-old female diagnosed with SLE 8 years ago. She was noncompliant to her medications consisting of oral steroids, azathioprine, and hydroxychloroquine. She had stopped these medications for 2 months prior to presentation to us. Cutaneous examination revealed multiple atypical target lesions and skin detachment affecting 35-40% of body surface area. Lesions were distributed predominantly photodistributed. There was also severe oral mucositis. Investigations revealed a markedly elevated anti-dsDNA antibody titer compared with her previous values, hypocomplementemia, elevated ESR. Skin biopsy revealed apoptotic pan-epidermolysis. In patient management with oral steroids, photoprotection and supportive measures was done. She completely recovered within 2 weeks and was discharged in good condition. Patient 2 was a 25-year-old female diagnosed with SLE 1 year ago. She also had grade IIa lupus nephritis. She was regular on her treatment with oral corticosteroids, azathioprine, and hydroxychloroquine. She presented to the emergency department with fever and rash of 1 day duration. On further questioning, she admitted to discontinuation of her SLE medications for 15 days prior to presentation. Examination revealed multiple flat atypical target lesions on her face, neck, trunk, and extensors of upper limbs. On day 2 of admission sheets of the epidermis detached involving 50-60% of her body surface area. She also had oral mucositis. Her anti dsDNA antibody titers were markedly raised compared with her previous values. Skin biopsy revealed apoptotic pan-epidermolysis. She was treated with oral steroids along with supportive care and photoprotection. She recovered within 3 weeks.

Conclusion: Toxic epidermal necrolysis-like presentation of SLE is an uncommon manifestation of ACLE. The absence of invoking drugs, predominant photodistribution, and paucity of mucosal involvement along with serological parameters aid in differentiating it from drug-induced TEN. These lesions indicate activity of the underlying lupus and call for more aggressive management of patients.

Commercial support: None identified.

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3411
TPN-associated zinc deficiency

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Report of a case: A 49-year-old white man with a 3-month history of poorly differentiated small bowel adenocarcinoma presented with a 2-week history of crusted erosions of the face and perineal area. He recently had been diagnosed with T3NxMx adenocarcinoma and had undergone resection of a significant part of the small bowel. His abdominal wall defect was left open after surgery due to poor wound healing. After 10 weeks on total parenteral nutrition (TPN), he developed painful, burning, crusted erosions over most of his face with accentuation over the central face. Physical exam revealed eroded plaques over the lateral metacarpophalangeal joints and periungually. Bullous plaques were present on the knees and elbows. Additionally, there were two deep erythematous vesicles over the ventral interphalangeal joints of the thumbs. Other symptoms included generalized fatigue and four to six loose stools daily. Punch biopsies were performed of the right cheek and left elbow.

Pathology: The biopsy specimen from an erythematous erosion on the cheek showed epidermal pallor with parakeratosis and a diminished granular layer. The specimen from a pustular plaque on the left elbow exhibited focal full thickness epidermal necrosis, with neutrophils in the blister cavity. Both biopsies were compatible with zinc deficiency.

Clinical course: The patient's zinc level was found to be 29 mcg/dL (normal 56-134 mcg/dL) and alkaline phosphatase level was low, both of which were suggestive of zinc deficiency. Prior to his dermatology appointment, he was given IV copper and iron supplementation. After seeing dermatology, these were discontinued and the patient's TPN was supplemented with an additional 10 mg of zinc daily. Within 5 days of initiating zinc supplementation, the patient experienced significant improvement of his facial erythema and crusting, as well as his diarrhea and fatigue.

Commercial support: None identified.

3063
A case of folliculotropic mycosis fungoides masquerading as acne

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Background: Mycosis fungoides (MF) is a common form of cutaneous T-cell lymphoma classically characterized by conspicuous patches and plaques. Rarely, it exhibits predilection for hair follicle and eccrine gland infiltration. This is termed folliculotropic mycosis fungoides. This is a rare variant of MF with neoplastic T-lymphocytes infiltrating the hair follicles, often sparing the epidermis. This entity can have a variable clinical presentation presenting a diagnostic challenge. Here, we will discuss one clinical presentation.

Case report: A 50-year-old African American male presented with a 6-month history of new onset acneiform lesions on the face, postauricular scalp and chest. Previous therapy included clindamycin gel, benzoyl peroxide gel, and doxycycline with no improvement in the lesions. Dermatologic exam revealed cystic papules, pustules and comedo-like lesions in a random distribution on the face, postauricular scalp, and chest. Though the eruption appeared acneiform, the history as well as the clinical picture did not support a diagnosis of acne. Biopsy was performed for definitive diagnosis, and a diagnosis of folliculotropic MF was made.

Discussion: Folliculotropic MF can present a diagnostic challenge both clinically and histopathologically. Our patient was misdiagnosed as having acne and incorrectly treated for 6 months before biopsy aided in determining the correct diagnosis. According to a WHO consensus report, the prognosis of folliculotropic MF is worse than that of tumor stage classical MF with one study showing a 10-year survival rate of only 26%. The variability in the clinical presentation of folliculotropic MF can often lead to delays in diagnosis and treatment. Effort expended to diagnose this condition at earlier stages can help improve survival amongst patients. This case report will highlight clinical features that should alert the clinician in considering folliculotropic MF in case the disease entity follows an atypical course.

Commercial support: None identified.

LYMPHOMA, CUTANEOUS/MYCOSIS FUNGOIDES

3211
A bibliometric analysis of the 100 most influential publications in cutaneous T-cell lymphoma

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Background: Citation counts provide a useful measure for analyzing the scientific impact of a journal article. Older articles, however, have a higher likelihood of gaining more citations given the length of its citable period. Citation index circumvents this bias by dividing the total number of citations by the number of years since the article's publication. To date, the most influential publications in the multidisciplinary discipline of cutaneous T-cell lymphoma (CTCL) has yet to be formally identified. Herein, we report and analyze the 100 most cited publications in CTCL.

Objective: This bibliometric study aims to identify the 100 most cited articles within the CTCL peer-reviewed literature and analyze each article's individual characteristics.

Methods: The 100 most commonly cited articles between 1970 and 2015 were identified using the Web of Science electronic database. The terms cutaneous T-cell lymphoma, mycosis fungoides, and Sezary syndrome were used as search criteria. Each of the articles' citation count, citation index, journal source, publication year, article type, institution, and country of origin were compiled and analyzed.

Results: The 100 most commonly cited articles were published in 37 journals, with 18 articles published in *Blood*. These consisted of 76 original investigations, 22 reviews and 9 proceedings paper. Tied at second, the *Journal of the American Academy of Dermatology* and the *Journal of Clinical Oncology* each contributed 9 articles. The most cited article was published in the *Proceedings of the National Academy of Sciences of the United States of America-Biological Sciences* with a total of 3905 citations, while the article with the highest citation index at 129.82 was published in *Blood*. The year 2007, which tied with 1998, recorded the highest number of cited CTCL articles, partly due to the increased interest with histone deacetylase inhibitor at that time. The majority (72%) of the articles were from institutions within the United States, with the National Cancer Institute being the most prolific of institutions contributing 22 articles.

Conclusion: This study identified the most significant publications in CTCL within the last 45 years. Our results highlight the impact of colleagues' work and seminal advances in the realm of CTCL.

Commercial support: None identified.

3323
A case of ichthyosiform mycosis fungoides mimicking pityriasis rotunda

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Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL). Apart from the classic type of MF, many atypical variants have been reported, including hyperpigmented, hypopigmented, unilesional, follicular and ichthyosiform MF. Ichthyosiform MF is very rare and this represents 1.8% of all MF cases. A 73-year-old man presented with localized brownish scaly plaques involving trunk, back and both extremities over a period of 10 years. The lesions were round-shaped ichthyosiform plaques of varying sizes five to ten centimeters in diameter, clinically similar to pityriasis rotunda. Histopathologic examination revealed a compact orthokeratosis and hypogranulosis in the atrophic epidermis and atypical lymphocytes in the upper dermis showed epidermotropism and formed Pautrier microabscess. Immunohistochemically, the specimen showed a CD2+, CD3+, CD5+ with predominance of CD4+ but loss of CD7. From these clinical and histopathologic findings, he was diagnosed with ME Our case showed ichthyosiform eruption as the sole manifestation and clinically presented with large oval shape scaly plaques. Herein, we report a patient with a rare case of ichthyosiform MF clinically mimicking pityriasis rotunda.

Commercial support: None identified.

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3162
A case of primary cutaneous follicle center lymphoma in a young man

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A previously healthy 16 yo male presents with a 2 year history of an asymptomatic violaceous plaque on the chest. There was no epidermal change and lesion had never drained fluid. Over the course of 6 months, he developed satellite papules around the larger plaque. He had been systemically well throughout.

Investigations: Initial biopsy performed was reported as pseudolymphoma. Routine labs were unremarkable as was Borrelia serology. He saw plastic surgery and had an excisional biopsy of the larger plaque. Specimens were then sent for flow cytometry and for opinions in Austria and Vancouver. The final diagnosis was follicle center B-cell lymphoma (B cells were positive for CD10, and many of the cells are positive for BCL6). Further studies including more extensive blood work and CT scan of chest, abdomen and pelvis were all negative.

Diagnosis: On pathology, the dense infiltration of B cells with a germinal center phenotype is consistent with a diagnosis of primary cutaneous follicle center cell lymphoma and flow cytometry revealed an increased number of polyclonal B cells. Clinical and radiographic correlation confirmed this to be primary cutaneous disease.

Treatment: The patient was initially treated with intralesional corticosteroid injections when the diagnosis was pseudolymphoma. The satellite papules flattened out with the intralesional injections, but the larger plaque remained. After the repeat biopsy, he was seen by pediatric hematologic oncology and after case discussion it was decided to offer a trial of rituximab. The patient was agreeable and received rituximab infusion which was tolerated well. Following this, at a 6 month visit, all plaques and papules were completely flat and no longer violaceous. The lesions remain flat 2 years following infusion.

Conclusion: This is a case of a rare presentation of primary cutaneous follicle center lymphoma in an otherwise healthy young man who was treated successfully with rituximab.

Commercial support: None identified.

3844
A red head with a plethora of plasma cells

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The dermatology inpatient consult service was asked to provide assistance with a 69-year-old woman admitted for newly onset, diffuse, bright red plaques involving the entire scalp and forehead. The patient had a medical history of multiple myeloma treated one year prior with chemotherapy including bortezomib, cyclophosphamide and dexamethasone. Patient reported that the plaques began after she experienced minor trauma to the scalp, beginning as a small red "bump" and later progressing to large, infiltrative plaques. She denied any symptoms in these areas—no bleeding, pain, or pruritus. She was started on broad spectrum antibiotics out of concern for cellulitis, but these had not been helpful. A 4 mm punch biopsy was performed on the forehead. Pathology was consistent with plasma cell myeloma, with diffuse CD138 positivity, and predominant IgG kappa expression by in situ hybridization. Identical plasma cell abnormalities were subsequently found upon bone marrow aspirate. Subsequent treatment consisted of stem cell transplantation and chemotherapy. However, due to numerous comorbidities and generally poor health, the patient elected not to pursue further therapies and she died within three months. Cutaneous involvement in multiple myeloma is quite rare and typically occurs in late stage disease, reflecting an increased tumor cell burden. This is generally a sign of poor prognosis, and most patients die within 12 months after the diagnosis. Patients are often found to have extensive plasmacytic infiltration of multiple organs at the time of death. While various forms have been reported, IgG multiple myeloma is the most frequent subtype to present with cutaneous involvement. Cutaneous involvement in multiple myeloma is one of four known neoplasms involving plasma cells, which also include extramedullary plasmacytoma without multiple myeloma, solitary plasmacytoma of bone, and plasma cell leukemia. All four types may affect the skin, either by direct extension to the skin from underlying bone lesions or metastatic lesions without contiguous bone involvement. When treatment is indicated, therapy generally includes autologous bone marrow transplant, chemotherapy, radiation therapy, and surgical excision of plasma cell infiltrates when possible.

Commercial support: None identified.

2752
A rare malignancy not to miss: A case and review of extranodal NK/T-cell lymphoma, nasal type

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A 20-year-old previously healthy Hispanic male was admitted to the hospital with 5 months of increasing left facial and periorbital swelling and palatal necrosis beginning as a hole in his palate. Four months prior to admission, he was treated with broad-spectrum intravenous antibiotics for presumed cellulitis with sinus extension without improvement. He subsequently underwent several sinus debridements without clinical response. Intraoperative biopsies were nondiagnostic, notable only for necrosis and mild squamous cell dysplasia. Systemic steroids were administered to cover for possible autoimmune etiologics but he continued to deteriorate with increasing necrosis of the palate. Physical examination revealed left periorbital erythema and edema with overlying crusted plaques on the left medical canthus, left lower eyelid, and left alar crease. A 4 cm through-and-through defect was noted at the midline of the hard palate. Thorough laboratory work-up was notable for elevated Epstein–Barr virus (EBV) titers and negative for infection and immunology serology. PET/CT demonstrated extensive disease activity with FDG-avidity throughout the left periorbital region with extension into the nose and nasooropharynx. Histopathologic examination of a biopsy from the nasal ala demonstrated a dense CD3 and CD56 positive atypical lymphocytic infiltrate in the dermis. EBV-encoded small nuclear RNA stain was positive, consistent with a diagnosis of extranodal NK/T-cell lymphoma, nasal type. Extranodal NK/T-cell lymphoma, nasal type, is a rare peripheral T-cell lymphoma associated with chronic EBV infection. It occurs more commonly in Asia and Latin America due to a high rate of latent EBV infectivity. The clinical course of this disease is locally aggressive and can metastasize beyond the head and neck region. Patients often develop rapidly expanding tumors that cause ulcerations and necrosis. Clinically, the early cutaneous manifestations of extranodal NK/T-cell lymphoma, nasal type can be nonspecific and mimic an infectious or inflammatory process. Progression of disease despite therapy for the latter should remind the clinician to consider this rare diagnosis. Definitive diagnosis is established by histologic examination with appropriate immunohistochemical stains. When detected early, prognosis for localized disease treated with combination chemotherapy and radiation is good. Locally advanced or metastatic disease portends a poor prognosis.

Commercial support: None identified.

2344
Adult T-cell leukemia/lymphoma presenting as multiple necrotic ulcers and digital gangrenes

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Introduction: Adult T-cell leukemia/lymphoma (ATLL) is considered a malignancy of mature T cells associated with human T-cell lymphotropic virus-1 (HTLV-1). Skin eruptions are common presentations, affecting approximately 50% of patients. We aimed to present a case of ATLL with atypical clinical and histological manifestations.

Case report: A 57-year-old woman presented with multiple necrotic, ulcerative papules and nodules and digital gangrenes. Histologic examination revealed necrotizing granulomatous vasculitis. She had been treated as vasculitis for 1 year until atypical lymphocytosis with flower cells was observed in her peripheral blood. Laboratory investigation showed the patient and four of her five brothers were seropositive for HTLV-1. A diagnosis of ATLL with cutaneous involvement was made by the presence of HTLV-1 proviral DNA in the skin biopsy specimen.

Conclusions: ATLL may rarely present as multiple ulceronecrotic papulonodules and digital gangrenes. The cutaneous necrotizing granulomatous vasculitis in our patient could obscure the underlying malignancy. The findings in this case indicate that ATLL encompasses a varied clinical and histologic spectrum.

Commercial support: None identified.

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3613

Blastic plasmacytoid dendritic cell neoplasm: A case series

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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematologic malignancy derived from the precursors of plasmacytoid dendritic cells. BPDCN is an aggressive malignancy that presents with cutaneous lesions and may have bone marrow or leukemic involvement. We present 3 cases of BPDCN with various clinical manifestations to highlight the spectrum of disease presentation and its novel treatment with SL-401 (interleukin 3 receptor antibody). Patient 1, a 45-year-old woman, presented with a quarter-sized purple plaque on her left dorsal forearm. Biopsy was consistent with BPDCN with characteristic expression of CD56 and CD 123. Her bone marrow biopsy was negative for infiltration. Patient 2, a 72-year-old man, presented with a violaceous cutaneous eruption that involved his scalp, forehead, periorbital area bilaterally, and mid to upper back. Bone marrow biopsy demonstrated a high percentage of blasts and atypical cells. Flow cytometry of both the bone marrow and lymph nodes was consistent with a diagnosis of BPDCN. Patient 3, a 64-year-old man, presented with a 2 month history of numerous nodules with eschars on the trunk and face, with other smaller nodules on the bilateral upper arms, chest and back. Bone marrow biopsy revealed a high number of blasts and a skin biopsy demonstrated an atypical dermal lymphoid infiltrate, both consistent with a diagnosis of BPDCN. The flow cytometry was also positive for CD4, CD56, and CD123 supporting his presentation. All 3 patients were found to be candidates for SL-401, a targeted therapy directed at the interleukin-3 receptor which is highly expressed in BPDCN. Patient 3 has been receiving ongoing treatment, while patients 1 and 2 are in the process of trial enrollment.

Commercial support: None identified.

3644

Characterization of cutaneous lymphomas at dermatology department of Pontificia Universidad Católica De Chile (1986-2015)

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Introduction: Cutaneous lymphomas (CL) are an heterogeneous group of cutaneous neoplasms. High clinical suspicion and adequate histopathologic techniques are very important for a correct and timely diagnosis to prevent disease progression.

Objective: To analyze epidemiologic, clinical and histopathologic features of patients with diagnosis of primary and secondary CL at Pontificia Universidad Católica de Chile (PUC).

Patients and methods: Clinical cases, demographic characteristics and histopathology of patients with diagnosis of primary and secondary CL at PUC between 1986 and 2015 were analyzed.

Results: 199 cases of primary (169 CTCLs and 30 CBCLs) and 21 cases of secondary CL were found. 66.2% of CTCLs were mycosis fungoides (MF), 16.5% lymphomatoid papulosis, 4.1% unspecified cutaneous peripheral T-cell lymphomas, 3.6% Sézary syndrome, 2.4% subcutaneous panniculitis-like, 2.4% NK/T-cell lymphomas, 2.4% primary cutaneous anaplastic large cell lymphomas, 1.8% pleomorphic lymphomas and 0.6% gamma/delta T-cell lymphomas. 59.8% of MF were classical, 24.1% hypopigmented, 12.5% folliculotropic, 1.8% pagetoid reticulosis, 0.9% palmar-plantar and 0.9% syringotropic. Patients with hypopigmented MF had mean age of 18 years compared with 54 years in classical MF cases. Patients with folliculotropic MF had the worst prognosis in MF group, evolving with recurrences and needing more than one treatment modality. 63% of CBCLs were marginal zone B-cell lymphomas, 20% follicle center lymphomas and 17% diffuse large B-cell lymphomas (leg type). 62% of secondary CL were NHL, 28% adult NHL associated with HTLV-1, 5% HL and 5% leukemia cutis.

Conclusion: This casuistic shows an idea of incidence and epidemiology of CL in Chile and Latin America. Incidence of CL is increasing and at an earlier age. Most frequent CL was MF with an important proportion of hypopigmented MF in young patients. We observed a higher proportion of marginal zone B-cell lymphomas than reported in literature.

Commercial support: None identified.

2791

Cutaneous T-cell lymphoma misdiagnosed as lipodermatosclerosis

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Background: Lipodermatosclerosis is an inflammation of subcutaneous fat of the lower legs due to chronic venous insufficiency which is classically manifest as an "inverted champagne bottle." Mycosis fungoides (MF) is a T-cell lymphoma primarily of the skin that manifests as patches, plaques, tumors or erythroderma. Occasionally, MF can mimic a pigmented purpuric dermatosis. Herein, we describe an obese woman with a 2 year history of a persistent indurated plaque on the right calf misdiagnosed as lipodermatosclerosis.

Observation: A 64-year-old woman presented with an indurated, erythematous, nontender plaque on her right leg. There was associated aching pain and numbness, but no peripheral edema was noted and her ankle was not involved. She had previously been evaluated by her primary care physician, a vascular surgeon, a local dermatologist and a dermatologist at a tertiary referral center, all of whom diagnosed lipodermatosclerosis and suggested topical corticosteroids and compression. The vascular surgeon had referred the patient to an oncologic surgeon for a biopsy, but biopsy was not performed due to concern about poor healing. The dermatologic consultation had noted "eczematous" changes on the trunk and thighs which responded moderately to topical corticosteroids. Vascular studies showed venous insufficiency in both legs, but worse on the unaffected leg. An incisional biopsy of the right distal calf was performed despite the patient's concerns about healing which revealed a monomorphic population of atypical predominantly dermal-based lymphocytes that were small to medium in size and did not show significant anaplasia. Staining found CD3 and CD4 positive T cells with a diminished expression of CD7 and no CD30 expression. A clonal T cell receptor gene rearrangement was also identified and a diagnosis of cutaneous T-cell lymphoma was made. A second biopsy of a plaque on the contralateral thigh 3 weeks later revealed CTCL also. The histomorphology and phenotype were deemed consistent with tumor and plaque stage lesions of mycosis fungoides. A reactive node was present in the right inguinal chain, but a PET/CT scan was otherwise negative. The patient was diagnosed with stage 2B MF and treated with radiation and oral bexarotene.

Comment: This case highlights another potential manifestation of MF and emphasizes the critical role that biopsy plays when multiple diseases share similar clinical manifestations.

Commercial support: None identified.

3355

Folliculotropic mycosis fungoides: Clinical and histopathologic features and response to phototherapy

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Background: Folliculotropic mycosis fungoides (FMF) is a variant of ME characterized clinically as having a variable skin eruptions, and histopathologically as folliculotropic infiltrates.

Objective: To investigate the clinicopathologic, immunophenotypic, molecular features and treatments of FME

Methods: This study was conducted on 15 patients with histopathologic evidence of folliculotropism who diagnosed with MF at one institution.

Results: The patients were between 52 and 68 years of age. The spectrum of clinical diagnosis was broad and includes rosacea, chronic deep folliculitis, large cell acanthoma, lichen planus-like keratosis, exfoliative dermatitis, and Ofuji's papuloerythroderma. Thirteen patients had early-stage MF (A or B), and two patients had late-stage MF (IVA). In all patients, the atypical lymphocytic infiltrate had a perifollicular distribution. The CD4/CD8 ratio was >10 in 8 patients. PCR detection of TCR γ gene rearrangement was conducted in 10 patients and showed monoclonality in 5 patients. Thirteen patients were treated with UVA-1, PUVA or PDT. Patients with early-stage MF had complete remission. Otherwise, patients with late-stage MF had poor response to the therapy.

Conclusion: FMF is a variant of MF that appears to have a variable clinical presentation. Therefore, biopsy is required to confirm the diagnosis of FME and UVA-1, PUVA, and PDT are clinically effective treatment in patients with early-stage FME

Commercial support: None identified.

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Cutaneous involvement with Epstein-Barr virus–positive plasmablastic lymphoma

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Plasmablastic lymphoma is an aggressive hematologic malignancy with postgerminal center B-cell differentiation to a plasmablastic lineage. It is often associated with immunodeficiency, such as from HIV infection or age-related immune functional decline. This systemic disorder has overlapping features of diffuse large B-cell lymphoma and plasmablastic plasma cell myeloma. An 84-year-old woman was hospitalized with a 2 month history of progressive violaceous papules and nodules present on the upper chest and back. They were accompanied by fatigue and cough. Complete blood cell count, chemistry panel, and infectious studies were without abnormalities. CT angiography of the chest showed bilateral pulmonary nodules and enlarged mediastinal lymph nodes. Histopathology from a skin biopsy revealed a nodular infiltrate throughout the reticular dermis, composed of large monomorphic cells with plasmacytic features. There were numerous mitotic figures throughout the infiltrate. A Grenz zone was present in the papillary dermis. The tumor cells strongly expressed CD79a, demonstrated kappa light chain restriction, and had partial expression of CD138 and CD20. In situ hybridization for EBV was diffusely positive. A diagnosis of plasmablastic lymphoma was made. After discussion with the patient's oncologist, she elected to pursue palliative measures and passed away within 2 months of diagnosis. EBV-positive plasmablastic lymphoma is a rare but aggressive hematologic malignancy. Clinically, patients are most likely to present with nasal/oral cavity, lymph node or GI tract involvement. Cutaneous involvement is rare, occurring in less than 6 percent of patients. The immunophenotype is one of postgerminal center plasmablast lineage. There is heterogeneity, but the majority express plasma cell markers CD38, CD138 and Mum1, while fewer express B cell markers CD79a or CD20. EBV expression is found in 59% of HIV-negative cases and is associated with a slightly better prognosis. The median survival is 19 months for this lymphoma, underscoring the aggressive nature.

Commercial support: None identified.

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Diagnosis of subcutaneous panniculitis-like T-cell lymphoma in a patient with multiple sclerosis: Therapeutic challenges

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Background: Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a cytotoxic cutaneous T-cell lymphoma (CTCL). 15% of SPTCL cases are complicated by a potentially fatal hemophagocytic lymphohistiocytosis (HLH), which is characterized by high fever, lymphadenopathy, splenomegaly, pancytopenia, and high concentrations of lactate dehydrogenase (LDH), ferritin, and triglycerides. Up to 20% of SPTCL patients may have an autoimmune disorder.

Objective: To describe the challenges in management of patients diagnosed with SPTCL in the setting of multiple sclerosis (MS) treated with interferon beta(β)-1b.

Case report: A 55-year-old white woman presented with 6 month history of subcutaneous nodules on chest and abdomen and recurrent fever of unknown origin. History included advanced MS treated with interferon-β-1b for several years. Multiple small and flesh-colored subcutaneous nodules on chest and abdomen were present. Lymphadenopathic exam was negative. Skin biopsy showed infiltrate with rimming of atypical lymphocytes in adipose tissue. Malignant cells were positive for CD3+, CD8+, and BF-1+ and negative for CD56 and for Epstein–Barr encoding region in situ hybridization. T-cell receptor gene rearrangement analysis showed clonality. PET-CT revealed disease limited to subcutaneous tissue, with no hepatosplenomegaly. Diagnosis of SPTCL was then made. Blood work was normal and recurrent fevers responded to ibuprofen. One month later, she was admitted with fever, anemia, thrombocytopenia, elevated LDH and ferritin, all suggesting a diagnosis of HLH. Bone marrow biopsy did not show overt evidence of HLH. Interferon-β-1b was withheld and systemic corticosteroids and cyclosporine were initiated.

Discussion: Interferon alpha and gamma are a treatment of choice for some CTCLs, including mycosis fungoides and Sézary syndrome; however, they are not recommended in patients with cytotoxic CTCLs at high risk of HLH. HLH induced by interferon-β-1a has been postulated in literature. Both HLH and MS may cause neurologic symptoms, further complicating a diagnosis of HLH. This case challenges the clinician to decide the approach to treatment that is expected to provide the highest benefit-to-risk ratio in concurrent MS and SPTCL.

Commercial support: None identified.

3746

Intravascular diffuse B-cell lymphoma revisited

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Introduction: Intravascular lymphoma was originally described in 1959 by Pfleger and Tappeiner under the term systemic endotheliomatosis. Many synonyms including malignant angioendotheliomatosis, angioendotheliomatosis proliferans systemica, proliferating endotheliomatosis, neoplastic endotheliosis, angio-endotheliotropic lymphoma and intravascular lymphomatosis have predated the current nomenclature. Intravascular diffuse large B-cell lymphoma is now part of the WHO-EORTC 2005 and corresponding WHO 2008 classification of B-cell lymphoma with primary cutaneous manifestations. Classically this entity involves the skin and central nervous in a polymorphous manner but extremely variable presentations and manifestations has been described.

Observation: An 88-year-old male with a history of recent stroke and a stinging-like pruritus of 6 months duration. There were no B symptoms and a negative review of systems. A discrete erythematous papule biopsy revealed and unexpected intravascular proliferation of large atypical lymphocytes filling some dilated vessels in the dermis and concordant immunohistochemistry confirming the diagnosis of intravascular B-cell lymphoma. A few months later, the patient later developed a livedo racemosa with erythematosis nodule primarily on the lower body. A systemic work up was negative aside from a second asymptomatic stroke. Symptomatic treatment for the pruritus and clinical follow up was undertaken with no chemotherapy for the time being.

Discussion: Intravascular B-cell lymphoma has been quoted as another great imitator. Unexplained neurologic symptoms with various skin finding are classic for this diagnoses. Two key histological differential diagnoses are benign reactive angioendotheliomatosis and primary cutaneous CD30+ anaplastic large cell lymphoma with intralymphatic spread. The former is characterized by endothelial cell occluding vessels and the latter by CD30-positive lymphocytes with lymphatic spread. Immunohistochemistry with D2-40 can differentiate this entity. Random skin biopsies have been reported of being high yield for intravascular lymphoma and was in our case beneficial. Intravascular lymphoma has a high rate of fatal outcome if generalized and less so if restricted to the skin. A high index of suspicion is important for this uncommon cutaneous lymphoma.

Commercial support: None identified.

2668

Blastoid mantle cell lymphoma: An unusual presentation

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A 69-year-old man with a 20-year history of chronic lymphocytic lenkemia (CLL) and a six-year history of mantle cell lymphoma (MCL) presented with a solitary lesion on his left leg. The patient had received multiple courses of chlorambucil for treatment of CLL and rituximab as well as CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) for treatment of MCL. Both conditions were in remission at the time of presentation. Physical examination revealed a 4x4 cm red to violaceous dermal nodule on the left anterior lower leg. Biopsy of the lesion demonstrated a sheet-like proliferation of highly atypical lymphoid cells in the dermis and subcutaneous fat. The tumoral cells were blastoid in appearance and possessed high nuclear to cytoplasmic ratios, vesicular chromatin, and large, irregular and prominent nucleoli. Multiple apoptotic bodies and mitoses were evident. Immunohistochemical staining for CD20, BCL-2, BCL-6, MUM-1, and cyclin D1 were positive in lesional cells. Sox-11, TDT, and CD10 were negative. Break-apart FISH for cyclin D1 was positive for the cyclin D1 rearrangement (11q13). Mantle cell lymphoma (MCL) is a rare, aggressive variant of non Hodgkin lymphoma (NHL). MCL is named based on its involvement of lymphocytes from the mantle zone of lymph nodes. MCL typically occurs in middle-aged males and represents 2-10% of all non-Hodgkin lymphomas. The disease is often identified at later stages, with involvement of multiple lymph nodes and/or the spleen. Skin involvement is rare, found in only 2-6% of patients and typically presents with solitary or multiple erythematous papules. MCL presents with a blastoid histological morphology in 10-20% of cases, and portends a poor prognosis.

Commercial support: None identified.

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Invisible mycosis fungoides—Not to be missed in chronic pruritus

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Pruritus without a visible dermatosis may be the first manifestation of hematologic malignancies such as Hodgkin disease, chronic lymphocytic leukemia and mycosis fungoides and may precede the definitive diagnosis by weeks to years. We present a case of 'invisible' mycosis fungoides associated with chronic generalized pruritus in an elderly patient. Our case highlights the importance of performing skin biopsies in patients with chronic unexplained pruritus, especially in the absence of cutaneous lesions and prompt the clinician to consider possible underlying malignancy, such as 'invisible' mycosis fungoides.

Commercial support: None identified.

3585

Loss of CD30+ expression after treatment with brentuximub vedotin (BV) in a patient with anaplastic large cell lymphoma: A new phenomenon

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Anaplastic large cell lymphoma (ALCL), which accounts for about 3% of all adult lymphomas, is a rare aggressive T-cell lymphoma.

Case: A 41-year-old African American male with stage IV ALCL, CD30+ and ALK presented with a left upper cutaneous lip mass. He was treated with chemotherapy for 6 cycles and brentuximab vedotin (BV) for 3 doses. Remaining nodules of the left chest and left neck were biopsied and showed CD30-positive lymphoproliferative disorder. He continued to receive BV therapy and re-presented for a 3-week history of growing and tender nodules on the chest and back.

Workup: Biopsies of both chest and back lesions showed a diffuse dermal infiltrate of medium-to-large sized atypical lymphocytes with frequent mitotic figures, admixed with scattered eosinophils. The atypical cells were CD3 positive and CD4 and CD8 double negative T cells. They were negative for TCR-gamma and CD56 immunostain, as well as ALK-1 and beta F1. Interestingly, the specimens were also negative for CD30, a marker that had previously been expressed by the patient's T-cell lymphoma of the skin.

Treatment: The patient underwent total skin electron beam radiation and was continued on BV, with resolution. He relapsed two months later and presented with extensive disease. He was matched for allogeneic stem cell transplant but in the process of receiving radiation, developed involvement in the bone, lungs, and skin. Biopsy of a cutaneous lesion was CD30 negative. He received three cycles of chemotherapy but unfortunately expired.

Discussion: Anaplastic large cell lymphoma is an aggressive disease, especially for ALK negative patients, who have a 5-year survival rate of 60%. BV is approved for relapsed or refractory systemic ALCL. This case highlights a rare phenomenon of BV tumor response with documented loss of CD30 expression, which has only been described in in vitro models and will be the first cases confirmed in a patient. With treatment with BV, his tumors shifted their phenotype and the skin biopsies confirmed a remarkable response to BV and the ability of the lymphoma to adapt. In addition, his systemic ALCL responded to the therapy until his diffuse relapse.

Conclusion: Our patient is the first reported case of confirmed tumor growth in ALCL with loss of CD30 expression after BV treatment. Recognition of this histopathologic finding is crucial in both the treatment of patients with ALCL as well as determining how this therapy can be in used in the future.

Commercial support: None identified.

3869

Mycosis fungoides bullosa with pyoderma gangrenosum-like presentation: Rarest of the rare case

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Introduction: Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma. Classically it present as disseminated eruption of erythematous, itchy patches which gradually progress to plaques, nodules and tumors. But several unusual variants of MF have been reported, mycosis fungoides bullosa is one such rare presentation which has poor prognosis. Since its description in 1871, less than 20 cases of MF bullosa have been published and there is only one case of MF bullosa simulating pyoderma gangrenosum. We report a first case of MF bullosa from our country and second case of MF bullosa with pyoderma gangrenosum like presentation along with vesiculo-bullous and erythematous infiltrated plaques of MF, worldwide.

Case report: A 55-year-old male presented with two well-defined, ulcerated plaques covered with necrotic slough, one in the left submandibular region and another on the chest. He also had multiple, annular to well defined, erythematous, infiltrated plaques on scalp, face, extremities, trunk and tense fluid-filled bullae on palms and soles. Some of the crusted plaques showed vesiculation on the surface. About 7 months back, it started as asymptomatic clear fluid-filled pea sized vesicles on apparently normal skin of the chest, these vesicles ruptured to form erosions discharging fluid, pus and blood and new lesions appeared to present state. Patient was initially treated on the lines of pemphigus vulgaris by a local practitioner. But histopathologic examination of skin biopsies from ulcer, tense bullae and annular plaques confirmed the diagnosis of MF bullosa, showing widespread subepidermal collection of CD3+ atypical lymphocytic cells with epidermotropism, folliculotropism, intra and subepidermal clefts filled with atypical lymphocytes. Biopsy from ulcer margin showed epidermal ulceration with CD3+ atypical cells in dermis. Direct immunofluorescence (DIF) was negative for IgG, IgA, IgM and C3 antibodies at basement membrane zone excluding autoimmune disease. Hence, our case, fulfilled the criteria for diagnosing MF bullosa including clinical presentation, characteristic histopathology, negative DIF and no other possible cause of vesiculobullous lesions.

Conclusion: Our case is rare presentation of MF bullosa which itself is a rare, unusual variant of mycosis fungoides. The important differential diagnosis are bullous pemphigoid, bullous pyoderma gangrenosum, mycosis fungoides, primary cutaneous anaplastic large T-cell lymphoma and tertiary syphilis.

Commercial support: None identified.

3279

Mycosis fungoides presenting as purpura annularis telangiectoides of Majocchi

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Mycosis fungoides (MF) is a cutaneous T-cell lymphoma that typically affects older adults. Classically, MF presents as erythematous annular patches and red-brown eczematous and psoriasiform plaques with a predilection for sun protected areas. We present a rare case of mycosis fungoides presenting as purpura annularis telangiectoides of Majocchi in a 66-year-old white male. The paticot initially presented with a one-year history of a progressive asymptomatic eruption of his buttocks and groin. His medical history was significant for hypertension and his only medication was valsartan-HCTZ. Physical exam revealed diffuse and confluent red-brown oval patches with central clearing and peripheral punctate petechiae in a well-demarcated bathing suit distribution. Punch biopsy showed a band like infiltrate composed of lymphocytes and numerous extravasated red blood cells in the superficial dermis, with larger atypical lymphocytes in the lower epidermis and in the dermoepidermal junction. Clonal rearrangement of the T-cell receptor gamma gene was positive by PCR. Laboratory data including a CBC, chemistry panel, LFT's, and lactate dehydrogenase were within normal limits. Peripheral blood flow cytometry was also negative. Using both histopathologic and clinical features, the diagnosis of a rare form of MF presenting as purpura anularis telangiectoides of Majocchi was made. Given the photoprotective distribution, the patient was started on NB-UVB therapy three times a week. At a two-month follow-up, the patient had cleared without any residual lesions. MF presenting as pigmented purpuric dermatoses (PPD) can be difficult to diagnose given the histologic overlap between the two. MF presenting as PPD is a rare occurrence but should be considered in long-standing and chronic PPD.

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Peripheral T-cell lymphoma, not otherwise specified with prominent cutaneous involvement

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A 33-year-old African American man presented to our emergency department with an approximately 1-year history of painful enlarging skin nodules. Examination revealed multiple, variably sized, indurated skin nodules, with central ulceration and yellow-brown crusting distributed on the scalp, face, umbilicus, buttocks, bilateral thighs and right arm. In addition, there was palpable matted lymphadenopathy in both the axillae and groin. Multiple skin biopsies and an excisional lymph node biopsy from the right axillae were obtained. Histopathologic analysis of the skin revealed a nodular lymphohistiocytic infiltrate filling the dermis, which consisted of many large and atypical lymphocytes. No significant epidermotropism was identified though there were some focal areas of perifollicular necrosis. A T-cell gene rearrangement study revealed a monoclonal population of cells which on further immunotyping was consistent with a mature CD4+ T-cell lymphoma. Similar analysis together with flow cytometry of the sampled lymph node revealed identical morphologic and immunophenotypic features of lymphoma as detected in the skin. A staging positron emission tomography computed tomography (PET-CT) scan revealed intense fluorodeoxyglucose uptake in the lymph nodes of neck, parotid glands, axillae, inguinal and iliac chains, as well as spleen. Bone marrow biopsy, flow cytometry of the blood and bone marrow and human T-cell lymphotropic virus-1/2 serologies were negative. In view of these findings, a diagnosis of peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS) was rendered with a stage of IIIES. PTCL-NOS, is a poorly defined and heterogeneous group of predominantly nodal T-cell lymphomas not meeting histopathologic or immunophenotypical criteria for the other well-defined subtypes of peripheral T-cell lymphoma. Initial treatment may include cyclophosphamide, hydroxydaunorubicin, oncovin and prednisone (CHOP)-based chemotherapy, radiation therapy and/or autologous hematopoietic cell transplantation. The prognosis is considered poor, with previously reported 5-year survival rates of under 20%. Our patient was initially treated with radiation to reduce the size of the larger and most symptomatic tumors. He then completed 6 cycles of CHOP-Etoposide, with follow-up PET-CT revealing interval resolution of all the previously identified foci of lymphoma. All skin lesions have been replaced by atrophic hypopigmented scars.

Commercial support: None identified.

3839

Persistent agmination of lymphomatoid papulosis—Case series and review of the literature

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Introduction: Persistent agmination of lymphomatoid papulosis (PALP) is a chronic recurrent disease with clustered papulonecrotic lesions circumscribed within a mycosis fungoides (MF)-like patch area, usually on the trunk and thighs. We report two cases of persistent agmination of lymphomatoid papulosis.

Case report: Case 1: A 33-year-old male presented with two asymptomatic, palm-sized, mild scaly erythematous patches studded with several agminated papules on the left anterior thigh for two years. The skin biopsy showed dense subepidermal small lymphocytic infiltration with significant epidermotropism of single cells or cell clusters (which were immunohistochemically CD3+/CD20-), and large CD30+ atypical cells in the dermis. The initial diagnosis was mycosis fungoides with CD30+ transformation. Staging work-up included normal findings in complete blood cell count, differential count, whole body positron emission tomography - computed tomography, and bone marrow biopsy. He was treated with photochemotherapy and localized electron beam radiation therapy, and there was no other organ involvement in the following eight years. The skin lesions would reappear on his trunk, arms or thighs after several months of remission. Given the clinical features with recurrent course, histological characters suggestive of lymphomatoid papulosis type A, we diagnosed this patient as persistent agmination of lymphomatoid papulosis (PALP) mimicking limited popular and patchy mycosis fungoides. Case 2: A 53-year-old female had recurrent mild itchy clustered pea-sized papules within a palm-sized patch over her bilateral thighs for more than one year. Pathology revealed perivascular and upper dermal diffuse infiltration of small lymphocytes and some large CD30+ atypical cells, which was compatible with lymphomatoid papulosis type C. The lesions had partial response to topical clobetasol, but did not remit completely.

Discussion: Persistent agmination of lymphomatoid papulosis was first described in 2007 and 16 cases had been reported in the English literature. Age of onset ranges from 6 to 62 years old. The lesions involve circumscribed areas of trunk and thighs with persistent localized eruptions of papulonodules. It runs a chronic course with lesions appearing up to 12 years, waxing and waning without complete resolution if left untreated. Histology displays features of a CD30+ lymphoproliferative disorder, 80% compatible with lymphomatoid papulosis type A. PALP differs from localized or regional lymphomatoid papulosis in its specific morphology with multiple anatomic areas, and MF-like characteristics. Papular mycosis fungoides should also be differentiated from PALP, but it lacks typical patches, does not resolve spontaneously, and the cells are CD30- immunohistologically. Clinical behavior and outcome of PALP are usually benign. Staging work-up has not revealed systemic involvement. Most of the cases had long-standing remissions after localized radiotherapy, but one progressed to MF-type cutaneous T cell lymphoma. There remains an ongoing debate concerning whether PALP represents a composite lymphoma such as anaplastic large-cell lymphoma, which will warrant further treatment and close follow-ups.

Commercial support: None identified.

2920

Plaque/patch stage mycosis fungoides successfully treated with ingenol mebutate

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Introduction and objectives: Topical treatment options for patch/plaque stage mycosis fungoides (MF) and folliculotropic MF (FMF) include, among others, topical potent steroids, topical chemotherapy (carmustin, mechlorazine), imiquimod, resiquimod, topical methotrexate and retinoids. Ingenol mebutate (PEP005) is a new topical field-directed treatment option for actinic keratosis. Furthermore, PEP005 has demonstrated in vitro and in vivo effectiveness on melanoma and melanoma cell lines. The action mechanisms of PEP005 are related to the induction of proinflammatory events (PMN oxidative burst and keratinocyte cytokine release) and apoptosis. Whether PEP005 is clinically effective for MF and FMF remains undetermined.

Materials and methods: In four male patients suffering from longstanding and extensive MF (n = 3) and FMF (n = 1), stage T2b, a single target lesion was selected for mebutate therapy (0.05%, 2 applications at 1 week interval). All patients received furthermore systemic methotrexate (15-20 mg/w). Biopsies were performed at 2 months as well as photographic recordings.

Results: All the patients experienced treatment related adverse effects including, burning sensations, slight oozing and crusting for 3 to 5 days. The skin biopsies of all the patients revealed signs of postinflammatory hyperpigmentation without further signs of MF of FME Immunohistochemistry did not favor MF or FME No monoclonal TCR rearrangement was observed in any of the biopsies.

Conclusion: Topical mebutate ingenol 0.05% may be considered as effective alternative topical treatment for localized plaques/patches of MF and FME Larger studies are required to establish efficacy and tolerance as well as the place of mebutate ingenol in the therapeutic armamentarium of MF.

Commercial support: None identified.

2922

Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma, rare subtype of cutaneous T-cell lymphoma in a Chinese patient

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Background: Primary cutaneous aggressive epidermotropic CD8 T-cell lymphoma (PCAETCL) is a rare subtype of cutaneous T-cell lymphoma (CTCL). Patients present with a rapidly progressive course, clinically manifest as widely distributed ulcerative lesions which are histopathologically characterized by epidermotropic infiltrates of CD8 cytotoxic T cells. PCAETCL runs an aggressive course with a high tendency to spread to extranodal sites. Unfortunately, treatment response to conventional therapies is poor, leading to an unfavorable prognosis.

Case study: We report a case of PCAECTL in a Chinese patient with a long standing psoriasiform rash presenting with new onset of ulcerative lesions. Histology revealed CD 8+ epidermotropic lymphoma. In view of the aggressive clinical history, immunohistochemistry findings and absence of systemic and visceral involvement, a diagnosis of primary cutaneous aggressive epidermotropic CD 8+ cytotoxic T-cell lymphoma was made. Patient received CHOP chemotherapy but suffered relapses with recurrent plaques and tumors over the body requiring subsequent radiotherapy.

Discussion: Differential diagnoses of other types of CD8+ lymphoma are discussed.

Conclusion: Primary cutaneous aggressive epidermotropic CD8 T-cell lymphoma is a rare lymphoma and its aggressive clinical course with poor treatment response is observed in this Chinese patient. It is a rare but important diagnosis not to be missed in patients presenting with ulceration of preexisting dermatoses or new primary ulcerative lesions.

Commercial support: None identified.

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Primary cutaneous EBV+ diffuse large B-cell lymphoma: A rare and aggressive cutaneous lymphoma

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The classification of primary cutaneous B-cell lymphomas has been a subject of debate over the past several years. Recently, the World Health Organization and European Organization for Research and Treatment of Cancer updated the classification of these cutaneous neoplasms. While much is understood about the three most common primary cutaneous B-cell lymphoma subtypes (primary cutaneous follicle center lymphoma, primary cutaneous marginal zone lymphoma, primary cutaneous diffuse large B-cell lymphoma leg type), more research is necessary to further define the less common provisional entities. Primary cutaneous EBV-positive diffuse large B-cell lymphoma is a rare and aggressive cutaneous neoplasm that was recently included as a provisional entity in the classification system for primary cutaneous B-cell lymphomas. Few case reports have been published regarding this newly described cutaneous lymphoma. It has a more aggressive clinical course and poorer prognosis than most of the primary cutaneous B-cell lymphoma subtypes. Although rare, EBV-positive diffuse large B-cell lymphoma is an important entity to consider when evaluating a patient with a suspected primary cutaneous lymphoma. Primary cutaneous EBV positive diffuse large B-cell lymphoma responds poorly to conventional treatments for other primary cutaneous B-cell lymphoma subtypes. Further research is needed to establish optimal treatment regimens for this aggressive cutaneous lymphoma.

Commercial support: None identified.

2343

Relative frequency, clinical features, and survival outcomes of 395 patients with cutaneous lymphoma: A subgroup analysis per 10-year period

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Background: Previous large-scale studies on cutaneous lymphoma (CL) have mainly been performed in the United States and Europe. Long-term changes in relative frequency in CL have not been investigated in Asian populations.

Objectives: We investigated the relative frequency, clinical characteristics, and survival outcomes of CL in Korean patients. Moreover, we evaluated the changes in the relative frequency of CL over a 20-year period.

Methods: The present retrospective cohort study included all 395 patients who presented with CL over a 20-year period in the dermatology department of a tertiary referral hospital in Korea.

Results: The 395 cases consisted of 289 cases of primary CL and 106 cases of secondary CL. Primary CL included T/NK-cell linage lymphoma (CTCL, 85.1%) and B-cell lineage lymphoma (CBCL, 14.9%). The relative frequency of CBCL increased over time, as shown by a decrease in the CTCL/CBCL ratio from 10.4 in 1994-2003 to 4.5 in 2004-2013. CTCL was more commonly associated with multiple and extensive skin lesions than was CBCL. The 5-year overall survival rate for all primary CL patients was 81%.

Limitations: This study is a retrospective, single center design.

Conclusions: Changes were seen in the relative frequency of CL during a 20-year period in Korean patients.

Commercial support: None identified.

2622

Racial differences in survival of patients with Sezary syndrome in the United States: A population-based study of 204 cases

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Introduction: Sezary syndrome is a rare leukemic variant of cutaneous T-cell lymphoma (CTCL) characterized by erythroderma, lymphadenopathy, and proof of neoplastic T cells in blood and skin. Limited data exists on racial difference in survival of patients with Sezary syndrome.

Methods: We analyzed patients with Sezary syndrome from 1973-2012 using data from Surveillance, Epidemiology, and End Results (SEER)*Stat – Version 8.2.1. Demographics were collected, and Chi-square test was performed to compare the age and sex by race. Z-score was obtained to compare the 5-year relative survival rate by race.

Results: We identified 204 patients with Sezary syndrome. Sixty-four percent were male, and median age at diagnosis was 68, white was the most common race (83%) followed by Black (11%) and Other (6%). There was no significant difference in the age, sex by race. Five-year relative survival was significantly lower in Black compared with white (15.8% vs 44.7%, Z-score = -3.693, $P < .01$). No significant difference in relative survival was found between white and other.

Conclusion: Our study showed poorer survival in black patients with Sezary syndrome. Further research is warranted to explore disparities in access to care, biologic aggressiveness, and treatment efficacy between racial groups in Sezary syndrome.

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3160

Rituximab infusion causing localized urticaria during the treatment for cutaneous lymphoid hyperplasia

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This is a case of a 64-year-old man with history of nonmelanoma skin cancer who presented for evaluation of red lesions on his left thigh that had been present for over 20 years. The patient had used topical steroids and intralesional kenalog with temporary relief of his itching but no improvement in the appearance. The patient otherwise denied any systemic symptoms like fevers, chills, night sweats, or weight loss. Punch biopsies revealed an atypical lymphoid infiltrate consisting of a mixture of CD3+ T cell and CD20+ B cells in the superficial and mid dermis without destruction of adnexal structures. Gene rearrangement studies were negative and there was no kappa/lambda light chain restriction. The patient was diagnosed with cutaneous lymphoid hyperplasia (CLH) and started on rituximab. During his first infusion, he was premedicated with 650 mg of acetaminophen and 50 mg of intravenous diphenhydramine. Fifty minutes into his first infusion, he developed localized urticaria over his tumor sites with severe pruritus. He denied any other systemic symptoms, shortness of breath, swelling, or rash. He was given 10 mg of dexamethasone and topical hydrocortisone, with significant improvement in his urticaria, and the rituximab was restarted and completed with no further complications. On each of the three subsequent infusions, he continued to develop similar localized urticaria, but with a less robust reaction than initially. There have been eight reported cases of a localized urticarial reaction to rituximab infusion during treatment of primary cutaneous B-cell lymphoma, but to our knowledge, this is the first case of an urticarial reaction during the treatment CLH and the only case where the patient experienced repeated episodes of urticaria with each infusion. Rituximab is known to cause a cytokine-release syndrome from activation of complement, macrophages and release of proinflammatory cytokines and vasoactive mediators in patients with a high burden of disease, like in chronic lymphoid leukemia. This patient's urticaria is thought to be caused by a similar cytokine release syndrome, but localized only to his cutaneous disease. This case is illustrative of a rare adverse effect of rituximab, and given rituximab's increasing popularity for the treatment of a variety of diseases, it is important to better understand the potential risks and side effects of this medication.

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2440

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL), gamma/delta (GD) type

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A 40-year-old man presented to our clinic with a two-year history of an asymptomatic, generalized rash associated with fatigue, weakness, weight loss, night sweats, arthralgias, and myalgias. Since the onset of the rash, he noted progressive deterioration of his health, requiring him to stop working due to fatigue and weakness. Outside punch biopsy revealed a deep perivascular lymphohistiocytic infiltrate. Special stains for microorganisms were negative. Chest x-ray revealed few scattered calcified granuloma. Although the findings were not specific, a working diagnosis of sarcoidosis was entertained. Prednisone treatment slightly improved his constitutional symptoms, but did not stem the progression of his rash. Examination revealed scaly, erythematous plaques and erythematous-to-brown plaques and nodules diffusely involving his trunk and extremities. There was neither lacrimal gland enlargement nor palpable lymphadenopathy. Incisional biopsy of two nodules was performed. Sections revealed a lobular lymphoid infiltrate composed of small, atypical lymphocytes with intermixed histiocytes and numerous apoptotic cells in the subcutis. The lymphocytes, some rimming adipocytes, showed moderate cytoplasm, mildly irregular nuclei, and mature chromatin. Immunohistochemical stains demonstrated staining of the atypical lymphocytes with CD2, CD3, CD4, CD8 (very dim), CD43, CD56 (dim), perforin, TIA, and TCR-gamma. CD5, CD7, betaF1, TdT, and TCL-1 were negative. T-cell receptor (TCR) beta and gamma chain genes showed a clonal population. Flow cytometry was normal. Bone marrow and liver biopsies did not show lymphomatous involvement. The morphologic, immunophenotypic, and molecular findings were diagnostic of a primary SPTCL, GD type. SPTCL is a rare peripheral T-cell lymphoma which has gained recognition in recent years. There appear to be two distinct subsets: alpha-beta (AB) and GD. The five-year overall survival rate for patients with AB and GD subtype is 82% versus 11%, respectively. Unfortunately, due to the rarity of the disease, there is no standard of care, and randomized controlled studies are lacking. The patient was started on multi-agent chemotherapy to treat his aggressive, rapidly progressing lymphoma.

Commercial support: None identified.

3762

Subcutaneous panniculitis-like T-cell lymphoma: A diagnostic challenge

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Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare variant of T-cell lymphoma characterized by infiltration of the subcutaneous tissue by neoplastic cytotoxic T-cells mimicking panniculitis with an aggressive clinical course. A 31-year-old, otherwise healthy male patient, presented with a 6-month history of multiple painful erythematous and purplish nodules with ulceration on the proximal limbs and trunk, as well as intermittent low-grade fever, night sweats and a weight loss of 13 lb. A previous skin biopsy reported a granulomatous infiltrate, and, thinking of a possible diagnosis of cutaneous tuberculosis, he was treated with rifampin/isoniazid/pyrazinamide with no improvement. Physical examination revealed a necrotic ulcer on the right arm, as well as the previously described dermatosis, with no peripheral lymphadenopathy. Laboratory findings showed increased LDH and ESR levels. Complete blood count, liver and renal function tests were normal. HIV, hepatitis B and C, and PPD tests were all negative. Ulcer debridement, and two excisional biopsies were performed. Histopathology showed an atypical lymphoid infiltrate affecting the entire dermis, as well as the fat lobules resembling a lobular panniculitis. Immunohistochemistry was positive for CD3/CD8, Ki-67 and TIA-1, and negative for CD20, CD30 and CD56. These findings were consistent with SPTCL. A contrast-enhanced CT of the chest and abdomen revealed mediastinal and retroperitoneal lymphadenopathy with hepatomegaly. The patient was referred to the Hematology Department, and CHOP chemotherapy was started. SPTCL is a rare neoplastic entity with infiltration of the subcutaneous tissue by atypical T-cells. Clinical presentation includes nodules, plaques, and ulcers on the extremities and trunk. Fever, chills, and weight loss are commonly seen. Few patients may have lymphadenopathy or hepatosplenomegaly. Histopathology shows an atypical lymphoid infiltrate predominantly in the subcutaneous tissue, in a lobular pattern. Immunohistochemistry is positive for cytotoxic T-cells that are CD3 +, CD 4-, CD8+, and CD56-. The tumor cells express TIA-1, perforin and granzyme A. Differentiating this entity from panniculitis and some infectious diseases may be difficult, making its diagnosis a clinical challenge. An appropriate clinical history, as well as histopathology and immunohistochemistry tools are of crucial importance for the accurate and prompt diagnosis and treatment of this disease.

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3805

Synchronous presentation of cutaneous T-cell lymphoma and chronic lymphocytic leukemia

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Cutaneous T-cell lymphoma (CTCL) is included in a heterogeneous group of lymphoproliferative disorders which present with clonal expansion of T cells that infiltrate skin. Secondary malignancies have been reported in patients with disorders such as CTCL, and often these behave more aggressively. An imbalance in the immune system has been proposed as a possible physiopathological mechanism. A 49-year-old Hispanic woman presented to our dermatology clinic for evaluation of a 7-month widespread dermatosis. Past medical history was unremarkable. She complained of asthenia, adynamia, fever, night sweats and progressive weight loss of approximately 45 pounds in the previous year. On dermatologic examination, there were numerous brownish-grey macules, some of them confluent of up to 3-4 cms in diameter on her chest, back, abdomen and extremities. Approximately eight ulcerated and erythematous nodules with an asymmetrical distribution were also present. The patient referred these lesions gradually appeared within the last 4 months. They were painful and exhibited a serosanguineous exudate. She was evaluated by multiple health providers, who requested blood tests and urinalysis, based on a presumptive infectious etiology. On laboratory examination, complete blood count with differential showed total leucocyte count of 40,000, with 91% lymphocytes, and urinalysis was positive for abundant gram-positive cocci; *Streptococcus pyogenes* grew in the urine culture. She received 5 doses of intramuscular ceftriaxone without any improvement. When she was evaluated in our dermatology clinic, two skin biopsies were performed from a macule and a nodular lesion. The infiltrate was compatible with large cell T-cell lymphoma and immunohistochemistry was positive for CD8, CD4, and CD30. She was referred to the hematology clinic, where she was evaluated. A peripheral blood smear showed large and mature lymphocytic cells as well as smudge cells, morphologically compatible with chronic lymphocytic leukemia (CLL). The patient was hospitalized to initiate chemotherapy. CTCL has been associated with previous, subsequent or synchronic second malignancies. This could be linked to a genetic predisposition, an altered immune system, the use of immunosuppressive agents, and/or radiotherapy. Authors have reported the occurrence of CTCL in the setting of CLL, although rare. The largest case series reports 14 patients with simultaneous CTCL and CLL; in nearly 60% of the patients the diagnosis of these two entities was concurrently made, in the rest of the patients the diagnosis of CLL was previously made. This is a unique case in which CLL and CTCL were diagnosed concurrently.

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3675

Syringotropic mycosis fungoides, a rare form of cutaneous T-cell lymphoma

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Syringotropic mycosis fungoides (STMF) is a rare variant of folliculotropic mycosis fungoides (FMF). STMF is characterized by prominent T-cell lymphocytic infiltration of both follicular epithelium and eccrine glands. We present a case of this rare form of MF and review its presentation and management. A 63-year-old white male presented with a progressive, dry rash on his legs for one year which eventually ulcerated on the posterior upper thigh and foot. On physical examination, scaly patches were noted on the buttocks. Plaques with punctate erythema were noted on the arms and left posterior thigh which exhibited folliculotropism and alopecia. An initial biopsy showed diffuse lymphohistiocytic inflammation. Due to the nonspecific histological findings and unremarkable rheumatologic bloodwork, a repeat biopsy was performed. The pathology demonstrated a dense, extensive and nodular lymphocytic infiltrate, which appeared hyperchromatic and hyperconvoluted. Approximately 99% of the cells stained positively for CD3 and 1% of the cells stained negatively for CD20 and CD30. Additional staining demonstrated marked positive staining for CD4 with diminished CD8 and negative CD56 staining. T-cell polymerase chain reaction detected a clonal T-cell receptor gamma (TCRG) population. There was no growth of tissue cultures for acid-fast bacilli, bacterial or fungal organisms. The results were consistent with peripheral T-cell lymphoma. The patient was referred to Northwestern lymphoma clinic where a multidisciplinary team preformed additional biopsies and diagnosed him with STMF stage T1b. Treatment with 8-methoxypsoralen (8-MPO) and UVA (PUVA) was recommended two times per week in addition to acitretin 25mg on weekdays. To date, the patient has shown a partial response. The CTCL team is considering adding spot or total skin electron beam therapy if the disease progresses. Data from the limited cases of STMF reported in the literature suggest that STMF primarily involves the limbs, trunk and palms or soles, presenting as erythematous, punctated patches with associated alopecia. First-line treatment has not been established, but the data show that STMF responds poorly to topical regimens, possibly as a result of ineffective penetration into the reticular dermis where T-cell infiltrates are most prominent. Data currently support PUVA and systemic retinoids or electron beam therapy as the best skin-directed therapies for this subset of MF.

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Syringotropic mycosis fungoides: A rare variant of CTCL

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A 62-year-old Italian-American man presented to the dermatology inpatient consult service in 2010 with erythroderma, and a 30-pound weight loss. Skin biopsy and flow cytometry revealed syringotropic mycosis fungoides. Over the last four years, the patient has had a progressive course with prominent follicular and ulcerative tumor burden despite various treatments. On physical examination the scalp, face, trunk and extremities have extensive pink scaling perifollicular plaques. The bilateral lower extremities, inguinal folds and perianal region have red, moist, malodorous, ulcerated plaques. In addition, there is profound alopecia of scalp and body hair, and atrophy of the nasal tip. Laboratory data: Flow cytometry of inguinal lymph node: 11% abnormal cells (CD4+, CD2+, CD5+, CD3-). Flow cytometry of blood: 16% abnormal cells (CD4+, CD2+, CD3-, CD5+, CD7+). Radiologic data: Total body PET scan: axillary, inguinal, iliac lymphadenopathy with several nodes containing increased glucose metabolism, cutaneous activity in right anterior abdominal wall and left lateral thoracic wall. Stage IVA (T4N3M0B1): Previous treatments included bexarotene, photopheresis, total skin electron beam therapy, CHOP, IV methotrexate and pralatrexate. Current treatment includes the HDAC inhibitor, vorinostat. Syringotropic mycosis fungoides (STMF) is an exceedingly rare variant of cutaneous T-cell lymphoma (CTCL), a malignancy that results from aberrant proliferation of skin-homing T-cells. STMF is classified as a subtype of folliculotropic MF (FMF). The clinical presentation of STMF is diverse and may be localized or diffuse. While more classic STMF lesions include punctate erythematous papules and plaques, there are other distinguishing clinical findings. A recent retrospective study of 19 patients found erythema and alopecia to be the most common clinical presentations. Other features include hyperkeratotic follicular prominence, pruritus, hyperesthesia, anhidrosis, poikiloderma atrophicans vasculare and palmoplantar keratoderma. Many of the skin-directed therapies of STMF have proven ineffective due to the periecerine location of the infiltrate. Treatments include PUVA, total skin electron beam therapy, methotrexate, IFN-α, systemic chemotherapy such as CHOP, and fludarabine. HDAC inhibitors including vorinostat represent a newer class of antineoplastic agents approved for the treatment of patients with refractory or recurrent CTCL.

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MELANOMA AND PIGMENTED LESIONS

2849

10-year retrospective study of subungual melanoma in a Dermatologic National Reference Center in Mexico City

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Introduction: Melanoma is a malignant neoplasm that arises mainly from skin melanocytes. It represents one of the most common forms of cancer in young adults and currently represents a significant public health problem. Although melanoma accounts for only 4% of all dermatologic cancers, it is responsible for 80% of deaths from skin cancer. There are four clinicopathological entities: superficial spreading melanoma, nodular melanoma, lentigo maligna and acral lentiginous melanoma. Epidemiologic studies in our country reveal that the most common type of melanoma is the acral melanoma which is the most common type in mestizo population. Subungual melanoma is a variant of acral lentiginous melanoma that originates in the nail matrix. In dark-skinned ethnic groups there is a 3.3 to 4.5 increased risk for this type compared to whites.

Material and methods: We retrospectively identified all the patients with melanoma diagnosis in the dermatopathology database in our institution between 2004 to 2014. Among 162 cases of cutaneous melanoma, 89 (55%) were female and 73 (45%) were male. 91 (56%) cases were classified as acral melanoma and from these 84.6% had an invasive component with Breslow thickness ranging from 0.3 mm to 7 mm. There were 26 subungual melanomas which represents 28% of acral melanomas and 16% of all melanoma cases. Female patients accounted for 65% of subungual melanomas and only 35% were male. 76.9% were diagnosed at an invasive stage, with Breslow thickness ranging from 0.45 mm to 5.5 mm. The most frequent topography of acral melanomas was the right foot with 42 cases. Subungual melanomas were located more frequently on the first finger of the right hand and the first toe of the right foot.

Discussion: Subungual melanoma is not an uncommon disease among Mexican mestizo population. In whites it is considered a rare tumor, found in 1-5% of total melanomas cases. This incidence rises up to 15-30% in darker skin types. Subungual melanoma has a poor prognosis due to frequent delayed diagnosis, the survival rate at 5-10 years is 30-13% respectively. It is imperative to provide an opportune diagnosis and appropriate management.

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2777

A case of vitiligo-like depigmentation induced by dabrafenib in patients with metastatic melanoma

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Introduction: BRAF, an upstream activator in the MAPK pathway, is mutated in approximately 40% to 60% of cutaneous melanomas. Dabrafenib is orally bioavailable small molecule agent that block mitogen activated protein kinase signaling in patients with melanoma and BRAFV600E mutation. We describe a patient with metastatic melanoma who developed vitiligo-like depigmentation with dabrafenib.

Case report: A 44-year-old woman with preauricular, cervical lymph node and pulmonary metastases from a left outer ear primary melanoma. Molecular testing of the primary tumor demonstrated BRAF V600E mutations, she received dabrafenib 150 mg twice daily. Two months later, she developed vitiligo-like depigmentation of the face, scalp, trunk and limbs. At week 12 the patient demonstrated notable clinical regression, computed tomography imaging showed no lung metastases and partial response in cervical lymph node, which was positive on positron-emission tomography. Other common adverse reactions for dabrafenib were hyperkeratotic hand-foot reaction, keratosis pilaris-like reaction, palmar-plantar erythrodysesthesia syndrome. All were resolved with topical therapy without the cessation of medication.

Discussion: The introduction of BRAF inhibitors (BRAFi) revolutionized BRAFV600-mutated metastatic melanoma treatment with improved response rate and overall survival compared to standard chemotherapy. The cutaneous adverse effects of the BRAFi in the treatment of metastatic melanoma have been well reported. The most common adverse reactions for dabrafenib as a single agent are hyperkeratotic hand-foot reaction, keratosis pilaris-like reaction, epidermal neoplasms (squamous cell carcinoma, keratoacanthoma, verrucal keratoses), and palmar-plantar erythrodysesthesia syndrome. Vitiligo-like depigmentation is a relatively harmless type of autoimmunity that can occur in patients with melanoma spontaneously or on immunotherapy, however it has not been reported with dabrafenib. The depigmentation results from strong antimelanoma immunity that also targets healthy melanocytes, as a result of shared expression of melanocyte differentiation antigens, is important as an indicator of robust antimelanoma immunity and associated improved survival.

Conclusion: Vitiligo-like depigmentation was induced by dabrafenib. In patients with metastatic melanoma this reaction may be associated with more favorable clinical outcome.

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3462

A comparative study of proliferative activity and tumor stage of pregnancy-associated and nonpregnancy-associated melanoma in gestational age women

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The influence of pregnancy on the development, progression, and prognosis of melanoma is controversial. A paucity of information regarding the impact of pregnancy on tumor proliferation, along with conflicting data regarding patient outcomes and cause-specific mortality, create uncertainty in how to advise women to proceed with family planning after a diagnosis of melanoma. Recommendations are generally based on age and tumor stage, and some physicians will advise patients to wait two to five years before becoming pregnant based on the high risk of early recurrence. However, as many women already delay childbearing, the decision of whether to proceed or wait becomes a difficult balance between concerns of tumor recurrence or progression and risks associated with advanced maternal age. In order to evaluate the impact of pregnancy on disease stage and tumor progression, we sought to compare clinical characteristics, histologic features, stage at diagnosis and proliferative activity in pregnancy-associated melanoma (PAM) and melanoma in non-pregnant women of reproductive age (non-PAM). We reviewed medical records and pathology reports from women diagnosed with melanoma between 2006 and 2015 to examine staging information and tumor proliferation rates using mitotic count and two immunohistochemical markers of proliferation; phosphohistone H3 and Ki-67. PAM was not associated with higher disease stage ($P = .067$). In fact, there was a significantly greater number of in situ cases in the PAM group compared to the non-PAM group ($P = .041$) and the majority of patients with PAM (50/50) and non-PAM (115/119) presented with stage I disease or lower. Among invasive melanomas, there was no significant difference in proliferative activity between groups by comparison of median mitotic count ($P = .37$), median pHH3 count ($P = .61$) or Ki-67 proliferation index ($P = .99$). Pregnancy status was also not associated with age at diagnosis, tumor site, Breslow depth, Clark level or ulceration. We found no predilection for higher stage disease in PAM. Furthermore, in this study of patients with primarily early stage disease, our data suggest that pregnancy does not have a significant impact on tumor proliferation. For patients undergoing close clinical surveillance, a history of PAM should not outweigh traditional factors, such as advanced maternal age, in planning future pregnancies.

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2739

A unique presentation of metastatic melanoma appearing ten years after the primary lesion that highlights the usefulness of SOX-10 in identifying melanomas of metastatic origin

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A 45-year-old female with a medical history of melanoma on the right triceps treated with Mohs and skin graft and one year of interferon therapy in 2005 presented with an enlarging right upper quadrant cutaneous nodule. The lesion appeared approximately one month prior and there were no inciting events prior to the appearance of the nodule. The patient had no systemic symptoms, pain, pruritus, perilesional ecchymosis or bleeding. The lesion was bullous, violaceous, and measured 5 x 5 x 3 cm. A CT scan of the abdomen was performed and demonstrated a 5.8 x 6.2 cm lesion with well-defined and enhancing rims in the skin and subcutaneous fat of the upper right abdominal wall, appearing to minimally infiltrate the underlying rectus abdominus musculature without intraperitoneal communication. After surgical excision, the lesion was found to have an abnormal appearing capsule and was sent to pathology for further evaluation. Preliminary pathological findings were consistent with invasive high grade undifferentiated malignant neoplasm. Further immunohistochemical testing revealed that the tumor cells were positive for SOX-10, Vimentin, EMA, Ki-67, and negative for Mart1, HMB45, pancytokeratin, desmin, smooth muscle actin, CD31, CD34, ERG and tyrosinase. Given the clinical history, the morphologic and immunophenotypic findings were found consistent with malignant melanoma of metastatic origin. Further testing revealed positivity for BRAF VE1 and BRAF V600E, further confirming the diagnosis. This is a unique presentation of metastatic melanoma that appeared ten years after the primary lesion was treated with Mohs and interferon therapy. Even though the lesion appeared vascular in nature, both clinically and surgically, the positivity for the SOX-10 marker and the clinical history helped hone the diagnosis of malignant melanoma of metastatic origin.

Commercial support: None identified.

3199

Antimelanogenic effect of sorbus aucuparia fruit extract in α-melanocyte stimulating hormone-induced B16F10 murine melanoma cells

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Melanogenesis is a physiological process that results in the synthesis of melanin pigments. The key enzyme of this process is tyrosinase, involved in the initial stages of melanin biosynthesis. Melanin plays an important role in protecting skin against ultraviolet light injury. However, abnormal accumulation of melanin pigments lead to hyperpigmentation disorders. Therefore tyrosinase inhibitors are most promising agents for preventing and treating pigmentation disorder and are used as skin-whitening agents in the cosmetic industry. In this study, we evaluated the effect of sorbus aucuparia fruit (SAF) extract on melanogenesis of α-MSH-induced B16F10 melanoma cells. We measured melanin content, tyrosinase activity, and the expression of melanogenesis-related proteins. As results, SAF extract reduced cellular melanin content and tyrosinase expression. In addition, SAF extract reduced melanin content in 3D-culture skin model (reconstructed human epidermis with melanocytes). Taken together, these results suggest that SAF extract could be useful as a hyperpigmentation inhibitor.

Commercial support: None identified.

2407

Attitudes and behaviors towards sun protection and melanoma in African Americans

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Introduction: The incidence rates of melanoma have increased over the past decade. Not much is known about melanoma in the black population, so our objective was to understand the frequency that black patients engage in skin-protective behaviors, as well as their self-perceived risk of developing melanoma and confidence in ability to perform skin self-examinations.

Methods: A total of 142 adult patients from the University Hospitals Case Medical Center outpatient dermatology clinic were surveyed on their frequency of sun-protective behaviors, self-perceived risk of developing melanoma, confidence in performing skin self-examinations, and confidence in being able to identify a melanoma. Patients who self-identified as African American, were at least 18 years old, and were fluent and literate in English were selected for inclusion.

Results: Of the 142 patients who were surveyed, 66.9% were on Medicaid. We found that black males were more likely to perceive themselves as being at risk for developing melanoma ($P = .0021$, adjusted OR 2.592, 95% CI 1.170-5.744). Patients with at least some college education were more likely to be confident in differentiating between a melanoma and other types of moles ($P = .037$, OR 2.589, 95% CI 1.054-6.358), as well as examining a mole for asymmetry ($P < .001$, OR 6.315, 95% CI 2.048-19.722). Current smokers were less likely to have been taught how to conduct a skin self-examination ($P = .028$, OR 2.746, 95% CI 1.104-6.830), and also less likely to be confident that they could examine a mole for asymmetry ($P = .038$, OR 0.298, 95% CI 0.096-0.921). 16.2% of surveyed patients reported never or rarely intentionally seeking shade, and 84.5% reported never or rarely applying sunscreen at least three times a week. 80.3% reported having no confidence at all in differentiating between a melanoma and other types of moles. 81.7% of patients reported having no confidence at all in being able to examine a mole for asymmetry. 71.1% of these patients did not believe they were at risk for developing melanoma, and only 17.8% reported being taught by a doctor how to conduct a skin self-examination.

Conclusion: The education provided to black patients for sun protection and skin-self examinations needs to be improved so that melanoma mortality rates among blacks can be decreased. More education is needed to improve black patients' confidence in being able to check their own skin, as well as improving their sun-protective behaviors.

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BAP1 expression in cutaneous melanoma in Chilean population

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Introduction: BAP 1 (BRCA1-associated protein-1) is a tumor suppressor gene whose germline mutation has been described in families predisposed to uveal melanoma, familial melanoma and other neoplasms. There is a highly positive correlation between the absence of immunohistochemistry (IHC) expression of BAP1 and the mutation of the gene that encodes it. Furthermore, researchers have found BAP1 loss of expression in 2 5 5.6% of sporadic cutaneous melanomas.

Objective: To determine BAP1 expression in melanomas in Chilean population.

Materials and methods: BAP1 IHC staining was performed in archival formalin-fixed, paraffin-embedded tissue sections from cases of cutaneous melanoma and a sample of atypical Spitzoid tumors from the Department of Pathology, Pontificia Universidad Católica de Chile (2006-2014).

Results: 102 patients were collected (total of 130 histologic samples). Of these seven patients had familial melanoma, 17 had multiple primary melanoma, 68 cases were sporadic cutaneous melanoma and 5 atypical Spitzoid tumors. 56.9% of all melanomas were in situ. All samples showed positive BAP1 immunohistochemical expression.

Discussion and conclusions: Using IHC we did not find BAP1 loss in sporadic melanomas neither in patients with familial, multiple melanoma tumors nor 5 atypical Spitzoid neoplasms, reflecting the absence of mutation in our population, in contrast to previously published. This could be explained by geographical and ethnic differences, although another possibility is that the frequency of BAP1 alteration in thin and in situ melanoma could be lower than in advanced invasive melanoma.

Commercial support: None identified.

3057

Clinical remission of stage IIIB, BRAF-negative, malignant melanoma with combined high dose IL-2 and aflibercept

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Background: The incidence of melanoma, the most fatal form of skin cancer, continues to rise faster than any other cancer type in the United States. While IL-2 monotherapy has classically been used to treat melanoma, data regarding the efficacy of aflibercept, a relatively newer agent, is lacking. Here, we describe a patient with metastatic melanoma of the scalp who achieved clinical remission after treatment with aflibercept, a novel VEGF decoy receptor, in combination with high-dose IL-2 therapy.

Case report: A 51 year-old man presented to our dermatology clinic with multiple nodules at the vertex of his scalp. After biopsy and staging imaging, he was diagnosed with T4N1M0, stage IIIB, B-RAF negative, malignant melanoma. Surgical resection was not advised due to his multiple lesions covering a wide area of his scalp. The patient received 3 mg/kg of aflibercept, infused intravenously every 14 days. The dose was increased to 4 mg/kg/dose every 2 weeks after 6 months. He completed 6 cycles of high-dose IL-2 in a closely monitored, intensive care unit setting. Aflibercept administration was notable for new onset hypertension (commencing three days after first infusion), an erythematous rash of the groin (responsive to antibiotic cream), and transient rectal bleeding. After six months of therapy, the patient's scalp lesions had lighted and decreased in size. All lesions were individually resected with pathology demonstrating no evidence of melanoma. Instead, benign dermal melanophages and chronic inflammation were seen.

Discussion: Aflibercept functions as a high-affinity, soluble decoy VEGF receptor that prevents intracellular and extracellular VEGF-A, VEGF-B, and placental growth factor (PlGF) from binding to their receptors. In a single-arm phase 2 study, aflibercept monotherapy was associated with a 50% progression-free survival of at least 4 months in patients with inoperable stage III or IV melanoma of cutaneous or uveal origin. The severity of hypertension, a well-known adverse effect of aflibercept, was associated with a positive response to the drug. The observation of clinical remission using a regimen of IL-2 and aflibercept has, to our knowledge, not yet been documented in patients with stage IIIB melanoma. Additionally, it is unclear whether synergistic action occurs with combined IL-2 and aflibercept. Randomized clinical trials are warranted to investigate superiority of the combined regimen compared to IL-2 alone.

Commercial support: None identified.

3612

Blue nevus-like metastatic uveal melanoma

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Cutaneous metastasis from uveal melanoma is not frequently encountered. Additionally, only rarely does metastatic uveal melanoma simulate the appearance of a blue nevus clinically or histopathologically. As a result, blue nevus-like metastatic melanoma is difficult to recognize and confidently diagnose. The use of cytogenetic analysis has been introduced as an additional diagnostic tool and includes the use of FISH (analysis of monosomy 3) and mutational analysis (analysis of BRAF). With this knowledge, targeted drug therapies may be used as adjunct treatment to prolong life and improve patient outcomes. We report the case of a 77-year-old female with a history of uveal melanoma status post iodine plaque therapy and nodular melanoma of the scalp status post excision, who presented with a cluster of blue macules in the same area of the scalp as her prior melanoma. Differential diagnosis included blue nevus, dermal melanocytosis, and blue nevus-like metastatic melanoma from preexisting uveal or nodular cutaneous melanoma. The histopathology demonstrated a focal collection of elongated, spindle-type, pigmented cells in the dermis scattered throughout a dense collagen matrix, which was consistent with a blue nevus-like metastatic melanoma, most likely from her previous uveal melanoma. Because she lived several hours away, the patient was returned to her primary dermatologist and oncologist for further workup, including a PET/CT and MRI of the brain. PET/CT showed hypermetabolic foci in the lungs, not thought to be related to metastatic disease and to be followed with serial CT scans. There was no evidence of metastatic disease on brain MRI. Mutational analysis for BRAF, a marker of cutaneous melanoma was negative. Because the remaining tissue from the biopsy was small, we were unable to perform FISH to check for monosomy 3, a marker of uveal melanoma metastasis. Therapy was discussed by the patient's oncologist, but she declined any further treatment and has since been lost to follow-up.

Commercial support: None identified.

3842

Clinicopathologic characteristics and cytogenetic profiles of melanocytic lesions of uncertain malignant potential: A retrospective chart review

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Background: Melanocytic tumors of uncertain malignant potential (MELTUMP), a subset of melanocytic neoplasms most of which are atypical Spitz tumors, pose a unique diagnostic challenge and often elude classification. Although fluorescence in situ hybridization (FISH) and comparative genomic hybridization (CGH) have allowed for better characterization of MELTUMP, further investigation is needed in identifying features associated with the presence or absence of cytogenetic abnormalities in patients given such provisional diagnosis. This study aims to identify the clinical, histologic, and CGH- or FISH-derived profiles of patients who carried the provisional diagnosis of MELTUMP.

Methods: Patients given the provisional diagnosis of MELTUMP and treated at the Washington Cancer Institute were identified via the electronic medical record. Data on known melanoma clinical prognostic factors and histopathologic features were collected. Patients whose biopsies did not undergo CGH or FISH profiling were excluded.

Results: Twelve patients (mean age 40.7 years old) were given a provisional diagnosis of MELTUMP and underwent CGH testing. Cases were sent out for formal pathologic consultation on an average of 1.6 times. Primary tumor sites include the back (n = 3), legs (n = 2), arm (n = 2), face (n = 2), abdomen (n = 1), thigh (n = 1), and sole (n = 1). Breslow depth was recorded in 10 patients, 6 of whom underwent a sentinel lymph node biopsy. Deep mitoses (n = 4), asymmetry (n = 6), sheets of melanocytes (n = 8) and high-grade cytologic atypia (n = 7) were the most common histologic features identified. Half of the patients showed chromosomal aberrations. Chromosomal copy gains were noted in 8 patients, with 6p and 11p being the most common. Five patients had chromosomal losses, with 3 having losses in 9p. Spitz nevus was the favored diagnosis in 42% of the cases, with two of those cases having gains in 11p. Multiple chromosomal gains and losses were noted in cases favoring melanoma after CGH. One case without any chromosomal aberrations persisted as a desmoplastic melanoma.

Conclusion: No statistical model could be used to fit the small sample size in this study. Larger studies are needed to identify histologic features associated with the presence/absence of cytogenetic abnormalities in patients given such provisional diagnosis.

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Concordance of reflectance confocal microscopy with histopathology in the diagnosis of lentigo maligna

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Background: Lentigo maligna (LM) is a form of melanoma in situ that may progress slowly, but is associated with higher rates of local recurrence compared to other subtypes of melanoma. Diagnosis of LM can be challenging, as blind biopsies are prone to sampling error due to the heterogeneous nature of LM and its characteristic wide subclinical extension. Reflectance confocal microscopy (RCM) provides noninvasive, real-time imaging of cell structure and may be a useful adjunct in diagnosing LM and defining its borders. Few studies have compared performance of RCM to histopathology in diagnosing LM, and specific clinical or microscopic features influencing RCM interpretation are not well described.

Objective: To determine the degree of concordance between RCM and conventional histopathologic analysis in the evaluation of suspected LM and to identify factors that may obscure diagnosis of LM with RCM.

Methods: Under IRB approval, 16 patients were seen by the Dermatology service at Memorial Sloan Kettering Cancer Center for evaluation of known or suspected LM. Cases included primary LM as well as recurrent and/or previously treated lesions. For each case, RCM was performed and images were assessed for LM using an accepted algorithm. A total of 59 biopsies were performed in areas of concern. RCM and histopathology interpretations were reviewed for degree of concordance. In cases of diagnostic discordance, clinical histories and images were analyzed for patterns leading to misdiagnosis with RCM.

Results: RCM and histopathology interpretations were concordant in 52/59 biopsy sites (88%). There were no false negatives (sensitivity 100%) and 7 false positives (specificity 71%) using RCM. The false positives included actinic keratosis (2), dermatofibrosis (2), solar lentigo (1), dermal melanocytosis (1), and a pigmented and traumatized seborrheic keratosis (1). Of note, 5/7 false positives occurred in the same patient with multiply recurrent LM previously treated by imiquimod. Features suggestive of LM in the false positive group included the presence of numerous atypical cells at the DEJ and follicular localization of these cells.

Conclusion: RCM shows excellent sensitivity for detecting LM although features of benign macules on a background of heavily sun-damaged skin can obscure diagnosis and limit its specificity. Further studies that characterize these baseline architectural changes in sun-damaged skin are needed to more reliably distinguish LM.

Commercial support: None identified.

3593

Confocal characterization of primary melanoma. Noninvasive prediction of histological prognostic markers

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Introduction: Reflectance confocal microscopy (RCM) is a noninvasive imaging technique that provides real-time evaluation of skin with cellular resolution. Recent RCM studies on melanoma morphology let the recognition of different tumor phenotypes.

Hypothesis: Melanomas can present in vivo features that translate biological and prognostic behavior, and these findings can be visible by RCM.

Objective: To detect dermoscopic and confocal criteria present in primary melanomas related to histological features that play an important role as prognostic markers.

Methodology: Retrospective study of clinical, dermoscopical and confocal images, in addition to further revision of histopathologic slides of primary melanomas diagnosed from February 2011 to February 2015. Only sporadic melanomas on trunk and limbs with high quality images available were included.

Results: 92 primary melanomas were reviewed; 44 male and 48 female with a mean age of 60.4 years old (SD 16.2) mainly located on posterior trunk (50%). The most frequent dermoscopic pattern was multicomponent (55.4%), and the predominant confocal global pattern was the so-called dendritic pattern (44.6%). Histologic melanoma subtypes included in situ (30.4%), superficial spreading (56.6%), lentigo maligna (6.5%) and nodular (5.4%) subtypes. Dermoscopic presence of pigment network was related to both lower Breslow and mitotic rate (both $P = .002$), in contrast to the presence of vessels was related to both higher mitotic rate and Breslow index ($P = .001$). Confocal presence of dermal nest was related to a higher mitotic rate ($P = .006$), similarly, presence of atypical basal cells and nucleated visible cells in dermis ($P = .03$). The observation of diffuse inflammatory infiltrate in dermis was strongly associated with mean increase in Breslow thickness of 0.6 mm ($P = .04$) and the increase of the number of the mitosis count ($P = .04$).

Limitations: Single center retrospective study, and only trunk and limbs melanomas were included.

Conclusions: Melanoma can be better characterized by dermoscopy and confocal microscopy in terms of prediction of Breslow and mitotic rate in histopathology.

Commercial support: None identified.

2359

Conservative surgery of a subungual melanoma in situ

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Subungual melanoma (SUM) is a rare subtype of melanoma. It arises from the nail matrix, but may involve the other components of the nail unit. This disease is frequently misdiagnosed, which leads to a delay in proper treatment and a poor prognosis, especially due to short matrix-to-bone distance. The final diagnosis must be confirmed by an adequate histopathologic examination. Excisional biopsies are regarded as gold standard in order to avoid sampling errors. The conservative surgery for SUM is currently recognized by the international literature (when at early stages), and offers to the patient a safe, effective and curative treatment, preserving their functional ability. In this article we intent to report a case of SUM successfully treated with conservative surgery (resection of the nail unit, preserving the digit).

Commercial support: None identified.

3907

Effect of beta-blockers on malignant melanoma risk of recurrence and overall mortality

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Introduction: Early data suggest beta-blockers, presumably through their antiangiogenic effects, may influence cutaneous malignant melanoma (CMM) recurrence and even overall survival, though conflicting reports have also been published.

Methods: Retrospective case-control study of patients diagnosed with CMM from the years of 1970 to 2014 at one academic medical center. 1339 patients met inclusion criteria. Patients with a diagnosis of melanoma prior to the study period, and those with evidence of lymph node, visceral and/or in-transit metastasis at the time of diagnosis were excluded. Those with a history of beta-blockers and/or phosphodiesterase 5 inhibitor use were compared to those without to evaluate for differences in melanoma recurrence and overall mortality.

Results: Of 1339 patients diagnosed with CMM, 74.1% had taken a beta-blocker. There was no statistically significant difference between the incidence of recurrent CMM in patients taking a beta-blocker (16.8%; 58/346) versus those who had not (16.5%; 162/993) ($P = .87$, Fisher's exact test) over an average follow-up period of 5.21 years (median follow-up, 7 years). However, the average length of time to recurrence of melanoma was longer in patients taking a beta-blocker (mean 3.19 years) than in those who had never taken a beta-blocker (mean 2.94 years), though this difference was not statistically significant ($P = 54$; two-tailed Student's t-test). There was no difference in overall mortality in those who took a beta-blocker versus those who did not (risk ratio 0.66; $P = .1256$, Fisher's exact test).

Limitations: Retrospective review, single institution, short length of follow-up.

Conclusion: The addition of a beta-blocker may provide a modest but measurable increase in disease-free survival following diagnosis of cutaneous malignant melanoma (CMM). The benign side effect profiles of these anti-angiogenic medications would likely allow easy adoption into a "cocktail" of targeted immunotherapies used in malignant melanoma. Phase II randomized clinical trials of propranolol in melanoma progression are underway.

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Efficacy evaluation of new drug for melanoma using MR molecular imaging

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Background: Major molecular imaging technology consist of optical, radionuclear and magnetic resonance molecular imaging. Molecular imaging, a type of in vivo, real time imaging, is a rapidly emerging technology that fusion science the fields of molecular biology, chemistry, pharmacology, medicine, genetics, biomedical engineering and physics.

Purpose : Molecular imaging has some advantage to the achievement of following important goal. (1) Assessment of the effects and shortening the developmental periods in new drugs development, (2) rapid, repeated and quantitative in vivo imaging in same individuals over whole experimental periods. So, molecular imaging studies are more precise and higher clinical impacts than conventional animal model study. This study aimed to development the advanced preclinical efficacy evaluation methods of new drug for melanoma using MR molecular imaging.

Method : For development of animal melanoma model for MR molecular imaging, we construct a lenti -viral vector encoding a heavy chain ferritine gene (hFTH). To generate stable B6 melanoma cell line that express hFTH, gene were transduced with lenti-viral vector B6 melanoma cell containing ferritine gene was subcutaneously inoculated in dorsal side of C57BL/6J mice. Oregonine, new antimelanoma drug, extract from leaves and barks of *Ahnus japonica* by large scale column chromatography and enzyme hydrolysis. New developed antimelanoma drug, (oregonine) and DTIC were intraperitoneal injection to animal melanoma model for MR molecular imaging. Then, T2 weighted images were acquired by 9.4 Tesler animal MRI (Bruker R).

Result: Efficacy of oregonine, new antimelanoma drug, are shown the comparable effectiveness with DTIC. Oregonine plus DTIC are shown more higher efficacy than oregonine only. So oregonine could be use as additive drugs with DTIC for melanoma management. In conclusion, melanoma animal models for the MR molecular imaging could be use a valuable tools in new drug development with highly clinical significances and more precisely preclinical efficacy evaluation.

Commercial support: None identified.

2774

Evaluation of nevus count in relation to melanoma survival in a cohort of patients from a region with high ultraviolet radiation in southern Europe

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Background: The incidence of cutaneous malignant melanoma is increasing in the last decades. The better understanding of risk and prognostic factors is essential to implement effective preventive strategies. A high nevi count is considered to be a risk factor for the development of melanoma. In a recent study developed in the United Kingdom and Spain, a high total nevi count also proved to be of favorable prognosis in melanoma patients.

Objective: To analyze if in our population (white, in a region with a high ultraviolet radiation along the whole year: Canary Islands, Spain) a low nevi count had an impact in the survival of melanoma patients.

Methods: We performed a retrospective observational study, analyzing the clinical records of the patients diagnosed with melanoma evaluated in our department from January 2000 to June 2015. Data collected included age at diagnosis, gender, site of primary melanoma, histologic subtype, Breslow thickness, staging of disease, date of last follow-up, date of death if applicable, cause of death and number of melanocytic nevi at diagnosis (low nevi count defined as <20). In situ melanomas, noncutaneous melanomas and patients without follow-up were excluded. Statistical analyses were performed with R core team.

Results: In the study period 557 patients were diagnosed of melanoma, with a 17% of melanoma in situ and 81% of invasive melanomas. 453 patients fulfilled the inclusion criteria. Women represented 54.7%. The mean age at diagnosis was 55.1 years. Superficial spreading melanoma was the most common subtype (61%), followed by nodular subtype. The most frequent body site was the trunk, followed by the legs in women and by the head and neck in men. Men were found to present with more advanced disease compared to women ($P < .02$). The mean Breslow thickness was of 1.97 mm. 59.4% of patients had <20 nevi, 27.6% had 20-50 and 12.1% >50. The median time of follow-up was of 4.8 years. The crude 5-year melanoma-specific survival rate was lower in patients with low nevi count (87.4% vs 92% in >20 nevi). The survival prediction model that included Breslow's thickness, age and nevi was better than the one that did not include nevi (log likelihood ratio test, $P = .09$).

Conclusion: The subgroup of patients with less than 20 nevi showed a tendency to develop a worse prognosis. Although we did not reach statistical significance, we think it might be affordable with a higher sample size and a longer follow-up.

Commercial support: None identified.

2521

Five year survival in patients with nodular and superficial spreading melanomas in the US population

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Introduction: Nodular melanoma (NM) is the second most common subtype of melanoma after superficial spreading melanoma (SSM) and is characterized by exclusive vertical growth phase. NM has a more rapid growth rate, more biologically aggressive behavior and an increased number of mitoses compared to other histologic subtypes, whereas SSMs are diagnosed as thinner lesions. We conducted a population-based retrospective data analysis to compare the five year relative survival of patients with NM and SSM.

Methods: We collected demographics, pathologic and survival data on patients with NM and SSM from 2004-2009 using data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER)*Stat software (version 8.2.1). Statistical tests included the Chi-square test to compare proportions, and Z-score to compare 5-year relative survival.

Results: Of the patients with melanoma, we identified 5011 patients with NM and 22,420 with SSM. Patients with NM were more likely to be 65 years or older (43% vs 25%, $P < .01$), male (63% vs 48%, $P < .01$), T3/4 (60% vs 7%, $P < .01$), N1-3 (26% vs 5%, $P < .01$) and M+ (4% vs 0.3%, $P < .01$) compared to SSM. Five-year relative survival was lower in NM compared to SSM (69.0% vs 98.3%, Z score 45.24, $P < .01$). Subgroup analysis showed inferior survival in NM in T1b (71% vs 99%, Z score 11.9, $P < .01$), T2a (91% vs 96%, Z score 2.9, $P < .01$), and T2b (70% vs 91%, Z score 5.7, $P < .01$). Survival difference remained significant after excluding patients with nodal or distant metastases at diagnosis in T1bN0M0 (78% vs 99%, Z score 7.2, $P < .01$), T2aN0M0 (95% vs 98%, Z score 2.6, $P < .01$), and T2bN0M0 (78% vs 95%, Z score 4.8, $P < .01$) suggestive of higher risk of recurrence in NM.

Conclusions: Five year relative survival is worse in NM compared to SSM especially in T1b, T2a, and T2b patients. This argues for consideration of melanoma subtype in the staging system as well as in melanoma treatment guidelines such as sentinel lymph node biopsy in T1 (less than 1 mm thick) melanoma.

Commercial support: None identified.

3187

How do we make decisions on sentinel lymph node biopsy? A decision tree from a cross-sectional study of primary malignant melanoma patients

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Background: Sentinel lymph node biopsy (SLNB) remains the standard of care for staging lymph nodes in patients with malignant melanoma (MM). It is recommended for patients having a tumor stage ≥T1b without evidence of regional or visceral metastases. However, not all the patients fulfilling this recommendation undergo the procedure.

Objective: To analyze the factors that accounts for the decisions on SLNB, and their hierarchy in the decision making process.

Methods: A cross-sectional study was conducted at the Melanoma Clinic of the Hospital Universitario Virgen Macarena (Seville-Spain). Between 2009 and 2014 484 patients with primary MM and lacking regional or at distance disease after imaging studies (CT-scan or PET-CT) were recruited. Study variables were age, sex, anatomic location, MM subtype, tumor stage (T1a-T4b), and mitotic rate (<1 mitosis/mm^2 vs ≥1 mitosis/mm^2). These independent variables were used to build a decision tree following the CHAID method. A two-tailed $P = .05$ was considered the threshold for significance.

Results: Among 271 patients with primary MM staged ≥T1b, the standard recommendation for SLNB, SLNB was performed in 63.1% (n = 171). Mean age was higher in the group of patients who didn't undergo SLNB (55.8 vs 48.8 years, $P = .001$). SLNB was performed more frequently in T2b stage (84.6%), followed by T2a (74.7%), T3a (69.2%), T1b (59.0%), T3b (58.1%), T4b (45.9%), T4a (40.0%), and T1a (11.3%). The decision tree showed that the first decision factor was the T-stage ($P < .001$). Patients with T2a, T2b or T3a tumors shown the higher frequency of SLNB (74.1%). After T-stage, the age was the most important factor ($P = .001$). In T1b, T3b, T4a or T4b cases the SLNB was carried out in 69.2% of patients aged <70 years and in 12.2% of patients ≥70 years. In patients with tumors T2a, T2b or T3a the SLNB was performed in 80.2% of patients aged <70 years and in 33.3% of those aged ≥70 years. After the age, the anatomic location was the most important factor in patients older than 70 years ($P = .04$) (40.0% for the limbs vs. 3.4% for head-&-neck). In patients <70 years the mitotic rate was a decision factor after tumor stage and age ($P = .016$).

Conclusions: Even though SLNB remains a standard of care for managing MM patients, a meaningful percentage of patients do not undergo the procedure. Beyond the accepted prognostic factors (T-stage, mitotic rate, ulceration), other clinical and even demographic factors are commonly accounted for that decision.

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Imprecision of Breslow thickness measurements in melanoma around AJCC staging cutoffs and their implications for patient management

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Background: Breslow thickness is the most important prognostic factor in clinically localized primary cutaneous melanomas and its accuracy has important implications on staging, and clinical management. A review of the Melanoma Institute Australia (MIA) and NSW Cancer Council database found an unexpectedly large number of melanomas reported as exactly 1.00 mm thick. Our study sought to determine the possible cause for this apparent aberration.

Methods: Using the Melanoma Institute Australia database, 200 cases of invasive cutaneous melanoma with a reported Breslow thickness measurement between 0.90 and 1.10 mm were selected. 125 of these were suitable for review, and their thickness was re-measured and recorded to two decimal places by two independent pathologists.

Results: Concordance of measurements between the two pathologists was high, with an intraclass correlation coefficient of 0.816 (95% CI 0.733-0.873). The original measurements showed clustering at 0.90, 1.00, and 1.10mm, whereas the review measurements did not. There was a statistically significant mean difference of 0.045 ($P = .0031$) between the original and remeasured Breslow thickness measurements. The original measurements staged 84 cases (72%) as T1 and 33 cases (28%) as T2. The reviewed measurements staged 58 cases (50%) as T1 and 59 cases (50%) as T2. This difference was statistically significant ($P < .001$).

Conclusions: This study identified the phenomenon of terminal digit bias in Breslow thickness measurement, which had a significant impact on staging. Awareness and education of this bias and recording Breslow thickness measurement to two decimal places may increase precision at critical staging intervals. We suggest standardization of guidelines in regards to Breslow thickness measurement accuracy.

Commercial support: None identified.

3438

Juvenile melanoma

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Case 1: A 6-year-old boy had a 14-month history of an erythematous papule on his left cheek. Excision revealed severe cytological atypia, deep mitoses and ulceration. S-100 stained strongly with patchy positivity for melan-A and focal positivity for HMB-45. Overall the features were consistent with an atypical Spitz nevus. Expert analysis of complete genome hybridization of the nevus concluded the final diagnosis was Spitzoid melanoma, childhood type. There was found to be loss of p16 staining which can correlate with biallelic loss of Chr 9p, at the location where CDKN2A encodes p16. Comparative genome hybridization highlighted the loss of Chr 9 with an inflection in the array at CDKN2A and CDKN2B. This supports a biallelic loss of the genes which can confer more metastatic potential than in an atypical Spitz tumor that has a monoallelic loss. Case 2: A 3-year-old girl had a one year history of a firm cystic lesion on the right cheek. Histopathology showed features of an atypical Spitz tumor of uncertain malignant potential. Compete genome hybridization again favored a diagnosis of Spitzoid melanoma. Multiple studies report that melanoma in childhood behaves differently to that of adulthood, with more atypical clinical features such as amelanosis and raised lesions, as found in this report. A review of evidence-based practice criteria for establishing the diagnosis of juvenile melanoma suggests that thorough analysis of histopathology and immunohistochemistry may allow for the correct diagnosis in most cases of childhood melanoma. Clinical and histopathologic findings of Spitzoid melanomas can correlate with comparative genome hybridization array. This can help classify and predict behavior of Spitzoid melanocytic neoplasms. Daniotti et al highlighted that mutations in CDKN2A are important in pediatric melanoma. This rare diagnosis is difficult to make and the prudent use of available investigations increases appropriate stratification of patients and diagnosis of juvenile melanoma.

Commercial support: None identified.

3149

Malignant melanoma arising in a chronic burn scar

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Neoplasia can occur after a history of a burn, the most common being squamous cell carcinoma, known as a Marjolin's ulcer. In 1982 Jean-Nicholas Marjolin first described development of skin carcinoma secondary to a burn and subsequently this phenomenon was termed Marjolin's ulcer. However, malignant melanoma secondary to a burn is relatively rare with only 39 cases being reported in the literature to the best of our knowledge. It has been reported that around 2% of chronic burns can turn into malignant tumors. We present a patient who attended dermatology clinic with a several year history of a chronic scar secondary to a steam burn on the left forearm. The scar had recently developed lumps within it, which initiated an urgent dermatology referral. A biopsy confirmed malignant melanoma and he proceeded to have a wider excision repaired with a split thickness skin graft. To date he has had no signs of recurrence. The pathogenesis of neoplasia secondary to chronic burns is unclear, however some people feel that a carcinogenic toxin is produced at the site of the burn. Another theory is that the scar could create an environment which encourages neoplastic growth once a carcinogen is present. This case highlights the need for prolonged surveillance of a patient with a history of a burn, as the latency can be as long as 71 years. A careful history is required when assessing these patients for the first time and then regular follow-up is advised for the prevention and detection of malignant melanoma.

Commercial support: None identified.

2954

Melanoma among patients with oculocutaneous albinism: 3 case reports

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Introduction: Patients with oculocutaneous albinism (OCA) are highly susceptible to develop UV-induced skin cancer and according to published series squamous cell carcinoma is the most common histopathologic subtype followed by basal cell carcinoma. Diagnosis of melanoma represents a greater diagnostic challenge in these patients due to its hypopigmented appearance and to date fewer than 40 cases of melanoma in OCA have been reported. Herein, we report 3 cases of amelanotic melanoma in 3 albino patients.

Case reports: Case 1. A 16-month old infant with OCA type I was diagnosed of melanoma of nevoid type with a Breslow thickness of 4.64 mm located on his forehead. Case 2. A 51-year-old albino woman was diagnosed of superficial spreading melanoma with a Breslow thickness of 0.78 mm located on her arm. Case 3. A 53-year-old woman with OCA type I was diagnosed of superficial spreading melanoma with a Breslow thickness of 0.45 mm located on her back. During follow-up, the patient developed a basal cell carcinoma on the nose that was treated with Mohs surgery.

Discussion: The occurrence of melanoma in individuals with OCA has been reported in the literature to be rare. This low incidence remains unexplained since it is well established the inverse relationship between the incidence of melanoma and the degree of skin pigmentation. We believe that due to their lack of pigment, such lesions may be misdiagnosed as other benign or malignant skin tumors or even as inflammatory disorders. Indeed, genome-wide association studies in different populations have identified an association between selected polymorphisms in pigmentation-related genes (TYR, TYRP1, OCA2, SLC45A2 and MC1R) and risk of melanoma. On the other hand, it has been suggested that patients with a total defect of melanin synthesis (OCA type 1A) would have a lower risk of developing skin cancer due to the fact that these patients do not synthetize pheomelanin which promotes the production of reactive oxygen species.

Conclusion: Differences in the sensitivity to skin carcinogenesis among patients with OCA may be explained, in part, according to the gene mutation. We underline the importance of dermoscopy for the evaluation of pink lesions in albino patients with special attention to the vascular pattern to improve early detection of amelanotic melanoma.

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3748

WITHDRAWN

3032

Painful nipple hyperkeratosis secondary to vemurafenib

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Vemurafenib is a selected BRAF kinase inhibitor approved for treating metastatic or unresectable melanoma, which unfortunately has numerous cutaneous side effects, including three previously reported cases of asymptomatic areola and/or nipple hyperkeratosis. We present the first case of painful bilateral nipple hyperkeratosis secondary to vemurafenib in an 84-year-old female. She was successfully treated with tretinoin 0.05% cream, which allowed her to comfortably continue treatment. With increased awareness of this condition, we found a second case of asymptomatic nipple hyperkeratosis secondary to vemurafenib in our clinic. As this medication gains acceptance for treatment of metastatic melanoma, it is imperative that dermatologists are aware of this potentially uncomfortable side effect, which could result in decreased compliance and impaired quality of life.

Commercial support: None identified.

3174

Melanoma in men treated with PDE5A inhibitors: A report from the RADAR (Research on Adverse Drug Events And Reports) project

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Introduction: The phosphodiesterase 5 (PDE5A) inhibitors sildenafil (S), vardenadil (V), avanafil (A), and tadalafil (T) are all FDA-approved for the treatment of erectile dysfunction and with no caveat regarding melanoma risk in the full prescribing information (FPI). However, an increased risk of melanoma related to S, V and T has been previously reported in literature. The aim of this study is to explore whether melanoma occurs subsequent to PDE5A inhibitor exposure in a large patient population.

Methods: We searched a large urban, academic-based electronic medical record (EMR) repository (3 million individuals, January 2010 to December 2014) for all male patients who were exposed to one of the drugs and were subsequently documented as diagnosed with melanoma (ICD9 codes 172.0-172.9) at least 3 months after drug exposure.

Results: Of 525,523 individual men, 8 of 1117 men exposed to V developed melanoma, 30 of 5933 men exposed to T developed M, 36 of 5507 men exposed to S developed M, and none of only 21 men exposed to A developed M. After adjustment for race and age, a significant association with melanoma was detected for T (OR: 1.6; 1.11-2.31, $P = .01$) and for S (OR: 2.07; 1.48-2.89, $P < .001$). Moreover, a trending towards significance ($P = .058$) was detected for V.

Conclusion: While not currently recognized as a warning, precaution or possible adverse reaction in the FPI for any one of the PDE5A inhibitors, these data that indicate a significant association with the development of melanoma in patients taking sildenafil and tadalafil do now warrant exploration to further define this safety signal relative to additional, and even, larger patient populations. This study underscores how ongoing, proactive, postmarketing pharmacovigilance plays an important role in the detection of adverse outcomes not previously detected as safety signals in already marketed drugs. Moreover, investigation into causality for any possible relationship between PDE5A inhibition and the development of malignant melanoma is warranted.

Commercial support: None identified.

2981

Patient preferences during total body skin cancer screening examination

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Background: Despite the continued rise of skin cancer in the US, many at-risk individuals do not receive regular skin checks for multiple reasons, including discomfort due to the personal nature of a total body skin exam (TBSE). The purpose of this study was to identify patient preferences for physician gender and disrobing practices, to better understand how the TBSE may be adjusted to maximize patient comfort.

Methods: An anonymous cross-sectional survey study of adults 18 years or older undergoing a TBSE was conducted at three institutions. The survey included questions regarding attitudes about skin cancer screening and preferences of patient comfort with a TBSE, including gender of screening provider, degree of disrobement and embarrassment during the exam. Distributional characteristics for each variable were assessed for normality. Univariate significance was assessed with chi-squared test, Student's t test, or one-way ANOVA, as appropriate.

Results: Of 483 participants (response rate 85.5%), 443 completed the gender preference survey questions (252 women, 191 men). One-third (33.7%, n = 85) of female participants had a preference for physician gender, compared to only 16.8% (n = 32) of male participants ($P < .001$). Women were more likely than men to ask for a gender-specific physician when scheduling (12.8% vs 4.9%, $P = .004$). Of those with a preference (n = 117), 98.8% of women and 37.5% of men preferred a female physician ($P < .001$). Gender preference for physician decreased inversely with patient age, from 50% of women <30 years, down to 24.2% of women ≥70 years. Regarding disrobing preferences, 31.3% of women did not want their genital area examined, compared to 12.5% of men ($P < .001$). In visits where the physician and patient were the same gender (n = 218), patients were more likely to be asked to remove underwear (46.9% vs 25.5%, $P = .01$), and women were more likely to have their breasts examined (81.2% vs 71.7%, $P = .03$).

Conclusions: Overall, these results suggest that the strong difference in preference for physician gender between women and men identifies a potential barrier for at-risk individuals to receive regular TSBEs if there is no option for the specific physician gender of choice. In order to enhance patient comfort in the clinical setting, scheduling practices and disrobing requirements should be evaluated to address this issue in hopes of promoting patient choice of provider.

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2522

Survival in desmoplastic melanoma patients with or without adjuvant radiation

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Introduction: Desmoplastic malignant melanoma (DMM) is a rare variant of melanoma with higher local recurrence rates compared with conventional melanoma. Adjuvant radiotherapy (AR) after excision is considered in patients with DMMs that are greater than 4 mm (ie, thick melanomas) in Breslow's depth to attain local control. However, its impact on survival is unknown. We conducted a population-based retrospective data analysis to assess the impact of AR on the survival of patients with thick DMMs.

Methods: We analyzed patients with T4 (thicker than 4 mm) DMM according to the AJCC's 6th edition from 2004-2012 using data from the Surveillance, Epidemiology, and End Results (SEER)*Stat software (version 8.2.1). Statistical tests included the Fisher's exact test to compare demographics and the Z-score to compare relative survival.

Results: Of the 1239 patients with DMM, we identified 346 patients with T4N0M0 DMM. Seventy percent of patients were male, 98% were white, 60% were older than 65 years, 78% were diagnosed with stage T4a, 18.5% stage T4b, and 3.5% diagnosed T4NOS. Sixty (17%) patients received radiation postsurgery. There was no significant difference in age, gender, and race between two groups. However, there were more T4b patients who did not receive radiation ($P = .01$). There was a statistically significant difference in the relative survival of patients with or without use of radiation treatment postsurgery at years 2 (100% vs 91.6%, Z-score = 2.057, $P = .04$) and 3 (98.9% vs 79.7%, Z-score = 2.41, $P = .02$, and 4 (98.7% vs 78.9%, Z-score = 2.388, $P = .02$). In the stage T4a subgroup analysis, there was still a statistically significant difference in relative survival of patients with or without use of radiation postsurgery at years 2 (100% vs 92.2%, Z-score = 2.243, $P = .02$), 3 (99.7% vs 83.2%, Z-score = 2.107, $P = .04$), and 4 (99.4% vs 82.7%, Z-score = 2.057, $P = .04$).

Conclusion: Our study showed that relative survival of stage T4 DMM patients with postsurgery radiation was significantly higher than patients without postsurgery radiation. This finding needs to be validated in prospective clinical trials.

Commercial support: None identified.

3253

Vemurafenib induced "fixed drug-like eruption" with acantholytic pattern: A case report

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Vemurafenib is a selective BRAF kinase inhibitor. This drug improves survival in stage III or IV melanoma. We describe a "fixed drug-like eruption" adverse effect, with a histological pattern of acantholysis, not previously reported.

Case: A 69-year-old, white male patient presented to the dermatology room with skin lesion on left pectoral region which was diagnosed of nodular melanoma. Local excision of the lesion and axillary lymphadenectomy were performed. Imaging studies confirmed the presence of pulmonary metastasis. Molecular testing showed a positive mutation for BRAF V 600. We decided to start on therapy with vemurafenib (960 mg twice a day). After one month of therapy he was admitted to the Emergency room because a purulent, left axillary mass. Subsequent biopsy of the mass was positive for melanoma metastasis. The patient developed a pruritic, maculopapular exanthem, confluent on the face and upper trunk region. On both hypothenar regions he showed two pseudovesicles erythematous plaques that subsequently evolved to blisters. In the oral cavity, erosions and a lichenoid network were observed. The histologic study of the trunk showed mixed perivascular inflammatory infiltrates in the dermis. In the hand lesion, there was a marked epidermal acanthosis with an intraepidermal blister, scattered acantholytic keratinocytes and mild dyskeratosis. Eosinophils predominated in the epidermal infiltrate. Direct immunofluorescence was negative. Drug withdrawal was necessary in order to achieve remission of skin lesions.

Discussion: Vemurafenib improves survival in patients with metastatic melanoma harboring the BRAF V600 mutation. The most common toxic effects are arthralgia, rash and fatigue. Less common effects are photosensitivity, alopecia, eruptive nevi and cysts. Squamous cell carcinoma and keratoacanthomas have also been described. The most severe reaction includes Stevens–Johnson syndrome or toxic epidermal necrolysis. Our patient had a severe drug-skin reaction and a fixed drug-like eruption on the hands. There were two cases in the literature of rash on the trunk with acantholytic dyskeratosis pattern typical to Grover-like rash. To our knowledge, this is the first reported case of intraepidermal blister with acantholytic dyskeratosis mimicking a fixed drug eruption. These cutaneous manifestations can be managed with topical treatment, but in our case the severity of the rest skin lesions forced the suspension of the drug.

Commercial support: None identified.

2361

Vemurafenib-associated neutrophilic panniculitis in a patient with metastatic amelanotic melanoma presenting with cancer of unknown primary origin

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The treatment of metastatic melanoma is challenging. The BRAF gene mutation is found in 40-60% of melanoma, the most common being the V600E mutation. Vemurafenib was approved by the Food and Drug Administration in 2011 as target therapy for the treatment with BRAF V600 mutation–positive metastatic melanoma. Herein we report a case of metastatic amelanotic melanoma with unknown primary cancer as the initial presentation. The patient presented with neutrophilic septal panniculitis one week after vemurafenib treatment, which is a rare cutaneous toxicity of BRAF inhibitor (BRAFi). We also review current literature on management of BRAFi-related cutaneous toxicities.

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2408

A 13-year retrospective study of basal cell carcinoma in a Canadian population: A comparison between anatomical location and histopathologic subtypes

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Background: It is unknown whether the histologic subtypes of basal cell carcinoma (BCC) arise from a common progenitor cell or whether other factors play a role in their pathogenesis. Although BCC is the most common type of skin cancer, there are no Canadian studies to document the histologic variants of this tumor and their relationship with age, gender and body site.

Objective: To investigate the relationship between the different BCC histopathologic subtypes and anatomic distribution of the BCC in a Canadian population.

Methods: Between 1993 and 2005, the charts of all patients diagnosed with BCC in a single private dermatology practice in Vancouver, Canada, were retrospectively reviewed. Only the first two histologically confirmed tumors were collected from each patient.

Results: From a total of 418 patients with 1005 tumors, 557 qualifying BCCs were identified; 418 were a first BCC diagnosis. Overall, nodular BCCs accounted for 58% of all tumors and 66% were situated on the head/neck (OR = 3.0, 95% CI = 2.1-4.3, $P < .0001$) and in older people (OR = 1.6, 95% CI = 1.1-2.1, $P = .02$). Superficial BCCs were often localized to the trunk (OR = 3.2, 95% CI = 2.1-4.9, $P < .0001$) and almost half were evident in those between the ages of 40-59 years (OR = 1.8, 95% CI = 1.2-2.7, $P = .004$). Infiltrative and mixed BCCs appeared predominantly on the head and neck (OR = 2.9, 95% CI = 1.6-5.2, $P < .0001$). Nodular (OR = 3.1, 95% CI = 2.1-4.5, $P < .0001$) and mixed BCCs (OR = 6.3, 95% CI = 1.5-26.9, $P = .004$) were more common in men. Infiltrative (OR = 2.4, 95% CI = 1.5-4.1, $P = .0003$) and superficial BCCs were more common in women (OR = 3.7, 95% CI = 2.5-5.7, $P < .0001$).

Conclusion: Our results show a preference of at least some BCC subtypes for certain anatomical locations and gender. This suggests possible differences in the pathogenesis of this malignancy.

Commercial support: None identified.

3909

A case of metastatic Merkel cell carcinoma with lymphoepithelioma like features negative for cytokeratin 20

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Merkel cell carcinoma (MCC), also known as neuroendocrine carcinoma of the skin, is an aggressive cutaneous neoplasm that has a poor prognosis with a high metastasis and recurrence rate. Merkel cell carcinoma arises most often on sun-exposed areas in fair-skinned individuals over age 50. It usually appears as a firm, painless, violaceous lesion on the head and neck region. Histopathologically, MCC usually appears as a dermal tumor nodule, which frequently extends into the subcutaneous fatty tissue. The tumor cells are small blue cells with basophilic nuclei and minimal cytoplasm. Mitoses are frequent and the apoptosis index is high. The "small round blue cell" histologic pattern of MCC must be differentiated from several other tumors, such as small-cell lung carcinoma, carcinoid tumor, malignant lymphoma, and small-cell melanoma. Therefore immunohistochemical staining is required. One of the hallmarks of Merkel cell carcinoma is positivity for cytokeratin 20 in a perinuclear dot like pattern. Here we present a rare case of an invasive poorly differentiated carcinoma with neuroendocrine differentiation with two rare histopathologic features—lymphoepithelioma like differentiation and cytokeratin 20 negativity. Weedon calls the lymphoepithelioma like differentiation pattern of MCC "exceedingly rare." While poorly differentiated carcinomas can lose CK 20 positivity, 95% of Merkel cell carcinomas express positivity for CK20. In our case a 91-year-old white male, with an extensive history of radiation treatments, presented in clinic for a rapidly enlarging post auricular mass measuring 6 x 4 cm that he states tripled in size over two months after originally presenting as a nonhealing ulcer. A punch biopsy revealed the presence of a carcinoma infiltrating the dermis with trabeculae of neoplastic cells also forming larger nests and syncytia. A strong lymphoid response and basaloid appearing areas were noted on dermatopathology. The carcinoma expressed the neuroendocrine markers synaptophysin and chromogranin. Notably pathology was negative for Ber-Ep4, CK20, and TTF-1. A PET scan and CT head/neck revealed metastatic involvement of the parotid lymph nodes. No lesions were noted in the lungs thus ruling out metastatic small cell neuroendocrine carcinoma of the lung. Wide local excision was performed along with a superficial parotidectomy with facial nerve preservation. One out of two intraparotid lymph nodes excised was positive for poorly differentiated carcinoma. A wide cervical facial advancement flap repaired the defect after frozen section pathologic examination revealed clear margins. Merkel cell carcinoma is a rare and deadly tumor and this case is unique given its two unusual histopathologic findings. We present this case with corresponding clinical and histopathology images to remind clinicians and pathologists that Merkel cell carcinoma can have unusual presentations under the microscope. We highlight the importance of thorough histopathologic investigation as well as thorough clinical workup with PET/CT to rule out metastasis of other neuroendocrine tumors such as small cell lung cancer.

Commercial support: None identified.

3087

A dose finding trial with a novel ingenol derivative (LEO 43204) for field treatment of actinic keratosis on the scalp

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Introduction: LEO 43204 is a novel ingenol derivative developed for improved chemical and biologic properties compared to ingenol mebutate. This phase 1/2 trial investigated the efficacy and safety of LEO 43204 gel in patients with actinic keratosis (AK) on the scalp.

Methods: This was a randomized, double-blind, parallel-group, vehicle-controlled 8-week dose-finding trial investigating efficacy and safety of 0.037% and 0.05% LEO 43204 gel as field treatment once daily for 2 consecutive days on the balding scalp (25-250 cm^2) with 5-20 clinically typical AKs in the treatment area. The 0.05% dose was selected based on the outcome of the dose escalation part of the trial. Six individual components of local skin responses (LSRs) were assessed on a scale from 0 to 4, yielding a max composite score of 24. Efficacy was assessed by AK count on days 29 and 57; LSRs and adverse events were assessed on days 1, 3, 8, 15, 29, and 57. Patients completed a Treatment Satisfaction Questionnaire (TSQM) on day 57.

Results: A total of 163 patients were randomized and received treatment. In each treatment group at least 96% of patients completed all treatments. The median age was 72 years; all were men, white, and had Fitzpatrick skin type I-III. The median history of AK was 9 years. At baseline the median number of AKs in the treatment area was 13. For both doses the reduction in AK count at week 8 compared to baseline was significantly greater than with vehicle (73% (0.037%); 79% (0.05%) vs 13% (vehicle); $P < .001$) and most (91% to 97%) of this effect was observed by week 4. For both active doses the composite LSR score peaked at day 3, rapidly declined thereafter and were almost back to baseline at 2 weeks. The peak composite LSR score for the active treatments was higher than for vehicle (8.6; 8.7 vs 1.5). Both active treatments were well-tolerated with the most common adverse drug reactions being application-site pain (including burning) (48%; 57% vs 6%) and application-site pruritus (25%; 27% vs 3%). There were no treatment-related serious adverse events. Global treatment satisfaction score was high for both active treatments and higher than vehicle (75%; 76% vs 36%; $P < .001$).

Conclusion: Both doses of LEO 43204 gel were effective as field treatment of AK on the balding scalp and statistically significantly superior to vehicle, were well-tolerated based on the adverse event profile and LSRs, and were associated with high global treatment satisfaction.

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2650

Abrikossoff's tumor: an atypical presentation

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Introduction: Abrikossoff's tumor or granular cell tumor (GCT) is usually benign. It might involve multiple anatomical sites, most frequently the head and neck. In the skin it has an unspecific clinical appearance, leading to a wide range of differential diagnoses.

Case report: A 55-year-old woman was referred to us with a hyperesthesic lesion, not painful, that appeared one year before in the lower abdomen after a strong trauma in this area. It was a brownish nummular tumor lesion, infiltrating but not adhered to deep planes, well defined, measuring 3 x 2 cm. With the clinical suspicion of atypical dermatofibroma, we made surgical excision of the lesion. Histopathology revealed a nonencapsulated tumor in the dermis and subcutaneous tissue disposed in sheets, nests and trabeculae organized irregularly. It lied between collagen bundles and surrounded skin appendages. Tumor cells were large and polyhedral with abundant eosinophilic granular cytoplasm surrounding a hyperchromatic nucleus. Cellular atypia, mitosis, vascular invasion and necrosis were not observed. Inmunohistochemical (IH) study showed positive S-100 and CD68. Hence, a histologic and IH diagnosis of a GCT was made.

Discussion: Abrikossoff's tumor is a rare benign neoplasm that might affect any part of the body. It usually appears from the second to the sixth decade of life and it is twice as common in women as in men. It's relatively more common among black people. This tumor usually presents as a slow growing, solitary and painless nodular mass, located mainly in head and neck areas, the tongue being the most frequent location. It histogenesis is disputed, but the neural origin is the most defended. Histopathology of the tumor shows polygonal cells arranged in sheets with granular eosinophilic cytoplasm and small nuclei, that infiltrates the dermis and subcutaneous tissue. "Pustulo-ovoid bodies of Milian" have been described as a constant histological finding. IH studies have shown the cells to express S-100 protein and CD-68, among others. GCT metastasis are rare (1-3%). Tumor size >5 cm, rapid growth, vascular invasion, necrosis and cell spindling are important indicators of malignancy. The treatment of choice is local surgical excision with a wide margin.

Conclusion: We present a case of cutaneous GCT, benign, localized in lower abdomen (an infrequent location), presenting as a histiocytoma-like lesion that appeared after a strong trauma in this anatomic area.

Commercial support: None identified.

2394

An overview of the skin surveillance and photoprotection behaviors in the liver transplant recipients in Queensland, Australia

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Introduction: Nonmelanoma skin cancers such as squamous cell carcinoma and basal cell carcinoma are commonly encountered cutaneous neoplasms in solid organ transplant recipients (OTRs) and can lead to significant morbidity. Patient education is therefore of paramount importance to encourage both timely assessments and treatment of suspected lesions in these high-risk individuals. The aim of this study was to review the skin surveillance and photoprotection behaviors to determine whether these were adequate amongst the liver transplant recipients in Queensland, Australia.

Methods: A total of 183 patients were recruited from the Princess Alexandra Hospital in Brisbane. All patients completed a health and sun survey questionnaire which collected information regarding the frequency of their skin surveillance and photoprotection behaviors.

Results: Less than one-third of the patients reported participating in physician assisted whole body skin examinations at a frequency of more than once a year. In regards to photoprotection, patients with a previous history of skin cancer were more likely to participate in photoprotection with hats and long sleeve clothing as well as sunscreen. However, again less than one-third of the participants reported practicing these photoprotection behaviors all the time when outdoors.

Conclusion: Our study provides a good snap shot of the skin surveillance and photoprotection in liver transplant recipients in Queensland, Australia. Our data highlight that there continues to be room for improvement in both patient education, regarding sun-protection measures and the need for regular skin surveillance by their general practitioner or dermatologist; particularly in this high-risk subgroup of OTRs. Presence of a dedicated transplant dermatology clinic which implements skin care guidelines based on the current evidence as well as recommendations made by the International Transplant Skin Care Collaborative (ITSCC) for skin care may provide an avenue to improve patient compliance when it comes to practicing photoprotection and well as skin surveillance behaviors in the future.

Commercial support: None identified.

3140

Assessment of quality of life (QoL) using Skindex-16 in patients (pts) with locally advanced basal cell carcinoma (laBCC) treated with vismodegib (VISMO) in the STEVIE study

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Sarah Williams,11 Alberto Fittipaldo,11 D. Scott Ernst,12 Axel Hauschild,13 Nicole Basset-Seguin,14 Johan Hansson15 11Roche Products Ltd, Welwyn Garden City, UK; 12Western Univ; London Regional Cancer Program, London, Ontario, Canada; 13Univ Hospital Schleswig-Holstein, Kiel, Germany; 14Univ Paris 7 & Hôpital Saint-Louis, Paris, France; 15Karolinska Institutet, Stockholm, Sweden

Background: VISMO is approved for use in adults with laBCC or metastatic BCC (mBCC) inappropriate for surgery or radiotherapy. STEVIE (NCT01367665) is an ongoing phase 2 study evaluating the safety of VISMO (150 mg/d in 28-d cycles) in pts with laBCC or mBCC. A secondary objective assesses the effect of VISMO on QoL using Skindex-16. Here we present Skindex-16 results for pts with laBCC.

Methods: Skindex-16 has 16 questions in three domains (symptoms, function, and emotions); it was designed for chronic diseases. Median change from baseline for each domain was assessed at Cycle 2 Day 1 (C2), Cycle 7 Day 1 (C7), and end of study (EOS) in all pts and subgroups (sex, age, and tumor location). Negative changes ≥10 points indicate a clinically meaningful improvement (CMI). Frequency of Skindex response was tabulated by clinical tumor response by the following four categories: complete response, partial response, stable disease, and progressive disease. Results are reported descriptively; no formal statistical hypotheses were tested. Data are derived from a planned interim analysis (cutoff November 6, 2013).

Results: CMIs in emotion scores were observed at all time points in pts with laBCC (n = 455), with median change from baseline of −14.3 at C2, −23.8 at C7, and −23.8 at EOS; they were consistent across all pt subgroups. Improved emotion scores at EOS were associated with complete and partial clinical responses (vs stable and progressive disease). Symptom scores were maintained through end of study in pts with laBCC, while CMIs were observed in subgroups (locations other than head/neck at C2 and end of study [both −10.4]) and in female pts and those aged ≥65 y (both −12.5 at C7). No CMIs were seen for function scores in pts with laBCC.

Conclusions: In pts with laBCC, VISMO was consistently associated with CMIs in emotion scores. Emotion scores were consistent with clinical response. The Skindex-16 has limited applicability to nonskin-related symptoms, including AEs. However, some CMIs in symptom scores were seen in limited subgroups of pts categorized by age, sex, and lesion location.

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3432

Baseline quality of life and psychosocial health of skin cancer patients

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Background: Despite the high prevalence of skin cancer, few studies have measured its effect on patient quality of life (QOL) and psychosocial health using disease-specific validated instruments.

Objective: To assess the baseline QOL and levels of psychosocial distress in patients with nonmetastatic skin cancer.

Methods: We conducted a cross-sectional study of 136 consecutive patients presenting for the treatment of nonmetastatic skin cancer between February and April 2015 across two surgical facilities in the same academic institution. Prior to treatment, patients completed a questionnaire documenting sociodemographic and medical information. Additionally, they completed validated psychometric measures of QOL [Skin Cancer Index (SCI)] and symptoms of anxiety and depression [Hospital Anxiety and Depression Scale (HADS)].

Results: The mean overall SCI score for the sample was 69.8 out of 100 (95% CI 66.3, 73.4). Decreased SCI scores, corresponding to decreased QOL, were associated with younger age ($P < .01$), higher income ($P = 0.01$), and a suburban/rural clinic location ($P < .01$). Women scored lower than men in the SCI appearance subscale ($P = .03$). Depression levels were greater for immunosuppressed patients ($P < .01$), those with severe chronic disease ($P < .01$), and those with lower income ($P = .04$). Anxiety levels were greater for younger patients ($P < .01$) and smokers ($P = .02$). 24% of patients met the threshold for clinical signs of psychosocial distress (HADS score ≥7). HADS anxiety scores negatively correlated with total SCI scores ($P < .01$).

Limitations: Limitations include cross-sectional study design, imputed patient survey data, and patient self-reported characteristics.

Conclusion: The SCI and HADS are validated tools sensitive to psychosocial changes in patients with nonmetastatic skin cancer. Younger patients, women, and those with higher income are most impacted by their skin cancers, while smokers, immunosuppressed patients, and those with severe illnesses are at risk for symptoms of anxiety and depression. Nonmetastatic skin cancers appear to have a moderate impact on patient QOL but use of disease-specific tools such as the SCI precludes value comparisons to the general population. Future studies will identify how patient-reported outcomes change with treatment of skin cancer.

Commercial support: None identified.

3361

BOLT 18-month analysis: efficacy and safety with sonidegib in locally advanced BCC (laBCC)

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Background: Durable clinical benefit and manageable tolerability were observed with the hedgehog pathway inhibitor (HPI) sonidegib in patients (pts) with laBCC in the phase 2 BOLT study. Updated efficacy and safety in pts with laBCC treated with sonidegib 200 mg using data collected up to 18 months (mo) after randomization of the last pt are reported here.

Methods: Tumor responses were assessed by central review by MRI per RECIST v1.1, photo per WHO guidelines, and histology in multiple biopsies, and a composite overall response (COR) for each pt was determined using criteria A (per protocol; more stringent) and B (similar to the criteria used in prior HP studies in BCC). The key distinction between these criteria is the stringency required to achieve a COR of complete response (CR); criteria A required negative histology and a CR (or CR equivalent) by all image modalities used in this analysis, whereas criteria B allowed a COR of CR with negative histology and either a CR or partial response (PR) by MRI or photo. In this analysis, objective response rate (ORR; CR + PR) and duration of response (DOR) were evaluated using both criteria. Safety was assessed in treated pts until 30 days after the last dose per CTCAE v4.03.

Results: Median duration of exposure was 11.1 mo in pts with laBCC treated with sonidegib 200mg (n = 66). ORRs using criteria A and B were similar, 37 (56%) and 40 (61%) pts, respectively. However, more pts achieved a CR with criteria B than A, 15 (23%) vs 3 (5%), respectively; PR was achieved in 34 (52%) pts with criteria A, and 25 (38%) with B. Responses were durable, with few responders progressing or dying per A (10/37 responders) and B (11/40). Adverse events (AEs) observed with sonidegib 200 mg in pts with laBCC were primarily grade 1/2, with the most common AEs (any grade/grade 3 or 4) including muscle spasms (56%/3%), alopecia (52%/not applicable [NA]), and dysgeusia (47%/NA).

Conclusions: In the BOLT 18-mo analysis, sonidegib 200 mg had a manageable safety profile and provided sustained tumor responses in pts with laBCC. Most pts responded to treatment with sonidegib 200mg using either response criteria. 12 additional pts had a CR with the less stringent BCC-RECIST-like criteria. These data support the potential of sonidegib 200 mg as a new treatment option in laBCC.

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3358

Clinicohistopathologic study of multiple basal cell carcinomas in Korea

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Background: Basal cell carcinoma (BCC) is the most common malignant skin tumor. Some studies reported that the number of patients who develop more than one BCC is increasing. To date, however, the characteristics of patients with multiple BCCs is not well elucidated in Korean literature.

Objectives: To investigate the incidence and characteristics of patients with multiple BCCs in Korea.

Methods: Fifty nine patients confirmed with more than two BCCs in Pusan National University Hospital for 16 years were included. We reviewed the clinical records of these patients.

Results: Among a total of 933 patients with BCC in our hospital for 16 years, 59 patients (6.3%) had multiple BCCs. Multiple BCCs were identified simultaneously on the date of diagnosis in 41 patients (69.4%), and had interval a mean of 9.2 months between first and subsequent lesion. There were 132 BCC lesions in 59 patients, they were mainly located on nose (39.2%) and cheek (22.5%). Fifty (84.7%) of 59 patients had same anatomic site of BCC lesions and 9 (15.3%) of 59 patients had different anatomic site of BCC lesions.

Conclusion: The result of this study showed that the subsequent BCCs are located nearby the first BCC. Encountering patients with BCC, physician should look closely around the lesion with consideration for multiple BCCs. Furthermore, occurrence of new BCCs as well as recurrence should be evaluated during follow-up periods.

Commercial support: None identified.

3248

Clinical characteristics of nonmelanoma skin cancers recurring within 5 years after Mohs micrographic surgery

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Background: Mohs micrographic surgery (MMS) has been used for decades to treat certain high-risk nonmelanoma skin cancers (NMSC) due to its high cure rate. However, clinical recurrences do occur in a small number of cases, cited as 1% in the literature. We examined specific clinical characteristics associated with NMSC recurrences following MMS including histopathology, immunosuppression, smoking status, and anatomical location.

Methods: We employed a retrospective chart review of 1471 cases of MMS performed at UC San Diego (UCSD) during 2008 and 2009. Medical records were reviewed to determine recurrence within 5 years following MMS for patients who had medical follow-up at UCSD. Patients who did not follow-up for at least 5 years at UCSD after the initial MMS were contacted via telephone and asked whether they had further treatments in the location of the initial MMS. We excluded 361 cases due to lack of follow-up, resulting in a total of 1110 cases for our study.

Results: We identified 5 (0.45%) recurrences from the 1110 cases of MMS performed in 2008 and 2009. There were 724 cases of basal cell carcinomas (BCC), 3 were recurrences (0.41%). There were 357 cases of squamous cell carcinomas (SCC); 2 were recurrences (0.56%). Three (60%) recurrences occurred in past smokers. Both SCC recurrences occurred in immunosuppressed patients. No recurrences were found in the 29 cases of other subtypes of NMSC including dermatofibrosarcoma protuberans and atypical fibroxanthoma. All recurrences were located on the cheeks, ears or nose. Time to the NMSC recurrence ranged from 11 to 38 months with a mean of 23.6 months. Review of MMS histopathology of these recurrent tumors showed that there were no errors or difficulty with the processing or interpretation of the slides.

Conclusions: Recurrence of NMSC following MMS at our institution is below the reported average. Our retrospective chart review identified specific clinical characteristics associated with NMSC recurrence including a history of smoking, anatomic location on the cheeks, ears or nose, and a history of immunosuppression for SCCs. As recurrences may not be evident in the years immediately following MMS, further longitudinal studies are warranted to further analyze clinical characteristics associated with recurrences.

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2336

Comparison between 2 mm margin excision, 4 mm margin excision, and Mohs excision, in periorbital basal cell carcinomas

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Introduction: The excision of periorbital basal cell carcinomas represents a particular challenge as 4-mm margins may result in the removal of a large area of healthy periorbital tissue, causing significant morbidity such as lagophthalmos, ectropion and exposure keratopathy. Studies have shown that treatment with 2-mm margins may be a safe and efficient alternative, especially for nodular basal cell carcinomas. However this has not been compared with Mohs excision.

Methods: All periorbital basal cell carcinomas treated at the Mohs Surgery Unit at the University of Ottawa, Ottawa, Canada, were retrospectively reviewed from 2011-2015. The largest preoperative size with 2-mm margin excision and with 4-mm margin excision were compared to the final largest postoperative size following Mohs excision.

Results: There was a statistically significant difference between the 2-mm margin excision group and the Mohs excision group ($P < .05$). 75% of the 2-mm margin excision group had a larger Mohs excision size, indicating that 2-mm margins would have been insufficient for complete tumor removal in these patients. 14% had more than a 1 cm difference between excision with 2-mm margins and the final Mohs excision. For the 4-mm excision group, 35% had a larger Mohs excision size and 10% had more than a 1 cm difference. However, there was no statistically significant difference between the 4-mm margin excision group and the Mohs excision group. For the patients with nodular basal cell carcinomas, 66% of the 2-mm margin excision group had a larger Mohs excision size, and 17% had more than a 1 cm difference ($P < .05$).

Conclusions: 2-mm margins appear to be insufficient for complete tumor removal in periorbital basal cell carcinomas, including nodular basal cell carcinomas. 4-mm margins may also be insufficient in a minority of cases. For periorbital basal cell carcinomas, where the maintenance of healthy tissue is of particular importance, Mohs excision appears to be the safest option.

Commercial support: None identified.

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3785

Correlation between microscopic localization of inflammation in frozen sections and subsequent site of nonmelanoma skin cancer

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Background: During Mohs micrographic surgery of nonmelanoma skin cancer (NMSC), inflammation present in histologic frozen sections has been found to occasionally presage detection of tumor on frozen sections of adjacent excision specimens. Previous work has indicated that inflammation can precede detection of additional tumor; the relationship between the microscopic location of the inflammation and the site of the additional tumor has yet to be elucidated.

Objective: To quantify the correlation between the location of inflammation without visible tumor on histologic frozen section and the location of subsequently detected NMSC.

Methods: In an urban academic medical center, from the period of June 2008 to October 2009, a retrospective cohort study was carried out. Two independent investigators reviewed glass slides and medical records pertaining to frozen sections associated with the staged excision of NMSC. Each clock-faced stage of Mohs was measured as (1) the proportion of cases with inflammation at this location that subsequently had tumor at the same location; (2) the proportion of cases that had neither inflammation nor subsequent tumor at the same location; (3) the probability of subsequent tumor at this location given that inflammation was previously seen at the same location; and (4) the probability that in the absence of preexisting inflammation at this location, the location was clear of tumor.

Results: Of the 3148 NMSC cases that were reviewed, 60 cases that exhibited inflammation on histologic frozen section of an excision specimen were followed by tumor in the subsequent excision specimen. There was a significant positive correlation between the presence of inflammation and the presence of nearby tumor at 6 of 12 segments (Pearson correlations, $P < .05$), with correlation coefficients from 0.196-0.323. The probability that tumor was absent when inflammation was not seen in preceding sections was 91%, with segment-specific values from 82-96%.

Conclusion: During Mohs micrographic surgery of NMSC with frozen sections, presence of histologic inflammation is modestly predictive of adjacent tumor, but lack of inflammation is a strong predictor that no additional tumor will be found.

Commercial support: None identified.

3783

Cutaneous squamous cell carcinoma with invasion through ear cartilage

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Cutaneous squamous cell carcinoma (cSCC) of the ear represents a high-risk tumor location with an increased risk of metastasis and local tissue invasion. It is uncommon for these cancers to invade through nearby cartilage. A 76-year-old man presented to the dermatology department with a nonhealing tumor on the anterior aspect of his left superior ear with symptoms including pain and bleeding. A diagnostic biopsy showed a moderately differentiated squamous cell carcinoma. Following curettage, a small full thickness defect in the cartilage of the left scapha could be seen. Permanent sections through the eroded cartilage revealed tumor invasion into the posterior ear skin. Although a uniform definition of high-risk cSCC does not exist, several key features are consistently considered high risk. These risk factors include clinical tumor size, location, tumor invasion depth, rate of tumor growth, tumor recurrence, degree of cytologic differentiation, presence of perineural invasion by tumor, and histologic subtype. Invasion by high-risk tumors is facilitated by matrix metalloproteases (MMP), specifically MMP-13 (collagenase 3) which preferentially degrades type II collagen found in cartilage. MMP-13 is expressed in malignant keratinocytes found in cSCC. Primary squamous cell carcinoma of the ear has a metastatic rate of approximately 15.5%. Cartilage destruction is a significant risk factor for metastatic disease. Tumor depth, large nerve perineural tumor invasion, and tumor diameter are the most important prognostic factors for determining risk of local recurrence and metastasis. Elective neck dissection or sentinel lymph node biopsy may be used to evaluate for metastases, however this issue is controversial. Histopathologic confirmation of a primary cSCC of the anterior ear with full thickness cartilage invasion extending to the posterior auricular skin appears to represent an interesting addition to the dermatology literature.

Commercial support: None identified.

2480

Description and approach to a rare case of linear pigmented basal cell carcinoma

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The linear basal cell carcinoma was first described by Lewis in 1985. It is a rare and distinct morphology variant. Since 1985, only 37 cases have been reported. The periocular region was the most affected, especially the lower eyelid and malar region, and they were followed by cervical and trunk. It occurs in equal proportion of men and women aged 40-87 years being 92% over 60 years. The case to be presented is a 77-year-old female patient, phototype III. The dermatologic examination detected a 2 years old lesion which was 2 cm long (in its longest axis) linear pigmented, in the left periocular region. Coloring from erythematous to gray, lightly pearled edges, precise limits. The patient denied symptoms and local trauma. The dermatoscopic examination concluded the absence of diagnostic criteria for a melanocytic lesion, presence of gray ovoid nests and sheet structures, characteristics consistent with basal cell carcinoma. Then it was held a confocal microscopy which showed blocks of basaloid cells, gap between the blocks and peripheral basaloid with the presence of large vessels and high flow. For treatment of the injury, it was decided to perform Mohs micrographic surgery, with complete resolution of the clinical picture. In histologic sections were shown features of nodular subtype of pigmented basal cell carcinoma. The case report describes a rare form of pigmented basal cell carcinoma, with characteristics that corroborate data found in literature. The dermoscopy allowed ascertain the ovoid nests, spider veins and leaf structures. Confocal microscopy showed tumor island and the palisade cells, allowing a more detailed analysis of the injury, aiding in the diagnosis and enabling better surgical planning. The surgical technique used was recommended by the literature: Mohs micrographic surgery. The histologic sections showed nodular subtype, which corresponds to the described subtype followed by pigmented (in 17 cases of BCC linear periocular only 2 were pigmented).

Commercial support: None identified.

2914

Determining useful predictors for management decisions in basal cell carcinoma

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Background: Basal cell carcinoma (BCC) is a common skin cancer that affects 3 out of 10 whites in the US. BCCs are categorized histologically and can be treated invasively with excision, Mohs micrographic surgery (MMS), or surgery, or conservatively, with electrodessication and curettage (EDC), topical chemotherapeutics, radiation, or cryosurgery.

Objectives: To determine if age, sex, biopsy margin status, lesion location (areas H, M, L as from the MMS appropriate use criteria), and BCC subtype are useful predictors of which treatment to pursue.

Methods: A retrospective chart review was done of 499 cases of BCC at the UCLA dermatology clinics from 2014. A logistic regression model was applied to examine how age, sex, margin status, location, and BCC subtype predict treatment route.

Results: 26 cases were eliminated due to lack of information. Of the remaining 473, 87 had excisions, 290 had MMS, 9 had surgery, 57 had EDC, 20 used topical therapy, 5 had radiation, and 2 had cryosurgery. Increasing age was found to significantly increase the probability of having an invasive procedure; for every year of age the odds increased by 3%. There was no difference in management between men and women. Due to low variability in margin status such that only three had clear margins, this variable could not be analyzed. Of those with positive margins, 42% of cases treated with excision or MMS had no residual tumor. 95% of lesions from Area H, 61% from Area M, and 90% from Area L were treated invasively. Nodular and aggressive types of BCC were 7.9 times more likely to be treated invasively relative to the superficial type ($P < .0001$).

Conclusion: Younger patients may be less likely to opt for invasive procedures due to aesthetic concerns. While our data indicate adherence to the MMS appropriate use criteria at UCLA, the discrepancy between the guidelines and our findings for area M are likely also the result of aesthetic considerations, as patients might be less willing to have a scar in an M area, which is usually exposed. As such, patients' concerns about aesthetics provide a reason that a shift away from the suggested guidelines to treating BCC might be considered. Lastly, pathologic reporting of margin status was found to have no bearing on treatment decision-making or outcomes, and does not appear to be necessary. Instead, histopathologic subtyping does appear to guide clinician decision-making.

Commercial support: None identified.

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2510

Development of squamous cell carcinoma on actinic keratosis after ingenol mebutate (Picato®) gel

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Background: Actinic keratosis (AK) is an area of dysplastic epidermal keratinocytes that undergo transformation due to substantial ultraviolet (UV) exposure. In turn, actinic keratosis has the potential to develop into both squamous cell carcinoma. Ingenol mebutate (Picato®) gel is a new short term topical treatment approved in 2012 by the US food and Drug Administration (FDA).

Patient and method: A 79-year-old female presented with a chief complain of numerous patches and plaques on her face with itching sensation. During the physical examination of her face, nine lesions were found with 1-to 2-cm sized well-defined erythematous patches and plaques with crusts. Biopsy was carried out at the lesions, and the biopsy specimens were consistent with actinic keratosis. We applied 0.015% ingenol mebutate gel on the affected area with a 0.5-cm margin once daily for 3 days consecutively.

Result: Transient local skin reactions (erythema, flaking, and crusting) were observed, but had resolved spontaneously by 2 weeks. Most of the lesions were improved clinically, but one lesion located on the forehead was mildly aggravated. Because the patient desired to observe the lesion without treatment, we decided to close follow-up. This lesion was still observed at 2 months follow-up period and got larger in size. The lesion was presented with a well-defined hyperkeratotic erythematous plaque measuring 1.5 x 1.5 cm with crusts on her forehead. Wide local excision was performed and the histopathologic result showed the extension of atypical keratinocytes into the dermis with nests of tumor cells and squamous differentiation. The patient was diagnosed with squamous cell carcinoma.

Conclusion: The occurrence of nodule on the forehead shortly after treatment and its fast growth rate could raise the possibility of an undesired effect of ingenol mebutate. When only the effects of inflammatory responses stimulate the dysplastic epidermal cells of AK dominantly at low dose concentration, the AK can be rather progress to rapidly growing SCCs through the activation of inflammatory substances, IL-1β and MMPs. Although this is a rare phenomenon, the progression of AK lesions by the inflammatory triggering effects at low concentration of ingenol mebutate should be acknowledged by clinicians. And they should not hesitate to change the treatment to surgical excision, a more invasive procedure, when the lesions progress abruptly.

Commercial support: None identified.

3189

Effectiveness and diagnostic performance of dermoscopy on routine teledermatology-based skin cancer triage. Interim results of a randomized study

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Background: After 10 years teledermatology (TD) has turned into a routine procedure for skin cancer triage. Even though the favorable results yielded by clinical TD the transmission of dermoscopic picture might even improve the quality and effectiveness of the routine TD-based triage of skin cancer.

Objectives: To analyze the potential benefits gained from the addition of dermoscopic pictures to a TD-based skin cancer triage system.

Methods: This study involves the first 4 months of a long-term controlled randomized study. Teleconsultations based on clinical pictures (CTC) and teleconsultations including clinical and dermoscopic pictures (CTC+DTC) were compared. Patients with lesions suspicious of skin cancer were randomized in a 1:1 ratio to CTC or CTC+DTC. The diagnostic performance of both CTC and CTC+DTC was analyzed (sensitivity, specificity, false positive rate, and false negative rate). Diagnostic confidence level (DCL) and nonreferral rate were compared between both procedures (CTC vs. CTC+DTC).

Results: 250 patients with an average age of 53.43 years (95% CI 50.91-55.94 years) were randomized (125 CTC and 125 CTC+DTC). The most common lesion consulted was seborrheic keratosis (29.20%, n = 72), followed by common acquired melanocytic nevus (26.00%, n = 65). Basal cell carcinoma was the most common malignant lesion (6.40%, n = 6 40%), followed by squamous cell carcinoma (3.20%, n = 8). 60.80% and 76.80% of patients managed through CTC and CTC+DTC were not referred to the skin cancer clinic, respectively. In pigmented lesion this percentage was 69.39% and 89.13%, respectively. The time spent by the GP was 7.44 minutes for CTC and 8.70 minutes for CTC+DTC ($P = .01$). There was no difference between the time spent by the dermatologist in the evaluation of CTC and CTC+DTC (1.04 minutes vs 1.22 minutes, $P = .14$). Dermoscopic pictures increased the teleconsultations rated with the highest DCL (61.60% vs 79.20%, $P = .01$). In the pigmented lesions group 86.96% of CTC+DTC were rated with the highest DCL ($P = .01$). Dermoscopic pictures improved sensitivity (0.60 vs 1.00) and specificity (0.81 vs 0.97) of skin cancer triage, with a lower rate of false positive (0.18 vs 0.03) and false negative (0.40 vs 0.00) results.

Conclusion: The interim results of this prospective randomized study provide meaningful favorable data ahead of the definitive results of a large-scale study on the effect of the addition of dermoscopic pictures to the routine TD-based skin cancer triage.

Commercial support: None identified.

3401

Efficacy and safety of sonidegib in patients (pts) with nevoid basal cell carcinoma syndrome (NBCCS)

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Background: NBCCS, a rare autosomal dominant disorder caused by mutations in the hedgehog (Hh) pathway regulator PTCH1, causes development of multiple BCCs, which necessitates numerous surgeries. Here, we describe the efficacy and safety of sonidegib, a systemic Hh pathway inhibitor (HPI), in pts with NBCCS treated in 2 double-blind, randomized phase 2 trials (NCT01350115 [A]; NCT01327053 [B; BOLT 18-mo analysis; median follow-up, 26.3 mo]).

Methods: In trial A, pts with NBCCS with ≥2 BCCs were randomized 6:1 to sonidegib 400mg daily or placebo (PBO) for 12 weeks (W), followed by surgical excision of the target BCC or tumor-free area at W16. The primary endpoint (PE), rate of clinical clearance of the main target BCC (assessed until W16), was met if the complete clearance rate was ≥50%. Histologic clearance of target BCCs and change in BCC tumor burden in up to 20 BCCs were also assessed. In trial B, pts with advanced BCC were randomized 1:2 to sonidegib 200 or 800 mg daily. The PE, objective response rate (ORR; complete response [CR] + partial response [PR]; met if ≥30% in either arm), was assessed per central review using mRECIST (locally advanced BCC) and RECIST 1.1 (metastatic BCC). Safety was assessed as mild/moderate/severe for >7 months after last dose in A and per CTCAE 4.03 until 30 days after last dose in B.

Results: The PE was not met in A; however, all sonidegib-treated pts (n = 7) had clinical clearance of target BCCs: 43% complete (100% improvement), 43% marked (76-99%), and 14% moderate (26-75%). In contrast, target BCCs worsened or showed slight clearance (1-25%) with PBO (n = 2). With sonidegib, histological clearance was observed in 4/7 pts and median tumor burden was reduced (change from baseline in total volume tumor measurement was -95mm 3 and change in longest dimension was -63.6 mm in 400 mg sonidegib group at W16); in pts with high tumor burden at baseline (>50 BCCs; n = 4), BCC number reduced after day 43 and decreased further beyond the treatment period. In B, ORRs in pts treated with sonidegib 200 (n = 3) or 800mg (n = 13) were 33% (1 PR) and 62% (1 CR, 7 PRs), respectively. Overall, safety was consistent with previous reports of sonidegib and other HPIs, with muscle spasms, myalgia, nausea, alopecia, and dysgeusia being common adverse events.

Conclusions: Given the clinical benefit and manageable safety profile observed in these studies, treatment with sonidegib may be a promising nonsurgical option for pts with NBCCS.

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Efficacy following discontinuation of sonidegib treatment in patients with locally advanced basal cell carcinoma (laBCC)

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Background: Despite the risk of significant morbidity and disfigurement, patients (pts) with laBCC may not perceive their disease as life-threatening. In BOLT, a phase 2 study of the hedgehog (Hh) pathway inhibitor sonidegib (NCT01327053), some pts discontinued (DC) treatment before disease progression (PD), potentially due to adverse events (AEs). This analysis assesses efficacy in pts with laBCC who DC sonidegib before PD using data from the 18-mo analysis (median follow-up, 26.3 mo; cutoff, July 11, 2014).

Methods: Pts with laBCC were randomized 1:2 to sonidegib 200 (n = 66) or 800 (n = 128) mg daily. Objective response rate (ORR; complete response [CR] + partial response [PR]) and duration of response (DOR) were assessed by central and investigator (INV) review per mRECIST. Safety was assessed per CTCAE v4.03 in treated pts until 30 d postlast dose.

Results: By the data cutoff, 86% of pts with laBCC DC treatment, primarily due to PD (29%/8%; 200/800 mg), AEs (27%/41%), physician decision (14%/9%), or pt decision (11%/21%). Response was durable in pts who DC treatment before reaching PD and was sustained postDC; median DOR by central review was 24.8 mo (800 mg) and not reached (200 mg), regardless of whether tumor assessment data was analyzed through 30 d postlast dose or through PD. Eleven pts who DC long before (≥180 d) PD were further profiled (200 mg, n = 4; 800 mg, n = 7); DC was due to AEs (n = 8, mostly Grade 1/2), physician decision (n = 1), or pt decision (n = 2). Seven pts had baseline tumor burden > 300 mm^2 (range, 150-2675 mm^2), and 7 pts had histologic clearance at last dose. At last dose, 7 pts had PRs, 3 had stable disease (SD) (1 of them had PR postDC), and 1 had an unknown response, as assessed by central review; by INV review, 3 pts had CR and 8 had PR. DOR ranged from 7.2-15.6 mo for 8 responders per central review, and ranged from 5.8-23.0 mo for 11 responders per INV review. By the data cutoff, 6/11 pts had PD (range, 4.7-14.8 mo postlast dose), as assessed by central review; by INV review, 10/11 pts had PD (range, 3.3-17.5 mo postlast dose). Based on previous established PK-GBI-1 relationship, GLI1 (biomarker for Hh pathway activity) is predicted and appears to remain inhibited after treatment DC, likely due to sonidegib's long half-life (28 d).

Conclusions: Sonidegib demonstrated clinical benefit persisting beyond treatment DC in pts with laBCC. Most pts who DC long before PD had objective responses and DC due to grade 1/2 AEs.

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Efficacy of sonidegib in patients with aggressive and nonaggressive subtypes of locally advanced basal cell carcinoma

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Introduction and objectives: BCCs with aggressive (eg, micronodular or infiltrative) histology are associated with higher rates of recurrence and, for certain subtypes, an increased likelihood of subclinical spread. The hedgehog pathway inhibitor sonidegib has demonstrated clinical benefit in >90% of patients (pts) with locally advanced (la)BCC in the BOLT phase 2 study, with durable tumor responses observed through a median follow-up of 20 months (mo). Here we evaluate the efficacy and safety of sonidegib in pts with aggressive vs nonaggressive histologic subtypes of laBCC based on a median follow-up of 26.3 mo (BOLT 18-mo analysis; cutoff July 11, 2014).

Methods: Pts with laBCC not amenable to curative surgery or radiotherapy received sonidegib 200 or 800mg daily (1:2 randomization). Objective response rate (ORR; confirmed complete response [CR] + partial response [PR]), duration of response (DOR), and progression-free survival (PFS) were assessed according to modified RECIST criteria. Safety was assessed in treated pts according to CTCAE v4.03 until 30 days post last treatment.

Results: ORRs in all pts with laBCC (n = 194) by central review were 56.1% and 45.3% in the 200 and 800 mg arms, respectively. Aggressive tumor histology was found in 57.7% of pts with laBCC. ORR was similar in pts with aggressive subtype (59.5% in 200 mg, 44.0% in 800 mg) and nonaggressive subtypes (51.7% in 200 mg, 47.2% in 800 mg). PFS events (progressive disease or death) occurred in 6/22 responders in the 200 mg group and 10/33 in the 800 mg group for pts with aggressive subtype, compared with 4/15 and 7/25 respectively in the nonaggressive groups. Median DOR was not reached in both aggressive and nonaggressive 200 mg groups. Median PFS was 22.1 mo and 19.4 mo in the aggressive 200 and 800 mg groups, and 30.5 mo in the nonaggressive 800 mg group. Median PFS was not reached in the nonaggressive 200 mg group. In pts with laBCC (n = 193), the most common adverse events (AEs; any grade; 200 mg/800 mg) were muscle spasms (56%/69%), alopecia (52%/61%), and dysgeusia (47%/59%). AEs leading to discontinuation in >5% of pts with laBCC were muscle spasms (200 mg/800 mg: 3%/9%), decreased weight (3%/6%), and alopecia (2%/7%).

Conclusions: Sonidegib demonstrated sustained, clinically meaningful responses in pts with laBCC, with similar efficacy observed in pts with aggressive and nonaggressive tumor histologies. The 200 mg dose showed an improved benefit-risk profile in pts with laBCC.

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Efficacy of sonidegib in patients with locally advanced basal cell carcinoma (laBCC) by tumor burden

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Background: Large BCCs can be difficult to manage with surgery and/or radiotherapy and are more likely to recur and lead to further advanced disease. Treatment with the hedgehog pathway inhibitor sonidegib resulted in tumor shrinkage in >90% of patients (pts) with laBCC in the phase 2 BOLT study (NCT01327053; Migden et al. Lancet Oncol. 2015). Here, efficacy by tumor burden in pts with laBCC treated with sonidegib using updated data (18-mo analysis; cutoff, July 11, 2014; median follow-up, 26.3 mo) is reported.

Methods: Pts with laBCC, not amenable to curative surgery or radiotherapy, were randomized to sonidegib 200 mg (n = 66) or 800 mg (n = 128) daily. Objective response rate (ORR; confirmed complete response [CR] + partial response [PR]), duration of response (DOR), and progression-free survival (PFS) were evaluated according to BCC-modified RECIST by central review. Tumor burden was evaluated based on target lesion size, with the median determined using combined data from both doses. Pts without photos or target lesions were excluded from the analysis.

Results: By the data cutoff, median duration of exposure was 11.1 and 6.3 mo for the 200 mg and 800 mg arms, respectively. Median tumor burden at baseline was 12.10 cm^2 (0.70-570.35 cm^2). The ORRs for all patients were 56.1% with sonidegib 200 mg and 45.3% for 800 mg. ORRs were numerically higher in pts with a tumor burden < the median [200 mg: 69.6%, n = 23; 800 mg 58.9%, n = 56] than in pts with a tumor burden ≥ the median [200 mg: 56.7%, n = 30; 800 mg: 42.9%, n = 49]. With both doses, > 50% of responders had DOR > 6 mo regardless of tumor burden (200 mg: 11/16 for pts with tumor burden < median, 10/17 ≥ median; 800 mg: 21/33 < median, 13/21 ≥ median). Median PFS was 22.1 mo with sonidegib 200 mg and 22.0 mo with 800 mg. With sonidegib 200 mg, 3 and 10 PFS events (progressive disease or death) occurred in pts with a tumor burden < the median and pts with tumor burden ≥ the median, respectively. At the 800 mg dose, 12 PFS events occurred in both subgroups.

Conclusions: Sonidegib continued to demonstrate meaningful clinical benefit and sustained tumor responses in pts with laBCC, with more objective responses occurring in pts with a tumor burden < the median. These results are not unexpected, as patients with a greater tumor burden may be more difficult to treat due to the extent of their disease.

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Efficacy of sonidegib in patients with metastatic BCC (mBCC)

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Background: In the BOLT phase 2 study, the hedgehog (Hh) pathway inhibitor sonidegib demonstrated durable clinical benefit in patients (pts) with mBCC. Updated efficacy data collected up to 18 months (mo) after randomization of the last pt (cutoff, July 11, 2014; median follow-up, 26.6 mo) are now reported.

Methods: Pts with mBCC were randomized to receive sonidegib 200 mg (n = 13) or 800 mg (n = 25) daily. Objective response rate (ORR; complete response [CR] + partial response [PR]), duration of response (DOR), and progression-free survival (PFS) were assessed by central and investigator review using RECIST v1.1.

Results: Median baseline tumor burden in pts with mBCC was 4.6 cm (range, 1.5-14.6 cm), and most pts had >1 lesion at baseline. The most common sites of metastases were lung (71%, 200 mg; 52%, 800 mg) and bone (14%, 200 mg; 22%, 800 mg). ORRs (200 mg/800 mg) were 7.7%/17.4% by central review and 23.1%/34.8% by investigator review. Tumor shrinkage per central review was observed in 92% and 84% of pts in the 200-mg and 800-mg arms, respectively. Importantly, disease control rates (DCRs; CR+PR+ stable disease [SD]) following 200 mg/800 mg treatment were high (92.3%/91.3% by central review and 84.6%/82.6% by investigator review). PFS was indicative of treatment benefit (median PFS was 13.1 mo per central and investigator review for 200 mg, and 11.1 mo and 14.3 mo, respectively, for 800 mg) and tumor responses were durable. Median DOR per investigator review was 17.7 and 10.2 mo in the 200 mg and 800 mg arms, respectively. Data from the BOLT primary analysis (cutoff, June 28, 2013) showed that both doses of sonidegib provided near-complete pathway inhibition (>98% decrease from baseline in GLI1 [biomarker for Hh pathway activity] levels) in pts with mBCC. Additionally, maintenance or improvement in quality of life (QOL) was reported in pts with mBCC treated with sonidegib 200 mg and 800 mg. Efficacy results in BOLT are further supported by the phase 1 study, of 6 pts with mBCC treated with daily doses of sonidegib ranging from 100-1500 mg, 3 had PRs, 2 had SD, and 1 pt had an unknown response.

Conclusions: Despite most pts having extensive disease at baseline, sonidegib provided meaningful clinical benefit and disease control in pts with mBCC in the BOLT 18-mo analysis. Durable tumor responses, extended PFS, and encouraging biomarker and QOL data support the potential use of sonidegib as a new treatment option for mBCC, a rare and difficult-to-treat disease.

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Frequency of nonmelanoma skin cancer recurrence in cancer patients receiving niacinamide or niacin: A retrospective case-control study

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Introduction: Niacinamide (NCM) has been shown to enhance repair of UV-radiation induced DNA damage in human keratinocytes and has reportedly decreased nonmelanoma skin cancer (NMSC) incidence in high-risk patients by 23%. Niacin (NC) has been used to decrease cholesterol in high risk cancer patients. The aim of this study was to retrospectively assess NMSC recurrence in cancer patients exposed to NCM or NC.

Methods: We searched a large (3 million patients), urban, academic electronic medical record (EMR) repository (01/2010-12/2014) to select all individuals (age18-89) with cancer (who have a known high risk for development NMSC) identified by ICD9 code (excluding melanoma and NMSC). Exposed population consisted of patients receiving NCM or NC. Patients who were exposed to both NCM and NC were excluded. We then determined which patients were documented with at least 2 recurrences of NMSC (NMSC removal procedure on 2 separate dates) after first exposure to NCM or NC. A control population consisted of age and gender matched patients from the same cancer cohort (ratio 1:5), with no documented NCM or NC exposure in the EMR. Association was assessed by Fisher's exact test while mean number of NMSC removal procedures were assessed by the independent sample test.

Results: While a total of 106,950 patients with a cancer diagnosis were detected, of these, 39 were documented as exposed to NCM, with 2 of these patients reported to have multiple recurrences of NMSC postNCM exposure (5.1% vs. 2.1% in control group). 903 patients were exposed to NC, of which 38 had multiple NMSC recurrences (4.2% on NC vs 3.8% in control group). No significant effect on frequency of NMSC recurrence was found in those exposed to NCM or NC (Fisher's exact test $P = .26$ and $P = .57$, respectively). The mean number of NMSC removal procedures postNC exposure was $1.76 + 1.42$ compared to $1.90 + 1.93$ in the control ($P = .59$).

Conclusion: No correlation between the use of niacinamide or niacin and a protective effect against NMSC recurrence was detectable in this large population of cancer patients. However, the retrospective nature of this study, and the inability to establish or rule out exposure to multivitamins containing NCM or NC, are study limitations. Regardless of the study limitations, these findings point to the need for further exploration with even larger prospective studies to more clearly establish the role of NCM or NC and NMSC recurrence in high risk cancer patients.

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Extramammary Paget's disease in Korea: A single center's experience

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Background: Extramammary Paget's disease (EMPD) is a rare intraepithelial neoplasm affects apocrine gland-bearing skin such as the scrotum, vulva and perineal region. The rarity of this disease cause difficulties in its characterization. To date, there are few retrospective studies which attempt to characterize EMPD in Korea.

Objective: The aim of this study was to investigate characteristics of Korean patient with EMPD including patient's demographics, presenting symptoms, treatment, and recurrence rates, and overall prognosis.

Methods: To elicit the clinical pattern of EMPD in Korea, we performed retrospective analysis of patient's clinical records. Sixty-three patients diagnosed with EMPD in Pusan National University Hospital from June 2002 to June 2015 were included.

Results: Incidence of EMPD was more frequent in men than women (51:12). The most frequently involved site was the scrotum in men and the vulva in women. The mean disease duration was 42.7 months (range, 3-144). Twelve of 63 patients (19.0%) had malignancy in internal organ including stomach, liver, lung and colon. Metastasis to the lymph nodes was found in 5 of 63 patients (7.9%). Twenty-three patients (36.5%) underwent Mohs micrographic surgery (MMS), 17 patients (27.8%) underwent conventional excisions, and 16 patients (26.2%) underwent nonsurgical methods such as topical imiquimod application, photodynamic therapy. Patients who underwent MMS experienced the lowest recurrence rate (4.3%) compared with patients who underwent nonsurgical treatment (37.5%) or conventional excisions (17.6%).

Conclusion: The results of our study showed the clinical features of Korean EMPD patients. Recognition of these characteristics of EMPD can be useful for the diagnosis and management of EMPD.

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Granulation tissue masquerading as BCC after treatment with vismodegib

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Vismodegib is a relatively new sonic hedgehog inhibitor used in the treatment of basal cell carcinoma in select patients including those with advanced disease or for whom traditional treatment modalities may not be viable options. In this report, we highlight the case of a 65-year-old female with an advanced, ulcerated basal cell carcinoma located on her left upper back/posterior shoulder. On presentation it measured greater than 100 square centimeters, having been neglected for over a decade. Prior to treatment with vismodegib she had undergone gross debulking with a surgical scalpel blade as well as 7 injections of 5-fluorouracil. She was treated with vismodegib over the course of several months (total of about 17 months), during which time she demonstrated only mild clinical improvement as measured by reduction in tumor size and mild re-epithelialization of the ulcer. A short break of about one month's duration was taken during treatment after she developed dysgeusia. As it appeared she had failed treatment, she was subsequently taken for surgical resection to excise what appeared to be residual tumor. However, extensive pathological examination (with complete tissue submission) revealed only granulation tissue with no evidence of residual tumor. A split thickness graft was placed three days postoperatively and at most recent check she continues to do well (now over 6 months postoperatively). We believe it is important for clinicians to be aware that gross disease may not correlate with microscopic disease after treatment with vismodegib. This case demonstrates that further sampling may be necessary to confirm suspected residual disease and to definitively state treatment failure has occurred.

Commercial support: None identified.

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Identification of metastasis-associated microRNAs in basal cell carcinoma

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Background: Basal cell carcinoma (BCC) is the most common cancer in humans; however, distant metastasis is exceedingly rare, occurring in less than 0.1% of cases, and mechanisms for this metastasis are unknown. Cutaneous metastatic cancer cells have been reported to secrete exosomes, membrane-bound vesicles containing miRNAs, that are critical for cancer-host crosstalk, and this could be occurring with metastatic BCCs (MBCCs).

Objective: To explore the expression levels of miRNAs purified from serum exosomes of MBCC and nonmetastatic BCC patients, and to assess the functional effects of MBCC exosomes on cultured fibroblasts and keratinocytes.

Methods: After institutional review board approval, serum samples were obtained from patients with MBCC and non-MBCC at Stanford Hospital and Clinics from 2012-2015. Tumor-derived exosomes were purified from the serum samples, and exosomal miRNAs were extracted. RNA-sequencing was used to assess exosomal miRNA expression levels. Quantitative real-time PCR (qPCR) analysis was performed to confirm the RNA-seq data. Associations of confirmed miRNAs with known cancers were identified by keyword search of miRNAs in MIRbase, PubMed, and Google Scholar. To determine the effect of MBCC exosomes on metabolic activity of cultured keratinocytes and fibroblasts, MTT and Ki-67 assays were performed. To assess the effect of MBCC exosomes on cell migration and invasion, transmigration assays were performed.

Results: Using RNA-seq, a total of 75 miRNAs were significantly differentially expressed between the MBCC and non-MBCC groups. qPCR confirmed the increased expression of 24 miRNAs and decreased expression of 10 miRNAs. Several miRNAs that were increased in MBCC exosomes have also been associated with other types of cancer, including hsa-mir-552 (increased in colorectal cancer metastases) and hsa-mir-508 (increased in aggressive esophageal squamous cell carcinomas). MBCC exosomes increased the metabolic activity, migration and invasion ability of fibroblasts but not keratinocytes, consistent with potential biologic effect on the dermis.

Conclusion: The miRNAs identified are candidate biomarkers for metastatic BCC that may be confirmed in future larger studies.

Commercial support: None identified.

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Importance of skin cancer screening after radiation therapy

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Secondary malignancies due to radiation therapy are relatively rare, yet serious and potentially mortal. Studies of patients exposed to both low and moderate doses of radiation have consistently found an increased risk of nonmelanoma skin cancers (NMSCs), including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). The highest incidences of NMSCs are found within the radiation field and sun exposed areas, with photosensitive individuals at an even greater risk of developing SCCs. The risk of NMSCs is increased in areas of radiation dermatitis, though it can also occur at sites of prior radiation without evidence of chronic radiation dermatitis. The risk is higher in patients irradiated before age 20 and persists for greater than 40 years after treatment, peaking at 20 or more years after exposure. Given the importance of screening for secondary NMSC in patients who have received radiation, we sought to investigate how often radiation oncologists refer patients to a dermatologist for total body skin examination (TBSE) postradiation therapy. We performed an IRB-approved patterns of care survey of radiation oncologists across the United States. Our results show only 10.89% of 709 respondents routinely refer patients to a dermatologist for TBSE following radiation therapy. Although surveillance for secondary NMSCs may not be indicated in all patients, we propose that dermatology referral be included in survivorship plans for appropriate patients. Given increasing survival rates following cancer therapy, appropriate adults should receive yearly dermatologic examinations of irradiated fields, following the guidelines already in place for survivors of childhood cancer. Skin cancer screening by a dermatologist has been shown to be cost effective, with higher sensitivity and specificity in identifying NMSCs, as compared to screening by primary care physicians. Additionally, TBSE by a dermatologist would help to identify NMSCs in an earlier state, preventing extensive surgical resection and reducing the likelihood of wound complications in a previously irradiated field. Patients should be educated about their increased risk for NMSCs and should be given information on self-examination for skin cancer and photoprotective measures, including daily use of broad-spectrum sunscreen.

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2513

Inframammary acrochordon-resembling atypical spindle cell neoplasm consistent with giant cell fibroblastoma

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Background: Giant cell fibroblastoma (GCF) is a rare, slow-growing soft tissue tumor, mainly affecting young males. We report a unique case of GCF associated with atypical spindle cell neoplasm in an adult female with unusual histopathology.

Case report: A 51-year-old white woman presented to our dermatology office for a skin cancer screening and complained of a soft enlarging nodule, below her right breast, which had been present for approximately ten years. She denied previous biopsy in the past, and denied a personal and family history of skin cancer. Physical examination revealed a 1.8-cm pedunculated protuberant soft nodule on the right inframammary fold, thought to be an acrochordon. A shave biopsy was performed and sent to a soft tissue pathologist for consultation. Histopathologic evaluation revealed poorly marginated and only moderately cellular intradermal spindle cell proliferation with a patternless architecture and focally striking irregularly shaped pseudovascular spaces. While most of the spindle cells had tapering nuclei and indistinct cytoplasm, there was also an admixed population of larger multinucleate cells with bizarre nuclei. Surprisingly, the lesion stained negative for CD34, prompting a diagnosis of atypical spindle cell neoplasm mostly consistent with GCF. Since such lesions may recur and evolve into the related dermatofibrosarcoma protuberans (DFSP), the patient was advised to have a small reexcision around the base with margins of uninvolved skin. The patient moved abroad and confirmed receiving the recommended treatment by an outside physician. We report this case to feature a variant of GCF which may easily be misdiagnosed or mistaken for an acrochordon.

Discussion: GCF presents as a firm, painless, slow-growing soft tissue tumor in the male pediatric population. It is commonly localized to subcutaneous tissue with occasional dermal involvement, and occurs anywhere on the body but the hands and feet. Histologically, GCF stains positive for CD34 and negative for S100 and HMB45, and is characterized by irregular pseudovascular spaces lined by pleomorphic giant cells. GCF is commonly associated with DFSP, a fibrohistiocytic tumor with high incidence of local recurrence and low metastatic potential in adult patients. Early diagnosis and prompt treatment with complete surgical resection is considered curative. GCF should be considered in the differential diagnosis when patients present with benign-appearing lesions.

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Interest of dermatologic supportive care with specific hydrotherapy after breast cancer treatment: A randomized multicenter controlled clinical study

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Introduction: Treatment of breast cancer in an adjuvant setting is associated with significant dermatologic adverse events. The skin toxicities induced by chemotherapy, surgery or radiotherapy negatively impact patients' quality of life (QoL), not only during but also several months after cancer treatment. This controlled study assessed the interest of a specific hydrotherapy performed just after cancer management on QoL and dermatologic adverse events.

Materials and methods: 68 women (mean 52 yo) in complete remission after a standardized (neo-) adjuvant treatment (chemotherapy, radiotherapy, surgery) for infiltrating breast carcinoma RH+ HER2- were included by oncologists. Specific hydrotherapy management was performed in Avène Les-Bains center (France) and mainly included daily thermal water showers and massages, with optimized skin care therapy during 3 weeks (HG, n = 33). In the control group (CG, n = 33), best dermatologic supportive cares were allowed. Patients were randomized after the end of radiotherapy (1 to 5 weeks) (inclusion visit) with at least 2 skin toxicities ≥ grade 1 (dry skin, hyperpigmentation, skin induration, pain of skin, pruritus, lymphedema, hand-foot syndrome, radiodermatitis, nail toxicity, other). Primary endpoint was the assessment of the European Organization for Research and Treatment of Cancer QoL Questionnaire Breast Cancer (EORTC QLQ-BR23) from D0 (hydrotherapy start) to D18 (hydrotherapy end). Secondary endpoints included measurements of dermatologic side effects due to anticancer treatments (assessed using National Cancer Institute-Common Terminology Criteria for Adverse Events, NCI CTCAE v4), dermatologic QoL (DLQI), health global status (EORTC QLQ-C30), psychological well-being and self-perceived general health (PGWBI) questionnaires.

Results: At D18, intergroup comparison demonstrated a significant difference in favor of HG for 9 different items: lymphedema ($P = .0015$), symptoms linked to cancer ($P = .0001$), side effects due to treatment ($P < .005$) and physical image ($P = .0139$) (EORTC QLQ-BR23); dry skin ($P < .0001$), nail loss ($P = .001$), pruritus ($P = .0113$), skin hyperpigmentation ($P < .05$) and skin induration ($P < .005$) (NCI CTCAE). In addition, the DLQI and the PGWBI global scores were significantly improved in HG patients compared to CG patients ($P < .0005$ and $P < .005$, respectively). The EORTC QLQ-C30 was also improved at the end of hydrotherapy: status of QoL ($P < .005$), emotional functioning ($P = .0001$), fatigue ($P = .017$).

Conclusion: QoL is severely impaired in female patients treated for breast cancer. Specific dermatologic supportive care in breast cancer survivors significantly improves patients QoL, well-being and reduces dermatologic symptoms due to anticancer treatments.

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Malignant degeneration of chronic ulcer in an long evolution leprosy patient

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Nonhealing trophic ulcers in leprosy are a common phenomenon, but acute malignant transformations them, are relatively rare. A case of squamous cell carcinoma developing in trophic ulcer in leprosy is presented. A 81-year-old man, with a history of chronic ulcers with torpid evolution of both legs secondary to Hansen's disease thirty years ago, presented to our external clinic with a 3-year history of trophic ulcer of the right foot. He presented with a rapid growing excrescence that was proposed for biopsy. The anatomopathologic features were consistent with squamous cell carcinoma. The nuclear magnetic resonance revealed a mass on the posterior region, of the right ankle infiltrating deep structures (tendons, muscles, bone). Amputation was performed. Squamous cell carcinoma (SCC) arising in chronic ulcers of leprosy patients is uncommon. Most occur in leprosy-endemic countries (India, Africa and Latin America). In Spain, few cases have been described Marjolin ulcers in patients with leprosy. Marjolin ulcer is a well-defined, but uncommon malignant ulcer that occurs in chronic wounds and cutaneous scars. Most of the tumors are relatively slow growing and tend to metastasize late with an average time of approximately 25 years. Various theories concerning pathogenesis of Marjolin ulcer have been proposed. Well-differentiated squamous cell carcinoma is the most common histological type of Marjolin ulcer. Biopsy with histopathologic interpretation remains the gold standard for the diagnosis, with radical surgical excision being the treatment of choice.

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3514

Management of common vismodegib (VISMO) related adverse events in patients with locally advanced basal cell carcinoma (laBCC): RegiSONIC Disease Registry Study

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Background: RegiSONIC (NCT01604252) is an ongoing prospective, observational cohort study collecting real-world data on treatment patterns and outcomes in patients (pts) with advanced BCC (aBCC) and/or BCC nevus syndrome (BCCNS). We present the incidence and management of common adverse events (AEs) associated with VISMO in pts with laBCC on VISMO (150 mg/d).

Methods: Pts enroll in 3 cohorts (C): newly diagnosed aBCC pts (C1), aBCC pts who previously received VISMO in a Genentech-sponsored study (C2), or pts with BCCNS who have aBCC or multiple BCCs of any stage (C3). Pts are being treated according to clinician's standard of care and clinicians were requested to report AEs, serious AEs, and AEs with fatal outcomes.

Results: As of Feb 15, 2015, 362 pts with laBCC were enrolled (344 in C1, 4 in C2, and 14 in C3). 96 (27%) of these pts were treated with VISMO (received VISMO ≤90 d of determination of laBCC); 64 (67%) were male and median age was 67 y (range, 34-99). 78 of the 96 (81%) pts experienced any protocol-specified AE, and serious AEs occurred in 14 (15%) pts. A total of 231 VISMO-related AEs occurred in 71 (74%) pts, leading to discontinuation in 20% (14/71), temporary interruption in 25% (18/71), and dose reduction in 8% (6/71; VISMO capsule does not enable dose reduction <150 mg/d; reductions included other dosing schedules, including dose holds). 64 muscle spasm AEs occurred in 48% (46/96) of pts; management included drug treatment (28% of AEs; most commonly cyclobenzaprine hydrochloride for 14% of AEs), nondrug treatment (5%), or discontinuation or interruption of VISMO (30%), while 59% had no treatment indicated. Pts may have multiple AEs and multiple treatments for each AE. 62 ageusia/dysgeusia AEs were reported by 53% of pts (51/96); management included drug treatment (3% of AEs; Biotene spray and megestrol acetate in 1 pt each) or discontinuation or interruption (24%), while 77% had no treatment indicated. 38 alopecia AEs were reported by 38% (36/96) of pts; management included drug treatment (11% of AEs; bimatoprost [1 pt], diflorasone diacetate [1 pt], and minoxidil [2 pts]), or discontinuation or interruption (24%), while 82% had no treatment indicated.

Conclusions: Muscle spasms, taste disturbances, and alopecia were common in VISMO-treated laBCC pts in the real-world setting, consistent with AEs reported from clinical trials. Common AE management strategies included interruption or discontinuation, and muscle spasms were also often treated with drugs.

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2916

WITHDRAWN

3652

Mullerian mixed tumor of the uterus with metastasis to the scalp

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Malignant mixed Mullerian tumors (MMMT) of the uterus are rare tumors that have both malignant epithelial and mesenchymal components. Genetic data suggest that both components of a MMMT arise from dedifferentiation of a uterine (endometrial) carcinoma. The carcinomatous components of MMT are extremely heterogeneous (squamous cell carcinoma, adenoid basal carcinomas, adenocarcinomas, poorly differentiated carcinoma among others) presumably because they arise from primitive embryonic tissues that develop into the genitourinary organs. Rare case reports of MMMT have shown a focal small cell component with neuroendocrine differentiation. A woman in her 60s presented with vaginal discharge. A workup revealed high grade carcinosarcoma/MMMT with invasion of the uterine wall. Six months later, she again had symptoms and a recurrence was detected by biopsy. Further radiographic workup revealed pulmonary nodules and a fine needle aspirate revealed a poor differentiated adenocarcinoma (CK+ positive and negative for TTF-1, CA-125 and p53). Two months later, the patient presented with multiple nodules on the scalp. Biopsy revealed a small cell carcinoma with intense immunoreactivity for synaptophysin consistent with a neuroendocrine carcinoma. A second biopsy demonstrated a malignant poorly differentiated carcinoma with a mainly non−small cell phenotype with a very focal small cell component. Both the non−small cell portions and small cell portions of this tumor stained prominently for synaptophysin, weak and focally for cytokeratin AE1/3 and negative for TTF-1. There was no mesenchymal component. Based upon integration of the clinical history with the histopathologic and immunophenotypic features of both skin biopsies and with knowledge of the heterologous nature of MMMTs, the nodules were interpreted as metastatic lesions from the MMMT. We share this case as the first report of a MMMT of the uterus with metastasis to the skin that shows neuroendocrine differentiation.

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2836

Multidisciplinary approach to metastatic primary cutaneous adenocarcinoma of the scalp

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Cutaneous adnexal tumors are a rare entity and can be a diagnostic and therapeutic dilemma. Distinguishing primary cutaneous tumors from metastatic carcinoma to the skin requires a thorough work-up. As with many rare tumors, there is no standard of care management. Herein, we present our multidisciplinary approach to a primary cutaneous adenocarcinoma of the scalp with lymph node metastasis. A 60-year-old male presented for management of a nodular growth on his scalp. He reported rectal bleeding but was otherwise healthy. Of note, his mother died of gastric cancer at age 30 and the patient had a benign breast tumor excised 20 years prior. Physical exam revealed a 2-cm by 2-cm fixed pink nodule on the parietal scalp. Biopsy showed ductal adenocarcinoma with apocrine features (CK-7, ER, PR positive; focal staining for p53; Her2Neu, Pax8, D2-40 negative). CT/PET scan and CT chest/abdomen/pelvis had no evidence of disease. Gastrointestinal work-up revealed normal endoscopy and colonoscopy. Failure to identify a visceral malignancy supported the diagnosis of a primary cutaneous adenocarcinoma. Staged excision went two stages down through galea and periosteum, showing persistent rare atypical cells at the deep margin. A firm, palpable postauricular lymph node was detected and ultrasound-guided biopsy was positive for tumor. MR head/neck showed two suspicious nodes. Head and neck surgery performed selective neck dissection and found adenocarcinoma in subcutaneous tissues with perineural invasion along with 2/20 positive nodes. Repair was performed by plastics surgery with rotational flap closure and split thickness skin grafting. Considering the aggressiveness of his disease and the high risk for metastasis, the medical oncology team initiated weekly cisplatin and paclitaxel chemotherapy. Image-guided adjuvant radiation started one week following the first chemotherapy dose with an anticipated 66 Gy in 33 fractions to the primary site and positive margin and 60 Gy in 30 fractions to the neck. The patient is under close surveillance to monitor his response to treatment. This case demonstrates the unique work-up and therapeutic challenges of an exceedingly uncommon tumor. Collaboration between a myriad of specialties is warranted for comprehensive management. Long-term follow-up will be required to evaluate the outcome and further reporting of additional cases may help define optimal treatment of these rare tumors.

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2809

Multiple pilomatricomas in a 41-year-old Asian woman

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Pilomatricomas are benign adnexal tumors which differentiate towards hair matrix cells. These lesions present most often as firm nodular tumors in the upper extremities, head and neck areas, with rare cases reporting pilomatricomas appearing on the trunk. Pilomatricomas can range from 0.5 to 3 cm in diameter with the classification of "giant" pilomatricoma reserved for tumors exceeding 5 cm in diameter. Four histopathologic stages have been described: early, fully developed, early regressive, and late regressive, all of which involve anucleated squamous cells known as "ghost" or "shadow" cells. There are known associations of this pathology with other conditions, most notably myotonic dystrophy, sarcoidosis, Gardner syndrome, Turner syndrome, Steinart disease, sternal cleft, and coagulative defects. Rarely, pilomatricomas can degenerate into pilonatricoma carcinoma. Treatment of this condition is excision of the tumor and the prognosis is favorable with virtually no recurrence. Pilomatricomas are most often seen in patients in their first two decades of life. We report a case of a 41-year-old Asian woman with no significant medical history who presented with painful lesions on her upper extremities bilaterally. The patient denied a family history of similar lesions and was worried she had skin cancer. On clinical exam, the patient had on each upper extremity, a round-shaped, blue and white colored, firm nodule. The lesions were completely excised without complications and were consistent with pilomatricomas on histology. Prior to our observations, Fernandez-Flores et al reported a 28-year-old male with multiple pilomatricomas associated with seminoma which was diagnosed several months before the pilomatricomas. In another case, a 22-year-old woman, also with no medical history, presented with multiple pilomatricomas distributed on her forearm, trunk, and eyebrow. Nevertheless, multiple pilomatricomas in an older patient and in the absence of associated disorders remains rare, which may be a product of underreporting rather than actual incidence. This case highlights the importance of considering pilomatricomas in the differential diagnosis in the setting of multiple growths, even in older patients.

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2897

Multiple tanning bed–induced acral squamous cell carcinomas mimicking arsenical keratoses

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Introduction: Squamous cell carcinoma arises in chronically sun-exposed skin. The major risk factor is ultraviolet light exposure, which includes artificial sources such as tanning beds. Other risk factors include, ionizing radiation, chemicals, HPV, and arsenic exposure. Arsenical keratosis can be caused by chronic exposure to arsenic via drinking water or occupational exposure and is characterized by keratoses of the palms and soles and multiple nonmelanoma skin cancers.

Observation: A 41-year-old woman presented with 2-year history of scaly, erythematous papules and plaques on her lateral feet, calves, and palms. The lesions were pruritic, tender and bled easily. She denied any history of radiation or arsenic exposure including ingesting well water or use of Fowler's solution. She has an extensive history of tanning bed use of over 20 years. Previous biopsies of multiple lesions revealed actinic keratoses and squamous cell carcinoma in situ. Prior treatments included, surgical excision, desiccation and curettage, cryosurgery, topical fluorouracil, and imiquimod. Total urine arsenic level was tested and was 62 ug/L [normal 0-50 ug/L] and 24-hour urine arsenic level was 41-ug/24 hr [normal 0-50 ug/24hr]. Therefore, with normal-high levels of arsenic, it is most likely that the patient's multiple squamous cell carcinomas can be attributed to her tanning bed use.

Comment: This patient demonstrates another possible manifestation of chronic UV exposure from excessive tanning bed usage. Treatments for this patient might include continued destructive measures, topical chemotherapy including "chemo-wraps" with 5-fluorouracil and oral retinoid therapy.

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Nonmelanoma skin cancer histologic subtype as a predictor for subclinical spread and number of Mohs stages required to achieve tumor-free margins

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Objective: Describe the behavior of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) in relation to several factors such as: histopathologic subtypes, location, number of Mohs micrographic surgery (MMS) stages required for tumor clearance, and repair type and size.

Methods: A retrospective medical chart review of 219 cases of nonmelanoma skin cancer (NMSC) treated with MMS was performed. The data obtained from each record included patient's age, gender, and immune status; anatomic location, if the tumor was primary or recurrent, initial lesion size, defect size after MMS, number of stages, type and size of reconstruction.

Results: Basal cell carcinoma (BCC) was diagnosed in 165 (75.3%) cases and distributed between six histologic subtypes: nodular (121; 73.3%), superficial (4; 2.4%), micronodular (21; 12.7%), morpheaform (13; 7.9%), basosquamous (5; 3.8%) and infundibulocystic (5; 1.8%). Squamous cell carcinoma (SCC) was diagnosed in 54 (24.7%) cases and was subdivided in SCC in situ (9; 16.7%) and SCC invasive (45; 83.3%). The mean number of stages required to clear the most aggressive BCCs (micronodular/morpheaform) (n = 34) was 2.03 while the least aggressive BCCs (nodular/superficial) (n = 125) required a mean of 1.56 stages ($P = 0.04$) There was no statistically significant difference between the mean number of stages between SCC in situ and invasive SCCs (1.56 and 1.67, respectively; $P = .701$). An association was found between the number of stages (1 vs. ≥2) and the location of tumor (high risk vs. non-high risk zone; $P = .001$). The initial mean size of recurrent tumors was 2.35 cm (n = 18); whereas it was 1.41 cm for the primary tumors (n = 201) ($P < .001$). Recurrent tumors had a mean final defect size of 3.42 cm and primary tumors had a mean final defect size of 2.01 cm ($P < .001$). The mean number of MMS stages for recurrent tumors was 2.22, while primary tumors required a mean of 1.61 ($P = .006$).

Conclusions: The most important predictors of extensive subclinical spread were location in high-risk zone, recurrent tumors, and morpheaform and micronodular BCC subtypes. Tumors with these features can be regarded as potentially exhibiting an aggressive clinical behavior and thereby can help us optimize surgical planning and patient orientation.

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3500

Preliminary effectiveness and safety in the first 88 patients with newly diagnosed locally advanced basal cell carcinoma treated with vismodegib in the RegiSONIC Disease Registry study

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Background: Treatment of advanced basal cell carcinoma (aBCC) is challenging, with limited treatment options for patients (pts) with disease no longer amenable to surgery or radiation. The Hedgehog pathway inhibitor vismodegib (VISMO) provides a new treatment option for such pts. The RegiSONIC Disease Registry (ClinicalTrials.gov ID, NCT01604252) is an ongoing prospective, observational cohort study designed to collect real-world data on treatment patterns and outcomes in pts with aBCC and/or BCC nevus syndrome (BCCNS). We present preliminary effectiveness and safety data from the first 88 non-BCCNS pts with newly diagnosed locally advanced BCC (laBCC) treated with VISMO.

Methods: The first pt was enrolled on June 20, 2012. Pts are enrolling in three cohorts: newly diagnosed (VISMO-naïve) aBCC (cohort 1), pts with aBCC who previously received VISMO in a Genentech-sponsored study (cohort 2), or pts with BCCNS who have aBCC or multiple BCCs of any stage (cohort 3). Pts are being treated according to clinician's standard of care and evaluated by the clinician's standard practice for assessing disease response (eg, diagnostic image, histopathologic evaluation, photography, clinical evaluation, laboratory evaluation), with data collection every ~3 months.

Results: As of February 13, 2015, 344 newly diagnosed laBCC pts without BCCNS were enrolled in cohort 1. Of these, 88 (26%) were treated with VISMO (received VISMO ≤90 days of determination of laBCC). In this subgroup, 59 (67%) were male and the median age was 67 years (range, 34-99). The median follow-up duration was 13.8 months (range, 0.2-31.8). The response rate was 69% (95% CI, 59-79), with complete response in 42 pts (48%) and partial response in 19 (22%). Median duration of response was 6.0 months (range, 0.0-27.8) by univariate analysis (not estimable by the Kaplan-Meier method). Median progression-free and overall survival were not estimable by the Kaplan-Meier method. Adverse events (AEs) of any grade were reported in 71 pts (81%) and serious AEs were reported in 12 (14%). Treatment was discontinued because of AEs in 14 (16%) pts. The most common AEs were ageusia/dysgeusia (50%), muscle spasms (45%), alopecia (36%), and weight loss (17%).

Conclusions: Data from the RegiSONIC study demonstrate a response rate similar to other VISMO clinical trials in patients with laBCC in a real-world clinical setting. Strategies to manage the most common AEs are needed to optimize treatment benefit.

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3548

Rapid local metastasis associated with primary eccrine carcinoma of the scalp treated with Mohs micrographic surgery

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Primary eccrine carcinoma of the skin is a very rare malignant adnexal tumor with eccrine differentiation somewhat resembling a syringoma, accounting for roughly 1 of 13,000 specimens submitted to a dermatopathology laboratory. There have been only about 140 cases reported in the literature since the first description of a case by Lennox et al in 1952. Usually presented in middle-aged patients and most commonly on the scalp as a large plaque or nodule with/without pain or alopecia, these tumors can be locally very aggressive and frequently metastasize (up to 60%), usually with a fatal outcome. Histologically, these tumors are composed of basaloid epithelium with uniform hyperchromatic nuclei and abundant eosinophilic cytoplasm forming infiltrative epithelial strands with lumen formation. The main differential diagnosis for this tumor is microcystic adnexal carcinoma (MAC). Immunohistochemistry often stains for high and low molecular weight cytokeratins with lumina highlighted by carcinoembryonic antigen (CEA) and epithelial membrane antigen (EMA) staining. We report a case of rapidly metastasizing eccrine carcinoma of the scalp five days after Mohs micrographic surgery in a 69-year-old male patient with a nodule on his scalp noted only two weeks prior to his visit to our dermatology clinic. A biopsy confirmed carcinoma with ductal differentiation consistent with eccrine carcinoma with squamous differentiation, staining strongly and diffusely for keratin 903 (high molecular weight keratin) and CK7. Stains for CEA and EMA are diffusely positive and focally highlight ductal structures. A stain for P63 is diffusively positive in the tumor whereas a stain for podoplanin (D2-40), which stains lymphatics, is negative. The tumor was treated with Mohs micrographic surgery with negative margins. Five days after surgery, a new lesion developed 10 cm from the vertex scalp primary. This lesion was biopsied to show moderately to poorly differentiated adenocarcinoma consistent with in-transit metastatic eccrine carcinoma with comparable histomorphology to the previous biopsy. The patient was referred for radiation therapy, which has been shown to be effective in some cases. Chemotherapy has not been used extensively and presumably lacks in efficacy. We will herein review known cases of eccrine carcinomas, differential diagnoses, histopathology, and summarize current treatment options for this rare disease.

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3926

Retrospective study of vulval BCC

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Basal cell carcinoma (BCC) is the most common human malignancy, which often occurs as a result of ultraviolet light on sun-exposed areas. A more rare location for the presentation of BCC is the non–sun-exposed genital area, where squamous cell cancer occurs frequently in the setting of human papillomavirus and chronic inflammatory lesions, such as lichen sclerosus et atrophicus. Therefore BCC of the vulva are a rare occurrence with a prevalence of 2-4% of all vulval cancers. To date only 250 cases have been described. This study was conducted to explore the clinical findings, treatment and outcome of patients with vulval BCC. We describe a retrospective single-center study examining 25 cases of vulval BCC from 2001 to 2015. The mean age of patients included in this study was 75 years old (range 38-102 years old). The mean duration of the presenting lesions was 3 years (range 1-15). The most common presentation was a lump (68%), with other presenting features included an eroded ulcer (12%), a polypoid lesion (10%), cystic lesions (6%), and finally a plaque-like lesion (4%). The mean diameter of the vulval BCC was 1.1 cm (range 0.3-2.5 cm). The majority of lesions were located in the anterior part of the vulva. We identified a negative HPV status in all the patients found to have vulval BCC and chronic vulval inflammation was noted in 12% of patients. A quarter of patients had candidiasis identified. In addition, of the patients included in the study 25% of cases had a previous skin cancer, 21% of cases had a previous solid organ malignancy (predominantly breast cancer), and 5% had a previous history of having undergone radiotherapy for a gynecological malignancy. Differential diagnoses offered at the time of clinical review included vulval cancer (70%), in which a BCC was suspected in 67% of cases and squamous cell carcinoma in 33%, psoriasis (10%), hydrocistoma (10%), and a fibroepithelioma polyp (10%). The histologic subtypes of BCC were reported as follows: nodular (69%), infiltrative (18%), and superficial (13%). All vulval BCCs were treated with definitive surgery in this study with either a wide local excision strategy (95%) being used or a hemivulvectomy (5%) being used. Reported recurrence rates were 11% in our population sample. This study demonstrates that the diagnosis of vulval BCC can be substantially delayed. The difficulty in treating this particular carcinoma comes in its variety of presenting features, with a lump typically being the most come. Although the etiology of vulvar BCC is not known, early diagnosis is important. Because BCC in these sites sometimes seems innocuous, biopsy of all suspect lesions is advisable.

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3551

Penile squamous cell carcinoma in two patients treated with mycophenolate mofetil in a dermatologic setting

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Cutaneous malignancy is rarely associated with the use of mycophenolate mofetil (MMF). Much of the literature available relates to transplant data and high doses of immunosuppression and the use of multiple agents. We describe two cases of penile squamous cell carcinoma (SCC) occurring in patients prescribed low dose (MMF) for two dermatological conditions. An 83-year-old man was diagnosed with bullous pemphigoid and commenced on (MMF) once daily, reducing to alternate days, after 2 years. He relapsed within two months and the higher dose was reinstituted, with potent topical steroid and minocycline. Concomitantly, he developed a penile rash. The histology demonstrated moderate dysplasia (PIN). Seven years after diagnosis, MMF was ceased due to disease remission, but 9 months later he developed a moderately differentiated SCC of the penis and had a partial penectomy. Further stains retrospectively carried out, show positivity for p16. The second case was an 87-year-old man referred with a penile ulcer, clinically suggestive of pyoderma gangrenosum (PG). This was confirmed on histology. Management included oral prednisolone followed by tacrolimus, with disease control. On tapering tacrolimus his (PG) recurred and the dose was increased. He was switched to (MMF) for 5 months, but relapsed and was recommenced on tacrolimus, achieving remission 2 years after diagnosis. He was discharged 4 years after remission, but later represented with a moderately differentiated SCC of the penis (p16 negative) and underwent a total penectomy.

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2401

Prevalence of actinic keratosis in general practice in Switzerland

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Actinic keratosis (AK) is a common intraepithelial lesion of squamous cell carcinoma of the skin (SCC). It develops mostly in elderly patients and on chronically sun exposed skin areas. Most of the studies on prevalence of AK originate from USA and Australia, and recently from Austria and Spain and are based on populations in dermatology practice. Switzerland is, however, the country leading in skin cancer incidence in Europe. Data on AK prevalence among the Swiss population is an important public health issue. Our study aimed to assess the prevalence of AK in the outpatient Swiss population in general practice. A total of 2844 consecutive patients (55.69% female) were enrolled in 49 general practitioners' offices. 718 (25.25%) of them were diagnosed with AK. 57.6% of the AK patients were male. The prevalence of AK increased steadily with patient age. Most of the AK developed on the head, arms and forearms. 50.74% of AK patients declared leisure-related UV exposure, while only 24.09% were exposed to UV occupationally. 15.74% of the patients were UV exposed both occupationally and during leisure. AK distribution among sun-exposed body sites and extent of disease varied by sex. In Switzerland, AK is a common diagnosis in the general practitioner's setting. Since it has been estimated that about 5% of AK may progress to invasive SCC, the prevention of AK, as well as patients' and general practitioners' education may play a critical role for subsequent SCC development. This is the first study on AK prevalence in Switzerland identifying patients most affected by AK in Switzerland. These results will help to define future approaches to target general practitioners for education, screening and specific intervention in patients with AK.

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3670

Recurrent dermatofibrosarcoma protuberans with suspected pulmonary metastasis in a 44-year-old

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Dermatofibrosarcoma protuberans (DFSP) is a rare, locally aggressive soft tissue sarcoma that typically presents in young and middle-aged adults. We review the presentation and management of a recurrent DFSP with suspected pulmonary metastases. A 44-year-old Chinese female presented with a 8 x 3 cm flesh-colored to violaceous irregularly shaped "keloid" in the right inguinal area along with two 1 cm smooth papules in the left suprapubic area. She had been referred for intralesional injections of the "keloid." Due to the tumor's irregular appearance a biopsy was performed. Spindle and stellate fibroblasts were present in the dermis and expanded into the subcutaneous tissue forming anastomosing and palisading bundles. Special stains were positive for CD34 and negative for factor XIII and S100. Fluorescent in situ hybridization (FISH) was positive for the fusion of COL1A1 (17q21) and PDGFB (22q13) loci. The large tumor was a DFSP while the two smaller papules near the tumor were keloids (biopsy proven). Review of her medical records revealed she had been previously diagnosed with DFSP in the same location in 2007. The DFSP had been excised; however, the patient never volunteered this information, likely due to a language barrier despite the use of interpreters. She was informed that this was a recurrent DFSP and referred to oncology. A computed tomography (CT) scan of the chest, abdomen and pelvis was significant for 4 nodular opacities measuring 0.2-0.3 cm in the right lung and another measuring 0.2 cm in the left lung. These lesions were concerning for possible metastatic disease but were deemed too small to biopsy. Therapy with imatinib mesylate was initiated at 600 mg per day with a plan to repeat the CT scan after 3 months and re-evaluate the tumor's size after 1 month for possible Mohs micrographic surgery. Clinical suspicion must be high to avoid inappropriate management of a DFSP in those with a personal or family history of keloids. Our case demonstrates the potential for DFSPs to recur years after the initial diagnosis, and for metastases to occur despite its low-grade classification. Recurrence rates depend on the type of surgery performed including: conservative surgical resection (26-60%), wide local excision (0-30%), and Mohs micrographic surgery (0-8%). Imatinib mesylate can be used to shrink large unresectable DFSPs to permit possible surgical resection of the residual tumor.

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3474

Review of tumors of follicular lineage in a hospital in the Canary Islands in the last 11 years

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Introduction: Appendage tumors are relatively rare, and their clinical appearance is commonly nonspecific. Classification systems tend to be controversial, but it is largely accepted grouping lesions according to their morphologic similarity to normal appendage structures. Follicular lineage tumors include benign and malignant neoplasms in addition to malformations and hamartomas. Tumors arising from pilosebaceous structures are expected to be found predominantly in the head and neck area.

Methods: In this retrospective observational study we collected information from January 2003 to December 2014 from the Doctor Negrín Hospital dermatology department database. We reviewed all the patients histologically diagnosed as follicular hamartomas and cysts, neoplasms and proliferations with follicular, matrical, follicular sheath (trichilemmal) and infundibular or isthmic differentiation. We decided to exclude trichilemmal and infundibular cysts (104 patients) because many of these lesions are assessed and treated in other services such as general or plastic surgery.

Results: We studied 288 patients. The average age was 52 years old (between 8 and 91). No gender differences. The most frequent tumors were, in descending order, fibrous papule, pilomatricoma, trichoepithelioma, inverted follicular keratosis and trichilemmoma. There were 4 cases of malignant tumors, all of them trichilemmal carcinoma (1.38%). The most frequent location were head and neck 79%, extremities 15%, and trunk 4%.

Conclusions: The follicular tumors are an infrequent problem in our department. They are predominantly located in the head and neck area. The great majority are benign; however, it was not possible to clinically differentiate the type of tumor, and whether if it was benign or malignant, so the histologic correlation is extremely important.

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Safety and efficacy of vismodegib and impact of treatment breaks in advanced basal cell carcinoma: Interim analysis of the STEVIE study in 499 patients

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Background: Vismodegib (VISMO) was the first Hedgehog pathway inhibitor approved for adults with locally advanced (la) or metastatic (m) basal cell carcinoma (BCC) inappropriate for surgery or radiotherapy. STEVIE (NCT01367665) is an ongoing safety study of VISMO in patients (pts) with laBCC or mBCC. Data from an interim analysis of 499 pts (data cutoff: November 6, 2013) are reported.

Methods: Pts with laBCC or mBCC receive VISMO 150 mg once daily until progressive disease, unacceptable toxicity, or withdrawal. The primary objective is safety; efficacy variables are secondary endpoints. Treatment breaks (TBs) of up to 8 weeks are allowed for management of toxicity and other reasons. An exploratory analysis was performed to assess the impact of TBs on the safety and efficacy profile of VISMO.

Results: Four hundred ninety-nine pts (laBCC: 468; mBCC: 31) were included in the analysis. Median duration of VISMO exposure was 36.4 weeks. Common treatment-emergent adverse events (TEAEs) included muscle spasms (64%), alopecia (62%), dysgeusia (54%), weight decreased (32%), asthenia (28%), and decreased appetite (25%); most were grade 1 or 2 in severity. Serious TEAEs occurred in 108 pts (22%). Overall response rate (investigator-assessed) in pts with measurable disease (RECIST 1.1) was 65% (313/482) (32% complete response [CR]; 33% partial response [PR]), including 67% (302/453) in pts with laBCC and 38% (11/29) in pts with mBCC. Median time to best response (all pts) was 3.7 months (mos) (3.7 mos laBCC; 6.5 mos, mBCC). Median durations of response were 22.7 and 10.0 mos, respectively. Median progression-free survival was 24.5 and 13.1 mos in pts (intent-to-treat population) with laBCC and mBCC, respectively. During the study, 368 (74%), 76 (15%), 41 (8%), and 14 (3%) pts received 0, 1, 2, and ≥3 TBs, respectively. The median duration of treatment was 31.9, 42.7, 57.0, and 64.9 weeks in pts with 0, 1, 2, or ≥3 TBs, respectively. Given the longer exposure period, pts with more TBs tended to experience a higher incidence of TEAEs. Overall response rate was 61% (30% CR; 31% PR), 65% (33% CR; 32% PR), 95% (51% CR; 44% PR), and 85% (39% CR; 46% PR) in pts with 0, 1, 2, or ≥3 TBs, respectively.

Conclusions: This interim analysis of STEVIE confirms the previously observed safety and efficacy of VISMO in a setting representative of routine clinical practice. Treatment breaks did not appear to compromise efficacy.

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3037

Skin cancer detection through teledermatology vs. face-to-face dermatology consultation

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Few studies have performed a head-to-head comparison of skin cancer detection rates between teledermatology and face-to-face dermatology consultations in the same patient population. We conducted a retrospective cohort study of all store-and-forward teledermatology consultations and an equivalent number of randomly selected face-to-face dermatology consultations at the Veterans Affairs (VA) Boston Healthcare System. The proportion of lesions requiring biopsies and incidence of detected nonmelanoma and melanoma skin cancers were compared between the two groups. There were 623 patients in the teledermatology and 637 patients in the face-to-face dermatology consultation cohort. The vast majority (95%) of patients were male in both cohorts, with no significant difference in age (62.6 ± 15.8 vs. 64.3 ± 16.1, $P = .1$). There was, however, a significantly higher proportion of patients with prior history of skin cancer evaluated by face-to-face consultations, 23% (144/637) vs 8% (50/623), $P < .001$. Face-to-face dermatology consultations had higher overall detection rate of skin cancers than teledermatology consultations, 11% (70/738) vs 4% (25/623), $P = .001$, even when adjusted for age and prior history of skin cancer (adjusted $P < .01$). Incidence of detected melanomas for patients evaluated via face-to-face dermatology vs. teledermatology consultation was 0.6% (4/637) vs 0% (0/623), while incidence of detected keratinocytic carcinoma (basal cell carcinoma and squamous cell carcinoma combined) was 10% (64/637) vs 3.9% (24/623), $P < .05$ respectively. There were also two cases of cutaneous T-cell lymphoma in the face-to-face consultation cohort, and one case of Merkel cell carcinoma in the teledermatology cohort. A significantly higher proportion of patients evaluated by face-to-face consultations received biopsies, 25.1% (160/637) vs 8% (50/623), $P < .001$ though yield of malignant tumors from biopsies was statistically equivalent between the two cohorts, 43.8% (70/160) vs 50% (25/50), $P = .4$. The current study directly compares the effectiveness of teledermatology and face-to-face consultations in detecting skin cancer in a predominantly older male patient population within the VA Boston Healthcare system. Results showed that face-to-face consultations detected nearly three times more skin cancers than teledermatology, even when adjusted for age and prior history of skin cancer.

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3326

Skin cancer surveillance in pediatric cancer survivors—A case of multiple basal cell carcinomas in a patient with a history of acute lymphoblastic leukemia, total body irradiation, chemotherapy, and allogeneic bone marrow transplantation

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Pediatric cancer survivors are at an increased risk for long-term effects from the therapy targeted for their primary malignancy. Children who have had hematopoietic stem cell transplantation (HSCT), chemotherapy, and irradiation are known to have an increased risk of developing cutaneous malignancies. Drug-induced immunosuppression has been known to increase the risk of developing squamous cell cancer (SCC) approximately 65- to 250-fold, basal cell cancer (BCC) by 10- to 16-fold, and melanoma 2- to 8-fold. Patients who receive a radiation dose of 35 Gy or greater to the skin have approximately a 40-fold higher risk of developing BCC compared to patients who did not undergo irradiation, but there is no confirmed association with increased squamous cell carcinoma or melanoma risk. It was found that even radiation doses of 1 Gy or higher were associated with a greater risk of BCC. BCC is also reported to be more aggressive in these patients with greater destruction and rates of recurrence, which has been attributed to possible irradiation-induced genetic alterations, defective vasculature in the area exposed to radiation, and/or modification of the patient's immune system. Limited data focusing on pediatric patients who received HSCT have also indicated there is a significant incidence of nonmelanoma skin cancer (NMSC) in these patients. Based on our experience caring for a 26-year-old patient in remission from pre-B cell acute lymphoblastic leukemia who received a cumulative irradiation dose of 5400 cGy (1200 cGy TBI, 1800 cGy spinal, and 2400 cGy cranial), allogeneic bone marrow transplantation, and chemotherapy (adriamycin, idarubicin, daunomycin, cytoxan, vincristine, prednisone, fludarabine), we recommend that dermatologists should collectively establish guidelines for surveillance. Our patient, as one example, has accumulated a dermatologic history of 30 biopsy-proven BCCs and numerous surgeries. Currently, there are guidelines provided by various regional oncology organizations, but no established protocol that involves dermatologists in the care of these patients. Evidence from the literature to date suggests that multidisciplinary teams that encourage collaboration between oncologists and dermatologists, preventive education regarding photoprotection, and regular dermatologic exams for prompt diagnosis and timely treatment would reduce morbidity in these patients.

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3925

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Spontaneous resolution of advanced basal cell carcinoma following short pulse treatment with hedgehog pathway inhibitor

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Introduction: Recently vismodegib (VSDG), a hedgehog pathway inhibitor, was approved for treatment of advanced basal cell carcinoma (BCC) after a phase II study showed significant tumor response after median treatment length of 10 months. Since VSDG approval, several prospective trials have further evaluated its safety and efficacy. Treatment length in these studies ranged from 5.5 to 9 months, both supporting results of the initial phase II trial. However, data and clinical experience are still limited and further evaluation is needed to define the role of VSDG in the treatment of advanced BCC, particularly the length of treatment necessary for tumor clearance.

Case report: A 51-year-old Hispanic male presented with a 6-month history of a nodule on his left lower eyelid. The patient received radiation for BCC to this area 1 year prior, but the tumor recurred and now obstructed his vision. He has a family history of melanoma, smokes half a pack of cigarettes a day and works as a handyman. Physical exam showed a 3.0 x 2.7 cm vascular, friable, nodule on his left lower eyelid with surrounding erythema and an injected conjunctiva. The patient subsequently received 2 biopsies, both showing nodular type BCC. The patient was started on 150 mg VSDG daily. Treatment abruptly ended after 15 days when the patient was incarcerated. Six weeks later the patient reported spontaneous involution of the tumor. Twelve weeks after treatment the patient had complete clearance with a 0.8 x 0.4 cm residual area of hyperpigmentation. Biopsy revealed chronic perifolliculitis with granulation tissue, hemosiderin deposition and scar, with no carcinoma identified.

Discussion/conclusions: No previously published study has reported resolution of BCC with VSDG after such short treatment length. The exact role of VSDG in treating BCC has not yet been clearly defined. Recent studies have evaluated other modalities of VSDG in the treatment of advanced BCC, including its use as an adjuvant to surgery and in operable BCC. This case highlights the need for further academic discussion when using a novel therapeutic agent.

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3263

Squamous cell carcinoma on African albino: A rare case in Spain

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Squamous cell carcinoma is a very high incident tumor on early-aged African albinism population, half-reducing their life expectation. A 24-year-old male from Equatorial Guinea, black race, with oculocutaneous albinism and HIV infection diagnosed on January 2015, was admitted to our the emergency room presenting a cutaneous lesion on head and face producing intense pain associated to marked affection of general status. 10 months earlier he was diagnosed of a well-moderate differentiated squamous cell carcinoma at Equatorial Guinea. The extension study was negative for metastasis, but the impossibility of surgical treatment made the patient travel to Spain. On physical examination, an irregular, suppurative ulcer of 20 cm approximately from the right parietal region to the right side of the neck destroying part of the homolateral auricle was found. Blood sample analysis revealed 22.33 103/µl. leucocytes with 19.56 103/µl. neutrophils, RCP 142.80 mg/L. ELISA HIV: positive, CD4 lymphocytes 500 CD4/mm3. Ulcer culture: *Streptococcus dysgalactiae, Providencia stuartii, Klebsiella pneumoniae*. Blood culture: *Streptococcus dysgalactiae*. Skin biopsy: moderately differentiated squamous cell carcinoma without perineural invasion. Cranial and face CT scan revealed a huge mass infiltrating the external auditory canal, parotid gland and temporomandibular joint, up to the hypopharynx. Chest and abdomen CT scan found lung metastasis and retroperitoneal lymphadenopathy. A stage IV right hemicranial squamous cell carcinoma was diagnosed, accompanied by secondary findings such as polymicrobial infection of the tumor with *S dysgalactiae* bacteremia and A1 stage of HIV chronic infection. He was treated actively with antibiotics and morphine. On an interdisciplinary session, surgery was dismissed and chemotherapy treatment was started. After 2 cycles, the tumor progressed and a sedation-analgesic perfusion was started. The patient died. Albinism has an incidence of 1/17,000 world habitants. In Africa, the incidence is 1/1500-5000 habitants. Intense solar radiation and the lack of suitable skin protection made these patients develop skin cancer at early ages. HIV infection increases skin cancer risk. The lack of access to sanitary care makes this tumor reach considerable big sizes that hinder adequate treatment. The most important risk factor for the albinism population to develop aggressive skin cancer is the lack of access and the precariousness of the sanitary care system.

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3571

Squamous cell carcinoma: Brain metastasis

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A 54-year-old male farmer, who lives in the outskirts of Honduras, presents a lesion on his lower lip, which consists of a nodule of several millimeters in diameter, is erythematous, indurated, and asymptomatic. Later on, the surface of the nodule ulcerated and extended progressively, causing important asymmetry on the right side of his face. The patient visited a general practitioner who diagnosed an oral infection and dispatched him with oral amoxicillin. After 1 week of therapy with no evident recovery, he was referred to a dermatologist. We received the patient with a white exophytic tumor, multilobulated on the surface, measuring 3 cm in diameter, infiltrating his right cheek, preauricular area asymptomatic, causing facial disfiguration. Upon the request of oral examination, purulent discharge drained spontaneously, without dental compromise. Bilateral cervical adenopathy was found and palpebral ptosis of the left eye was observed. The neurologic evaluation revealed 13/15 on the Glasgow Coma Scale with major affection on the verbal parameter. He was admitted to the hospital with a treatment of antibiotics and a skin biopsy of the lip was performed. The results reported intercellular and intracellular edema, polymorphic ISLOTS with different sizes, composed of polygonal cells with big nucleus and pleomorphism; many with intercellular bridges. There are few mitoses, 0-1 in 10 fields at 40x. The stroma revealed dilated capillary vessels, some infiltrating the endothelial wall and lumen. It concluded: squamous cell carcinoma, well differentiated with lymphovascular infiltration. According to protocol, a cranial MRI was performed and its results reported the presence of a mass of great size that involved the base of the skull, sellar region, pterygopalatine area, right orbit, both maxillary sinus and ethmoidal cells, adenopathy in the neck, segments III and IV on the right side and segment III on the left side, all less than 9 mm. Therapy was initiated with 50 g of cisplatin, 500 mg of 5 fluorouracil for 4 days, and 16 mg of dexamethasone. Unfortunately, 48 hours after, the patient filed for discharge. One month later, he died. Squamous cell carcinoma is a malignant neoplasm of keratinocytes that show full thickness epidermal dysplasia. It may arise de novo or from actinic keratosis, a premalignant precursor lesion that shows partial thickness epidermal dysplasia. Actinic keratosis progresses to full thickness malignancy at an estimated rate of 0.025% to 16% for an individual lesion per year. Squamous cell carcinoma lesion progresses from in situ (Bowen disease) to invasive lesion once the tumor cells invade the basement cell membrane of the dermoepidermal junction. The incidence of nonmelanoma skin cancers varies globally, but it is thought to be increasing overall since the 1960s. Although the vast majority of the squamous cell carcinoma cases present early stages of the disease, a minority of cases progress to regional or distant metastasis (approximately 2-5%), accounting for 20% of all skin cancer–related deaths. In Honduras, little is known about the epidemiology of this disease and few publications related are found. In 1999, a study identifying the incidence of skin cancer in 22,324 medical files, revealed that 12% of them corresponded to squamous cell carcinoma. In 2008, a group of oncologists studied 25 patients who underwent tumor resection as an initial therapy for nonmelanoma skin cancer between 2004 and 2009. Of these patients, 40% accounted for squamous cell carcinoma, nonrecurring after a 5-year follow-up. No information regarding metastasis has ever been published in our country. Given the rapid onset and progression of our patient with a fatal outcome, we encourage early identification of precursor lesions with proper treatment, for even though metastasis is rare according to international literature, the behavior for each individual may vary.

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2945

The role of reflectance confocal microscopy in the diagnosis and management of squamous cell carcinoma in situ

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Background: Reflectance confocal microscopy (RCM) is increasingly used for noninvasive in vivo diagnosis of nonmelanoma skin cancer.

Objective: A pilot prospective study to evaluate the role of RCM in the diagnosis of squamous cell carcinoma in situ (SCCIS) and monitoring of response to nonsurgical interventions.

Methods: Ten patients with a total of 11 SCCIS were identified. The clinical, confocal, histologic features and fluorescence diagnosis were recorded.

Results: Four SCCIS lesions underwent RCM imaging prior to biopsy while 11 SCCIS lesions were followed-up with RCM imaging. There were clinical features of persistent SCCIS postphotodynamic therapy (PDT) in 4 out of 11 follow-up cases. On RCM imaging, all 8 (4 new SCCIS and 4 follow-up) cases displayed atypical honeycomb or epidermal disarranged pattern. Three out of 8 cases (37.5%) showed presence of numerous dendritic cells in the epidermis while small bright refractive cells were seen in the epidermis in 4 out of 8 cases (50%). Round blood vessels in the superficial dermis were seen in 4 cases (50%) with SCCIS. Eight lesions were treated with PDT only while 3 lesions underwent a combination of PDT with cryotherapy or imiquimod. Clinical persistence of SCCIS in follow-up cases were confirmed with RCM imaging and fluorescence diagnosis in 2 follow-up cases. There were no features of SCCIS on RCM imaging in the 7 lesions which were clinically cured.

Conclusion: There was good correlation between histologic and confocal features in patients who underwent RCM imaging prior to biopsy. Our study suggests that RCM may be a complementary noninvasive tool in the diagnosis of SCCIS although a biopsy is often necessary as the depth of RCM imaging is limited to the level of papillary dermis. It is useful in monitoring response to nonsurgical treatment by avoiding unnecessary biopsies especially in lesions with persistent residual postinflammatory erythema.

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3056

Topical imiquimod for the treatment of recurrent oral squamous cell carcinoma and regression of pulmonary metastasis while on acitretin

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Oral squamous cell carcinoma (OSCC) is the tenth most common type of cancer that has historically been treated with surgery or radiation with or without chemotherapy, all of which lead to significant posttreatment morbidity. Topical imiquimod cream has been approved by the FDA for treatment of nonhyperkeratotic actinic keratosis, superficial basal cell carcinoma, and external genital warts. Off-label use has demonstrated effectiveness in treatment of mucosal neoplasms. Acitretin is an oral retinoid indicated for the treatment of psoriasis. It is also used as a chemopreventive agent for the prevention of cutaneous squamous cell carcinoma in immunosuppressed patients. An 81-year-old white female presented with recurrent oral squamous cell carcinoma and lung nodules consistent with metastasis. She was refractory to treatment with two wide local excisions and subsequent radiation therapy. Advanced tumor stage decreased the likelihood of cure from surgical resection, chemotherapy, or radiotherapy. Tumor directed treatment of the right retromolar trigone (RMT) was initiated with topical imiquimod 5% cream daily. The patient was also started on acitretin 10 mg daily for pulmonary metastasis. Subsequent examination two weeks later showed complete regression of the oral lesion. The imiquimod cream was gradually tapered to once weekly applications without recurrence of the lesion. Two months after starting treatment with topical imiquimod, a biopsy was performed of the RMT and found to be negative for disease. No side effects were noted other than mild tenderness from erosions as the lesion was resolving. A PET/CT was performed to evaluate for metastatic disease. Results showed earlier noted widely spread minute lung nodules were stable or markedly reduced in size. No new lung nodules were noted. We report the resolution of recurrent oral squamous cell carcinoma with topical imiquimod cream and the regression of pulmonary metastasis of cutaneous squamous cell carcinoma with oral acitretin. Given the considerable risks associated with traditional treatment regimens for OSCC, topical imiquimod may offer a reasonable and well-tolerated alternative treatment option with optimal results for patients with multiple comorbidities. Further studies are warranted to investigate its utility as a single agent therapy for OSCC. This is the first reported case describing topical imiquimod in treatment of OSCC.

Commercial support: None identified.

3282

Trichilemmal carcinoma: Case report

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Trichilemmal carcinoma, a low-grade malignant lesion, is a rare adnexal tumor originated from hair follicle cells that usually appears on sun-exposed skin areas of elderly patients. This paper reports a case of an 83-year-old woman presented with a 5-year history of a developing tumor on malar region, measuring 4 cm in greatest diameter. Initial differential diagnosis included squamous cell carcinoma and basal cell carcinoma. An incisional biopsy was performed. Histologically, it revealed epithelial cells cords infiltrating the dermis, showing enlarged and hyperchromatic nuclei, with small nucleoli and numerous mitotic figures. A pilar type keratinization was demonstrated, compatible with trichilemmal carcinoma. Immunohistochemical tests showed a positive epithelial membrane antigen (EMA) in rare cells, whereas carcinoembryonic antigen (CEA) and P16 were negative. The patient was referred to the department of oncologic surgery to excise the tumor. The diagnosis of trichilemmal carcinoma is established by histopathologic examination, completed when is necessary by immunochemistry (usually negative for CEA and EMA, although positive results have been occasionally documented for the latter).The pathogenesis of trichilemmal carcinoma remains unknown, but sun-exposure, postsurgical radiation for other lesions, immunosuppression or a preexisting burn scar are predisposing factors. The tumor usually manifests in the elderly as a solitary nodule, with a 3:1.6 female-male ratio. It is commonly located on the scalp, forehead, neck, trunk and the upper extremities. A differential diagnosis is required; thus, other skin cancers should be excluded. Simple excision with adequate margins is the treatment for a solitary lesion. Despite an indolent course and benign clinical evolution, the tumor has potential for local invasion and recurrence, which implies the need of a careful follow-up.

Commercial support: None identified.

2769

Treatment patterns and key factors associated with high treatment costs among commercially insured patients with advanced basal cell carcinoma

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Background: Although basal cell carcinoma (BCC) can be effectively treated, advanced BCC (aBCC), including locally advanced BCC (laBCC) and metastatic BCC (mBCC), could be challenging to treat and is associated with substantial health care costs.

Objectives: To describe the treatment patterns and identify key factors associated with high treatment costs for aBCC patients.

Methods: Commercially insured adult patients were selected if they had ≥2 claims with a BCC diagnosis (ICD-9:173.x1) separated by ≥30 days on or after October 1, 2011 (BCC-specific ICD-9 codes release date). ABCC patients (including mBCC and laBCC) were identified using an algorithm based on metastasis diagnosis, use of radiation therapy, and medical oncologist/other specialist visits. The index date was defined as the first aBCC qualifying diagnosis or event. Patients were continuously enrolled in a health plan for ≥6 months before (baseline) and ≥12 months after the index date (study period) and had ≥1 BCC diagnosis during baseline. Patient characteristics, treatment patterns and treatment costs were measured during the study period. Key factors associated with high BCC treatment costs (ie, the top 20% most costly aBCC patients) were assessed using multivariable logistic regression.

Results: A total of 847 aBCC (laBCC: 826, mBCC: 21) patients were identified, with a mean age of 75 years and 57% male. During the study period, the most common physical comorbidities were diabetes (25%), malignancy [excluding skin cancer] (20%), and chronic pulmonary disease (16%); 13% of patients had any mental comorbidity and 15% had malaise and fatigue. The most common treatments observed among aBCC patients were radiation therapy (94%) and surgeries (59%), including cryosurgery (48%), reconstructive surgery (21%), surgical excision (17%), malignant destruction (15%), and Mohs surgery (11%). Among the 94 patients receiving Mohs surgery, 93% also had reconstructive surgery and 15% had radiation therapy within 60 days following the Mohs surgery. Drug treatment was less frequent, with 2% of patients using imiquimod and 0.4% using vismodegib. Younger age (age < 65), men, and Northeast region were significantly associated with high BCC treatment costs (ie, ≥$15,156).

Conclusions: The majority of the aBCC patients received radiation therapy and over half received surgeries. Key factors associated with high treatment costs included age, gender, and region.

Supported by Novartis Pharmaceuticals Corporation.

2424

UV recall or inflammation of actinic keratoses? Post cetuximab reaction for a voriconazole induced aggressive cutaneous squamous cell carcinoma in a heart transplant patient

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Importance: High-risk cutaneous squamous cell carcinoma (cSCC) that occurs more commonly in immunosuppressed patients is associated with rapid local growth, high rates of metastasis, and local recurrence. The advent of cetuximab, an EGFR inhibitor, has been well received in this patient population in terms of safety and efficacy. We report a new inflammatory cutaneous reaction following the cessation of cetuximab therapy.

Observations: A heart transplant patient, maintained on voriconazole for a history of disseminated aspergillosis, presented with extensive and unresectable cSCC of the scalp and face. He was treated with first line cetuximab monotherapy and showed near resolution of the cSCC in question. However, one month after cessation of cetuximab therapy, the patient developed facial edema with inflammation of existing lesions as well as accentuation of previously nonnoticeable papules and plaques.

Conclusions and relevance: Cetuximab is an alternative therapy for the treatment of SCC in transplant patients and may be used as first line monotherapy when surgery or radiotherapy is contraindicated. Importantly our case raises awareness for a possible UV recall versus inflammatory reaction of previous actinic keratoses following therapy with cetuximab.

Commercial support: None identified.

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3134

VDA-1102, a first-in-class VDAC/HK modulator entering phase 1/2 drug development, for treatment of actinic keratosis and cutaneous squamous cell carcinoma

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Background: Phosphorylation of glucose to glucose-6-phosphate by hexokinase (HK) is the first enzymatic reaction in the glycolytic pathway, which prepares glucose for entry into the Krebs cycle that supplies cells with energy and the precursors necessary for numerous metabolic processes. Unlike the HK1 isozyme that is ubiquitously expressed, high levels of the HK2 isozyme are found mainly in transformed cells where it is required for cancer initiation and transformation. HK2 attaches to the mitochondria via interaction with the VDAC1 channel. VDAC1/HK2 association allows a high rate of glycolysis and blocks pro-apoptotic signals.

Methods: VDA-1102, a novel, selective, targeted VDAC1/HK2 modulator, is being developed as a topical treatment of actinic keratosis (AK) and squamous cell carcinoma (SCC).

Results: VDA-1102 demonstrates selective detachment of HK2 from VDAC1 (IC50 = 90 nM) without affecting the interactions of HK1, thus affecting cancer cells but not their surroundings. It inhibits the proliferation of many tumor types and is especially efficacious (IC50 < 1 μM) against a variety of skin cancer cell lines including AK, SCC, melanoma, basal cell carcinoma (BCC) and cutaneous T-cell lymphoma. Topically administrated VDA-1102 was tested in a UVB-induced skin cancer model in SKH1 hairless mice, a validated model for AK and SCC. All of the tested VDA-1102 doses (2.5% and 5% ointment qd, and 40% topical solution intermittent dosing) led to approximately 70% reduction in the number of cutaneous lesions ($P < .0001$; similar to ingenol mebutate), and 70% reduction in the total area of lesions ($P < .0001$), without any topical or systemic side effects. Histopathology of the treated skin showed a reduced rate of cell division ($P = .0009$), increased apoptosis (caspase-3, $P = .0003$), and an effect on the levels of HK2 in the tissue (pharmacodynamics marker). Toxicology studies in several species have established that VDA-1102 has a very broad therapeutic window.

Conclusions: Selective VDAC/HK2 modulators, such as VDA-1102, exhibit significant antitumor efficacy against AK, cutaneous SCC, and other skin cancer types, with a promising safety profile. This first-in-class drug employs a new targeted anticancer mechanism of action, and differs from the currently used topical AK and SCC drugs, which induce severe inflammation or necrosis as part of their mechanism of action. The phase 1 human clinical trial with VDA-1102 ointment is scheduled for January, 2016.

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3888

Vulvar metastasis

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Introduction: Cutaneous vulvar metastasis are uncommon representing only 5-8% of all vulvar cancers. They are usually accompanied by metastasis involving other organs and therefore are associated with a poor prognosis. The majority of patients present either single or multiple nodules or masses. Labia majora of the vulva are the most frequent localization.

Case reports: We describe 2 new cases of metastatic tumors of the vulva as a manifestation of two different entities. Case report 1: A 44-year-old woman with a previous history of rectal adenocarcinoma that had been treated with chemotherapy and radiotherapy, presented with a 15-days history of vulvar edema and itching. On physical examination she presented multiple erythematous and indurated papules over the labia majora and mons pubis accompanied by a generalized vulvar edema and erosions in the perianal region. Biopsy showed a metastatic adenocarcinoma that was infiltrating the dermis. The immunohistochemical studies demonstrated that cells were positive for CK19. Case report 2: A 60-year-old woman noticed a firm and painful vulvar mass which had been progressing. She had been treated one year before of a leiomyosarcoma in the scalp. On physical examination, an indurated erythematous nodule of approximately 3 cm was visualized in the left labium majora. She underwent complete surgical excision of the lesion. Histologic evaluation revealed a metastatic high grade leiomyosarcoma.

Discussion: Primary cancer of the vulva is uncommon, accounting less than 1% of all cancers in women. Metastatic cutaneous tumors of the vulva are even more rare representing only 5-8% of all vulvar cancers. The most common symptoms included the presence of nodules, masses, pain and ulceration. They can be accompanied by bleeding, pruritus or edema. The vulvar site most frequently involved was the labium majora and they usually appear after the diagnosis of the primary tumor. Squamous carcinoma of the cervix followed by ovarian carcinoma and rectal adenocarcinoma represented the most common primary sites of metastatic tumors to the vulva. Metastatic tumors of the vulva represent a poor prognosis and they usually are accompanied by multiple simultaneous metastases to other sites. Vulvar lesions should be suspected as metastatic in a patient with a prior history of malignant carcinoma and by the absence of a mucocutaneous intraepithelial lesion.

Commercial support: None identified.

3780

What our patients know: SLUCare Dermatology patients and skin cancer

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Background: Melanoma and nonmelanoma skin cancers are the most commonly diagnosed cancers and diagnosis rates continue to rise. It is important to understand what patients know regarding skin cancer and sun protective behaviors, as knowledge often helps dictate behavior.

Objective: The objective of this research project is to determine underlying patient knowledge as well as gaps in knowledge with regards to skin cancer, including melanoma, squamous cell carcinoma and basal cell carcinoma of patients presenting to dermatology clinic.

Methods: An 18-item survey was distributed to SLUCare dermatology patients during routine clinic visits. Various demographic questions were used to identify patient characteristics and groups that may be linked to an inferior knowledge base and thus, may be most in need of additional education. All knowledge-based questions were created from information found in American Academy of Dermatology pamphlets and website. The study population included patients 18-99 years of age who presented to SLUCare general Dermatology clinics and were able to complete the survey.

Results: Two hundred surveys were distributed equally among two sites, with 170 completed surveys used in analysis. Of those who responded, 104 (61.2%) were female and 55 (32.4%) were male; 62.9% (107) of patients were established, while 23.5% (42) were new. A history of skin cancer history was present in 28.8% of responders. Age of responders varied, with the 51-65 year old group being the highest represented and the > 66-year-old group the lowest. Mean overall score was 66% (SI) = 17.6%). Females scored significantly higher when compared to males ($P = .025$). A significant difference in survey scores was also seen among different age groups with participants between the ages of 36-50 years scoring significantly higher than those great than 66 years old ($P = .022$). Interestingly, higher scores were obtained by new patients when compared to established patients, however the difference was not significant ($P = .184$). Differences in scores between participants with and without a history of skin cancer, as well as participants with varying sunscreen use habits were not significant.

Conclusions: Our results reveal lower than expected general knowledge regarding skin cancer. The survey results shed light upon subgroups that may have inferior knowledge and ultimately underscore the importance of patient education.

Commercial support: None identified.

PEDIATRIC DERMATOLOGY

3503

A boy and his guinea pig: the importance of taking a pet history

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A 9-year-old boy presented with a 4-week history of a pruritic and gradually enlarging periorbital scaly erythematous plaque affecting his right upper and lower eyelids. There was a family history of systemic lupus erythematosus (LE) in his maternal grandmother. Otherwise, he was fit and well. Examination revealed an area of well-demarcated erythema with scattered follicular crusting affecting the right periorbital region, with associated mild eyelid edema. Initial treatments prescribed in the community, including hydrocortisone acetate, miconazole nitrate 2% cream, oral antibiotics and antiviral agents were of limited benefit. The differential diagnoses included tinea faciei and discoid LE in view of the family history. Initial investigations including antinuclear antibody, extractable nuclear antigen screen, double-stranded DNA, bacterial and viral skin swabs were all negative. Skin scrapings were taken during the initial consultation. On further exploration of the history, his mother reported that their pet guinea pig Fluffy had been treated for left-sided periorbital hair loss a month prior to the patient's symptoms. The veterinarian's diagnosis was a likely fungal infection and clinical pictures of Fluffy were very similar to the child. In light of this information, he was commenced on clobetasone butyrate 0.05%/oxytetracycline 3%/nystatin 100,000 units/g cream twice daily. The plaque responded to this treatment. Three days later treatment was changed to terbinafine hydrochloride 1% cream o.d. and clobetasone butyrate 0.05% cream o.d. Fungal elements (3+) were seen on microscopy of skin scrapings. A heavy growth of *Microsporum canis* was isolated on fungal culture, confirming a zoophilic tinea faciei. Tinea faciei is a dermatophyte infection affecting the glabrous skin of the face. It can affect all ages, but there is a peak in childhood, often due to direct pet contact. The clinical presentation can vary greatly. Most cases respond to topical antifungal treatments, as did our patient. This case highlights the importance of including a pet history when reviewing patients, especially in pediatric cases that present with a facial rash. Other important pet histories in our clinic included untreated staphylococcal scalded skin syndrome in a dog transferred to a child which involved emergency referral to a vet. A comprehensive history will facilitate reaching an accurate diagnosis and ensure appropriate treatment is commenced in a timely manner.

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2561

A case of concurrent plexiform neurofibroma and phakomatosis pigmentovascularis

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Case: We report a case of a 10-year-old boy who developed a plexiform neurofibroma at the site of a preexisting phakomatosis pigmentovascularis (PPV) lesion. The patient was known for a lesion on the left shoulder consisting of a congenital melanocytic nevus, a Becker's nevus and a vascular malformation. This lesion was diagnosed as a PPV. On follow-up at 10 years of age, the patient had developed a soft mass at the site of the PPV. The mass was tender with arm mobilization. MRI of the shoulder showed a 10.0 x 8.5 x 2.0 cm mass with a target sign highly suggestive of a plexiform neurofibroma, which was subsequently confirmed on histopathology. Aside from a single cafe-au-lait spot on the abdomen, the rest of the cutaneous exam was normal. His ophthalmologic exam was normal. The patient did not meet the criteria for neurofibromatosis type 1 (NF1)

Discussion: PPV is a rare entity that combines a vascular malformation with a pigmentary nevus. A previous case has been described of a PPV lesion occurring at a different site than a plexiform neurofibroma in a female patient with segmental NF1. To our knowledge, this is the first time that a plexiform neurofibroma superimposed on a PPV lesion has been described.

Commercial support: None identified.

3219

A rare case of congenital unilateral nevoid telangiectasia

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Unilateral nevoid telangiectasia (UNT) is a rare cutaneous vascular condition first described by Blaschko in 1899. It is characterized by unilateral superficial telangiectasias occurring most often in the cervical and upper thoracic dermatomes in a linear pattern. The condition occurs in a 2:1 female to male ratio and cases can be divided into those that are congenital versus acquired. While most UNT cases are acquired and often found in females, only about 15% of cases are congenital and are furthermore reported mostly in males. Acquired cases have been hypothesized to occur in association with hyperestrogenemic states such as pregnancy, puberty, oral contraceptive use and hormonal therapy, alcoholism, and liver disease, including hepatitis B and C infections. Conflicting evidence is present as to whether there is an absolute increase in the presence of estrogen and progesterone receptors in the skin as many case reports show no increase. Instead, others hypothesize that the condition is actually a result of somatic mosaicism and that cutaneous lesions are genetically predisposed to becoming visibly evident under conditions of elevated estrogen. Sixteen congenital cases of UNT have been reported in the literature. Our patient is a newborn baby girl who presented at birth with red blanchable reticulate patches in a dermatomal distribution extending from the right shoulder down to the flexural aspect of the arm. There were also a few coalescing reticulate patches on the right superior chest and back. The patient was born to a healthy mother by spontaneous vaginal delivery without complications. Maternal history was significant only for yeast infection and trichomonas infection diagnosed during her ninth month of pregnancy, for which she received treatment. Otherwise, the mother related being healthy and was not taking any additional medications besides prenatal vitamins. The infant was again seen in follow-up two weeks later at which time the patches were noticeably lighter. She continued to be in good health and gynecomastia was present on exam. Finally, the baby was reevaluated at three months old and all patches on the right arm, superior chest, and superior back had resolved. There was also no further evidence of gynecomastia. This case illustrates a rare occurrence of congenital unilateral nevoid telangiectasia and the interesting finding of gynecomastia as a possible indicator of a hyperestrogenemic state.

Commercial support: None identified.

3234

A study of cutaneous tuberculosis in children

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Background: Cutaneous tuberculosis is still highly prevalent in India and continues to be an important cause of morbidity in children.

Aim: The study the clinical spectrum of pediatric cutaneous tuberculosis and to correlate them with Mantoux reactivity and BCG vaccination status.

Materials and methods: A prospective observational study was conducted on patients attending an outpatient dermatology department of a tertiary care hospital in Delhi to analyze the clinical pattern of cutaneous tuberculosis in paediatric population. A detailed clinical examination, investigations, such as hemogram, serology for HIV, Mantoux test, chest X-ray, cytology, and histopathology were carried out in all children. They were treated with antitubercular therapy (directly observed treatment short course-DOTS regimen), and the clinical response was followed up.

Results: Twenty children (≤16 years) out of a total of 55 patients seen with cutaneous tuberculosis during a 1-year period, were included in this study. Of these, 8 (40%) had lupus vulgaris (LV), 7 (35%) had scrofuloderma (SD), 5 (25%) had lichen scrofulosorum (LS), 3 (15%) had tubercular gumma and 1 (5%) had tuberculosis verrucosa cutis (TBVC). Four (20%) patients concomitantly had more than one type of skin tuberculosis. Affirmative clinicopathologic correlation was observed in all the patients. Regional lymph nodes were involved in seven (35%) patients, 3 (15%) patients had lung involvement while 1 (5%) each had involvement of GIT and bone. No correlation was found between Mantoux reactivity and the extent of disease. Of the 17 (85%) children in whom the data regarding vaccination status was available, 7 (35%) had been vaccinated and 10 (50%) had not. Among the vaccinated group no child had disseminated disease. Three children in the nonvaccinated group had disseminated disease. Family history of tuberculosis was positive in seven (35%) patients. HIV test was negative by ELISA in all patients.

Conclusion: BCG vaccination at birth seems to provide protection against disseminated disease in children. However, BCG coverage still remains poor in migrant population from villages. The main source of childhood cutaneous tuberculosis is infected household contacts and chemoprophylaxis needs to be more widely adapted in Indian pediatric population. Due to immaturity of immune system in children, systemic association is common and warrants a thorough look for underlying focus.

Limitations: Small sample size.

Commercial support: None identified.

3177

A case of pediatric keratosis lichenoides chronica

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A 9-month old girl with neurologic damage from an encephalocele and craniosynostosis presented with a pruritic eruption of edematous, erythematous and hyperkeratotic papules and plaques on her extremities and fine erythematous plaques on her face. Impetiginized atopic dermatitis was suspected, but did not respond to fluticasone cream and oral azithromycin. A biopsy demonstrated marked interface with apoptotic keratinocytes throughout the epidermis, consistent with erythema multiforme. Despite negative HSV stains, the patient was given a 1-month course of acyclovir to treat possible latent HSV. Additional treatments included hydroxyzine, fluocinolone oil, and emollients. Six months later, despite treatment, the patient's eruption persisted; however, the morphology had evolved to hyperkeratotic papules coalescing into retiform plaques on the extremities, with persistence of the facial eruption. Alopecia of the frontal scalp and eyebrows was noted. A second biopsy showed lichenoid dermatitis with patchy parakeratosis, focal epidermal atrophy, and marked colloid bodies. Considering the clinical and histopathologic features, the patient was diagnosed with pediatric keratosis lichenoides chronica (KLC). She was treated with NBUVB therapy biweekly for 4 weeks, without significant improvement, and was lost to follow-up. KLC is a disorder of keratinization that is very rare in children. It is characterized by linear, hyperkeratotic papules that coalesce into retiform plaques, primarily on the dorsal extremities and buttocks. Aside from the age of onset, pediatric KLC is differentiated from adult cases by pruritus, an early facial eruption of fine erythematous plaques, alopecia of the frontal scalp, eyebrows and eyelashes, and familial occurrence. Histologically, KLC features focal parakeratosis, variable atrophy and acanthosis, lichenoid inflammation and interface changes with abundant necrotic keratinocytes. KLC is a chronic condition and few effective treatments have been reported. Anecdotal success with PUVA and/or oral retinoids, UVB phototherapy and tacrolimus ointment has been reported. The diagnosis of KLC is often delayed due to nonspecific initial presentation and tendency for morphologic change over time. Our case highlights the difficulty in diagnosis, with preliminary diagnoses of atopic dermatitis and erythema multiforme prior to the final diagnosis of pediatric KLC, after evolution to the classic clinical and histopathologic features.

Commercial support: None identified.

3088

A review of tinea capitis in a cohort of Asian children

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Background: Tinea capitis is a common dermatologic disorder worldwide but is relatively less common in Singapore. Locally, inflammatory variants of tinea capitis, such as kerion and favus, are more commonly seen. Unfamiliarity of this condition commonly leads to delayed diagnosis, inappropriate or inadequate treatment and poor outcomes (eg, scarring alopecia). We describe our experience with pediatric tinea capitis in a tertiary pediatric hospital in Singapore.

Objectives: We aim to perform a retrospective review of pediatric patients diagnosed with tinea capitis at KK Women's & Children's Hospital and provide more information on the epidemiology, disease presentation, natural history, investigations, treatment and outcomes.

Methods: We performed a retrospective study of children aged 16 years and younger with tinea capitis, as confirmed by positive fungal culture, identified over a 10-year period at our center through microbiological laboratory records. Patients' case records were reviewed and information recorded included demographics, comorbidities, exposure history, clinical presentation, investigation results, treatments and outcomes.

Results: 7 patients were identified (5 females and 2 male patients). The mean age of presentation was 5 years and 7 months (range: 1 year and 9 months to 9 years and 2 months). The mean duration of symptoms before presentation was 5 weeks (range: 1 week to 16 weeks). There was positive contact with animals in 3 patients. No other comorbidities or risk factors were identified. Clinical findings included boggy plaques in 2 patients, multiple papules in 1, erythematous patches in 2, and pustular lesions in 2. Four patients had associated nonscarring alopecia. Fungal culture was positive for Microsporum species in 4 patients and Trichosporon species in 3 patients. All patients were treated with oral antifungals (4 griseofulvin, 1 itraconazole, 2 terbinafine). All patients improved after treatment with oral antifungal therapy with no observed recurrence of disease.

Conclusions: Tinea capitis in children is rare in our predominantly South Asian population. Most cases present with inflammatory lesions (eg, kerion). All patients responded to oral antifungal therapy with minimal sequelae and recurrence.

Commercial support: None identified.

3258

Adalimumab long-term safety/efficacy results for pediatric patients with chronic plaque psoriasis from a phase 3, randomized study

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Introduction: Results of long-term safety and efficacy of TNF-α—inhibitor adalimumab (ADA) are reported for pediatric patients (pts) with severe chronic plaque psoriasis who participated in the 52-week (wk) follow-up period (PerD) of this phase 3 trial (NCT01251614).

Methods: This multisite international study included a 16-wk double-blind treatment PerA, a 36-wk treatment withdrawal PerB, a 16-wk ADA double-blind retreatment PerC, and a 52-week follow-up PerD conducted in parallel to the blinded periods. In PerA, pts were randomized 1:1:1 to ADA 0.8 mg/kg every other week (eow); ADA 0.4 mg/kg eow; or MTX 0.1-0.4 mg/kg weekly. ADA pts received matching MTX placebo; MTX pts received matching ADA placebo. Responders were pts achieving ≥75% improvement in Psoriasis Area Severity Index (PASI75) and Physician's Global Assessment 0 or 1 (PGA 0/1). PerD participants included: (1) nonresponders at end of PerA continued to PerD and received open-label (OL) ADA 0.8; (2) pts maintaining disease control in PerB off treatment continued in PerD off treatment; (3) responders at end of PerA who lost disease control in PerB, and at completion of PerC, continued in PerD on respective blinded PerC treatment (ADA 0.8 if initially randomized to MTX or ADA 0.8; ADA 0.4 if initially randomized to ADA0.4). All pts could switch to OL ADA 0.8 in PerD.

Results: Of 114 enrolled pts, mean age was 13.0 years, range 5-18. All 108 pts who entered PerD received ADA except 8 who entered offtreatment in PerB and maintained disease control off-treatment in Per D. Treatment groups for efficacy are defined by PerA dose/PerD dose: MTX (N = 37)/ADA 0.8 (N = 36); ADA 0.4 (N = 39)/0.4 (N = 36); ADA 0.8 (N = 38)/0.8 (N = 36). PASI75 was achieved at wk16 PerA by 32.4%, 43.6%, 57.9%, respectively; at wk16 PerD by 86.1%, 50.0%, 61.1%, respectively; and at wk52 PerD by 86.1%, 47.2%, 72.2%, respectively. PGA 0/1 was achieved at wk16 PerA by 40.5%, 41.0%, 60.5%, respectively; at wk16 PerD by 77.8%, 38.9%, 50.0%, respectively; and at wk52 PerD by 75.0%, 50.0%, 55.6%, respectively. Treatment-emergent adverse events per 100 pt years in PerD by initial randomized treatment (MTX, ADA 0.4, ADA 0.8) were any event 463.0, 362.8, 387.2; serious event 3.2, 4.0, 9.8. There were no serious infections.

Conclusion: In this pediatric population, efficacy was maintained through 52 weeks of ADA treatment. Overall safety profile was similar for both ADA doses. No malignancies and no deaths related to study drug were reported.

AbbVie Inc participated in the study design; study research; collection, analysis and interpretation of data; and writing, reviewing and approving of this publication. All authors had access to the data, and participated in the development and review.

3373

Body dysmorphic disorder and suicidal ideation in a 15-year-old girl who witnessed sexual abuse

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A 15-year-old female patient attended our psychodermatology clinic with body dysmorphic disorder, acne and a scar on her abdomen. During the consultation the patient complained, her skin conditions had an enormously negative impact on her life. She avoided social activities and isolated herself at home most of the time. She was diagnosed with having depression and social anxiety disorder. She was also suicidal. Her acne was treated with topical agents and a referral was made to child mental health department. During the consultation with the psychiatrist became clear that the patient had witnessed sexual abuse four years previously. At this time her body dysmorphic disorder symptoms started. She was commenced on Sertraline and referred to a counsellor for cognitive behavioral therapy. Her suicidal ideation stopped and her depression settled with this and her dermatologic treatments. The patient was referred as well to plastic surgeons for correction of her abdominal scar. Research to date has indicated that childhood abuse in general is associated with psychiatric disorders and suicidal ideations in later life. Research has examined the unique association between body dysmorphic disorder and suicidal ideation on one hand and childhood sexual abuse on the other. A study examining all form of child abuse in body dysmorphic disorder patients found that 28.0% of participants (75 subjects) reported sexual abuse. Even more interesting was the severity of sexual abuse was significantly associated with current body dysmorphic disorder severity. Our case emphasizes the need for dermatology health care professionals to ask about sexual abuse in childhood/early life, especially when a patient present with body dysmorphic disorder and suicidal ideation. Dermatologists often shy away of checking about sexual abuse and suicidal ideation in their patients. But body dysmorphic disorder and social anxiety disorder are more commonly associated with sexual abuse than dermatologists may realize.

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Bullous erythema ab igne in a bone marrow transplant patient

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Erythema ab igne (EAI) is a dermatosis characterized by localized reticulated erythema and hyperpigmentation resulting from chronic exposure to infrared radiation that induces injury to the epidermis and superficial vascular plexus. The condition is typically noted with frequent use of heating pads or chronic exposure to heat sources. The bullous form is less common and is a result of excessive thermal radiation resulting in an acute thermal burn. We present the case of a 17-year-old Nigerian female with a history of sickle cell disease complicated by numerous vasoocclusive crises who underwent recent allogeneic stem cell transplantation. She had a long history of back pain relating to her vasoocclusive crises and frequently used a heating pad for pain relief. Dermatology was consulted for a new bullous eruption that developed day 16 posttransplant. She was febrile for 48 hours prior to developing eruption and was being empirically treated for possible fungal pneumonia. Given recent transplant, the differential diagnosis of her bullous eruption included life-threatening etiologies, such as deep fungal infection and graft-versus-host disease. On exam, a reticulated hyperpigmented patch was noted on the left lower back and flank with exquisitely tender bullae localized to the areas of hyperpigmentation. While discussing the symptoms with the patient's mother, she confirmed frequent use of a heating pad at the site of the eruption noting the reticulated patch was chronic and preceded transplant. Given the history and examination, a diagnosis of bullous EAI was made. The heating pad was discontinued and topical emollients were applied. The bullae resolved three days after discontinuation of the heating pad, though the reticulated hyperpigmentation persisted. This case illustrates a common condition with an unusual presentation in a complicated patient. Pediatric patients with chronic pain often use heating pads and EAI has long been recognized as a complication of heating pad use. Bullous transformation related to thermal burns may be underrecognized in pediatric patients with chronic pain. The majority of bullous eruptions in a posttransplant patient are emergent, specifically in the case of graft-versus-host disease or deep fungal infection. Bullous EAI, a much less dire entity, should be considered in the differential diagnosis of a bullous eruption in a chronically ill child.

Commercial support: None identified.

2349

WITHDRAWN

3425

Case report: Successful treatment of a huge-mixed hemangioma on the forehead using pulse dye laser combined topical timolol maleate 0.5% and intralesional steroid injection

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Infantile hemangioma (IH) is the most common tumor in infants, approximately more than 40% were located on the face. Many new treatments have been used such as pulse dye laser (PDL), topical β-blocker, imiquimod, topical steroid. However, the effect of PDL in the treatment of hemangioma is just on the superficial vascular as well as topical timolol maleate 0.5% has been proved as an effective treatment for superficial hemangioma. Besides, treatments for huge, deep or mixed hemangioma required systemic propranolol, steroid and also leave some side effects for the children. This is a case report about a huge-mixed hemangioma on the forehead that is treated successfully using PDL combined topical timolol maleate 0.5% and intralesional steroid injection. A 9-month-old girl has a huge-mixed hemangioma on the forehead, which grew rapidly from a small lightly red macule to ten times size within first few month of age. Examination showed mixed hemangioma with 5cm in diameter and 2cm in depth. She was treated with PDL at 13.5 J/cm^2 – 1.5 ms – 7 mm spot size combined injected intralesional 1 mg/0.25 ml dexamethasone phosphate mixed with 40 mg/1 ml triamcinolone acetonide. She was maintaining treated with topical timolol maleate 0.5% solution twice a day right after that. After 6 months she was continued treated some telangiectasias with PDL for the second time at 12J/cm^2 – 1.5 ms – 7 mm spot size and maintaining topical timolol 0.5% solution. One independent assessor (blinded to patient allocation) evaluated photographs after each month compared to baseline using 100-mm visual analog scale (VAS) (from -5 to +5) in lesion size, thickness and color. An investigator global assessment scale (IGA) (0 to 3) will be used to evaluate any evidence of complications or adverse events (-3 to +3). Parent was asked to rate the side effects and improvement in size (0 to 3) at the end of treatment. After 5 months, IH nearly disappeared with lightly red color, 2 cm in diameter and 0.2 cm in size, average VAS was +4 and average IGA was 0. After 8 months, IH was just a lightly pink macule, 1.5 cm in diameter, average VAS was +4.7, average IGA was 0, and parent rated 0 for side effects and 3 for improvement in size. This is the huge-mixed hemangioma that successfully treated using combination of three methods: PDL, intralesional steroid injection and topical timolol maleate 0.5%.

Commercial support: None identified.

2964

Clinical and epidemiologic characteristics of childhood vitiligo: A study of 701 patients from Brazil

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Background: Vitiligo is the most common disorder of skin pigmentation. Approximately 0.5% to 2% of the world population is affected by the disease, and 25% of cases begin before 10 years of age. Although prevalent, there are few Brazilian studies on the characterization of childhood vitiligo.

Objective: To evaluate clinical and epidemiological characteristics of childhood vitiligo.

Methods: Descriptive, retrospective study conducted by obtaining data records of patients under the age of 18, in which vitiligo was diagnosed until 15 years of age at Instituto de Dermatologia Prof Rubem David Azulay and at private clinics in São Paulo and in Rio de Janeiro. Variables such gender, clinical form, age of onset, location of initial lesions, autoimmune associated diseases, emotional factors, autoantibodies, Koebner phenomenon, family and personal medical history, presence of halo nevus and stability of the lesions, were evaluated. Descriptive analysis of the data was performed, expressed by the frequency, the mean and standard deviation in the total sample, and by types and subtypes of childhood vitiligo. It was also performed to compare the clinical and epidemiological variables between two types of vitiligo (segmental and nonsegmental).

Results: Predominance of females (62%). The most common subtype was generalized vitiligo (53.8%). The average age of disease onset was 5.9 years. The most affected initial site was head/neck (44.22%). The Koebner phenomenon was present in 38.2%, emotional triggering factors were present in 67.0% of the patients, halo nevus was present in 17.4% and associated autoimmune disease in 6.5% of the patients. Family history of vitiligo was observed in 16.9% of the patients and stability was reported by 20.1% of patients. The presence of positive family history did not significantly influence the age of onset. We found a significant difference between segmental vitiligo and non-segmental vitiligo regarding the age of onset, Koebner phenomenon, hypothyroidism, anti-TPO antibodies, family history of psoriasis and halo nevus. However, there was no significant difference regarding the stability of the lesions and the presence of emotional triggering factors between the 2 groups.

Conclusion: Childhood vitiligo has its own characteristics. Vitiligo different subtypes have distinct characteristics. Our study presents a great number of patients, helping to elucidate the peculiarities of vitiligo with childhood onset.

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Giant congenital juvenile xanthogranuloma clinically mimicking hematoma

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Background: Juvenile xanthogranuloma (JXG) is a benign, self-limited disease of infants and children occurring early in life with 20% present at birth. They are firm papules or nodules measuring 5 mm to 2 cm. Early JXGs can be more erythematous, but become increasingly yellow over time. JXGs usually run a benign course with regression by 3-6 years old with potential pigmentary alteration or atrophic scarring upon resolution. Extracutaneous involvement can occur, most commonly in the eye, with children having multiple lesions being at greatest risk. Giant JXGs are a rare variant greater than 2 cm in diameter. Unlike more common JXGs, the giant variant is typically present at birth, at an increased risk of ulceration, and may only partially involute over time.

Observation: A 6-week-old male presented with a firm swelling of his right vertex scalp measuring 3 cm x 2 cm. His labor was difficult, given that he was 10 pounds, and after birth, his entire scalp was red and swollen. Over the subsequent 2 weeks, the redness subsided except for one spot that continued to become larger in size. Their pediatrician, an outside dermatologist, and a neurologist evaluated the lesion and ordered an ultrasound, which showed a soft tissue swelling with "fluid" per the mother, but no diagnosis was given. Exam revealed a non-tender nodule stable in size since 2 weeks old with overlying alopecia. Within the nodule, smaller papules were noted with a yellowish hue. A repeat ultrasound was performed which showed a hyperechoic within the dermal layer and a hypoechoic collection deep to the dermis, but above the periosteum. Findings were most consistent with a scalp hematoma, specifically a caput secundum. Given that the history and exam findings were atypical for a hematoma, a biopsy was performed which showed a nodular infiltrate of histiocytes consistent with JXG. Evaluation by ophthalmology revealed no ocular involvement.

Comment: Giant congenital JXGs are a rare variant of JXGs that can be mistaken for other infantile swellings and tumors including hematomas, infantile hemangiomas, Langerhans cell histiocytosis and other soft tissue neoplasms. Keep this diagnosis in mind when evaluating large congenital tumors in the neonatal period. A "watch and see" approach is still recommended as giant congenital JXGs do spontaneously regress and are not believed to be independently associated with systemic involvement.

Commercial support: None identified.

3201

Harlequin ichthyosis baby still alive on isotretinoin for five months: A case report

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Harlequin fetus (HI) is a rare and the most severe form of the congenital ichthyosis with an autosomal recessive inheritance. Incidence of the disease is nearly 1 in 3,000,000 live births. The vast majority of affected individuals are homozygous for mutations in the ABCA12 gene, which cause a deficiency of the epidermal lipid transporter, resulting in hyperkeratosis and abnormal barrier function. Although HI infants have historically have high mortality in the perinatal period due to their profound epidermal compromise, sepsis and respiratory failure, the prognosis of HI infants has vastly improved over the past many years due to advances in neonatal intensive care and oral retinoid therapy. We report a case of harlequin baby born to a consanguineous mother (gravida 7) at 36 weeks of pregnancy, by caesarean section, with severe thick fissured scales, severe ectropion, eclabium and digital contractures. Mother had a similar baby in her 4th pregnancy who died 3 days after delivery. However, this baby was admitted in neonatal intensive care unit (NICU) and treated with oral isotretinoin (1 mg/kg per day). Presently baby is 5 months old, doing well and on regular follow-up.

Commercial support: None identified.

3655

Hemimaxillary enlargement, asymmetry of the face, tooth abnormalities, and skin findings (HATS): A case report

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Background: Hemimaxillary enlargement, asymmetry of the face, tooth abnormalities, and skin findings (HATS) is a nonprogressive developmental disorder characterized by unilateral abnormalities of the maxillary bone, teeth, gums, and skin. Also known as segmental odontomaxillary dysplasia, the hallmark of this syndrome is the constellation of oral abnormalities, including partial anodontia, abnormal tooth spacing, delayed tooth eruption, and gingival hyperplasia. Up to 48% of patients with HATS syndrome have abnormalities of the overlying facial skin.

Case report: We report a 12 year-old girl who presented with facial asymmetry and an enlarging plaque on the left face from zygoma to mandible. She was born with a pink, slightly raised lesion on the cheek, which began to darken and develop hair at age one. At age six, a tumor (and one tooth) of her left maxilla were excised. The skin lesion remained indistinctly bordered, light brown, and covered with pale downy hair until puberty, when the hair became dark, terminal hair and her facial asymmetry worsened. On examination, the patient had an asymmetric prominence of the left cheek and fullness of the left upper lip. There was a caramel brown hyperpigmented plaque with well-defined borders extending from the left nasal sidewall, medial canthus, and lower eyelid to the preauricular region and jawline with overlying dark brown hairs. There was left-sided gingival hypertrophy and several upper left teeth were absent. There were no abnormalities noted on the right. Biopsy of the plaque showed hyperpigmentation and hypertrichosis. Prior maxillary tumor biopsy was consistent with fibrous dysplasia. Dental x-rays showed absence of first premolar, delayed eruption of second premolar, and slight left-sided microdontia.

Discussion: The acronym HATS, coined by Welsch and Stein in 2004, captures the wide range of findings, particularly the cutaneous abnormalities, associated with segmental odontomaxillary dysplasia. Common skin findings include hypertrichosis, lip hypopigmentation, discontinuity of the vermilion border, and facial erythema. Skin biopsies often are described as consistent with a Becker nevus, although there are clinical dissimilarities. The diagnosis is based on clinical presentation, dental radiographic findings, and histology of the affected maxillary bone. The main goal of treatment is the restoration of dental function. Associated hypertrichosis and hyperpigmentation are amenable to laser therapy.

Commercial support: None identified.

3915

Herpes zoster in an immunocompetent varicella vaccinated child

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An 18-month old boy presented with a painful rash lasting two days. The patient was born at term after a normal pregnancy, was otherwise healthy, and received his varicella vaccination at 12 months. Upon examination, a zosteriform skin eruption was present at dermatomes L2, L3, L4 on the left. The eruption was erythematous, patchy, and studded with vesicles. The child was afebrile with no other dermatologic findings. A vesicle was unroofed and swabbed for varicella zoster virus (VZV) PCR. The patient was prescribed acyclovir and the lesions healed after two weeks. The child's mother was pregnant, but had a history of chickenpox and developed no infection over the following eight weeks. There was no family history of compromised immunity. Subsequently, VZV was detected in the specimen by PCR. Given that the patient's mother was pregnant and the patient had many unvaccinated contacts at daycare, a strain-specific differentiation was performed and the VZV was identified as the Oka vaccine strain. Patients vaccinated against VZV to prevent chickenpox can suffer rare complications, including vaccine-related zoster (shingles). The vaccine is effective in preventing chickenpox, but the medical community should be aware that vaccination could lead to shingles just as natural infection with wild-type VZV. The administration of VZV vaccine is associated with substantial reduction in chickenpox-related morbidity. Considering the vast number of vaccines administered worldwide, short-term side effects of vaccination are relatively uncommon. Late-onset reactions such as zoster are even rarer. We report one such complication: vaccine-related herpes zoster dermatitis. Among VZV vaccine recipients, shingles has been reported but is uncommon. Estimates propose a frequency of 0.18 cases per 1000 vaccine patient-years. One study found the incidence of zoster (from both vaccine-strain and wild-type) to be approximately 48 cases per 100,000 person-years in vaccinated children, and 250 cases per 100,000 person-years in unvaccinated children (from wild-type only). Among those vaccinated in the latter study, not all zoster occurrences were shown to be caused by vaccine-strain VZV. Of the postvaccination zosteriform eruptions, 50-85% were associated with vaccine-strain VZV; the remainder was wild-type VZV. This suggests vaccinees may become infected with wild-type virus, display minimal clinical manifestations, and develop shingles. Clinical characteristics of vaccine-related zoster among children are similar to those of wild-type zoster. Using VZV vaccine to prevent chickenpox considerably reduces morbidity from wild-type VZV infection. However, the vaccine strain establishes neuronal latency; hence, reactivation of vaccine virus in and transmission from healthy and immunocompromised individuals is possible. Consequently, vaccinated patients with subsequent zoster should be considered contagious. Appropriate barrier precautions are warranted since both vaccine-strain and wild-type VZV may cause zoster. In cases with a history of VZV vaccination, physicians should document the presence of VZV by submitting samples for PCR. Additionally, the requisition should note that vaccine-strain VZV may be involved. In such cases, local health departments should be consulted, since timely differentiation of vaccine or wild type disease is clinically useful in situations with pregnant or immunocompromised contacts, where postexposure treatment may be indicated.

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Hospitalization of a 9-month-old boy due to multiple arthropod bites, likely caused by the Hobo spider (*Tegenaria agrestis*)

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Hobo spiders (*Tegenaria agrestis*) are a type of spider that has been associated with dermonecrotic injuries in the Pacific Northwest. In North America, they are distributed from Oregon to British Colombia and east to Montana and Colorado. After the bite, a small area of induration occurs within 30 minutes and is followed by expanding erythema of up to 5-15 cm, with blister formation at 15-35 hours. An eschar may develop with underlying necrosis and systemic symptoms appear within 10 hours of the bite. We report a case of a previously healthy 9-month-old boy who was admitted to the hospital unresponsive, hypoglycemic, hypokalemic, cyanotic, and in rhabdomyolysis as a consequence of four arthropod bites, identified by the patient's father as hobo spider bites.

Commercial support: None identified.

3951

Infantile hemangiomas: Analysis of untreated lesions to establish early systemic treatment criteria

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Infantile hemangioma (IH) is the most common tumor of newborns. This vascular birthmark affects 10% of infants, with characteristic initial rapid proliferation followed by gradual spontaneous involution over 10 years. While the majority of IH resolve without sequelae, a subset are associated with significant morbidities, including disfigurement, painful ulceration, visual impairment and airway compromise. The 2014 FDA-approval of propranolol (Hemangeol; Pierre Fabre) has transformed medical management of IH. Data supporting the tolerability, safety and efficacy of propranolol has endorsed its use as first-line treatment, replacing oral corticosteroids. Only a subset of IH require systemic treatment. For these infants, early medical intervention may be more effective than delaying treatment until after significant growth and associated complications occur. So, there is a need for additional data to define the best candidates for early initiation of treatment. This retrospective review of untreated IH will illustrate the unfavorable outcomes that occurred as a result of inadequate or delayed medical management, and assess the relative risk of several parameters in predicting serious sequelae, including skin type, location, topography (concavity vs. convexity), surface area, per cent superficial vs. deep distribution; cliff-drop vs. sessile border; surface change, telangiectasia, halo pallor and evidence of erosion.

Commercial support: None identified.

3588

Incontinentia pigmenti: A case report and discussion

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Background: Incontinentia pigmenti (IP) is an X-linked dominant, multisystem disease that presents shortly after birth and is typically antenatally lethal in males. It is due to a mutation in the IKBKG or NEMO gene, whose normal function is to protect against apoptosis. The disease progresses through four cutaneous stages that include vesicular, verrucous, hyperpigmented and hypopigmented skin findings. The linear and whorled, Blaschkoid cutaneous appearance is secondary to mosaicism resulting from randomized X chromosome inactivation. The most common sites of involvement in IP are the hair, skin, nails, teeth, eyes and central nervous system.

Case description: A full term, 1-day-old neonate, presented via an inpatient consult for an evolving rash and low grade temperature. The patient was being treated in the NICU with several antimicrobial medications. On physical examination, there were extensive areas of erythematous papules and vesicles, coalescing into plaques in a whorled, linear pattern. The pathology from a punch biopsy of one of the lesions revealed eosinophilic, spongiotic dermatitis consistent with IP. Inpatient ophthalmologic examination showed possible retinal involvement prompting an MRI of the brain which showed numerous areas of restricted diffusion, likely secondary to cytotoxic edema, compatible with IP. Genetic confirmation was done at follow up, which demonstrated a heterozygous, partial deletion of the NEMO gene. At the four-month follow up visit, the patient's skin lesions showed an overlap of the first three stages of disease. Repeat eye exam was normal, and the patient continued to be seizure free. Patchy areas of alopecia were present. Supportive care of the intermittently flaring, cutaneous lesions was continued with the use of emollients and topical steroids.

Conclusion: IP is a rare, genetic disorder, with only 900 to 1200 cases having ever been reported in the literature. While the cutaneous findings can be very distinct, IP can present with varying levels of severity, and can at times be less recognizable, especially to nondermatologist physicians. Increased awareness of this condition will lead to a minimization of unnecessary medical intervention, as well as early recognition and counseling regarding IP's genetic implications and extracutaneous manifestations.

Commercial support: None identified.

3175

Juvenile myelomonocytic leukemia presenting with leukemia cutis in a child with multiple juvenile xanthogranulomas

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Introduction: Juvenile xanthogranuloma (JXG), a common form of non-Langerhans cell histiocytosis, is a generally benign, self-limiting disease of infants and children. They often present with lesions in the skin, although extracutaneous manifestation may occasionally occur. There is an important association of multiple JXG with the development of childhood leukemia, most commonly juvenile myelomonocytic leukemia (JMML).

Case report: We report a case of a 15-month-old Chinese boy who presented together with his monozygotic twin, for multiple JXG. The lesions appeared in both twins at 6 months of age as yellowish-brown firm round papules and nodules located mainly on the head and neck region. They were otherwise well with no systemic complaints. The parents declined biopsy then and opted for continued surveillance. The JXG regressed spontaneously after 2 years. The patient represented at 4 years old with Sweet syndrome–like rash and 1 month history of fever. Full blood count showed leukocytosis with marked neutrophilia and associated anemia. Bone marrow biopsy showed hypercellular marrow with myeloid hyperplasia, left shift maturation. Peripheral blood revealed blasts and monocytosis. Gene mutation analysis revealed PTPN11 gene mutation and trisomy 8. Skin biopsy showed atypical dermal inflammatory cells with leukemic infiltration. These findings confirmed the diagnosis of JMML with leukemic cutis. The patient underwent uneventful matched-sibling donor cord blood transplantation with successful engraftment. The leukemia relapsed 1 year later the patient was eventually underwent a definitive haploidentical bone marrow transplant.

Discussion: JMML is an uncommon hematologic malignancy in young children, accounting for less than 2% of childhood leukemia. It often presents with lymphadenopathy, anemia/thrombocytopenia, hepatosplenomegaly and skin involvement. Somatic PTPN11 mutations are the most frequent molecular lesions in JMML—35% of nonsyndromic JMML cases. There is definite association between multiple JXGs and JMML. A regular surveillance full blood count is key to detect early disease. Incidence of skin lesions in JMML has been reported to be 36-48% with most presenting as nonspecific reactive maculopapular rash, also known as leukemids. An annual review even after regression of skin lesions is necessary to follow up on recurrence of JXG, and/or the development of associated JMML that can rarely present as leukemic cutis, as described in our case.

Commercial support: None identified.

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Juvenile xanthogranuloma. Report of two uncommon cases

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Juvenile xanthogranuloma (JXG) is the most common non-Langerhans histiocytic disorder. It may presents as single or multiple yellowish papules or nodules, predominantly located on the head and neck, but it may also involve other tissues. JXG usually appears during the first year of life, and the spontaneous regression of the cutaneous lesions is frequent. We report two special cases of JXG. The first one is a 7 months of age girl who consulted for presenting multiple well-demarcated nodules affecting face, scalp and extremities that reached one and a half centimeters larger diameter. It began to regress spontaneously without treatment after 3 months, which results in conspicuous scars. The second case is a 6 months girl that showed a mass in the posterior cervical region from the third month of life measured 35 x 25 mm. It was composed of small yellowish nodules of rubbery feel. The pathology sample showed a proliferation of histiocytes with foamy cytoplasm and multinucleated Touton-type giant cells with eosinophils, lymphocytes and plasma cells in the inflammatory infiltrate. Immunohistochemical stains were positive for CD68 and negative for CD1a and S100, establishing the diagnosis of JXG. In both cases, additional studies (ophthalmologic examination, abdominal ultrasound and blood tests) ruled out systemic involvement. The macronodular and giant JXG variants are rare forms of presentation, being necessary an histological study for the diagnosis in doubtful cases. Management should be conservative, because of the benign clinical course and spontaneous regression of lesions.

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3718

Langerhans cell histiocytosis mimicking lichen nitidus with bone involvement

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Langerhans cell histiocytosis is a clonal proliferation of immature myeloid dendritic cells precursors with a wide clinical spectrum: from exclusively cutaneous involvement to multisystem illness, which could be life-threatening. We report the case of a 6-month-old Hispanic boy, previously healthy, with a history of 4 months of widespread pruritic hypopigmented papules mimicking lichen nitidus. Pregnancy and childbirth presented no complications. Both parents were healthy and unrelated. The skin biopsy showed a pagetoid spread and dermal infiltrate of large cells, with reniform nuclei and abundant eosinophilic cytoplasm, which exhibited strong immunoreactivity for CD1a, CD207 (langerin) and S-100 protein. The radiographic skeletal survey and skull series revealed 4 osteolytic lesions: right posterior parietal bone (25 mm); left frontal bone (10 mm); left humerus (20 mm); and right femur (50 mm). A brain magnetic resonance imaging ruled out pituitary gland involvement. Other complementary studies (full blood count; coagulation; liver and kidney function; urine analysis; chest radiography, and abdominal ultrasound) were carried out with normal results. The final diagnosis was multisystem nonrisk-organ LCH with cutaneous and multiple bone involvement. The patient was treated according to the LCH-III protocol with oral prednisone and intravenous vinblastine and, at the sixth week of treatment, the patient had achieved complete remission. To date, widespread hypopigmented papules as a type of cutaneous LCH has been related exclusively with skin-only and multisystem nonrisk-organ LCH (skin and bone). With these several cases documented, we suggest early biopsy of hypopigmented rash in children.

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2896

3918

Linear epidermal nevus syndrome

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Epidermal nevi are cutaneous hamartomas that can be isolated cutaneous lesions or may be associated with a variety of underlying syndromes, especially if it is of a linear type. They are of ectodermal origin and hence can be associated with other neurocutaneous abnormalities. Some of these syndromes are well defined, which include Schimmelpenning syndrome, phacomatosis pigmentokeratotica and Becker nevus syndrome, whilst other syndromes involving epidermal nevi remain less well defined. We present a female child referred to the dermatology service at 7 years of age with a linear epidermal nevus on the right anterior chest, right axilla, right arm and back. On that occasion no other symptoms or signs were noted related to an underlying syndrome. On annual follow up it was noticed when she was 8 years old that she had a slight scoliosis and was referred to the orthopedic department for an opinion. At this time, no other neurocutaneous abnormalities were found. Over the next 3 years, when under review in both dermatology and orthopedics clinics, there was only slight progression in her scoliosis until she was 12 years old. During this time her linear epidermal nevus did not change and topical therapy, such as Dermol 500, were used to control axillary odor. When she was 12 years old, she had a dramatic increase in the curvature of her spine. It was noted that Cobb's angle, which had been stable at approximately 24 degrees, changed rapidly over a 3-month period to 43 degrees, resulting in a rapid increase in her scoliosis. She was subsequently referred to a specialist spinal unit who initially treated her with a thoracic spine brace and subsequently she required operative correction for the scoliosis to allow normal functioning. Our patient demonstrates that the dermatologist must be vigilant in a patient presenting with an epidermal nevus for any associated signs of a neurocutaneous abnormality, given the ectodermal origin. It is also important to note that the associated signs may not be evident when a patient is first seen. Indeed, our patient's presentation shows the rapidity of onset that is possible of such associated symptoms. This underlines the need to be vigilant over time, so careful follow up of a patient with a linear epidermal nevus is essential.

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Lupus erythematosus profundus in children, a case series

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Lupus erythematosus profundus (LEP), also known as lupus panniculitis is a variant of lupus erythematosus cutaneous (LEC) that affects subcutaneous tissue. LEP occurs in 1% to 3% of patients with LEC, and it may be a single manifestation of the disease or it can be associated to discoid lupus erythematosus (DLE) or systemic lupus (SLE). Overall, the average age of presentation ranges from 30 to 60, and the disease is more common in women. It is a rare finding in children, with only 19 fully reported prior cases in the English literature. We performed a multicentric retrospective study in three public dermatology reference centers in Mexico City, where we accomplished a research in three databases from April 1993 to July 2015 for the histopathologic reports compatible with LEP. Subsequently, we reviewed the medical files. In total, we found 10 children under 18 years with histopathologic and clinical diagnosis of LEP. The average age at presentation was 9 years, with a predilection for the female gender (80%). The most common involved areas were the cheeks, nose, zygomatic region and scalp. None of them presented association with LED or LES at their time of presentation, nor systemic symptoms. The histopathologic features were usually lobular or mixed panniculitis with lymphocytes and plasma cell rich inflammatory infiltrate. Other common findings were the formation of lymphoid follicles and hyaline fat necrosis. Four cases were treated with hydroxychloroquine at 4 mg per kilogram and a single intralesional triamcinolone injection (10 mg). This four cases presented remission of the lesions after two months of treatment. None of them progressed to SLE during the follow-up period (1-7 years). For the rest of the patients, there are limited data during the follow-up in the medical files. The role of laboratory testing is not well established in diagnosing LEP. In our patients, laboratory tests performed included blood counts, metabolic profiles, ANA, anti-dsDNA and other autoimmune studies, which were not significant. LEP is rare in children and is a difficult diagnosis to make without the use of histopathology. Treatment with antimalarials has been shown to be effective. It is still unknown what is the risk of these patients for developing future SLE. The major adverse outcome associated with the disease is subcutaneous atrophy once the inflammation resolves.

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3574

New growth within a nevus sebaceous in a 10-year-old girl

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Nevus sebaceous (NS) presents at birth or early childhood as a yellowish, hairless plaque on the scalp, face, or neck and can develop both benign and, less frequently, malignant neoplasms of both epidermal and adnexal origins. A 10-year-old girl presented for evaluation of an NS on her right cheek, present since birth. Within the previous few months, the patient's mother noticed a new growth within the lesion and one episode of bleeding. The new lesion was not painful or pruritic. The patient had no known family history of skin cancer. Examination revealed 4 cm x 1 cm orange-yellow to slightly pink Blaschkoid plaque with prominent plugged comedones containing a 4 mm hyperkeratotic exophytic papule. A punch biopsy performed to rule out malignant transformation revealed verrucous epidermal hyperplasia with parakeratosis and hypergranulosis along with prominent sebaceous glands, consistent with a verruca vulgaris growing within a nevus sebaceous. Koilocytes were not observed. The lesion was human papillomavirus (HPV) (v/11/16/18/31/33 negative. The most frequently reported benign neoplasms associated with NS are trichoblastoma, a tumor of hair follicle origins, and syringocystadenoma papilliferum (SCAP), a tumor of sweat gland origin, most likely apocrine. Basal cell carcinoma (BCC) is thought to be the most frequent malignant tumor occurring in NS, but squamous cell, sebaceous, and apocrine carcinomas have also been reported. Multiple neoplasms can occur within the same lesion, but the coexistence of more than three lesions is rare. Viral warts have been noted within NS, in 2.3% to 11.6% of cases, including the HPV-induced trichilemmoma. Although warts are uncommon in NS, the presence of HPV DNA may be more common than previously thought. HPV could represent either a commensal infection or an essential factor in the pathogenesis of NS. It will certainly be interesting to see if there is a change in the prevalence of NS with the advent of prophylactic HPV vaccination for the prevention of infection by high-risk HPV genotypes. Although our patient's HPV type was not typeable high-risk, and malignant transformation is thankfully rare, it does raise the question of perhaps considering early recommendation of HPV vaccine in this particular population.

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2535

Naxos/Carvajal disease in an 11-year-old Brazilian girl

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Naxos disease and Carvajal syndrome are rare genodermatoses that combines palmoplantar keratoderma, woolly hair and cardiomyopathy. We report a case of an 11-year-old girl who presented palmoplantar keratoderma and woolly hair, associated with severe biventricular dilated cardiomyopathy of early onset. In Naxos disease, patients are born with woolly hair and develop palmoplantar keratoderma during the first year of life, evolving in adolescence with arrhythmogenic right ventricular dysplasia. Carvajal syndrome is a variant with the same cutaneous findings, but left ventricular involvement and clinical overlap with dilated cardiomyopathy, leading to early morbidity. An 11-year-old female patient was admitted to the Cardiology Department of our hospital with a 15-day history of progressive dyspnea that rapidly evolved into congestive cardiac failure. She presented with signs of poor perfusion, drawing, and tachypnea. Dermatologic examination revealed linear and focal hyperkeratosis on her palms and soles, and thin, pale, and curly hair. Chest X-ray showed cardiomegaly and signs of congestive heart failure. Echocardiography showed dilated cardiomyopathy with severe biventricular systolic dysfunction (ejection fraction of 24%). The girl received vasoactive drugs and was admitted to the intensive care unit. Due to the severity of the condition, she was listed for cardiac transplantation. Her parents were not consanguineous and there was no other affected member in the family. According to these findings and although it was not possible to perform genetic testing, the diagnosis of Naxos disease/Carvajal syndrome was considered, once she had the characteristic triad of wooly hair, palmoplantar keratoderma and cardiomyopathy. In Naxos disease a mutation of the plakoglobin gene on 17q21 chromosome is observed, while in Carvajal syndrome the defect is in desmoplakin gene on chromosome 6p42. Both plakoglobin and desmoplakin are part of the desmosomal structure, responsible for cell adhesion and resistance of skin and myocardial cells. The presentation of these syndromes varies according to the gene mutation and may be seen as syncope, tachycardia, heart failure or sudden death. For cases with woolly hair and palmoplantar keratoderma, the dermatologist should provide a cardiac assessment, considering Naxos/Carvajal disease. When an early diagnosis is made, an increase in life expectancy may be provided by suitable treatment of the heart failure and arrhythmias.

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3733

Otologic involvement in lamellar ichthyosis: An easily overlooked entity

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Several forms of inherited congenital ichthyosis are called "nonsyndromic ichthyosis" because they lack primary involvement of any tissue other than the epidermis. However, these conditions can indeed be viewed as being syndromic as they affect nonkeratinized tissues. Perhaps the most notable example is ocular damage, such as exposure keratitis, that occurs as a consequence of ectropion. Other less recognized sequelae of inherited ichthyoses, such as conductive hearing loss, may occur as well. We describe a case of identical twin boys with congenital lamellar ichthyosis (TGM1 loss-of-function; OMIM 242300) who undergo disimpaction and debridement of their external ear canals under general anesthesia every 6 months. Both have conductive hearing loss due to impacted concretions of cerumen and keratinous debris within the external ear canal. Histopathologic examination of the debrided material shows dense spherules composed of cerumen, desquamated corneocytes with cholesterol clefts, and minute fragments of vellus hairs. The histopathologic diagnosis is secondary keratosis obturans. The most likely differential diagnosis, cholesteatoma of the external auditory canal (CEAC), was ruled out due to absence of osteonecrosis. The dermatologic management of children with lamellar ichthyosis may overshadow other less prominent symptoms. To our knowledge, only one study, Huang et al, has examined otologic manifestations of ichthyosis. Their study was based on 135 surveys of patients with various types of congenital ichthyoses, 30% of whom reported having lamellar ichthyosis. Approximately 80% of respondents reported ear pruritus, 66% reported difficulty hearing, and 29% reported frequent otalgia. 28% had abnormal hearing test results, and 16% had used hearing aids. Importantly, many of the patients who self-reported hearing trouble had never been examined by an audiologist. With this in mind, an ear and hearing examination (with appropriate referral for otolaryngologic and audiologic evaluations) should be a part of the periodic evaluation of patients with lamellar ichthyosis. Additionally, young patients with keratosis obturans may benefit from adjunctive or alternative treatments, such as cerumenolytics, as a way to maintain patent ear canals and to avoid periodic debridement under general anesthesia.

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Parents' behaviors, motivations, and barriers to American Academy of Dermatology sun protection recommendations for Hispanic and black children ages 4-12

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Background: Excessive exposure to ultraviolet radiation during childhood and adolescence increases the chance of developing skin cancer in adulthood. Sun safe behaviors early in life may decrease the risk of future skin cancers. Although incidence rates for skin cancers are lower in Hispanics and blacks compared to white non-Hispanics, skin cancers in these minority populations have a poor prognosis because of delayed diagnosis and advanced stage presentations. At this time, there are few studies investigating the sun safety behaviors of Hispanic and black children. The primary objective of this study is to identify the current behaviors, motivations, and barriers to American Academy of Dermatology (AAD) sun protection recommendations in Hispanic and black parents. The results of this study will inform the development of an evidenced-based, interventional approach to promote healthy behaviors early in childhood.

Methods: Starting July 2015, parents with children between the ages 4-12 were recruited from UHealth general pediatric outpatient clinic and were asked to complete a 52-question survey available in English or Spanish. Survey collection will continue until 200 survey responses have been collected and will be analyzed using SPSS software. Correlations with demographic factors will be sought.

Results: A total of 54 responses were collected during the first two weeks of survey administration (93% response rate). The median age of the children was 8.61 years (SD = 2.716), most of whom were white Hispanic 38.9% (n = 21) and black 37% (n = 20). Preliminary results demonstrate a significant difference between parent education level and overall knowledge of sun protection and skin cancer ($P = .009$). Differences between parent education level and consistency of sun safe behaviors have not been shown to be significant ($P = .466$). Hispanic parents were found to use sunscreen on their children more often than black parents ($P = .001$). Final results from the analysis of the questionnaires will be presented and discussed.

Conclusion: Dermatologists and pediatricians will benefit from this study by better understanding the behaviors, motivations, and barriers that affect black and Hispanic parents' adherence to sun protection recommendations for children ages 4-12. To our knowledge, there are no large-scale studies investigating these issues in the Hispanic and black pediatric population.

Limitations: These preliminary conclusions are based on a limited subset of data.

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2698

PENS syndrome: Clinical spectrum and dermoscopy findings

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Introduction: The acronym PENS, 'papular epidermal nevus with "skyline" basal cell layer', was proposed for the first time in 2011 (Torrelo et al) characterizing a new type of keratinocytic nevus, presenting as single or multiple small keratotic papules and plaques of "gem-like" appearance, with rough surface. Lesions may be present since birth or develop during the first year of life in a random distribution, affecting trunks and limbs. Histopathology demonstrates diffuse compact orthokeratotic hyperkeratosis, acanthosis and columnar basal cells with uniform small nuclear in a palisade arrangement. In 2012, Tadini et al described a new neurocutaneous phenotype, defined as PENS syndrome, evidencing neurologic abnormalities, such as epilepsy or psychomotor delay, in association with the dermatologic condition. Here we report two Brazilian patients, with clinic and histopathologic findings characteristic of PENS syndrome, and further report dermoscopic findings.

Case 1: A nine-year-old male patient presented with seven papules and plaques of "gem-like" appearance, up to 1.5 cm, with rough and yellowish surface, scattered on the trunk, legs and arms. The lesions were present since birth and the patient had no neurologic symptoms. Skin biopsy showed orthohyperkeratosis, acanthosis, and a palisade of cuboidal-polygonal dark basal cells, forming a "skyline" appearance. Dermoscopy showed well defined edges, bulbous projections, a reversed thickened network, and some punctuate vessels. Neuroimaging evaluation (MRI) showed no signs of neurologic involvement.

Case 2: A three-year-old female patient with six roundish and yellowish plaques with rough surface, up to 1.3 cm, scattered on limbs and arms. Age of onset was also at birth. Parents did not report any neurological symptoms. Histopathologic and dermoscopy findings showed similar features with the patient reported in case one.

Discussion: PENS syndrome is a rare and recently described neurocutaneous disorder, characterized by keratinocytic nevus that do not follow Blaschko's lines or any particular distribution pattern, and may be associated with neurologic abnormalities. Here we report two patients with PENS syndrome, with typical clinical and histopathologic features, and further present for the first time dermoscopy findings of this condition.

Commercial support: None identified.

3774

Pediatric psoriasis—Epidemiology and disease particularities

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Background: The onset of psoriasis may appear at any age; however, not many epidemiologic studies exist addressing the features of the disease inside the pediatric population.

Material and method: We studied the cases of psoriasis in patients aged 1 year to 18 years, who referred to our clinic over a three year period. The study group had 125 patients, in which we analyzed disease features according to age, clinical subtype, topography, associated comorbidities and treatment.

Results: The average age for our study group was 9.2 years, with a 1.1, 4 male: female sex ratio. According to age groups there were: 7.2% patients under 2 years, 13.6% aged 2-5 years, 50.4%, 6-11 years, 28.8%, 12-18 years. The most frequent clinical subtype for both sexes was psoriasis vulgaris, 39.2%. The scalp was affected in 39.2% cases, extension sites of the limbs, 27.2%, elbows and knees, 15.2%, trunk, 35.2%, face, 10.4% and palms and soles, 13.6% and 8.8%, nails. We found associated comorbidities in 54 (43%) patients, 67% infectious diseases, 35%, other skin diseases, of which over half (53%) atopic dermatitis, 20% anemia, 13% endocrine and metabolic diseases. Treatment modalities were: exclusive topical therapy in 60% of cases, phototherapy and photochemotherapy, in 38.4% and in 1.6%, systemic therapy. The two cases where systemic therapy was needed, were an 8 year old boy and a 17 year old girl, presenting with erythrodermic psoriasis and they received therapy with acitretin.

Conclusions: In our study population, children aged between 6-11 years old were most often affected by the disease. The most frequent clinical subtype was psoriasis vulgaris and the scalp was the most often involved. Infectious diseases were most frequently associated, followed by other skin conditions, mostly atopic dermatitis. The patients responded well to topical therapy, 98.4%. In the most severe cases, good results were obtained with systemic retinoids.

Commercial support: None identified.

3596

Rare finding of a scalp dermatofibrosarcoma protuberans in a 3-year-old boy

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Dermatofibrosarcoma protuberans (DFSP) is a rare, slow-growing dermal mesenchymal neoplasm with an annual incidence of 0.8-5 cases per million individuals. A 3 year-old white male patient had a 3.0 by 3.5 cm magenta colored flat-topped, progressively growing nodule on the right parietal scalp that was non-tender. Histopathology showed monomorphous spindle cell proliferation in the dermis with dermal proliferation expanding into and through the surrounding adipose and adnexal structures. An immunohistochemical stain demonstrated proliferation to be diffusely positive for CD34. DFSP is characterized by slow, infiltrative growth that initially presents as a small papule evolving over time into an indurated nodule. These lesions have a peak incidence in the second to fifth decade of life with a rate of metastasis estimated at 1-6%. This neoplasm is relatively uncommon in childhood with fewer than 200 cases reported in the literature to date. Pediatric DFSP is most often mistaken for a vascular malformation. When appearing as an atrophic plaque, as in this case, the diagnosis may be challenging and delayed. DFSP on the scalp of children is quite rare with fewer than 10 scalp lesions reported. One reported pediatric patient with recurrence of a scalp DFSP due to incomplete resection ultimately was treated successfully with adjuvant imatinib mesylate before and after repeat resection. Imatinib, which is well tolerated in children with chronic myeloid leukemia, has demonstrated great efficacy in a limited number of pediatric DFSP cases. Pediatric DFSP shares the same histopathologic feature of monomorphic fusiform pattern as adult DFSP and similarly stains positive for CD3. Translocation in chromosomes 17 and 22 is also found in most pediatric DFSPs, resulting in fusion of the COL1A1 gene with the PDGFB gene that triggers tumor cell proliferation. The current standard treatment of DFSP is wide local surgical resection or Mohs micrographic surgery with adequate tumor-free margins to prevent local recurrence that is most often attributed to the infiltrative nature of DFSP deep into the subcutaneous tissue, fascia and underlying muscle. When DFSP is not amenable to surgery or recurs, imatinib and radiotherapy can be considered as alternatives. In the pediatric population, caution must be taken due to radiation-related risk of growth defects or gonadal dysfunction. Pediatric DFSP has an excellent prognosis if recognized early followed by complete resection.

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3004

Rare primary cutaneous aspergillosis in critically ill neonate

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Aspergillus species are known to cause severe morbidity and mortality in patients who cannot mount an appropriate immune response. In critically ill neonates, there have been several case reports of invasive aspergillosis but rarely isolated primary cutaneous aspergillosis infection. Here, we present a case of a critically ill neonate of 24 weeks' gestation with primary cutaneous *Aspergillus niger*. Patient had multiple medical problems including extreme prematurity, twin gestation, respiratory distress and pneumoperitoneum requiring percutaneous penrose drain. On day 6, patient was noted to have blisters on the left side of his penis spreading to the abdomen with skin breakdown and sloughing. Wound cultures of skin lesion were obtained and patient was started on antibiotics, fluconazole and acyclovir. Skin lesions developed into white plaques with desquamation, crusting and yellow drainage over abdomen, left penis and upper back. On day 10, fungal wound culture grew moderate *A niger* and light *Candida albicans* so patient was switched from fluconazole to liposomal amphotericin B at 5 mg/kg daily, voriconazole, topical nystatin and on day 26, micafungin was added. Blood cultures remained negative throughout the hospital course. The rash continued to progress with development of numerous erosions that had coalesced into white-yellow plaques on antecubital fossa, abdomen, back, lower extremities including dorsal feet and ankles. By day 32, there was necrosis around the penrose with bowel visible through the abdominal lesion. He developed necrosis over the left foot with subsequent amputation of two left toes and areas of necrosis over dorsal right foot. Our patient died on day 39 of life due to extreme prematurity and disseminated cutaneous aspergillosis. This case illustrates key points to immediately obtain pan cultures and initiate empiric antibiotics, antivirals, and antifungals in critically ill patients with worsening skin lesions. Due to his extreme prematurity, steroid requirement while on ventilation, and penrose drain placement, it is likely that our patient was unable to mount an appropriate immune response leading to disseminated cutaneous fungal infection. The fungal wound culture grew *A niger* and *C albicans* on three separate plates so it was unlikely to be a contaminant. After a NICU investigation, our patient's source of aspergillus was not determined, but there was suspicion for possible exposure in utero during the twin's birth in a toilet.

Commercial support: None identified.

3165

Report of 3 cases of juvenile generalized pustular psoriasis—A rare disease of this age group

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Introduction: Generalized pustular psoriasis(GPP) is a rare but potentially severe variant of childhood psoriasis, classically presents with extensive pinpoint sterile pustules on a background of erythrodermic and painful skin. The pustular variant has a prevalence rate of 0.6% in childhood psoriasis, with a slight male preponderance in the ratio 3:2. Juvenile GPP presents early in life, often preceding the development of psoriasis vulgaris.

Case reports: We report 3 cases of GPP in children with no prior history of psoriasis – one presented with the acute exanthematic pattern and two presented with the subacute annular pattern. Patient 1 is a 6-year-old boy who presented with an extensive painful pustular eruption that developed 3 weeks prior to presentation, associated with fever and upper respiratory symptoms. Patient 2 is a 3-month-old boy who presented with erythematous papules and plaques, studded with pinpoint pustules over his scalp, face, limbs and trunk. Patient 3 is a 3-month-old boy who presented with annular rashes with mild scaling over abdomen following a mild cold, which slowly spread to involve the entire trunk, face and limbs with appearance of pinpoint pustules over 2 weeks. There was pitting of his fingernails. In all 3 patients, complete blood counts revealed neutrophilia and skin biopsies showed subcorneal spongiform pustules with neutrophilic infiltration, consistent with pustular psoriasis. The swab cultures were negative for bacterial and fungal growth. All 3 patients responded to treatment with oral acitretin.

Discussion: GPP in childhood frequently present without preexisting features of psoriasis, often with an abrupt onset of pustulosis, commonly following infection as a primary trigger. The presentation of GPP alone may represent a distinct pattern of immune activation associated with recessive mutation in IL36RN, a gene encoding messenger protein cytokine involved in the signaling pathway. Mutation analysis of the IL36RN gene allows for an early diagnosis of suspected GPP even at its first episode of pustulosis. Due to rarity of disease, there is neither adequate literature on retinoid drug trials nor recommended treatment guidelines for juvenile GPP. The use of oral acitretin in children is reserved for severe psoriasis variants like GPP. The clinical response has been excellent with complete clearance seen as early as 3 weeks after initiation. Clinical prognosis is often good. They also achieved longer disease remission.

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3313

Regressed, sclerotic congenital melanocytic nevus

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Introduction: Congenital melanocytic nevi (CMN) naturally evolve throughout their lifespan that includes relatively proportionate growth with the growing child, darkening, textural or surface changes (eg, papillomatous, verrucous, or cerebriform), hypertrichosis and later in life lightening of pigmentation. Despite the natural evolution of these lesions that includes malignant transformation (contingent on the size of the lesion), CMN rarely spontaneously involute, particularly in the absence of halo depigmentation.

Report: We report a case of a 2-day-old infant who presented at birth with a medium sized congenital melanocytic nevus involving the distal left leg and much of the left foot with concomitant, ipsilateral lymphadenopathy. An extensive workup that included imaging, skin and lymph node biopsies excluded the possibility of a congenital melanoma. Over the course of several years, the affected skin became sclerotic and began to lighten in color in the absence of any halo phenomenon. By three years of age, the CMN had completely regressed and the dermal sclerosis had softened. The child was left with mild leg length and girth discrepancy, rocker-bottom foot deformity, and gait abnormalities. Lymphadenopathy remains present to date.

Conclusion: Spontaneous regression of CMN via sclerosis is an extremely rare occurrence (less than 10 cases in the literature) and is thought to be mediated by an immunological mechanism different than that induced by halo phenomenon. We review the literature on this phenomenon and postulate how it leads to regression of the nevus.

Commercial support: None identified.

3584

Scars and forelocks: A case of a 3-year old girl with circumscribed morphea and poliosis circumscripta

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Introduction: Morphea is a fibrosing condition of the skin, subcutaneous tissue and bone due to the imbalance in collagen production and degradation. Poliosis is a patch of white hair, with the involvement of the surrounding skin of the hair follicle. Both conditions are rare autoimmune diseases.

Case summary: In this report, we have a 3-year old girl who presented with a 9-month history of a hyperpigmented plaque on the left cheek, gradually enlarging with increasing induration and tautness, and no other associated symptoms. During the cutaneous examination, the patient presented with an irregularly shaped, hyperpigmented plaque, surrounded by a violaceous rim, with a shiny surface and firm consistency, with a few areas of indentation, and loss of hair follicles on the left side of the face and neck. A solitary, well-defined, round, white patch topped with a white forelock on the left frontal scalp was also found during cutaneous examination. On skin punch biopsy of the hyperpigmented plaque, findings were consistent with morphea. The dilemma was in trying to classify what type of morphea the patient had. Although the patient showed clinical findings of circumscribed morphea, morphea on the face would usually present as linear morphea. Linear morphea and poliosis presenting in the face and scalp are seen in cases of Parry-Romberg syndrome. However, the classic finding of en coup de sabre in linear morphea was not present in the patient. The patient was treated with a combination of topical glucocorticoids and vitamin D derivative, where an effective response was noted after 4 weeks of treatment. Close follow-up is necessary to monitor disease progression.

Conclusion: Although it is possible that these are two separate disease entities, the presence of both morphea and poliosis in one patient requires further investigation and careful monitoring of the disease condition. The nature of morphea as a chronic disease, the setting of poliosis as a poorly understood entity, and the presence of severe, debilitating sequelae like Parry-Romberg syndrome are indications to watch out for recurrences or exacerbation of the disease. Lastly, the presence of these conditions in a 3-year old child will have a psychosocial impact in the future.

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Skin disorders encountered at a pediatric homeless clinic: A retrospective chart review

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Background: Limited information about skin problems in homeless children exists in the current literature.

Objective: To investigate the skin conditions commonly seen in a pediatric homeless clinic as compared to that of a large tertiary care children's hospital dermatology clinic.

Methods: A retrospective chart review of all children treated by pediatric dermatologists at UMOM, a licensed clinic under the auspices of Phoenix Children's Hospital serving the homeless, was conducted from January, 2010 to September, 2013. Age, gender, diagnosis, procedures, investigational studies, immunization history, insurance status, past medical history and treatment plans were recorded. The current housing situation and time spent in the shelter was also recorded. A list of ICD9 diagnoses billed during the same time frame from children seen in the dermatology clinic at Phoenix Children's Hospital was obtained and compared to the list from the UMOM homeless clinic. No child was excluded from the analysis.

Results: There were 100 visits for 76 patients from the UMOM homeless clinic during the study period. Patients ranged in age from newborns to 24 years of age in the homeless cohort. Within the homeless clinic visits, 62% of patients reported living in a shelter. The most common diagnoses seen were atopic dermatitis (37.7%), acne (28.6%), warts (6.5%), molluscum contagiosum (5.2%), nevi (5.2%), ingrown toenails (5.2%), and insect bites with hypersensitivity reaction (3.9%). Among the children seen at the Phoenix Children's Hospital Dermatology Clinic, the top diagnoses were atopic dermatitis, acne, hemangiomas and nevus-non neoplastic. The homeless clinic population at UMOM had only 12 children under 2 years of age, which may account for why there were fewer infantile hemangiomas reported.

Limitations: The retrospective nature of the study, its reliance on electronic medical records that at times were incomplete and the relatively small sample size of the homeless pediatric population are potential limitations to this study. The Phoenix Children's Hospital tertiary care dermatology clinic may have referral bias.

Conclusion: Homeless and nonhomeless children suffer from similar conditions such as atopic dermatitis and acne. With the growing homeless pediatric population and their exposure to unsheltered environments, further studies are needed to investigate the dermatologic conditions of this population.

Commercial support: None identified.

3272

Subcutaneous fat necrosis of the newborn as a complication of therapeutic hypothermia for birth asphyxia

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Introduction: Neonates with hypoxic ischemic encephalopathy (HIE) are routinely treated with therapeutic hypothermia in order to improve neurological outcome. We describe a neonate who developed an abscess-like presentation of subcutaneous fat necrosis of the new born (SCFN) after undergoing whole-body cooling for HIE.

Case report: A full-term boy was born to a 37-year-old mother via an emergency cesarean section due to changes in the cardiotocographic examination. At delivery the neonate showed signs of HIE so that a whole-body cooling was initiated. A cooling blanket was set to maintain a target temperature of 33.5°C for 72 hours and then was gradually rewarmed. On the fifth day of life the neonate developed red and violaceous subcutaneous nodules and indurated plaques on the back and the posterior aspect of the arms. Days after, a red, soft, fluctuant central abscess appeared on the middle back area. A punch biopsy of the indurated plaque showed necrosis of the fat lobules in the subcutaneous adipose tissue admixed with an inflammatory infiltrate and radially oriented needle-shaped clefts in the cytoplasm of adipocytes and some histiocytes. According to these findings a diagnosis of SCFN was made. The abscess was drained and the lesions resolved after six months.

Discussion: SCFN of the newborn is a self-limited inflammation of the subcutaneous adipose tissue that typically develops during the first week of life in full-term neonates. Birth asphyxia and hypothermia are the most commonly associated risk factors. On the other hand, large, randomized, double-blind control trials have indicated neuroprotective benefits of inducing hypothermia in neonates with birth asphyxia; therefore, a growing number of neonatal intensive care units are implementing whole-body cooling programs. The risk of SCFN in neonates undergoing this therapy is unknown although some cases have been described in the literature. Thus, induced hypothermia may play a further role in the development of SCFN.

Conclusion: Clinicians should recognize this association as more neonates are undergoing therapeutic cooling to minimize the mortality and morbidity due to HIE.

Commercial support: None identified.

3936

Sun protection beliefs among Hispanic caretakers and the practices employed in their children

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Background: The disparity of skin cancer at time of diagnosis is multifactorial and affected by socioeconomic status, education, and awareness of skin cancer. Among Hispanic populations, detection of cutaneous malignancy is frequently delayed, which results in a poor prognosis. Better understanding of the sun protection beliefs among Hispanic caretakers and the use of sun protection in their children is paramount to promoting skin cancer awareness and sun safe behaviors, as these attitudes are believed to be a determinant of a child's future sun protection practices.

Objective: The purpose of this study was to elucidate the perceived benefits of sun protection and use of photoprotective practices employed by Hispanic caretakers in children.

Methods: This cross-sectional study was conducted in an outpatient pediatrics clinic at MetroHealth Medical Center that serves primarily Hispanic individuals. The principal caretaker of a child electively completed a questionnaire assessing demographics, sun exposure patterns, photoprotective practices, and potential barriers to using photoprotection in pediatric groups. Paired Student *t* test and descriptive statistics were used for analysis.

Results: A total of 88 complete surveys were obtained, and 86% of surveys were completed in Spanish. There was a statistically significant difference in the use of sunscreen, long-sleeve shirts, wide-brim hats, and sunglasses in sunny, hot days compared to cloudy, hot days ($P < .01$ for all). Sunscreen application was reported as the most effective method to reduce skin cancer risk, decrease photoaging, and prevent sunburns in our sample. However, noteworthy barriers to using sunscreen existed; agreed causing eye irritation (56.8% of sample) and not knowing which to use (44.3% of).

Conclusions: Parental use of photoprotection in children primarily consisted of applying sunscreen. Current analysis indicates that while many understand the benefits of sunscreen use, it is only applied when the perceived risk of UVR-mediated damage is high. The existence of a large number of barriers to use may contribute to this. These preliminary results reveal the importance of stressing the use of all photoprotective practices, especially in scenarios where perceived risk of sun damage is low.

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3583

Synovitis in children with harlequin ichthyosis: An underrecognized comorbidity

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Background: Harlequin ichthyosis (HI) is an autosomal recessive skin disorder due to mutations in ABCA12, leading to deficiency of transporter protein that limits epidermal lamellar body secretion. Affected neonates are tightly encased in an erythematous, deforming membrane that is fissured to resemble the checkered costume of a harlequin. Survivors have extensive erythroderma and scaling, leading to frequent infections, feeding issues, and thermoregulation, but rarely has joint pain been mentioned in patients with HI.

Observation: We describe three children with HI whose synovitis lead to considerable discomfort and difficulty with ambulation, necessitating rheumatologic evaluation and intervention. Case 1: Four year old white–African American boy presented with 4 month history of arthritis in his bilateral legs, resulting in limping and limitation of activity. The pain was worst in the morning after sleep. MRI of left lower extremity showed synovitis and tenosynovitis of left ankle. Examination showed generalized erythroderma and fine scaling. He had sharply demarcated, boggy swelling of anterior lower legs and dorsal aspect of feet with tenderness to palpation of left > right ankle and dorsum of foot. His range of motion (ROM) of left ankle was reduced. Interestingly, he also had several nodular lesions on the legs showing non-caseating granulomas on histological examination. Daily naproxen was given. Case 2: Six year old Hispanic boy had 3 year history of muscle and joint aches, morning stiffness, and difficulty walking, requiring intermittent use of a cane. Examination demonstrated tenderness on palpation of bilateral knees without bogginess or swelling. Daily naproxen was initiated. Case 3: Three year old white girl developed arthritis of bilateral fingers and hand swelling 1 year before presentation. Examination revealed bilateral wrist, hand, finger, ankle, and toe edema with limited ROM. Pain has improved with methotrexate, but she has continued to experience considerable discomfort and swelling has persisted.

Discussion: Joint pain has not been considered a cardinal feature of HI, but in all 3 children with harlequin ichthyosis beyond infancy, joint pain was an incapacitating and painful feature. Recognition of the systemic complications of HI and more aggressive management based on ongoing biomarker analysis should be considered.

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The influence of itch: Quality of life in pediatric patients with chronic pruritus

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Background: Chronic pruritus is challenging to treat with a narrow range of treatment options. The physical exam findings can be difficult to reconcile with the impact that the patient feels the pruritus has on his/her daily life. Insight into patients' quality of life (QoL) impact can help guide treatment to optimize clinical improvement.

Methods: Children, 8-17 years old, who reported itch greater than 6 weeks, were recruited out of pediatric dermatology clinics at an academic institution. The children were administered the KidsItchyQoL, a 35-item QoL instrument which asked about the social, emotional and functional impact of their itch during the past week on a 4-point Likert scale. We selected those items in which at least 70% of patients reported some impact of itch.

Results: Analysis include our initial 21 patients, the majority having atopic dermatitis (76%) and with a median itch duration of 8 years. Certain experiences were universally reported; 100% reported scratching and used lotions. Interestingly, 95% of patients reported worsening itch with changing seasons. The social impact was considerable: 71% of patients felt embarrassed and 76% worried about what others thought. The overall lowest reported impact was ability to make friends, which was still reported in a third of patients. The responses demonstrated functional impacts such as sleep disturbances (81%), difficulty wearing certain clothes (71%) and trouble focusing on schoolwork (71%). The emotional consequences were narrower, with patients most frequently feeling frustrated (91%) and "driven crazy" (81%). The most frequently reported skin symptoms were pain (81%), bleeding (76%) and scarring (86%).

Conclusion: There was consistency in several factors affecting quality of life. It is evident that chronic itch has a substantial impact on social and daily functioning and as well as considerable emotional impacts. Evaluating more patients will better clarify the influence on quality of life and determine factors that correlate with this impact.

Commercial support: None identified.

3171

Topical timolol for the treatment of infantile hemangiomas in Asian children

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Objective: To review a cohort of patients with infantile hemangiomas treated with topical timolol and evaluate the treatment efficacy.

Methods: Retrospective review of the medical records of children with infantile hemangiomas treated with topical timolol from year 2012 to 2014 at the outpatient Pediatric Dermatology clinics, KK Women's and Children's Hospital.

Results: A total of 66 patients with infantile hemangiomas were treated with topical timolol. 36 of them had superficial, 23 had mixed, 1 had deep and 6 had both superficial and deep hemangiomas. There were 43 girls and 22 boys. The most common site was head/neck with 32 patients, followed by the trunk with 21 patients, upper limb with 11 patients and lastly the lower limbs with 7 patients. 29 patients were treated using Timolol 0.5% eye drops and 37 patients were treated using Timolol XE 0.5% ophthalmic solution which has a more viscous consistency allowing it to stay on more easily. The frequency for both treatments was twice to thrice daily. The median age at the start of treatment was 4 months old (range: 1 to 40 months). Treatment outcome was graded as good (>50% reduction/growth arrest) for 35 patients (50%), moderate (25-50% reduction in size) for 8 patients (12%) and poor (<25% reduction/continued growth) for 17 patients (21%). There were 6 patients who defaulted follow-up. Those patients who were treated earlier at 2 to 3 months or had thinner superficial lesions did better. The location and size of the lesions did not affect treatment outcome. There were no reported major adverse complications.

Conclusion: Topical Timolol treatment of infantile hemangiomas remains a suitable treatment option despite the increasing trend towards oral propranolol. This is especially so for hemangiomas which are non-life threatening and non-functionally threatening. Parents may also be more comfortable with a topical as opposed to oral therapy.

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3662

Thyroid dermopathy and acropachy in pediatric patients: A rarity

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The cutaneous manifestations of Graves' disease (GD) include thyroid orbitopathy, pretibial myxedema (PTM, also known as thyroid dermopathy) and thyroid acropachy (TA). PTM and TA, occurring in up to 4% and 1% of all cases respectively, is rarely reported in pediatric patients. We present a case series of two pediatric patients with emphasis on the clinical presentation of the cutaneous manifestations of GD. Patient 1: A 14 year-old male presented with weight loss, anxiety and palpitations. Physical exam was remarkable for a pulse of 116, enlarged six centimeter goiter, and exophthalmos. Laboratory studies confirmed GD with undetectable TSH (<0.005 mcu/mL), elevated total T4 (18.4 ng/dL), and elevated thyroid peroxidase antibodies (16 IU/mL). Seven months after initial presentation while on methimazole therapy, the patient noted hyperpigmented, indurated plaques on the bilateral anterior lower legs. A punch biopsy from the leg revealed the presence of mucin intercalated throughout the collagen bundles with no fibroblastic proliferation, consistent with PTM. Patient 2: A 16 year-old female presented with shortness of breath, insomnia and palpitations and acutely worsening dyspnea on exertion. Physical exam was remarkable for a pulse of 123, a seven centimeter goiter, and exophthalmos. Laboratory studies confirmed GD with depressed TSH (0.05 mcu/mL), elevated free T4 (10 ng/dL) and elevated thyroid peroxidase antibodies (14 IU/mL). After developing an allergic reaction to methimazole, she underwent radioactive I-131 thyroid ablation. Seven months later, she developed hyperpigmented anterior lower extremity plaques along with persistent acral swelling. Punch biopsy from the leg was diagnostic of PTM. Radiographs of the hands revealed subtle periosteal reaction along the radial aspect of the second metacarpals bilaterally, diagnostic of TA. PTM and TA are hypothesized to result from stimulation of dermal fibroblasts provoking a cytokine cascade with increased glycosaminoglycans and retention of water, particularly in dependent areas. Our cases serve to expand the currently limited literature on thyroid dermopathy and acropachy. To our knowledge, this is the second case of thyroid acropachy in a pediatric patient since 1973. Notably, return to euthyroid state does not prevent development of cutaneous disease. Local topical and systemic steroids, gamma globulin, plasmapheresis and rituximab have been used with variable success, thus further research is needed.

Commercial support: None identified.

2556

Transient neonatal zinc deficiency: A review of two pediatric cases

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Case 1: A 3mo exclusively breastfed male born via cesarean at 38wks due to oligohydramnios presented for evaluation of a worsening rash on his face, diaper area, hands that first developed at age 1mth. Exam revealed fairly well-demarcated erythematous scaly plaques in a periorificial distribution. Laboratory evaluation revealed low alkaline phosphatase (69, nl 85-270) and low zinc (15, nl 60-120ug/dL). Case 2: An underweight 4mo exclusively breastfed male born after induction at 37wks due to oligohydramnios was evaluated for a rash on his face, trunk, and extremities that first developed at age 2mths. Exam revealed brightly erythematous moderately well-demarcated periorificial plaques and ill-demarcated thin, mildly erythematous plaques on trunk and extremities. Laboratory evaluation revealed normal alkaline phosphatase and low zinc (25ug/dL). The differential diagnosis for both cases included acrodermatitis enteropathica (AE) and transient neonatal zinc deficiency (TNZD). Maternal breast milk zinc concentrations were tested and found to be low (0.15ug/g, ~15% of normal) in both cases. Dermatitis in both infants responded within days of starting zinc supplementation and clear skin was noted at 2 week follow-up appointments. The infants were small for age at time of presentation (growth chart by weight: 12% and 0%, respectively). This also improved with zinc supplementation (51% and 12% at 9mo, respectively). Both infants continued supplemental zinc until introduction of complimentary nutrition without recurrence. It is important to distinguish TNZD from AE. TNZD presents in exclusively breastfed infants and resolves upon weaning, while AE typically presents after the infant is weaned from breastfeeding. AE is a result of impaired intestinal zinc absorption due to mutations in SLC39A4 encoding the zinc uptake transporter Zip4 requiring lifelong zinc supplementation to avoid sequelae of zinc deficiency. In contrast, TNZD is a result of a mutation in SLC30A2 encoding the zinc efflux transporter ZnT-2 found in mammary epithelial cells. This mutation only manifests in exclusively breastfed infants. Misdiagnosing patients with TNZD as having AN can lead to chronic zinc toxicity secondary to over supplementation. Interestingly, the highest level of SLC30A2 is in placental tissue. Decreases in placental and amniotic fluid zinc levels are correlated with oligohydramnios, seen in both our cases, leading us to speculate about a possible correlation.

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Treatment of anogenital warts with imiquimod 5% cream in 22-month and 18-month old infants

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Anogenital warts are benign epidermal tumors caused by human papillomavirus (HPV) acquired in children through vertical, autoinoculation, heteroinoculation, contaminated fomite, and sexual transmission. Fortunately, most anogenital warts are self-limited making active nonintervention a reasonable initial approach. However, for those with symptomatic or persistent anogenital warts, intervention is usually necessary. Imiquimod has been shown to be an effective treatment option for anogenital warts in adults and children. However, in infants (less than 2 years of age), reports of effectively treated cases remain relatively few. Here we present two cases anogenital warts in infants treated with topical imiquimod 5% cream. Case 1: A healthy 22-month old girl presented with a 1-month history of rapidly growing perianal lesions. On physical exam, she had numerous grouped pink verrucous perianal papules consistent with condyloma. Biopsy and HPV typing were performed, which were consistent with condylomatous changes and positive for types 6 and 16, respectively. She was treated with imiquimod 5% cream regimen that was well tolerated: application to the perianal warts for 8 hours at night, three times a week for a period of 6 weeks with the use of mupirocin cream when imiquimod was not used. The patient was followed up every 2 weeks with complete resolution of lesions by 4 weeks. Case 2: A healthy 18-month old girl presented with a 2-month history of rapidly growing perivulvar lesions. On physical exam, she had pink verrucous perivulvar papules consistent with condyloma. Anoscopy and vaginoscopy did not show any internal lesions. Biopsy and HPV typing were consistent with condylomatous lesions and positive for types 6 and 11, respectively. She was treated with imiquimod 5% cream regimen for a period of 8 weeks that was well tolerated with complete response. Our patients presented with rapidly growing perianal (case 1) and perivulvar warts (case 2) that were treated with imiquimod 5% cream with no serious adverse effects. Interestingly, marked improvement was observed by 2 weeks of therapy in both cases. Our report adds to the number of effectively treated anogenital warts with imiquimod 5% cream in infants reported in the literature. The ease of use, safety profile, efficacy, lower recurrence rates, and potential for long-standing immunity make imiquimod a viable alternative treatment option especially in pediatric patients with larger area of involvement.

Commercial support: None identified.

3724

Urticaria pigmentosa in a 6-month old Filipino male with G6PD deficiency

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Introduction: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzyme defect of red blood cells. Around 200 million people are deficient in this enzyme. In the Philippines, this X-linked hereditary deficiency has a prevalence rate of 4.5% to 25.7%. Clinical manifestations of patients with G6PD deficiency may be induced by trigger factors such as certain drugs like diphenhydramine, an H1 antihistamine. Mastocytosis is a rare group of disorders of mast cell proliferation. The most common cutaneous manifestation of mastocytosis is urticaria pigmentosa presenting as multiple pruritic hyperpigmented macules, papules and patches over the face, trunk, and extremities, usually sparing the palms and soles. Darier's sign is usually positive. Histopathologic examinations with both Giemsa and CD 117 stains will reveal abundance of mast cells. In East Avenue Medical Center, a tertiary government hospital in the Philippines, only three cases were noted from 1992-2015. H1 antihistamines such as diphenhydramine are the first-line treatments for such cases in addition to topical steroids, and mast cell stabilizers.

Case report: This is a case of a six-month old Filipino boy presenting with multiple pruritic brown macules, papules, and patches on the face, trunk, extremities including the palms and soles. Darier's sign is positive. This patient has mild motor developmental delay and has G6PD deficiency. Histopathologic examination with Giemsa and CD 117 staining revealed abundance of mast cells that are the typical histologic features of mastocytosis. He was given cetirizine instead of diphenhydramine, ketotifen, a mast cell stabilizer, emollients, and triamcinolone lotion, a mid-potent topical steroid. Clinical improvement of cutaneous lesions was noted after one month.

Conclusion: Urticaria pigmentosa and G6PD deficiency are both rare disorders. The combination of these two together with motor developmental delay have not been reported previously suggesting that this might be a new syndrome with an unknown etiology. The symptoms of urticaria pigmentosa may be relieved with the use of H1 antihistamines such as diphenhydramine. But it is important to always do a thorough history to detect other co-morbidities such as G6PD deficiency so as to avoid giving medications that might cause hemolytic anemia.

Commercial support: None identified.

3750

Two cases of neonatal lupus

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Neonatal lupus erythematous (NLE) is an entity that occurs 0.6-2.2 of every 100,000 children annually with female ratio predominance of 2:1. The etiology is thought to be caused due to transplacental passage of maternal autoantibodies such as Ig6 against Ro (SSA), La (SSB) or U1-ribonucleoprotein. The clinical manifestations involve dermatologic, cardiac and hepatic involvement. Dermatologic lesions presents with annular erythematous plaques predominantly in periorbital region, neck, and scalp. Cardiac involvement occurs in about 65% of patients which can vary from rhythm abnormalities to complete congenital heart block or heart failure that generally do not resolve. This is a self-limited disease, therefore the treatment consists of supportive therapy until resolution in 2-6 months. Overall we describe two cases with almost identical clinical and histopathologic manifestations. They presented to the hospital with dermatosis of multiple erythematous plaques varying in size with well circumscribed elevated borders affecting face, skull, thorax, upper and lower extremities. One mother had systemic lupus erythematosus (SLE) diagnosed before pregnancy, while the other had nonrelevant medical history. Lab work requested for both mothers returned positive for anti SSA and anti SSB in both cases confirming the diagnosis for NLE. Biopsies reported superficial and media perivascular dermatitis with marked interstitial mucinosis. No cardiovascular lesions found on either patients. Treatment consisted of hygiene education and sunblock every 2 hours throughout whole body with follow up at 6 months. This disease is poorly recognized resulting in misdiagnoses with other entities. Therefore, it is of great importance to incorporate clinical information in order to provide a more prompt diagnosis. Although in some cases, the mothers do not progress to SLE there is an increased risk in these mothers to debut with SLE along their lifetime. Nevertheless, they must be followed carefully in order to provide the necessary treatment and prevent progression of disease.

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3027

Vulvar xanthelasmoid mastocytosis in a child with urticaria pigmentosa

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Background: Cutaneous mastocystosis is a mast cell dependent disease that most commonly presents in childhood as solitary mastocytomas or urticaria pigmentosa. Xanthelasmoid mastocytosis represents a rare clinical entity on the spectrum of cutaneous mastocytoses.

Case description: A five year-old female presented to our pediatric dermatology clinic with a several month history of papular, pruritic lesions on the buttocks and genitals. Past medical history included biopsy proven urticaria pigmentosa. A review of systems was negative for headaches, facial flushing, itching, fatigue, or diarrhea. No other pertinent family, allergic, or social history was noted. On exam, the patient had multiple firm, well-circumscribed smooth yellow papules of varying sizes located on the vulva and perineum. Widespread red-brown patches were also noted on the neck, chest, and back. The patient's guardian declined a biopsy of the genital lesions.

Discussion: Xanthelasmoid mastocytosis is a rare clinical entity, occasionally seen in conjunction with urticaria pigmentosa. These lesions often present in infants and arise as small, hard, yellow papules. They are usually widespread, but have rarely been reported in the genital region. Darier's sign is inconsistent in such lesions. Histologically, mast cell infiltrates are seen in the deep dermis, which is thought to yield their yellow color. Like other childhood forms of cutaneous mastocytoses, the recommended treatment is with antihistamines and avoidance of mast cell degranulation stimulators. Since these lesions can last into adulthood, surgical removal can be contemplated but may not be a viable option due to the risk of negative physical and psychological sequelae.

Conclusions: Here we present a case of vulvar xanthelasmoid mastocytosis in a young girl with urticaria pigmentosa. Our case is of interest due to the rare nature of such lesions as well as the genital location and late age of onset in our patient. Dermatologists should be aware of this unique entity as manifestations of cutaneous mastocytoses seem to exist on a spectrum.

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PHARMACOLOGY

3335
A report of tigecycline-associated angiokeratoma formation

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Introduction: Angiokeratomas represent benign growth of abnormally dilated vascular tissue. They are often observed as cutaneous manifestations of certain enzymatic deficiencies, but they can also occur in asymptomatic individuals. Recently, angiokeratoma formation has been reported in association with certain medications. We describe the first reported case of angiokeratoma appearance associated with the use of tigecycline, an intravenous antibiotic reserved for multidrug resistant bacterial infections.

Case report: A fifty-nine year old female on chronic immunosuppression due to severe rheumatoid arthritis presented with a one-week history of two dark-colored papules, one on each lower extremity. The first papule had appeared several days following cessation of a six-week course of intravenous tigecycline for an unrelated soft tissue infection. Standard laboratory evaluation and infectious workup were negative. A biopsy revealed histopathologic features consistent with an angiokeratoma. Five more similar-appearing papules erupted over the next two weeks, culminating in a total of seven newly appearing angiokeratomas over a three-week span. Since these lesions were asymptomatic, treatment was deferred. Seven weeks following the initial papule's appearance, six of the angiokeratomas had spontaneously resolved without any treatment, leaving no cutaneous signs of their former locations.

Discussion: The timeline of gradual angiokeratoma progression and resolution in this patient suggests that a temporary factor was associated with the pathogenesis of angiokeratoma formation. Despite the onset of angiokeratoma appearance occurring a few days after discontinuing tigecycline, the time course of the angiokeratoma eruption in relation to the course of tigecycline suggests that this antibiotic may have been associated with their formation. We hypothesize that subcutaneous formation of angiokeratomas began prior to tigecycline cessation, but only cutaneously appeared after tigecycline was stopped. Due to its lengthy half-life of sixty hours, over 25% of the steady state concentration may still have been present in the patient's serum on the day of the first angiokeratoma appearance, four days after tigecycline cessation. Finally, the resolution of angiokeratomas in the absence of tigecycline suggests it may have been associated with their formation. Future investigations are warranted to delineate the pathogenesis of tigecycline-associated angiokeratomas.

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3448
An evaluation of vasoconstriction potency response for fluticasone propionate gel, 0.025% compared to current marketed reference corticosteroid formulations of known potency

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Background: The vasoconstriction response produced from exposure to topical corticosteroids has proven to be an effective indicator of steroid delivery through the epidermal barrier of the skin. Although the vasoconstriction response to steroids is not known to be directly related to their biochemical activity in skin diseases, it is well known that the vasoconstriction response is an indicator of steroid delivery and to some extent predicts comparative efficacy in treatment of skin disease.

Objective: Evaluate the vasoconstriction potency response of fluticasone propionate gel, 0.025% in comparison with fluticasone propionate cream, 0.05% and three other reference corticosteroid formulations of known potency.

Methods: This was an open-label study on 24 healthy adults. Subjects had twelve 4-cm^2 sites demarcated on each forearm of which 10 per arm were evaluated for vasoconstriction response to five gel formulations which contained fluticasone propionate. Four reference formulations (diprolene cream af, 0.05%; betamethasone dipropionate cream, 0.05%; triamcinolone acetonide cream, 0.1%; fluticasone propionate cream, 0.05%) and 1 test formulation of fluticasone propionate gel, 0.025% (test gel) were each dosed onto two side by side site pairs on each arm for a 16-hour duration. All sites remained unoccluded after application and two sites on each forearm remained untreated to serve as controls. Two hours after all product removal, a visual blanching score was obtained and a chromameter assessment made. Higher scores of blanching correlated to a steroid product that is more potent than one which showed lower scores. The study was based on the McKenzie-Stoughton vasoconstriction potency method. This test shows statistical difference between formulations where there is a 2-level, or greater, potency difference.

Results: The test gel was significantly different from diprolene cream AF, 0.05%, betamethasone dipropionate cream, 0.05%, and triamcinolone acetonide cream, 0.1%, but not significantly different from fluticasone propionate cream, 0.05%. The test gel has a potency ranking no greater than a 5, but a ranking of 6 was not ruled out. Adverse events were minimal and unrelated to the treatments.

Conclusions: The test gel was found to have the same potency ranking as fluticasone propionate cream, 0.05% and was well tolerated.

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2647
Antimalarials for oral erosive lichen planus: A retrospective study of 8 patients

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Background: Treatment of oral erosive lichen planus (OELP) is considered a therapeutic challenge. Various systemic and topical agents that are aimed at the control of symptoms, rather than cure the lesions, have been used with varying results.

Objective: In this study, we review the therapeutic response to antimalarial drugs in eight patients with OELP. All of them had been previously treated with other drugs without obtaining a favorable response.

Methods: Eight patients diagnosed with oral erosive lichen planus were treated with antimalarial agents. The first clinical evaluation was made after a month of treatment and then every 2 to 3 months. Baseline ophthalmologic examinations were performed, and laboratory values were monitored before and during treatment.

Results: Six women and two men from 56 to 82 years (mean 66 years) received oral antimalarials drugs. The ratio of interval required for a favorable clinical response was 1-3 months (mean 2.4 months). Pain relief and reduced erythema and erosions were observed after of a mean of 2.4 months.

Conclusion: Antimalarials may be useful for the treatment of oral erosive lichen planus. They are easily administered and affordable with few adverse effects.

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3294
Association of additional malignancies not previously recognized in the FDA Full Prescribing Information for ustekinumab: An analysis of the FDA Adverse Event Reporting System (FAERS)

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Introduction: Ustekinumab (U) is an interleukin (IL)-12 and IL-23 inhibitor, approved for the treatment of moderate to severe psoriasis (Ps) and for active psoriatic arthritis (PsA). Two long-term studies, with up to 5 years of follow-up, concluded that U did not increase the rate of malignancy in patients with psoriasis. Moreover, according to the Full Prescribing Information (FPI), occurrence of malignancies other than nonmelanoma skin cancer in U-treated patients was similar to what would occur in the general U.S. population. Nevertheless, U has now been reported to be associated with lymphoma. The aim of this study was to determine if there is a detectable association between U and malignancy in the Food and Drug Administration Adverse Event Reporting System (FAERS) database.

Methods: We searched the FAERS database (January 2004 through December 2015) for terms related to U combined with cancer/malignancy, and calculated the proportional reporting ratio (PRR) for detection of a safety signal, defined as number of events >3, chi-square result (>4) and the PRR (>2).

Results: Similar to the FPI, signals for breast cancer, prostate cancer, colon cancer, rectal cancer, and melanoma were found in the FAERS database. Unlike the FPI, safety signals were detected for several additional malignancies, namely B-cell lymphoma (9), myeloid leukemia (N = 10), bladder cancer (N = 6), cervix carcinoma (N = 4), epithelioid sarcoma (N = 11), gastric cancer (N = 4), lung cancer (N = 22), esophageal cancer (N = 109), ovarian cancer (N = 5), metastatic ovarian cancer (N = 10), plasmacytoma (N = 6), renal cancer (N = 8), testis cancer (N = 44) and thyroid cancer (N = 4).

Conclusion: Safety signals from the FAERS database suggest that ustekinumab is associated with several malignancies not recognized in the full prescribing information. However, limitations to the interpretation of FAERS data are the voluntarily reported aspect of data collection and redundant reporting. Exploration of this finding that ustekinumab is associated with malignancies not previously recognized in the full prescribing information is warranted.

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3167
Association of melanoma and nonmelanoma skin cancer with antihypertensive drugs: A report from the Research on Adverse Drug events And Reports project

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Introduction: Some antihypertensive drugs may increase the risk of skin cancer, but findings are inconsistent regarding the possible association of exposure to these agents including angiotensin-converting enzyme inhibitors (ACEIs), angiotensin-receptor blockers (ARBs) and thiazides (TZs) with occurrence of malignant melanoma (MM), basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). The aim of this study was to investigate further these possible associations.

Methods: The Northwestern Medicine Enterprise Data Warehouse repository was searched to detect patients, age 18-89 years, with two consecutive prescriptions for an ACEI, ARB or TZ. Subsequent diagnoses of MM, BCC or SCC occurring at least 2 months after exposure to one of these drugs were identified using ICD9 codes. The control population, from the same repository, consisted of non-antihypertensive drug-exposed individuals. Adjusted odds ratio was obtained using logistic regression analyses.

Results: Between Jan. 2010 and Feb. 2015, a total of 635,687 individuals with documented age, race and gender were detected. Of 5772 patients with prior exposure to an ARB: 23 MM, 45 BCC and 18 SCC were detected. Of 15,617 patients with prior exposure to an ACEI: 28 MM, 94 BCC and 35 SCC were detected. Of 3400 patients exposed to a TZ: 9 MM, 18 BCC and 13 SCC were detected. After adjusting for age, gender and race, a significant increased risk of melanoma was determined for ARBs (OR: 2.21; 95% CI: 1.45-3.36) and TZ (OR: 2.03; 95% CI: 1.04-3.92). An increased risk of basal cell carcinoma was determined for ARBs (OR: 1.36; 95% CI: 1-1.83) and ACEIs (OR: 1.31; 95% CI: 1.06-1.62). Finally, an increased risk of squamous cell carcinoma was determined for ARB, ACE and TZ (OR: 1.75; 95% CI: 1.08-2.8; OR: 1.59; 95% CI: 1.12-2.25; OR: 3.47; 95% CI: 1.99-6.04; respectively).

Conclusions: These findings serve to delineate the association of malignant melanoma and nonmelanoma skin cancer subsequent to ACEI, ARB and TZ exposure. This may have clinical relevance related to the choice of antihypertensive agent, particularly for patients with known risk factors for skin cancer. Given the widespread use of these drugs, increased pharmacovigilance, along with education for both patients and health practitioners, are warranted.

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3166
Comparison of the pharmacoeconomic profiles of treatment regimens for field pattern actinic keratoses

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Actinic keratosis (AK) is a common premalignant skin condition estimated to have an estimated prevalence of 39.5 million persons and warrants 5.2 million office visits in the United States each year. Currently, there is no universal agreement on the treatment of AKs. The objective of this paper is to create a model for health care providers to employ in determining the most cost effective treatment modality for AKs. The model is based on the efficacy of the treatment, of which compliance rate is an inherent factor. This study will introduce a static model comparing different treatment options taking into account compliance rates, the average wholesale price, and efficacy data from pivotal studies to determine the relative efficacy of the different treatment options. We collected efficacy data from package inserts based on the treatment regimen used in the package insert or off-label common practice usage, cost data from Medi-Span Price Rx, and compliance data from various clinical trials (for therapies with similar regimens since AK data was not available) to estimate compliance data for our studied treatments of AKs. The model also allows providers to input their own data to generate relative efficacy rates based on their own practice. The drugs studied included: 5% fluorouracil cream, 0.5% fluorouracil cream, aminolevulanic acid plus blue light photodynamic therapy, 3% diclofenac sodium gel, 3.75% imiquimod cream, 0.015% ingenol mebutate gel, and 5% imiquimod cream. Using the best available compliance data combined with efficacy and cost, aminolevulanic acid plus photodynamic therapy is the most effective treatment option for AKs (66% efficacy). We ran the model a second time with a theoretical 100% compliance rate of all treatment modalities and aminolevulanic acid plus photodynamic therapy was still the most effective (69% efficacy). This paper aims to provide guidance to physicians considering field pattern treatment of AKs and to choose the most efficient treatment considering price, patient adherence, and outcome. Using the best available compliance data, aminolevulanic acid plus photodynamic therapy is the most efficacious treatment option for AKs. While this study does have limitations, such as lack of available compliance trials for the treatment regimens and therefore, coming up with estimates for best available rates, we hope it can serve as a guideline for providers in choosing a cost effective modality for the treatment of AKs.

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3673
Evaluation of risk of SSRI-associated impotence and low libido in men exposed to finasteride

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Introduction: Finasteride (F) exposure is associated with sexual dysfunction and depression when used to treat androgenic alopecia in men. Another class of drugs, selective serotonin reuptake inhibitors (SSRI), such as citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline are prescribed for depression, are also associated with sexual dysfunction.

Methods: To evaluate sexual dysfunction adverse drug-drug interactions between F and SSRIs, we searched a large, urban, academic-based electronic medical record archive (3 million individual records, May 1998-June 2015) to detect all men exposed to oral F ≤ 1.25 mg/day, and with no record of impotence, low libido, nor phosphodiesterase-5 inhibitor (sildenafil, tadalafil, and vardenafil) use prior to F exposure.

Results: We detected 6803 men (median age 33, interquartile range 28.5-41 years) exposed to F ≤ 1.25 mg/day of whom 864 also were prescribed an SSRI. Data were analyzed using globally optimal classification tree analysis (GO-CTA), a nonparametric statistical methodology for which no distributional assumptions are required and that explicitly maximizes model classification accuracy for each specific sample and hypothesis. For GO-CTA, the index of classification accuracy is effect strength for sensitivity (ESS), a normed index on which ESS = 0 indicates the accuracy that is expected by chance, and ESS = 100 indicates perfect, errorless prediction. The rate of impotence diagnosis was 76 of 864 (8.8%) among men prescribed both F and an SSRI vs 207 of 5,939 (3.5%) among men prescribed F and no SSRI (risk ratio 2.5; number needed to harm 5.3; effect strength score 14.8%; $P \leq .001$). The rate of low libido diagnosis was 34 of 864 (3.9%) among men prescribed both F and an SSRI vs 84 of 5,939 (1.4%) among men prescribed only F and no SSRI (risk ratio 2.3; number needed to harm 60; effect strength score 16.4%, $P = .001$).

Limitations: Limitations of this study include a need to evaluate causality since these findings warrant further exploration of this drug-drug interaction and their associations with low libido and impotence.

Conclusions: There is evidence that exposure to both F and an SSRI results in a clinically significant drug-drug interaction with an associated increased risk of both impotence and low libido in men who were prescribed both F and an SSRI in this study population.

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3599
Lichenoid dermatitis from interferon alpha-2a in a patient with metastatic renal cell carcinoma and seronegative HCV

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Cutaneous reactions to interferon, including a lichenoid drug reaction, are most commonly reported in patients undergoing treatment for hepatitis C virus (HCV) infection. There have been case reports of interferon-induced lichen planus in seronegative HCV patients with lymphoproliferative disorders and melanoma. We report the case of a 71-year-old man undergoing treatment with interferon for metastatic renal cell carcinoma (RCC) who developed an eruption 2 months after starting interferon. Clinical and histological findings from biopsies supported a diagnosis of interferon-induced lichen planus. To our knowledge, this is the first known case of a lichenoid drug eruption from interferon in a seronegative HCV patient with metastatic RCC.

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2484

Nicotine replacement therapy in recurrent aphthous ulcers

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Complex aphthosis is a painful ulcerative condition of the oral/genital mucosa which can cause significant functional morbidity. Typical treatments include topical anesthetics/corticosteroids and systemic colchicine, dapsone and thalidomide. We present a case of treatment resistant complex aphthosis in a non-smoker who's condition was also complicated by treatment with intravenous immunoglobulin and methotrexate for autoimmune dysautonomia. She was ultimately successfully treated with nicotine replacement therapy.

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2657

Perforating folliculitis in a HIV-infected patient with hepatocellular cancer treated with sorafenib

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A 53-year-old African American man presented with a four-month history of acneiform type rash on his arms and legs. His medical history included HIV with a CD4 count of 266 and hepatocellular carcinoma status post chemoembolization, radiofrequency ablation. Medications included calcium (1 tablet PO qd), prednisone (20 mg PO qd), lopinavir/ritonavir (200/50 mg, 2 tablets PO bid), and tenofovir/emtricitabine (1 tablet PO bid). The patient was also taking sorafenib (200 mg PO bid), a multikinase inhibitor, for hepatocellular carcinoma. Four months after sorafenib induction, the patient developed small papules, slowly evolving into painless, non-pruritic, indurated, brown papules. A dermatologic examination revealed innumerable papules on the chest, abdomen, and left flank, which coalesced into a plaque. Upon closer examination the papules that composed the plaques were noted to have follicular prominence. Papules noted on the left posterior shoulder, arms, face, and anterior thighs had keratotic cores. Thin, exfoliative scale covered the palms and fingers, while the patient's feet were positive for hyperkeratosis. A punch biopsy of a papule located on the right posterior upper arm was performed. On pathology, the perforated hair follicle showed inflammatory cells, degenerated extracellular matrix, and collagen within the keratotic plug. The centrally dilated and distorted, follicular infundibulum was plugged predominately with compact parakeratosis with focal basophilic cellular debris and perifollicular fibrosis. There was also mild, superficial, chronic, perivascular inflammation. The distinctive feature of perforating folliculitis of transepidermal penetration and elimination was not seen in multiple sections and levels, but the findings were compatible with a partially resolved lesion of a perforating disorder such as perforating folliculitis. The patient was managed by discontinuation of the sorafenib (200 mg PO bid) for two weeks, which eliminated the occurrence of new papules. Because of the efficacy of sorafenib against hepatocellular carcinoma the patient was advised by oncology to continue use of the drug (200 mg PO bid). He began to develop new papules when the drug was restarted, but due to the tolerability of the papules, he did not discontinue use.

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2441

Rifampicin-induced bullous pemphigoid

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Introduction: Bullous pemphigoid (BP) is an acquired autoimmune disease that affects mainly the elderly and is characterized by subepidermal blistering. Although in most cases, the causative agent remains unidentified, certain medications have been implicated in the pathogenesis of the disease. We report a case of BP in a young patient that appeared after treatment with rifampicin.

Case report: 17 years male, native of Colombia, residing in Spain for a year, on rifampicin and isoniazid treatment for tuberculosis lung after initial treatment with rifampicin, isoniazid, pyrazinamide and ethambutol. He was attended at the dermatology department by itchy vesicular eruption in the upper back, neck, nose, cheeks and forehead. The initial diagnosis was herpetic eczema and was prescribed treatment with valacyclovir 1 g every 8 hours for 7 days and cloxacillin 500 mg every 6 hours for 5 days. Ten days after treatment, lesions persisted. Viral and bacterial culture were negative. We perform a second skin biopsy with direct immunofluorescence, and included in the differential diagnosis: drug-induced lupus, prurigo pigmentosa, bullous pemphigoid (BP) and linear dermatoses Ig A. Direct immunofluorescence demonstrated linear C3 deposits confirming the diagnosis of PA. We started treatment with prednisone with good response. Subsequently there appeared a strong residual hyperpigmentation.

Discussion: Over the years, more than 50 medications have been associated with bullous pemphigoid. In everyday clinical practice, the differential diagnosis between classic BP and drug induced BP can prove to be quite difficult. As no clear cut histologic or clinical criteria can be set, one must follow indications from the presenting symptoms of the patients, the recent history of received medications and the histopathologic picture of the disease to set a possible diagnosis. Unfortunately, even if a suspect drug is identified, rechallenging a patient is impossible and no definite proof can be established. Considering the fact that after withdrawal of a suspect medication most patients respond rapidly to treatment and do not experience relapses of the condition, the possibility of drug induced BP must always be considered by the treating physicians. Drug reported by the patient, only rifampin previously reported as causal agent in the PA. Conclusion The development of vesicles and bullae in a young patient who has recently introduced new drugs requires discard drug induced BP.

Commercial support: None identified.

2442

Paronychia and excess granulation tissue with ibrutinib: A newly reported side effect

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Ibrutinib interferes with malignant B-cell proliferation via inhibition of Bruton's tyrosine kinase (BTK), which is involved in the NF-KB pathway. Common side effects reportedly include nausea, abdominal pain, vomiting, constipation, upper respiratory tract infection, fatigue, bruising, rash, musculoskeletal pain and peripheral edema. We have observed the development of severe paronychia and excessive granulation tissue formation in two patients within one year of starting ibrutinib, which has previously not been reported in the literature. The first case was a 79 y/o gentleman with a history of mantle cell lymphoma treated with ibrutinib. About one year after initiation of treatment with ibrutinib, he noticed development of excessive granulation tissue around multiple toenails with painful inflammation of the lateral nail folds consistent with paronychia. No other medication or traumatic trigger could be identified. He was treated with topical steroids and antibacterial dilute vinegar soaks and was lost to follow up. The second patient was a 79 y/o male with a history of CLL, treated with ibrutinib. Four months after starting ibrutinib he noticed inflammation around the cuticle of his left index finger. He was treated with azithromycin, nail avulsion linezolid, itraconazole, oral and topical acyclovir with no improvement. Subsequently, a biopsy of the area was performed and showed some perivascular lymphohistiocytic inflammation with neutrophils. Tissue cultures were negative for bacteria and fungus. He was started on treatment with dilute acetic acid soaks and clobetasol ointment twice daily with some improvement. We postulate that alteration of downstream NFKB mediated pathways may explain the observation of two cases of paronychia and excessive granulation tissue seen in patients taking ibrutinib. It is important to recognize this clinical finding as a potential adverse drug reaction to avoid inappropriate or aggressive treatments targeting presumed infectious etiologies, as this is inflammatory in nature.

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3679

Topical imiquimod—Be aware of the unexpected

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We are reporting a rare but serious side effect of imiquimod and its implications on daily practice. An elderly lady was commenced on imiquimod for SDCCs on her chest. Within 5 days superficial erosions occurred to the treatment area. 3 weeks later, the GP prescribed 7 days of erythromycin on suspicion of superinfection. Erythromycin had been tolerated well previously. In the 6th week, the patient represented with atypical targetoid lesions affecting trunk and both arms. She admitted to general malaise throughout treatment. She was hospitalized hypotensive and feverish but an initial septic screen including antistreptolysin O titer, throat and skin swabs was negative. Punch biopsies from chest and arm showed nonspecific inflammatory changes with eosinophils and subepidermal eosinophilic blisters. The rash progressed into confluent denuded areas with positive Nikolsky sign covering 20% of the body surface. A frozen skin section confirmed full thickness necrosis. Mucous membranes remained unaffected. The patient recovered fully after withdrawal of imiquimod and intense skin care. An overlap syndrome of TEN/SJS (toxic epidermal necrolysis/Stevens–Johnson) secondary to imiquimod was diagnosed. A lymphocyte transformation test was negative but due to its low sensitivity of 60-70%, imiquimod cannot be excluded as trigger. Alternatively, other mechanisms may mediate the reaction such as systemic absorption of imiquimod and direct keratinocyte TLR7 activation. The timeline of events associated with continuous application of imiquimod favors the drug as culprit. There is no literature mentioning imiquimod as trigger of SJS/TEN. Official regulatory bodies for medicines such as the FDA and MHRA do not highlight recent concerns regarding imiquimod causing serious adverse reactions. In 2007 an American postmarketing surveillance report investigated the association of imiquimod with cases of SJS/TEN but the evidence was not convincing. The British National Formulary mentions SJS as rare side effect. This case raises awareness of a rare but serious side effect of a commonly used drug. In daily practice potentially harmful side effects need to be mentioned as part an informed consent to treatment for medico-legal reasons. Diligent adverse drug event reporting is required to capture more cases. On suspicion of a drug eruption, a good history with a thorough timeline of events cannot be replaced by current laboratory testing.

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2867

Urticariform plaques: delayed hypersensitivity reaction type IV to enoxaparin

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Introduction: The low-molecular weight heparins as enoxaparin are widely used to prevent and treat thromboembolic disorders. Cutaneous reactions secondary to enoxaparin injections include delayed hypersensitivity skin reactions described as erythematous, itchy infiltrated plaques at injection sites.

Case report: A 55 years-old female with no personal or family history of interest was attended in our dermatology unit complaining an itchy rash for four days of evolution. The patient only referred one treatment for 15 days with enoxaparin which it had suspended 5 days before the start of the eruption. This was located in the injection points. The examination revealed the existence of two urticariform plaques which were very well defined and localized on the iliac crests. They coincide with the inoculation points of enoxaparin. The clinic of the patient was compatible with delayed hypersensitivity reaction type IV to enoxaparin. The diagnosis was confirmed by skin biopsy. The patient began treatment with a regimen of topical methylprednisolone and she was practically asymptomatic in one week.

Discussion: Heparin's most common adverse event is hemorrhage; late side effects include telogen effluvium, alopecia, osteoporosis, lipodystrophy, and a reversible increase of liver enzymes. Heparin may cause all types of allergic reactions, particularly cell-mediated type IV and antibody-mediated type II reactions. Very rarely also immediate type I reactions occur. The delayed hypersensitivity reaction type IV is a sensitization or induction period of at least 7-10 days, but more often after weeks to months, patients develop pruritic erythematous lesions at the injection sites. The latency period in previously sensitized individuals lasts typically from 1 to several days. Manifestations include erythematous plaques at the injection sites. These are sometimes followed by formation of vesicles and bullae. The main differential diagnoses include local hematoma, infections, such as erysipelas, contact dermatitis, and particularly heparin-induced skin necrosis. If the eruption is local, the enoxaparin could be changed by other low molecular weight heparin. In case of generalized rash, we must discontinue treatment with this type of heparins. To do always allergies study.

Conclusion: The diagnosis of delayed reaction of hypersensitivity to enoxaparin is a clinical diagnosis in which the history and examination are the protagonists.

Commercial support: None identified.

PHOTOBIOLOGY, PHOTOTHERAPY AND PHOTOSENSITIVITY DISEASES

2483

A case of widespread actinic granuloma with associated drug-induced lupus erythematosus

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Actinic granuloma is a rare, idiopathic skin disease affecting cutaneous sun-exposed sites of middle-aged adults. The disease is triggered by an immune response caused by factors that modify the antigenicity of elastic tissue and many systemic diseases have been associated with this condition. We report a case of a 71-year-old male with a sudden onset widespread pruritic eruption comprising of annular plaques. The plaques were photodistributed and the patient had been recently commenced on hydralazine. The clinical presentation, biochemical investigations and biopsy pointed toward a diagnosis of hydralazine-induced lupus, but on skin biopsy actinic granuloma was found. These two conditions have rarely been associated with each other and this case highlights the importance of biopsy in photodistributed dermatoses as well as investigation for other systemic associations.

Commercial support: None identified.

2783

A prospective study of daylight photodynamic therapy for treatment of actinic keratoses in an Irish population

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Photodynamic therapy has been shown to be a highly effective treatment for actinic keratoses (AKs), however therapy is often limited by pain. Daylight mediated PDT is emerging as an effective treatment for AKs, with limited side effects. The aim of this study was to evaluate the efficacy of daylight PDT and to determine patient satisfaction. Patients attending the dermatology clinic with grade 1 and/or 2 actinic keratoses on scalp and/or face were recruited. The lesions to be treated were photographed, mapped and numbered. 16% methyl ester of 5-aminolevulinic acid in cream base was applied to the treatment area. The patients then spent 2 hours exposing the area to daylight. Patients completed DLQI questionnaire before and after treatment and recorded pain severity on a scale of 1-10. Patients were reviewed 2 weeks following treatment to assess response. The primary outcome was therapeutic response at 2-week follow-up. Secondary outcome was patient satisfaction. 25 patients were recruited for this study. The mean number of AKs at baseline was 6.12 (±2.01). The mean UV index on day of treatment was 4.77. All patients showed a marked improvement at 2 week follow up with a mean number of AKs of 2.00 (±0.97). The mean lesion response rate at 2 weeks was 68.33% (±14.82). 22 patients (88%) reported no pain or mild pain during the treatment (pain score 0-3) and 3 patients (12%) reported moderate pain (pain score 4-7). There was no significant association found between therapeutic response rate and maximal pain score. The mean DLQI score pretreatment was 1.40 (±0.91). This did increase to a mean of 3.08 (±2.24) during treatment, but decreased to a mean of 2.12 (±0.83) at 2-week follow up. The most frequently reported adverse event was erythema. 60% reported scaling and 80% reported itching. 84% reported pain and 96% reported burning sensation during treatment. This was reported to have subsided by 2 days posttreatment. Daylight PDT is an effective treatment for patients with actinic keratoses in Ireland and is well tolerated with minimal side effects.

Commercial support: None identified.

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2540

A retrospective review on the use of 308 nm excimer lamp phototherapy at the National Skin Centre, Singapore

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Background: Excimer light phototherapy (308 nm) is a form of targeted phototherapy shown in controlled studies to be effective in the treatment of localized vitiligo and psoriasis. This study aims to assess its role in a predominantly Asian population at the National Skin Centre, Singapore.

Materials and methods: We retrospectively reviewed the clinical data of 247 patients who were started on excimer lamp phototherapy at the National Skin Centre over a 5-year period from 2008 to 2012. The phototherapy system used was the (308 ± 2 nm) VTRAC excimer lamp system (Photomedex, Horsham, PA). The data analyzed included the diagnoses, epidemiological data, clinical responses and adverse effects.

Results: Most patients were Chinese (68.4%) followed by Indians (14.2%) and Malays (8.9%). The patients treated had ages ranging from 3 to 74 years old, with 55.5% of them being men. The most common skin disorder treated with excimer lamp phototherapy was vitiligo (80.6%) followed by psoriasis (15.4%), endogenous eczema (1.6%) and mycosis fungoides (0.4%). Majority of patients with vitiligo (90.2%) and psoriasis (97.4%) had tried other treatments including topical corticosteroids and NBUVB before starting on excimer phototherapy. 37% of patients with vitiligo achieved at least 50% improvement after a mean number of 18 sessions of excimer lamp phototherapy while 35.3% of patients with psoriasis achieved at least 50% improvement after a mean number of 15.7 sessions. One-third of patients experienced some minor adverse effects during the treatment, most commonly erythema (22.3%) and pruritus (5.7%). No patient had to stop phototherapy because of adverse effects.

Conclusion: Excimer lamp phototherapy is a safe and well-tolerated treatment in our local population, with fairly good efficacy in recalcitrant vitiligo and psoriasis that had persisted despite other treatments.

Commercial support: None identified.

2533

Actinic reticuloid in the setting of HIV

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Background: Actinic reticuloid (AR) is a rare, severe variant of chronic actinic dermatitis (CAD), an eczematous hypersensitivity reaction to ultraviolet (UV) rays. HIV infection has been linked to CAD/AR and may play a role in the disease process.

Case report: A 63-year-old white male with a medical history of recent HIV diagnosis (CD4 255, not on antiretroviral treatment) presented with a 14-month history of a progressive, eczematous eruption. Early in the disease course, affected areas were limited to sun-exposed body surfaces but the condition progressed over time to involve covered areas. Clinically, there was scaling erythema of the face with ectropion. Involving the trunk, arms, and legs were erythematous papules coalescing to form infiltrated plaques. There was hyperkeratosis of the soles and an infiltrative, dyshidrotic eruption of the palms. Histology revealed epidermal acanthosis, epidermotropism, and a strongly CD8+ lymphocytic infiltrate in the dermis with few giant cells and eosinophils. Polymerase chain reaction (PCR) for T-cell receptor (TCR) gene rearrangement was negative. A diagnosis of AR was made. The patient was started on antiretroviral therapy and systemic prednisone which led to significant cutaneous improvement.

Discussion: AR is a photosensitive dermatosis considered to be a severe variant of CAD. Clinically, patients present with infiltrated papules coalescing to form lymphomatoid plaques typically on sun-exposed sites. When severe, non–sun exposed sites can be affected. It is important to exclude cutaneous T-cell lymphoma in suspected cases of AR as the two conditions share some clinical and histologic features. In AR, the infiltrate is typically CD8+ and PCR for TCR gene rearrangement will be negative. The pathogenesis of CAD/AR has not been fully elucidated but is thought to be a delayed type hypersensitivity reaction to UV rays. CAD/AR has also been linked to HIV and has been reported as the presenting manifestation in several HIV patients. One hypothesis suggests that progression of HIV infection leads to decreased CD4:CD8 ratio with subsequent loss of control of the antiself response. CD8+ lymphocytes are then able to react to some photoinduced antigen essentially unchecked, simulating a pseudolymphomatous process.

Conclusion: AR is an uncommon variant of CAD and may serve as the initial presentation of HIV infection. Its pathogenesis in HIV patients is thought to be fueled by unchecked, reactive CD8+ lymphocytes.

Commercial support: None identified.

3561

Actinic prurigo

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Actinic prurigo is a rare photodermatosis characterized by acute eruptions of papules or papulovesicles and persistent eroded nodules that are intensely pruritic. Photosensitivity to UVA and UVB is severe. Sun exposed sites, particularly the dorsal nose, cheeks, chin, earlobes, forehead and extensor forearms are most commonly involved. Cheilitis, conjunctivitis and pruritus are also characteristic. Postinflammatory scarring and hypopigmentation may be prominent. Actinic prurigo was first described in South and Central American and among Native Americans in Canada and the United States. Cases were later reported among European whites and Asians. Usually, it begins in childhood before the age of ten years. It is more common in girls, with a female to male ratio estimated to be 2-6:1. Actinic prurigo often resolves by adolescence, but may persist indefinitely. Here we report a case of actinic prurigo undiagnosed until the patient was in her 30s. We also detail the evaluation and treatment options. Actinic prurigo differs from polymorphous light reaction (PMLE) as it may involve covered sites, such as the buttocks. Hardening does not occur. Although generally worse in spring and summer, actinic prurigo is perennial. Distinguishing actinic prurigo from PMLE, atopic dermatitis, insect bites, prurigo nodularis, lupus erythematosus or if scarring is severe, erythropoietic protoporphyria is important, particularly if the patient presents to the provider in adulthood. Sunlight avoidance and potent corticosteroids are first line treatments; however, these are often insufficient. Thalidomide may be more useful, but teratogenicity limits its use. Hydroxychloroquine has been reported not to be efficacious, although in the case we present here, our patient had a dramatic response.

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2860

Comparison of sunburn protection offered by beach umbrella against high SPF sunscreen in a randomized in use study

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Seeking shade is one way to avoid sun exposure. Other methods include wearing protective clothes and applying sunscreens. Shade works by physically shielding skin from direct harmful UV rays. However, UV rays can also reach the skin from other angles. There is a lack of clinical evidence that shade can provide sufficient protection when used in real life and it is not clear whether people still need to wear protective clothes or sunscreen under the shade. We directly measured sunburn protection offered by a beach umbrella in comparison to a high SPF sunscreen in a randomized, evaluator-blinded, in-use clinical study. Eighty-one subjects were divided into two groups, one using only a beach umbrella and the other using only SPF 100 sunscreen as its sun protection measure. The subjects in both groups were kept side-by-side for three and half hours at a beach in a park in Texas. Clinical sunburn evaluation was conducted at baseline and 24 hours following the exposure for all exposed body sites for each subject. Overall, the beach umbrella offered poor sunburn protection compared to high SPF sunscreen. Of the subjects in the umbrella group, 78% showed an increase of erythema on one or more body sites vs. only 25% of the subjects in the sunscreen group. Of the total body sites evaluated, 49.5% worsened after exposure for the umbrella group vs. 6.1% for the sunscreen group. For all the body sites evaluated, the umbrella group showed a significant increase in clinical sunburn scores. We conclude that shade, such as that offered by a beach umbrella, may not provide sufficient sun protection for an extended exposure. It is important to consider multiple sun protection measures and combine them, rather than relying on a single approach.

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3154

Curettage-assisted aminolevulinic acid photodynamic therapy in the treatment of erosive pustular dermatosis of the scalp: A case series

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Erosive pustular dermatosis of the scalp (EPDS) is a rare inflammatory disease of unknown etiology that usually occurs in the elderly. It is characterized by sterile pustules, and chronic crusted erosions that can lead to cicatricial alopecia and skin atrophy. Treatments such as topical steroids, topical and oral retinoids, topical tacrolimus, calcipotriol, oral and topical dapsone, and cryotherapy have met with varying success partly because of difficulty penetrating the hyperkeratotic crust, and the tendency of EPDS to recur after any treatment that induces trauma to the skin. Only 2 cases of successful treatment of EPDS with ALA-PDT have been reported. EPDS has been reported to improve, and be induced by, methylaminolevulinate PDT. In this case series, we present 8 patients (ages 67-93) with EPDS who had failed several topical and/or oral treatments and were then successfully treated with gentle curettage followed by 5-aminolevulinic acid (ALA) photodynamic therapy (PDT). In our treatment protocol, curettage, which was followed by daily application of a petrolatum-based ointment, was performed 1-2 weeks prior to PDT rather than immediately prior to application of the photosensitizer in order to minimize the postoperative discomfort such as stinging and burning sensation from ALA-PDT. The PDT protocol included a 1 hour application of a 20% 5- ALA solution followed by exposure to blue light for 16 minutes and 40 seconds. One patient required a second treatment because of partial improvement. Follow-up has ranged from 3-10 months, and to date, there have been no recurrences and no adverse effects (ie, no burning, stinging, or postprocedure pain). ALA-PDT targets mitotically active cells in inflammatory lesions, which may explain its success in EPDS, an inflammatory dermatosis. However, in the authors' experience, performing ALA-PDT without prior curettage in EPDS often results in suboptimal response because the massive hyperkeratosis of the lesions inhibits the accumulation of ALA within cells. Curettage of the hyperkeratosis prior to PDT in EPDS utilizes the same concept as that of ablative fractional resurfacing laser-assisted PDT for actinic keratoses, allowing for a more even and deeper effect of the ALA-PDT. Contrary to topical and oral medications that show inconsistent efficacy in EPDS and possible adverse effects, ALA-PDT showed high efficacy and was not associated with any adverse effects in our series.

Commercial support: None identified.

2833

Evaluation of the short-term efficacy and tolerance of a sonic brush compared to manual cleansing on post-IPL recovery

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Background: Intense pulsed light (IPL) treatments are most commonly used for reducing brown spots and redness on the face, neck, and chest. IPL recovery time varies with initial redness and swelling within the first 24 hours followed by peeling and brown "micro-crust" regions that dissipates typically within 2 to 3 weeks. In an effort to expedite recovery time and improve short-term performance, we investigated the use of a sonic cleansing brush introduced 1 day after performing IPL.

Objective: Assess the effect of a sonic skin care brush on IPL recovery time and appearance of skin within 2 weeks of IPL treatment.

Methods: Ten women between the ages of 30 to 65 with uneven skin tone and moderate wrinkles were enrolled in this 2-week, split-face pilot study investigating the incorporation of a sonic skin care cleansing brush randomized to one side of their face versus manual cleansing beginning 24 hours post-IPL. Study participants were instructed to cleanse twice daily with a gentle cleanser and the sonic brush (with radiance brush head) on 1 side of their face for 30 seconds twice a day versus manual cleansing. Participants were additionally provided a moisturizer and sunscreen to use through the duration of the study. Participants returned to the clinic at 3, 7, 10, and 14 days for investigator assessments and complete questionnaires. Objective investigator assessments of wrinkles, smoothness, evenness of skin tone, radiance, and overall skin appearance were assessed using the Fitzpatrick 0-9 scale. Tolerance evaluations both objective investigator assessment (peeling, erythema, edema, and dryness) and subjective tolerance (burning, stinging, itching, and tingling) were graded using a 0-3 scale.

Results: Following IPL treatment, the side of the face randomized to the sonic brush had greater improvements in objective measures of smoothness at 7, 10 and 14 days post IPL (Wilcoxon signed rank $P = .023$, 0.010, and 0.046, respectively), evenness at days 10 and 14 ($P = .024$ and 0.033), radiance at 7 and 10 days ($P = .034$ and 0.028), and overall skin appearance at 7, and 10 days ($P = .014$ and 0.024). The sonic brush was well tolerated at all visits with no differences in tolerance scores (objective and subjective) between the side cleansed with the sonic brush versus manual cleansing; all tolerance measures returned to 0 at day 14 for both cleansing methods. 100% of participants reported that sonic cleansing improved reduction of brown spots/micro-crusts.

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3937

Duration of efficacy for daily facial sunscreen product

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Objective: To determine the time duration of photoprotection/efficacy of facial moisturizer containing UV filters under controlled, clinical testing and ad lib use.

Background: Proper use of sunscreens is complex if not confusing, eg, recreational vs. daily, amount applied, frequency of application, and ideal performance, ie, SPF and/or broad-spectrum protection. The AAD position statement on sunscreens states "...using a broad-spectrum (UVA and UVB protection) sunscreen with SPF 30 or higher and meeting the UVA protection criteria..." This recommendation has evolved from applying daily SPF 15 broad-spectrum protection to the current SPF 30. The escalation in SPF number over time, ie, 15 to 30, is based, in part, on the premise that consumers do not apply the dose of product used to determine in vivo SPF. Further, current directions for use state "...reapply every 2 hours..." when outside. Arguably, the SPF 30 and reapplication lose some practicality in the context of sunscreens designed for low intensity, incidental UV exposure.

Method: The SPF of a daily facial moisturizer, SPF 15 broad-spectrum protection, was determined 8 hr after single application using the current FDA method except for the time at which SPF was determined. Separately, subjects in Cincinnati OH were instructed to apply ad lib an SPF 15 broad-spectrum protection facial moisturizer product in the morning and go about normal activities for the day. The area treated was determined using UV imaging photography assessed before and at select time points after product application.

Results: The static SPF of a facial moisturizer SPF 15 broad-spectrum protection is maintained over 8 hr of limited activity. Facial products are applied at or near the tested SPE ie, 2 mg/cm^2. UV protection with facial moisturizers differing in SPF are maintained over 8 hr under normal conditions, ie, office work, homemaking.

Conclusion: Daily incidental UV exposure, largely to face, accounts for a large portion of the cumulative lifetime UV damage. However, sunscreen products are, generally speaking, considered for recreational use, ie, high intensity, intermittent use. This pattern of exposure, albeit important, in not the manner in which the majority of modern, urban populations are affected by sunlight. In the present study, it is shown that a single application of a facial moisturizer SPF 15 broad spectrum protection provides long lasting, ie, 8-hr, protection under normal daily activities.

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3753

Extracorporeal photopheresis in the treatment of CTCL: A single center long term experience

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Introduction: Initially extracorporeal photopheresis (ECP) was designed for the treatment of cutaneous T-cell lymphoma (CTCL), Sezary syndrome variant. Further indications have been documented in recent years, eg, systemic sclerosis, graft-vs-host-disease, solid organ transplant rejection. The present study describes our experience with ECP alone or in combination with interferon alpha, PUVA, total skin electron beam, steroids and chlorambucil in treating CTCL patients.

Materials and methods: 26 patients with CTCL over a period of 25 years were evaluated in a retrospective manner. Multiple standard clinical and laboratory findings usually identified as indicators for response to treatment were evaluated. Age at disease onset, time elapsed before treatment and clinical stage were included. Analysis encompassed erythroderma, WBC, LDH, and CD4/CD8 ratio.

Results: At the time of diagnosis of CTCL mean patient's age was 58.6 years (range 37-78). Male to female ratio was 1.25:1. All 26 patients received ECP for more than 10 cycles. The mean number of ECP cycles was 54.2 (range 14-148 cycles). Overall survival rates were estimated by Kaplan–Meier method and compared using log-rank tests. The median overall survival was 5.9 years (range, 0.8-17.8 years) regardless of cause of death or blood involvement. A reduction of specific laboratory parameters correlated with response to treatment.

Conclusion: Patients with CTCL receiving ECP treatment with or without combination of immune-modulatory therapy experience higher response rates and longer survival than controls. Our study suggests that the use of extracorporeal photopheresis can have a significant positive effect on survival of a subset of CTCL patients.

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HIV photodermatitis presenting as vitiligo in photodistributed areas

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A 56-year-old Hispanic man with untreated HIV (CD4+ lymphocyte count of 43) presented with pruritic patches in sun-exposed areas. Medications included methadone. Physical examination revealed erythematous and depigmented patches on the face, ears and dorsal arms. Laboratories for autoimmune disease, syphilis, tuberculosis, and porphyria were negative. Histology of an erythematous patch showed lichenoid dermatitis with eosinophils, consistent with lichenoid drug eruption or lichenoid photodermatitis. MART-1 immunostain highlighted absence of melanocytes and Fontana-Masson stain detected no melanin deposits. Staining for T cell markers revealed a decreased CD4+/CD8+ ratio of 0.6, with prominent exocytosis of CD8+ T cells into the basal layer of the epidermis, suggesting a direct cell-to-cell interaction with melanocytes. The patient was treated with topical corticosteroids and encouraged to initiate antiretroviral therapy and photoprotection.

Discussion: HIV is a photosensitizing condition, even in the absence of photosensitizing medications. Here we present a rare clinical presentation of HIV photodermatitis presenting with lichenoid inflammation and the loss of melanocytes. The differential diagnosis for this case includes primary inflammatory vitiligo or photodermatitis leading secondarily to vitiligo. We favor the latter because of the clinical history, the photodistribution of depigmented areas, and the presence of a dense lichenoid infiltrate with eosinophils. Postinflammatory hypopigmentation was another consideration, but the absence of melanocytes argues again it.

Conclusion: Vitiligo is increasingly being reported in patients with a background of immunosuppression, including HIV. Though the exact link between HIV, photodermatitis, and vitiligo is unknown, our patient's low CD4+/CD8+ lymphocyte ratio suggests that cell-mediated cytotoxicity may be involved in melanocyte destruction.

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3009

Impact of sun exposure and actinic damage on shrinkage of surgical specimens

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Introduction: The shrinkage of surgical specimens (SS) of human skin is known, which has been attributed mainly to the retractile properties of the SS, contrary to the classical hypothesis attributing it to the action of formalin. Has been studied the influence of sex and localization, being observed bigger contraction at younger ages and the SS located in the trunk and extremities. However it has never studied the impact of chronic sun exposure (CSE) and actinic damage (AD) on the shrinkage of the SS.

Objectives: To evaluate the impact of CSE and AD on the shrinkage of the SS.

Methodology: A cross-sectional, descriptive observational study was performed in patients who had undergone surgery during a ten-month period. It included consecutive patients and data were gathered on age, CSE, AD and specimen width and length before surgical excision (before SE), at 5 minutes postsurgery (ex vivo) and after 24 h of fixation in 10% buffered formalin (postfixation).

Results: 251 patients were collected with a mean age of 63.9 years (standard deviation [SD] 19.2), of which 182 (72.5%) reported CSE and 177 (70.5%) reported AD. The mean shrinkage between before SE to postfixation in patients with / without CSE was 0.18cm (SD 0.22) / 0.26cm (SD 0.32) and 0.41cm (SD 0.39) / 0.48cm (SD 0.33), and in those with / without AD was 0.18cm (SD 0.23) / 0.24cm (SD 0.31) and 0.40cm (SD 0.39) / 0.52cm (SD 0.35) of width and length, respectively. A greater shrinkage of SS of patients without CSE / AD of 30.8%/25.0% and 14.6%/23.1% between before SE to postfixation, of 10.5%/2.2% and 5%/18.2% between before SE to ex vivo and 93.6%/93.1% and 63.7%/60.5% between ex vivo to postfixation of width and length was observed, respectively. There were statistically significant differences ($P < .05$) between measures of length of SS of patients with/without AD between before SE to postfixation and of width of SS of patients with/without CSE and AD between ex vivo to postfixation.

Limitations: The skin of SS was diseased and no other potentially influential factors were studied.

Conclusions: The skin under CSE or AD seems to have less contractile capacity than not exposed to the sun continuously. This is probably due to damage from the sun on the dermis and epidermis. It should be taken into account in the assessment of discrepancies between surgical and histopathologic measurements of SS.

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3912

Hydroa vacciniforme and granulomatous uveitis in association with EBV

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An 8-year-old Hispanic female presented to pediatric dermatology with an asymptomatic, recurrent rash on the bilateral temporal face, chest, and shoulders present for 5 months. Physical examination revealed several small 1-2 mm white dome-shaped papules with central umbilication on the face and chest. There were also rare, scattered erythematous papules and papulovesicles, with several ovoid shallow scars on the bilateral temples, cheeks and nose. Biopsy was performed and revealed superficial and deep perivascular and periadnexal infiltrates. Immunohistochemical staining utilizing EBV LMP-1 staining was positive in many perifollicular epithelia. Complete blood count (CBC) and liver function tests (LFTs) were within normal limits. EBV serologic testing was consistent with recent infection. Ophthalmologic evaluation revealed a granulomatous uveitis. The patient's clinical and laboratory findings were felt to be consistent with EBV-associated hydroa vacciniforme. Hydroa vacciniforme (HV) is a rare pediatric photodermatitis characterized by symmetric papulovesicular lesions that heal with varioliform scarring on sun exposed areas. It can be associated with EBV infections, particularly if necrotic lesions are present. This EBV-associated HV may manifest as a more severe form of disease that is associated with lymphoproliferative disorders, such as hydroa vacciniforme-like lymphoma (HVLL). HVLL is a rare EBV positive cutaneous T-cell lymphoma that usually occurs in children. In addition to the typical lesions seen in HV, HVLL may present with facial edema, ulcerative lesions, large hemorrhagic bullae, and atrophic scars on both sun-exposed and non—sun-exposed skin. Therefore, sun exposure is not thought to induce HVLL. HV more commonly affects males who also have a later onset and longer disease course (mean duration of HV is 9 years). Patients may experience pruritus or a burning sensation a few hours or days after sun exposure, followed by the onset of erythematous macules that progress to necrotic crusts. HV is rarely associated with ocular and oral involvement as well as deformities of the hands, ears, and nose that are typically related to scarring. Ocular manifestations include photophobia, conjunctivitis, anterior uveitis, keratitis, and corneal opacities. Laboratory evaluation, including CBC with differential and LFTs, may identify severe HV and its variants which can be associated with high fevers, facial swelling, liver damage, and hematologic abnormalities. Sun protection is vital for the management of HV. Suggested treatment for EBV-associated HV includes acyclovir (28-72 mg/kg/day, divided into 2-5 doses) or valacyclovir (60 mg/kg/day divided twice daily) for 2-4 week periods, or continuously. Our patient was treated with acyclovir 40mg/kg/day divided twice daily for 4 weeks, along with sun protection.

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Linear nevoid psoriasis responsive to narrowband UVB phototherapy

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Linear nevoid psoriasis is a rare form of psoriasis with few cases reported in the literature. The main differential diagnosis is inflammatory linear verrucous epidermal nevus (ILVEN). While ILVEN is usually refractory to therapy, linear nevoid psoriasis responds well to antipsoriatic treatment. We report the first case of linear nevoid psoriasis treated with narrowband-UVB with good response. A 4-year-old girl presented with a disseminated dermatosis that appeared during her first year of life. Physical examination revealed irregular, erythematous confluent papules and plaques with fine scaling affecting the left axillary region, left upper thigh and left iliac region, arranged in a linear distribution along Blaschko's lines. An erythematous plaque was found on her scalp. Presumptive diagnoses of lichen striatus, linear psoriasis and ILVEN were considered. A skin biopsy revealed hyperkeratosis, parakeratosis, regular psoriasiform hyperplasia, agranulosis, Munro's microabscesses, blood vessel dilation and a perivascular lymphocytic infiltrate in the upper dermis. A diagnosis of linear Blaschkoid psoriasis was made. Fluocinolone acetonide cream once daily was prescribed with mild improvement after three weeks. Later, nb-UVB phototherapy was initiated; she is currently receiving 700 mJ/cm^2, two to three times a week with excellent improvement after 37 sessions. Linear nevoid psoriasis is a rare variant of psoriasis presenting along Blaschko's lines at birth or early in life. The main differential diagnosis is ILVEN, which can be clinically and histologically identical. Linear psoriasis usually has a later onset and presents with asymptomatic or slightly itchy lesions; scalp and nail involvement is possible. ILVEN may appear during the first months of life, lesions are more pruritic, and it is resistant to antipsoriatic therapy. The pathogenesis is unclear. It has been explained by genetic mosaicism, where certain cells react differently from other cells in the same anatomic area, due to chromosomal abnormalities. Treatment consists of topical corticosteroids, calcipotriol, methotrexate and psoralen UVA phototherapy (PUVA). Previous reports have described successful treatment with systemic psoralens and UVA exposure (PUVA) either alone, or in combination with oral methotrexate. This is the first reported case of linear nevoid psoriasis treated with nb-UVB with good response. We expect further improvement as we increase the dose and more sessions are received.

Commercial support: None identified.

2802

Metal oxide sunscreens protect skin primarily by absorption, not by reflection or scattering

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The inorganic metal oxide sunscreens titanium dioxide and zinc oxide have been considered to protect against sun burning ultraviolet radiation by physically reflecting/scattering the incident photons and thus protecting the skin. Earlier publications suggested, however, that the primary action of UV protection by these sunscreen agents is through absorption and not by reflection. The purpose of this work was to quantitate the contributions of each of these modes of action to the protection provided by these inorganic UV sunscreen filters. An optical integrating sphere was used to measure the transmission and the reflectance of titanium dioxide and zinc oxide. The average range of reflection for zinc oxide and titanium dioxide throughout the UV range was only 4-5%, providing minimal UV protection via this mechanism. The remainder of the UV protection is provided by semiconductor band gap-mediated absorbance of the UV photons. At wavelengths above the semiconductor band gap, absorption energy levels (in the long UVA and visible wavelengths), these sunscreen filters are predominantly reflectors of light (up to 60% reflection) and nonabsorbing. We conclude that titanium dioxide and zinc oxide provide UV protection primarily via absorption of UV radiation, and not through significant reflection or scattering means.

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3617

Miliaria crystallina in a patient with chronic myelogenous leukemia on dasatinib

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A 40-year-old female with chronic myelogenous leukemia (CML) presented with a one day history of vesicles on her upper and lower extremities. Patient was diagnosed in 2009 with CML and had been treated in the past with nilotinib, hydroxyurea, as well as combination of clofarabine, idarubicin, and cytarabine. Nine days prior to presentation, patient was started on dasatinib 100 mg by mouth daily. On the morning of presentation, the patient was in a shaded area outside and within fifteen minutes developed vesicles on her upper and lower extremities which were nontender and nonpruritic. She went to the emergency department where dermatology was consulted to evaluate for possible bullous drug eruption. She no fevers or chills and had normal oral intake. On exam, there were 1-3 mm clear delicate vesicles on her upper extremities extending from her apical shoulder to her distal forearm as well as her anterior thighs and lower legs sparing her feet which displayed new nonpitting edema. No oral or genital lesions were noted. Her labs showed neutropenia (ANC 154) with a platelets of 15 K/uL. Her sodium was 132 meq/mL, phosphorous 5.1 mg/dL. Punch biopsies taken from her thigh showed a paucinflammatory subcorneal vesicle centered over the acrosyringium. Conservative therapy was advised and the patient reported that the lesions self-resolved within a few days of their formation with some lesions leaving 1-2 mm postinflammatory hyperpigmentation. Chronic myeloid leukemia, which accounts for 20% of all adult leukemias, is caused by a constitutively active tyrosine kinase, BCR-ABL, which drives malignant growth in leukemic stem cells. Dasatinib is a tyrosine kinase inhibitor with affinity for BCR-ABL and KIT. It is FDA approved for the treatment of CML, including CML with imatinib resistance, and has several cutaneous adverse effects, including morbilliform rash, skin lightening, phototoxicity, panniculitis, and edema. Miliaria crystallina is an asymptomatic occlusion of the acrosyringium commonly reported in neonates, hypernatremic patients, and has not been reported in association with dasatinib. It has been reported in a CML patient who had undergone induction chemotherapy with liposomal doxorubicin erupting with clear vesicles on day 5 posttreatment. It may be that in our case the miliaria could have been due to one of her prior treatments; however, dasatinib was the only new medication that she had been given. This case highlights a unique association of dasatinib with miliaria crystallina which may be confused with a more significant bullous drug eruption.

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2995

Patch and photo patch test in suspected chronic actinic dermatitis patients

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Introduction: Chronic actinic dermatitis is characterized by persistent eczematous eruption on sun exposed body areas for >3 months; sensitivity to UVL and often visible light and histologically characterized by features of dermatitis with few atypical mononuclear cells. Many patients are positive to multiple contact allergens and have a background of preexisting allergic contact or endogenous (atopic or seborrheic) dermatitis.

Method: We reviewed all cases of chronic actinic dermatitis, who were diagnosed and treated, in our institute during last 5 years. Detailed history and clinical examination was carried out. Patch test was done using Indian standard series and parthenium acetone extracts. Photo patch test was performed by using Scandinavian photo patch antigen series with the addition of parthenium and compositae mix by standard method.

Results: One hundred one patients including 69 were male and 32 females (ratio 2.15:1) were recorded. Mean age at diagnosis was 49.89 years. Mean duration of illness was 6.52 years (range: 0.5-30 years). Most common occupation was farmer in 30 (29.70%) patients. Lichenified hyperpigmented plaques over photoexposed sites was the most common presentation. Photosensitivity was seen in 64 (63.36%) patients. Fifty two patients (56.43%) patients had aggravation in summer and winter exacerbation was observed in 5 patients. Exposure to parthenium was observed in 70 ((69.30%), hair dye in 27 (26.73%), and history of atopy was present in 20 (19.80%) patients. Patch test was performed in all 101 patients and photo patch test in 86 patients. Patch test was positive in 71 (70.29%) patients and photo patch test was positive in 12 (13.95%) patients. Parthenium with acetone extract (1:100) and (1:200) was most common positive allergen as it was positive in 52 (51.48%) patch test and 3 (3.48%) photo patch test. Partheniolide was positive in 10 cases, colophony in six, fragrance mix and p-phenylenediamine (PPD) base in 5 patch tests, compositae mix in 4, nitrofurazon, potassium dichromate, thiuram mix and epoxy resin in three each. Photo patch tests showed positive results for parthenium and perfume mix in 3 each, balsam of Peru in 2, thiuram mix, compositae mix and promethazine hydrochloride in one patient each.

Conclusion: Parthenium, perfume mix, PPD most common positive allergens in CAD like pattern of dermatitis in our series. Parthenium, perfume mix and balsam o Peru were common photopatch test positive in patients with CAD.

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Photoonycholysis mediated by 8% clobetasol nail lacquer

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A 12-year-old boy with personal history of twenty-nail dystrophy underwent treatment with 8% clobetasol propionate in nail lacquer prescription. Two weeks after the beginning of the treatment the patient started with intense pain in his nails. One week later he developed black eruptive macules under the nail plate, mostly in the third finger of his left hand and in the fifth finger of his right hand. After investigating the composition of the nail lacquer, a clinical diagnosis of photoonycholysis mediated by benzophenone was made. We recommended the patient to avoid the nail lacquer and sun protection of the nails. 6 weeks after the treatment was stopped the photoonycholysis lesions had disappeared. Photoonycholysis is a likely side effect of therapies with some antibiotics, such as tetracycline derivatives or fluoroquinolones, psoralens, captopril or thiazide diuretics, due to cutaneous photosensitization. It usually appears after more than two weeks of exposure to the drug and it often follows a photosensitivity reaction in the skin. However, it can also appear in the absence of photosensitive reaction. Onychodynia is the first symptom in most patients, followed by discoloration of the nails and onycholysis from 1 to 4 weeks. Additionally, photoonycholysis has been reported in porphyria cutanea tarda, erythropoietic porphyria, variegate porphyria, erythropoietic protoporphyria and pseudoporphyria. It is known that benzophenone is a phototoxic substance whose action occurs within ultraviolet A (UVA) and ultraviolet B (UVB) spectrum. Photosensitization of benzophenone provokes an oxidation of linolenic acid, resulting in formation of free radicals which react with oxygen. Minor structural changes in the benzophenone molecule influence its phototoxic properties. The importance of this case resides in the fact that some benzophenone derivatives are used as UV filters in sunscreens, some of which have shown positive photopatch responses.

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3133

Realistic sunscreen durability—A randomized, double-blinded, controlled clinical study

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Background: The American Academy of Dermatology and FDA recommend reapplying sunscreen at two hour intervals. Additionally, the sun protection factor (SPF) of sunscreens is tested using a thickness of 2 mg/cm^2. However, studies show that sunscreen under real-life conditions is neither applied sufficiently and often not reapplied. Recently developed sunscreen products claim to offer improved water resistance and photostability. This study investigated the durability of two current sunscreens with different SPF protection over an eight hour period.

Methods: Participants (n = 50) were randomized into two study groups utilizing either 2 mg/cm^2 (FDA testing concentration) or 1 mg/cm^2 (real-life application levels) amounts of sunscreen. Two current SPF 15 and 70 sunscreens were applied to test spots on each participant's back. In vivo SPF values were obtained at baseline, 3.5, and 8 hours post initial application during which subjects completed 30 minutes of moderate exercise followed by 80 minutes of water exposure. All participants and evaluators were blinded of their study group or product used.

Results: Participants in both dose study groups revealed only a 15-20% overall decrease in their SPF protection 8 hours after application. The study group that received half the FDA test concentration of sunscreen also achieved approximately half or less the labeled SPF. At 8 hours, the test sites that received SPF 70 maintained an average SPF greater than 60 (2 mg/cm^2 application) and 20 (1 mg/cm^2 application). Similarly, the SPF 15 product test sites revealed an in vivo protection of 12 (2 mg/cm^2) and 6 (1 mg/cm^2).

Conclusions: This study demonstrates that current sunscreens may be durable on skin even following significant exercise and water exposure suggesting that reapplication intervals may be longer than currently recommended. In addition, the higher SPF sunscreen maintained a skin-cancer protective level of SPF following extended use. High SPF sunscreen may provide an additional margin of safety especially for people who do not reapply frequently. Advances in sunscreen technology should continue to involve higher SPF products that can offer durable real-use protection.

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3587

Retrospective review antinuclear antibodies in phototherapy

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Background: Dermatologists often order a pretreatment antinuclear antibody (ANA) titer prior to initiation of phototherapy to screen for photosensitive disorders. Checking an ANA rarely alters the treatment course of the patient. However, the patient is often subjected to additional testing and clinician visits such as rheumatology consultations if the pretreatment ANA is positive, leading to potentially avoidable delays in treatment and increased healthcare costs. The need for obtaining an ANA in all patients prior to initiating psoralen and ultraviolet A (PUVA) therapy has remained an issue of debate ever since data from early studies suggested that PUVA therapy could potentially cause patients to develop a positive ANA. Accordingly, early guidelines recommended obtaining an ANA in all patients prior to initiation of PUVA treatment in order to exclude diseases for which PUVA is contraindicated such as systemic lupus erythematosus (SLE). Subsequent studies suggested that obtaining an ANA prior to PUVA administration may not be necessary for all patients. The most recent American Academy of Dermatology guidelines on the role of phototherapy in patients with psoriasis and psoriatic arthritis suggest obtaining a pretreatment ANA only if indicated based on the patient's history. Although most of the controversy has surrounded PUVA therapy, clinicians often check an ANA prior to phototherapy with narrowband ultraviolet B (NB-UVB) or ultraviolet A1 (UVA1). We hypothesize that routinely checking ANA in all patients prior to phototherapy leads to delay in treatment and does not lead to the patient being excluded from receiving phototherapy for medical reasons.

Objectives: 1. Determine the outcome if patients have a positive ANA. Specifically, we wanted to determine if the positive ANA caused delay in treatment and whether the patient required clearance by a rheumatologist. 2. Determine if patients developed a positive ANA during or after phototherapy. 3. Determine if patients developed a connective tissue disease during or after phototherapy.

Study design: A retrospective chart review of patients ≥18 years old in whom phototherapy was prescribed at the University of South Florida in Tampa between January 1, 2006 and June 17, 2013. Patients <18 years old or those who were unable to start phototherapy due to nonmedical reasons were excluded. Patients who received phototherapy were identified by several methods including a manual review of phototherapy log books, a review of prior authorizations utilized for coverage determination, and searching phototherapy CPT codes. Data related to patient demographics, disease being treated, pretreatment ANA, subsequent ANAs, time from the initial visit to the onset of phototherapy, duration and number of treatments, and type of phototherapy received were also obtained.

Results: There were 509 total patients with ANA assessments. The ANA was positive in 20 patients and negative in 489. There were no statistically significant differences in the baseline variables of patients with a positive or negative ANA. The time between obtaining an ANA and the commencement of phototherapy was statistically significant between those with a positive or negative ANA. Patients with a negative ANA had a median time to treatment of 25 days compared to those with a positive ANA of 49 days. The median time between ordering phototherapy and first treatment was 19 days for patients with a negative ANA and 76 days for patients with a positive ANA, a statistically significant delay in treatment ($P = .0039$). Of the 20 patients with a positive ANA, clearance was obtained by a rheumatologist in 19 cases; one was cleared by the ordering dermatologist. No patients developed a photosensitive connective tissue disease during treatment. Seventy-nine patients had follow-up ANAs. Of these, 6 had a pretreatment positive ANA and 7 had a positive follow-up ANA. All 7 of these patients' original ANA was negative.

Conclusions: Pretreatment ANA assessment is often unnecessary and leads to increased health care costs and delayed treatment. Of the patients with a positive ANA all were eventually cleared. Furthermore, a positive ANA significantly delays care if they need to be seen by a rheumatologist. Dermatologists are excellent at diagnosing photosensitive dermatoses such as SLE and dermatomyositis. If the patient has a condition for which phototherapy is recommended, a dermatologist can more often than not rule out a photosensitive connective tissue disease based on history, review of systems, physical exam, and skin biopsy.

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Skin photorejuvenation effects of light emitting diodes: A comparative study of yellow and red light emitting diodes in vitro and in vivo

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Red-colored light-emitting diodes (LEDs) can improve skin photorejuvenation and regeneration by increasing cellular metabolic activity. We evaluated the effectiveness of visible LEDs with specific wavelengths for skin photorejuvenation in vitro and in vivo. In methods, normal human dermal fibroblasts (HFs) from neonatal foreskin were cultured and irradiated in vitro by LEDs at different wavelengths (410-850 nm) and doses (0-10 J/cm^2). In vivo experiments were performed on the skin of hairless mice. Collagen (COL) and matrix metalloprotcinase (MMP) expression were evaluated via semiquantitative reverse transcription (RT)-PCR, western blot analysis, and a procollagen type I C-peptide enzyme immunoassay (EIA assay). Hematoxylin—eosin and Masson's trichrome staining were performed to evaluate histologic changes. In results, COL I was upregulated and MMP-1 was downregulated in response to LED irradiation at 595 ± 2 nm and 630 ± 8 nm in HFs. A peak EIA assay result was achieved at a dose of 5 J/cm^2 with an LED at 595 ± 2 nm. In vivo, COL I synthesis was upregulated in response to both 595-nm and 630-nm LED irradiation, and this impact was prolonged to 21 days after irradiation after a single 100 J/cm^2 dose. The histologic changes were consistent with the RT-PCR and western blot results. In conclusion, treatment with 595 ± 2 nm 630 ± 8 nm LEDs upregulated COL I expression and downregulated MMP expression, and the effects persisted at least 21 days after irradiation. These findings suggest that yellow and red-colored LEDs might be useful for skin photorejuvenation.

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2463

Solar urticaria: Study of 20 patients

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Introduction: Solar urticaria (SU) is a subtype of physical urticaria and an uncommon photodermatosis. It is characterized by a transient pruritic erythema or wheals after sun exposure.

Objective: To report the epidemiologic and clinical data, phototesting outcome and treatment of 20 patients with SU.

Methods: A retrospective study of 20 patients with SU, diagnosed in our center from 2009 to 2015, was performed. All patients were exposed to natural sunlight, and a phototest with ultraviolet light (UV) (specific UVA and UVB devices), visible light and solar simulator was carried out.

Results: 10 men and 10 women were included with mean age of 41 years. The mean duration of the disease was 72.4 months. An autoimmunity study was conducted in all patients, being all negative. Serum/urine porphyrin tests were done in 50 % of patients, being all negative. Total IgE plasma level was measured in 16/20 patients (80%), being high in 11/16 (68.75%). 70% of patients had a medical history of atopy, predominantly allergic rhinitis in 11 patients, 5 patients with atopic eczema, and bronchial asthma in 2 patients. Besides, 3 patients had physical dermographism, and 2 other dermatoses (polymorphic light eruption). Two cases were associated with lymphoma: one with non-Hodgkin lymphoma and the other with a cutaneous marginal zone lymphoma. The action spectrum was found in the visible light range in 5 patients (30%), visible light combined with UV-A range in 4 (25%), from the UV-A to the UV-B range in 2 (10%), visible light combined with UV-A range and UV-B range in 1 (5%), in the UV-A range in 1 (5%), and finally with fluorescent light in 1 patient. Symptoms could have not been provoked by phototesting in 4 patients (20%).

Discussion: Patients were divided into two groups for treatment: those with high tolerance were treated with antihistamines and sunscreens and an increased dose of natural exposition was prescribed. For those with low tolerance, a phototherapy treatment was implemented to induce hardening. The association between SU with atopy is higher than in the previously published series. The association in two cases with lymphoma has not been previously described in the literature. The action spectrum findings are similar to those previously described in the literature. The treatment algorithm described above might be effective in other cases, considering that almost all our patients showed a partial improvement.

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3657

Treatment of lipodermatosclerosis with UVA-1

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An 85-year-old female presenting with a 1.5-year history of bilateral leg edema, erythema, and pain. She had previously been diagnosed with cellulitis and treated with intravenous antibiotics while in the hospital, as well as PICC line placement and outpatient treatment with intravenous antibiotics. Serologies for ANA, rheumatoid factor, anti-double-stranded DNA, HLA-B27, CCP antibody, SS-A, and SS-B were negative. Both MRI and ultrasound were performed for each leg, and failed to demonstrate a deep venous thrombosis, evidence of infection, or osteomyelitis. Despite antibiotic therapy, she continued to have waxing and waning of her disease. After repeated admissions, dermatology was consulted and the patient was found to have poorly marginated, circumferential, red brown patches with fine white scaling involving the bilateral lower extremities. The areas involved had a firm, bound down appearance with atrophy giving an "inverted champagne bottle" appearance below the knee. Both legs demonstrated 1+ pitting edema and tenderness to palpation. Based on clinical appearance and history, our patient was diagnosed with lipodermatosclerosis. She was treated with clobetasol under occlusion, ACE wraps, and leg elevation. She initially had improvement with this, however her pain and inflammation returned despite continued treatment. Pentoxifylline was added to her regimen and this was also not successful. Due to treatment failure, she was treated with UVA-1, with three treatments weekly for a total of 20 treatments. With light therapy, her legs softened significantly, and she had marked improvement in her pain and erythema. After treatment with UVA-1, she only required Ace wrapping of her legs for maintenance with no recurrence of fibrosis, erythema, or pain. Both lipodermatosclerosis and localized scleroderma have been shown to have increased pyridinolines, which are hydroxylysine aldehyde derived cross-links in collagen, that are absent in healthy tissue. UVA has been shown to decrease these collagen cross-links. We believe that UVA-1 lead to remodeling of the extracellular matrix in our patient, as well as a decrease in inflammation, leading to her improved clinical findings. UVA-1 should be considered as an adjuvant to standard compression therapy in refractory cases of lipodermatosclerosis.

Commercial support: None identified.

3374

Vitamin D synthesis after UVB exposure in Asians

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Background: Ultraviolet B (UVB) irradiation is the main source of vitamin D in human. Sunlight exposure to obtain adequate vitamin D without or with minimal cutaneous damage is encouraging in a sunny climate. However, the sufficient amount of UVB to achieve adequate vitamin D status for Asian skin has never been determined.

Objectives: To determine the efficacy of frequent and short UVB exposures to improve vitamin D status in Asian ethnic people.

Materials and methods: Twenty five healthy Thai volunteers with skin type III-V were included. Participants exposed 30 % of their body surface area (BSA) to broadband UVB (BBUVB), 4 SEDs per session, twice weekly for 8 weeks. Blood samples for 25-hydroxyvitamin D3, 25-hydroxyvitamin D2, and parathyroid hormone levels were evaluated at baseline and every 4 weeks for 16 weeks. Cutaneous changes such as skin lightness (L), melanin (M) and erythema (E) index were assessed every 4 weeks.

Results: Twenty one volunteers completed the study. All but one subject were women. The mean age was 47 ± 14.01 years. Serum 25-hydroxyvitamin D3 level significantly increased by 2.88 ± 3.39 ng/ml at week 4 and 2.60 ± 3.32 ng/ml at week 8, from the mean baseline value of 23.63 ± 6.47 to 26.50 ± 6.98 and 26.23 ± 5.80 ng/ml ($P = .001$, $P = .002$), respectively. Mean serum 25-hydroxyvitamin D3 level declined steadily to 24.27 ± 5.97 and 22.88 ± 5.36 ng/ml after withdrawal of UVB exposure for 4 and 8 weeks, respectively ($P = .014$, $P = .001$). Serum 25 (OH) D3 level at baseline and 2 months post-irradiation was not different, ($P = .475$). No significant change of skin L, M, E index and serious side effects were observed throughout the study.

Conclusion: In skin type III-V or Asian skin, exposed 30% of their BSA to 4 SEDs of BBUVB twice weekly for 4-8 weeks increased serum vitamin D3 level significantly. The amount of UVB is equivalent to 5 minutes of midday sun exposure in Bangkok, Thailand.

Commercial support: None identified.

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PIGMENTARY DISORDERS AND VITILIGO

3281
Search for clinical and laboratory markers of severity and instability of vitiligo: A cross-sectional observational hospital based study

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Introduction: Vitiligo has always been troubling dermatologists due to unsatisfactory results every now and then, in spite of many treatment options available; keeping doctors on their toes in acquiring more and more knowledge about the disease. Vitiligo has recently been found to be associated with atopic diathesis and proposed explanations include melanocyte destruction by proinflammatory state of atopy, Koebnerization of vitiligo by scratching in pruritic atopic dermatitis and common genetic mutation(s) like vitamin D receptor polymorphisms in both vitiligo and atopic diathesis. The association of vitiligo with increased serum homocysteine (Hcy), decreased serum vitamin B-12 and decreased serum folic acid levels has also been studied and mechanisms proposed for increased Hcy levels causing 'pigmentary dilution' include melanocyte destruction, mutation in catalase gene and inhibition of histidase and tyrosinase.

Materials and methods: A cross-sectional observational study was conducted on 40 vitiligo patients and 40 matched controls and criteria for atopic diathesis, serum Hcy, vitamin B12, folic acid levels compared.

Results: History of atopy (47.5% vs 20%; $P < .05$) and clinical atopic diathesis were significantly associated with vitiligo (42.5% vs 15%; $P < .05$). Out of the following criteria: recurrent cough and cold, bronchial asthma, xerosis, chronically relapsing dermatitis, pruritus and family history of atopy; 5% of controls and 20% of cases fulfilled more than 3 criteria. Leukotrichia ($P < .05$) and early age of onset (22.4 vs 34.4 years; $P < .05$) were significantly found in patients of atopy. Mean Vitiligo Area Scoring Index (VASI) and mean percentage body surface area (BSA) involved was more in patients of atopy, but not significantly ($P > .05$). Elevated serum Hcy levels (72.5% vs 10%; $P < .05$) and reduced serum vitamin B-12 levels (70% vs 25%; $P < .05$) were significantly associated with vitiligo. No significant association was found with reduced serum folic acid levels. High VASI (39.47% vs 7.67%; $P < .05$) and larger mean percentage BSA (45.5% vs 10.5%; $P < .05$), unstable disease (72.5% vs 27.5%; $P < .05$); and leukotrichia were significantly associated with elevated Hcy levels.

Conclusion: Atopic diathesis, elevated serum Hcy and reduced serum vitamin B12 levels may be used as markers of severity and instability of vitiligo and included in work-up done on the first visit. There are no Indian studies on the same.

Commercial support: None identified.

3521
A rapid assessment of vitiligo lesion stability in view of melanocyte grafting

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Background: The assessment of stability status is crucial in view of melanocytes grafting. Until now, a delayed evaluation of stability status of vitiligo lesions was judged by three imprecise indicators: history, Koebner's phenomenon and test grafting. Therefore, it is important to discriminate active stage from stable stage.

Aim of the study: to introduce new and simple methodologies in order to develop a rapid and not delayed accuracy of staging.

Materials and method: Clinical assessment and disease activity: we proposed to separately identify the two more common clinical types of vitiligo: amelanotic with sharply demarcated borders and hypomelanotic with poorly defined lesions borders. Clinical pictures were taken at the time of the examination and a skin biopsy was performed concomitantly. All patients were examined one year after their first visit. The vitiligo was classified as stable if no new lesions had appeared and as spreading or active if there had been an increase in the number and/or size of existing vitiligo lesions. Histologic assessment: Skin biopsies from 71 patients were performed at the edge of vitiligo lesions. 8 to 10 sections from each patient were successively stained with hematoxylin-eosin and immunostained with HMB45, monoclonal antibodies against CD8 T-lymphocytes and E-cadherin. Statistical analysis: Statistical analysis was performed with the Windows 15.0 version of SPSS software (SPSS Inc, Chicago, IL, USA). $P < .05$ were regarded as significant.

Results: We have noticed a worsening in 46 patients and stability in 23 patients. The stable lesions were statistically associated to an amelanotic aspect with sharply defined borders ($P < .001$), and histologically by the lack of an inflammatory infiltrate of CD8-T lymphocytes in the epidermis and the dermis ($P = .017$) and a down-expression of E-cadherin at the membrane of keratinocytes ($P = .044$).

Discussion: The clinical aspect of the vitiligo and particularly of the borders may exactly reflect the depigmenting process in course. We demonstrated that amelanotic aspect with sharply defined borders is associated to stability status of the vitiligo lesions.

Conclusion: A simple and careful clinical examination of perilesional skin with or without histopathologic study of the edge may allow reliable and immediate evaluation of the actual stability of vitiligo lesions.

Commercial support: None identified.

3720
Automated microneedling and topical 5-flurouracil solution may help in treating acral vitiligo

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Introduction: Acral vitiligo is considered one of the most distressing dermatological disorders. Although surgical treatment is considered the treatment of choice in these patients after disease stability, yet it is time, cost and effort consuming. It also needs skillful experience. Microneedling was used with little success for treating acral vitiligo either solely or combined with excimer laser.

Aim of the study: An automated microneedling device has been tried to induce repigmentation in stable acral vitiligo patches. 5-Flurouracil is used topically during the procedure.

Patients and methods: Twenty patients with stable acral vitiligo were treated with an automated microneedling device in combination with topical 5-flurouracil solution. Each patient received sessions every 2 weeks.

Results: Repigmentation was noticed in sixteen patients after variable number of sessions.

Conclusion: Automated microneedling with topical 5-flurouracil solution may provide a simple, effective method for treating resistant and stable cases of acral vitiligo.

Commercial support: None identified.

3706
Clinical and instrumental efficacy of a dermocosmetic with Uniwhite peptide, niacinamide, vitC and hyaluronic acid on reducing actinic lentigo and improving photoaging

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Introduction: This monocentric open-label study assessed the clinical and instrumental efficacy and tolerability of a night cream containing uniwhite peptide (2%), niacinamide (4%), vitamin C derivative (4%) and hyaluronic acid (0.1%) for photoaging skin applied once daily during 8 weeks.

Methods: Forty-six white volunteers were included 53 to 70 yo. At inclusion, subjects presenting crow's feet wrinkles graded 2 to 6 (0-8 scale) and at least one facial target lentigo. Product was applied on the face and neck. Assessments were performed at baseline, after 4 and 8 weeks: Clinical evaluation of wrinkles, facial complexion homogeneity & luminosity; instrumental evaluation of lentigo intensity and sharpness, wrinkles depth and melanin content Subjects answered a questionnaire at each postbaseline visit.

Results: All subjects completed the study. Mean age was 64 yo. In vivo evaluation showed a significant progressive improvement in skin luminosity, complexion homogeneity and crow's foot wrinkles depth, at each visit ($P < .05$). These results were confirmed by clinical evaluation on digital photographs with significant improvement of the lentigo, complexion homogeneity, lightening effect and facial complexion. Lentigo software analysis ($n = 39$) showed a significant decrease of the color contrast between lentigo and surrounding skin, as well as a decrease in the target area indicating a depigmenting effect on target lentigo ($P < .005$). A decrease in melanin component was also observed at each visit ($P < .001$), confirming a lightening effect of the product. From the first visit, 80% of subjects considered that the product had a redensifying effect and 91% felt a deeply nourished skin.

Conclusion: In this 8-week study, this face and neck night cream containing peptide, niacinamide, ascorbic glucoside and hyaluronic acid, was well tolerated and effective to improve actinic lentigo and clinical aspects of photoaging, both through clinical in vivo and instrumental noninvasive evaluation.

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3763
12-Hydroxystearic acid: A peroxisome proliferator-activated receptor ligand that has antimelanogenic and antiinflammatory activity

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Peroxisome proliferator-activated receptors (PPARs) have been pursued as biological targets for skin rejuvenation, antiinflammation and antiaging benefits. The goal of this research was to explore the cellular mechanisms of a new PPAR pan-agonist, 12-hydroxystearic acid (12-HSA), for its role in modulating melanogenesis and to confirm clinical efficacy in treating skin hyperpigmentation. 12-HSA reduced melanogenesis in a melanoderm model. Our study of cocultures showed that 12-HSA inhibited melanosome transfer from melanocyte to keratinocyte as measured by flow cytometry using double immunofluorescence labelling. In human monocytes stimulated with lipopolysaccharide (LPS), 12-HSA demonstrated moderate, yet dose dependent antiinflammatory potential as indicated by reduction in PGE2 production quantified by EIA. A half face, double blind, randomized IRB-approved clinical study was conducted to evaluate 12-HSA in a cosmetic formulation for reducing the appearance of pigmentation. Formulations were applied twice a day for 3 weeks and changes in skin were recorded using spectrophotometer (CM2600d). In line with the in vitro results and its role as a PPAR ligand, the formulation containing 12-HSA significantly lightened facial pigment spots over vehicle control, in ITA (individual typology angle) and L^* (lightness) as measured by spectrophotometer. For the underarm lightening study, female patients with skin types III or IV (Fitzpatrick scale) exhibiting a moderate level of even darkening across their underarms were enrolled in an IRB-approved clinical study. Impact of the product on hyperpigmentation, erythema and dryness was measured over 4 weeks of application of cream using expert visual assessment and expert underarm mapping. A significant lightening benefit was demonstrated in the 12-HSA under arm compared to the vehicle control after 10 days of application, which was maintained through the end of the study. Our research clearly indicates that the PPAR pan-agonist 12-HSA inhibits melanogenesis potentially through inhibition of melanosome transfer and/or antiinflammatory activity. Furthermore, 12-HSA safely and effectively reduced hyperpigmentation in as short a period as 3 weeks in both face and underarm in vivo clinical studies.

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2738
Assessment of intraerythrocyte zinc levels in vitiligo patients

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Background: Vitiligo is a common pigmentary disorder. Many studies across decades and all over the world have attempted to illustrate the pathogenesis behind it. The pathogenesis of vitiligo is not completely understood, although the disorder appears to be resulted from the complex interaction between immune abnormalities, otoisotoxic and environmental factors. Trace elements are essential for normal functioning of the immune system. In this study, we investigated the levels of zinc in erythrocytes and their relationship with disease severity in patients with vitiligo.

Objectives: The aim of this study was to determine the zinc levels in serum and erythrocytes of patients with vitiligo by using atomic absorption spectrometric technique and to investigate the relationship between those levels and disease activity.

Methods: Fifty-two (20 women and 32 men) vitiligo patients and age matched 52 controls were enrolled in the study. The diagnosis of vitiligo was determined according to physical examination and wood light. We measured zinc levels in serum and erythrocytes by atomic absorption spectrophotometric technique.

Results: Intraerythrocyte zinc levels of vitiligo patients and control group patients were found close to each other. Erythrocyte zinc levels of the control group were as 581.24 ± 95.48 [280-924] mg/dL (standard deviation: 95.48) and of the vitiligo group were as 602.12 ± 107.89 [400-872] mg/dL (standard deviation: 107.89). Serum zinc levels were additionally calculated as 88.94 ± 13.43 [41-117] mg/dL (standard deviation: 13) in the control group and 92.84 ± 15.51 [60-134] mg/dL (standard deviation: 16) in the vitiligo group ($P < .001$). 0.7% and 4% increases of intraerythrocyte and serum zinc levels in the vitiligo group respectively were not statistically significant ($P = .15$).

Conclusions: We did our study to find out whether the assessment of zinc deficiency by intraerythrocyte zinc levels instead of serum zinc concentrations in patients with vitiligo could be more informative or not. But any measurement was not superior over each other's according to the results of our study. Furthermore, the relationship between disease severity and erythrocyte zinc levels were also not correlated. Some other studies with intralesional or affected hair zinc levels in vitiligo may give us different results to make a healthier interpretation about the association of vitiligo and zinc.

Commercial support: None identified.

3439
Clinical and instrumental efficacy of a dermo-cosmetic serum with azelawhite complex and glycolic acid on reducing actinic lentigo and improving photoaging

Ana Beatris Rossi, MD, PFCD, Toulouse, France; Thérèse Nocera, MD, PFDC, Toulouse, France; Priscilla Lapalliud, PhD, PFDC, Toulouse, France

Introduction: The aim of this open-label clinical study was to assess the clinical and instrumental efficacy and tolerability in use conditions of a serum containing azelawhite complex (2% of peptide and 8% of azelaic acid) and glycolic acid (3%) for photoaged skin during 12 weeks. We have already demonstrated the "antiaging" effect of this association on human cutaneous explants.

Methods: Forty-two white volunteers (45 to 70 yo) were included in this monocentric open-label clinical study. At inclusion, subjects presented periorbital wrinkles graded 3 to 6 (1-9 scale) and at least one target lentigo. The tested product was applied on the face and neck twice daily. At baseline and after 4, 8 and 12 weeks of product use, clinical and instrumental assessments of photoaging signs of the face were performed. At each visit, a board certified dermatologist evaluated subjects' skin for clinical tolerability and graded a target lentigo according a modified MASI. Instrumental chromameter measurements of the skin color (ITA), 3-D skin surface profile (AEVA) and skin elasticity (cutometer) were performed. Macroscopic high definition images of the skin were taken with DermLite. Subjects answered a questionnaire at each postbaseline visit.

Results: All subjects completed the study. Mean age was 57 yo. The local MASI score for the target lentigo improved significantly after 4, 8 and 12 weeks ($P < .001$). These clinical results were confirmed by instrumental evaluation, with a significant increase of ITA values indicating a lighter color of the lentigo at each visit ($P < .001$), as well as the color contrast analysis of the lentigo images compared to the surrounding skin ($P < .001$). AEVA assessment showed a significant improvement of the rough structures (deep wrinkles) after 4 weeks of product use ($P = .008$). Product was considered efficacious in reducing photoaging signs by 62% of subjects at week 4 and 67% at week 12.

Conclusion: The twice-daily application of a serum containing azelawhite complex and glycolic acid over 12 weeks, was well tolerated and improved clinical aspects of photoaged skin, confirmed by dermatologist. Subjects and instrumental noninvasive evaluation.

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3703
Clinical efficacy of a dermocosmetic skin lightening cream in woman suffering from melasma

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Introduction: The aim of this intraindividual comparative study was to assess the clinical and instrumental efficacy of a skin lightening cream containing azelaic acid (12%) and glycolic acid (5.2%) for melasma during 16 weeks. The dermatologic safety of the product and the quality of life impact on subjects were also evaluated.

Methods: Thirty-three females' volunteers were included. The tested product was applied twice-daily on face hyperpigmented affected area. This melasma treated area was compared to healthy unaffected area at all assessment time (at baseline and after 8, 12 and 16 weeks (W)). Primary parameter was the clinical assessment of the modified MASI a compared to uninvolved skin. Instrumental chromameter measurement (ITA° value), macrophotographies and image ranking scoring using 4 point-scale (1 = least melasma to 4 = strongest melasma) were also performed. Quality of life was assessed with MelasQol. scale. Product tolerance was also assess by the dermatologist during the study.

Results: Thirty-one subjects (mean age: 47 years old) presenting combined (epidermal and dermal) or dermal melasma (as selected by Wood lamp) were analyzed. Two subjects have been withdrawn without relation with the tested product. The modified MASI score improved significantly after 8, 12 and 16 weeks (2.6; 2.1; 1.5) compared to baseline (3,8) ($P < .001$). The clinical scoring of macrophotographies also showed the decrease of melasma severity from strongest to least ($P < .001$). The parameter skin tan value (ITA°) by chromametric measurement confirmed the clinical assessment. A significant progressive decrease of the color difference between the melasma treated area and the surrounding non-pigmented area was observed from W8 to W16 ($P < .001$). The significant decrease of the MelasQol. score from 27.9 at baseline to 18.6 at W16 showed the improvement of the subjects' quality of life ($P < .001$). The skin tolerance was judged "good" by the dermatologist.

Conclusion: The twice-daily application of a dermocosmetic cream containing azelaic and glycolic acids over 16 weeks improved clinical severity of melasma pigmented areas through dermatologist, subjects and instrumental evaluations, with a good tolerance.

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3091

New severity assessment method for melasma

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Introduction and objective: Melasma is one of the most common pigmentary skin diseases. It is common patchy brown, tan, or blue-gray facial skin discoloration and typically appears on the upper cheeks, upper lip, forehead, and chin. The most common severity assessment method of melasma is Melasma Area Severity Index (MASI) score. However, the ordinary MASI scoring system has some problems due to the observer's subjective visual judgment. This study aimed to develop a new advanced severity assessment method of melasma based on computerized optical imaging analysis system.

Material and methods: In this study, we propose a new computerized optical imaging analysis method for the quantitative assessing of melasma. In order to quantitative analyze the involvement area, we were divided into frontal, cheek and chin region in patients. After that, the divided images were processed to define the melasma lesions by the multithreshold method and gradient mask were apply to correct the curvature error of facial contour. Degree of darkness and homogenesis were measured based on intensity of gray level and difference of gray level in melasma lesions.

Result: The proposed new quantitative assessment method for melasma is more objective and accurate than ordinary MASI method. In addition, a new assessment method is able to quantify a minute difference of pigmented pattern among melasma patients.

Conclusion: We developed the quantitative assessment method for melasma using computerized optical imaging analysis. Based on the results, our new computerized optical imaging system could be used as valuable tools to assess the severity of various pigmentary skin diseases including melasma.

Commercial support: None identified.

2744

Repigmentation in three cases of perineum vitiligo induced by photodynamic therapy

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Vitiligo is an acquired depigmentary disorder of the skin which results from the destruction of melanocytes. The depigmentation in genitalia site has a deleterious effect on the psychosexual function of many individuals. So far, very few data about perineum vitiligo treatment are available. Here, the authors report repigmentation in three cases of perineum vitiligo treated by photodynamic therapy (PDT). In all the patients, 5-aminolevulinic acid of 20% concentration was used after occluded 3 hours, following irradiation with red light (630 nm) with the same parameters (80 mw/cm^2, 20 min), one session every two weeks were made. During the treatment with PDT, no other treatments to vitiligo were done. Case 1: A 24-year-old unmarried female reported perineum vitiligo of 4 years, the lesion was nonprogressive for about 3 years. 3 months before PDT treatment, the patients received topical tacrolimus twice daily treatment for 6 months with no beneficial. Physical examination showed that the lesion was 6 cm^2. She received 11 sessions and 40% of the lesions repigmented. Case 2: A 20-year-old unmarried female with perineum vitiligo of 2 years, The lesion spread progressively for the first half year and was nonprogressive thereafter. She failed to respond to the medical treatment administrated to her before PDT. Examination revealed total area of the lesion was 30 cm^2. She received 12 sessions and 90% of the entire lesion showed good repigmentation 2 weeks after the last treatment. Case 3: A 50-year-old married female of 3 years' duration, the lesions had been progressive in the first year and spread almost the whole perineum. She was refractory to medical treatments, which she had received earlier. This patient underwent only 2 sessions and break the treatment because of the severe itching occurred after PDT. She received 30% repigmentation of the examination 3 months after the last treatment. During the treatment, the patients suffer mild burning or pain, itching and after the sessions erythema was noted, which were well-tolerated by most patients and generally disappeared several hours after treatments except for the 50-year-old patient with severe itching. This is to our knowledge the first study of PDT in perineum vitiligo. All the three patients yielding repigmentation who were satisfied with the treatment. Further studies with more patients are necessary to determine if PDT is a good option of treatment in perineum vitiligo.

Commercial support: None identified.

2354

Progression of idiopathic eruptive macular pigmentation in a girl from the child to adolescence

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A 14-year-old girl suffered from brownish round macules and patches over face, trunk and proximal limbs since she was 7 years old. She has no underlying medical disease or familial history of pigmentation disorders. The lesions were asymptomatic and there was no preceding redness or inflammation. After 7 years of loss follow up, she came back to our clinic. There were progressions of generalized brownish patches over whole face, chest, back and upper extremities. Physical examination revealed normal development of neurocutaneous system. Blood levels of mercury, lead, arsenic and cadmium were within normal limits. The histopathologic examinations for lesional skin showed increased basal layer pigmentation and increased melanocytic activity by dihydroxyphenylalanine reaction stain. Electron microscopy examination of the lesion skin revealed an increase in numbers and an increase in maturity of melanosomes in both basal and suprabasal keratinocytes. However, the cell number of melanocyte was within normal range. The diagnosis of idiopathic eruptive macular pigmentation (IEMP) was rendered. Oral transamic acid and topical Triluma cream were given, however, no significant responses were noted during one year of follow up. IEMP is characterized by rounded or oval-shaped, brownish macules without previous erythema or other symptom. The lesions mainly involved neck, chest, back and proximal extremities. Our case presented with an unusual course of aggressive progression and extensive face involvement in the seven years follow up. The pathogenesis of IEMP remains unclear. Endocrine factors, inflammatory stimuli, and autoimmune phenomenon were hypothesized. Asians and Egyptians were seem to be more vulnerable for IEMP according to reported case numbers. Ethnicity or Fitzpatrick skin type may be considered as risk factors. IEMP generally tends to regress spontaneously in months years without treatment. However, in our case, the disease runs an intractable and progressive course from year 7 to year 14. Similarly, a case of 21 year history of IEMP has been reported before, suggesting that IEMP may not be necessarily self-remitting. Topical steroids, hydroquinone, and tretinoin were not proved to be helpful in most reports. IEMP is a relatively rare disorder and should be considered as differential diagnosis for child or young adults with hyperpigmentation disorders. The management of IEMP may be difficult for extensive and nonremitting cases.

Commercial support: None identified.

3875

Transepidermal delivery of hydroquinone and clobetasol propionate using ablative fractional radiofrequency and ultrasound in the treatment of melasma

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Background: Melasma is a common disorder of hyperpigmentation that has a significant negative impact on the quality of life in affected individuals and is often difficult to treat. A range of treatments for melasma exist, with varying degrees of efficacy and success. Depigmenting agents have been the gold standard for the treatment of melasma for decades. But, some drugs that are absorbed do not penetrate deeply enough to reach the desired target in the tissue. Fractional ablation penetrates the skin by creating microchannels which reach beyond the stratum corneum, creating a direct path for drugs to reach the deeper skin tissue.

Objective: This present study intends to evaluate the clinical efficacy and the safety of the combination of fractional ablative radiofrequency technology paired with an acoustic pressure wave ultrasound technology to topically push the 4% hydroquinone and 0.05% clobetasol propionate through the albeit perforated melasma treated skin.

Methods: The study enrolled 20 patients of Fitzpatrick skin types I-IV with refractory facial melasma. Initially, patients were treated every other week, during 3 months (6 treatments) with fractional radiofrequency device (RF Pixel Microplasma) for skin perforation employing 50W and 1 pass, followed by acoustic pressure ultrasound. The treatment settings of the acoustic pressure ultrasound handpiece were 80% of the ultrasound energy output and 50 Hz for the ultrasound sonotrode vibration rate. Immediately 4% hydroquinone and 0.05% clobetasol propionate were applied on the perforated skin surface. Clinical and instrumental evaluations for improvement in pigmentation were conducted at baseline and at each subsequent follow-up visit at 2, 4, 8 and at 12 weeks. The effects of treatment were evaluated by three physicians not involved in the study and by standardized digital photographs (VISIA, Canfield Imaging Systems, USA) based on improvement of pigmentation and reduction in melasma size.

Results: This study shows the improvement of melasma through the enhanced penetration of hydroquinone and clobetasol propionate using ablative fractional radiofrequency and ultrasound and acoustic pressure. The image analysis showed that hyperpigmentation was significantly reduced at 2, 4, 6 and 12 weeks after treatment. The therapy was well tolerated, safe and no adverse events were reported during the study.

Conclusion: This study has demonstrated the improvement of melasma through the enhanced penetration of hydroquinone and clobetasol propionate by using a paired model for transepidermal drug delivery which could be a safe, tolerable, and effective alternative modality for the treatment of melasma.

The RF Pixel Microplasma was lent to the group for this study.

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PSORIASIS AND OTHER PAPULOSQUAMOUS DISORDERS

3227

2511

3110

A novel molecular disease classifier for eczema and psoriasis

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Novel specific therapies for eczema and psoriasis have been developed and they mark a new era in the treatment of these complex inflammatory skin diseases. However, within their broad clinical spectrum, eczema and psoriasis phenotypes overlap making an accurate diagnosis impossible in special cases, not to speak about predicting the clinical outcome of an individual patient. Here, we developed a novel method to reliably diagnose indistinct cases. We identified a robust molecular classifier (MC) consisting of the genes NOS2 and CCL27 that diagnosed eczema and psoriasis in a cohort of 129 patients suffering from classical forms, but also from subtypes of eczema and psoriasis, with sensitivity and specificity >95 %. Furthermore, the MC identified histologically misdiagnosed patients (n = 5) and gave a clear prediction for therapeutic response in 5 indistinct patients that was in line with the subsequent clinical course. Moreover, we established immunofluorescence stainings for iNOS and CCL27 protein on paraffin-embedded sections and also here, patients were diagnosed with sensitivity and specificity >88%. This disease classifier proved to be superior to current gold standard methods to distinguish eczema and psoriasis and may thus build the basis for molecular diagnosis of chronic inflammatory skin diseases required to establish personalized medicine in the field.

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3811
A real word review of treatment duration and persistence among European psoriasis patients

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Introduction: Psoriasis (PsO) is a chronic disease that imposes a heavy burden on patients and has yet no cure. Biologic agents have demonstrated strong efficacy in PsO, improving the signs and symptoms of the disease however the high cost of these drugs may limit their long-term use. The aim of this study is to assess the duration of biologic therapy and the impact of these drugs over time as well as measure persistence with these agents.

Methodology: We used patient data collected as part of an online treatment survey conducted among a panel of dermatologists between April 2014 and June 2015 across the five largest EU countries (France, Germany, Italy, Spain and the UK), and analyzed the records of 6013 biologic experienced patients suffering from moderate to severe plaque psoriasis. We reviewed the characteristics of patients and classified them according to the duration of their current biologic therapy into 3 roughly even sized samples. "Short-term" patients had been on their current biologic for ≤8 months (n = 1174); "medium-term" patients had been on their current biologic for >8 - ≤25 months (n = 1245); "long-term" patients had been on their current biologic for >25 months (n = 1182). We also analyzed the recorded duration of patients' most recent previous line of biologic therapy to assess persistence on treatment (n = 731). All data were tested for statistical significance using two-sided t-tests with a significance level of 0.05.

Results: On average patients had been on their current biologic for 22.9 months with no significant differences between brands bar Stelara which had a significantly shorter mean treatment duration (17.9 months). "Long-term" patients were significantly older vs the other two groups (48.6 years; $P < .05$) and as expected had longer overall disease durations (15.3 years) but they were also significantly more likely to have a PASI ≤10 (77.0%) and a BSA ≤10% (82.0%). This was in line with doctors' perceptions as the "long-term" group had the greatest proportion of patients deemed to have mild PsO (20.6%). The "short-term" group had a significantly greater percentage of moderate to severe patients vs the other groups. While "long-term patients" were significantly more likely to have had mild PsO at diagnosis (20.6%) there were no significant differences in perceived severity at the time of their 1st biologic initiation. However, "long-term patients" were more likely to suffer from comorbidities vs the other groups (69.1%) with cardiovascular disease (9.7%), ankylosing spondylitis (1.9%) and diabetes (11.6%) significantly more common in these patients. "Long-term patients" were also significantly more likely to be treated with anti-TNF inhibitors (77.7%) with Humira the most common choice (38.2%). Stelara was more frequently associated with "medium-term" patients (39.3%). Use of concomitant topical treatments was also significantly higher in "medium-term" patients (58.9%) although there were no statistically significant differences in steroid use between groups. With regards to stop and switch patients, the mean duration of their previous line of biologic therapy was 14.5 months. This was 17.8 months for switch patients and 15.1 months for patients stopping biologic therapy altogether (non- significant). Among those switching, patients spent 17.9 months on their 1st biologic before switching, 18.8 months on their 2nd and 13.0 months on their 3rd or more biologic (significantly less vs the duration of the 1st and 2nd biologic). Although only 4.1% of patients analyzed had stopped biologic therapy, the most common reason given for the stop was patient remission (36.4%). However, only 25% of these patients had been in remission for more than 12 months.

Conclusion: Our results confirm that long-term use of biologics can be beneficial to patients and that many continue to respond to their therapy for several years. However, a considerable proportion of patients stops or switches biologic due to lack of efficacy and/or tolerability issues. This emphasizes physicians' need for a large and varied armamentarium of biologic agents and novel small molecules. It also stresses the importance of therapeutic strategies such as treat-to-target that optimize patient outcomes and ensure maximum persistence on therapy.

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3450
A statistical tool to convert published PASI 75, PASI 90 and PASI 100 response rates into absolute PASI values

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Introduction: While relative improvements in PASI (eg, PASI 75) are often used for assessing the benefits of psoriasis therapies in clinical trials, absolute PASI values provide more clinically relevant information about the severity of disease long term. Treatment goals defined by absolute PASI targets may enable a more standardized quality of care. Thus, there is a trend to describe efficacy via the proportion of patients reaching an absolute PASI ≤ 1, ≤3, or ≤5. Because absolute PASI data are rarely published, we developed a tool to estimate these from commonly reported data. This will enable metaanalysis using absolute PASI. The objective of this analysis was to show the applicability of this tool using phase 3 ixekizumab data.

Methods: The tool is a parametric model based on a transformation of truncated multivariate normal distribution to reflect the nature of PASI data. The model takes into account the PASI threshold used as an entry criterion, mean and standard deviation at baseline, and PASI response rates. Using data from three phase 3 studies of ixekizumab, the tool was used to estimate the percentages of patients with PASI ≤1, ≤3 or ≤5 and these were compared to actual percentages. Within each study PASI values of the individual treatment arms (80 mg ixekizumab every 2 weeks, 80 mg ixekizumab every 4 weeks, 50 mg etanercept biweekly and placebo) and the treatment differences were analyzed at week 12.

Results: We found strong correlations between the estimated and the actual percentages of patients with absolute PASI ≤ 1, ≤3, and ≤5 at 12 weeks across the active treatment arms of the 3 studies (r = 0.9972, r = 0.9987, r = 0.9992, respectively). Across the 3 combined cutpoints the tool underestimated the percentages of patients on average by -0.8%. The correlations between estimated and actual treatment differences in percentages of patients with absolute PASI ≤ 1, ≤3, and ≤5 were also high (r = 0.9984; r = 0.9988; r = 0.9999, respectively).

Conclusions: This new tool shows good statistical properties enabling comparison of proportions of patients achieving absolute PASI thresholds using commonly reported data from ixekizumab phase 3 trials. This work will make future comparisons of absolute PASI data between treatments using published data possible in order to inform treatment guidelines, physicians, patients and reimbursement bodies.

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3461
Adalimumab dose escalation, deescalation, and reescalation in patients in the REVEAL study

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Introduction: The safety and efficacy of adalimumab (ADA) treatment in patients (pts) with psoriasis (Ps) has been demonstrated; however, not all pts maintain a high level of response over time. Here, we report the effectiveness and duration of escalating and deescalating ADA dosing between 2 regimens: every other week (eow) and every week (ew).

Methods: These analyses include open-label extension (OLE) data from REVEAL trial. Pts initially received 40 mg ADA eow. From OLE weeks (wks) 24 to 252, pts whose PASI response was <50% could dose escalate to 40 mg ew, and were reevaluated at 6 and 12 wks, then every 12 wks. Pts in the dose escalation (DE) population who achieved PASI75 were deescalated back to eow. Pts who deescalated and fell below PASI50 again could reescalate to ew; no further deescalation was allowed. Absolute and percentage changes in PASI scores were reported at last visit before DE or deescalation.

Results: Pts in the OLE study were predominantly male, white, with mean age of 44 years. In total, 299 former REVEAL pts underwent initial ADA DE, mean PASI score was 14.5 and mean percentage change from baseline (BL) in PASI was -26.2 at escalation. Approximately half of the initial DE population (144/299; 48%) attained a PASI75 response and deescalated back to eow, after median duration of 17 wks on ADA ew. Remaining 155 pts (52%) did not achieve PASI75 and remained on escalated ew dose for median duration of 29 wks. Among the 144 pts who deescalated, the mean PASI score at deescalation was 3.6; mean percentage PASI change from BL was -81.5. 68 pts of the deescalation group (47%) lost a PASI50 response and underwent reescalation to ew, after median duration of 24 wks. Remaining 76 pts (53%) who deescalated retained at least a PASI50 response and remained on eow dosing for median duration of 60 wks without reescalating. Mean PASI score for pts who reescalated was 12.9 at reescalation; mean percentage change from BL was -36.1. Pts who reescalated to ew remained in study with ew dosing for median duration of 44 wks. DE was not associated with additional safety concerns in the OLE study.

Conclusions: ADA was effective in eow and ew dosing regimens and exhibited safety consistent with known safety profile. Approximately 25% of pts who required DE to ADA ew successfully de-escalated and remained on eow dosing without need for dose reescalation (median 60 wks). Most deescalations occurred within 4 months after initial escalation.

AbbVie Inc, funded this study and participated in the study design, study research, data collection, analysis and interpretation of data, and writing, reviewing, and approving this abstract for presentation.

2572
Adalimumab is associated with reduced risk of joint-related signs and symptoms compared with methotrexate in patients with moderate to severe psoriasis

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Objective: Population-based studies have shown that psoriatic arthritis (PsA) is highly prevalent among patients with moderate to severe psoriasis. Adalimumab (ADA) has shown superiority to placebo in reducing the risk of psoriatic arthropathy adverse events (AEs) among patients with psoriasis and comorbid PsA.[2] This study assessed the effect of ADA vs methotrexate (MTX) on joint-related signs and symptoms (ie, joint pain, swollen joints) among moderate to severe psoriasis patients with and without comorbid PsA.

Methods: Data from 4 randomized phase 3 trials (M10-255, NCT00679731; BELIEVE, NCT00574249; REVEAL, NCT00237887; and CHAMPION, NCT00235820) were pooled for patients treated with ADA vs MTX (5-25 mg once weekly). Treatment-emergent joint-related signs and symptoms were reported in the trials. The cumulative incidence of joint-related AEs by Week 16 was compared between ADA and MTX using the Cox proportional hazards model, adjusting for baseline demographics, patient-reported presence of swollen/tender/stiff joints, the Psoriasis Area and Severity Index (PASI) score, and disease duration. A subgroup analysis was conducted among psoriasis patients without comorbid PsA at baseline.

Results: A pooled 1558 patients (ADA n = 1285, 82.5%; MTX n = 273, 17.5%) were included. The mean age was 43.9 years and the majority were male (67.4%). A quarter of patients had PsA at baseline (ADA group 26.9%, MTX group 17.2%) and 28.9% reported swollen, tender, or stiff joints. By Week 16, a significantly greater proportion of MTX patients (12.5%) than ADA patients (7.6%) reported joint-related AEs (unadjusted hazard ratio [HR] 0.58, 95% confidence interval [CI] 0.39-0.86, $P = .007$). Among psoriasis patients without comorbid PsA, a numerically greater proportion of MTX patients reported joint-related AEs than ADA patients (11.5% vs 7.8%). After adjusting for baseline characteristics, ADA was associated with a 48% lower risk of reported joint-related AEs when compared with MTX (HR 0.52, 95% CI 0.35-0.78, $P = .002$) among all patients, and a 43% lower risk among psoriasis patients without comorbid PsA (HR 0.57, 95% CI 0.36-0.90, $P = .016$).

Conclusion: ADA treatment was associated with a reduced risk of reported joint-related signs and symptoms when compared with MTX among moderate to severe psoriasis patients with and without comorbid PsA.

Design, study conduct, and financial support for the study were provided by AbbVie; AbbVie participated in the interpretation of data, review, and approval of the abstract; all authors contributed to the development of the publication.

3444
Adalimumab significantly improves PASI scores in head region among patients with moderate-to-severe psoriasis: Analysis from REVEAL and CHAMPION

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Introduction: Psoriasis affecting the head region is often problematic due to its visible location and resistance to therapy. This analysis evaluates the efficacy of adalimumab (ADA) treatment of the head region in patients with moderate-to-severe psoriasis.

Methods: Of the patients from the phase 3, randomized, placebo-controlled REVEAL (Menter A, et al. J Am Acad Dermatol. 2008;58:106-15) and CHAMPION (Saurat JH, et al. Br J Dermatol. 2008;158:558-66) trials, those with psoriasis involving the head were included in this pooled analysis. The intent-to-treat populations received ADA 80 mg at week 0, then 40 mg every other week or placebo through week 16. The methotrexate arm from CHAMPION was excluded. Improvements in overall and each component of the head region PASI score as well as quality of life (Dermatology Life Quality Index; DLQI) were evaluated at week 16 for ADA-treated patients vs placebo.

Results: Of 1372 patients in this analysis (451 placebo; 921 ADA); 66.1% were male and mean age was 44.2 years (range 18-82). At baseline, PASI scores were 19.1 overall and 16.7 for the head region; mean DLQI was 11.4. Mean improvement in overall PASI score from baseline to week 16 was 17.0% placebo, 80.1% ADA, for the head region it was 18.7% placebo, 83.0% ADA ($P < .001$). Mean improvement in PASI scores at week 16 in the head region by PASI components were: 14.5% placebo, 76.4% ADA for erythema; 19.0% placebo, 80.1% ADA for induration; 15.9% placebo, 75.4% ADA for desquamation; and 14.2% placebo, 73.2% ADA for area ($P < .001$ for all). The proportions of patients achieving PASI 75/90/100 in the head region at week 16 were 76.8%/66.7%/62.7% ADA and 16.2%/11.6%/10.9% placebo ($P < .001$ for all). Among ADA-treated patients, mean changes from baseline in DLQI scores at week 16 were -10.1 for PASI 100 responders in the head region vs -6.4 for PASI 100 nonresponders in the head region.

Conclusions: After 16 weeks of ADA treatment, patients achieved significant improvements overall and in each component of the head region PASI scores compared with placebo. Additionally, complete clearance of head psoriasis with ADA therapy resulted in greater improvements in quality of life. Due to the design of the PASI instrument, the benefit to the scalp can only be inferred.

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3391
An analysis of the incidence of adverse pregnancy outcomes among women with psoriasis in Newfoundland and Labrador

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Psoriasis is a chronic inflammatory skin disease affecting 2% of the world's population. In the current study, we sought to examine the effect of psoriasis case/control status and severity on several outcomes of pregnancy, including method of delivery, gestational age, size for gestational age, birth weight, and presence of congenital anomaly at birth. A retrospective cohort study design was used to analyze pregnancy outcomes among women with and without psoriasis, by case status and disease severity. Medical records of psoriasis patients at a dermatology clinic (Newlab Clinical Research Inc, St. John's (NewLab)) were linked via a unique identifier to a dataset of live birth registration records in Newfoundland and Labrador, and the associations between psoriasis case status and disease severity and the incidence of caesarean delivery, small for gestational age (SGA) birth, low birth weight (LBW), preterm birth (PTB), congenital anomaly, and overall negative pregnancy outcome were analyzed. This is the new results of the 1653 records of patients in the NewLab psoriasis clinical database who were eligible for inclusion. In the study 385 could be linked to the Newfoundland & Labrador Centre for Health Information (NLCHI) dataset for 1992-2012 giving a linkage rate of 23.3%. The 385 psoriasis patients represented 615 live births in the live birth dataset. Significant associations were noted with mean parity and age at first birth in psoriasis cases and controls ($P < .0001$). Unadjusted rates of caesarean and vaginal delivery in psoriasis patients and controls ($P < .03$). Unadjusted rates of overall negative pregnancy outcomes psoriasis and controls ($P < .01$). No significant differences were noted in marital status, urban/rural residence, and education level of psoriasis patients and controls or unadjusted rates were small for gestational age, low birth weights, preterm birth or congenital anomalies. Current analysis adds to the existing literature on pregnancy outcomes among women with psoriasis. It suggests that psoriasis severity may be predictive of overall negative pregnancy outcome but not with individual outcomes. This cohort represents the largest number of pregnancy outcomes studied to date. The study limitations include the effect of psoriasis on pregnancy outcomes in the absence of data on comorbidities, lifestyle factors or treatment. Research is warranted to control for these variables.

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3813
An exposure response model to describe the relationship between ixekizumab concentrations and the static Physicians' Global Assessment (sPGA) score and the Psoriasis Area and Severity Index (PASI) in patients with moderate to severe plaque psoriasis

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Objectives: Ixekizumab is an anti-IL-17A monoclonal IgG4 antibody currently in development for the treatment of psoriasis. This analysis aimed to describe the relationship between observed systemic exposure to ixekizumab (trough concentrations - Ctrough) and key efficacy endpoints at Week 12 (static Physician Global Assessment [sPGA] and Psoriasis Area and Severity Index [PASI] score) using data from 3 phase 3 studies.

Methods: Ixekizumab was administered subcutaneously (SC) as a 160 mg initial dose (Week 0) then an induction dose of 80 mg every 2 weeks (Q2W) or every 4 weeks (Q4W) to Week 12. Efficacy endpoints were sPGA score ((0,1) or (0)) and PASI (at least a 75%, 90%, or 100% improvement from baseline in PASI score [PASI 75/90/100]) at Week 12. The relationship between ixekizumab Ctrough and efficacy was explored through logistic regression modeling to determine the probability of a patient being a responder or a nonresponder. The dataset included 2888 patients, 2097 on ixekizumab and 791 on placebo. All analyses were done using NONMEM 7.3.0.

Results: The relationship between ixekizumab Ctrough and sPGA and PASI scores was described well using logistic regression models. Median Ctrough levels were 9.09 μg/mL for Q2W and 2.95 μg/mL for Q4W dosing. The model predicted response rate for sPGA (0,1) was 86% for Q2W and 84% for Q4W dosing and sPGA (0) responses were 42 and 37% for the Q2W and Q4W regimens, respectively. The predicted responses compared well with observed response rates. The relationship between ixekizumab Ctrough and PASI endpoints were also well described and the model was able to predict the observed response rate well. For PASI75, the model predicted response rate was 93% and 90% for Q2W and Q4W, respectively. Similarly, for PASI90, the model predicted response rates were 74% and 68% and for PASI100 the model predicted response rates were 39% and 34% for the Q2W and Q4W regimens, respectively.

Conclusions: The relationship between ixekizumab Ctrough levels and sPGA and PASI scores was described well using exposure response modeling. Based on exposure data, the model predicted high response rates for both dosing regimens and rates were consistent with the observed clinical data. Higher exposures in patients on the 80-mg Q2W dosing regimen resulted in consistently greater predicted response rates (increases of 2% to 6%) compared with the 80 mg Q4W dosing regimen across sPGA and PASI endpoints.

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An innovative topical therapy for the palmoplantar hyperkeratosis

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A study on the topical treatment of the palmoplantar hyperkeratosis in 25 subjects of 18 years of age and above, both males and females, selected between January and June 2015 was carried out at the psoriasis outpatient clinic of the Dermatological Department of the University of Bari, Italy. The selected sample consisted for the 84% (21 patients) of individuals affected by palmoplantar psoriasis, mainly characterized by scaling and hyperkeratosis with mild erythema and infiltration: the remaining 16% (4 patients) was divided as follows: 75% (3 patients) of subjects was affected by chronic hand eczema, mainly characterized by a squamous hyperkeratosis morphology, 25% (1 patient) was affected by pityriasis rubra pilaris with the typical clinical picture of palmoplantar keratoderma with a yellow-orange chromatic shade. The tested product consists of sodium lactate, at a concentration of 30%, of which the keratolytic, elasticizing, emollient properties and the capacity to promote the correct regeneration of the cutaneous tissue were evaluated. For each patient, a technical card was filled out to quantify, according to the physician's judgement, the following cutaneous parameters before and after 2 months of therapy: degree of xerosis, thickening, and scaling. The study has provided the possibility to evaluate considerable clinical improvements with respect to the considered parameters. Through the DLQI test (Dermatology Quality of Life Index), administered before and after therapy, it was also possible to assess the improvement of the quality of life in patients at the end of the treatment. The importance of this study stems from the necessity to treat, with the highest specificity, all of those cases of palmoplantar desquamating hyperkeratosis that, associated to several dermatosis, severely affect activities like the grip and the walking abilities, and have a strong impact on the quality of life both in the professional and social environment.

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3229

Analysis of major adverse cardiovascular events in the Psoriasis Longitudinal Assessment and Registry Study (PSOLAR)

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Objective: To compare the risk of MACE in psoriasis patients with new or ongoing exposure to biologic (bio) therapy vs topical/phototherapy (top/photo).

Methods: PSOLAR is an international psoriasis registry which follows patients who are eligible to receive systemic therapy based on standards of clinical practice. MACE is defined as cardiovascular death, stroke, and myocardial infarction. Cohorts were developed for new and ongoing use of all bios combined, TNFIs, ustekinumab separately, and top/photo, and observed through Aug 23, 2014; MTX was excluded from all groups. Demographics and clinical characteristics are described. Cumulative incidence rates in 100/PY with 95% CIs are summarized. Cox hazard regression methodology was used to identify risk factors, including bio therapies, for first MACE, with a reference group of top/photo.

Results: Data were analyzed from 7666 pts (6835 bio-exposed, 831 top/photo-exposed) for 19006 pt years. Demographics, clinical characteristics, and observation time were generally comparable among bio cohorts. Top/photo cohort was slightly older in age, lighter in weight, and was balanced with respect to gender in context of the bio cohorts. The cumulative incidence rates of MACE for combined bios, TNFIs and ustekinumab respectively were in per 100 PY (95%CI): 0.22 (0.15-0.30), 0.23 (0.15-0.35), and 0.19 (0.10-0.35). Multivariate analysis showed that increasing age (HR 1.78, $P < .0001$), male gender (HR 2.57, $P = .0098$), and history of hypertension (HR 2.534, $P = .0078$) were associated with increased risk of MACE. HRs for combined bios, TNFIs and ustekinumab respectively were: 0.648, 0.727, 0.526, but did not reach statistical significance.

Limitations: Bias in observational data, mismatched populations, unmeasured clinical variability (eg, meds and biomarkers), and inability to detect small differences in risk.

Conclusions: Results from PSOLAR suggest a nonsignificant decreased risk with TNFIs or ustekinumab in comparison with top/photo therapy in patients with psoriasis.

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3728

Assessment of HLA Cw6 genotype and correlation to ustekinumab response in a large cohort of patients with moderate-to-severe psoriasis

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Objectives: The link between the HLA-Cw6 allele in psoriasis (PsO) patients (pts) and improved clinical response to ustekinumab (UST) therapy was reported previously (Talamonti et al). The aim of this retrospective analysis was to determine the association of HLA-Cw6 status and response to UST in a large, well-controlled clinical trial population.

Methods: DNA was collected from approximately 600 North American participants in the UST Phoenix 1, Phoenix 2, and ACCEPT Ph3 PsO clinical trials. HLA-Cw6 genotype was assessed by SNP-chip imputation then correlated to PASI and PGA responses. Association between HLA-Cw6 status and efficacy (short and long-term) of UST or likelihood for dose escalation was evaluated.

Results: The prevalence of HLA-Cw6 was 44.6%. The HLA-Cw6 genotype in this combined population was associated with longer disease duration and earlier age of disease onset. Both HLA Cw6 positive as well as negative pts demonstrated relatively high response rates to UST (wk24 PASI75 responses were 86% vs 76%, respectively). A modestly higher percentage of HLA-Cw6 positive pts achieved PASI 50, 75, 90 and 100 at wks 4, 12, 24, and 28, vs HLA-Cw6 negative pts. The largest delta between positive and negative pts (17.9%) was observed for PASI75 response at wk12 with smaller differences noted at later timepoints for PASI90 (11.8% at wk24) and PASI100 (10.2% at wk28) response rates. HLA-Cw6 positive pts had modestly higher long-term efficacy rates than those that were HLA-Cw6 negative with statistical significance reached for PASI75 response rates (82.6% vs 64.4%, respectively) at the 5 year final efficacy assessment in Phoenix 1. Lastly, a larger percentage of HLA-Cw6 negative pts underwent a shortened dosing interval and/or dose escalation through year 5 in Phoenix 2. 57% of HLA-Cw6 positive pts did not require dose escalation vs 50% of negative. Among pts who received initial treatment of UST 45 mg, 41% of negative and 32% of HLA-Cw6 positive pts required both dose escalation and dose interval adjustment.

Conclusions: While a differential response to UST is evident in HLA-Cw6 positive vs HLA-Cw6 negative pts, the difference is modest particularly for response rates of more complete responses (PASI90 and PASI100); thus, the clinical utility of this marker as a predictor of response to UST appears to be limited.

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Association between complete or near complete resolution of psoriasis and improvements in health related quality of life, itching and skin pain: An integrated subanalysis of UNCOVER-2 and UNCOVER-3

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Introduction: While a 75% improvement in the psoriasis area and severity index (PASI) is considered a clinically significant improvement, evidence suggests that residual psoriasis continues to have a significant impact on the patient. The objective of this analysis was to evaluate the improvements in patient reported outcomes (PROs) among patients achieving complete (PASI 100) or near complete (PASI 90) resolution of their psoriasis compared to lower levels of treatment response using data from 2 phase 3 trials of ixekizumab.

Methods: Data were integrated from 2 phase 3 trials in which patients with moderate to severe psoriasis were randomized to groups receiving ixekizumab every 2 (IXE Q2W; N = 736) or 4 weeks (IXE Q4W; N = 733) following a 160-mg starting dose, etanercept (ETN; 50 mg biweekly; N = 740), or placebo (PBO; N = 361). PROs included an Itch Numeric Rating Scale (Itch NRS), which ranges from 0 (no itch) to 10 (severe itch), the Dermatology Life Quality Index (DLQI) and a skin pain visual analog scale (VAS) which ranges from 0 (no pain) to 100 (extreme pain). All treatment groups were combined. At week 12, proportions of patients achieving a DLQI (0,1), Itch NRS = 0 or skin pain VAS = 0 were compared pairwise using logistic regression model between groups of patients achieving <75% improvement in PASI (PASI < 75 [N = 901]), 75% to 89% improvement in PASI (PASI 75-89 [N = 482]), 90% to 99% improvement in PASI (PASI 90-99 [N = 576]), and 100% improvement in PASI (PASI 100 [N = 587]). Missing data were imputed using last observation carried forward.

Results: Among patients achieving a PASI 90-99, and PASI 100, significantly more patients reported no impact of psoriasis on their quality of life with 64.8% and 82.3%,respectively reporting a DLQI (0,1) compared to 31.5% in the PASI 75-89 group ($P < .001$). Similarly, more patients in the PASI 90-99 and PASI 100 groups reported an itch NRS = 0 (39.4% and 63.8%, respectively) and a skin pain VAS = 0 (49.5% and 66.5%, respectively) compared to patients in the PASI 75-89 group (23.7% reporting Itch NRS = 0 and 36.6% reporting skin pain VAS = 0; $P < .001$ for each comparison to PASI 90-99 and PASI 100 groups).

Conclusions: Significantly more patients among those achieving a PASI 100 or PASI 90 reported that their psoriasis no longer impacted their quality of life and had no itching and skin pain compared those achieving PASI 75 but not higher. These data suggest PASI 90 or PASI 100 may be considered a treatment goal.

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2658

Association between tumor necrosis factor inhibitor therapy and reduced risk of major adverse cardiovascular events in patients with psoriasis

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Background: We have reported previously from population-based cohorts that use of TNF inhibitors (TNFi) was associated with a 50% reduction in myocardial infarction risk in patients with psoriasis or psoriatic arthritis.

Objective: To determine whether use of TNFi is associated with change in risk of major adverse cardiovascular events (MACE, ie, myocardial infarction, stroke, and CV death) in patients with psoriasis. Compared to the original study, this study has a longer follow-up period in a population with psoriasis ± psoriatic arthritis.

Methods: This was a retrospective cohort study using the Kaiser Permanente Southern California (KPSC) health plan. At inclusion, patients had at least 4 ICD-9 diagnostic codes for psoriasis (696.1) and no antecedent MACE codes. Subjects were followed from1-1-2004 to 12-31-2014. Ustekinumab is not on formulary at KPSC, so 69 patients given ustekinumab were excluded from the study. Multinomial logistic regression estimated confounder-adjusted propensity scores for treatment and propensity score-adjusted multivariable Cox regression assessed differences in MACE incidence rates.

Results: Of 15,354 patients included, 1605 received TNFi for at least 2 months, 3599 were TNFi naïve and received oral agents or phototherapy (oral/photo cohort), and 10,350 were not treated with TNFi, other systemic therapies, or phototherapy (topical cohort). The median duration of follow-up for TNFi, oral/photo, and topical cohorts were 9.5, 8.5, and 8.1 years. The incidences of MACE in the TNFi, oral/photo, and topical cohorts were 8.45, 11.63, and 11.79 per 1000 patient-years, respectively. After adjusting for MACE risk factors, the TNFi cohort had a significantly lower hazard of MACE compared with the topical cohort (propensity score-adjusted hazard ratio, 0.60; 95% CI, 0.48-0.76). The oral/photo cohort had a similar hazard of MACE compared with the topical cohort (propensity score-adjusted hazard ratio, 0.98; 95% CI, 0.86-1.11). In a sensitivity analysis that excluded oral therapy, propensity score-adjusted hazard ratios for TNFi, photo, and topical cohorts were 0.59 (95% CI, 0.49-0.70); 0.98 (95% CI, 0.84-1.15); and 1.00 (reference), respectively.

Conclusions: We observed a significantly lower risk of MACE in patients with psoriasis who used TNFi compared to those who used topical agents or oral/phototherapy. The results add to evidence indicating a protective effect of TNFi on CV outcomes in patients with psoriasis.

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3213

Associations between baseline disease characteristics and total amount of calcipotriene/betamethasone dipropionate aerosol foam used in patients with psoriasis vulgaris: posthoc analysis from PSO-FAST

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Introduction: PSO-FAST was a double-blind, phase III study in which 426 patients with psoriasis vulgaris were treated with fixed combination calcipotriene 0.005% (Cal)/betamethasone dipropionate 0.064% (BD) aerosol foam versus aerosol foam vehicle for 4 weeks (NCT01866163). The aerosol foam formulation led to significantly greater treatment success rates and lower modified psoriasis area and severity index (mPASI; excluding head) scores compared with foam vehicle (week 4: treatment success, 53 vs 5%, odds ratio [OR] 30.3, 95% CI 9.7 to 94.3, $P < .001$; mean decrease in mPASI from baseline, 72 vs 26%). Here we report posthoc analyses evaluating the associations between baseline disease characteristics and mean total amount of Cal/BD foam used.

Methods: Patients (aged ≥18 years) with mild-to-severe body psoriasis (involving 2-30% body surface area [BSA]) were randomized 4:1 to once-daily Cal/BD foam or vehicle. Total amount of Cal/BD foam used by each patient over the study period was determined by calculating the difference between the weight of dispensed cans and the weight of those returned, multiplied by 0.41 (correction to account for the propellant gases). Total amount of Cal/BD foam used was evaluated according to three baseline psoriasis assessments: extent of BSA affected, PGA and mPASI. Treatment success (ie, clear/almost clear for patients with at least a two-step improvement from baseline by week 4, according to physician's global assessment of disease severity [PGA]) was assessed according to body mass index (BMI) and body weight.

Results: 323 patients were randomized to Cal/BD foam. At week 4, the mean (± standard deviation [SD]) total amount of Cal/BD foam used was 120.8 ± 85.7 g (n = 293). The total amount of Cal/BD foam used was higher with larger baseline BSA (<5%, 88 ± 71 g; 5− < 10%, 118 ± 73 g; 10− < 15%, 167 ± 91 g; 15−20%, 184 ± 80 g; > 20%, 214 ± 100 g) and increasing severities of baseline PGA (mild, 95 ± 76g; moderate, 122 ± 84 g; severe, 149 ± 106 g) and mPASI (<4, 85 ± 79 g; 4− < 8, 104 ± 74 g; 8− < 12, 134 ± 71 g; 12− < 16, 204 ± 93 g; 16− < 20, 192 ± 106 g; > 20, 240 ± 100 g). Treatment success rates were generally similar when stratified according to BMI and body weight.

Conclusions: The total amount of Cal/BD foam used increased with increasing baseline BSA, PGA and mPASI. Treatment success rates were generally consistent, independent of BMI and body weight. Patients used appropriate amounts of Cal/BD foam irrespective of baseline disease characteristics (severity and extent).

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Baseline Characteristics Associated with Psoriatic Arthritis in Patients with Psoriasis in the BELIEVE Study

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Introduction: Patients (pts) with psoriasis (Ps) are at risk of developing psoriatic arthritis (PsA). This analysis sought to identify baseline (BL) characteristics associated with PsA in pts with Ps from the BELIEVE trial

Methods: BELIEVE was a 16-week, randomized, vehicle-controlled European multicenter clinical trial on the efficacy and safety of adalimumab with and without calcipotriol/betamethasone treatment in pts with Ps who had previous failure, intolerance, or contraindications to ≥2 systemic treatments. Pts met at least 2 of 3 criteria: Ps Area and Severity Index (PASI) ≥10; affected body surface area (BSA) ≥10%, and/or Dermatology Life Quality Index ≥10. PsA diagnosis was based upon patient-reported medical history. BL characteristics of pts with/without PsA were compared using Fisher exact test and T-way analysis of variance. Predictive value of palmoplantar, nail, or scalp involvement, PASI, or BSA for PsA was assessed by univariate logistic regression (ULR); backward elimination in a multivariate logistic regression (MLR) model was used to identify independent predictors. Data for intertriginous Ps were not available for analysis.

Results: Of 750 pts, 205 (28.1%) had PsA for a mean duration of 9.3 yrs. PsA pts were older (47.3 v 44.2 yrs; $P = .002$) than Ps-only pts, and had longer duration of plaque Ps (22.5 v 20.6 yrs; $P = .046$), higher nail involvement (69.6% v 60.6%; $P = .026$), greater BSA affected by Ps (55.6% v 32.0%; $P = .030$), and greater PASI score (20.5 v 19.1; $P = .05$). On ULR, PsA was significantly associated with BL nail involvement (OR, 1.49 [95% CI, 1.05-2.11; $P = .023$]) and BL PASI greater than median score of 17.2 (OR, 1.50 [95% CI, 1.06-2.08; $P = .015$]). The incidences of PsA were 51.1% (142/457) and 23.2% (62/267) in pts with and without nail involvement, respectively. Incidences of PsA were 32.1% (117/361) and 24.0% (88/366) in pts with a PASI > 17.2 and ≤17.2, respectively. Palmoplantar scalp involvement, and BSA greater than median of 29.0% were not significantly associated with PsA. Nail involvement and PASI > 17.2 were identified as independent predictors for PsA using backward elimination in a MLR model with all above potential predictors (nail involvement: OR, 1.45 [95% CI, 1.02-2.05; $P = .039$]; PASI > 17.2: OR, 1.47 [95% CI, 1.05-2.04; $P = .022$]).

Conclusions: This exploratory analysis in pts with moderate to severe Ps suggests that nail involvement and more severe Ps are associated with significantly higher odds of having PsA.

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3455

Biologics in psoriasis

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Aim: Psoriasis is defined as "immune mediated inflammatory disease (IMID)" concurrently recovery of immunologic mechanism of disease has understood. Last 20 years biologics have taken place as a novel and specific agents for moderate to severe psoriasis treatment. In this study we aimed to evaluate the treatment response of biologics from moderate to severe psoriasis patients concurrently with comorbidity, disease period, demographic specifications and family history.

Background and design: Files of psoriasis patients were reviewed retrospectively. All patients registrations were evaluated by age, family history and presence of some diseases such as diabetes, hypertension, depression, liver and kidney failure and joint and nail lesions. Adalimumab, etanercept, infliximab and ustekinumab were also evaluated by efficacy, duration of efficacy and side effects.

Results: Fifty five psoriatic patients registrations were reviewed. Patients median age were 46.74 ± 13.73, 34.5% of patients were woman as 65.5% were man. Disease period were vary from 3 to 41 years. Median disease period were found 19.30 ± 10.13 years. While 4 (8.3%) of all patients were 2nd degree relative, 10 (20.8%) of patients were found as 1st degree. 30% of patients are diagnosed as psoriatic arthritis. Nail lesions were found in 46.7% patients. Comorbidities were found as follows: hypertension 8.7%, diabetes 4.3%, depression 5.5% and liver dysfunction in 3.6%. None of the patients have kidney problem. The used biologics for psoriasis treatment were defined as follow: etanercept 26 (47.3%), infliximab 19 (35.2%), adalimumab 18 (33.3%), ustekinumab; 3 (5.5%). The longest period for stay on drug were found as 85 months. The number of patients who used drug combinations were 11,12 and 10 in adalimumab, etanercept and infliximab groups, respectively. The mean pretreatment PASI values were 14.74 ± 9.4 in adalimumab,11.33 ± 3.87 in etanercept, 20.66 ± 13.42 in infliximab and 19.85 ± 11.95 in ustekinumab groups. The mean PASI values at 3rd, 6th and 12th months were as follows: for adalimumab 6.08 ± 6.67, 5.75 ± 9.64 and 5.88 ± 11.28; for etanercept 4.43 ± 5.37, 2.43 ± 3.03 and 1.10 ± 1.01; for infliximab 9.66 ± 17.58, 4.25 ± 6.18, 3.80 ± 2.94. Reactive lymphadenopathy was observed in a patient using adalimumab. No side effects were seen in patients treated with etanercept and infliximab.

Conclusion: We find out that treatment response to adalimumab, etanercept and infliximab were effective and safe in moderate to severe psoriatic patients

Commercial support: None identified.

3781

Biologics therapy in psoriasis patients with viral hepatitis, HIV, and cardiovascular diseases

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Biologic therapies have significantly improved the lives of patients with psoriasis due to their efficacy, convenience, and tolerability. However, the management of psoriasis patients with co-existed conditions such as hepatitis B and C (HBV, HCV), Congestive Heart Failure (CHF), and HIV using biologics therapy can be challenging. Authors will report their experience of biologics therapy in these individuals at a state of the art Psoriasis Biologics Clinic providing care for a total of 374 indigent patients with psoriasis. Of 13 reported cases, 5 had viral hepatitis, 5 had cardiovascular disorders, and 3 had HIV. All 5 patients with concurrent viral hepatitis had plaque psoriasis with 2 having psoriatic arthritis (PsA) (2M, 3F, mean age 51.5 yrs, average duration 8.8 yrs). Three patients had HBV and two had HCV. All the patients had received at least one biologic agent: four treatments of etanercept and one treatment of adalimumab. Patients were evaluated by a hepatologist and were cleared to use the biologics with regular monitoring. Of 5 psoriasis patients with cardiovascular disorders, 4 had plaque and 1 had guttate psoriasis with two of them having PsA (5M, mean age 54.6 yrs, average duration 10.2 yrs). One patient had myocardial infarction (MI) and CHF, one had NSTEMI, one had a pacemaker implant, and two of them had cardiomyopathy with stent implantation. After basic screening for biologics therapy, two of them received treatment of ustekinumab and three of them adalimumab. Patients were monitored closely in our psoriasis clinic in consult with a cardiologist. From our 3 HIV positive patients all had plaque psoriasis with two having PsA (3M, mean age 54.6 yrs, average duration 12.3 yrs). All were receiving HAART therapy under the care of infectious diseases (ID) physicians. Two received etanercept and one adalimumab treatments, and were followed up closely in our psoriasis clinic in consult with their ID physicians. All 13 patients under biologics therapy showed drastic improvements in their psoriasis symptoms. None of the patients showed signs or symptoms of neither liver failure, nor viral hepatitis, HIV, or CHF exacerbation while receiving biologics. In conclusion, biologics therapy may be considered for the treatment of moderate to severe psoriasis or PsA cases with concurrent disorders such as HCV, HBV, CHF, and HIV. However, close monitoring and regular follow-ups should be performed in order to optimize the quality of care in these individuals.

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2602

Cardiovascular (CV) event risk assessment in psoriasis (Ps) patients treated with tumor necrosis factor-alpha inhibitors (TNFi) versus phototherapy

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Objective: Ps is a risk factor for CV disease; more immune activity in Ps is associated with more inflammation and higher CV event risk. Thus, Ps treatments that better control inflammation may be associated with a lower CV event risk. This study compared the risk of major CV events in Ps patients (pts) receiving TNFi vs phototherapy.

Methods: Using a large US claims database (Q1 2000-Q3 2014), adult Ps pts with ≥2 TNFi prescription fills or phototherapy (PUVA, UVB NB, or UVB BB) sessions were classified in the TNFi or phototherapy cohorts, respectively. The index date was defined as the first TNFi or phototherapy initiation date. Pts had continuous health plan enrollment ≥6 months prior to and ≥1 month after index date. Pts previously treated with biologics were excluded. Pts were observed from index date until first major CV event (myocardial infarction, stroke or transient ischemic attack, or unstable angina) that led to hospitalization. Pts without a major CV event were censored at the end of continuous health plan enrollment, 12 months after treatment discontinuation, or at the initiation of a treatment defining the other cohort, whichever occurred first. Major CV event risk was compared between cohorts using Kaplan-Meier (KM) analyses (log-rank test) and Cox proportional hazards models adjusting for potential confounding factors.

Results: A total of 11,410 TNFi and 12,433 phototherapy (PUVA: 1117; UVB: 11,316) pts met the inclusion criteria. Mean age was 44.9 and 48.8 years, and there were 45.9% and 52.0% of females in the TNFi and phototherapy cohorts, respectively. The median follow-up time was 39.9 months for the TNFi cohort and 28.6 months for the phototherapy cohort. After 4 months of follow-up, the TNFi cohort started presenting significantly lower major CV event risk (KM estimates) compared to the phototherapy cohort, and the effect remained statistically significant until the end of the observation period. KM estimates of major CV events at 6, 12, and 24 months after the index date were 0.4%, 0.8%, and 1.4% for the TNFi cohort and 0.7%, 1.4%, and 2.7% for the phototherapy cohort, respectively (all $P < .05$). After adjusting for potential confounding factors, the TNFi cohort had a significantly lower hazard of major CV events compared to the phototherapy cohort (hazard ratio [HR]: 0.77; $P = .046$).

Conclusions: Ps pts treated with TNFi had a significantly lower risk of major CV event compared to those treated with phototherapy.

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Certolizumab pegol for the treatment of patients with moderate-to-severe chronic plaque psoriasis: An overview of 3 randomized controlled trials

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Background: Plaque psoriasis (PsO) is the most common form of PsO and comprises 80-90% cases. It imposes a substantial burden on quality of life (QoL). Certolizumab pegol (CZP), a pegylated Fc-free anti-TNF drug, has demonstrated efficacy in PsO patients (pts) in a phase 2 clinical trial. CZP has shown rapid sustained clinical improvements of both skin and joint signs and symptoms with an acceptable safety profile in a phase 3 trial of psoriatic arthritis (PsA) pts. Here, we describe the phase 3 clinical program currently underway to assess the efficacy and safety of CZP in pts with moderate-to-severe plaque PsO.

Methods: The CZP PsO clinical program consists of 2 identical phase 3, multicenter, randomized, double-blind, placebo (PBO)-controlled trials (CIMPASI-1, NCT02326298, and CIMPASI-2, NCT02326272), and a phase 3 multicenter, randomized trial that is active- and PBO-controlled (CIMPACT, NCT02346240). In all studies, pts are ≥18 years old with moderate/severe plaque PsO of ≥6 months' duration (PsO Area Severity Index [PASI] ≥12, body surface area [BSA] PsO ≥10% and Physician's Global Assessment of PsO [PGA] ≥3). Pts are candidates for systemic PsO therapy without prior exposure to CZP or >2 biologics. In CIMPACT, pts with prior etanercept (ETN) exposure are also excluded. CIMPASI-1 and CIMPASI-2 aim to demonstrate and compare the efficacy of 2 CZP doses, CZP 400 mg Q2W and 200 mg Q2W, in a PBO-controlled manner in PsO pts. Pts are randomized 2:2:1 to CZP 400 mg Q2W; CZP 400 mg at Wk 0, 2, and 4 followed by CZP 200 mg Q2W; or PBO. Co-primary endpoints are the proportion of pts achieving at Wk 16: 1) PASI75 response and 2) PGA clear or almost clear (with ≥2 category improvement). CIMPACT aims to compare the efficacy of 2 CZP doses, CZP 400 mg Q2W and 200 mg Q2W, to PBO or ETN in PsO pts. Pts are randomized 5:5:3:1 to CZP 400 mg Q2W; CZP 400 mg at Wk 0, 2, and 4 followed by CZP 200 mg Q2W, ETN 50 mg twice weekly; or PBO. The primary endpoint of CIMPACT is Wk 12 PASI75 response. In all 3 studies, other variables assessed include PsO (BSA, modified Nail Psoriasis Severity Index) and QoL (Dermatology Life Quality Index, Short Form-36, EuroQol) outcomes. Adverse events are monitored throughout. Following initial treatment periods described here, pts enter maintenance periods in each trial at Wk 16, during which long-term safety and efficacy data on various dosing regimens will be collected.

Conclusion: These studies will assess the efficacy and safety of CZP in pts with moderate-to-severe plaque PsO.

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3340

Clinical and immunological effects of subcutaneous methotrexate in psoriasis—First data from a 52-week phase III trial (METOP)

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Methotrexate (MTX) is one of the most frequently prescribed systemic therapies for psoriasis, but high quality clinical trials, especially with s.c. administration, are sparse. We report the results from a 52-week phase III trial in which 120 patients were randomized 5:1 to receive weekly s.c. injections of either MTX or placebo (PLC) for the first 16 weeks followed by a cross-over of placebo patients to active drug. The starting dose of MTX was 17.5 mg and could be increased to 22.5 mg at Week 8. The primary endpoint was the proportion of patients with a 75 % improvement of the psoriasis area severity index (PASI75) at week 16. Biopsies obtained from representative plaques at baseline and week 16 were available from a subgroup of patients (n = 27) and analyzed by histology, immunohistochemistry, and quantitative RT-PCR. At week 16, the PASI75 response rate was 41% in the MTX compared to 10% in the placebo group ($P = .0026$). PASI75 response rates at week 52 were 45% in the MTX/MTX group and 35% in the PLC/MTX group. PASI90 response rates were 18% (MTX) compared to 0% (PLC) at week 16, and 28% at week 52 (for both, the MTX/MTX and MTX/PLC groups). A physicians' global assessment (PGA) of clear or almost clear was achieved by 28% (MTX) and 7% (PLC) at week 16, and 40% (MTX/MTX) and 38% (PLC/MTX) at week 52, respectively (all analyses mITT-NRI). At least one SAE occurred in 1.1% (MTX) and 13.8% (PLC) of patients in the first 16 weeks, and in 2.2% (MTX/MTX) and 3.4% (PLC/MTX) of patients between week 16 and 52. No MTX-related SAEs were observed in the study. Of the patients with biopsies available, 14/27 were MTX PASI75 responders. In these patients a reduction of cutaneous IL-17A mRNA levels (to 10%) and IFN- mRNA levels (to 25%) by week 16 compared to baseline was observed parallel to a decrease of infiltrating CD3-positive T cells and CD11c-positive dendritic cells and a normalization of different parameters of epidermal dysfunction (Ki-67 expression, epidermal thickness, parakeratosis, presence of epidermal microabscesses). These effects were weaker in MTX PASI75 non-responders (7/27) and mostly absent in patients receiving placebo (6/27). The study documents safe and stable clinical responses of patients with psoriasis to subcutaneous MTX, with clear or almost clear skin achieved by approximately 4/10 patients at one year. Clinical effects were linked with effects of MTX on psoriasis-characteristic inflammatory pathways.

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Clinical characteristic of pustular psoriasis in 53 Thai patients

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Background: Pustular psoriasis is a rare variant of psoriasis. Limited data regarding the clinical characteristics, treatment outcome and clinical course of pustular psoriasis are available.

Objectives: To study clinical features, treatment outcome and clinical course of pustular psoriasis in Thai patients.

Materials and methods: A retrospective cohort study of pustular psoriasis patients with age more than 15 years who attended Dermatology clinic at Siriraj Hospital from July 2002 to October 2014 was conducted. Clinical features, treatment modalities, treatment response and clinical course were reviewed. We defined "complete response" as total clearing of the pustular lesions, "partial to good response" as ≥50% clearance, and "poor response" as <50% clearance of pustular lesions at the end of follow-up.

Results: Of the 53 pustular psoriasis cases, female to male ratio was 1.9:1. The mean age was 42.2 years (SD = 15.8) and mean age at onset was 36.6 years (SD = 17.2). Twenty-three patients had concomitant plaque type psoriasis vulgaris and the mean time to develop pustular psoriasis after plaque type psoriasis was 7.9 years. The common precipitating factors were inadequate sleep (30.2%), infection (30.2%) and drug (28.3%). Systemic steroid withdrawal (60% of drug-induced pustular psoriasis) was found to aggravate pustular psoriasis with an average time of 1.7 weeks after withdrawal. The common manifestation of pustular psoriasis was exanthematic type (60.4%) followed by localized type (22.6%). Topical steroid (98.1%) was the most common topical treatment while acitretin was the most frequently prescribed systemic treatment (75.5%), followed by methotrexate (43.4%). Regarding course of disease, 12 (22.6%) patients had complete response from treatment in a mean period of 3.45 weeks and 36 (67.9%) patients had partial response in a mean period of 5.4 weeks. Five patients (9.4%) had no response. None of the patients developed severe complications from pustular psoriasis or treatment related-disease.

Conclusion: Pustular psoriasis is a rare condition in Thailand. Exanthematic pustular psoriasis is the most common type and acitretin remains the most common prescribing drug. Most of the pustular psoriasis patients had a benign clinical course and can be controllable.

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Clinical outcomes associated with switching or discontinuation of anti-TNF inhibitors for nonmedical reasons in psoriatic disease patients

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Objective: To evaluate real-world clinical outcomes associated with nonmedical switching of anti-tumor necrosis factor (TNF) agents among patients with psoriasis (Ps) or psoriatic arthritis (PsA).

Methods: An online, physician-administered chart review was used to collect data on patients with a diagnosis of Ps or PsA who had a response for ≥6 months to an anti-TNF therapy. Physicians selected 2 cohorts that were matched based on primary diagnosis: patients who switched or discontinued from the anti-TNF therapy on which they had achieved a response for nonmedical reasons (switchers/discontinuers) and patients who did not discontinue for nonmedical reasons (continuers). Nonmedical reasons for switching/discontinuing included increased copay, change of insurance, job loss, and other economic factors that limited affordability of medication. Data for switchers/discontinuers were assessed for 12 months from the date of discontinuation (index date) and data for continuers were assessed for 12 months from the date of an office visit within 2 months of the matched switcher/discontinuer's index date. Generalized linear models were used to compare disease control and flares between cohorts with adjustment for baseline characteristics.

Results: 157 matched pairs of switchers/discontinuers and continuers were analyzed (N = 314); 83% of patients in both cohorts had a diagnosis of Ps, and 17% had a diagnosis of PsA. Mean age of the cohorts was similar (45 vs 46 years, P = .39). The percentage of males was significantly greater among switchers/discontinuers than continuers (70% vs 54%, P = .001). At baseline, there was no significant difference (P = .79) in disease severity between cohorts. During the follow-up period, more switchers/discontinuers than continuers had disease flares (86% vs 58%; adjusted odds ratio [OR] = 4.2, P <.001). Flares were more frequent among switchers/discontinuers than continuers (3.1 vs 1.6 flares; adjusted OR = 1.92, P = .002). Only 43% of switchers/discontinuers had well-controlled disease symptoms per the physician, a rate significantly lower (adjusted OR = 0.06, P <.001) than continuers (92%).

Conclusions: Switching or discontinuation of an anti-TNF therapy for nonmedical reasons was associated with significantly worse clinical outcomes among patients with Ps and PsA.

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Comparative effectiveness of biologic therapy in the Psoriasis Longitudinal Assessment and Registry (PSOLAR) Study

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Background/objective: PSOLAR is an observational study which evaluates safety and clinical outcomes in psoriasis patients. Physicians prescribe treatments including UST, ADA, ETN, and IFX per standard clinical practice. To compare the effectiveness of ustekinumab (UST) to adalimumab (ADA), etanercept (ETN) and infliximab (IFX) for the treatment of psoriasis at 6 months in a real-world setting.

Methods: Physician's Global Assessment (PGA) scores and body surface area (BSA) affected with psoriasis were assessed at the time of starting a new biologic on registry and at 6 months. Only patients who remained on therapy at 6 months were included; however, discontinuation before 6 months due to lack of effect was counted as treatment failure. Patients could be included in only one treatment group, and patients using concomitant systemic psoriasis therapies were excluded.

Results: Overall, there were 2076 new users of biologics, including UST (n = 1041), ADA (n = 662), ETN (n = 257), IFX (n = 116). Baseline characteristics (eg, age, gender, race, BMI) were generally comparable among treatment groups, while baseline PGA scores and BSA affected with psoriasis were more variable. Results from adjusted logistic regression analyses (including adjustment for baseline severity) showed that patients on ADA were less likely to achieve a PGA of 0/1 at 6 months versus patients on UST (odds ratios: 0.69 [P =.0016]). Similarly, patients on ETN and IFX were less likely to achieve a PGA score of 0/1 at 6 months compared to patients on UST (odd ratios: 0.56 [P = .0005], and 0.40 [P <.0001], respectively). Change in percent BSA affected with psoriasis at 6 months versus baseline was significantly greater for UST compared to ADA (1.85%, P = .0019) and for UST compared to ETN (3.45%, P <.0001), and trended greater for UST compared to IFX (1.80%, P = .1048).

Limitations: Observational studies are subject to potential confounding from unmeasured variables, as well as selection and information bias. This study did not control for patients' baseline disease status with respect to timing of or response to their previous therapy, dosing regimen or adjustments in dosing.

Conclusion: Data comparing the effectiveness of available biologic treatments for psoriasis are limited. In this large observational study, UST revealed higher clinical effectiveness (PGA and BSA responses) than TNF inhibitors after 6 months of usage.

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Comparison of a selective IL-23p19 inhibitor (BI 655066) with ustekinumab in patients with moderate-to-severe plaque psoriasis: Analysis of scalp, palmoplantar, and nail psoriasis subgroups

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Involvement of scalp, palmoplantar surfaces, or nails in psoriasis has a considerable negative impact on patient quality of life. In addition, these sites are considered relatively resistant to therapy. We assessed the efficacy of BI 655066, a selective IL-23 inhibitor for the treatment of scalp, palmoplantar and nail psoriasis (NCT02054481). In this multicenter, randomized, double-blind (within BI 655066 dose groups) phase II study, 166 patients with moderate-to-severe chronic plaque psoriasis were assigned to receive subcutaneous injections of BI 655066 (18 mg single injection; 90 mg or 180 mg at Weeks 0, 4 and 16) or ustekinumab (45 mg or 90 mg, based on body weight, at Weeks 0, 4 and 16). Psoriasis Scalp Severity Index (PSSI) and Palmoplantar Psoriasis Area and Severity Index (PPASI) were used to evaluate scalp and palmoplantar psoriasis, respectively. Nail Psoriasis Severity Index (NAPSI) was assessed on the hands only. Assessments were performed at baseline and (in those who had respective features at baseline) at Weeks 1, 2, 4, 6, 8, and every 4 weeks through Week 48. Patients who were documented to have no signs or symptoms were assigned a total score of zero for that visit. Median percentage improvements from baseline for BI655066 (90 mg and 180 mg, pooled) were compared with those for ustekinumab. One hundred and fifty four (92.8%) patients had scalp psoriasis, 42 (25.3%) patients had palmoplantar psoriasis and 96 (57.8%) patients had nail psoriasis. Scalp and palmoplantar disease responded rapidly; by Week 2, BI 655066-treated patients showed improvements from baseline in PSSI and PPASI of 50% and 51%, compared with 37% and 30% for ustekinumab-treated patients. By Week 6, patients in both BI 655066 and ustekinumab groups had complete clearance of scalp psoriasis, which were maintained throughout the study. For PPASI, complete clearance was seen at Week 6 for BI 655066 and Week 16 for ustekinumab and maintained throughout the study. Nail disease resolved more slowly, with 30% improvement in NAPSI for BI 655066 at Week 6 compared to 0% for ustekinumab. By Week 12, improvements in NAPSI were 41% and 36% for BI 655066 and ustekinumab, respectively, and by Week 24, the improvements in NAPSI were 61% and 67%, respectively. Selective blockade of IL-23 by BI 655066 demonstrates promising efficacy in the treatment of scalp, palmoplantar, and nail psoriasis, and suggests a more rapid improvement may be achieved with BI 655066 compared with ustekinumab.

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3765

Comparison of efficacy of ixekizumab and ustekinumab in the treatment of plaque psoriasis: An indirect comparison via etanercept

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Introduction: Psoriasis is a common, lifelong, and life-shortening chronic inflammatory skin disease manifested by prototypic red, thick, and scaly plaques. Ustekinumab (UST) is currently considered one of the most effective drugs for treatment. While at least a 75% improvement in Psoriasis Area and Severity Index (PASI 75) score from baseline is regarded as an optimal treatment goal for the first generation of biologic therapies, experience with UST and IL-17 inhibitors (including ixekizumab [IXE]) has shown that higher levels of improvement, such as PASI 90, can be consistently obtained in patients with moderate to severe psoriasis.

Methods: We indirectly compared UST (45 mg/90 mg) and IXE (80 mg every 2 weeks [Q2W] or every 4 weeks [Q4W]) via the common comparator etanercept based on the respective active comparator studies (ACCEPT, UNCOVER 2 and 3) using methods by Bucher (BU) and a modified version of Signorovitch (SG), which adjusts for baseline differences of studies, for PASI 75 and PASI 90 endpoints at Week 12.

Results: Differences in response rates between treatments showed significantly better efficacy outcomes for IXE vs UST across all dose comparisons, endpoints, and comparison methods. For IXE Q2W, PASI 75 rates were 23.9% (95% confidence interval: 15.7%-32.1%) higher than UST 90 mg using BU and 24.0% (15.3%-32.8%) higher when adjusting for baseline differences between studies using SG. PASI 90 rates differed by 25% (17.3%-33.7%) and 26.3% (17.5%-35.1%), respectively. For IXE Q4W, PASI 75 rates were 16.8% (8.5%-25.1%) higher than UST 90 mg using BU and 18.8% (10.1%-27.6%) higher when baseline differences were accounted for. PASI 90 rates differed by 19.1% (10.8%-27.3%) and 21.3% (12.6%-30.0%), respectively. Comparing IXE Q4W with UST 45 mg, PASI 75 rates were 23.1% (13.7%-32.5%) higher applying BU and 25.0% (15.2%-34.8%) higher for SG. Differences in PASI 90 rates were even larger, with 27.4% (18.2%-36.5%) using BU and 29.8% (20.4%-39.3%) using SG.

Conclusions: IXE demonstrated better efficacy compared to UST in terms of both PASI 75 and PASI 90 rates via indirect comparisons irrespective of dosing regimens. Weight-based dosing could not be taken into account. Baseline differences between studies are one of the main critiques against indirect comparisons. Using the modified SG approach to adjust for these, the observed treatment differences were slightly larger, underlining the robustness of results.

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3420

Comparison of guselkumab with placebo and adalimumab on health-related quality of life in a phase 2b clinical trial X-PLORE

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Background: Using data from X-PLORE, a phase 2b clinical trial, we investigated the impact of subcutaneous injections of guselkumab (GUS) on health related quality of life (HRQoL) when compared with placebo (PBO) and adalimumab (ADA) in patients with moderate to severe plaque psoriasis.

Methods: Moderate to severe plaque psoriasis patients with Psoriasis Area Severity Index (PASI) score ≥12, Physician's Global Assessment (PGA) ≥3 and BSA ≥10% (n = 293) were randomized to receive PBO, GUS (five dose groups: 5 mg q12wk, 15 mg q8wk, 50 mg q12wk, 100 mg q8wk, 200 mg q12wk), or ADA (80 mg at wk0, followed by 40 mg at wk1 and then every other wk). At wk16, patients initially assigned to PBO were to receive GUS 100 mg q8w through wk40. HRQoL was assessed using Dermatologic Life Quality Index (DLQI) and were compared between GUS with PBO at wk16, or between GUS and ADA at wk16 and 28. A DLQI score of ≤1 was defined as no impact of psoriasis on HRQOL.

Results: At baseline, the median DLQI score was 14, indicating very large effect of psoriasis on patient HRQoL. At wk16, patients in each GUS dose group had significantly greater improvement in HRQoL as demonstrated by greater improvement in DLQI scores, a greater proportion of patients achieving a DLQI score ≤1, or a greater proportion of patients achieving a reduction of ≥5 points in DLQI, when compared with patients in the PBO group, especially in higher dose GUS groups (P < .01 or < .001). A greater improvement in DLQI score was observed as early as wk4, and sustained through wk52 in all GUS treatment groups. Improvements of DLQI score were comparable between the ADA and GUS groups except for 5mg group at wk 16 and 28, while at wk28, higher GUS dose groups (ie, 100 mg q8w or 200 mg q12w) were more likely to achieve a DLQI score of ≤1 (64.1% and 83.3%, respectively) than patients in the ADA group (45.3%) (P = .068 and P < .001, respectively). Overall, improvement in DLQI was correlated with improvement in PASI at wk16 and 28.

Conclusion: GUS treatment significantly improves disease specific quality of life, especially in high dose groups (100 mg q8wk or 200 mg q12wk).

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Comparison of outcomes between psoriasis (Ps) patients (Pts) who switched from etanercept (ETA) to adalimumab (ADA) versus to ustekinumab (UST)

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Background: When Ps symptoms are not adequately controlled with ETA, pts may switch to a biologic with a different mechanism of action, such as UST, or to another tumor necrosis factor (TNF) inhibitor, such as ADA.

Objective: To compare health care resource utilization (HRU), health care costs, and dose escalation in Ps pts who switched from ETA to UST vs ADA.

Methods: In the Truven Health Analytics MarketScan database (2000-14), adult Ps pts who switched from ETA to UST or ADA on/after 9/25/2009 were identified. Pts who used a biologic approved for Ps other than ETA any time before the first UST/ADA prescription fill date (index date) were excluded. Pts were continuously enrolled in their health care plan for ≥6 months before (baseline) and ≥12 months after the index date (study period). HRU and costs (2014 US $) were measured over the 12-month study period following the index date and compared between UST and ADA pts using multivariate generalized linear regression models. Dose escalation, defined as a dose increase between injections equivalent to ≥45 mg/84 days for UST and ≥40 mg/28 days for ADA, were captured from the index date until the first dose escalation. ADA/UST discontinuation (treatment interruption ≥90 days), or the end of the study period, whichever occurred first. Dose escalation rates were compared between UST and ADA pts using multivariate Cox proportional-hazard models.

Results: Overall, 365 UST and 1335 ADA pts were selected. Median age was 48 in both treatment cohorts and pts were mainly male (ADA = 56.0%; UST = 58.6%; P = .36). Pts generally had similar baseline characteristics; however, a greater proportion of ADA pts had psoriatic arthritis (ADA = 13.7% vs UST = 6.6%; P <.01). Over the study period, UST pts had significantly more days with medical services (adjusted incidence rate ratio [IRR] = 1.11; P = .02), mainly driven by higher incidence of outpatient visits (adjusted IRR = 1.13; P <.01). After adjustment for potential baseline confounding factors, UST pts had higher total annual health care costs by $14,456 (unadjusted: $49,418 vs $35,233), mainly driven by higher pharmacy costs by $13,682. UST pts were also more likely to have a dose escalation (12.1% vs 8.9%; adjusted hazard ratio = 1.66; P <.01) than ADA pts.

Conclusions: Pts who switched from ETA to UST incurred higher HRU and costs over the 12-month study period than pts who switched to ADA. UST pts also had higher rates of dose escalation than ADA pts.

Design, study conduct, and financial support for the study were provided by AbbVie; AbbVie participated in the interpretation of data, review, and approval of the abstract; all authors contributed to the development of the publication.

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Comparison of the pharmacokinetics of ixekizumab following subcutaneous administration using a prefilled syringe versus an autoinjector in patients with moderate-to-severe psoriasis

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Introduction: Many biologic agents for the treatment of psoriasis are available as self-administered injections via an autoinjector. In clinical trials of ixekizumab, an anti-IL-17A monoclonal IgG4 antibody with high binding affinity, treatment has been delivered subcutaneously (SC) via prefilled syringe (PFS). The primary objective of the study was to evaluate the effect of drug delivery, either by PFS or autoinjector, on the pharmacokinetics (PK) of ixekizumab for 2 weeks after administration of a 160-mg initial dose.

Methods: This open-label, phase 3 study randomized patients with moderate-to-severe psoriasis to an injection device (PFS or autoinjector). To achieve an equal number assigned to the PFS and autoinjector within weight and injection site category, randomization was stratified by weight (<80 kg, 80 to 100 kg, >100 kg), injection assistance (yes/no), and injection site (arm, thigh, or abdomen). Following a 160-mg initial dose at week 0, patients received SC 80 mg ixekizumab as one injection every 2 weeks. Blood samples were collected following the initial 160-mg dose on days 2, 4, 7, 10, and 14 for PK analysis. Serum samples were analyzed for ixekizumab using a validated enzyme-linked immunosorbent assay method. PK parameters were determined using noncompartmental analysis methods. The primary parameters were maximum concentration (C_{max}) and area under the curve (AUC[0-tlast]) where tlast is time of the last sample (14 days ± 24 hours). Patients with 3 or fewer serum samples or missing day 14 values were not included in the PK analyses.

Results: Of 204 randomized patients, 192 were included in the PK analysis (PFS: 94; autoinjector: 98). The majority of patients were male (70%) and white (87%) with a mean age of 46.5 years. Baseline characteristics were similar between groups. The PFS and autoinjector showed similar maximum concentration (geometric mean Cmax [90% CI]: 15.0 μg/mL [13.9-16.1] vs 14.8 μg/mL [13.8-15.9]). The geometric mean AUC (90% CI) with the PFS was 157 μg*day/mL (147-168) vs 154 μg*day/mL (144-165) with the autoinjector. Variability in these parameters was also similar for each device group, with percent coefficient of variation estimates in the 41-46% range. The time to maximum concentration (median Tmax [min-max]) was also similar between the PFS (3.97 days [1.88-13.96]) and autoinjector (4.00 days [1.88 14.01]).

Conclusions: Ixekizumab PK results were similar between the PFS and the autoinjector.

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Consistent High Efficacy Adalimumab PASI75 Responders: a Post Hoc Analysis of REVEAL

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Introduction: A high proportion of patients (pts) with moderate to severe psoriasis (Ps) treated with adalimumab (ADA) achieve a Ps Area and Severity Index (PASI) 75. Among PASI75 responders at Week 33 of the REVEAL trial, PASI90/100 responses at Week 33 were 67% and 33%, respectively. This post hoc analysis was conducted to assess, among pts treated with ADA who achieved a PASI75 response, whether this high-efficacy response was consistently maintained and affected other efficacy endpoints (eg, DLQI).

Methods: REVEAL (NCT00237887) was a 52-week, double-blind, randomized, placebo (PBO)-controlled phase 3 study of ADA for moderate to severe plaque Ps. At Week 16, ADA-treated pts with ≥PASI75 response continued onto Period B. Pts from the ADA arm of Period B with a ≥PASI75 response at Week 33, were rerandomized in Period C to continue ADA 40 mg eow or to receive PBO, and sustained responses were assessed at Week 52. Pts were considered to have a consistent high-efficacy response if their PASI score at every visit after Week 33 until Week 52 was never >2 points higher than their Week 33 PASI score.

Results: A total of 250 pts achieved a PASI75 response at Week 33 and were rerandomized to continue ADA treatment; 245 pts had a study visit after Week 33 and were evaluable for consistent high-efficacy response. A total of 76.3% of pts (187/245) were consistent high- efficacy responders through Week 52. PASI75/90/100 response rates after 52 weeks of continuous ADA treatment were 84%/58%/33%, respectively. The mean change from baseline in PASI scores among high-efficacy responders at Week 52 was −16.7 and was significantly greater than in pts without a consistent high-efficacy response (−14.5; $P = .018$). Mean Dermatology Life Quality Index scores at Week 52 were 0.8 among high-efficacy responders compared with 4.3 among those without a consistent high-efficacy response. Of the ADA-treated pts with postweek 33 PASI data, 10 (6.0%) of the PASI90 responders and 1 (1.2%) of the PASI100 responders at re-randomization lost their PASI75 response by Week 52.

Conclusions: Evaluation of an enriched population of pts who had PASI 75 response at Weeks 16 and 33 after initiating ADA demonstrated that the majority of these pts had consistent high-efficacy response with continued ADA therapy beyond Week 33. Pts with consistent high-efficacy responses had better quality of life scores compared to those without consistent high-efficacy responses.

AbbVie Inc participated in the study design; study research; collection, analysis and interpretation of data; and writing, reviewing and approving of this publication. All authors had access to the data and participated in the development and review.

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Cost per responder of apremilast and etanercept in patients with moderate to severe plaque psoriasis using results from LIBERATE

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Background: Previous cost-per-responder analyses for moderate to severe plaque psoriasis have been performed using efficacy data for apremilast and etanercept from a network metaanalysis. The LIBERATE study is the first phase 3b trial of the oral phosphodiesterase 4 inhibitor apremilast in biologic-naive patients with moderate to severe plaque psoriasis to include an active control treatment arm. Efficacy data from LIBERATE demonstrated that apremilast and etanercept each independently produced significant improvement in the signs and symptoms of psoriasis at Week 16 vs placebo. The purpose of this analysis was to compare the cost per responder after 16 weeks of therapy with apremilast 30 mg BID or etanercept 50 mg QW in adults with psoriasis using results from the LIBERATE study.

Methods: A responder in the analysis was defined as a patient achieving a ≥75% reduction from the baseline Psoriasis Area and Severity Index score (PASI-75) at the end of the placebo-controlled period in LIBERATE. Cost and efficacy comparisons were made at Week 16. US wholesale acquisition cost as of August 2015 and dosing used in the LIBERATE trial were used to derive drug treatment costs.

Results: At Week 16, the PASI-75 response rate was 39.8% for apremilast and 48.2% for etanercept. The cost per PASI 75 responder at Week 16 was $5742.55 lower for apremilast compared with etanercept (apremilast: $20,835.38; etanercept: $26,577.93).

Conclusions: As compared with etanercept, apremilast had a lower wholesale acquisition cost per PASI-75 responder at Week 16 in patients with moderate to severe plaque psoriasis.

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Cost-effectiveness of apremilast in moderate to severe psoriasis in the UK

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Background: The treatment strategy for moderate to severe plaque psoriasis is highly individualized and dependent on many factors. In the absence of a universal treatment strategy, switching between various treatment options, including biologics, is a common practice among prescribers. We assessed the cost-effectiveness of placing a novel oral treatment, apremilast, after the failure of conventional systemic therapy but before biologics for moderate to severe plaque psoriasis from a UK payer perspective.

Methods: A 10-year Markov transition cohort model was developed comparing alternative treatment sequences: (1) apremilast followed by adalimumab followed by etanercept and (2) adalimumab followed by etanercept. Patients failing etanercept received best supportive care (BSC) as the last line of treatment in both sequences. Response was defined as a ≥75% reduction in Psoriasis Area and Severity Index score (PASI-75) at the end of the trial periods (12 to 16 weeks). Nonresponders moved to the next treatment line. A 20% all-cause annual dropout rate was assumed for each treatment. Efficacy inputs were obtained from a network metaanalysis. Unit costs were sourced from the British National Formulary, National Health Service (NHS) reference costs, and other published sources. A 3.5% annual discount rate was applied to costs and quality-adjusted life-years (QALYs). Utility gains by PASI response were obtained from apremilast clinical trial data.

Results: Placing apremilast before biologics as a treatment extension strategy resulted in an incremental cost-effectiveness ratio (ICER) of £20,593 per QALY gained. The apremilast arm had an additional 0.75 years in which patients achieved PASI-75 and an additional 0.09 QALYs (5.78 vs 5.69). Total time spent on biologics and in BSC was reduced by 0.44 and 1.01 years, respectively. Total costs were increased by £1882. Results were robust to a series of sensitivity and scenario analyses. Similar results were obtained when combinations of other biologics, including ustekinumab, were used in a 2- to 5-drug sequence. The probabilities of cost-effectiveness were 0.50 and 0.80 at willingness-to-pay thresholds of £20,000 and £30,000.

Conclusions: Placing apremilast after the failure of conventional systemic therapy but before biologics as a treatment extension strategy resulted in more QALYs and an ICER below £30,000 compared with routine NHS practice in the treatment of moderate to severe plaque psoriasis in the UK.

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3207

Current status of observations of malignancies in the psoriasis longitudinal assessment and registry (P.S.O.L.A.R.) study

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Objective: To report cumulative incidence and results of analysis of malignancies excluding nonmelanoma skin cancers (NMSC) in PSOLAR.

Methods: PSOLAR is a multicenter, longitudinal, observational study evaluating long-term safety and clinical outcomes for pts eligible to receive treatment for psoriasis with biologics and/or conventional systemic agents. The incidence of malignancies excluding NMSC (eg, basal/squamous cell carcinomas) overall and by treatment is reported. The rules for attribution of a malignancy to a therapy use a definition of exposure based on whether pts had ever been exposed to a given therapy at any time prior to the event. In cases of exposure to >1 therapy, the rule for attribution of malignancy to a treatment is ustekinumab (UST) 1st, infliximab (IFX)/golimumab (GLM) 2nd, other biologics 3rd (nearly all adalimumab (ADA) or etanercept (ETN)), or nonbiologic therapy 4th, which is consistent with the prespecified analytic plan. Analysis using Cox hazard regression was used to identify predictors of malignancy and included medication exposure defined as UST vs no biologic and biologics other than UST (primarily ADA, IFX and ETN) vs no biologic.

Results: PSOLAR is fully enrolled and, as of Aug 23, 2014, has 40,388 total pt-years of follow up with 12,093 pts. Age and gender adjusted cumulative rates of malignancy (excluding NMSC) overall and across treatments were: overall 0.68 events/100 pt years of observation (PY) [95%CI: 0.60, 0.76; 274/40388PY], UST 0.51/100 PY[95% CI: 0.39, 0.66; 60/12472PY], IFX/GLM (almost exclusively IFX) 0.81/100 PY[95% CI: 0.58, 1.10; 41/5176PY],other biologics (almost exclusively ETN/ADA) 0.73/100 PY [95% CI: 0.61, 0.88, 116/15991PY],and non-biologic therapy 0.75/100 PY[95% CI: 0.56, 0.99; 57/6749PY]. Multivariate analysis, based on any time exposure, revealed that increasing age ($P < .001$), and previous malignancy history ($P < .001$) were significant predictors of malignancy. No statistically significant increased risk of malignancy with the use of any biologics was observed.

Conclusions: Overall cumulative rates of malignancies are comparable across treatments. Age and previous malignancy were found to be associated, however, no biologics or immunomodulators were found to be associated with an increased risk of malignancy.

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3830

Disease burden in patients with severe psoriasis

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Introduction and objectives: Moderate to severe psoriasis is associated with a significant burden of disease and negatively impacts an individual's quality of life. Here we evaluated the patient-reported burden of illness of patients with moderate to severe psoriasis enrolled in phase 3 clinical trials of secukinumab.

Materials and methods: Baseline data from four phase 3 trials of secukinumab were pooled for analysis. Patient-reported burden of illness was evaluated using skin-related quality of life assessed with the Dermatology Life Quality Index (DLQI) and EuroQol 5-Dimensions visual analog scale (EQ-5D VAS). Patient-reported severity of psoriasis-related symptoms (itching, pain, and scaling) were assessed with the Psoriasis Symptom Diary (PSD). Each PSD item was completed using a 0-to-10 numeric rating scale. Descriptive statistics (mean, standard deviation and ranges for continuous variables and frequencies and percentages for categorical variables) were computed and summarized by psoriasis severity at baseline assessed by Psoriasis Area Severity Index (PASI) (moderate: PASI ≤20 or severe: PASI >20), and previous biologic therapy status (naïve or experienced).

Results: Of 2403 patients randomized across 4 trials, 1151 (48%) were classified with severe disease at baseline and were mostly male (72%) with mean age of 44 years and mean (SD) baseline PASI score of 30.3 (9.0). At baseline, most patients had previous experience with biologic therapy—severe: n = 959 (83%); moderate: n = 942 (75%). Patients with severe disease reported worse baseline scores than those with moderate disease: DLQI total score, 14.3 vs 12.0, respectively; mean EQ-5D VAS score, 59.1 vs 66.6; and mean psoriasis-related itching (6.7 vs 6.0), pain (5.7 vs 4.9), and scaling (6.7 vs 6.1). Among the patients with severe disease, those with previous biologic therapy were slightly younger than the naive patients (43.9 vs 46.6), baseline PASI scores were similar (30.1 vs 30.9). Patients naive to previous biologics reported worse scores for all PRO measures than those with previous biologic therapy.

Conclusions: The burden of illness for psoriasis patients with severe disease is high. Further, patients with severe disease with no previous biologic experience report greater impact on PROs than those with previous biologic experience. Ensuring adequate treatment to achieve clear skin is essential to optimize patient outcomes.

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3573

Dosing patterns with and cost impact of etanercept and ustekinumab for psoriasis in a real-world setting

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Background: There is a lack of evidence on the actual versus expected dosing patterns and costs of biologics used for psoriasis.

Objective: To estimate actual dosing of etanercept (ETN) and ustekinumab (UST), compare it to recommended dosing in the US Package Insert (USPI), and to describe total annual psoriasis-related costs in biologic-naïve psoriasis patients on these therapies.

Methods: Adults (age 18-63) with psoriasis initiating ETN or UST (index event) from 2011-2013 were identified in the MarketScan Commercial Database. Patients were required to have 12 months of continuous enrollment pre- and postindex without any psoriasis-related biologic use during the preindex period. Patients with other biologic-indicated comorbid conditions were excluded. Actual-to-expected dose ratios were computed for ETN/UST users while persistent on therapy. Ratios >1 indicated that actual drug dose was greater than the expected dose. Expected dose was calculated according to USPI for both therapies. However, as UST was approved as a weight-based dosing regimen, expected UST dose was based on clinical trial data reporting 69% of psoriasis patients weighing ≤100 kg ("low weight"). Specifically, patient weight was randomly assigned to match this distribution with low index dose patients being assigned as "low weight." Annual psoriasis-related costs consisting of biologics, nonbiologic psoriasis therapies, and psoriasis-related health care utilization were calculated. Chi-square and t-tests were used to compare categorical and continuous variables between ETN and UST, respectively.

Results: A total of 2997 patients met the study selection criteria with approximately two-thirds initiating ETN (n = 2128). The ETN and UST cohorts were similar in terms of age (45.2, both) and baseline Deyo Charlson Comorbidity Index Score (0.3, both). ETN patients were more likely to be female (49.4% versus 44.1%, $P = .008$). While persistent, the actual dose of ETN patients were closer to the expected dose than UST patients (ratio: 0.949 versus 1.169, $P < .001$). Total psoriasis-related costs were lower for etanercept than ustekinumab patients during the 12 months follow-up period ($28,291 versus $37,537, $P < .001$). Both index biologic costs ($24,629 versus $34,962, $P < .001$) and non-biologic, other psoriasis costs ($1807 versus $1850, $P = .034$) were lower for etanercept patients.

Conclusions: During the first year of psoriasis treatment, patients initiating ETN had 20% lower actual-versus-expected dosing ratio while persistent and 25% lower total annual psoriasis-related costs than UST patients.

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3803

Drug survival of biologic medications in psoriasis

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Background: Recently, drug survival has become an important clinical issue in psoriasis and is directly connected to treatment efficacy.

Objective: To investigate the drug survival of adalimumab, infliximab, etanercept, and ustekinumab in the treatment for psoriasis.

Methods: Survival analysis was performed in patients who received adalimumab, infliximab, etanercept, and ustekinumab for the treatment of psoriasis, drawn from the Clalit Health Services database. Multivariate analysis was performed, adjusting for demographic variables, metabolic syndrome and its components, psoriatic arthritis, coadministration of methotrexate or acitretin and previous biologic treatment exposure.

Results: Among 664 patients treated with biologics, ustekinumab had a significantly higher survival rate than tumor necrosis factor inhibitors (TNFIs). High socioeconomic status and concomitant methotrexate use were positive predictors for drug survival. None of the biologic agents' survival was significantly affected by previous exposure to one or two other different biologics.

Conclusion: Ustekinumab had the highest drug survival of all biological agents, although its use as a third-line treatment in most of the patients in the CHS. Previous exposure to previous different biologic agent was not observed to be a predictor for treatment drop-out necessarily.

Commercial support: None identified.

3221

Early clinical response as a predictor of subsequent response to tofacitinib treatment: Results from two phase 3 studies of subjects with moderate to severe plaque psoriasis

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Background: Ability to predict efficacy of psoriasis treatment has important clinical implications. Biomarkers or patient characteristics that can reliably predict treatment response in psoriasis patients remain elusive. Tofacitinib is an oral Janus kinase inhibitor that is being investigated for psoriasis. An exploratory analysis of data from a phase 2 tofacitinib psoriasis study suggested that early clinical response could predict subsequent efficacy.

Objective: To identify and validate that early clinical response can reliably predict later efficacy.

Methods: Identification of predictors of response was conducted on data from phase 3 study OPT Pivotal 1 (OPT 1; NCT01276639). Univariate logistic regression modeling was used with PASI75 response at Week (Wk) 16 as the dependent variable, and percent change from baseline PASI (at Wk 2, 4, 8, 12) and selected baseline characteristics (age, gender, weight, body mass index [BMI], C-reactive protein [CRP], duration of disease, previous biologic therapy, PASI, body surface area [BSA] impacted by psoriasis, age at onset of psoriasis) as predictor variables. Predictive ability was evaluated by area under the receiver operating characteristic curve (AUC-ROC). For continuous variables, the threshold maximizing the Youden Index, defined as "sensitivity + specificity − 1", was selected. Predictability of identified variables was confirmed in study OPT Pivotal 2 (OPT2; NCT01309737) with identical design as OPT1.

Results: None of the selected baseline variables showed good discriminatory ability for PASI75 response at Wk 16 (AUC-ROC ≤60%). Only PASI improvement from baseline at Wk 8 and 12 demonstrated good discriminatory power to predict PASI75 response at Wk 16 (AUC-ROC ≥86% and ≥94%, respectively). Thresholds having highest predictability for PASI75 response at Wk 16 were 50% and 72% PASI improvement at Wk 8 and 12, respectively. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were 87%, 71%, 78% and 83% for the threshold of 50% PASI improvement (PASI50) at Wk 8, while the corresponding values were 86%, 90%, 91% and 84% for the threshold of 72% PASI improvement at Wk 12. Validation with PASI50 response at Wk 8 was carried out in OPT2. In all tofacitinib-treated subjects, sensitivity, specificity, PPV and NPV were 88%, 69%, 80% and 81%, respectively.

Conclusion: Achieving PASI50 at 8 weeks after initiation of tofacitinib therapy is a reliable predictor of PASI75 response at Wk 16.

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3003

Early age of onset of psoriasis (<25 years of age) may be a predictor for cardiovascular disease in patients with severe psoriasis

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Psoriasis is a chronic inflammatory skin disease that affects 2-3% of the world's population and is associated with multiple comorbidities. These include comorbidities associated in increased cardiovascular risk such as hypertension, obesity, dyslipidemia and diabetes. As well early age of onset has been associated with decreased longevity of 20 years. It is estimated that in the United States psoriasis is associated with more than 1200 excess cardiovascular related deaths. To date no known predictive factors have been able to identify patients at risk. Our previous studies have shown that patients with severe psoriasis, cardiovascular risk is increased and linked to the male gender (OR 3.64; CI 0.75-6.93), early age of onset (OR 8.85; CI 2.53-4.49), and increasing age (OR 1.07; CI 1.03-1.111). We present the index case of a patient with severe psoriasis with no history of angina, no cardiac symptoms, but because of early age of onset, underwent cardiac assessment. This is a single case report illustrating severe cardiac disease. MC is a 67-year-old male, smoker with controlled hypertension, on valsartan. Age of onset of psoriasis 16 years. Psoriasis controlled with adalimumab for 5 years. No cardiac symptoms with heavy work. Brother with cardiovascular disease, age 50. BP 130/70. Heart rate 76. BMI 24.3. PE otherwise normal. EKG - nonspecific ST changes. Stress test Bruce protocol - extensive ST segment depression, ic, multivessel disease. Coronary angiogram - 100% blockage of RCA, 90% occlusion of the osteo OM2 lesion with circumflex 70% calcified proximally. Left main - 50-60% ulcerated irregular plaque distally. Grade 2 LV function. Urgent coronary artery bypass grafting of 4 vessels. Framingham score 17, <30% risk of CV disease over 10 years. Approach Jeopardy = 100%; Duke Jeopardy 12/12. Age of onset of psoriasis may be a valuable tool for predicting cardiovascular risk in patients with severe psoriasis. This index case illustrates that early age of onset of psoriasis may be associated with extensive and potentially lethal coronary artery disease. Screening patients with early age of onset will help detect patients at risk of sudden cardiac death and thus help prevent some of the 12,000 premature cardiovascular deaths associated with severe psoriasis seen yearly in the United States (and the some 120,000 worldwide).

Commercial support: None identified.

3421

Ease of use and confidence with a prefilled syringe to administer ixekizumab in a phase 3 trial evaluated with subcutaneous administration assessment questionnaire (SQAAQ)

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Introduction: Many biologic agents are available as self-administered subcutaneous (SQ) injections. In order for patients/caregivers to feel confident in their ability to administer therapy, an injection device should be easy to use. Availability of a prefilled syringe (PFS) and autoinjector allows patients/caregivers to choose a preferred device. Ixekizumab (IXE) is an anti-IL-17A monoclonal IgG4 antibody with a high binding affinity that is delivered by a SQ injection currently in development for the treatment of plaque psoriasis. The objective of this study was to report the usability, and patient-reported experience with IXE delivered via PFS.

Methods: This was an analysis of the 12-week, open-label period of a phase 3 study in patients with moderate-to-severe psoriasis who were randomly assigned to an injection device (autoinjector or PFS). Presented are analyses of the patients in the PFS group. The starting dose of IXE was 160 mg at Week 0, followed by 80 mg given every two weeks. Patients/caregivers reported their experience injecting with the prefilled syringe at weeks 0, 4, and 8 using the Subcutaneous Administration Assessment Questionnaire (SQAAQ), a 12-item questionnaire that provides an assessment of ease of use and confidence using a device to administer a SQ injection of drug on a 7-point Likert scale ranging from "strongly disagree" to "strongly agree." Observed data are reported.

Results: Of the 102 patients in the PFS group, 96 completed the 12-week period. At Week 0, 85% or more of patients/caregivers agreed/strongly agreed with each item on the SQAAQ; at Week 8 >90% agreed/strongly agreed. Among the items, at Week 0, 90% of patients/caregivers reported that they agreed/strongly agreed that the PFS was "overall, easy to use," "easy to learn how to use" and that they were "confident my dose is complete." At Week 8, 97%, 94%, and 99% agreed/strongly agreed, respectively. Overall the safety and efficacy profile was consistent with what has previously been reported. There were no serious adverse events or discontinuations associated with using the device. Mean % improvement in PASI at Week 12 was 92% (LOCF).

Conclusions: The vast majority of patients and caregivers who used the PFS reported on the SQAAQ that the device was overall easy to use and they were confident in using the device when using it for the first time at Week 0. IXE delivered via PFS had similar efficacy and safety findings as previously reported.

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3400

Ease of use and confidence with an autoinjector to administer ixekizumab in a phase 3 trial evaluated with the Subcutaneous Administration Assessment Questionnaire (SQAAQ)

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Introduction: Many biologic agents are available as self-administered subcutaneous injections. In order for patients/caregivers to feel confident in their ability to administer therapy, an injection device should be easy to use. Ixekizumab (IXE) is an anti-IL-17A monoclonal IgG4 antibody with high binding affinity currently in development for the treatment of psoriasis. The objective of this study was to report the usability, and patient-reported experience with IXE delivered via autoinjector.

Methods: This was an analysis of the 12-week, open-label period of a phase 3 trial in patients with moderate-to-severe psoriasis who were randomly assigned to an injection device (autoinjector or prefilled syringe). Presented here are analyses of the patients in the autoinjector group. The starting dose of IXE was 160 mg at Week 0, followed by 80 mg every two weeks. Patients or caregivers reported their experiences injecting with the autoinjector at weeks 0, 4, and 8 using the Subcutaneous Administration Assessment Questionnaire (SQAAQ), a 12-item questionnaire that provides an assessment of ease of use and confidence using a device to administer a subcutaneous injection of drug using a 7-point Likert scale ranging from "strongly disagree" to "strongly agree." Observed data are reported.

Results: Of the 102 patients in the autoinjector group, 94 completed the 12-week period. At Week 0 over 90% of patients/caregivers agreed/strongly agreed with each of the items on the SQAAQ and at Week 8 over 95% agreed/strongly agreed with each item. Among the items, over 90% of patients/caregivers reported that they agreed/strongly agreed that the autoinjector was "overall, easy to use," "easy to learn how to use" and that they were "confident my dose is complete" based on SQAAQ responses at Weeks 0, 4 and 8. Overall the safety and efficacy profile was consistent with what has previously been reported. There were no serious adverse events or discontinuations associated with using the device. Mean percent improvement in PASI at week 12 was 88% (LOCF).

Conclusions: The vast majority of patients and caregivers who used the autoinjector reported on the SQAAQ questionnaire that the device was overall easy to use and that they were confident in using the device when using it for the first time at Week 0. IXE delivered via an autoinjector had similar efficacy and safety findings as observed in the clinical trials for ixekizumab.

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2585

Effect of apremilast and etanercept on pruritus and health-related quality of life in patients with moderate to severe plaque psoriasis: Results from the LIBERATE study

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Background: Itching is one of the most bothersome psoriasis symptoms (J Am Acad Dermatol. 2014;70:871). We examined pruritus and health-related QOL up to Wk52 in the phase 3b, double-blind, double-dummy LIBERATE study.

Methods: Biologic-naive pts were randomized (1:1:1) to placebo (PBO), apremilast 30 mg BID (APR), or etanercept 50 mg QW (ETN) through Wk16; thereafter, all pts continued APR or switched from ETN or PBO to APR through Wk104. Pruritus was evaluated through Wk52 using a VAS (0-100 mm; 0 = no itch at all, 100 = worst itch imaginable) and QOL using the Dermatology Life Quality Index (DLQI; 0-30; 30 = worst QOL). The achievement of minimal clinically important differences (MCID) in pruritus VAS (improvement ≥30%) (Acta Derm Venereol. 2013;93:609) and DLQI scores (improvement ≥5points) (Br J Dermatol. 2008;159:997) is reported. This study was not powered for APR vs ETN comparisons.

Results: 250 pts who received ≥1 dose of study drug and had both baseline (BL) and ≥1 posttreatment PASI evaluations were included in the analysis (PBO n = 84; APR n = 83; ETN n = 83). At Wk16, mean change from BL in pruritus VAS was greater with APR (−35.6 mm) and ETN (−36.4 mm) vs PBO (−22.5 mm; nominal $P = .0026$ vs APR, nominal $P < .0001$ vs ETN). Greater improvement (ie, decreases) in pruritus occurred as early as Wk2 with APR and ETN vs PBO. At Wk16, mean change from BL in total DLQI score was greater with APR (−8.3) and ETN (−7.8) vs PBO (−3.8; $P < .0001$ vs APR, nominal $P = .0004$ vs ETN). More pts achieved MCID at Wk16 for pruritus (PBO 53.6%; APR 79.5%; ETN 83.1%) and DLQI (PBO 41.7%; APR 65.1%; ETN 65.1%) with APR or ETN vs PBO. At Wk52, pruritus improvements were sustained in pts who continued APR (−35.9 mm) and pts who switched from PBO or ETN to APR at Wk16 (PBO/APR −35.8 mm; ETN/APR −34.6 mm). At Wk52, DLQI improvements were sustained in pts who continued receiving APR (−8.9) and pts who switched from PBO or ETN to APR at Wk16 (PBO/APR −6.6; ETN/APR −8.0). At Wk52, 75.7% of pts who continued APR achieved DLQI MCID vs 71.2% and 59.4% of pts who switched from ETN or PBO to APR at Wk16. AEs were consistent with known safety profiles of apremilast and etanercept.

Conclusions: APR improved pruritus and QOL vs PBO at Wk16; improvement was sustained at Wk52 in pts who continued on APR or switched from ETN to APR.

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2795

Effect of metabolic syndrome on sexual function among female psoriatic patients

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Background: Psoriasis is a chronic skin disorder affecting 1-3% of the population. It is associated with impairments in health related quality of life even in mild cases, and excess mortality in severe cases. Effects of either psoriasis or metabolic disease on sexual function were studied to some extent, but the effects of both diseases on sexual life were not studied.

Aim of the work: the study is a cross sectional study, to examine effect of metabolic syndrome (MS) and psoriasis on sexual function. It was done at Dermatology Department, Suez Canal University.

Patients and methods: This study enrolled 17 cases with MS (cases); and 58 cases without MS (controls). All patients were subjected to; full history of the disease, other skin diseases and systemic disorders, clinical and dermatological examination, laboratory investigations, measurement of psoriasis severity by PASI and female sexual function index (FSFI) questionnaire was completed to determine FSD.

Results: The most common age group was fifth decade (50.0%). There was an increase of weight, BMI, waist circumference, blood pressure, fasting blood glucose (FBG), cholesterol, triglycerides and CRP and significant decrease of height in cases with MS in comparison to cases without MS. In addition, there was a decrease of age of onset, and increase of disease duration and PASI score in cases in comparison to controls and there was statistical decrease of desire, arousal, lubrication, orgasm, satisfaction and pain in females with MS in comparison to females without MS. There was statistical increase of females with FSD in cases with MS in comparison to cases without MS (94.1% vs 8.1% respectively). This was confirmed by the decrease of total FSD score in cases with MS in comparison to cases without MS (15.62 ± 4.64 vs 30.34 ± 2.72 respectively). Finally, there was positive (proportional), powerful, statistically correlation between PASI and either of BMI, disease duration, FBG and cholesterol. On the other hand, there was inverse (negative), moderate or powerful, statistical correlation between PASI and all variables of FSD scales, regardless presence or absence of MS.

Conclusion: the results of the present study revealed increased SD in psoriatic females with metabolic syndrome. It sheds light on the possible synergistic effects of both diseases on sexual life.

Commercial support: None identified.

3484

Effect of psoriasis activity and topical treatment on serum lipocalin-2 levels

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Background: Psoriasis has been considered as not only skin disease but systemic disease related to obesity, cardiovascular disease and metabolic syndrome. Adipokines influence the pathogenesis of psoriasis and its associations with comorbidities. Lipocalin-2 has been linked to insulin resistance, obesity, metabolic syndrome, atherosclerosis and diabetes.

Objective: Aim of this study was to investigate the associations between serum lipocalin-2 levels and the disease severity, markers of inflammation, indicators for metabolic syndrome and changes after topical treatment in patients with psoriasis.

Methods: Thirty-seven patients with active plaque-type psoriasis and 15 healthy controls were recruited in the study. Blood samples were collected before therapy and after 14 days of application. Serum lipocalin-2 concentrations were examined by enzyme-linked immunosorbent assay. The results were correlated with Psoriasis Area and Severity Index (PASI), body mass index (BMI), inflammatory and biochemical markers, lipid profile, duration of the disease and with effectiveness of topical treatment.

Results: Lipocalin-2 serum levels were significantly increased in psoriatic patients in comparison to the controls ($P = .023$). No significant correlations between lipocalin-2 and indicators of inflammation, nor BMI or PASI were noted. A significant correlation between lipocalin-2 and low-density lipoprotein-cholesterol was shown. As a result of the topical treatment serum lipocalin-2 level did not significantly change ($P = .9$), still remaining higher than in the controls, despite clinical improvement.

Conclusion: Lipocalin-2 might be a marker of psoriasis and convey cardiovascular and metabolic risk in psoriatic patients. Lipocalin-2 may not be a reliable indicator of inflammation. Lipocalin-2 is not useful in determining severity of psoriasis or monitoring the efficacy of antipsoriatic treatment.

Commercial support: None identified.

2615

Effects of adalimumab on health-related quality of life in psoriasis patients with and without comorbid psoriatic arthritis: Value of reducing PASI scores and systemic inflammation

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Objective: Adalimumab treatment has been associated with significant improvements in health related quality of life (HRQL) among patients with moderate to severe psoriasis. The objective of this study was to assess the extent to which these HRQL improvements are mediated by the effect of adalimumab on skin signs and systemic inflammation, and the extent to which these effects differ between patients who have psoriasis with and without comorbid psoriatic arthritis (PsA).

Methods: HRQL outcomes were analyzed during the 16-week double-blind period of randomized treatment with adalimumab vs placebo in the REVEAL trial of patients with moderate to severe psoriasis (NCT00237887). The 36-item Short Form Health Survey (SF-36) measures HRQL in 8 health domains, which are further aggregated into physical and mental component summaries (PCS, MCS). The effect of adalimumab vs placebo treatment on each of the SF-36 scores was partitioned into effects that were mediated by improvements on the scores of the Psoriasis Area and Severity Index (PASI) or on levels of C-reactive protein (CRP), both measured at Week 16, while adjusting for baseline characteristics. The incremental effect on PsA, as a moderator of effects on HRQL, was also assessed.

Results: The study included 1212 patients, with 27.8% having self-reported comorbid PsA. At baseline, all SF-36 domains and summary scores were significantly worse in patients with comorbid PsA than those without comorbid PsA. The PASI score was a significant mediator of the effect of adalimumab on all SF-36 scores. Among patients with comorbid PsA, CRP was a significant mediator of the effect of adalimumab on PCS, physical functioning, bodily pain, and general health. In patients without PsA, the effect of adalimumab on PASI mediated 91% of the total improvement in PCS scores. Among patients with PsA, the effect of adalimumab on PASI and CRP mediated 64% and 18% of the improvement in PCS, respectively (all $P < .05$).

Conclusions: Among patients who had psoriasis without PsA, improvements in the PASI score with adalimumab treatment accounted for almost all improvement in HRQL. However, among patients who had psoriasis with comorbid PsA, improvements in both PASI score and in CRP (as proxy for systemic inflammation) accounted for HRQL improvement.

Design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract, all authors contributed to the development of the publication.

3447

Efficacy and safety of apremilast with or without topical or phototherapy: Subanalysis of the population with < PASI-75 in the ESTEEM 1 phase 3, randomized, controlled trial in patients with moderate to severe plaque psoriasis

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Background: The phase 3 randomized ESTEEM 1 trial evaluated efficacy and safety of apremilast 30 mg BID (APR30) vs placebo (PBO) in patients (pts) with moderate to severe plaque psoriasis. The results in pts with <PASI-75 treated with and without (w/o) topical/phototherapy during Wks32 to 52 of ESTEEM 1 are reported.

Methods: Pts were randomized 2:1 to APR30 or PBO. At Wk16, PBO pts switched to APR30 (PBO/APR30). All pts were treated with APR30 through Wk32, followed by a randomized treatment withdrawal phase up to Wk52. The primary endpoint was PASI-75 at Wk16. At Wk32, in addition to APR30, pts with <PASI-75 could receive topical therapies and/or ultraviolet B phototherapy (T/P) at the discretion of the investigator.

Results: Of the 380 pts with <PASI-75 at Wk32, 210 received T/P (PBO/APR30+T/P; n = 84; APR30/APR30+T/P: n = 126) and 170 did not receive T/P (PBO/APR30 w/o T/P: n = 51; APR30/APR30 w/o T/P: n = 119). Topical agents used in pts with <PASI-75 in the PBO/APR30 and APR30/APR30 groups, respectively, included corticosteroids (67.9%, 62.7%), vitamin D analogs (16.7%, 11.9%), corticosteroids + vitamin D analogs (38.1%, 46.0%), and a calcineurin inhibitor (1.2%, 0.8%); 11.9% (PBO/APR30) and 8.7% (APR30/APR30) of pts received UVB phototherapy. At Wk52, PASI-75 was achieved by more pts receiving T/P vs w/o T/P (PBO/APR30: 15.6% vs 4.4%, respectively; APR30/APR30: 12.2% vs 6.9%, respectively). At Wk52, mean percent decreases (ie, improvements) from baseline in PASI score were: −61.3% (PBO/APR30+T/P) vs −52.6% (PBO/APR30 w/o T/P) and −58.2% (APR30/APR30+T/P) vs −57.3% (APR30/APR30 w/o T/P). During Wks32 to 52, the safety population included 378 pts: 210 pts received T/P (PBO/APR30+T/P; n = 84, pt-yrs = 28.0; APR30/APR30+T/P; n = 126, pt-yrs = 44.3) and 168 pts did not receive T/P (PBO/APR30 w/o T/P; n = 51, pt-yrs = 15.5; APR30/APR30 w/o T/P; n = 117, pt-yrs = 36.4). AEs occurring in ≥5% of pts during Wks32 to 52 were upper respiratory tract infection, nasopharyngitis, and back pain. Diarrhea/nausea rates were low (<5%) and similar among the PBO/APR30 and APR30/APR30 groups, regardless of T/P use. Based on exposure-adjusted incidence rates/100 pt-yrs, rates of AEs (including serious AEs) were similar in pts with vs without T/P use across both groups.

Conclusion: In pts with <PASI-75 at Wk32, APR30 with or without T/P demonstrated an acceptable safety/tolerability profile. The trend toward higher PASI responses in pts receiving T/P with APR30 warrants further investigation.

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3354

Efficacy and safety of oral tofacitinib in North American patients with moderate to severe plaque psoriasis: Pooled analyses of data from randomized phase 3 studies

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Background: Tofacitinib is an oral JAK inhibitor that is being investigated for psoriasis (PsO).

Objective: To evaluate the efficacy and safety of tofacitinib 5 or 10 mg BID in North American (NA) patients (pts) with moderate to severe chronic plaque PsO.

Methods: Efficacy and safety data at 16 weeks (wks) were pooled for NA pts from two pivotal randomized phase 3 studies (OPT-1, OPT-2; both 52-wks with initial 16-wk placebo (PBO)-controlled phases). First-year safety data were pooled for NA pts who participated in OPT-1, OPT-2, and a 56-week randomized phase 3 study (OPT Retreatment).

Results: Baseline characteristics of the 16-wk cohort (n = 894): 70.7% male; mean age 46.6 years; median disease duration 17.2 years, median PASI 18.0; median affected BSA 20%; median DLQI 12. At 16 wks, efficacy responses for the tofacitinib 5 and 10mg BID, and PBO groups, respectively, were: 40.2%, 54.3%, 9.0% for PASI75; 17.3%, 30.7%, 2.2% for PASI90; 36.6%, 49.2%, 7.9% for PGA clear/almost clear; and 26.2%, 45.9%, 4.7% for DLQI ≤1 ($P < .0001$ for both tofacitinib doses vs PBO for all endpoints). Clinically meaningful reductions in itch were also observed with both tofacitinib doses vs PBO (median change from baseline in itch severity item score: -3.6, -4.7 vs 0.0). In the PBO controlled period, rates of AEs and SAEs in the tofacitinib 5mg BID, 10mg BID and PBO groups were: 59.9%, 64.6%, 50.3%, and 2.3%, 2.2%, 2.8%, respectively. Incidence rates (IRs, pts with events per 100 pt-years) were: 0.98, 1.92, 2.03 for serious infections; 0, 0, 0 for opportunistic infections; 1.97, 4.81, 0.00 for herpes zoster; 0.00, 0.96, 0.00 for all nonmelanoma skin cancer (NMSC [0, 0, 0 for basal cell; 0.00, 0.96, 0.00 for squamous cell]), and 1.97, 0.96, 0.00 for all non-NMSC malignancies. All 95% CIs overlapped between 5 and 10mg BID. First-year (n = 1373) rates of AEs (70.2%, 74.9%) and SAEs (4.8%, 5.1%) were similar for both doses of tofacitinib (5 and 10 mg BID, respectively). IRs (pts with events per 100 pt-years) for tofacitinib 5 and 10 mg BID were: 1.47 and 2.43, respectively, for serious infections, 0.98 and 3.35 for herpes zoster, 1.23 and 2.00 for NMSC, 1.72 and 0.88 for non-NMSC malignancies. All 95% CIs overlapped between 5 and 10mg BID.

Conclusion. In this NA cohort, both tofacitinib doses were significantly more efficacious than placebo over 16 wks. The greatest responses were achieved with tofacitinib 10 mg BID. Safety in the NA population was consistent with the global population.

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2643

Efficacy and safety of secukinumab by age group in patients with moderate-to-severe plaque psoriasis: Pooled analysis of 4 phase III trials

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Introduction and objectives: Secukinumab, a fully human monoclonal antibody that selectively targets interleukin-17A, has been demonstrated to be highly efficacious in the treatment of moderate-to-severe psoriasis, starting at early time points, with a sustained effect and a favorable safety profile. This pooled analysis reports the safety and efficacy of secukinumab in patients aged 18-29, 30-49, and ≥50 years.

Methods: Data were pooled from the ERASURE, FIXTURE, FEATURE, and JUNCTURE phase III trials. Patients were randomized to receive subcutaneous secukinumab (300 mg or 150 mg) or placebo at Baseline (Week 0), Weeks 1, 2 and 3, and then every 4 weeks from Week 4 to 48. Psoriasis Area and Severity Index (PASI) nonresponders from the placebo group at Week 12 were re-randomized to secukinumab (300 mg or 150 mg). FIXTURE included a subcutaneous etanercept 50 mg group, with administration twice weekly to Week 12 and then weekly to Week 51 in addition to secukinumab (300 mg or 150 mg) and placebo. In all trials, the coprimary endpoints were PASI75 and Investigator's Global Assessment (IGA; modified 2011) of 0/1 (clear/almost clear) at Week 12.

Results: Patients aged 18-29, 30-49, and ≥50 years accounted for 14.7% (n = 252), 48.5% (n = 829), and 36.7% (n = 628) of the pooled population, respectively. At Week 12, PASI75, 90, 100, and IGA 0/1 responses with secukinumab 300 mg were observed in 80%, 64%, 33%, and 73% of patients 18-29 years; 82%, 58%, 28%, and 65% of patients 30-49 years; and 76%, 52%, 24%, and 62% of patients ≥50 years, respectively. With secukinumab 150 mg, PASI75, 90, 100, and IGA 0/1 responses at Week 12 were observed in 74%, 48%, 18%, and 55% of patients 18-29 years; 68%, 40%, 12%, and 51% of patients 30-49 years; and 69%, 40%, 14%, and 51% of patients ≥50 years, respectively. With etanercept, PASI75, 90, 100, and IGA 0/1 responses at Week 12 were observed in 49%, 22%, 2%, and 31% of patients 18-29 years; 40%, 21%, 4%, and 26% of patients 30-49 years; and 48%, 20%, 6%, and 27% of patients ≥50 years, respectively. For all secukinumab groups, efficacy responses increased to Week 16 and were sustained to Week 52. The safety profile of secukinumab was generally balanced between age groups. The most common adverse events for all age groups were nasopharyngitis and headache.

Conclusions: Across all age groups, secukinumab provided a rapid and strong response with a favorable safety profile to patients with moderate-to-severe psoriasis.

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3428

Efficacy of ixekizumab in moderate to severe psoriasis patients who have or have not received prior biologic therapies: An integrated analysis of 3 phase 3 studies

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Introduction: There is evidence that response rates to a biologic therapy may be lower in patients who have had previous exposure to other biologic therapies. Ixekizumab (IXE) is an anti-IL-17A monoclonal antibody with a high binding affinity that has been studied in phase 3 clinical trials in patients with moderate-to-severe psoriasis. In this integrated analysis, we evaluated the efficacy of IXE compared to placebo in patients who have or have not had previous exposure to biologic therapy.

Methods: Data were integrated from the 12-week induction phase of three phase 3 trials. Patients were randomized to treatment groups receiving 80 mg IXE every 2 (IXE Q2W; N = 1169) or 4 weeks (IXE Q4W; N = 1165) following a 160-mg starting dose, or placebo (PBO; N = 792). Psoriasis Area and Severity Index (PASI) 75, PASI 90, and PASI 100 response rates at week 12 were evaluated in subgroups of patients with or without previous exposure to biologic therapy. Significance was determined via the Cochran-Mantel-Haenszel test stratified by study; missing values were imputed as nonresponse.

Results: In this analysis, 883 (28.2%) patients had prior exposure to biologic therapy and 2243 (71.8%) patients were naive to biologic therapy. In these subgroups, PASI 75 response rates were 89.5% and 88.4% in the IXE Q2W and 77.5% and 83.1% in the IXE Q4W groups vs 2.7% and 5.2% in placebo ($P < .001$), respectively. PASI 90 response rates were 73.0% and 68.7% in the IXE Q2W and 53.7% and 66.9% in the IXE Q4W groups vs 0 and 1.7% in the placebo group ($P < .001$). In addition, the proportions of patients achieving complete resolution of their psoriasis plaques (PASI 100) were 36.6% and 39.1% in the IXE Q2W and 32.0% and 34.7% in the IXE Q4W groups vs 0 and 0.3% in the placebo groups ($P < .001$). Overall, there were no unexpected safety signals.

Conclusions. In this integrated analysis across three phase 3 trials, regardless of previous biologic treatment, both dose regimens of ixekizumab resulted in high levels of treatment response.

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2515

Efficacy of ixekizumab in patients with psoriatic arthritis: Results of a phase 3 randomized, double-blind, active- and placebo-controlled study

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Background/purpose: Psoriatic arthritis (PsA) is a chronic immune-mediated inflammatory disease which includes manifestations of peripheral arthritis, enthesitis, dactylitis, and spondylitis, and dermatologic skin and nail changes. Ixekizumab (IXE) is an IgG4 monoclonal antibody that binds with high affinity and specificity to the proinflammatory cytokine IL-17A.

Methods: In a phase 3 trial, 417 biologic disease-modifying antirheumatic drug (bDMARD)-naive patients with active PsA were randomized to up to 24 weeks of placebo (PBO; n = 106); adalimumab (ADA) 40 mg (n = 101) once every 2 weeks (Q2W; active control); or IXE 80 mg Q2W (n = 104) or Q4W (n = 107) following 160 mg initial dose at Week 0. Endpoints assessed at 12 and 24 weeks included response rates for: the American College of Rheumatology (ACR) 20 (primary endpoint), ACR50, ACR70, Psoriasis Area and Severity Index (PASI)75, PASI90, PASI100, and static Physician Global Assessment of psoriasis (sPGA) (0,1 = cleared and/or mild) and sPGA (0 = cleared); and change from baseline in Van der Heijde modified Total Sharp Score (mTSS; assessed at 16 and 24 weeks); and percent change from baseline in body surface area (BSA) psoriasis and Nail Psoriasis Severity Index (NAPSI) scores. Continuous and categorical endpoints were analyzed using the mixed-effect model for repeated measures and logistic regression, respectively.

Results: A total of 382 patients completed 24 weeks of the study. Compared to PBO, at 12 and 24 weeks, a significantly greater percentage of patients treated with IXE, both doses, achieved significantly greater responses on the ACR20 (57-62% IXE versus 30% PBO), ACR50, ACR70, PASI75, PASI90, PASI100, and sPGA (0), sPGA (0,1) (all $P < .01$), and greater improvement of radiographic progression of joint structural damage ($P < .025$). Both IXE groups had significantly higher percent improvement on BSA and NAPSI ($P < .01$) versus PBO. Efficacy results with ADA versus PBO were significant on most measures. Incidence rates of adverse events (AE) and serious adverse events were assessed at 24 weeks and were higher for IXE and ADA compared to PBO. Discontinuation due to an AE was similar across all groups. No deaths occurred.

Conclusion: In bDMARD-naive patients with active PsA, ixekizumab showed significant clinically meaningful improvements in disease activity, plaque psoriasis and nail clearance, and inhibition of structural progression. Ixekizumab was well tolerated with no unexpected safety findings.

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3118

Efficacy of long-term (104-week) treatment with apremilast in patients with psoriatic arthritis: Results from a phase III, randomized, controlled trial and open-label extension

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Background: PALACE 3 compared the efficacy and safety of apremilast (APR) with placebo (PBO) in patients with active PsA, including active skin disease, despite prior conventional DMARDs and/or biologics. We report the efficacy and safety for patients receiving APR 30 mg BID (APR30) over 104 weeks in PALACE 3.

Methods: Patients were randomized (1:1:1) to PBO, APR30, or APR20 mg BID (APR20) stratified by baseline (BL) DMARD use (yes/no) and psoriasis involvement of the body surface area (<5%/≥5%). The PBO-controlled phase continued to Week 24, with an early escape option at Week 16. At Week 24, all remaining PBO patients were re-randomized to APR30 or APR20. Double-blind APR treatment continued to Week 52; subsequently, patients could continue APR for up to 4 additional years as an open-label extension. The primary study endpoint was ACR20 response at Week 16. Other assessments included percent change from BL in swollen and tender joint counts (SJC/TJC) and patients' physical function (HAQ-DI).

Results: 505 patients were randomized and received ≥1 dose of study medication (PBO: n = 169; APR30: n = 167; APR20: n = 169); 71% of patients receiving either dose of APR during Weeks 0 to 52 completed 52 weeks in the study. Among 343 patients in both treatment arms who completed 52 weeks of APR treatment and had ≥1 dose of exposure in the second year, 282 patients (>82%) continued to receive treatment at the time of the data cutoff. Sustained decreases in disease activity were achieved with APR30 through 104 weeks of treatment, as demonstrated by ACR20 mean response rates of 61.3% at Week 52 and 66.5% at Week 104 in the APR30 group. These findings are highlighted by results observed in the more clinical practice-related assessments of percent change from BL in SJC and TJC: SJC decreases of 67.6% at Week 52 and 74.7% at Week 104 and TJC decreases of 55.3% at Week 52 and 66.5% at Week 104. Improvements in ability to perform activities of daily living were shown by the HAQ-DI mean improvement (ie, decrease) of −0.35 at Week 52 and −0.41 at Week 104 in the APR30 group. The proportion of patients with HAQ-DI score exceeding the minimal clinically important difference ≥0.30 threshold were 53.1% at Week 52 and 51.6% at Week 104 in the APR30 group.

Conclusion: Over 104 weeks, APR30 demonstrated sustained, clinically meaningful improvements in disease activity and physical function. APR continued to demonstrate a favorable safety profile and was generally well tolerated.

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2994

Efficacy of tofacitinib for the treatment of nail psoriasis: Two 52-week phase 3 studies in patients with moderate to severe plaque psoriasis

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Background: Tofacitinib is an oral JAK inhibitor that is being investigated for psoriasis (Pso); phase 3 studies have shown efficacy and safety of tofacitinib in patients (pts) with Pso.

Objective: To evaluate Nail Psoriasis Severity Index (NAPSI) in pts with existing nail Pso from two 52-week phase 3 pivotal studies in moderate to severe plaque Pso (OPT Pivotal 1, NCT01276639; OPT Pivotal 2, NCT01309737).

Methods: Adult pts were randomized 2:2:1 to receive tofacitinib 5, 10 mg, or placebo, BID. At Week 16, placebo pts were rerandomized to tofacitinib 5 or 10 mg BID. Change in NAPSI score from baseline and the proportions of pts achieving ≥75% or 100% reduction in NAPSI (NAPSI75 or NAPSI100) at Weeks 16/52 were assessed; for NAPSI75 and NAPSI100 non-responder imputation was applied. Data were pooled across studies; nominal P values for treatment comparisons are presented for Week 16.

Results: 1196 (64%) pts had nail Pso: 487 (5 mg BID), 476 (10 mg BID) and 233 (placebo). Median age was 46.0 years, 77% were male, 80% were white, 24% also had psoriatic arthritis and median PASI score was 20. Mean [standard error; SE] number of nails affected at baseline were 7.3 [0.1] (5 mg BID), 7.3 [0.1] (10 mg BID), 7.4 [0.3] (placebo to 5 mg BID) and 7.3 [0.3] (placebo to 10 mg BID). Baseline mean (SE) NAPSI scores were 27.0 [0.9] (5 mg BID), 27.3 [1.0] (10 mg BID), 26.6 [2.0] (placebo to 5 mg BID) and 25.5 [1.8] (placebo to 10 mg BID). At Week 16, mean (SE) % reduction from baseline in NAPSI score was significantly greater with tofacitinib 5 and 10 mg BID vs placebo (-17.4 [6.1] and -34.2 [6.1] vs 35.0 [9.3]; $P < .01$). The percentage of pts achieving NAPSI75 with tofacitinib 5 and 10 mg BID and placebo were 16.9%, 28.1% and 6.8%, respectively, and for NAPSI100 were 10.3%, 18.2% and 5.1%, respectively. Significantly more pts achieved NAPSI75 and NAPSI100 with both tofacitinib doses vs placebo ($P < .01$) and with 10 mg vs 5 mg BID ($P < .01$). Nail Pso continued to improve up to Week 52. At Week 52, mean (SD) changes from baseline in NAPSI score were -65.6 (3.7) and -75.5 (2.5); NAPSI75 was achieved by 24.6% and 41.0% of pts and NAPSI100 by 16.4% and 29.2% of pts that received tofacitinib 5 and 10mg BID, respectively; similar values were observed at Week 52 in pts who advanced to tofacitinib from placebo at Week 16.

Conclusions: Tofacitinib led to significant improvements in NAPSI at 16 weeks which were maintained through 52 weeks in pts with moderate to severe Pso with nail Pso at baseline.

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3002

Endothelium-dependent vasodilation is reduced in the cutaneous circulation of psoriatic patients

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Psoriasis, a chronic systemic inflammatory disease, is an independent risk factor for cardiovascular disease. Impaired vascular function in conduit and resistance vessels is evident in adults with plaque psoriasis; however, potential deficits in microcirculatory endothelial function in psoriatic patients remain unclear. Further, examining cutaneous vascular function has particular clinical relevance for this population because the skin-related symptoms are the outward manifestation of this systemic inflammatory disease process. We hypothesized that cutaneous endothelial function would be impaired in nonlesional skin of psoriatic patients. Three intradermal microdialysis fibers were placed in the forearm skin of 8 healthy adults (NP: 3M, 5F; 49 ± 3 yr) and 8 adults with moderate (>5% body surface area affected) plaque psoriasis (P: 3M, 5F; 48 ± 3 yr) for localized drug delivery. Microdialysis sites were perfused with lactated Ringer's (control), ascorbate (antioxidant), or BEC (arginase-inhibitor) while an index of skin blood flow was measured using laser Doppler flowmetry during a standardized local heating protocol (42°C) to elicit endothelial nitric oxide synthase (eNOS)-mediated vasodilation. Nitric oxide (NO)-dependent vasodilation was quantified following the perfusion of the nonspecific NOS inhibitor L-NAME. Data were expressed as a percentage of maximum cutaneous vascular conductance (%CVCmax; 28 mM sodium nitroprusside). The local heating-induced plateau at the control site was attenuated in psoriatic patients (NP: 99 ± 1% CVCmax vs P: 82 ± 6 %CVCmax; $P = .03$), which is mediated by reduced NO-dependent vasodilation (NP: 58 ± 5 %CVCmax vs P: 45 ± 8 %CVCmax; $P = .10$). Arginase-inhibition, but not ascorbate, tended to improve the local-heating induced vasodilation in psoriasis patients (Ringer's: 82 ± 6 %CVCmax vs BEC: 93 ± 2 % CVCmax; $P = .15$). These results suggest that cutaneous endothelial function is impaired in psoriatic adults due to reduced NO bioavailability and that arginase upregulation contributes to the microvascular dysfunction in these patients.

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3889

Erythrodermic psoriasis following terbinafine use

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Background: Terbinafine has been linked with the occurrence of psoriasis de novo or with its exacerbation. We report a case of erythrodermic psoriasis following terbinafine use.

Case report: A 67-year-old man with a 24-year history of mild psoriasis (scalp and elbows), well controlled with topical medications, was admitted to our hospital due to erythroderma. Ten days prior to its onset, he started taking terbinafine 250 mg/d for tinea cruris. He had been on enalapril, acetylsalicylic acid, simvastatin and inhaled steroids for several years due to his comorbidities. On admission, the patient had widespread erythema with diffuse scaling. He denied fever, urinary, respiratory or gastrointestinal symptoms. The white cell count was 14,080/mm^3 with mild neutrophilia. Liver and kidney function tests were within the normal range. Serologies for hepatitis B, C and HIV were negative. Since no classic triggers of erythroderma were identified, terbinafine was suspended. Therapy consisted of wet wraps with moisturizers and topical steroids, which resulted in a dramatic improvement after five days. In addition, methotrexate 7.5 mg/week and folic acid 5 mg/week were started, but soon suspended due to increased transaminases. Despite significant improvement with wet wrap therapy, PUVA was started for better disease control. After 12 sessions, he had complete resolution of the erythroderma, without recurrence after a 3-month follow-up.

Discussion: Cutaneous adverse effects are reported in 2.7% of patients taking oral terbinafine. Psoriasis exacerbation has been reported after its use, especially plaque and pustular psoriasis. When considering a medication as responsible for the exacerbation of a disease it is important to evaluate if there is chronological correlation. According to previous reports, the latency period between administration of terbinafine and the exacerbation of psoriasis is less than 4 weeks, categorized as short interval. Our patient developed erythroderma 10 days after starting terbinafine, which supports the association. Dermatologists should be aware of the association between oral terbinafine and psoriasis flare-up, including erythroderma. Similarly to any medication adverse event, further investigation and observation are needed to establish a solid conclusion.

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2957

Evaluation of efficacy and safety of ABP 501 in a phase 3 study in subjects with moderate to severe plaque psoriasis: 52-week results

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Background and objectives: ABP 501 is being developed as a biosimilar candidate to adalimumab (Humira), a fully human recombinant anti-TNF monoclonal antibody and has the same amino acid sequence as adalimumab. Evidence from analytical comparisons and phase 1 human pharmacokinetic study indicates that ABP 501 is similar to adalimumab. The objective of this study was to demonstrate clinical similarity between ABP 501 and adalimumab reference product in adults with moderate to severe plaque psoriasis. Results of clinical similarity based on efficacy and safety at week 16 have been previously reported. Here we report results of efficacy and safety at 52 weeks comparing subjects receiving ABP 501 or adalimumab for the entire duration of the study.

Methods: In this double-blind, active-controlled study subjects were randomized 1:1 (ABP 501: n = 175; adalimumab: n = 175) to receive study treatment subcutaneously 80 mg on week 1/day 1 and 40 mg at week 2 and every 2 weeks thereafter. At week 16, subjects achieving ≥PASI 50 response remained on study for up to 52 weeks and were rerandomized in a blinded fashion such that all subjects initially randomized to ABP 501 continued to receive ABP 501; those on adalimumab either continued on adalimumab or switched to ABP 501 in a 1:1 fashion. Subjects continued on treatment until week 48; the final efficacy assessments were conducted at week 50 and the end of study visit was week 52.

Results: Baseline characteristics were comparable in the two groups [ABP 501/ABP 501 (A/A), adalimumab/adalimumab (B/B)]. The mean PASI percent improvement from baseline at week 16, 32 and 50 (evaluated descriptively) was 86.6, 87.6 and 87.2 in group A/A and 88.0, 88.2 and 88.1 in group B/B, respectively. At the end of study incidence of subjects developing anti-drug antibodies was 68.4% in A/A group and 74.7% in B/B group. Incidence of treatment-emergent adverse events (TEAEs) was 86.2% in A/A group and 78.5% in B/B group. The most frequently reported TEAEs in ≥5% of subjects were nasopharyngitis, headache, upper respiratory tract infection, arthralgia, back pain, psoriasis and hypertension. Incidence of serious TEAEs was 4.6% in A/A group and 5.1% in B/B group.

Conclusions: At the end of 52 weeks the overall efficacy, safety and immunogenicity were comparable among the two groups.

This phase 3 study was sponsored by Amgen. Amgen provided all costs associated with the study conduct, data analysis and preparation of this abstract.

3417

Evaluation of inflammatory bowel disease in patients with plaque psoriasis studied in phase 3 trials of Ixekizumab (UNCOVER trials): Adjudicated data from the induction period

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Introduction and objectives: New onset or flares of inflammatory bowel disease (IBD) including worsening of active Crohn's disease (CD) and ulcerative colitis (UC) have been reported during treatment with biologic agents for psoriasis. The objective of this integrated safety analysis was to report the adjudicated incidence of CD and UC in 3 phase 3 clinical trials of ixekizumab, an anti-IL-17A monoclonal antibody.

Methods: In each trial during an induction period, patients were randomized to one of 3 treatment arms: (1) IXE every 2 (IXE Q2W; N = 1167) or every 4 weeks (IXE Q4W; N = 1161) following a 160-mg starting dose; (2) etanercept (ETN; 50 mg biweekly; N = 750); or (3) placebo (PBO; N = 791) for 12 weeks. After the induction period, patients continuing in the trial may receive IXE Q4W, IXE Q12W or PBO during a maintenance period depending on the study design of the individual trial. We collected information on all cases of suspected IBD reported during the induction period as a treatment-emergent adverse event or serious adverse event. This information was reviewed in a blinded fashion by external experts. These cases were adjudicated according to EPIMAD criteria into the following categories: definitive, probable, or possible.

Results: Of the 3858 patients enrolled in the trials, 2 patients were reported to have suspected CD and 2 were reported as suspected UC during the induction period. Adjudicators classified 1 CD case reported during induction as "probable." This event occurred at day 64 and the patient received IXE Q2W. The other suspected CD was classified as "possible." This event occurred at day 88 and the patient received IXE Q4W. Both of the suspected UC cases were adjudicated as "definitive." Importantly, both of these patients had a prior history of UC and both received IXE Q2W.

Conclusion: Of the 3858 total patients enrolled in the UNCOVER program the incidence of CD and UC was uncommon during the first 12 weeks of treatment with IXE. Additional analysis and adjudication of longer term data is currently ongoing and are required to further understand the relationship between IBD and IXE treatment.

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Evaluation of the Psoriasis Skin Appearance and Bothersomeness (PSAB) measure in patients with moderate to severe psoriasis treated with ixekizumab compared to etanercept and placebo: Results from UNCOVER-2

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Introduction: Psoriasis is characterized by red, thick and scaly skin lesions. While measures like the PASI are used by clinicians to assess the severity of psoriasis lesions, they do not capture the impact that the appearance of these lesions has on the patient. In this analysis, patients report how bothered they are by the redness, thickness, or scaliness of their skin lesions using a novel and validated instrument, the Psoriasis Appearance and Bothersomeness measure (PSAB), before and after treatment with ixekizumab, an anti-IL-17A monoclonal antibody, high dose etanercept, or placebo.

Methods: In the UNCOVER-2 trial, 1224 patients were randomized to receive 12 weeks of subcutaneous placebo (N = 168), etanercept (50 mg twice weekly; N = 358), or a single injection of 80 mg ixekizumab every 2 weeks (IXE Q2W; N = 351) or every 4 weeks (IXE Q4W; N = 347) following a 160 mg starting dose at Week 0. Using the PSAB at baseline and Week 12, patients were asked to indicate on a numeric rating scale (NRS) how bothered they are by any redness or discoloration, thickness, and scaling or flaking on their skin due to their psoriasis from 0 (not at all bothered) to 10 (extremely bothered). The scores from the 3 NRS items are summed for a total score ranging from 0 to 30 with higher scores indicating greater bothersomeness. Treatment comparisons were made using an ANCOVA model including treatment, pooled center and baseline PSAB value as covariates and missing data was imputed using the last observation carried forward.

Results: Mean (SD) baseline PSAB was 24.1 (6.4) across all groups. At week 12, mean (SD) PSAB was 4.0 (6.2), 5.0 (7.5), 11.4 (9.8) and 21.0 (8.2) in the IXE Q2W, IXE Q4W, etanercept and placebo groups, respectively. The improvements in PSAB were significantly greater in the ixekizumab treatment groups compared to etanercept and placebo with an LS Mean (SE) change from baseline of -20.1 (0.42) in IXE Q2W, -18.9 (0.42) in the IXE Q4W, -12.4 (0.42) in the etanercept group and -3.4 (0.61) in the placebo group ($P < .001$).

Conclusions: At baseline, moderate to severe psoriasis patients reported a high degree of bothersomeness (average of 24.1), reflecting the overall impact of the redness, thickness and scaliness of their psoriasis plaques. Both ixekizumab dosing regimens resulted in significantly greater improvements in the PSAB compared to improvements observed after treatment with etanercept or placebo.

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2526

Evaluation of timely versus delayed use of tumor necrosis factor inhibitors in the treatment of psoriatic arthritis: Economic and clinical results from a modeling study

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Objective: Progression of psoriatic arthritis (PsA) can lead to irreversible joint damage, functional impairment, and associated health care costs. Tumor necrosis factor inhibitors (TNFis) improve signs and symptoms of PsA, and, in contrast to other DMARDs such as apremilast and methotrexate, have been shown to slow the rate of radiographic progression. The economic impact of using apremilast before TNFis is not fully understood. We evaluated clinical outcomes and costs associated with timely versus delayed use of TNFis among patients with PsA.

Methods: A Markov model was developed to evaluate costs and outcomes of PsA treatment with TNFis (adalimumab, etanercept, infliximab, or golimumab) and/or apremilast over a 1-year time horizon. Patients received either a TNFi (timely TNFi use) or apremilast (delayed TNFi use) as initial treatment. Those who did not achieve an ACR20 response in the first 12 weeks of therapy or who subsequently lost ACR20 response either switched to a different TNFi or initiated a first TNFi. Joint responses (ie, ACR20 response) were evaluated for all patients; skin responses (ie, PASI75) were evaluated among patients with comorbid moderate/severe psoriasis (ie, affecting ≥3% of their body surface). Efficacy inputs and distributions of patients treated with TNFis were based on randomized controlled trials and market share data, respectively. Outcomes were response rates at year 1 and the number of patients who would need to be treated (NNT) to see 1 responder. Total costs and cost per responder were also calculated.

Results: After 1 year, patients with timely use of TNFis had higher ACR20 response rates, lower NNTs, and higher costs vs those with delayed use (70% vs 60%, 1.42 vs 1.68, $39,754 vs $31,515, respectively). Among the subgroup with moderate/severe psoriasis, timely use of TNFis was associated with higher combined ACR20+PASI75 response rates, lower NNTs, and higher costs compared with delayed TNFi use (41% vs 30%, 2.44 vs 3.33, $41,457 vs $33,510, respectively). The cost per ACR20 responder was higher ($56,492 vs $52,835) among all patients, however, among patients with psoriasis the combined ACR20+PASI75 cost per responder was lower for timely use of TNFis ($100,954 vs $111,686).

Conclusion: In this economic model, timely use of TNFis was a more effective strategy for managing PsA and was a more cost-effective strategy for managing patients with both joint and skin involvement.

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3184

First line biologic agent therapy for moderate-to-severe psoriasis in cancer survivors

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Introduction: Individuals with psoriasis are reported to have decreased quality of life associated with potentially debilitating features that are responsive to biological agents (BAs) that are known to pose some increased risk of malignancy. Consequently, patients with a history of cancer who have moderate-to-severe psoriasis typically pose a dilemma for selection of the most appropriate therapy to minimize the debilitating features of psoriasis yet balance the risk to benefit concurrent with anticancer therapy. This study aims to assess the current utilization of BA antipsoriasis treatments in patients diagnosed with cancer.

Methods: We searched the Northwestern Medicine Enterprise Data Warehouse (NMEDW), nearly 4 million individuals comprising an NCI Comprehensive Cancer Center as well as a NIH-designated Skin Disease Research Center (2010-2014) for patients who were prescribed medication as treatment for their moderate or severe psoriasis within 24 months after a diagnosis of cancer.

Results: 15 patients met the search criteria. Of these, 7 were prescribed systemic treatment for psoriasis, of which 3 were prescribed a BA and 14 received at least 1 topical agent. Systemic agents included methotrexate, acitretin, and 2 BAs (adalimumab and infliximab). Of the 7 (46.7%) prescribed a systemic treatment, 4 received a systemic agent as the initial treatment for psoriasis after cancer diagnosis. Of the 3 prescribed a BA, 2 received a BA as their first treatment for psoriasis after cancer diagnosis. Mean time between cancer diagnosis and BA was 6 months.

Conclusion: Although topical agents are most commonly used for psoriasis treatment within 24 months after cancer diagnosis, after weighing risk to benefit, biologic agents are used, despite they are reported to increase cancer risk. Further exploration is warranted for treatment outcomes related to biological agent use in cancer patients who have moderate-to-severe psoriasis.

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2607

Five year open-label extension study of safety and efficacy of etanercept in children and adolescents with moderate to severe plaque psoriasis

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Background: Treatments for moderate to severe plaque psoriasis in adults are not currently approved for children and adolescents in the US. This open-label extension (OLE) study evaluated long-term safety and efficacy of etanercept for pediatric psoriasis.

Methods: Patients aged 4-17 years who had completed a 48-week, randomized, double-blind, placebo-controlled parent study were eligible to participate in this 264-week OLE study. Patients who did not complete the parent study could enroll in the OLE if they had achieved at least a 50% improvement in Psoriasis Area and Severity Index (PASI 50) by week 12 with no serious adverse event (SAE) or other clinically significant adverse event (AE) considered related to etanercept. Patients received subcutaneous etanercept at 0.8 mg/kg (maximum 50 mg) once weekly for up to 264 weeks. Safety outcomes included incidence of AEs (including infections), SAEs, and serious infectious events (SIEs). Efficacy outcomes included rates of PASI 75 and PASI 90 responses and static physician global assessment (sPGA) status of clear/almost clear (score 0/1).

Results: Of 181 patients who enrolled in the OLE and received etanercept, 69 completed 264 weeks on study. A total of 161 (89.0%) patients reported an AE through week 264, most commonly upper respiratory tract infections (37.6%), nasopharyngitis (26.0%), headache (21.5%), acne (18.2%), streptococcal pharyngitis (14.9%), sinusitis (13.3%), skin papilloma (13.3%), cough (12.2%), influenza (11.6%), and oropharyngeal pain (11.0%). SAEs were reported by 5 (2.8%) patients (elective abortion, anxiety, intestinal obstruction, osteonecrosis, thyroid cyst) and SIEs were reported by 2 (1.1%) patients (cellulitis, infectious mononucleosis); only the case of cellulitis was considered related to treatment. No opportunistic infections, malignancies, or deaths occurred during the study. Rates of PASI 75 responses (~60%-70%), PASI 90 responses (~30%-40%), and sPGA status of clear/almost clear (~40%-50%) were maintained in patients who stayed on study through week 264.

Conclusions: Long-term etanercept therapy administered to children and adolescents with moderate to severe plaque psoriasis did not elicit any new safety signals and efficacy was maintained in patients who remained on study up to 264 weeks.

This study was sponsored by Immunex, a wholly owned subsidiary of Amgen Inc. and by Wyeth, which was acquired by Pfizer in October 2009.

3738

Fixed combination calcipotriene plus betamethasone dipropionate aerosol foam is more efficacious than topical suspension, with similar tolerability, in patients with psoriasis vulgaris: The phase III PSO-ABLE study

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Introduction: An innovative aerosol foam formulation of fixed combination calcipotriene 0.005% (Cal)/betamethasone dipropionate 0.064% (BD) has been developed to improve topical psoriasis treatment. In the PSO-ABLE study, efficacy and safety of Cal/BD aerosol foam was compared with Cal/BD topical suspension (susp) and vehicle formulations. Patient preferences and treatment convenience were also evaluated. Here we present efficacy and safety data.

Methods: PSO-ABLE was a phase III, investigator-blinded study. Patients (pts) aged ≥18 years with mild—severe psoriasis vulgaris (trunk and/or limbs) were randomized 4:4:1:1 to once-daily Cal/BD foam, Cal/BD susp, foam vehicle or susp vehicle for up to 12 weeks (wks) (NCT02152956). Primary efficacy endpoint: treatment success (defined as the proportion of pts who achieved clear/almost clear with a ≥two-step improvement, according to the physician's global assessment of disease severity) at wk 4 for Cal/BD foam vs wk 8 for Cal/BD susp, as per proposed and approved FDA labels, respectively. Other endpoints: proportion of pts achieving ≥75% reduction in psoriasis area and severity index (PASI75); time to treatment success (TTTS). Safety was monitored throughout.

Results: 463 pts were randomized to Cal/BD foam (n = 185), Cal/BD susp (n = 188), foam vehicle (n = 47) or susp vehicle (n = 43); mean age was 54.1 years. Significantly more Cal/BD foam-treated pts achieved treatment success at wk 4 vs Cal/BD susp-treated pts at wk 8 (36 vs 23%; OR 2.6, 95% CI 1.5, 4.5; $P < .001$). 52% of Cal/BD foam-treated pts achieved PASI75 at wk 4 vs 35% of Cal/BD susp-treated pts at wk 8 (OR 2.2, 95% CI 1.4, 3.5; $P < .001$; vehicles: 0% foam; 8% susp). Median TTTS with Cal/BD foam was 6 wks; this could not be determined for Cal/BD susp as 50% treatment success was not achieved within 12 wks. Adverse event (AE) frequency at 12 wks was similar for Cal/BD foam (42%) and Cal/BD susp (45%); most common was upper respiratory tract infection (n = 5, 2.7% and n = 9, 4.8%, respectively). For both active treatments, 2% of pts withdrew because of AEs. Adverse drug reactions (ie described as causally related to treatment) were reported in 14 pts (8%) using Cal/BD foam and seven (4%) using Cal/BD susp; all were single events except itch (Cal/BD foam, n = 5, 3%) and worsening psoriasis (Cal/BD susp, n = 3; 2%).

Conclusions: Four weeks of Cal/BD aerosol foam treatment showed superior efficacy compared with 8 wks with Cal/BD susp, with a similar tolerability profile.

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2936

Generalized pustular psoriasis of von Zumbusch associated with IL-36RN mutation

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Generalized pustular psoriasis (GPP) is characterized by a widespread sterile pustular eruption within erythematous scaly plaques or erythrodermic skin. It is known to be associated with systemic symptoms such as fever and malaise. This disease is often chronic and may be life threatening. DITRA (deficiency of interleukin thirty-six—receptor antagonist) is a recently described hereditary auto-inflammatory disorder characterized by repeated attacks of generalized pustular psoriasis accompanied by a high-grade fever, general malaise and a pro-inflammatory state. The recombinant interleukin-1 receptor antagonist anakinra has been used successfully in patients with DITRA. We present a new case of DITRA in a 35-year-old male patient with a 17-year history of psoriasis. One year after the onset of psoriasis, he developed generalized pustular psoriasis secondary to a streptococcus throat infection. Since then, the patient has had multiple exacerbations of his psoriasis, which manifests as erythroderma with numerous pustules forming lakes of pus. His cutaneous flares are associated with fever, general malaise, vomiting with dehydration, and increased inflammatory markers. These severe episodes necessitated regular hospitalizations. Identified triggers include noncompliance with treatment, decrease in corticosteroid dosage or a concomitant medical illness such as staphylococcus or streptococcus infections. Multiple treatments have been attempted, but control of his cutaneous disease remains challenging. His current treatment regimen involves prednisone 20mg daily, acitretin 25mg daily and subcutaneous adalimumab 80 mg weekly. Psoriasis severity combined with a von Zumbusch pattern prompted a search for the IL36RN mutation. Genetic analysis revealed an autosomal recessive pathogenic homozygous mutation of the IL-36RN gene, variant c.348C > T (p.Ser113Leu). Anakinra, an interleukin-1 receptor antagonist, will be introduced by rheumatology shortly.

Commercial support: None identified.

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Gynura pseudochina downregulates nuclear factor-κB leading to an improvement of chronic plaque psoriasis

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Background: Long term usage of topical corticosteroids in chronic plaque psoriasis often complicates by cutaneous and systemic side effects. *Gynura pseudochina* leaf extract has long been used in traditional medicine in Southeast Asian countries. Essentially, the previous in vitro study showed that the extract can reduce an activation of nuclear factor kappa B (NF-κB) pathway which plays an important role in the pathogenesis of psoriasis.

Objective: To determine the efficacy and safety of *G pseudochina* leaf extract ointment in comparison with 0.1% triamcinolone (TA) cream as a treatment for mild to moderate chronic plaque psoriasis and to elucidate the mechanism of action of the leaf extract in vivo.

Materials and methods: Twenty-five patients with mild to moderate plaque psoriasis completed a 4-week trial with twice daily application of *G pseudochina* leaf extract ointment on psoriatic lesions on one side of the body and 0.1% TA cream on the other. Targeted Area Score (TAS) and Psoriasis Severity Index (PSI) scores were assessed at baseline, weeks 1, 2, 3 and 4. Physician's Global Assessment (PGA) scores were obtained through assessment of the clinical photographs. Pre and post treatment skin samples were taken. Phosphorylation of NF-κB/RelA, Ki-67 and epidermal thickness were analyzed by immunohistochemistry.

Results: After 1 week of therapy, TAS in erythema, desquamation, induration and PSI scores decreased significantly on both treated sides ($P < .05$) and continuously declined during the further course of the treatments. No significant differences between the two treatments were observed using TAS of erythema and induration, PSI and PGA scores. Immunohistochemical staining revealed diminution of phosphorylated NF-κB/RelA, Ki-67 and epidermal thickness in the section treated with the *G pseudochina* leaf extract ointment. The ointment was well tolerated with minimal side effects such as staining, itching and stinging. No laboratory abnormalities were detected.

Conclusion: *G pseudochina* leaf extract ointment is an effective treatment for mild to moderate chronic plaque psoriasis, comparable with 0.1%TA cream.

Commercial support: None identified.

3203

Hyperkeratotic palmar psoriasis. Patient difficult to treat with an excellent response to etanercept therapy

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Introduction: Psoriasis palmoplantar (PPP) is a disease with high impact on patients' quality of life. There are several conventional therapies that try to treat it but, many times, it means a challenge to the dermatologist. In the last decade, development of biological treatments have improved the course of the disease.

Case report: We report a case of a 47-year-old man, laborer construction retired, with a 8 years history of hyperkeratotic palmar psoriasis. Furthermore, he was affected by hypertension. The patient presented severe palmar hyperkeratosis and fissuring that makes difficult to carry out his daily activities. Skin biopsy of his palm hand, was informed by morphologic pattern of psoriasis and patch tests were negative. Several treatments were prove in our patient with low efficacy including occlusive high potency topical corticosteroids, methotrexate 15 mg/week and acitretin 25 mg/day. Cyclosporine was contraindicated because of his hypertension and he could not come to hospital 3 times a week for psoralen UVA therapy. We started alitretinoin 10 mg/day treatment, with a complete resolution of the lesions in one month but had clinical recurrence in 6 months. We decided to start etanercept 50 mg twice a week, during 12 weeks and later, maintenance therapy of 50 mg/week for 6 months, with an excellent response. At present, the patient has no lesions at all.

Conclusion: There is no specific treatment for PPP. In cases where conventional therapies have failed, anti−tumor necrosis factor agents (etanercept, adalimumab, infliximab) and ustekinumab, have proved effective. However, paradoxically psoriatic effects with biologic treatment have been reported. We report a case of hyperkeratotic palmoplantar psoriasis that had not responded to several conventional therapies but responded well to treatment with etanercept without adverse effects.

Commercial support: None identified.

2458

High-frequency power Doppler ultrasonography in the assessment of nail psoriasis

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Background: Nail psoriasis is usually investigated and diagnosed by clinical examination. Power Doppler ultrasonography (PDUS) is a real-time and noninvasive imaging technique for studying skin diseases.

Objective: To show the potential of the latest ultrasonographic equipment using high-frequency probes and very sensitive power Doppler for assessment of patients affected by nail psoriasis.

Methods: The study was conducted in 36 patients with a diagnosis of nail psoriasis and 43 healthy participants, using an ultrasonographic system equipped with a linear variable-frequency transducer ranging from 18 to 22 MHz and a Doppler frequency ranging from 6.6 to 12.5 MHz. A semiquantitative score (0-5) of PDUS signal was used for the assessment of blood flow at nail bed and matrix area.

Results: The thickness of nail plate and nail bed and PDUS score was higher in patients with nail psoriasis compared to healthy controls.

Conclusions: This study provides evidence that high-frequency PDUS is a feasible, reliable and comprehensive approach to assessing psoriatic nail disease. Conflict of interest statement: The authors declare that there are no conflicts of interest.

Commercial support: None identified.

2797

Impact of antipsoriatic therapy on endothelial function

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Background: Endothelial dysfunction (EF) is one of the first events in the process of atherosclerosis, which is known to be associated with psoriasis. Nevertheless, the effect of antipsoriatic treatments on cardiovascular morbidity and EF is still unclear.

Objective: To investigate the effect of short-term antipsoriatic treatments on EF values as a potential marker of its effect on cardiovascular morbidity.

Methods: EF was evaluated in 26 patients with moderate-to-severe psoriasis by measuring microvascular blood flow, expressed as the reactive hyperemic index (RHI), before and after phototherapy (8 weeks) or systemic antipsoriatic treatment (12 weeks).

Results: Antipsoriatic intervention was effective (PASI ↓5 = 46.1%), while the average RHI did not improve during the study. Patients with baseline preserved EF exhibited a decline in RHI (RHI difference = −0.2 ± 0.4, $P = .053$), while patients with abnormal baseline RHI presented non-significant RHI improvement (RHI difference = 0.1 ± 0.2, P = NS).

Conclusion: There was no positive effect on EF of short-term antipsoriatic treatment. It is possible that a longer period of treatment and EF evaluation would uncover a positive endothelial effect, especially in patients with baseline abnormal EF.

Commercial support: None identified.

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Impact of ixekizumab on palmoplantar plaque psoriasis compared to placebo and etanercept: Results from UNCOVER 2

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Introduction: Psoriasis on the hands and feet (palmoplantar) has a significant impact on quality of life, impacts function, and is frequently resistant to the full range of therapeutic modalities. Ixekizumab (IXE) is an anti-IL-17A monoclonal antibody, which has been shown to be effective in treating psoriasis in clinical trials. The objective of this analysis was to evaluate the efficacy of IXE treatment for patients with moderate-to-severe palmoplantar involvement compared to etanercept (ETN) and placebo (PBO).

Methods: In the double-blind UNCOVER 2 trial, patients were randomized to receive subcutaneous PBO (N = 168), ETN (50 mg twice weekly; N = 358), or a single injection of 80 mg IXE every 2 weeks (IXE Q2W; N = 351) or every 4 weeks (IXE Q4W; N = 347) following a 160 mg starting dose at Week 0. Psoriatic involvement on hands and feet was assessed with the Palmoplantar Psoriasis Area and Severity Index (PPASI) (severity score range: 0 to 72). The percentage of patients with 100% reduction from baseline on the PPASI was analyzed in patients with baseline scores ≥8 (moderate-to-severe palmoplantar involvement). Treatment groups were compared using Cochran-Mantel-Haenszel test; missing data were imputed using non-responder imputation.

Results: At baseline, the percentage of patients with palmoplantar psoriasis in each treatment group was: PBO, 32.7%; ETN, 26.5%; IXE Q2W, 29.6%; IXE Q4W, 29.4%. Of those patients with PPASI scores ≥8 (n = 105), the overall mean (SD) baseline score was 19.4 (12.3). At 12 weeks, the percentage of patients within this population who had achieved 100% reduction in the PPASI score was statistically significantly greater with IXE Q2W (51.6% [n = 16 of 31], $P < .001$) and IXE Q4W (45.5% [n = 10 of 22], $P = .031$) compared to PBO (5.6% [n = 1 of 18]). In addition, IXE Q2W showed superiority over ETN (29.4% [n = 10 of 34], $P = .039$). There were no unexpected safety findings for patients treated with IXE.

Conclusion: At Week 12, both IXE dose regimens were superior to PBO, and IXE Q2W was superior to ETN for 100% improvement in patients with moderate-to-severe palmoplantar plaque psoriasis. Additional studies of the effect of IXE in larger populations of patients with palmoplantar plaque psoriasis are required.

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Impact of ixekizumab treatment on depressive symptoms: An integrated analysis of three phase 3 clinical studies in patients with moderate-to-severe psoriasis

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Introduction: Depression is a common comorbid condition with psoriasis, and both illnesses may be associated with immune-mediated systemic inflammation. Ixekizumab, an anti-IL17A monoclonal IgG4 antibody with a high binding affinity, has demonstrated efficacy for moderate-to-severe psoriasis. The efficacy of ixekizumab on depressive symptoms was evaluated in patients with plaque psoriasis and comorbid depression at baseline.

Methods: Depression outcomes were integrated using data from the 12-week induction period of three randomized, controlled trials. During induction, patients were randomized to receive subcutaneous placebo (PBO; N = 791) or 80 mg ixekizumab as one injection every 4 weeks (IXE Q4W; N = 1,161) or every 2 weeks (IXE Q2W; N = 1,167) following a 160-mg initial dose at Week 0. Depressive symptoms were assessed at Weeks 0 and 12 using the Quick Inventory of Depressive Symptomology − Self Report 16 items (QIDS-SR16). Patients presenting with comorbid depression at baseline (QIDS-SR16 total score ≥11) were included in this analysis (PBO, n = 93; IXE Q4W, n = 120; IXE Q2W, n = 107).

Results: In this population with depressive symptoms, QIDS-SR16 median (range) total score at baseline was 14.0 (11-24) with no significant differences across groups. At Week 12, patients treated with ixekizumab had a significant and clinically meaningful decrease in depressive symptoms versus placebo (QIDS-SR16 total score mean change: IXE Q4W, −6.5 ± 4.5; IXE Q2W, −6.9 ± 5.2; and PBO, −3.6 ± 4.6; $P < .001$, both dose comparisons). The percentage of patients who met response criteria for depressive symptoms (QIDS -SR16 total improvement ≥50% from baseline) was 49.1% NRI with IXE Q4W and 59.8% NRI with IXE Q2W vs 27.1% NRI with placebo ($P \leq .001$, both dose comparisons). The rate of remission of depressive symptoms (QIDS-SR16 score ≤ 5) at Week 12 was significantly greater for IXE Q4W (33.6% NRI) and IXE Q2W (45.2% NRI) vs 17.8% NRI for PBO ($P < .05$, both dose comparisons). The Pearson correlation (r) between improvement in psoriasis (PASI) and depression (QID-SR16) from baseline to Week 12 was .0.15.

Conclusions: In an integrated analysis of patients with plaque psoriasis and depressive symptoms at baseline, ixekizumab was superior to placebo, achieving a clinically meaningful response in ~50% and remission of depressive symptoms in 39.1% at Week 12.

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Impact of ixekizumab treatment on scalp psoriasis: Results from the UNCOVER-2 trial

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Introduction: Scalp psoriasis can be difficult to treat and negatively impacts quality of life. Ixekizumab (IXE) is a monoclonal antibody to IL-17A, a cytokine in psoriasis pathogenesis. In the UNCOVER trial, IXE was superior to both placebo (PBO) and etanercept (ETN) on skin clearance measures in patients with moderate-to-severe plaque psoriasis. The objective of this secondary analysis was to compare the effect of IXE therapy on scalp psoriasis compared to PBO and ETN.

Methods: Patients were randomized to receive subcutaneous PBO (N = 168), ETN (50 mg twice weekly; N = 358), or a single injection of 80 mg IXE every 2 weeks (IXE Q2W; N = 351) or every 4 weeks (IXE Q4W; N = 347) following a 160 mg starting dose at Week 0. Scalp psoriasis was assessed with the Psoriasis Scalp Severity Index (PSSI) (range: 0 to 72). Least squares (LS) mean changes were calculated using mixed effects models for repeated measures. Treatment groups were compared using the Cochran-Mantel-Haenszel test for categorical data. Missing data were imputed using nonresponder imputation.

Results: At baseline, the percentages of patients with scalp psoriasis in each treatment group were: PBO, 89.9%; ETN, 89.9%; IXE Q2W, 91.2%; IXE Q4W, 89.9%. Overall mean (SD) baseline PSSI score was 20.2 (15.22). Significant differences in the percent improvement of PSSI were observed as early as Week 1 with IXE Q2W (37.0%) and IXE Q4W (37.7%) vs ETN (8.4%) and PBO (4.3%) ($P < .001$; each comparison). At Week 12, the percent improvement from baseline in PSSI was 93.0%, 86.5%, 68.9%, and 3.7% with IXE Q2W, IXE Q4W, ETN and PBO, respectively. Improvement was significantly greater with both IXE dose regimens vs ETN (both, $P < .001$). At 12 weeks, the percentages of patients with no scalp psoriasis with IXEQ2W (74.4%) and IXEQ4W (64.1%) were significantly greater as compared with PBO (7.3%) and ETN (44.7%) (all, $P < .001$). There were no unexpected safety findings with IXE treatment.

Conclusions: IXE dosing regimens were superior to PBO and ETN for improvement in scalp psoriasis with onset of efficacy as early as Week 1. Over 60% of IXE-treated patients achieved complete resolution of their scalp psoriasis by week 12, which was significantly more than those treated with either ETN or PBO.

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Impact of ixekizumab treatment on sexual function in moderate-to-severe psoriasis patients: 12 week results from two phase 3 trials UNCOVER-2 and UNCOVER-3

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Introduction: Impaired sexual function is often an unrecognized complication of psoriasis. Ixekizumab, an anti-IL-17A monoclonal IgG4 antibody with high binding affinity, is being developed as a psoriasis treatment. We evaluated the impact of ixekizumab on sexual function in psoriasis patients enrolled in two phase 3, double-blind trials (UNCOVER-2 and UNCOVER-3).

Methods: Patients were randomized to subcutaneous placebo (PBO), high-dose etanercept (ETN; 50 mg twice weekly), or 80 mg ixekizumab as one injection every 4 (IXE Q4W) or 2 weeks (wks) (IXE Q2W) for 12 wks, following a 160-mg initial dose. 1224 patients were randomized in UNCOVER-2 (PBO, n = 168; ETN, n = 358; IXE Q4W, n = 347; IXE Q2W, n = 351) and 1346 in UNCOVER-3 (PBO, n = 193; ETN, n = 382 ETN; IXE Q4W, n = 386; IXE Q2W, n = 385). The Dermatology Life Quality Index Item 9 was used to assess how much skin caused any sexual difficulties ranging from 0 = not at all to 3 = very much at Wks 0, 2, 4, and 12. In patients with baseline sexual difficulty or impairment, the percentages of patients reporting improvements in any sexual difficulty (score ≥1) and impaired sexual function (score ≥2) were compared using logistic regression. Missing data were imputed by nonresponder imputation.

Results: In both trials at baseline, a similar percentage of patients in each group reported that their skin caused sexual difficulties (all patients: 45% UNCOVER-2; 43% UNCOVER-3). Among patients with sexual difficulties in UNCOVER-2 and UNCOVER-3, significantly more had improvement in sexual difficulties at Wk 2 with IXE Q4W (49% and 52%) and IXE Q2W (54% and 55%) vs ETN (30%, $P < .001$ and 37%, $P < .05$) or PBO (20%, $P < .001$ and 27%, $P < .001$). By Wk 12 more patients who were treated with IXE Q4W (68% and 78%) and IXE Q2W (80% and 81%) vs ETN (51%, $P < .001$ and 69%, $P < .05$) or PBO (24%, $P < .001$ and 27%, $P < .001$), experienced improvement. Improvement in the percentage of patients with impaired sexual function was consistent with improvement in sexual difficulty. A similar pattern of improvement was observed in males and females. Across all groups, all patients with complete resolution of psoriasis (PASI 100) were more likely to have no sexual difficulties at Wk 12.

Conclusions: In these trials, more patients treated with ixekizumab reported improvements in sexual difficulty than with ETN with significance observed as early as Wk 2. Patients with complete resolution of psoriasis were more likely to achieve no sexual difficulties.

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3012

Impact of treatment of psoriasis on carotid intima-media thickness

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Introduction: Psoriasis is a chronic immune-mediated inflammatory disease, which shares inflammatory pathways with atherosclerosis, reason why the two entities could be associated. Increased carotid intima-media thickness (IMT) is an accepted indicator of subclinical atherosclerosis and has been reported in severe psoriasis.

Objectives: Pilot study to quantify the degree of decrease long-term of IMT in patients that started treatment for severe psoriasis.

Methodology: In 14 patients with severe psoriasis (PASI >8 or BSA >8% or DLQI >8), the carotid IMT was measured by high-resolution B-mode ultrasonography, being calculated before starting phototherapy or systemic or biological therapy and after 6 -11 month treatment. Difference between initial and 6-11 month IMT values was determined.

Results: The mean age of patients was 45.3 years (18-66 years), 9 were male and 6 female, the average period with psoriasis was 17.2 years (2-45 years), the PASI/BSA/DLQI before treatment was 9.2 (7-16.6)/16.6 (12-31.5)/9.14 (1-25) and then 2.3 (0-7.5)/2.2 (0 -8)/3.6 (0-17), with an improvement of 75.5%, 86.7% and 60.1% respectively. Phototherapy was used in 2 patients, systemic treatment in 6 (4 with methotrexate, 1 with cyclosporine and 1 with acitretin) and biological treatment in 6 (5 with etanercept and 1 with adalimumab). Right/left carotid IMT before the treatment was 0.610 mm/0.630 mm and after 0.604 mm/0.588 mm, with a decrease of 1% and 6.7% after treatment, respectively. When comparing phototherapy, systemic treatments and biological treatments right/left carotid IMT before treatment was 0.621 mm/0.652 mm, 0.564 mm/0.576 mm and 0.653 mm/0.677 mm and then 0.706 mm/0.642 mm, 0.548 mm/0.527 mm and 0.625 mm/0.631 mm, respectively. A decrease in right carotid IMT of 2.8% after systemic treatment and 4.3% after biologic treatment, while a 13.7% increase after phototherapy was observed. Left carotid IMT decreased was observed in all cases, which was 1.5% with phototherapy, 8.5% with systemic treatment and 6.8% with biological treatment.

Limitations: Small patient numbers and self-controlled study design.

Conclusions: The treatment of psoriasis appears to decrease the IMT, favoring the reduction of atherosclerosis mainly to use systemic and biological treatments. Further analysis is recommended to confirm and complete our findings.

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Improvements in depression and anxiety with brodalumab therapy in AMAGINE-1, a phase 3 study for moderate to severe plaque psoriasis

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Introduction: Patients with psoriasis have increased risk for depression and anxiety. Brodalumab, a human anti−IL-17 receptor A antibody, has shown efficacy in treating moderate to severe plaque psoriasis in phase 3 clinical trials.

Objective: To assess improvements in depression and anxiety in patients with psoriasis treated with brodalumab from a phase 3 study (NCT01708590).

Methods: Patients with moderate to severe plaque psoriasis received brodalumab (140 or 210 mg) or placebo every 2 weeks (Q2W), with an additional dose at week 1, for 12 weeks. Patients completed the Hospital Anxiety and Depression Scale (HADS) at baseline and week 12. Outcome measures were improvement from baseline score and shift from baseline severity group (normal [score 0−7], mild [8−10], moderate [11−14], or severe [15−21]). Continuous data were compared between brodalumab and placebo arms using ANCOVA adjusted for baseline HADS and stratification factors (multiple imputation).

Results: There were 661 patients in the study: 222 brodalumab 210 mg Q2W, 219 brodalumab 140 mg Q2W, and 220 placebo. At baseline, patients were 73% male, mean (SD) age 46 (13) years, psoriasis duration 20 (13) years, and Psoriasis Area and Severity Index 20 (7). Mean (SD) HADS anxiety scores were 6.7 (4.3), 6.6 (4.2), and 6.4 (3.8) in 210 mg, 140 mg, and placebo arms, respectively; corresponding mean (SD) HADS depression scores were 5.5 (4.2), 5.2 (4.1), and 5.3 (3.9). Through week 12, adverse event rates were balanced among groups and one patient in each reported depression. At week 12, mean (95% CI) improvements in HADS anxiety scores were 1.8 (1.3, 2.2), 1.5 (1.0, 1.9), and 0.1 (-0.2, 0.5) in 210 mg, 140 mg, and placebo arms, respectively, and model-based treatment differences from placebo were 1.5 and 1.3 in 210 mg and 140 mg arms, respectively; corresponding mean (95% CI) depression score improvements were 2.0 (1.5, 2.5), 1.7 (1.2, 2.2), and −0.2 (−0.6, 0.2), and model-based treatment differences from placebo were 2.1 and 1.9 ($P < .001$ for all). The majority of patients receiving brodalumab shifted to less severe HADS severity groups; over 60% of patients with moderate and severe anxiety (N = 37 [140 mg] + 42 [210 mg]) or depression (N = 30 [140 mg] + 30 [210 mg]) at baseline improved to mild, normal, or moderate at week 12.

Discussion: In this study, the majority of patients with moderate to severe plaque psoriasis receiving brodalumab showed improvements in HADS anxiety and depression scores.

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Improvements in extraarticular manifestations of psoriatic arthritis over 96-weeks of certolizumab pegol treatment

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Introduction: Previous reports of RAPID-PsA (NCT01087788) demonstrated clinical efficacy of certolizumab pegol (CZP) in patients (pts) with psoriatic arthritis (PsA) over 96 weeks (wks). This abstract focuses on the efficacy of CZP for the treatment of extra-articular manifestations (EAMs) of PsA including psoriasis, nail psoriasis, enthesitis and dactylitis over 96 wks.

Methods: RAPID-PsA was double-blind and placebo-controlled to Wk24, dose-blind to Wk48 and open-label to Wk216. Pts had active PsA and had failed ≥1 DMARD. Here we present data for pts randomized to CZP at Wk0 (combined 200 mg Q2W and 400 mg Q4W doses). The primary clinical endpoint (ACR20 at Wk12) has been reported previously. EAM data are presented for pts with baseline (BL) involvement and include psoriasis (% body surface area [BSA] affected for pts with BL BSA ≥3%), nail psoriasis (modified nail psoriasis severity index [mNAPSI] for pts with BL mNAPSI > 0; for some pts nail analyzed changed to Wk96), enthesitis (Leeds enthesitis index [LEI] for pts with BL LEI > 0) and dactylitis (Leeds dactylitis index [LDI] for pts with at least 1 digit affected and a difference in circumference ≥10%). We also present data for pts with total resolution of each EAM, ie. % of pts with BL involvement achieving complete clearance (score of 0 for mNAPSI, LEI or LDI, or 0% BSA). Data shown are observed values.

Results: Of 409 pts randomized, 273 received CZP from Wk0. At BL, 166 (60.8%) of these pts had psoriasis (mean BL BSA: 24.2%), 197 (72.2%) nail psoriasis (mean BL mNAPSI: 3.3), 172 (63.0%) enthesitis (mean BL LEI: 3.0) and 75 (26.7%) dactylitis (mean BL LDI: 51.3). Rapid reductions in mean psoriasis BSA were seen to Wk24 (5.6%) and were maintained to Wk96 (3.7%). Similar improvements were observed in all EAMs assessed, including nail psoriasis (mean mNAPSI, Wk24: 1.4; Wk96: 0.7), enthesitis (mean LEI, Wk24: 1.0; Wk96: 0.7) and dactylitis (mean LDI, Wk24: 2.4; Wk96: 0.0). A large proportion of pts with BL EAM involvement went on to achieve total resolution. At Wk24, 26.8% of pts had total resolution of psoriasis, and 48.5% at Wk96. Similarly, for pts with nail psoriasis, 38.5% had total resolution at Wk24 and 65.2% at Wk96. For enthesitis and dactylitis the respective proportions achieving total resolution were 65.2% and 73.8% at Wk24, and 71.0% and 89.5% at Wk96.

Conclusions: Improvements in EAMs of PsA were observed following CZP treatment and were maintained to Wk96 of RAPID-PsA. These improvements were seen in all EAMs measured, including nail psoriasis, enthesitis, dactylitis and psoriasis.

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Improvements in fingernail lesions in patients with moderate-to-severe psoriasis treated with ixekizumab versus placebo and etanercept: Results from UNCOVER-2

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Introduction and objectives: Psoriasis affecting fingernails can be difficult to treat. Ixekizumab is an anti-IL-17A monoclonal IgG4 antibody with high binding affinity. We evaluated the effect of ixekizumab on fingernail psoriasis in patients enrolled in UNCOVER-2.

Materials and methods: This phase 3, double-blind trial randomized 1224 patients to receive subcutaneous placebo (PBO; N = 168), high-dose etanercept (ETN; 50 mg twice weekly; N = 358), or 80 mg ixekizumab as one injection every 4 weeks (wks) (IXE Q4W; N = 347) or 2 wks (IXE Q2W; N = 351) for 12 wks following a 160-mg initial dose. At Wk 12, ixekizumab-treated patients achieving sPGA 0,1 (responders) were rerandomized to PBO, IXE Q4W, or 80 mg IXE every 12 wks (IXE Q12W). Wk 12 ixekizumab nonresponders received IXE Q4W through Wk 60. PBO nonresponders received 160 mg IXE at Wk 12, then IXE Q4W through Wk 60. ETN nonresponders received PBO at Wk 12, then IXE Q4W at Wks 16-60. In prespecified analyses of patients with baseline psoriatic fingernail involvement (PBO, n = 113; ETN, n = 229; IXE Q4W, n = 219; IXE Q2W, n = 209), severity was assessed by Nail Psoriasis Severity Index (NAPSI; 0 = none, 80 = severe). Least squares mean changes were calculated using mixed effects models for repeated measures.

Results: Mean ± SD baseline NAPSI was 27.0 ± 20.2 for patients with psoriatic fingernails (N = 770). At Wk 12, there were significantly greater NAPSI improvements with IXE Q4W (-7.4 ± 0.8) and IXE Q2W (-8.6 ± 0.9) vs PBO (-0.8 ± 1.1, $P <$ .001 each) as well as with IXE Q2W vs ETN (-5.5 ± 0.8, $P < .001$). At Wk 60, significantly greater NAPSI improvements from baseline were observed for ixekizumab-treated responders re-randomized to IXE Q4W (-19.9 ± 1.2) and IXE Q12W (-14.7 ± 1.3) vs those switched to PBO (-7.4 ± 2.1, $P \leq .01$ each). A higher percentage of patients had NAPSI 0 at Wk 60 in IXE Q4W (53.0%) and IXE Q12W (25.4%) than PBO (6.7%, $P <$.001 each) At Wk 60, nonresponders who switched from PBO or ETN to IXE Q4W also experienced NAPSI improvements (-21.5 ± 19.2 and -22.4 ± 21.9, respectively). Overall, there were no unexpected safety signals with ixekizumab.

Conclusions: In this trial, ixekizumab provided significant and sustained improvement in fingernail psoriasis. Improvement with IXE Q2W was significantly greater than with ETN at Wk 12. Nonresponders who switched from ETN or PBO to ixekizumab had improvements similar to ixekizumab responders on extended treatment. Up to 50% of ixekizumab-treated patients had no nail psoriasis at Wk 60.

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Improvements in health-related quality of life and symptoms of depression with tofacitinib: Results from two randomized phase 3 studies in patients with moderate to severe psoriasis

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Background: Psoriasis (PsO) impairs health-related quality of life (HRQoL) and is associated with depression and anxiety. Tofacitinib is an oral JAK inhibitor that is being investigated for PsO.

Objective: To assess the effect of tofacitinib on HRQoL, depression, and anxiety in patients (pts) with moderate to severe PsO.

Methods: OPT Pivotal 1 (OPT1; NCT01276639) and 2 (OPT2; NCT01309737) were identical 52-week phase 3 studies. Pts received tofacitinib 5 mg (OPT1/OPT2: N = 363/382), 10 mg (N = 360/381), or placebo (N = 177/196) twice daily (BID). At Week 16, placebo-treated pts were re-randomized to tofacitinib 5 or 10 mg BID.

Assessments: Short Form-36 (SF-36) mental and physical component summary score (MCS and PCS; population norm mean = 50); Hospital Anxiety and Depression Scale (HADS); ≥75/90% improvement in PsO Area and Severity Index vs baseline (PASI75/90).

Results: At baseline, HRQoL was impaired in both studies (mean MCS 42.5−43.4; PCS 44.9−47.9), and 27.4−35.1% and 33.5−42.8% of pts met HADS criteria for depression and anxiety (subscale score ≥8), respectively. At Week 16, mean MCS change from baseline was greater in pts who received tofacitinib 5 mg BID (OPT1/OPT2: 4.2/4.0) and 10 mg BID (6.0/5.4) vs placebo (0.8/2.3; $P < .05$). A smaller proportion of depression cases were reported at Week 16 for tofacitinib 10 mg BID (OPT1/OPT2: 15.9/16.2%) vs placebo (31.9/26.8%; $P < .01$ in both studies) and tofacitinib 5 mg BID (17.4/24.0%) vs placebo ($P < .001$ in OPT1 only). A smaller percentage of anxiety cases were reported for tofacitinib 5 and 10 mg BID vs placebo in OPT1 (26.2% and 24.0% vs 37.7%; $P < .05$) but not OPT2 (28.2% and 26.2% vs 28.7%). Across studies at Week 16, fewer pts achieving PASI90 with tofacitinib 5 and 10mg BID had depression (16.2% and 12.0%) vs those achieving PASI75/90 (20.5% and 14.8%) or < PASI75 (23.1% and 21.6%). By Week 52, mean MCS were similar to the population norm in pts who received tofacitinib 5 mg BID (49.1/49.5) and 10 mg BID (50.7/50.0). Reduced rates of depression were maintained at Week 52 (OPT1/OPT2: 5 mg 14.7/21.1%; 10 mg 13.5/13.5%). At Week 52, the percentage of pts with anxiety in the tofacitinib 5 and 10 mg BID groups was 17.0% and 16.5% in OPT1, and 24.2% and 22.4% in OPT2.

Conclusion: Tofacitinib 5 and 10 mg BID improved HRQoL vs placebo in pts with moderate to severe PsO and reduced the proportion of pts with symptoms of depression, slightly more at 10 mg BID. Pts with greater PASI responses were less frequently depressed.

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Improvements in health-related quality of life measured by SF-36 and EQ-5D in patients with moderate to severe plaque psoriasis treated with brodalumab

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Introduction: Brodalumab, an IL-17RA monoclonal antibody, was efficacious in phase II/III trials in patients with moderate to severe plaque psoriasis (PsO), based on sPGA and PASI.

Objectives: To evaluate the impact of brodalumab on health-related quality of life (HRQOL) measured by the SF-36v2, the EQ-5D, and EQVAS.

Methods: Data from the double-blind, placebo-controlled induction phase of a phase 3 brodalumab RCT in patients with moderate to severe plaque PsO were analyzed (AMAGINE-1). Patients were randomized (1:1:1) to brodalumab 210 mg Q2W, 140 mg Q2W, or placebo. Secondary endpoints included change in SF-36v2 from baseline to Week 12 (Wk12), and EQ-5D/EQVAS scores across groups at Wk12. Data were analyzed as randomized, using an analysis of covariance model adjusting for baseline values and randomization stratification factors. Multiple imputation handled missing data.

Results: Patients treated with brodalumab achieved significantly greater improvement in all SF-36 scales scores, and greater EQ-5D, EQVAS scores, compared with placebo at Wk12 (all $P < .001$). Baseline EQ-5D and EQVAS mean (SD) for placebo (N = 216), brodalumab 140 mg (N = 216), and 210 mg (N = 221) were: 0.62 (0.29); 0.61 (0.32); 0.60 (0.32), respectively. At Wk12, EQ-5D mean scores (95% CI) Were: 0.61 (0.57, 0.66) for placebo (N = 218); 0.83 (0.79, 0.86) for 140 mg (N = 219); and 0.85 (0.82, 0.88) for 210 mg (N = 221) (all $P < .001$ vs placebo). Mean change (95% CI) scores from baseline to Wk12 in each of the SF-36 scales for placebo (N = 216), brodalumab 140 mg (N = 216), and 210 mg (N = 221), respectively, were: Physical function: -0.3 (-1.3, 0.7), 3.5 (2.4, 4.6), 3.1 (2.1, 4.0); Role—physical: -0.4 (-1.4, 0.7), 4.1 (3.0, 5.3), 3.8 (2.7, 4.9); Bodily pain: 0.0 (-1.2, 1.2), 7.2 (5.8, 8.7), 7.7 (6.2, 9.2); General health: -0.3 (-1.2, 0.6), 4.1 (3.0, 5.2), 4.2 (3.1, 5.2); Vitality: 0.8 (-0.2, 1.8), 5.0 (3.8, 6.1), 4.6 (3.4, 5.8); Social function: 0.2 (-1.0, 1.4), 7.2 (5.8, 8.6), 8.0 (6.6, 9.5); Role—emotional: -0.5 (-1.7, 0.7), 4.8 (3.5, 6.1), 4.7 (3.4, 6.0); Mental health: 0.7 (-0.4, 1.8), 5.3 (4.1, 6.6), 6.1 (4.9, 7.3); PCS: 0.4 (-1.3, 0.6), 4.2 (3.2, 5.3), 4.0 (2.9, 5.0); and MCS: 0.5 (-0.6, 1.6), 5.7 (4.4, 6.9), 6.2 (5.0, 7.5). All $P < .001$ vs placebo.

Conclusions: Patients treated with brodalumab experienced significant improvement in all aspects of HRQoL measured by the SF-36v2 and EQ-5D. Brodalumab significantly improves patient-reported outcomes in patients with moderate to severe plaque psoriasis.

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Improvements in patient-reported outcomes (PROs) among moderate to severe plaque psoriasis patients treated with brodalumab: Results from AMAGINE-1

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Introduction: Brodalumab, an IL-17RA monoclonal antibody, was efficacious in phase II/III trials in patients with moderate to severe plaque psoriasis (PsO), based on sPGA and PASI.

Objectives: To evaluate the impact of brodalumab on: the Psoriasis Symptom Inventory [PSI, an 8-item patient-reported outcome instrument measuring itch, redness, scaling, burning, stinging, cracking, flaking, and pain (scored from 0 to 32)], the Dermatology Life Quality Index (DLQI); and treatment satisfaction.

Methods: Data from a double-blind, placebo-controlled, randomized trial in moderate to severe plaque psoriasis was analyzed. Patients were randomized (1:1:1) to brodalumab 210 mg Q2W, brodalumab 140 mg Q2W, or placebo. Outcomes at Week 12 (Wk12) included the percentages of patients achieving: PSI responder definition (total score ≤8 with no item score >1); PSI total score = 0 (not at all severe on all signs and symptoms); improvement of ≥5 on DLQI from baseline; DLQI score of 0/1; different degrees of satisfaction with treatment. For DLQI and PSI, percentages were compared using Cochran-Mantel-Haenszel model, adjusting for baseline stratification factors and dichotomized baseline values. Nonresponder imputation was used for the binary outcomes. Treatment satisfaction was compared using ordinal logistic regression adjusting for the baseline stratification factors, and worst-case imputation was used.

Results: Baseline PSI and DLQI scores were similar across groups. At Wk12, significantly greater percentages of patients treated with brodalumab achieved: Improvements ≥5 on DLQI; DLQI = 0/1; PSI responder definition; and PSI = 0, compared with placebo (all $P < .001$). A significantly greater percentage of patients on brodalumab dosages had better treatment satisfaction compared with placebo ($P < .001$). At Wk12 the following proportions (95%CI) of patients: 4.1% (1.9%, 7.6%); 53.0% (46.1%, 59.7%); and 60.8% (54.1%, 67.3%) were PSI responders; 0.5% (0.0%, 2.5%); 17.4% (12.6%, 23.0%); and 21.6% (16.4%, 27.6%) had PSI total score = 0; 5.0% (2.5%, 8.8%); 42.9% (36.3%, 49.8%); 55.9% (49.1%, 62.5%) had DLQI 0/1; 21.6% (16.1%, 28.0%); 73.8% (67.0%, 79.9%); 83.6% (77.7%, 88.4%) had DLQI improvement≥5, in placebo (N = 220), brodalumab 140 mg (N = 219), and 210 mg (N = 222) respectively; All $P < .001$ vs placebo.

Conclusions: Results indicate that brodalumab significantly improved patient-reported outcomes (PSI, DLQI and treatment satisfaction) in patients with moderate to severe plaque psoriasis.

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Insurance coverage of biologics for moderate-to-severe psoriasis: A database review

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Background: With the variability in health insurance coverage for psoriasis systemic therapies, recent shifts in coverage for biological therapies have yet to be evaluated.

Purpose: To determine changes in insurance coverage of biologics for moderate to severe psoriasis between 2009 and 2014, with a focus on insurance policies as stated in prior authorization (PA) forms, coverage denials, and time course of approval process.

Methods: A retrospective chart review was performed on patients with a diagnosis of psoriasis (ICD-9 696) seen at the George Washington University Medical Faculty Associates Department of Dermatology between January 1st, 2009 and December 31st, 2014. Exclusion criteria included <9% body surface area (BSA), loss to follow-up, lack of biologic treatment, biologic treatment via clinical trial, and lack of health insurance. For all other patients, metrics collected included age, gender, BSA, health insurance plan, prior therapies, prescribed biologic, PA necessity, time in days between PA submission and coverage decision, and provided denial justifications.

Results: 864 patients with a diagnosis of psoriasis within the time period were identified, 114 of whom met the inclusion criteria. PA requirement increased from 15.6% of patients prescribed a biologic in 2009 to 75.0% patients prescribed a biologic in 2014. The mean duration in days between PA submission and coverage decision from the insurance company increased from 4.0 days in 2009 to 6.7 days in 2014. PA denial rates increased from 0% in 2009 to 20.8% in 2014. The most common reason for coverage denial was failure to attempt alternative therapies prior to requesting biologics. Other denial reasons included prescribed dosage discrepancies and inability to determine benefit. Upon analysis of PA forms of 4 insurance companies, the number of coverage requirements increased from 2009 to 2014.

Conclusion: Insurance coverage of biologics for moderate-to-severe plaque psoriasis has become increasingly regulated between the years of 2009 and 2014. Given both the cost burden and potential benefits of these therapies, further examination of healthcare coverage and treatment accessibility is warranted for optimal patient outcomes.

Commercial support: None identified.

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Is lichen planus a marker for dyslipidemia and metabolic syndrome?

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Background: Lichen planus (LP) is a distinct autoimmune inflammatory, self-limiting papulosquamous disorder of unknown cause that affects the skin, mucous membranes, nails and hair. Previous studies have established a link between LP and diabetes mellitus (DM). Recent studies have suggested that patients with LP could have higher risks of developing cardiovascular diseases. Disturbances in the lipid metabolism due to underlying inflammation and oxidative stress which releases inflammatory cytokines could be accountable. Certain other dermatological conditions such as psoriasis and androgenic alopecia are associated with cardiovascular risk factors which could possibly be explained by the underlying proinflammatory state.

Objective: To compare the prevalence of metabolic syndrome (MetS) and dyslipidemia in patients of LP and in healthy controls. We have also compared inflammatory markers in these groups.

Patients and methods: This case control study included 39 consecutive patients aged ≥18 years with LP (biopsy proven) with minimum disease duration of 6 months and 78 age- and sex-matched controls recruited from a tertiary care hospital in South India. Patients were recruited from March 2012 to August 2013. Fasting plasma glucose, lipid profile, ESR and CRP values were measured. Anthropometric measurements, body composition and dual-energy X-ray absorptiometry scan findings were compared.

Results: MetS was diagnosed in 59% of cases of LP based on the International Diabetes Federation (IDF) - 2006 criteria as compared to only 32% of controls, showing a highly significant difference (OR = 3.047, 95% CI = 1.375, 6.754, $P = .006$). We found dyslipidemia in 35.9% of cases as compared to 21.8% of controls ($P = 0.108$) in accordance with National Cholesterol Education Program—Third Adult Treatment Panel definition (NCEP ATP III). However, there was no difference between the inflammatory markers studied among the cases and controls.

Conclusion: The present study found a higher prevalence of MetS in patients with LP as compared to healthy controls and suggests that LP may be associated with MetS and dyslipidemia. Screening for MetS in patients with LP is advisable due to the long term complications associated with it.

Commercial support: None identified.

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Ixekizumab improves physical function, quality of life, and work productivity in biologic disease-modifying antirheumatic drug-naive patients with active psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a chronic immune-mediated inflammatory disease associated with psoriasis, peripheral arthritis, enthesitis, dactylitis, and spondylitis. PsA has a negative impact on patients' (pts) quality of life (QoL), physical function, and work productivity. Ixekizumab (IXE) is an anti-IL-17A IgG4 monoclonal antibody with high binding affinity.

Methods: In a phase 3 trial (SPIRIT-P1), 417 biologic disease-modifying antirheumatic drug (bDMARD)-naïve pts with active PsA were randomized to receive 24 weeks (wks) of placebo (PBO, N = 106), adalimumab 40 mg once every 2 wks (Q2W; N = 101, active control), or ixekizumab (IXE) 80 mg every 4 wks (Q4W; N = 107) or Q2W (N = 103) following a 160-mg starting dose at Wk 0. Patient reported outcomes (PROs) included Health Assessment Questionnaire – Disability Index (HAQ-DI), Short Form-36 Health Survey Physical Component Summary (SF-36 PCS), Dermatology Life Quality Index (DLQI), Itch Numeric Rating Scale (NRS) and Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP). Continuous PRO data were evaluated using a mixed-effects model for repeated measures. Categorical PRO data were compared using a logistic regression model; missing values were imputed with the nonresponder imputation (NRI) method, treating inadequate responders (IRs) as nonresponders.

Results: Patients treated with IXE Q4W or IXE Q2W reported significantly greater improvements compared to PBO in HAQ-DI, SF-36 PCS, DLQI, and Itch NRS at Wks 12 (16 for DLQI) and 24. ($P \leq .001$). Significantly greater improvements were also seen in all IXE groups versus PBO for WPAI-SHP (all components, except Absenteeism) at Wks 12 and 24 ($P < .05$). Compared to placebo, a greater percentage of IXE patients achieved the minimally clinically important difference for HAQ-DI (improvement from baseline in HAQ-DI ≥0.35, $P < .01$) at Wks 12 and 24, and the percentages of patients who had no negative effect on QoL as assessed by DLQI score of 0,1 or 0 were significantly greater in each IXE group at Wks 16 and 24. Greater treatment responses as assessed by Psoriasis Area Severity Index (PASI 75/90/100) were associated with greater improvements in DLQI ($P < .05$). Adalimumab, serving as an active reference arm, also demonstrated efficacy versus PBO across the assessed parameters.

Conclusions: In bDMARD-naive patients with active PsA, IXE significantly improves QoL, physical function, and work productivity as early as Wk 12.

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3017

Ixekizumab shows efficacy and safety in patients who failed biweekly etanercept therapy: Analysis From UNCOVER-2, a phase 3 randomized clinical trial in psoriasis

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Introduction: Clinical observations suggest that the efficacy of biologics in psoriasis can be affected by previous treatment with another biologic. In this analysis, we evaluate the efficacy and safety of ixekizumab (IXE), an anti-IL17A monoclonal antibody with high binding affinity, in patients (pts) who previously failed to reach static Physician Global Assessment (sPGA) 0 or 1 after 12 weeks (wks) on bi-weekly etanercept (ETN).

Methods: In UNCOVER-2, a double-blind phase 3 clinical trial, pts with moderate-to-severe psoriasis were randomized to receive IXE 80 mg every 2 wks (IXE Q2W; N = 351) or every 4 wks (IXE Q4W; N = 347) after a 160-mg starting dose, or ETN (50 mg bi-weekly; N = 358), or placebo (PBO; N = 168) during a 12-wk induction period. At wk 12, pts who had not achieved sPGA 0/1 were considered "nonresponders" and administered IXE Q4W for wks 12-60. ETN-nonresponders received 2 injections of PBO at wk 12, then IXE Q4W through wk 60 starting at wk 16 (4 wk wash-out). Missing data were imputed using nonresponder imputation.

Results: In this trial, 358 pts were randomized to biweekly ETN in the induction period and 200 (56%) were ETN-nonresponders (sPGA≥2) at wk 12; only 15.5% of these nonresponders achieved PASI 75. After 12 wks of IXE Q4W (wk 28), 83.5% had reached PASI 75, 57.0% had PASI 90, and 22.0% had PASI 100. Following 44 wks of IXE Q4W (wk 60), 82.5% of ETN-nonresponders had PASI 75, 68.5% had PASI 90, and 43.5% had PASI 100. After 4 wks of IXE Q4W, 45.5% of ETN-nonresponders achieved sPGA 0/1 rising to 73% after 12 wks. Serial Dermatology Life Quality Index (DLQI) scores among these pts showed that while 21.5% had achieved DLQI 0/1 after 12 wks of bi-weekly ETN, 58.0% had DLQI 0/1 at wk 60 (44 wks of IXE Q4W). During wks 12-60, 158 (79%) ETN-nonresponders experienced ≥1 treatment-emergent adverse event (TEAE); the majority of these 158 events were mild (35%) or moderate (54%). There were 9 (4.5%) pts with ≥1 serious AE (SAE) and 8 (4%) discontinuations due to AEs. This was comparable to TEAEs in PBO-nonresponders (N = 155) who began IXE Q4W with a starting dose at wk 12 (total patients with ≥1 TEAEs – 81%; mild = 27% and moderate = 42% TEAEs; 12 [8%] pts with ≥1 SAE; 8 [5%] discontinuations).

Conclusions: In this trial, IXE showed high clinical efficacy in pts who previously failed to reach sPGA 0/1 after 12 wks treatment with bi-weekly ETN. Pts switching from ETN to IXE Q4W had a safety profile similar to those switching from PBO to IXE Q4W.

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Ixekizumab, a novel anti–IL-17A antibody, exhibits low immunogenicity during long-term treatment in patients with psoriasis

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Objectives: Anti-drug antibodies (ADA) can result in reduced biologic efficacy over time in patients (pts) with psoriasis. Here we evaluate treatment-emergent ADA (TE-ADA) to ixekizumab, an anti-IL-17A monoclonal antibody, for association with maintenance of efficacy and safety.

Methods: The presence of ADAs was evaluated in pts from the induction period (0-12 weeks [wks]) of 3 randomized, controlled trials [RCTs] and the maintenance period (12-60 wks) of 2 of the 3 RCTs with the same randomized, blinded design. The induction period analyses included ADA-evaluable pts randomized to 80 mg ixekizumab either every 2 wks (IXE Q2W; N = 1150) or 4 wks (IXE Q4W; N = 1143) following a 160-mg starting dose. The maintenance period analyses included IXE responders at wk 12 who were rerandomized to IXE Q4W (N = 397) or IXE Q12W (N = 382). ADA serum trough levels were assessed using a highly drug-tolerant affinity capture elution screening assay.

Results: Serum levels of TE-ADA were divided into negative, low, moderate, and high titer groups. At 12 wks, the vast majority of pts were TE-ADA negative (IXE Q2W: 91.0%; IXE Q4W: 86.6%). Additionally, among IXE Q2W and Q4W pts, respectively, 5.7% and 8.0% had low, 1.6% and 3.0% had moderate, and 1.7% and 2.4% had high TE-ADA titers at 12 wks. When evaluating efficacy during the induction period in pts receiving IXE Q2W, only pts with high TE-ADA titers had reduced responses in PASI compared to TE-ADA negative pts, with 12-wk mean percent improvement from baseline PASI (last observation carried forward [LOCF]) of 91.7%, 85.7%, 88.7%, and 53.5% for pts with negative, low, moderate, and high TE-ADA titer, respectively. The 12-wk PASI 75 response rates (nonresponder imputation) were 90.7%, 84.8%, 83.3%, and 36.8% for IXE Q2W pts with negative, low, moderate, and high TE-ADA titers, respectively. At 60 wks for IXE Q2W pts re-randomized to IXE Q4W during the maintenance period, 84.8% were TE-ADA negative, 14.2% had low, 0.9% had moderate, and none had high TE-ADA titer. Efficacy at 60 wks was similar between all TE-ADA groups with mean percent improvement from baseline PASI (LOCF) of 94.3% for negative, 97.0% for low, and 100% for moderate TE-ADA titer pts. IXE Q4W data was similar. No safety findings were correlated to ADA.

Conclusions: TE-ADA levels against ixekizumab did not affect maintenance of response up to 60 wks among initial responders to ixekizumab. There was no correlation between TE-ADA and safety findings.

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LAS41008 (dimethyl fumarate) improves health related quality of life and physician's global assessment in the treatment of moderate to severe chronic plaque psoriasis: The BRIDGE study

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Introduction: Psoriasis is a debilitating disease; impairment of patient's health-related quality of life (HrQoL) is comparable with that observed in other chronic conditions. HrQoL is a factor in the choice of medicinal product in clinical practice.

Objective: To investigate safety, efficacy and impact on HrQoL of LAS41008 in the management of patients with moderate to severe chronic plaque psoriasis.

Patients and methods: The efficacy, safety and effect on HrQoL of LAS41008 (dimethyl fumarate; DMF) were assessed in this 16-week, double-blind study. Patients were randomized to either LAS41008 (DMF), to LASW1835 (DMF and ethylhydrogenfumarate salts) or placebo in a 2:2:1 ratio, followed by a 52-week off-treatment period. The coprimary efficacy endpoints were clinical response by Physician's Global Assessment (PGA) and Psoriasis Area and Severity Index (PASI™5) at week 16. Dermatology Life Quality Index (DLQI) at week 16 was a secondary endpoint. Treatment comparisons were based on *P* values from an asymptotic Wald test for risk difference. ANCOVA model was used for DLQI scores.

Results: Overall, 671 patients were efficacy evaluable (267 LAS41008, 273 LASW1835 and 131 placebo). Mean age was 44.4 (SD = 14.5) years and 64.7% were male. At baseline, around 60% of the patients had moderate PGA scores (PGA = 3), mean PASI score was 16.3 (SD = 6.0) and mean DLQI score 11.5 (SD = 6.6). At week 16, a greater proportion of patients had clear/almost clear PGA scores on LAS41008 than placebo (33.0% vs 13.0%, respectively, $P < .0001$) and significantly better DLQI scores were reported in LAS41008-treated patients compared to placebo, 5.4 (SD = 6.1) and 8.5 (SD = 6.9), respectively (adjusted mean treatment difference of -3.23, $P < .0001$). Similarly with LASW1835, 37.4% were clear/almost clear (PGA). Mean DLQI score was 6.0 (SD = 7.2).

Conclusions: Study data show LAS41008 provides benefits in both HrQoL and PGA after 16 weeks in patients with moderate to severe chronic plaque psoriasis.

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Lichen planus in a 12-year-old male with Noonan syndrome

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Lichen planus (LP) is a chronic inflammatory dermatosis of the skin and mucous membranes which is uncommon in children. We report a rare case of LP in a 12-year-old African American male with a history of Noonan syndrome (NS). Our patient presented with six months of extremely pruritic, flat-topped, purple-brown lesions involving his face and body. Histopathology revealed hyperkeratosis, hypergranulosis, a moderate irregular acanthosis, and a band-like infiltrate of lymphocytes and histiocytes in the upper dermis. Based on clinical and histopathologic findings, diagnosis was consistent with LP. The patient was treated with clobetasol 0.05% ointment and fluocinolone 0.025% cream with improvement. The classic presentation of LP features flat-topped, intensely pruritic, polygonal, violaceous papules and plaques with Wickham striae on flexural surfaces and mucous membranes. LP is uncommon in children, representing just 1-4% of cases. NS is an autosomal dominant genetic disorder involving the RAS-MAPK pathway that comprises characteristics such as short stature, facial dysmorphism, congenital heart defects, and learning disabilities. Dermatologic manifestations include woolly hair, abnormal pigmentation including multiple nevi, lentigines, and café au lait macules, and keratosis pilaris. There are no known reports of concurrent LP and Noonan syndrome. This case highlights the presentation of a common disease in an uncommon population.

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Lichen planus pigmentosus inversus: A case report of a rare entity

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Case report: A 71-year-old woman presented with a 5-year history of progressive, asymptomatic erythematous hyperpigmented rash involving the intertriginous areas. She had no history of trauma to the areas of involvement. The patient was in good health, without a history of hepatitis or malignancy. Medications included bupropion, aspirin, and fluoxetine. Physical examination revealed annular violaceous to brown macules and patches with the long axis following the flexural fold and involving the inframammary chest, axillae, and gluteal cleft. Oral mucosa, hair, and nails were uninvolved. She had no other sites of skin involvement. Dermoscopic evaluation revealed diffuse erythematous brown patches containing multiple granular gray-brown dots and an overlying scale. Laboratory data, complete blood cell count, liver function tests, and electrolytes were within normal limits, including negative serologic tests for syphilis, HIV, hepatitis B and C viruses. Skin biopsies of the gluteal cleft revealed an atrophic epidermis, interface dermatitis with focal basal vacuolization, scattered dyskeratotic cells present along the dermoepidermal junction, marked pigment incontinence with melanophages in the papillary dermis. Topical calcineurin inhibitor therapy was initiated after the diagnosis of LPP inversus was made.

Discussion: Lichen planus pigmentosus-inversus (LPP inversus) is a rare variant of lichen planus, with only 21 total cases reported in the medical literature. It presents as asymptomatic to mildly pruritic hyperpigmented macules and/or patches involving intertriginous and flexural areas and skin folds, most commonly the axilla and groin. The etiology of LPP inversus is thought to be T-cell mediated cytotoxic activity against basal keratinocytes. Treatment success with calcineurin inhibitors and high potency corticosteroids has been limited. Spontaneous regression has been documented. This represents a rare clinical variant of lichen planus.

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Long term effect of achieving PASI90 compared with PASI75 response on patient-reported outcomes in patients with moderate to severe psoriasis

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Background: The impact of psoriasis treatments on health-related quality of life (HRQL) has become a topic of increasing importance when determining treatment algorithms.

Objective: This study assessed the long-term effect of achieving 90% reduction in the Psoriasis Area and Severity Index (PASI90) compared with achieving 75% reduction (PASI™5) on patient-reported outcomes (PRO) in patients (pts) with moderate to severe psoriasis.

Methods: Pts from phase 3 psoriasis clinical trials (NCT00570986, NCT00679731, NCT00237887) who achieved ≥PASI™5 in the short term (Week 12 or 16 depending on the primary trial endpoint) and maintained their response in the long term (Week 52) were pooled into 4 groups based on PASI reduction at 2 time points: Week 12–16/Week 52, respectively (PASI90/90; PASI90/75–89; PASI™5–89/90; PASI™5–89/75–89). PROs included visual analog scales for skin pain (VAS-Pain) and pruritus (PRU), the Dermatology Life Quality Index (DLQI), and the physical/mental component summaries of the SF-36 Health Survey (PCS, MCS). PROs were compared between Week 52 PASI90 and PASI™5–89 achievers using multivariable regression, adjusting for baseline characteristics, corresponding baseline PRO score, and presence of short-term PASI90 response.

Results: 849 pts were included in the analysis (PASI90/90: n = 526; PASI90/75–89: n = 131; PASI™5–89/90: n = 122; PASI™5–89/75–89: n = 70). Compared with PASI™5–89/75–89, PASI™5–89/90 achievers had similar short-term scores but significantly better long-term incremental improvements in VAS-Pain (Δ = -4.3 vs 2.6), PRU (Δ = -0.9 vs -1.2) and DLQI (Δ = -1.8 vs 0.2) by Week 52. Compared with PASI™5–89/75–89, PASI90/90 achievers had significantly better short- and long-term scores for VAS-Pain, PRU, and DLQI, and better long-term scores for PCS and MCS. After adjusting for baseline characteristics, the differences in PRO scores between PASI™5–89 and PASI90 achievers at Week 52 were statistically different (all P <.05), although numerical differences were limited with regard to clinical meaningfulness: DLQI 0.6 vs 2.8, VAS-Pain 3.1 vs 12.2, PRU 0.7 vs 2.2, PCS 53.8 vs 52.6, and MCS 52.6 vs 50.9, respectively.

Conclusions: Pts with psoriasis initially achieving and maintaining ≥PASI™5 response have sustained improvements in skin pain, pruritus, and HRQL. Pts achieving PASI90 experience incremental benefits over PASI™5, but the long-term clinical meaningfulness of these benefits appears to be limited.

The design, study conduct, and financial support for the study/trial were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract.

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Long term safety and tolerability of apremilast in patients with moderate to severe psoriasis: Results from the LIBERATE study

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Background: LIBERATE (Evaluation in a Placebo-Controlled Study of Oral Apremilast and Etanercept in Plaque Psoriasis) was a phase 3b study evaluating the efficacy and safety of apremilast and etanercept vs placebo in biologic-naïve patients (pts) with moderate to severe plaque psoriasis. Safety during the Wk 16 to ≤52 apremilast-extension period is reported here.

Methods: Pts were initially randomized (1:1:1) to placebo (PBO), apremilast 30 mg BID (APR), or etanercept 50 mg QW (ETN). At Wk 16, pts continued on APR or switched to APR from PBO or ETN. All pts received APR from Wk 16 through Wk 104.

Results: The APR-extension period (Wks 16 to ≤52) included 226 pts (PBO/APR n = 73, pt-yrs = 44.3; APR/APR n = 74, pt-yrs = 45.3; ETN/APR n = 79, pt-yrs = 48.7). During this period, most AEs were mild to moderate in severity. Common AEs (≥5% of pts) including diarrhea, nausea, and headache did not increase with prolonged APR exposure in the APR/APR group vs pts who received APR during Wks 0 to 16. Based on exposure-adjusted incidence rates (EAIR)/100 pt-yrs, no increase in rates of serious AEs occurred during the APR-extension period (4.11 to 9.16, across groups) vs the Wk 0 to 16 period (3.93 ETN and 12.47 APR). Similarly, discontinuation rates due to AEs were low and did not increase (EAIR/100 pt-yrs, 4.11 to 6.78, across groups) vs the Wk 0 to 16 period (EAIR/100 pt-yrs, 7.87 to 12.40, across groups). One serious infection (mastoiditis, APR/APR) and no MACE or malignancies were reported during the Wk 16 to ≤52 extension period. Rates of depression and depressed mood with APR were low, occurring in 2 pts (Wks 16 to ≤52, APR/APR), each with a prior history or with depression at baseline. Suicidal ideation (n = 1, PBO/APR) was reported for Wks 16 to ≤52. At Wk 52, mean percent change from baseline in weight was −1.19% (PBO/APR), −0.70% (APR/APR), and −0.04% (ETN/APR). Weight loss of > 5% was experienced by 18.6% (PBO/APR), 10.0% (APR/APR), and 8.0% (ETN/APR) of pts during the APR-extension period.

Conclusion: Switching from ETN to APR at Wk 16 did not result in any clinically significant safety findings through Wk 52 in pts with moderate to severe plaque psoriasis.

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Long-term safety of adalimumab in clinical trials for adult patients with moderate to severe plaque psoriasis

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Introduction: Adalimumab (ADA) is an anti–tumor necrosis factor antibody approved to treat adults with moderate to severe plaque psoriasis (PsO). A comprehensive safety analysis of long-term ADA clinical data in PsO revealed no evidence of cumulative toxicity (Am J Clin Dermatol 2011;12[5]:321-37); since then, more trials were initiated.

Aims: To update the long-term safety profile of ADA in PsO.

Methods: Safety data were evaluated for adults with moderate to severe plaque PsO treated with ADA in 17 phase 2–4 trials, including open-label extensions. Treatment-emergent adverse events (AEs) were collected from the first dose to 70 days after the last dose or the cutoff date (Dec 31, 2014) and coded using MedDRA, version 17.1. AE incidence rates are expressed as events per 100 patient-years (E/100 PYs) of exposure to ADA.

Results: As of Dec 31, 2014, the ADA clinical safety database contained data for 3500 PsO patients, representing 5268.7 PYs of ADA exposure. Overall, there were 16,181 AEs, yielding an incidence of 307.1 E/100 PYs. The numbers of events and their incidence rates were 3688 and 70.0 for AEs related to ADA; 436 and 8.3 for serious AEs; 260 and 4.9 for AEs leading to discontinuation; and 10 and 0.2 for AEs leading to death, respectively. Of the 9 treatment-emergent deaths (0.3% of patients), 1 was considered related (congestive heart failure [CHF]). Event numbers and incidence rates for infections, serious infections, opportunistic infections, and tuberculosis were 4505 and 85.5, 92 and 1.7, 1 and <0.1, and 16 and 0.3, respectively. Event numbers and incidence rates were 76 and 1.4 for any malignancy, 10 and 0.2 for melanoma, and 33 and 0.6 for nonmelanoma skin cancer. The standard incidence ratio for any malignancy in these patients was 0.92 (95% CI, 0.63−1.31) compared with the US 2000−2007 SEER database, indicating no overall difference in risk vs the general population. Event numbers and incidence rates for myocardial infarction, CHF, cerebrovascular accident, demyelinating disorder, and lupus-like reaction/SLE were 14 and 0.3, 13 and 0.2, 11 and 0.2, 1 and <0.1, and 2 and <0.1, respectively. There were 208 allergic reaction events and 584 injection site reaction events, representing rates of 3.9 and 11.1 E/100 PYs, respectively.

Conclusion: No new safety signals were found in a comprehensive analysis of ADA PsO clinical trials. The AE rates remained stable and consistent with other labeled indications over increased ADA exposure time.

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Metabolic syndrome and psoriatic arthritis among Brazilian patients with plaque psoriasis—Preliminary results of the BEYOND study

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Background: Previous studies suggest that psoriasis (Pso) is associated with risk of metabolic syndrome (MetS) and psoriatic arthritis (PsA); however, there are limited data regarding this issue in Latin America.

Objective: This preliminary analysis of BEYOND study aimed to examine the prevalence of MetS and PsA among Brazilian patients with plaque-type psoriasis.

Methods: BEYOND is a cross-sectional, multicenter study conducted in Brazil aiming to investigate the burden of disease in adult Pso patients. This subsample involved patients who underwent physical examinations to assess the PsA prevalence based on Classification Criteria for Psoriatic Arthritis (CASPAR), and MetS prevalence based on a modified version of National Cholesterol Education Program Adult Panel III criteria and by questions regarding history of cardiovascular diseases. Past medical history of PsA, MetS, and other cardiovascular comorbidities were also assessed by patient report.

Results: 64 patients were enrolled, who were predominantly men (53.1%), white/-white (68.8%), retired (34.4%), completed high school (35.9%), and a mean age (SD) of 55 (± 11.3) years old. The prevalence of PsA according to CASPAR criteria was 45.1% (23/51); of these, 88.1% were newly diagnosed by the study. Regarding the most frequent CASPAR individual items observed, 88.2% had negative test for rheumatoid factor; 80.4% presented radiologic evidence of juxtaarticular new bone formation, and 45.1% had inflammatory articular disease. A mean CASPAR score (SD) of 4.53 (0.87) was found in the study sample. The study specific procedures found a MetS prevalence of 54.1% (33/61) and the patients' self-report of MetS diagnosis only 3.3% (2/61). The frequencies of cardiovascular comorbidities were: dyslipidemia (88.5%), hypertension (70.5%), obesity (50.8%) and diabetes (36.1%).

Conclusion: These findings suggest that MetS and PsA are underdiagnosed in this cohort of Pso patients. This emphasizes the importance of increase the awareness of these comorbidities among Brazilian medical community, in order to permit early diagnosis and adequate treatment.

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More rapid improvement in quality of life with fixed combination calcipotriene plus betamethasone dipropionate aerosol foam versus topical suspension (PSO-ABLE study in patients with psoriasis vulgaris)

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Background and objective: The phase III, PSO-ABLE study (NCT02132936) demonstrated superior efficacy with fixed combination calcipotriene 0.005% (Cal)/betamethasone dipropionate 0.064% (BD) aerosol foam at wk 4 vs Cal/BD topical suspension (susp) at wk 8, with comparable safety up to wk 12, in patients (pts) with mild-to-severe psoriasis of the body. Changes in health-related quality of life (HRQoL) are presented here.

Methods: Pts assessed HRQoL using dermatology life-quality index (DLQI) and generic EQ-5D questionnaires at baseline, wks 4, 8, 12. A DLQI score of 0 (range 0 to 30) and EQ-5D utility score of 1 (weighted range −0.594 to 1) indicate perfect health. The proportion of pts who achieved a DLQI score of 0/1 (no/low impairment) was also determined.

Results: 465 pts were randomized (4:4:1:1) to treatment with once-daily Cal/BD foam (n = 185), Cal/BD susp (n = 186), foam vehicle (n = 47) or susp vehicle (n = 43). Mean baseline DLQI scores were 7.0 (Cal/BD foam), 7.9 (Cal/BD susp), 7.0 (foam vehicle) and 9.3 (susp vehicle), indicating moderate impact on HRQoL. DLQI scores improved by wk 12 in all groups; mean change in DLQI at wk 4 was significantly greater with Cal/BD foam than Cal/BD susp (−4.3 vs −3.8; adj diff −1.0; $P = .005$); differences were not significant at wks 8 (−4.5 vs −4.4; adj diff −0.7; $P = .075$), and 12 (−4.6 vs −4.3; adj diff −0.8; $P = .069$). DLQI score improvements were significantly greater with both active treatments vs their respective vehicles at each time point ($P < .05$). Significantly more pts using Cal/BD foam than Cal/BD susp achieved DLQI scores of 0/1 at wks 4 (46 vs 32%; $P = .013$) and 12 (63 vs 44%; $P = .003$), with a non-significant difference at wk 8 (54 vs 43%; $P = .060$). Mean baseline EQ-5D utility scores were 0.80 (Cal/BD foam), 0.82 (Cal/BD susp), 0.82 (foam vehicle) and 0.77 (susp vehicle). At wk 4, a significantly greater improvement in mean EQ-5D utility score was seen with Cal/BD foam vs Cal/BD susp (0.09 vs 0.03; adj diff 0.05; $P < .001$). From wk 8, improvements in utility scores for both Cal/BD formulations were comparable (wk 8: 0.08 vs 0.05; adj diff 0.03; $P = .06$; wk 12: 0.07 vs 0.05; adj diff 0.02; $P = .21$). Both active treatments had significantly greater wk 4 improvements in EQ-5D utility scores vs their respective vehicles ($P < .05$).

Conclusion: In PSO-ABLE, Cal/BD aerosol foam improved HRQoL more rapidly than Cal/BD topical suspension, in pts with psoriasis vulgaris.

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Network metaanalysis and cost per responder of tumor necrosis factor, interleukin, and phosphodiesterase inhibitors in the treatment of psoriatic arthritis

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Objective: Multiple disease-modifying therapies are available to treat psoriatic arthritis (PsA) including anti-TNF and interleukin inhibitors and a phosphodiesterase (PDE)-4 inhibitor. We conducted a network metaanalysis (NMA) to indirectly compare the efficacy and cost per responder (CPR) of these therapies.

Methods: A systematic literature review was used to identify Phase III randomized controlled trials (RCTs) of biologics (adalimumab [ADA], certolizumab pegol [CZP], etanercept [ETN], golimumab [GOL], infliximab [IFX], secukinumab [SEC], ustekinumab [UST]) and PDE-4 inhibitor (apremilast [APR]) for PsA. Efficacy was estimated as the probabilities of achieving ACR20 and PASI75 at week 24 by a Bayesian NMA. FDA-approved dosages were used and for the investigational product SEC, 150 and 300mg Q4W were used. Numbers needed to treat (NNT) were calculated as the reciprocal of incremental response rate of each therapy versus placebo. Comparisons were made in terms of cost per incremental ACR20 or PASI75 responder. Drug costs were based on Wholesale Acquisition Cost (July 20, 2015), and IFX 4-hour infusion cost was obtained from Medicare payment information. Analyses were repeated among subgroups of biologic-naive patients.

Results: A total of 17 RCTs were identified, 13 included ACR20 and/or PASI75 at week 24. NNT for ACR20 at week 24 were 2.3 (95% credible interval 1.8–3.2) for ADA, 2.3 (1.7–3.4) for GOL, 2.3 (1.8–3.3) for SEC 300 mg, 2.7 (1.8–4.3) for IFX, 3.0 (2.3–4.0) for SEC 150 mg, 3.1 (2.2–4.6) for CZP, 3.2 (2.1–5.5) for ETN, 4.5 (3.2–6.7) for UST 90 mg, 5.7 (3.7–9.2) for UST 45 mg, and 6.3 (4.4–9.4) for APR. The NNT for PASI75 at week 24 were 1.5 (1.3–2.0) for GOL, 1.5 (1.2–1.9) for IFX, 1.6 (1.3–2.1) for ADA, 1.7 (1.3–2.3) for SEC 300 mg, 2.1 (1.6–2.7) for UST 90 mg, 2.3 (1.7–3.3) for SEC 150 mg, 2.3 (1.8–3.1) for UST 45 mg, 2.7 (1.9–4.0) for CZP, 6.4 (2.9–15.8) for ETN, and 6.7 (3.6–13.0) for APR. The 24-week ACR20/PASI75 CPR were estimated at $44,618/$30,336 for ADA, $45,669/$30,184 for GOL, $55,222/$30,133 for IFX, $61,775/$123,299 for ETN, $70,951/$61,910 for CZP, $77,241/$54,422 for SEC 300 mg, $77,407/$81,836 for APR, $97,845/$76,775 for SEC 150 mg, $139,922/$56,103 for UST 45 mg, and $221,745/$101,004 for UST 90 mg. NNT and CPR results were similar for biologic naive patients.

Conclusion: At week 24, ADA, GOL, and IFX had the lowest incremental CPR for both ACR20 and PASI75.

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Network metaanalysis of new biologic agents targeting IL-23/Th17 pathway for moderate to severe plaque psoriasis

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Introduction: Targeting proinflammatory cytokines such as tumor necrosis factor-α (TNF-α) has been an effective therapeutic approach for patients with moderate to severe plaque psoriasis. A new generation of biologics targeting IL-23/Th17 pathway has been developed. This study aimed to assess the clinical effectiveness of these new therapeutic agents using network metaanalysis.

Methods: Randomized trials were identified by a systematic literature review. Study quality was assessed by Jadad score. Network metaanalysis was used to make direct and indirect comparisons among the therapeutic options.

Results: 39 clinical trials (n = 22,457) met the inclusion criteria. Guselkumab and tildrakizumab were excluded due to small numbers of patients and/or Jadad scores below 4. There were 26 direct comparisons in the network. Ixekizumab 80 mg Q2W is ranked the most effective, followed by brodalumab 210 mg Q2W and infliximab 5 mg/kg- I Q6/8W. The probability of either an anti-IL17A or an anti-IL17RA agent was the most efficient treatment for a particular case reached almost 80%. A high degree of consistency between the direct and the indirect evidence was observed.

Conclusions: New agents targeting the IL-23/Th17 pathway seem to be more effective than most of the classical anti-TNF-α drugs. Future treatment recommendations also must consider adverse effects and cost.

Commercial support: None identified.

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Numbers needed to treat and costs per responder for novel treatments of moderate to severe psoriasis

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Objective: The clinical benefits of novel treatments for moderate to severe psoriasis (biologics and apremilast) have been well established, including variations in patient response across different therapies. We estimated the number needed to treat (NNT) to achieve a 75% reduction in the Psoriasis Area and Severity Index (PASI-75) with biologic agents and evaluated the incremental drug cost per PASI-75 responder for biologic treatments relative to apremilast.

Methods: A systematic literature review was conducted to identify randomized controlled trials of novel treatments in patients with moderate to severe psoriasis. Relative probabilities of achieving PASI-75 response with each treatment during the clinical trial period (10 weeks for infliximab; 12 weeks for etanercept, ustekinumab, and secukinumab; and 16 weeks for adalimumab and apremilast) were estimated using a Bayesian network metaanalysis. The NNT was estimated as the reciprocal of the difference in estimated PASI-75 response rates between each biologic treatment and apremilast (apremilast was chosen as the reference based on its lower price and lower efficacy). Costs were assessed in 2015 US dollars including drug acquisition and administration. The incremental cost per PASI-75 response for each biologic was estimated for the clinical trial period and annually.

Results: A total of 20 trials meeting all inclusion criteria were identified. Compared with apremilast, the NNT to achieve 1 additional PASI-75 response during the clinical trial period was 1.96 (95% credible interval: 1.69–2.31) for secukinumab 300 mg, 2.09 (1.77–2.52) for infliximab, 2.58 (2.07–3.28) for secukinumab 150 mg, 2.72 (2.18–3.59) for adalimumab, 2.75 (2.21–3.58) for ustekinumab, and 5.71 (3.70–9.86) for etanercept. The 1-year incremental cost per PASI-75 responder relative to apremilast was $20,419 ($17,375–$24,735) for infliximab; $48,405 ($39,331–$64,926) for adalimumab; $61,941 ($53,770–$75,308) for secukinumab 300 mg; $71,187 ($57,936–$93,983) for ustekinumab; $80,788 ($65,827–$104,187) for secukinumab 150 mg; and $136,223 ($93,500–$250,072) for etanercept 50 mg. A similar ranking of these biologic treatments was observed for cost per PASI-75 responder during the clinical trial period.

Conclusions: Infliximab and adalimumab had the lowest incremental cost per PASI-75 responder among the biologic treatments compared with apremilast.

Design, study conduct, and financial support for the study were provided by AbbVie; AbbVie participated in the interpretation of data, review, and approval of the abstract; all authors contributed to the development of the publication.

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Occlusivity and moisturization potential of a new lotion formulation of halobetasol propionate, 0.05%

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When a topical treatment for psoriasis and other corticosteroid-responsive dermatoses is indicated, patients often prefer a lotion to a cream. However, lotions are perceived to be less occlusive, and consequently less hydrating, than creams. Therefore, since ultrapotent topical corticosteroids are a cornerstone of such topical treatments, a novel lotion formulation of halobetasol propionate, 0.05% (HBP lotion) that provides the beneficial occlusion and moisturization of a cream was developed. The objective of this study was to determine and compare the occlusivity and moisturization potential of HBP lotion and ultravate (HBP) cream when applied to skin whose barrier integrity has been challenged by dry shaving. A single center, evaluator-blinded, randomized within subject study was conducted in 16 healthy volunteers (aged 18-55 years). On Day 1, the stratum corneum barrier was challenged by dry shaving the skin surface of both volar forearms with a disposable razor and six test sites (3/arm; area = 25cm^2) were identified: 2 sites each for HBP lotion, ultravate cream, and dry shaved controls. On Day 2, transepidermal water loss (TEWL) and conductance measurements were performed. Then, a single application of ~100 mg of each test article was applied to the designated test sites of the volar forearms in duplicate, and was maintained in situ for 6 hours by protecting the arms with a raised perforated guard secured with nonocclusive tape. TEWL and conductance measurements were performed 2, 4, and 6 hours postapplication of the test articles. TEWL values did not vary between HBP lotion and ultravate cream (2h: $P = .12$; 4h: $P = .80$; 6h: 0.37), which suggests that the two HBP formulations provide similar occlusivity and can participate equally in the management of dry and inflammatory skin conditions. Additionally, HBP Lotion treated sites had significantly greater conductance compared to: (1) dry-shaved controls at all time points (each, $P < .001$) and (2) ultravate cream at 2h and 4h (each, $P < .001$). Both HBP lotion and ultravate cream improved skin moisturization at 6h. However, at 2h and 4h following single applications of HBP lotion and ultravate cream conductance results indicated greater skin moisturization with HBP lotion than ultravate cream, suggesting that HBP lotion more rapidly penetrates the outer skin layers to ensure optimal hydration during treatment.

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One-year biologic cost per patient with psoriatic diseases in a managed care population

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Background: The rising health care cost in specialty pharmacy has led providers to place economic factors into treatment decisions. Current evidence on biologic costs in psoriatic diseases is lacking.

Objective: To determine the annual drug and administration cost of US-approved biologics per patient with psoriasis (PsO) and/or psoriatic arthritis (PsA) in a managed care population comprising beneficiaries predominantly enrolled in a large managed care health plan.

Methods: This is a retrospective cohort study using administrative data for individuals in the HealthCore Integrated Research Database (HIRDSM). The cohort included patients initiating a tumor necrosis factor inhibitor [TNFi] (adalimumab [ADA], etanercept [ETN], golimumab [GOL], infliximab [INF]) or a non-TNFi (ustekinumab [UST]) between Jul 1, 2009 and Jan 31, 2015. Patient entry criteria were age ≥ 18, continuous enrollment during the 180 days prior to and 360 days postindex, and PsO and/or PsA diagnosis in the 6 months preindex. The index event and date was defined as the first biologic use following 6 months of enrollment. Unit biologic and administration costs as of Jan 1, 2015 were applied to the real-world dosing and administration data to calculate annual per patient cost. Costs were stratified by drug mechanism, disease indication, and new versus established users.

Results: A total of 8081 patients with PsO and/or PsA met the eligibility criteria (ADA: n = 3,161; ETN: n = 4,721; GOL: 94; INF: n = 547; UST: 458, mean age 45.1, 42.9% female). Among new users (n = 4093), non-TNFi users (UST) had numerically greater cost per patient ($36,745) compared with TNFi users ([ADA]: $27,949; [ETN] $30,090; [GOL]: $24,474; [INF]: $26,646). Among established users (n = 4988), the cost per patient for non-TNFi users ($28,771) was within the cost range of TNFi users ([ETN]: $28,125; [INF]: $31,813). ADA had numerically greater cost than other agents in both new ($27,397) and established users ($30,590) with only PsA. UST and INF had numerically greater cost than other agents in new ($36,574-$38,395) and established users ($31,842-$33,793) with PsO ± PsA, respectively.

Conclusion: Although similar annual biologic cost per patient may be expected among established users of TNFi and non-TNFi, new non-TNFi users were found to incur at least 22% greater annual cost than new TNFi users. Average cost varied considerably across psoriatic indications and individual agents.

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Oral Candida colonization: A case-control study in Asian patients with psoriasis

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Background: Various microorganisms including bacteria, virus, and fungi can act as superantigens to activate specific T cells and initiate the pathogenic cycle of psoriasis. The linkage between Candida and psoriasis has been investigated since 1980; however data addressing oral Candida colonization in patients with psoriasis especially in Asian patients are limited and inconclusive.

Objective: This prospective study was aimed to investigate oral Candida colonization in patients with psoriasis in comparison with demographically matched healthy controls.

Methods: Sixty patients with psoriasis aged older than 18 years were recruited to closely match with sixty healthy controls for age and gender. All participants were recruited from the same geographic region (Bangkok, Thailand). Specimens were collected using oral rinse and tongue swab techniques to identify Candida colonization in oral cavity.

Results: Each group consisted of 28 men and 32 women. At the time of the study, 27 (45.0%) patients used only topical treatment and the remaining of the patients (55%) were on systemic treatment including methotrexate, acitretin, cyclosporine, and phototherapy. The mean PASI score was 6.0 ± 5.5. Our study showed that the diagnostic yield of oral rinse technique was better than that of swab technique. Oral Candida colonization was found in 30% and 20% of patients with psoriasis using oral rinse technique and swab technique, respectively. There was a significant difference between prevalence of oral Candida colonization in patients with psoriasis and in controls using oral rinse technique (30% vs 13.3%, $P = .03$). *Candida albicans* was the predominant oral Candida species isolated. Psoriatic patients with systemic treatment was significantly associated with increased risk of Candida colonization than psoriatic patients with topical treatment (odds ratio = 4.24, 95% CI = 1.19-15.03).

Conclusion: Psoriatic patients had significantly higher prevalence of oral Candida colonization than healthy controls. The presence of oral candidiasis was significantly associated with systemic treatment. Further studies are warranted to determine the clinical significance of Candida colonization in patients with psoriasis.

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Oxidative damage and nuclear factor erythroid 2-related factor 2 protein expression in normal skin and keloid tissue

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Background: Reactive oxygen species (ROS) play an important role in the induction of apoptosis under pathological conditions. Recently, a significant increase in ROS production and disrupted apoptosis mechanisms in keloids have been reported. Nuclear factor erythroid 2-related factor 2 (Nrf2) represents one of the most important cellular defense mechanisms against oxidative stress and is implicated in the regulation of apoptosis. Recently, it has been reported that Nrf2 upregulates Bcl-2, an anti-apoptotic protein.

Objective: To compare Nrf2 protein expression in normal skin tissues to keloid tissues.

Methods: ROS generation in keloid tissues was evaluated with OxyBlot analysis. Western blotting and/or immunohistochemical staining approaches were used to study expression of Nrf2 or Bcl-2 in keloid and normal skin tissues. Cellular fractionation was performed to examine subcellular distribution of Nrf2. Transfection of fibroblasts with Nrf2-specific siRNA was conducted to understand the relationship between Nrf2 expression and apoptosis induction.

Results: Protein oxidation, a marker of oxidative stress, is increased in keloid tissues. Western blot analysis clearly showed that Nrf2 and Bcl-2 are downregulated in keloid tissues. Immunohistochemical staining of Nrf2 confirmed the results of the western blot analysis. Transfection of fibroblasts with the Nrf2-specific siRNA results in increased apoptosis and decreased cell viability.

Conclusion: Collectively, our data indicate that Nrf2 expression is downregulated in keloid tissues, and that Nrf2 is involved in the development of apoptosis in Nrf2 siRNA-transfected fibroblasts. We propose that a defective antioxidant system and apoptotic dysregulation may participate in keloid pathogenesis.

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Patient choice of dosing frequency among moderate-to-severe plaque psoriasis patients with adalimumab, etanercept, and/or ustekinumab experience

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Introduction: Various biologic therapies, with different dosing frequencies, have demonstrated efficacy in treating moderate-to-severe plaque psoriasis (PsO). One key aspect of patient(pt)-centered PsO care is the pt's choice in treatment selection.

Objective: To determine which dosing frequency pts are more likely to choose for injectable biologic treatment.

Methods: Pts, identified through administrative claims, had ≥1 PsO diagnosis and ≥1 claims for methotrexate, cyclosporine, or injectable biologics(adalimumab = ADA, etanercept = ETA, or ustekinumab = UST). Pts were surveyed on current and past biologic experience and how dosing frequency related to specific choice of therapy. Pts were grouped into 6 injectable biologic cohorts based on current and past biologic use over time—only one or any pair of ADA, ETA, or UST. Among the following options for a maintenance biologic injection frequency, pts were asked which they would choose: time ranges (once every 1-2 weeks (wk), once every 3-4 wks, once every 1-2 months (mos), or once every 2-3 mos) and a specific number of wks (between 1 and ≥12). A stratified (biologic naive vs experience) random sample design was used, and estimation was done using SAS/STAT 9.2 with finite population correction.

Results: 219 pts, who had experience, based on administrative claims, with any injectable biologic, completed the survey. The majority of pts ever-exposed only to ADA and/or ETA(based on pt-reported use) chose a "1-2 week" dosing interval(ETA only = 60.0%; ADA only = 51.7%; ADA+ETA = 54.1%). The majority of pts ever-exposed to UST chose a 2-3 month dosing interval(UST only = 81.3%; ETA+UST = 72.2%; ADA+UST = 80.0%). When asked to choose an interval based on a specific number of wks, pts with ADA and/or ETA experience mostly chose an interval of every 1-, 2- or 4-wks. The majority of those with any UST experience chose every ≥12 wk dosing. It was observed that some pts never exposed to UST chose longest dosing, every 2-3 mos = 10.3%-23.8%; every ≥12 wks = 14.8%-18.8%.

Conclusions: Results demonstrated that among pts exposed to only one biologic, the majority chose a dosing interval consistent with the biologic with which they were familiar. However pts ever exposed to UST(either UST only or also exposed to another biologic) chose the longest dosing interval option. Treatment sequence and outcomes were unknown. Health care providers are encouraged to understand pt choice of and rationale for biologic dosing frequency during shared decision-making.

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Persistence of biologic therapy in psoriasis patients with comorbidity

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Background: Psoriasis often requires a lifelong therapy and drug survival is considered as a marker for treatment success. There is a need for more data on persistence to treatment of biologics in psoriasis patients with comorbidity.

Objective: To estimate long-term drug survival rates of different biologics in a cohort of patients with psoriasis and to evaluate predictors of treatment adherence.

Patients and methods: This was a retrospective analysis of 67 patients with plaque-type psoriasis treated with biologics (adalimumab, efalizumab, etanercept, infliximab, ustekinumab) in routine clinical care. Drug survival rates and outcome parameters were analyzed. Patients were eligible for biologic treatment, had a Psoriasis Area and Severity Index (PASI) > 10, a body surface area affected > 10%, a Dermatology Life Quality Index (DLQI) > 10.

Results: In total, 125 treatment periods with adalimumab (n = 37), efalizumab (n = 9), etanercept (n = 55), infliximab (n = 13) and ustekinumab (n = 11) were administered to 67 psoriasis patients. 64.2% of the patients enrolled were male. Median (1st-3rd quartile) age was 47 (39-52) years and disease duration 23 (17-31) years. The observation period lasted 4.2 (0.5-6.2) years. The difference in drug survival in patients with psoriasis adjusted to coexistence of psoriatic arthritis (PsA) between adalimumab and infliximab ($P = .028$), etanercept and infliximab ($P = .01$) was statistically significant. Patients with PsA in general demonstrated significantly greater rates of drug survival ($P = 0.010$). The difference in drug survival according to comorbidity was statistically significant between adalimumab and infliximab ($P = .005$), etanercept and efalizumab ($P = .027$) and etanercept and infliximab ($P = .001$). Patients with comorbidity in general demonstrated a significantly shorter drug survival time than patients without comorbidity ($P = 0.33$).

Conclusion: Efficacy of biologic therapy is reduced with time. Patients with the comorbidity of metabolic syndrome experienced a loss of adherence to biologic therapy.

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Pityriasis lichenoides chronica induced by adalimumab in a patient with psoriasis with response to methotrexate

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Introduction: Tumor necrosis factor alpha (TNF-α) inhibitors have been demonstrated to be effective in treating immunomediated inflammatory diseases, such as psoriasis, rheumatoid arthritis and inflammatory bowel disease. However, these biologicals may induce infections, neoplasms, or autoimmune diseases. Cutaneous side effects have been reported, including dermatitis, psoriasis-like rash, vasculitis, keratosis follicularis, dermatitis herpetiformis, alopecia, folliculitis, pemnosis-like eruptions, granuloma annulare and sarcoidosis. Until now, there is only one reports describing the appearance of pityriasis lichenoides chronica (PLC) in association with adalimumab treatment in a patient with severe psoriasis. We report the first cases of pityriasis lichenoides chronica (PLC) developed while on adalimumab and successfully treated with methotrexate.

Case report: A 45-year-old man hypertensive, diabetic and no drug allergies, with a history of severe, recalcitrant psoriasis for which he received biologic treatments (ustekinumab and etanercept) without control of the disease. He started adalimumab and within the second month, there was significant clinical improvement. However, 10 weeks after commencing treatment, he developed new cutaneous lesions consisting of erythematous papules, with central scaling, affecting the trunk, the buttocks, and extremities, sparing the face, palms, and soles. These were asymptomatic and did not coincide with intercurrent illness or other new pharmacologic therapy. Microscopic examination of a skin biopsy showed findings consistent with PLC. No clonal rearrangement of the TCR was detected. It was decided, on the assumption of a synergistic action, to start methotrexate (MTX) therapy (15 mg/week) and adalimumab was continued because of the severity of psoriasis. Complete remission was achieved in 6 weeks with residual pigmentation and bowel disease was controlled. This was discontinued but 15 days later PLC recurred and MTX was again introduced and led to new remission.

Discussion: The pathogenesis of PLC is not well understood. However, CD4+ T helper cells are heavily implicated, and alterations in T-cell function and cytokine production, secondary to TNF inhibition, may be responsible for triggering the disease. The treatment of PLC relies on antibiotics and/or phototherapy. In case of failure, immunosuppressants are recommended. The course of PLC is variable, spontaneous regression is possible. MTX is effective for PLC, and represents an interesting therapeutic option because of the synergistic action of MTX and TNF-α inhibitors in psoriasis.

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Predicting PASI90 response among adalimumab-treated patients with moderate to severe psoriasis

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Objective: A 90% reduction from baseline on the Psoriasis Area and Severity Index (PASI90) has been used to assess the effectiveness of biologic treatments in psoriasis. This study compared PASI90 response between patients with psoriasis who were treated with adalimumab and placebo, and identified predictors of PASI90 response among the adalimumab-treated patients.

Methods: Patients with moderate to severe psoriasis who were randomized to adalimumab or placebo in 2 phase 3 clinical trials were included in the analyses (REVEAL, NCT00237887; CHAMPION, NCT00235820). The double-blind follow-up period in both studies was 16 weeks. The cumulative rate of achieving PASI90 response was compared between adalimumab and placebo arms using Kaplan-Meier analysis and a log-rank test. A subgroup analysis was conducted for patients achieving PASI50 at any time during the 16 week follow-up period. A baseline prediction model for achievement of PASI90 response at Week 16 was developed among patients receiving adalimumab in REVEAL and validated using independent data from CHAMPION.

Results: In the pooled trial population (adalimumab n = 921; placebo n = 451), the mean age was 44 years and 67% were male. The cumulative rate of PASI90 response by Week 16 was 53.6% for adalimumab and 4.1% for placebo ($P < .001$). Among patients achieving PASI50, which occurred for 90.2% receiving adalimumab and 23.5% receiving placebo, the cumulative rate of PASI90 achievement by week 16 was 65.3% for adalimumab and 23.0% for placebo ($P < .001$). In data from adalimumab-treated patients in REVEAL (n = 787), significant predictors of PASI90 response included younger age (odds ratio per year [OR] 0.98), male gender (OR 1.49), and lower weight (≤75 kg, OR 3.40; 75–100 kg, OR 2.66; reference >125 kg). The model provided moderate predictive value (C statistic 0.65) when validated among adalimumab-treated patients in CHAMPION (n = 104).

Conclusions: The majority of adalimumab-treated patients achieved PASI90 response by Week 16. Among those adalimumab-treated patients achieving PASI50, nearly two-thirds ultimately achieved a PASI90 response. In contrast, fewer than a quarter of placebo-treated patients with a PASI50 response achieved a PASI90 response. Younger age, male gender, and lower weight were associated with a greater chance of achieving PASI90 with adalimumab.

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Predictors of response to tofacitinib or etanercept in a phase 3 randomized, noninferiority study in patients with moderate to severe chronic plaque psoriasis

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Background: Tofacitinib is an oral Janus kinase inhibitor that is being investigated for psoriasis. In the phase 3 study, OPT Compare, tofacitinib 10 mg BID was noninferior to etanercept 50 mg BIW.

Objective: To ascertain whether certain baseline characteristics can predict a differential response to tofacitinib 10 mg BID vs etanercept 50 mg BIW.

Methods: In this posthoc analysis of data from OPT Compare (NCT01241591), efficacy at 12 weeks of tofacitinib (10 mg BID) vs etanercept (50 mg BIW) was evaluated overall and in subgroups according to the following baseline characteristics: age, gender, race, geographic region, PASI, PGA, affected BSA, weight, BMI, CRP, and treatment history. Descriptive statistics for differences (and 95% CIs) in the percentage of PASI75 responders between the tofacitinib and etanercept groups were compared.

Results: Of the 1101 patients enrolled in this study who received study medication/placebo, 330 and 335 received tofacitinib 10 mg BID and etanercept 50 mg BIW, respectively. Baseline characteristics were similar between these two treatment groups; most patients were male (70–72%) and white (86–87%). Mean body weight was 83–85 kg, mean PASI score was 23 in both groups, mean affected BSA was 31–32%. In addition, 93–94% had received prior systemic agents, and 72% in both groups had received prior phototherapy. Overall, PASI75 and PASI90 responses at Week 12 were achieved by 63.6% and 36.1% of tofacitinib recipients and 58.8% and 32.2% of etanercept recipients, respectively. The percentage of PASI75 responders at Week 12 was similar between the tofacitinib and etanercept groups when analyzed by age, race, geographic region, baseline PASI, PGA, affected BSA, and treatment history. Subgroups with higher PASI75 response at Week 12 to tofacitinib vs etanercept were females (difference 16.6%, 95% CI 3.1%, 30.1%); patients with higher CRP (≥0.3 mg/dL; difference 12.8%, 95% CI 1.6%, 24.0%); heavier patients (90 to <120 kg; difference 13.3%, 95% CI 0.45%, 26.2%); and patients with higher BMI (30 to <40 kg/m^2; difference 19.5%, 95% CI 6.8%, 32.3%). No subgroup of patients responded better to etanercept than tofacitinib.

Conclusion: Tofacitinib 10 mg BID was noninferior to etanercept 50 mg BIW and the difference in efficacy between the treatment groups was small for most subgroups of patients. Nevertheless, females, patients with higher baseline CRP, and heavier patients responded better to tofacitinib than to etanercept.

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Pregnancy outcomes in women with psoriasis and psoriatic arthritis exposed to ustekinumab

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Background: Ustekinumab (UST) is indicated for moderate to severe psoriasis (PSO) and psoriatic arthritis (PsA) in adult patients, with a Food and Drug Administration pregnancy class B designation. No adverse developmental outcomes (pre- and postnatal) were observed in preclinical (animal) studies of UST, and limited published data exist concerning the effects of UST on human pregnancies. Studies have suggested PSO may be a potential risk factor for adverse pregnancy outcomes. To characterize pregnancy outcomes in women treated with UST for approved indications, data from clinical trials, registries, and spontaneous reports are presented.

Methods: This dataset includes individual patient cases within the company safety database through 31 December 2014. Cases retrieved include prospectively reported (ie, pregnancy outcome not known when first reported) and retrospectively reported (ie, pregnancy outcome known when first reported) cases with maternal UST use for PSO or PsA during pregnancy or within 2 months prior to conception and with a known pregnancy outcome.

Results: Eighty seven pregnancy reports (86 PSO, 2 PsA, some cases may report >1 indication, 58 prospective, 29 retrospective) were identified. Average maternal age was 31 years. Of the 87 reports, the majority of pregnancies (57/87, 65.5%) resulted in live births (LB, [including 3 premature births]). Congenital anomalies (CA) were reported in 1 pregnancy (1.2%): stenosis (spontaneous report). Spontaneous abortion (SA) was reported in 16 pregnancies (18.4%). Elective termination (ET) was reported in 14 pregnancies (16.1%). Of the 87 pregnancy reports, 16 reported exposure in all 3 trimesters (12 LBs, 3 SAs, 1 ET) and 37 reported exposure in the first trimester: 23 LBs (including 3 premature), 6 SAs, and 8 ETs.

Conclusion: Review of pregnancy outcomes after maternal exposure to UST for PSO and PsA indications identified 87 pregnancies with known outcomes: 57 LBs (including 3 premature) and 1 CA. The rate of SAs was generally comparable to the rate reported for the general population (15% to 20%). Consistent with the literature, SAs in this case series were associated with older maternal age (34.42 yrs). The limited available data suggest that UST exposure may not impact pregnancy outcomes but additional experience is needed.

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Prevalence of psoriasis: An Indian perspective

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Objective: The study aimed to understand the epidemiology and trends in prevalence of psoriasis over five-year period in patients attending a tertiary care hospital in India.

Background: Psoriasis is a common chronic condition of skin that may require lifelong treatment and affect patient's physical and mental status. Treatment selection is influenced by age, sex, occupation, and general health, ability to comply with the treatment, previous treatment as well as type, extent duration and natural history of disease. Although psoriasis occurs worldwide, the prevalence varies considerably between races and regions. It can present at any age and has been reported at birth and also in older people. Psoriasis is often associated with nail changes and arthritis if carefully looked for. An increased prevalence of smoking and alcohol consumption is related with incidence and severity of psoriasis.

Design/methods: The current study is a retrospective, observational study where subjects were identified from patient's records that were diagnosed with psoriasis between July 2010 and June 2014 in Department of dermatology in a tertiary care hospital in India. The epidemiologic data includes demographic characteristics of individual summarized using descriptive statistics.

Results: Out of total 16,129 patients attending outpatient department of dermatologic diseases, there were 771 patients diagnosed with psoriasis; amounting to 4.78% prevalence rate of psoriasis during stipulated five-year period. The mean age of patients was 43.34 ± 16.72 years and maximum number of cases (52.9%) were in age group of 31-50 years. The prevalence of psoriasis among children (age 0-18 years) was 5.2%. Male to female ratio was 1.4:1. Most of the patients were private sector employees 274 (35.55%). A positive family history of psoriasis was found in 62 (8.04%). There was a nonsignificant seasonal variation in the incidence of psoriasis ($P = .674$). 154 (19.97%) patients reported joint pain and 343 (44.48%) had nail changes associated with psoriasis like discoloration, pitting, subungual hyperkeratosis, onycholysis. History of alcohol consumption was present in 296 (38.39%) and of smoking in 201 (26.07%).

Conclusion: Studies on prevalence of disease are tools to assess the burden of disease in a population. Paucity of data in this field necessitates further research as to help us better understand the disease in relation to time and space in a given geographic area.

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Product of the Physician Global Assessment and body surface area (PGA×BSA): A measure of psoriasis severity tested in patients with active psoriatic arthritis and treated with certolizumab pegol

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Introduction: Previously, the use of the product of Physician Global Assessment (PGA) and body surface area (BSA) (PGA×BSA) to assess psoriasis severity has been investigated in patients (pts) with psoriasis, with the aim of assessing this tool as a possible alternative to the time-consuming Psoriasis Area and Severity Index (PASI).

Methods: RAPID-PsA (NCT01087788), is a double-blind, placebo (PBO)-controlled study investigating efficacy of certolizumab pegol (CZP) in psoriatic arthritis (PsA) pts. Skin outcomes were assessed in all pts with ≥3% BSA at baseline (BL). PGA×BSA was calculated by multiplying pt PGA scores (0–5) with pt BSA (0–100%). Outcomes reported for pts treated with CZP or PBO were percentage improvement from BL in PGA×BSA and PASI, achievement of PASI75 response and ≥75% improvement in PGA×BSA (PGA×BSA75). Further analyses investigated Spearman correlations between PGA×BSA and PASI or the Dermatology Life Quality Index (DLQI); cross tabulations assessed whether pts achieving PASI75 also achieved PGA×BSA75 and vice versa. Observed data are reported.

Results: 252 pts had ≥3% BSA at BL (166 CZP, 86 PBO) and were included in these analyses. At BL, pts had mean: PASI 11.7, PGA×BSA 79.4 and DLQI 10.8. For CZP-treated pts, PGA×BSA and PASI demonstrated similar sensitivities to treatment between BL and Week 24, with mean improvements of 76.6% with PGA×BSA (n = 140) and 75.3% with PASI (n = 144). With PBO, mean improvements were 28.9% with PGA×BSA (n = 80) and 41.5% with PASI (n = 35). 75% improvement was achieved by similar percentages of patients with CZP (PGA×BSA75: 59.0%, PASI75: 61.4%) and PBO (PGA×BSA75: 15.1%, PASI75: 15.1%). At BL, PGA×BSA and PASI were strongly correlated ($r = 0.78$; n = 225), and both PGA×BSA ($r = 0.46$; n = 225) and PASI ($r = 0.50$; n = 249) were moderately correlated with DLQI. For Week 24 percentage improvement from BL, strong correlations were again seen between PGA×BSA and PASI ($r = 0.85$; n = 186), with moderate correlations to DLQI (PGA×BSA r = 0.41, n = 179; PASI r = 0.41, n = 203). Cross tabulations showed high concordance between PASI75 and PGA×BSA75 at Week 24 (156/186; 83.8%). Discordance was seen in 30 (16.2%) pts, with 12 (6.5%) achieving PASI75 but not PGA×BSA75, and 18 (9.7%) PGA×BSA75 but not PASI75.

Conclusions: PGA×BSA is sensitive to changes in skin manifestations in PsA pts treated with CZP. Furthermore, PGA×BSA correlates strongly with PASI, and achievement of 75% improvement was similar for PGA×BSA and PASI.

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2587

Psoriasis plaque resolution by body region and plaque signs with adalimumab and etanercept: An indirect comparison

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Objective: Psoriasis plaque resolution is a desirable outcome in managing patients with chronic plaque psoriasis. The Psoriasis Area and Severity Index (PASI) captures the features of psoriasis plaques by incorporating the types of plaques (erythema, induration, and scaling) and the affected area in 4 body regions (head, trunk, upper and lower limbs). This study compared psoriasis plaque resolution, measured by PASI components, between patients receiving adalimumab (ADA) and etanercept (ETN).

Methods: Patients with moderate to severe psoriasis randomized to ADA or placebo (PBO) arms in 2 phase 3 psoriasis trials (REVEAL: NCT00237887; CHAMPION: NCT00235820) were compared to those randomized to ETN or PBO in 2 separate phase 3 psoriasis trials (M10-114: NCT00691964; M10-315: NCT00710580). Rates of plaque resolution by body region and by plaque signs at Week 12, defined as achievement of PASI component scores = 0, were compared between ADA and ETN after adjusting for cross-trial differences in patient characteristics using propensity score weighting and subtracting off the corresponding PBO arm rates (ie, ADA − PBO vs ETN−PBO). Achievement of Dermatology Life Quality Index (DLQI) = 0 (ie, absence of skin-related impairment of quality of life) at the primary trial endpoint was also compared.

Results: After adjustment, baseline characteristics were balanced between the pooled ADA trials (ADA n = 875, PBO n = 427) and the pooled ETN trials (ETN n = 260, PBO n = 130). When compared to ETN, ADA was associated with significantly greater PBO-adjusted percentages of patients achieving regional plaque resolution (trunk: 44.3 vs 26.7%; upper limbs: 27.9 vs 14.8%; lower limbs: 21.5 vs 5.7%; all $P < .01$) and whole-body plaque sign resolution (induration: 25.4 vs 6.7%; desquamation: 20.2 vs 7.7%; erythema: 15.0 vs 6.0%; all $P < .01$). No significant differences were observed between ADA vs ETN in rates of head-specific plaque resolution (49.7 vs 48.7%). Additionally, a significantly greater proportion of ADA patients achieved DLQI = 0 when compared to ETN patients (27.7 vs 11.7%; $P < .01$).

Conclusions: When compared to ETN, substantially more ADA-treated patients with moderate to severe psoriasis achieved plaque resolution in the trunk, upper limbs, and lower limbs and in terms of whole-body erythema, induration, and scaling signs. ADA-treated patients were also associated with greater improvement in dermatology-related quality of life.

Design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract; all authors contributed to the development of the publication.

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Psoriasis skin and blood gene expression before and after treatment with adalimumab

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Adalimumab is an efficacious anti-TNF biologic in the treatment of psoriasis. However, the effect of adalimumab on genome-wide gene expression changes in peripheral blood compared to skin is not well characterized. Thirty adult subjects with >10% body surface area of chronic plaque psoriasis were recruited for the study. Lesional skin and peripheral blood mononuclear cell samples prior to and one month following treatment with adalimumab were collected. The skin samples were analyzed using genome-wide RNAseq, and the blood samples were analyzed using genome-wide Affymetrix microarrays. Data preprocessing and analysis were conducted using the EdgeR and Affy packages in R/Bioconductor. In the skin, paired analysis before and after treatment revealed changes in pathways important to epidermal development and keratinocyte differentiation. Such important genes as keratin 6A and 6B, tubulin B6, desmocollin and desmoglein 3 were among the top differentially expressed genes. In peripheral blood, pathways involved in hematopoietic cell lineage and immune response were found to be differentially expressed, including genes such as the Fc receptor-like A and 5, as well as immunoglobulin heavy chains. Using a principal components approach, we show that expression of genes in posttreatment skin resembles that of healthy controls. Thus, treatment of psoriasis with adalimumab appears to be associated with modulation of keratinocyte and epidermal proliferation in the skin and with immunologic changes in the blood. We discuss the ramifications of these relationships between skin and blood gene expression changes induced by adalimumab treatment for psoriasis.

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3468

PURE study design: A new registry of patients with moderate to severe chronic plaqUe psoRiasis in Canada and Latin AmErica (LACan)

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Background: Treatment options for the management of chronic moderate to severe plaque psoriasis include phototherapy, oral systemic agents and biologic therapy. Secukinumab, a fully human monoclonal antibody that selectively targets IL-17A, was recently approved for this population. Long-term observational data are required to understand the true impact of secukinumab in a clinical practice setting. The PURE registry is a multinational observation study that will assess the real-life safety and effectiveness of the management of patients with moderate to severe psoriasis.

Methods: This study is a multinational, prospective, observational two cohort study of adult Canadian and Latin American patients with psoriasis that are treated with secukinumab (cohort 1) or another approved therapy (cohort 2) as per routine clinical judgment of the treating physician. Approximately 2500 patients (1250 per cohort) will be recruited by community and hospital dermatologists. Decision regarding treatment must have been reached prior to patient enrolment in the study. Study includes a 5-year follow-up with assessments at baseline, 3 and 6 months and every 6 months thereafter. The primary objective of the observational study is safety. With 1250 patients, a 95% confidence interval for the proportion with any adverse events (assume 60%) and serious infections (assume 30%) will be ± .3%, and for serious adverse events (assume 5%) will be ± 1.2%. The study has 90% power to detect odds ratios of 1.30, 1.35 and 1.75 respectively for any adverse event, serious infections, and serious adverse events with 5% significance. Other measures captured will include effectiveness (Investigator's Global Assessment (IGA mod 2011), Psoriasis Area and Severity Index (PASI)) along with Patient Reported Outcomes (Dermatology Life Quality Index, Work Productivity and Activity Impairment Questionnaire, Hospital Anxiety and Depression Scale, Psoriasis Epidemiology Screening Tool, Psoriasis Symptom Diary and Treatment Satisfaction Questionnaire). Health care resource utilization will also be assessed.

Implications: This is the first Canadian and Latin American observational study assessing the real-life safety and effectiveness of secukinumab in the management of moderate to severe psoriasis. The inclusion of patient reported outcomes and health care utilization assessments will provide a comprehensive evaluation of this new treatment in comparison to other approved therapies.

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3541

Psoriasis-associated fatigue: A review of pathogenesis, metrics and treatment

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Fatigue has been recognized as a substantial symptom of psoriasis and psoriatic arthritis. Because of its subjective nature and the lack of effective therapeutics, fatigue is often ignored by clinicians. Here we synthesize data and observations from a literature review of all relevant articles via PubMed that highlight the importance of qualifying and quantifying fatigue amongst patients with psoriasis and psoriatic arthritis as well as highlight the need to develop novel therapeutics to target this debilitating element of a multisystem disease. Fatigue in psoriasis is triggered by complex interactions of inflammation—both directly via inflammatory cytokines and indirectly by factors of disease activity and psychiatric distress that inherently influence somatic manifestations of fatigue. Significant evidence from animal models demonstrates the importance of the same cytokines thought to be key in the disease process of psoriasis (IL-1, TNF-α, IL6) to be also significant in the pathogenesis of fatigue. But how does this relationship extrapolate to a human model? Because fatigue is not easily quantifiable, clinicians and investigators in these trials have had to rely heavily on self report instruments to gauge fatigue. Four of these aforementioned metrics (SF-36, FACIT-F, FSS and VAS) are reviewed. These screening tools are limited by patient literacy, recall bias, selective recall and digit preference. Nevertheless, much of what we know about the interaction of fatigue and psoriasis comes from clinical trial studies. Given the overlapping pathophysiology of psoriasis and fatigue, it is not surprising that in review of the literature, biologic agents including TNFα inhibitors etanercept and adalimumab, have shown meaningful reductions in fatigue symptoms. Given the prevalence and significance of psoriasis-associated fatigue and the promising data of the effect of TNFα inhibitors in this phenomenon, new efforts are needed in order to understand its pathophysiology, to develop new metrics for its evaluation and to investigate therapeutic strategies to target it clinically.

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3734

Pustular psoriasis induced by hydroxychloroquine: A case report to confirm a rare association

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A 70-year-old white female came to our clinic due to an abruptly onset generalized pustular eruption, which developed 5 days before. Systemic symptoms included fever and malaise. At the time of the visit physical examination revealed extensive erythematous patches with pustules on the entire body. Previous history of mild psoriasis was reported, although ended for several years. Her medical history was notable for mixed connective tissue disorder. As result of recent worsening of joint pain and increase of ANA titer, hydroxychloroquine therapy was started two weeks before the appearance of cutaneous eruption. Routine laboratory data showed an increase of inflammatory markers, white blood cell count with marked neutrophilia, ESR and Per. Positivity to ANA (1:640, speckled pattern) was found related to the history of connective tissue disorder. The clinical picture was compatible with acute generalized pustular psoriasis, therefore biopsy was performed to confirm the diagnosis. Suspecting a drug-induced phenomenon, hydroxychloroquine was stopped, and local and systemic therapy with corticosteroids was started. At the follow-up visit, two weeks after, skin and general conditions improved with no appearance of new lesions. Hydroxychloroquine is one of the most important options in patient suffering for rheumatic disease. Adverse cutaneous reactions are rare and includes urticarial and bullous eruptions. Stevens–Johnson syndrome, TEN and erythema multiforme. Few data are reported in the literature regarding associations with pustular psoriasis. However, in psoriatic patient, even after several years of remission, this drug can induce abruptly reappearance or worsening of the disease. Clinicians should remember this association, investigate about possible previous history of psoriasis and limit its prescriptions in this type of patients.

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Pustular psoriasis mimicking SCLE

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A 46yo female presented with new onset unusual rash 6 weeks after beginning adalimumab. Her pustular psoriasis had been controlled on acitretin, but due to lipid and liver abnormalities, a decision was made to switch treatment. Hepatitis C and alcohol consumption precluded use of methotrexate, and a decision was made to pursue biologics. Upon induction, she developed large red annular and polycyclic plaques on the trunk and forearms. Most had central clearing with a trailing edge of scale, and most were studded with pinpoint pustules. Labs were significant only for a stable but elevated alkaline phosphatase and positive antinuclear antibody (1:160 titer). Anti-double-stranded DNA, anti-SSA/Ro, anti-SSB/La, antiribonuclear protein, and anti-Smith antibodies were negative. A biopsy taken from one of these plaques revealed a superficial perivascular lymphocytic infiltrate, along with mounds of parakeratosis containing neutrophils, some extending beneath in a spongiform pattern. There was significant spongiosis, with irregular epidermal hyperplasia. Taken together, a diagnosis of pustular psoriasis was made. Drug-induced subacute cutaneous lupus erythematosus (DI-SCLE) presents clinically and histopathologically in a manner similar to idiopathic SCLE, with photosensitive symmetric, nonscarring annular and polycyclic, papulosquamous lesions, usually on sun-exposed skin. The characteristic plaques with trailing scale of SCLE were pronounced in this case, however, a predominant involvement in sun-protected areas and findings of pustules within the plaques were unusual, and more typical of psoriasis. Interestingly, the pustular variant of psoriasis is the most common subtype in patients receiving adalimumab for conditions other than psoriasis. Histologically, SCLE is typified by basal layer vacuolar degeneration and thinning of the epidermis, neither of which was seen in this case. In contrast to the idiopathic form, systemic involvement in DI-SCLE is rare. In one study, 70-90% of patients had anti-Ro/SSA and anti-La/SSB positivity, and up to 1/3 of cases are positive for antihistone antibodies. Patients on TNF-alpha inhibitors were 8x more likely to develop SCLE compared to age- and sex-matched controls. The mechanism by which this patient's paradoxical SCLE-like psoriasis flare while on treatment with an agent known to induce SCLE is unclear, and evidence in the literature to support this occurrence is lacking.

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3182

Rate of severe infection in patients who are prescribed systemic therapy for psoriasis

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Introduction: Systemic biologic and immunosuppressive agents are widely used to treat psoriasis, but the potential for severe infection continues to be viewed as unpredictable. The aim of this study is to investigate risk of severe infection in patients who undergo systemic therapy for psoriasis.

Methods: We searched a large, urban, single-center electronic medical record repository to detect all patients (aged 18-89 years) who were prescribed one systemic agent for psoriasis (January 2010-July 2015). We then detected the subset of patients that developed a severe infection subsequent to systemic agent exposure. Severe infection was defined by ICD-9 code and was limited to first infection for those who required hospitalization and/or IV or IM antibiotics.

Results: 145 (1.8%) of 8250 psoriasis patients who received a systemic agent developed a severe infection. Severe infections for each medication were detected in: 15 of 1175 (2.9%) patients treated with infliximab; 25 of 1395 (1.8%) patients treated with cyclosporine; 71 of 4208 (1.7%) patients treated with methotrexate; 20 of 1175 (1.7%) patients treated with adalimumab; 9 of 571 (1.6%) patients treated with etanercept; 3 of 223 (1.3%) patients treated with acitretin; 1 of 81 (1.2%) patients treated with ustekinumab. No cases of severe infection were found for secukinumab, golimumab and apremilast (N = 2; N = 27 and N = 40, respectively). Of the 2 cases found for alefacept 1 developed a severe infection, however, due to the small sample size, alefacept was excluded from the analyses. There was no significant difference in the rate of severe infection between each agent ($P = .64$). Of the 145 patients who developed a severe infection, the most common were cellulitis/abscesses (N = 29, 20.0%), gastrointestinal (N = 24, 16.6%), septicemia (N = 15, 10.3%), bacteremia (N = 13, 9%), mycoses (N = 10, 6.9%), and herpes zoster (N = 9, 6.2%).

Conclusions: Findings from this population indicate that infection rates between medications are not distinguishable. Although these rates of infection are consistent with prior reports, unlike prior reports there was no significant difference between biologic and nonbiologic agents. Based on findings in this population, choice of systemic agent is not predictive of greater or lesser risk for severe infection.

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3525

Reduction in C-reactive protein levels with adalimumab therapy in patients with moderate to severe hand and/or foot psoriasis

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Introduction: C-reactive protein (CRP) is a biomarker of systemic inflammation and predictor of cardiovascular risk. We evaluated post hoc the relationship between adalimumab (ADA) therapy and high sensitivity (hs)-CRP levels in patients with moderate to severe hand and/or foot psoriasis from the 16-week placebo (PBO)-controlled period of a phase 4 randomized trial (REACH).

Methods: Patients were randomized 2:1 to ADA 40 mg every other week (following 80 mg at week 0) from weeks 1−15 or matching PBO, followed by a 12-week, open-label extension. The primary endpoint was the proportion of patients achieving Physician's Global Assessment of hands and/or feet (hfPGA) 0/1 (clear or almost clear) at week 16. In this post hoc analysis, changes in hs-CRP were measured as observed from baseline to week 16 among patients treated with ADA versus PBO. The impact of baseline characteristics (history of psoriatic arthritis [PsA] and body mass index [BMI]) and hfPGA responses on changes in hs-CRP levels were also evaluated.

Results: 72 patients (24 PBO, 49 ADA) were included in the analyses, for 65 patients (19 PBO, 44 ADA) hsCRP measurements were available both at baseline and at week 16. Despite a relatively low body surface area (BSA) % involvement (mean 7.7), median hs-CRP levels at baseline among patients with hand and/or foot psoriasis were 1.6 mg/L (PBO n = 19) and 2.2 mg/L (ADA n = 44). At week 16, overall median changes in hs-CRP were +0.10 mg/L (PBO n = 19) and 0.55 mg/L (ADA n = 44). Analyzed by hfPGA response at week 16, median changes in hs-CRP for hfPGA 0/1 responders were 0.0 mg/L (PBO n = 1) and 0.80 mg/L (ADA n = 14); and for non-responders, +0.30 mg/L (PBO n = 15) and 0.40 mg/L (ADA n = 23). The baseline median hs-CRP level was greater for patients with history of PsA (5.5 mg/L, n = 6) compared with those without PsA (1.8 mg/L, n = 57). At week 16, median changes in hs-CRP for patients with PsA were 2.35 mg/L (ADA n = 6) (no patients with a PsA history had been randomized to PBO); and without PsA were +0.10 mg/L (PBO n = 19) and 0.40 mg/L (ADA n = 38). Median hs-CRP levels were also reduced with ADA therapy regardless of baseline BMI.

Conclusions: Patients with moderate to severe hand and/or foot psoriasis, particularly those with PsA, had elevated hs-CRP levels at baseline despite low BSA involvement. Treatment with ADA 40 mg every other week resulted in greater reductions in hs-CRP levels among these patients compared with PBO regardless of baseline characteristics.

The authors and AbbVie scientists designed the study, and analyzed and interpreted the data. AbbVie funded the research and provided writing support. All authors contributed to the development of the content; all authors and AbbVie reviewed and approved the abstract.

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Relationship of serum vitamin D with psoriasis severity and adalimumab response in Chinese patients with moderate to severe plaque psoriasis from a phase 3, randomized, placebo-controlled, double-blind study

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Introduction: There is a paucity of data assessing serum 25-hydroxyvitamin D (25[OH]D) status in patients with moderate to severe psoriasis. In a phase 3 adalimumab (ADA) trial of Chinese patients with moderate to severe psoriasis, we examined post hoc if screening 25[OH]D levels correlated with baseline disease activity or treatment response to ADA.

Methods: This multicenter study included a 12-week, double-blind, placebo (PBO)-controlled period (Period A) followed by a 12-week open-label period. Period A patients were randomized 4:1 to ADA 40 mg every other week following an initial 80 mg dose, or matching PBO. Serum 25[OH]D levels and PASI scores were measured at screening. Patients did not receive Vitamin D supplement. We calculated the Pearson correlation coefficient between screening 25[OH]D and screening PASI scores, and between screening 25[OH]D and % change of PASI from screening to week 12. Patients were subdivided into 4 quartiles based on their screening 25[OH]D values. Adjusted treatment effects (PBO vs ADA) were compared by controlling for these quartiles as strata using Cochran-Mantel-Haenszel test.

Results: Of 425 ITT patients in Period A, 75.4% were men; all were Asian; mean age was 43.2 years; mean disease duration was 15 years. 25[OH]D levels and PASI scores were available for all ITT patients (87 PBO, 338 ADA). The mean screening 25[OH]D was 41.9 nmol/L (standard deviation [SD] 19.29) for PBO, and 45.1 nmol/L (SD 22.98) for ADA. The mean PASI score at screening was 25.3 (SD 10.87) for PBO and 27.7 (SD 11.85) for ADA, and at baseline, 25.6 (SD 10.98) for PBO and 28.2 (SD 12.00) for ADA. The PASI75 response rate at week 12 was 77.8% for ADA vs 11.5% for PBO ($P < .001$). The correlation coefficients between screening 25[OH]D and screening PASI scores were −0.082 ($P = .092$), and between screening 25[OH]D and % change of PASI scores from screening to week 12, 0.001 ($P = .984$). Significant correlation between 25[OH]D levels and PASI scores was not observed. In all 4 screening 25[OH]D quartiles, significantly ($P < .001$) more ADA-treated patients vs PBO achieved PASI75 response: 75.9% ADA vs 16.7% PBO [treatment difference 59.2%] in the lowest quartile; 79.4% ADA vs 21.1% PBO [treatment difference 58.3%] in the highest.

Conclusion: ADA was effective in the treatment of Chinese patients with moderate-severe psoriasis. This analysis revealed no impact of serum 25[OH]D levels on psoriasis disease activity or on responsiveness to ADA treatment.

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2599

Relative efficacy and costs per responder for adalimumab versus secukinumab in the treatment of moderate to severe psoriasis

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Objective: With availability of multiple biologics for moderate to severe psoriasis, comparative effectiveness research has utility in clinical decision making. Without head-to-head studies, a need exists to determine relative efficacy among biologics accounting for differences in study populations. This study compared relative efficacy and resultant cost per responder between adalimumab (ADA) and secukinumab (SEC).

Methods: An indirect comparison was conducted using patient-level data from an ADA trial (REVEAL) and published aggregate data from the pivotal SEC trials (ERASURE and FIXTURE). To adjust for cross-trial differences, patients in REVEAL were reweighted to match the mean and standard deviation of baseline characteristics in the SEC trials, specifically, age, weight, BMI, sex, race, duration of psoriasis, body surface area, baseline PASI score, physician assessment of severity, and prior biologic. PASI75 and PASI90 response rates and numbers needed to treat (NNTs) to achieve an additional PASI75/90 response relative to placebo were compared at the study's primary endpoint. Annual incremental costs per PASI75/90 response were calculated.

Results: Before matching, there were significant differences in weight, race, and baseline PASI between ADA and SEC trials. After matching, all baseline characteristics were balanced. Relative PASI75/90 rates were similar for ADA compared to SEC 150 mg (rate difference: −0.5% [−9.3%, 8.3%] and 6.5% [−2.1%, 15.0%]), and lower for ADA compared to SEC 300 mg (−10.6% [−19.0%, −2.2%] and −9.4% [−17.7%, −1.0%]). NNTs to achieve 1 additional PASI75 response were 1.6, 1.6, and 1.4 for ADA, SEC 150 mg, and SEC 300 mg, respectively. Annual incremental costs per additional PASI75 responder were $20,789 lower for ADA vs SEC 150 mg and $8309 lower for ADA vs SEC 300 mg. NNTs to achieve 1 additional PASI90 response were 2.2, 2.6, and 1.8 for ADA, SEC 150 mg, and SEC 300 mg, respectively. Annual incremental costs per additional PASI90 responder were $51,113 lower for ADA vs SEC 150 mg and $8009 lower for ADA vs SEC 300 mg.

Conclusions: After adjusting for cross-trial differences, ADA and SEC 150 mg had similar PASI75/90 rates; both were lower than SEC 300 mg. Annual costs per PASI75/90 responder were more than $20,000 lower with ADA than with SEC 150 mg and more than $8000 lower with ADA than with SEC 300 mg.

Design, study conduct, and financial support for the study were provided by AbbVie; AbbVie participated in the interpretation of data, review, and approval of the abstract; all authors contributed to the development of the publication.

2475

Relative efficacy of adalimumab versus secukinumab in active psoriatic arthritis: A matching-adjusted indirect comparison

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Objective: The phase 3 FUTURE 1 and FUTURE 2 trials demonstrated efficacy of secukinumab (SEC) for active psoriatic arthritis (PsA). However, there are limited data comparing the effectiveness of SEC with established PsA treatments. This study compared the relative efficacy of adalimumab (ADA) 40 mg versus SEC 150 mg and 300 mg for the treatment of PsA.

Methods: An indirect comparison was conducted using individual patient data from the ADA pivotal trial (ADEPT) and published data from FUTURE 1 and 2. To adjust for the cross-trial differences, individual patients in ADEPT were re-weighted to match the mean baseline characteristics in the FUTURE trials. Specifically, age, weight, gender, race, baseline methotrexate use, psoriasis ≥3% body surface area, baseline PASI score, presence of dactylitis and enthesitis, and HAQ-DI were included in the baseline matching. The ACR 20/50/70 and PASI 75/90 response rates relative to placebo at week 24 were compared. Numbers needed to treat (NNTs) to achieve one additional ACR 20 and PASI 75 responder were also calculated.

Results: After matching, mean baseline characteristics were balanced across the ADEPT and FUTURE 1 and 2 trial populations. Compared to SEC 150 mg, ADA demonstrated higher relative ACR 20/50/70 (mean differences, 9.5% [+4.3%, 23.3%], 3.0% [-10.1%, 16.0%], and 6.0% [-4.4%, 16.5%], respectively) and PASI 75/90 response rates (13.1% [4.5%, 26.7%] and 6.7% [-6.4%, 19.9%]). Similarly, ACR 20/50/70 and PASI 75 were higher with ADA compared to SEC 300 mg (mean difference: 5.3% [-10.3%, 20.8%], 6.2% [-7.7%, 20.2%], 6.0% [-5.6%, 17.6%], and 7.3% [-10.1%, 24.7%], respectively). The NNTs to achieve one additional ACR 20 responder were 2.3 for ADA vs 3.0 for SEC 150 mg and 2.7 for SEC 300 mg. The NNTs to achieve one additional PASI75 responder were also lower for ADA (1.7) vs SEC 150 mg (2.2) and SEC 300 mg (1.9).

Conclusions: In the absence of head to head trials comparing ADA and SEC, the current indirect comparison which adjusts for differences across trial populations provides valuable and reliable evidence for physicians and payers. After adjusting for cross-trial differences in baseline characteristics, ADA was associated with higher relative ACR and PASI rates and lower NNTs compared with SEC 150 mg or 300 mg at week 24 among patients with PsA.

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Research objectives and design of the Corrona Psoriasis Registry: A large prospective cohort of psoriasis patients in the United States

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Background: Psoriasis is a chronic, immune-mediated inflammatory disease that affects approximately 3% of the US population and can be associated with serious comorbidities including obesity, diabetes, cardiovascular disease and other autoimmune diseases. Secukinumab, a first-in-class IL-17A inhibitor, was recently approved for moderate to severe plaque psoriasis in the US, EU, and other countries around the world. While clinical trial data capture efficacy and safety for an average of 12 months under controlled circumstances, long-term data are still limited. Large long-term prospective registries will help to determine the treatment safety and effectiveness in the real world, and help improve clinical decision-making.

Methods: The Corrona Psoriasis registry was launched in April 2015 in collaboration with the National Psoriasis Foundation (NPF) to study the comparative safety of approved systemic psoriasis therapies in a national cohort of patients in a real world setting. Secondary objectives include analyses of epidemiology, comorbidities, treatment practices, and comparative effectiveness. The registry is designed as a prospective, multicenter, observational registry for patients with psoriasis. Eligibility criteria for enrollment include: ≥18 years of age, dermatologist-diagnosed psoriasis, and initiating or switching to a systemic therapy in the previous 12 months. Systemic therapy includes FDA-approved biologic and nonbiologic (methotrexate, cyclosporine, and apremilast only) treatments for psoriasis. Data are collected from both the participating dermatologist and patient approximately every 6 months during regular outpatient visits. The Registry collects data on patient demographics, lifestyle factors, comorbidities, medication use, adverse events, and detailed physician and patient assessments including Psoriasis Area Severity Index (PASI), Investigator Global Assessment (IGA), body surface area (BSA), Dermatology Life Quality Index (DLQI), EQ-5D, and Work Productivity and Activity Impairment measures.

Results: Corrona and the NPF plan to recruit approximately 200 sites within the US with a target enrollment of 10,000 patients and an expected follow-up duration of at least 8 years.

Conclusions: This registry will establish a real-world database of the patient population and contribute to the clinical knowledge base of psoriasis research. Corrona is actively recruiting dermatology sites who are interested in participating in this registry.

This study is sponsored by Corrona, LLC. Initial funding for this registry is provided by Novartis Pharmaceutical Corporation. Corrona, LLC has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, Astra Zeneca, BMS, and others.

3218

Response of persistent juvenile pityriasis rubra pilaris to secukinumab

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A 54-year-old white female presented with a generalized variably pruritic eruption present since the age 2. No other immediate family members were similarly affected. Physical examination revealed sharply marinated generalized orange-red plaques confluent on trunk with discrete islands of sparing on the face, neck, and extremities. The palms and soles were notable for thin waxy yellowish keratoderma with associated subungual hyperkeratosis. Multiple shave biopsies revealed broad epidermal rete, alternating parakeratosis and orthokeratosis, focal follicular hyperkeratosis, and focal acantholytic dyskeratosis. A diagnosis persistent juvenile pityriasis rubra pilaris (PRP) was made. The patient had been previously treated with methotrexate (MTX), isotretinoin, acitretin, infliximab, and adalimumab with limited improvement. Given the prior failure of first line oral systemic and biologic therapies, that patient was started on secukinumab 300 mg SC weekly for 5 weeks and then once a month thereafter. The patient had rapid near full body clearance after 1-2 injections with regression of the palmar-plantar keratoderma. Secukinumab is a fully human antibody targeting IL-17A with broad effects on keratinocyte proliferation and epidermal maturation. While the etiopathogenesis of PRP is incompletely understood, this case suggests that in select patients with persistent juvenile PRP, IL-17 inhibition may be a relevant therapeutic target.

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3901

Rupioid psoriasis preceded by varicella presenting as Koebner phenomenon

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Introduction: Psoriasis is a common, chronic, hyperproliferative skin disorder. Morphologically classifications include plaque, guttate, pustular, nummular, gyrate, and rupioid features. Rupioid psoriasis is characterized by the presence of conic, thick, adherent plaques while Koebner phenomenon is described as the appearance of psoriatic lesions in uninvolved skin as a consequence of trauma.

Case report: A 16-year-old Mexican female presented with a 5-month history of erythematous patches covered by scaly, thick, conic, silvery, adherent plaques, with variable size and shape, affecting the skin of scalp, forehead, retroauricular folds, arms, elbows, forearms, trunk, thighs, knees, legs and with a total body surface area (TBSA) of 11%. She complained of fissuring and pain of plaque area with movement of limbs. No nail or joint affection was found. One month prior to skin manifestations, she had primary varicella, after which she developed these plaques in numerous residual lesion. A skin biopsy was performed revealing epidermal parakeratotic hyperkeratosis with scarce neutrophils, regular and moderate acanthosis with agranulosis. Superficial dermis showed papillomatosis, edema, congested and dilated capillaries with moderate lymphocytic infiltrate, consistent with psoriasis. CBC, chemistries and hand X-rays were within normal rages. Topical treatment consisted of 1% coal tar/2% salicylic acid shampoo for scalp, tacrolimus 0.1% ointment twice a day for face, 20% salicylic acid ointment to body plaques only at night, and an emollient cream several times a day. 4 weeks later, PASI score was 90% improvement for face plaques and 60% for body lesions. Topical treatment was continued, switching to calcipotriol/betamethasone dipropionate ointment at night for one month and then every other day. After 4 months of treatment, complete remission occurred and patient continued to be free of disease at one year of follow-up.

Discussion: There are rare case reports of hyperkeratotic psoriasis, of which only one is a pediatric patient. Poor response to topical treatment, psoriatic arthritis and nail involvement have all been typically described in these patients. There are only six case reports of varicella infection followed by guttate or plaque psoriasis. This is the first known report of rupioid psoriasis secondary to a varicella primary infection that presented as Koebner phenomenon in a pediatric patient.

Commercial support: None identified.

3478

Safety and efficacy of adalimumab in combination with different doses of methotrexate in patients with psoriatic arthritis: Subanalysis of ADEPT

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Introduction: The ADEPT study demonstrated that adalimumab (ADA) treatment reduced disease activity in patients (pts) with psoriatic arthritis (PsA) (Mease PJ, et al. Arthritis Rheum. 2005;52(10):3279-3289). This post hoc analysis explored the safety and skin efficacy of ADA in combination with methotrexate (MTX) in pts with PsA in ADEPT.

Methods: ADEPT (NCT00195586) was a 24-week randomized placebo (PBO)-controlled study of ADA 40 mg every other week in pts with moderate to severe PsA. Randomization was stratified by MTX use (yes/no) and extent of psoriasis (PsO: <3% or ≥3% of body surface area [BSA]). For this analysis, pts were grouped by baseline MTX (low dose, ≤15 mg/wk; high dose, >15 mg/wk). Efficacy endpoints were changes in PsO Area and Severity Index (PASI) response rates in pts with ≥3% affected BSA at baseline (nonresponder imputation). Adverse events (AEs) were monitored and reported as events per 100 pt-years (E/100PY).

Results: Of the 162 pts randomized to PBO and 151 randomized to ADA, 70 (43%) and 70 (46%), respectively, were taking MTX and had ≥3% BSA involvement at baseline. Overall, PASI50/75/90 response rates were significantly higher with ADA vs PBO ($P < .001$) at Weeks 12 and 24 regardless of MTX dose. PASI50/75/90 response rates with ADA at Week 24 were 100/92/75% in the low-dose MTX subgroup (n = 12), 82/65/41% in the high-dose MTX subgroup (n = 17), and 63/46/32% in the ADA-only (n = 41) subgroup. AE rates were highest among pts taking high-dose MTX for both PBO (915 E/100PY) and ADA (1028 E/100PY) arms. Rates of serious and severe AEs were highest in the PBO arms of the no MTX and low-dose MTX subgroups, and lowest in the high-dose MTX PBO arm. Rates of discontinuation due to an AE were lowest in the high dose MTX subgroup of the ADA arm.

Conclusions: In pts with PsA, treatment with ADA monotherapy or in combination with MTX regardless of dose provided greater response rates in PASI-related endpoints at Weeks 12 and 24 compared with PBO. AE rates were highest among pts receiving high-dose MTX alone or in combination with ADA.

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2347

Safety and tolerability of apremilast up to 182 weeks: Pooled analyses from phase 3 clinical trials

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Background: Apremilast (APR), an oral phosphodiesterase 4 inhibitor, has been shown to be efficacious in the treatment of moderate to severe plaque psoriasis (ESTEEM 1 and 2) and psoriatic arthritis (PALACE 1-3) in randomized, placebo-controlled, phase 3 trials. Safety of APR was assessed over 3 yrs in these studies.

Methods: Safety findings are reported for the APR-exposure period 0 to ≤182 wks based on data available through February 14, 2015.

Results: In the pooled ESTEEM 1 and 2 analysis, the APR-exposure period (all pts who received APR, despite when initiated [0 to ≤182 wks]) included 1,184 pts treated with APR 30 mg BID (APR30; 1902.2 pt-yrs). During the 0 to ≤52 wk APR-exposure period, AEs occurring in ≥5% of pts included diarrhea, nausea, headache, and tension headache. Most cases of diarrhea and nausea were mild to moderate in severity, occurred during the first wk of dosing, and generally resolved within 1 month. During the 0 to ≤182 wk period, AEs occurring in ≥5% of pts were upper respiratory tract infection (6.7%) and nasopharyngitis (6.0%). Based on exposure-adjusted incidence rates (EAIR)/100 pt-yrs, AEs/serious AEs and discontinuation of study drug due to AEs did not increase with long-term exposure compared with the 0 to ≤52 wk APR-exposure period. For the overall exposure period, EAIR/100 pt-yrs for serious AEs was 5.9 (EAIR 0 to ≤52 wks: 6.4) and for discontinuation due to AEs was 7.0 (EAIR 0 to ≤52 wks: 10.2). During the 0 to ≤182 wk APR-exposure period, no increases in rates of MACE (EAIR 0.5), malignancies (EAIR 1.2), depression (EAIR 1.8), or suicide attempt (EAIR 0.1) were noted compared with the 0 to ≤52 wk APR-exposure period. No serious opportunistic infection (EAIR 0.0), reactivation of TB infection, or clinically meaningful effects on laboratory measurements were reported. Three deaths (1 per yr) occurred during the 0 to ≤182 wk APR-exposure period (EAIR 0.2). Mean (median) percent change from baseline in weight was −1.53% (−1.20%); weight loss >5% was experienced by 21.9% of pts. Results of pooled safety analyses from the ESTEEM and PALACE 1-3 trials including 1905 pts treated with APR30 (3527.5 pt-yrs) over the same APR-exposure period were consistent with those from the ESTEEM pooled safety analysis.

Conclusions: APR30 demonstrated an acceptable safety profile and was generally well tolerated for up to 182 wks, with no new signals or increases in severity or frequency of AEs with long-term APR30 treatment.

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3510

Safety of adalimumab dosed every week and every other week in patients with hidradenitis suppurativa or psoriasis

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Introduction: Adalimumab (ADA) is approved for the treatment of moderate to severe plaque psoriasis (Ps) at a dose of 40 mg every other week (eow) and is being investigated for the treatment of hidradenitis suppurativa (HS). We report the safety of ADA dosing 40 mg eow and every week (ew) in these patient (pt) populations.

Methods: In 2 phase 3, double-blind, placebo-controlled studies, pts with HS who received ADA ew in period A (12 weeks) were randomized to receive placebo (Pbo), or 40-mg ADA eow or ew in period B (24 weeks). In an open-label extension (OLE) study for phase 2/3 studies in Ps, pts received 40-mg ADA eow; from weeks 24 to 252, pts with <50% improvement in PASI could escalate the dose to 40-mg ew; afterwards, they were re-evaluated at 6 and 12 weeks and then every 12 weeks. Upon achieving a PASI75 response, pts who dose-escalated were deescalated to eow. Pts who deescalated and fell below PASI50 again were reescalated to ew and kept there. Adverse events (AEs) are presented as number of events and events per 100 pt-years (n, [E/100 PY]).

Results: Overall, 300 pts with HS in period B and 1605 with Ps in the OLE were included. In patients with HS, the AE rate was lower in the eow (163 [492.4]) and ew (167 [471.8]) groups compared with Pbo (188 [591.2]). Serious AEs were reported at higher rates in the eow (7 [21.1]) and ew (5 [14.1]) groups compared with the Pbo group (2 [6.3]); however, rates of AEs leading to discontinuation were comparable. Infection rates in the eow (46 [139.0]) and ew (45 [127.1]) groups were lower compared with the Pbo group (55 [173.0]). Other AEs of interest occurred infrequently. Among pts with Ps, the rates of AEs and serious AEs were comparable between the eow and ew groups (any: eow 662.5 [237.6] v ew 517 [232.5]; and serious: eow 181 [6.5] v ew 17 [7.6]); the rate of AEs leading to discontinuation was higher with ew dosing (eow 80 [2.9] v ew 22 [9.9]). Infection rates were lower with ew dosing (144 [64.8]) compared with eow dosing (2029 [72.8]), and rates of serious infections were comparable (eow 33 [1.2] v ew 2 [0.9]).

Conclusions: Regardless of treatment assignment, the incidence of AEs appears higher in pts with HS, compared with pts with Ps, which may be due to inherent characteristics of the HS population. In pts with HS or Ps, the safety of ADA ew and eow dosing regimens was comparable and consistent with the expected AE profile of ADA.

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2709

Safety profile of patients achieving complete or near complete resolution of moderate-to-severe psoriasis after 12 weeks of etanercept or ixekizumab: Integrated analyses from UNCOVER-2 and UNCOVER-3

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Background and objective: New biologics targeting IL-17A enable a majority of psoriasis patients (pts) to achieve higher clearance levels than the current treatment goal of 75% reduction in the Psoriasis Area and Severity Index (PASI 75). Because high levels of clearance can be associated with safety concerns with certain existing drugs, the need to balance efficacy with safety is of high importance. Ixekizumab (IXE) is an anti-IL-17A IgG4 monoclonal antibody with high binding affinity. The objective of this analysis was to assess whether more adverse events (AEs) are associated with greater clearance levels after 12 weeks (wks) of treatment.

Methods: Data were integrated from the induction period (0-12 wks) of 2 phase 3 trials where pts were randomized to receive subcutaneous placebo (N = 361), high dose etanercept (ETN, 50 mg twice weekly; N = 740), or a single injection of 80 mg IXE every 4 (IXE Q4W; N = 733) or 2 wks (IXE Q2W; N = 736) following a 160-mg starting dose. Changes in disease severity were measured as improvements in PASI. Treatment-emergent adverse event (TEAE) and serious adverse event (SAE) rates for the ETN and IXE groups were analyzed in categories of patients achieving <75%, 75% to <90%, 90% to <100% and 100% improvement in PASI (last observation carried forward), and compared with the Cochran-Armitage Trend test.

Results: At Wk 12, 7%, 34%, and 40% of ETN, IXE Q4W, and IXE Q2W pts, achieved complete resolution of psoriasis plaques (PASI 100); 16%, 31%, and 31% achieved near complete resolution (PASI 90 to <100). TEAE rates were not significantly different across the PASI response categories within each treatment group (ETN, $P = .58$; IXE Q4W, $P = .82$; IXE Q2W, $P = .10$). Pts with lower levels of skin clearance were more likely to discontinue due to TEAEs in the ETN ($P = .013$) and IXE Q4W ($P = .003$) groups than pts with higher levels of clearance. Rates of SAEs overall, SAEs of infection, and TEAEs of Candida infection were not significantly different ($P > .05$) across PASI response categories for any treatment group.

Discussion: Pts achieving complete or near complete resolution of psoriasis plaques with ETN or IXE had no increase in AE rates versus pts achieving lower levels of clearance. Pts achieving higher levels of clearance were less likely to discontinue due to AEs. Thus, higher levels of efficacy may be achieved in pts with moderate-to-severe psoriasis without increases in AE rates for at least the first 12 wks of treatment.

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3414

Secukinumab administration by autoinjector maintains efficacy in plaque psoriasis over 2 years: Results of the JUNCTURE study

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Introduction: Secukinumab, a fully human monoclonal antibody that selectively targets IL-17A, is highly efficacious in the treatment of moderate to severe psoriasis, starting at early time points, with a sustained effect and a favorable safety profile. Here, efficacy and safety data are reported after 2 years of treatment in the JUNCTURE study, a phase 3 study in which subjects self-administered secukinumab using an autoinjector.

Methods: Subjects were randomized 1:1:1 to secukinumab 300 mg, 150 mg or matching placebo. Treatments were given at Baseline, Weeks (Wk) 1, 2, 3 and then every 4 weeks from Wk 4 until Wk 208, or Wk 12 for subjects on placebo. After Wk 12, subjects in the placebo group who achieved a PASI 75 response continued on placebo, while those who did not achieve a PASI 75 response were re-randomized 1:1 to secukinumab 300 mg or 150 mg. Coprimary endpoints were secukinumab efficacy compared to placebo for PASI 75 and IGA mod 2011 0/1 response rates at Wk 12. Secondary endpoints included PASI 75, 90, 100 and IGA mod2011 responses over time. Approximate Year 2 data correspond to data collected at the Week 112 site visit. Year 2 data from 88 subjects in the 300 mg secukinumab dose group, and 89 subjects in the 150 mg secukinumab dose group were analyzed using multiple imputation methodology.

Results: As reported previously, a high level of PASI 75, 90 and 100 responses were maintained to Year 1 (PASI 75, 90 and 100 responses for the 300 mg dose were 86.2%, 72.1% and 46.9%, respectively, and 74.5%, 53.9% and 33.6% for 150 mg at 52 weeks). Year 2 PASI 75 response rates were 81.4% for subjects receiving secukinumab 300 mg and 64.9% for those receiving 150 mg. Year 2 PASI 90 response rates were 68% for those receiving 300 mg and 44.3% for those receiving 150 mg, respectively; corresponding PASI 100 scores were 45.8% and 25.3%. Previously at Year 1, in subjects receiving secukinumab 300mg and 150mg, IGA mod 2011 0/1 response rates were 74.7% and 59.3%, respectively. Year 2 IGA mod 2011 0/1 response rates were 62.6% and 44.5%, respectively. No new or unexpected safety signals were observed to Year 2.

Conclusions: Secukinumab treatment with an autoinjector achieved clear or almost clear skin in a majority of subjects with moderate to severe plaque psoriasis up to 2 years. The favorable safety profile of secukinumab was consistent with previous studies.

Supported by Novartis Pharma AG, Basel, Switzerland.

3384

Secukinumab administration by prefilled syringe maintains efficacy in moderate to severe plaque psoriasis over 100 weeks: Results of the FEATURE trial

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Introduction: The FEATURE study examined secukinumab efficacy and safety in moderate to severe plaque psoriasis when self-administered using a prefilled syringe (PFS). Here, data from up to two years (100 Wks) of treatment are reported.

Methods: Subjects were randomized 1:1:1 to secukinumab 300 mg, 150 mg, or matching placebo (PBO). Treatments were self-administered using a PFS at Wks 0, 1, 2, 3, and 4, then every 4 wks until Wk 12 (PBO) or Wk 208 (secukinumab). PBO group nonresponders were rerandomized to secukinumab 300 mg or 150 mg after Wk 12. Coprimary endpoints were PASI 75 and IGA mod 2011 0/1 response rates at Wk 12 vs PBO. Secondary endpoints included PASI 90 and PASI 100. Here, Wk 100 interim efficacy analyses were performed using multiple imputation (MI) methods on data from 86 (300 mg) and 88 (150 mg) subjects who received secukinumab at any point during the study.

Results: Secukinumab was superior to PBO at Wk 12 with respect to PASI 75 response and IGA mod 2011 0/1 response, and substantial PASI 75, 90, and 100 responses were maintained to Wk 52. At Wk 100, median treatment exposure at any dose was 624 (33–763) days, for 274.3 subject-years overall experience. Wk 100 analysis in all subjects receiving secukinumab from either baseline or Wk 12 showed PASI 90 response, 59.7% of subjects with 300 mg and 41.3% with 150 mg secukinumab. At Wk 100, 40.8% and 22.2% of subjects had PASI 100 with secukinumab 300 mg and 150 mg, respectively. PASI 75 responses were seen in 79.6% of subjects with secukinumab 300 mg and in 58.4% receiving secukinumab 150 mg, and IGA mod 2011 0/1 scores were recorded for 55.2% and 41.1% of subjects receiving secukinumab 300 mg and 150 mg, respectively. No new or unexpected safety signals were observed to Wk 100.

Conclusions: Substantial and durable PASI 90 and PASI 100 responses at Wk 100 were achieved using long-term administration of secukinumab by PFS. The safety profile of secukinumab was consistent with previous studies, with no new or cumulative safety findings seen.

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2564

Secukinumab exhibits a favorable safety profile during 104 weeks of treatment in subjects with moderate to severe plaque psoriasis

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Introduction: Secukinumab, a fully human monoclonal antibody that selectively targets IL-17A, is highly efficacious in the treatment of moderate to severe psoriasis, starting at early time points with a sustained effect and a favorable safety profile. This study is an extension of two secukinumab phase 3 studies (ERASURE and FIXTURE) in moderate to severe psoriasis. Here, we evaluated overall safety of secukinumab from Week (Wk) 52 to Wk 104.

Methods: Subjects were eligible for inclusion in the extension on completion of either core study with at least a partial response (PASI ≥50) to secukinumab at Wk 52. PASI 75 responders in each secukinumab dose group of the core studies were randomized 2:1 to continue the same doses of secukinumab (300 mg or 150 mg) or receive placebo (300 mg to PBO or 150 mg to PBO) every 4 wks. Adverse events (AEs), and AEs of special interest (serious infections, candidiasis, neutropenia, inflammatory bowel disease [IBD], malignancy, major adverse cardiovascular events [MACE]) were analyzed from Wk 52 to Wk 104.

Results: At Wk 104, AEs were reported in 76.6% and 70.1% of subjects who received any secukinumab 300 mg treatment (300 mg and 300 mg to PBO groups; n = 552) or any secukinumab 150 mg treatment (150 mg and 150 mg to PBO groups; n = 522), respectively. Infections were the most frequent AEs, in both the any secukinumab 300 mg (53.1%) and any secukinumab 150 mg (41.6%) treatment groups, with nasopharyngitis being the most common infection (24.1% and 17.0%, respectively). Serious adverse events were reported for 5.6% and 6.3% of subjects receiving any secukinumab 300 mg or 150 mg dose, respectively. Rates for AEs of special interest at Wk 104 were as follows for any secukinumab 300 mg and 150 mg dose, respectively: candidiasis (2.5%, 1.5%), neutropenia grade ≥2 (3.1%, 2.8%), serious infections (1.3%, 1.1%), IBD (0.2%, 0.2%), malignancy (0.4%, 0.8%), and MACE (0.2%, 0.4%). Treatment-emergent anti-drug antibodies (TE-ADA) and neutralizing antibodies (NA) were rare (6 (0.6%) subjects had TE-ADA, of whom 2 (0.2%) tested positive for NA) and were not associated with loss of secukinumab efficacy or issues of clinical concern. No deaths and no cases of reactivation of latent tuberculosis were reported.

Conclusions: Secukinumab was not associated with any new or unexpected safety findings to Wk 104. This analysis of safety data supports a favorable safety profile of secukinumab over 104 wks in subjects with moderate to severe psoriasis.

Supported by Novartis Pharma AG, Basel, Switzerland.

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Secukinumab improves signs and symptoms of psoriatic arthritis: Results of phase 3 FUTURE 2 study stratified by concomitant methotrexate use

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Introduction: Concomitant methotrexate (MTX) use with biologics is common in patients with psoriatic arthritis (PsA). We report the effect of secukinumab, an anti–interleukin-17A monoclonal antibody, on signs/symptoms of PsA in the FUTURE 2 study (NCT01752634), and results of an exploratory analysis for ACR responses with/without concomitant MTX.

Methods: 397 PsA patients were randomized to subcutaneous secukinumab 300 (n = 100), 150 (n = 100), 75mg (n = 99) or placebo (PBO; n = 98) at baseline (BL), Weeks (Wks) 1–4 and then every 4 wks from Wk 8. MTX at a stable dose (≤25 mg/wk) was permitted. Primary endpoint: ACR20 response at Wk 24; secondary endpoints: ACR50 response, PASI75/90 response and HAQ-DI; exploratory endpoints: DLQI and ACR70.

Results: Of 397 patients randomized, 47% received concomitant MTX (secukinumab 300 mg: n = 44; 150 mg: n = 44; 75 mg: n = 47 and PBO: n = 50); mean dose ranged from 16.1-18.0 mg/wk across treatment groups. In the overall study population, significantly more patients on secukinumab achieved ACR20 response vs PBO at Wk 24, with secukinumab 300 and 150 mg providing the highest response rates. ACR20/50/70 response rates were improved with secukinumab 300 and 150 mg vs PBO regardless of concomitant MTX use. In the overall study population, mean change from BL in HAQ-DI at Wk 24 was −0.56, −0.48 and −0.32 with secukinumab 300, 150 and 75mg, respectively, vs −0.31 with PBO. In patients with psoriasis affecting ≥3% of body surface area, PASI 75/90 response rates at Wk 24 were 63%/49%, 49%/33% and 28%/12% with secukinumab 300, 150 and 75 mg, respectively, vs 16%/8% with PBO. In DLQI, mean changes from BL with secukinumab 300, 150 and 75 mg were −8.48, −8.77 and −7.43, respectively, vs PBO (−2.13).

Conclusions: Secukinumab 300 and 150 mg significantly improved joint and skin symptoms in patients with PsA, with associated improvements in physical function and skin-related quality of life. Improvements in signs and symptoms of PsA were demonstrated with secukinumab 300 and 150mg in both the concomitant MTX and without MTX sub-groups.

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Secukinumab inhibits radiographic progression in patients with psoriatic arthritis: Results of phase 3 FUTURE 1 study stratified by concomitant methotrexate use

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Introduction: We report the effect of secukinumab, with and without concomitant methotrexate (MTX), on radiographic progression in psoriatic arthritis (PsA) patients in an exploratory subgroup analysis of the randomized, double-blind, placebo (PBO)-controlled study (FUTURE 1, NCT01392326).

Methods: 606 patients with active PsA were randomized to secukinumab or PBO. Patients on secukinumab received 10 mg/kg intravenous (i.v.) loading dose at baseline (BL), Weeks (Wks) 2 and 4, followed by subcutaneous (sc) secukinumab 150 (IV→150 mg) or 75 mg (IV→75 mg) every 4 wks (q4wk) from Wk 8. PBO was given on the same schedule. At Wk 16, PBO patients with ≥20% reduction in tender or swollen joint count (nonresponders) were rerandomized to secukinumab 75 or 150 mg sc q4wk; responders received secukinumab 75 or 150 mg sc q4wk from Wk 24. van der Heijde modified total Sharp score (mTSS) and erosion and joint space narrowing (JSN) scores were determined at BL, Wks 16/24 (depending upon response) and Wk 52. Analysis of radiographic progression at Wk 24 used linear extrapolation for patients with X-ray assessments at Wk 16. Wk 52 analyses used evaluable data.

Results: In the overall study population, secukinumab significantly inhibited radiographic progression from BL to Wk 24 vs PBO. There was lower mean change in mTSS score from BL to Wk 24 in patients on secukinumab compared to those on PBO, irrespective of concomitant MTX use. Inhibition of radiographic progression with secukinumab was sustained from Wk 24 to Wk 52. Improvements in mean change in erosion and JSN scores were also observed with secukinumab throughout the study.

Conclusions: Secukinumab provided significant and sustained inhibition of radiographic disease in patients with PsA. Within the limitations of suboptimal statistical power, the exploratory analysis does not suggest a clinically meaningful difference in radiographic progression between the secukinumab with MTX and secukinumab without MTX subgroups.

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Secukinumab is effective in reducing dactylitis and enthesitis using multiple measures in patients with psoriatic arthritis: Results from two phase 3 randomized, multicenter, double-blind, placebo-controlled studies (FUTURE 1 and 2)

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Introduction: Dactylitis and enthesitis are common disabling manifestations of psoriatic arthritis (PsA). We report the effects of secukinumab on dactylitis and enthesitis in the phase 3 FUTURE 1 and 2 studies (NCT01392326 and NCT01752634, respectively).1,2

Methods: In FUTURE 1, 606 patients with active PsA were randomized to placebo (PBO) or intravenous (i.v.) secukinumab 10 mg/kg at baseline (BL), Weeks (Wks) 2 and 4, then subcutaneous (sc) secukinumab 150 mg (IV-150 mg) or 75 mg (IV-75 mg) every 4 wks from Wk 8. In FUTURE 2, 397 patients were randomized to sc secukinumab (300, 150 or 75 mg) or PBO at BL, Wks 1, 2, 3 and 4, and then every 4 wks from Wk 8. The primary endpoint for both studies was ACR20 response at Wk 24; the proportions of patients with resolved dactylitis and enthesitis at Wk 24 were secondary endpoints. Dactylitis counts, Leeds Dactylitis Index (LDI) and Leeds Enthesitis Index (LEI) were also assessed.

Results: At BL, 324 (53.5%) and 372 (61.4%) patients in FUTURE 1 and 138 (35%) and 253 (64%) patients in FUTURE 2, respectively, had dactylitis and enthesitis. At Wk 24, more patients in the secukinumab IV-150 and IV-75 mg and 300 and 150 mg sc groups had complete resolution of dactylitis and enthesitis vs PBO in both studies. Corresponding reductions in LDI, LEI and mean dactylitis counts were observed.

Conclusions: Secukinumab reduced the number of dactylitic digits and enthesitis sites in patients with PsA and was associated with a greater proportion of patients achieving complete resolution of dactylitis and enthesitis vs PBO.

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Secukinumab is predominantly prescribed at the recommended 300 mg dose to psoriasis patients in the United States

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Background: Secukinumab is a novel, fully human monoclonal antibody indicated for the treatment of moderate to severe plaque psoriasis, and has been available to US patients since March of 2015. According to the US product label, the recommended dose is 300 mg. For some patients, a dose of 150 mg may be acceptable.

Methods: Secukinumab Service Request Forms (SRFs) jointly filled by physicians and patients for initial secukinumab prescription from March 1, 2015 to May 31, 2015 were analyzed. All patients provided written informed consent. Information on the prescribed secukinumab dose and patient characteristics was analyzed descriptively.

Results: The analysis included 5050 secukinumab SRFs completed by 1989 unique physicians. Patients were from all regions of the US: Northeast (14.5%), Midwest (20.2%), South (45.6%), and West (19.7%). The patient sample was roughly balanced by sex (females, 45.7%; males, 53.8%; missing data, 0.5%) and distributed across a wide range of age groups: 18-24 years (2.6%), 25-34 (10.6%), 35-44 (20.4%), 45-54 (25.1%), 55-64 (25.2%), 65+ (16.2%). 2494 patients (49.4%) had previously used a biologic (missing or unknown for rest of data), with 60% (1486) using 2 or more biologics. Overall, the initial secukinumab dose was 300 mg for 99.9% of the patients (5046) and 150 mg for only 4 patients (0.1%). A majority of the SRFs requested the autoinjector pen as the injection device (4543; 90.0%) rather than the pre-filled syringe (507; 10.0%).

Conclusions: Using a large number of secukinumab SRFs filled by US patients and their physicians distributed from all regions, this analysis found that secukinumab is predominantly prescribed at the recommended 300 mg dose. Therefore, secukinumab is being prescribed in accordance with the product label.

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3348

Secukinumab maintains reductions in PASI through second year of treatment: A randomized extension of the ERASURE and FIXTURE studies in plaque psoriasis

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Background: Secukinumab, a fully human anti-IL-17A monoclonal antibody, has been demonstrated to be highly efficacious in the treatment of moderate to severe plaque psoriasis, starting at early time points, with a sustained effect and favorable safety profile. This trial is an extension of two secukinumab phase 3 studies in moderate to severe psoriasis (ERASURE and FIXTURE). This abstract focuses on absolute changes in PASI at Week (Wk) 104 in subjects who were PASI75 responders at Wk 52 of the core studies.

Methods: PASI75 responders from the secukinumab treatment arms of both trials were randomized 2:1 to continue the same doses of secukinumab (300 mg or 150 mg, continuous-treatment) or receive placebo (300 mg to PBO or 150 mg to PBO, treatment-withdrawal) every 4 wks up to Wk 104, or until relapse (defined as a reduction in maximal PASI improvement from baseline by >50%). At core study baseline, all subjects had a PASI ≥12. Absolute change from core study baseline PASI was calculated. Multiple imputation was used for missing data. Safety and tolerability of secukinumab up to Wk 104 were also evaluated.

Results: A majority of subjects in the 300 mg (87.1%) and 150 mg (72.8%) continuous-treatment arms reached Wk 104 without relapse, vs only 16.0% and 12.7%, respectively, in the 300 mg and 150 mg treatment-withdrawal arms. In the continuous-treatment arms, mean (median; range) PASI was reduced from 22.1 (19.8; 11.2-72.0) at core study baseline to 1.6 (0.6; 0.0-23.4) over 104 wks with secukinumab 300 mg (n = 335 at Wk 104), and from 22.4 (19.2; 12.0-72.0) to 2.6 with 150 mg (n = 239 at Wk 104). Reductions in mean PASI at Wk 52 [from 22.1 to 1.0 with 300 mg (n = 363) and from 22.9 to 1.8 with 150 mg (n = 297)] were sustained to Wk 104. In the 300 mg treatment-withdrawal arm (n = 136), mean PASI was reduced in 27 subjects who experienced relapse from 13.0 one wk following relapse to 1.7 twelve wks after retreatment (from Wk 4 after relapse). In the 150 mg treatment-withdrawal arm (n = 123), mean PASI was reduced from 13.1 following relapse to 2.9 twelve wks after relapse and retreatment (n = 50). No new or unexpected safety findings were identified. Immunogenicity was low and consistent with the core studies.

Conclusions: Continuous treatment with either secukinumab 300 mg or 150 mg achieved strong and sustained reductions in PASI over 2 years, with no new or unexpected safety findings. Patients who relapsed following treatment withdrawal at Wk 52 regained response upon retreatment.

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Secukinumab provides more effective relief from psoriasis impact on personal relationships and influence on clothes worn than etanercept and placebo

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Introduction and objectives: Secukinumab is highly efficacious in the treatment of moderate to severe plaque psoriasis, with fast onset, a sustained effect, and a favorable safety profile. The objective of the current pooled analysis is to evaluate its impact on personal relationships and clothes worn as measured by the Dermatology Life Quality Index (DLQI).

Materials and methods: Patients aged ≥18 years were randomized 1:1:1 in ERASURE to subcutaneous treatment groups (secukinumab 300 mg, secukinumab 150 mg, and placebo) and 1:1:1:1 in FIXTURE (including an etanercept 50 mg twice-weekly group). The DLQI was administered at baseline, Weeks 1, 8, 12, 24, 36, and 52, with total, subscale, and item scores computed at all visits. This analysis used data for secukinumab 300 mg and etanercept from baseline to Week 52, placebo data up to Week 12, and focused on the personal relationship subscale (q8 and q9) and items assessing the influence on clothes worn (q4), impact on relationships with partners/close friends/relatives (q8), and sexual difficulties (q9). Treatment differences in mean scores were evaluated using van Elteren and proportions of DLQI subscale and item responders (score = 0, indicating no impact) using Chi-square statistics.

Results: Subjects on secukinumab (n = 572) achieved greater mean improvement in the personal relationship subscale and q4, q8, and q9 than subjects on placebo ($n = 572$; all $P < .0001$) and etanercept ($n = 319$; personal relationships: $P < .05$ at Weeks 8 & 12; q4: all $P < .0001$; q8: $P < .05$ at Weeks 8 & 12; q9: all $P < .01$). The response rates were higher for secukinumab 300 mg than for placebo (all $P < .0001$; personal relationships Week 12 response rates: 48% vs 16%; q4: 58% vs 12%; q8: 45% vs 16%; q9: 37% vs 10%) and etanercept (personal relationships: all $P < .05$ except for Weeks 4 & 36; q4: all $P < .05$; q8: all $P < .05$ except for Weeks 4 & 36; q9: numerically higher starting at Week 8; personal relationships Week 12 response rates: 48% vs 38%, Week 52: 55% vs 47%; q4 Week 12: 58% vs 37%, Week 52: 66% vs 47%; q8 Week 12: 45% vs 37%, Week 52: 52% vs 45%; q9 Week 12: 37% vs 34%, Week 52: 40% vs 36%).

Conclusions: Secukinumab 300 mg provides greater improvements and more effective relief from psoriasis impact on personal relationships and clothing worn than etanercept and placebo.

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Secukinumab provides more effective relief from skin-related quality-of-life impact than etanercept in moderate to severe psoriasis

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Introduction and objectives: Secukinumab is highly efficacious in the treatment of moderate to severe plaque psoriasis, with early onset, a sustained effect, and a favorable safety profile. This pooled analysis focuses on evaluating the impact of secukinumab treatment versus etanercept on skin-related quality of life as measured by the Dermatology Life Quality Index (DLQI).

Materials and methods: Patients aged ≥ 18 years were randomized 1:1:1 in ERASURE to subcutaneous treatment groups (secukinumab 300 mg, secukinumab 150 mg, and placebo) and 1:1:1:1 in FIXTURE (including an etanercept 50 mg twice-weekly group). The DLQI was administered at baseline and Weeks 4, 8, 12, 24, 36, and 52 with total, subscale, and item scores computed at all visits. This analysis used secukinumab 300 mg and etanercept data from baseline to Week 52. DLQI response was defined as no effect of skin problems on health-related quality-of-life (total score of 0 or 1, subscale of 0, and item score of 0). The effects of treatment on DLQI total scores, subscale scores (symptoms/feelings, daily activities, leisure, work/school, personal relationships, and treatment), and item scores were evaluated using the van Elteren and proportions of DLQI responders using Chi-square statistics.

Results: Subjects treated with secukinumab 300 mg (n = 572) achieved greater mean improvement in DLQI total, 4 out of 6 subscales (all $P < .05$; symptoms/feelings, daily activities, work/school [except at Week 24], and treatment), and 8 out of 10 item scores (all $P < .05$; q1: itchy, sore, painful, stinging; q2: embarrassed; q3: shopping, home, garden; q4: clothing worn; q5: social or leisure activities; q7: work or studying (except at Week 24); q9: sexual difficulties; q10: treatment problems) than subjects treated with etanercept (n = 326) from Week 4 through Week 52. Secukinumab 300 mg achieved higher DLQI response rates for DLQI total and 5 subscales (except personal relationships) than etanercept starting at Week 4 through Week 52 (all $P < .05$ except personal relationships). Item-level response rates were numerically higher for secukinumab 300 mg versus etanercept for all items ($P < .05$ Week 8-52 for q1, q2, q3, q4, q5, q7, q10).

Conclusions: Overall, secukinumab provides greater improvements and relief from skin-related quality-of-life impact than etanercept in psoriasis.

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Secukinumab provides more effective relief from skin-related quality-of-life impact than placebo in moderate to severe psoriasis

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Introduction and objectives: Secukinumab is highly efficacious in the treatment of moderate to severe plaque psoriasis, starting at early time points, with a sustained effect and a favorable safety profile. This pooled analysis focuses on evaluating the impact of secukinumab treatment versus placebo on skin-related quality of life as measured by the Dermatology Life Quality Index (DLQI).

Materials and methods: Patients aged ≥ 18 years were randomized 1:1:1 in ERASURE to subcutaneous treatment groups (secukinumab 300 mg, secukinumab 150 mg, and placebo) and 1:1:1:1 in FIXTURE (including an etanercept 50 mg twice-weekly group). The DLQI was administered at baseline and Weeks 4, 8, 12, 24, 36, and 52 with total, subscale, and item scores computed at all visits. This analysis used secukinumab 300 mg and placebo data from baseline to Week 12. DLQI response was defined as no effect of skin problems on health-related quality of life (total score of 0 or 1, subscale of 0, and item score of 0). The treatment effects on DLQI total scores, subscale scores (symptoms/feelings, daily activities, leisure, work/school, personal relationships, and treatment), and item scores were evaluated. Proportions of DLQI responders were also compared.

Results: Subjects treated with secukinumab 300 mg (n = 572) achieved greater mean improvement in DLQI total, subscale, and item scores than subjects treated with placebo (n = 572) from Week 4 through Week 12 (all $P < .001$). Secukinumab 300 mg achieved higher DLQI response rates for total, subscales, and items than placebo at all visits through Week 12 (all $P < .001$; Week 12 DLQI 0/1: 58% vs 8%; symptoms/feelings: 48% vs 4%; daily activities: 59% vs 12%; leisure: 56% vs 17%; work/school: 52% vs 21%; personal relationships: 48% vs 16%; treatment: 55% vs 18%; q1—itchy, sore, painful, stinging: 56% vs 5%; q2—embarrassed: 58% vs 10%; q3—shopping, home, garden: 54% vs 21%; q4—clothing worn: 58% vs 12%; q5—social or leisure activities: 57% vs 18%; q6—sports: 43% vs 17%; q7—work or studying: 52% vs 21%; q8—partner/friend/relative: 45% vs 16%; q9—sexual difficulties: 37% vs 10%; q10—treatment problems: 53% vs 18%).

Conclusions: Secukinumab provides greater improvements and relief from skin-related quality-of-life impact than placebo in moderate to severe psoriasis.

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Secukinumab treatment does not induce blood pressure change in subjects with moderate to severe plaque psoriasis: Results from the FIXTURE study

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Introduction: Psoriatic disease is known to be associated with various comorbidities, one of which is high blood pressure. Secukinumab, a fully human monoclonal antibody that selectively targets IL-17A, is highly efficacious in the treatment of moderate to severe psoriasis, starting at early time points, with a sustained effect and a favorable safety profile. Here we analyze data from a large phase 3 study (FIXTURE) to assess the effect of secukinumab treatment on blood pressure in subjects with moderate to severe psoriasis.

Methods: In this double-blind, placebo-controlled study, subjects (N = 1306) with moderate to severe psoriasis were randomized (1:1:1:1) to subcutaneous secukinumab (300 mg or 150 mg), etanercept (ETN, 50 mg) or placebo (PBO). Subjects received secukinumab at Baseline, Weeks 1, 2 and 3, and then every 4 weeks from Week 4 to 48. Changes in sitting systolic and diastolic blood pressure and pulse were assessed in secukinumab 300 mg (n = 312), secukinumab 150 mg (n = 315) and ETN (n = 303) groups.

Results: Demographics and baseline characteristics were comparable across all treatment arms. At Baseline, diastolic blood pressure was 80.0 mmHg in subjects receiving secukinumab 300 mg, 81.0 mm Hg in subjects receiving secukinumab 150 mg and 79.8 mm Hg in subjects receiving ETN. Baseline systolic blood pressure was 126.7 mm Hg, 128.1 mm Hg and 126.3 mm Hg in subjects receiving secukinumab 300 mg, 150 mg or ETN, respectively. At Week 52 diastolic blood pressure was 80.3 mm Hg, 81.0 mm Hg and 80.2 mm Hg and systolic pressure was 126.1 mm Hg, 127.4 mm Hg and 125.9 mm Hg, respectively for subjects receiving secukinumab 300 mg, 150 mg or ETN. The change in diastolic blood pressure from Baseline to Week 52 was 0.4 mm Hg, 0.0 mm Hg, and 0.2 mm Hg, and change in systolic blood pressure was -0.4, -1.0 and -0.6 mm Hg for subjects receiving secukinumab 300 mg, 150 mg and ETN, respectively. Mean sitting pulse at Baseline was 72.8 bpm, 74.6 bpm and 74.0 bpm for subjects receiving secukinumab 300 mg, 150 mg and ETN, respectively, with a change from Baseline to Week 52 of, -0.6, -0.4, and -0.7 bpm, respectively.

Conclusions: Secukinumab treatment was not associated with clinically relevant changes in blood pressure or pulse in subjects with moderate to severe plaque psoriasis in the phase 3 FIXTURE study.

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Secukinumab treatment provides faster and more effective relief from patient-reported quality-of-life impact than ustekinumab in subjects with moderate to severe plaque psoriasis

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Background: Secukinumab, a fully human monoclonal antibody (mAb) that selectively targets IL-17A, is highly efficacious in the treatment of moderate to severe plaque psoriasis, starting at early time points, with a sustained effect and a favorable safety profile. CLEAR is a phase 3b study comparing the efficacy and safety of secukinumab versus ustekinumab, an anti-IL-12/23 mAb, in adults with moderate to severe plaque psoriasis. This analysis focused on the treatment effect on skin-related quality of life as measured by the Dermatology Life Quality Index (DLQI).

Methods: Data from baseline to week 16 for patients aged ≥ 18 years randomized 1:1 to subcutaneous treatment groups (secukinumab 300 mg and ustekinumab 45 mg or 90 mg according to body weight at baseline) were used for this analysis. The DLQI was administered at baseline and weeks 4, 8, 12, and 16 with total and subscale scores computed at all visits. DLQI response was defined as no effect of skin problems on health-related quality of life (DLQI total score of 0 or 1).Time to response was computed as the period from the randomization date to the time when DLQI 0/1 response had occurred. Median time to response was compared between treatment groups using Kaplan-Meier methods with a log-rank test.

Results: Mean (SD) baseline DLQI total scores were similar for both treatment arms. secukinumab 13.4 (7.63), ustekinumab 13.2 (7.57). The mean DLQI total score as well as all subscale scores (symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment scores) improved (decreased) continuously over the treatment period in both treatment groups, with more pronounced improvements in the secukinumab arm than the ustekinumab arm at all visits (weeks 4, 8, 12, 16).($P < .001$ on DLQI total score). Up to week 16, 80.7% of subjects treated with secukinumab achieved DLQI response (0/1) versus 69.3% treated with ustekinumab ($P < .0001$). The median time to DLQI response (0/1) was significantly shorter for secukinumab compared to ustekinumab (8 weeks vs 12 weeks, $P < .0001$).

Conclusion: Secukinumab treatment provides stronger and faster relief from patient-reported quality of life than ustekinumab in patients with moderate to severe plaque psoriasis.

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Secukinumab treatment provides more effective relief from patient-reported psoriasis-related pain, itching, and scaling than ustekinumab

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Background: Secukinumab is highly efficacious in the treatment of moderate to severe plaque psoriasis, with fast onset, a sustained effect, and a favorable safety profile. CLEAR is a phase 3b study comparing the efficacy/safety of secukinumab versus ustekinumab, an anti-IL-12/23 mAb, in adults with moderate to severe plaque psoriasis. This analysis examined the treatment effect on psoriasis-related pain, itching, and scaling.

Methods: This analysis used baseline to Week 16 data for patients aged ≥ 18 years randomized 1:1 to subcutaneous treatment arms (secukinumab 300 mg and ustekinumab 45 mg or 90 mg according to body weight at baseline). Psoriasis-related pain, itching, and scaling over the last 24 hours were assessed using a 0-10 numerical rating scale with higher scores indicating greater severity. Mean treatment difference at Week 16 was examined via analyses of covariance adjusting for geographical region, body weight stratum, and baseline score. The percentage of subjects reporting complete relief of symptoms (score = 0) was compared between treatment arms. Time to complete relief was computed as the period from randomization to the Week when a symptom score of 0 occurred. Median time to complete symptom relief was compared between treatment arms using Kaplan-Meier methods with a log-rank test.

Results: The full analysis set included 336 subjects randomized to secukinumab 300 mg and 339 subjects to ustekinumab. Mean changes from baseline to Week 16 for pain, itching, and scaling were significantly greater for secukinumab (−3.3, −5.0, and −5.7) than for ustekinumab (−2.8, −4.6, and −5.2; all $P < .05$). Significantly more secukinumab-treated subjects achieved complete pain (80.3% vs 69.7%), itching (64.0% vs 52.2%), and scaling (74.4% vs 56.1%) relief by Week 16 than ustekinumab-treated subjects (all $P < .05$). The median time to complete itching (12 vs 16 Weeks) and scaling relief (8 vs 16 Weeks) was significantly faster for secukinumab than for ustekinumab (both $P < .001$). The median time to pain relief was 8 Weeks for both treatment arms, but the Kaplan-Meier curves were statistically different, and the log rank test favored secukinumab ($P = .0056$).

Conclusion: Secukinumab 300 mg alleviates patient-reported, psoriasis-related pain, itching, and scaling significantly faster and better than ustekinumab.

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Secukinumab withdrawal leads to loss of treatment responses in a majority of subjects with plaque psoriasis with retreatment resulting in rapid regain of responses: A pooled analysis of two phase 3 trials

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Introduction: Here, we assessed the rates of regain of clinical responses following retreatment of subjects with moderate to severe psoriasis who had relapsed following per-protocol withdrawal of secukinumab during the extension of the ERASURE and FIXTURE studies. This abstract focuses on data up to 2 years.

Methods: In this analysis subjects who had PASI 75 responses at the end of the core studies (Week [Wk] 52) were randomized in the extension study 2:1, to continue on the same dose of secukinumab or receive placebo (PBO) every 4 wks. Subjects who relapsed in the two PBO arms (300 mg-PBO and 150 mg-PBO) were retreated with secukinumab upon relapse. Relapse was defined as a loss of >50% of the maximum PASI gain compared with Baseline in the core studies.

Results: In total, 995 subjects entered this part of the extension study; the treatment groups were comparable with respect to Wk 52 Baseline characteristics. The percentage of subjects in the continuous-treatment groups who reached Wk 104 without relapse was 87.1% (secukinumab 300 mg, N = 363) and 72.8% (secukinumab 150 mg, N = 301). In the treatment-withdrawal groups, 16.0% (secukinumab 300 mg-PBO, N = 181) and 12.7% (secukinumab 150 mg-PBO, N = 150) reached Wk 104 without relapse. In patients in the 300 mg withdrawal group who did relapse and were re-treated, 94.8% of subjects re-captured PASI 75, 70.3% PASI 90, and 38.4% PASI 100 responses after twelve wks of re-treatment with secukinumab 300 mg. There were no new or unexpected safety findings in the extension study.

Conclusion: Secukinumab provided strong and sustained efficacy over 104 wks, clearing psoriasis while maintaining a favorable safety profile. In subjects relapsing after being withdrawn from therapy, retreatment with secukinumab restored efficacy in the vast majority of patients by 12 wks post restart of treatment.

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Secukinumab, a new anti–IL-17a biologic therapy, induces rapid clinical, histologic, and molecular resolution of psoriasis while preserving full T cell activation potential

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Introduction: We report the histopathologic and molecular basis of disease resolution, and T cell activation in subjects treated with secukinumab.

Methods: Moderate to severe plaque psoriasis patients were administered 300 mg secukinumab (n = 24) or placebo (PBO) (n = 12) for 12 wks. PASI score and biopsies of lesional (LS) and non-lesional (NL) skin were obtained at Baseline (BL), Wk 1 or 4, and 12. and biopsies were assessed for epidermal growth, differentiation and maturation, mitotic rate, T-cells, and monocyte derived cell types. Primary endpoint: % of subjects attaining skin histological disease reversal by Wk 12. Activation of circulating T-cells was evaluated ex vivo by quantifying cell activation markers. Transcript profiles were measured and compared to clinical and histological endpoints.

Results: Histologic disease reversal by Wk 12: 14/23 (61%), secukinumab; 0/12 (0%), PBO ($P < 001$). PASI90 response Wk 12: 14/24 (58%), secukinumab. Histological disease reversal correlated with % ΔBL PASI score ($r = -0.77$, $P < 001$). Inflammatory infiltrates in LS were reduced by secukinumab, but background levels of immune cells remained in NL and LS skin. Secukinumab did not affect ex vivo T cell activation at Wk 4. Progressively, LS transcript profile reverted to that of NL skin from Wk 1 to Wk 12. Secukinumab caused significant reduction in upregulated IL-17-pathway genes and beta-defensin-2, both in LS skin and in circulation. Expression of LS transcripts mirrored low response, but residual LS transcript expression persisted even in responders (a phenomenon termed "molecular scar").

Conclusions: Secukinumab has rapid and profound effects on psoriasis skin histopathology and psoriatic signature genes, confirming that its target IL-17A is a major driver of pathophysiologic changes in psoriatic skin in a majority of patients. Resident skin immune cells and responses to global T-cell activation were not altered by secukinumab. The authors acknowledge the contribution to this research of Nicole Hartmann, Thomas Peters, and Anke Hasselberg.

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3377

Secukinumab-treated subjects experience low rates of Candida and recurrent Candida infections: A pooled analysis from 10 phase 2 and 3 clinical studies in psoriasis

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Introduction: Interleukin (IL)-17 signaling is important for mucocutaneous defense against Candida albicans and genetic deficiency of IL-17 results in compromised Candida immunity. Therefore, subjects receiving anti-IL17A therapies may be at increased risk of Candida infections. Clinical trials have shown that secukinumab, a fully human monoclonal antibody that selectively targets IL-17A, is highly efficacious in the treatment of moderate to severe psoriasis (PsO).

Methods: We conducted a pooled analysis of Candida infections from 10 randomized, phase 2/3 PsO studies in 3430 subjects, including 1410 subjects treated with secukinumab 300 mg, 1395 with secukinumab 150 mg, and 323 subjects on etanercept (ETN).

Results: During the first year of treatment, 41/1410 (2.9%) subjects on secukinumab 300 mg, 21/1395 (1.5%) on secukinumab 150 mg and 4/323 (1.2%) of subjects on ETN experienced Candida infection. Of these subjects, some experienced more than one episode of Candida (recurrent candidiasis). 14/41 (34%) on secukinumab 300 mg, 1/21 (5%) on secukinumab 150 mg, and 2/4 (50%) on ETN. The number of Candida episodes in the first year was mostly 1 or 2 (3 episodes occurred in one subject on secukinumab 300 mg and in one subject on ETN), and mostly recurred within the same location (oral, vulvovaginal, interrigo). In about ~75% of subjects with recurrent Candida, there were confounding factors, including antibiotic use, but there was no concomitant diabetes mellitus reported. All infections were nonserious, resolved spontaneously or responded to standard treatment, and none led to treatment discontinuation. Eight subjects with recurrent Candida in the first year on secukinumab 300 mg were enrolled into a long-term extension study to continue receiving 300 mg therapy; the majority of these subjects (5) did not experience any Candida infection in the second year of treatment.

Conclusions: Candida infections were uncommon in subjects with moderate to severe PsO treated with secukinumab, and recurrent infections were even less uncommon. Both were more likely to happen in the first year of treatment and may have been dependent on confounding factors. The data further suggest that such infections are easily managed and do not impact the course of secukinumab therapy.

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Selective blockade of IL-23p19 with BI 655066 is associated with clinical responses superior to ustekinumab in patients with moderate-to-severe plaque psoriasis: Results from a 48-week phase II study

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IL-23 is pivotal for induction and maintenance of the central inflammatory axis in psoriasis. BI 655066, a humanized IgG1 monoclonal antibody that selectively inhibits IL-23, was compared with the IL-12/23 inhibitor ustekinumab (UST) in patients with moderate-to-severe chronic plaque psoriasis (NCT02054481). In this multicenter, randomized, double-blind (within BI 655066 dose groups) phase II study, 166 patients were assigned to receive subcutaneous injections of BI 655066 at three different dose regimens (18 mg single injection; 90 mg or 180 mg at Weeks 0, 4, and 16) or UST (45 mg or 90 mg, based on body weight, at Weeks 0, 4, and 16). Psoriasis Area and Severity Index (PASI) was assessed at Weeks 0, 1, 2, 4, 6, and 8, followed by assessment every 4 weeks thereafter through to Week 48. In patients with psoriatic arthritis (PsA), pain was assessed by visual analog scale and expressed as median percentage change from baseline. Safety was assessed at all visits by recording adverse events (AEs). BI 655066 had a rapid onset of effect with 69% and 66% of patients (180 mg and 90 mg, respectively) achieving PASI 50 by Week 4, vs 45% of UST patients. By Week 8, 83% and 80% of BI 655066 patients (180 mg and 90 mg, respectively) had achieved PASI 75 vs 60% of UST patients. By Week 12, the proportion of patients achieving PASI 90 (primary endpoint) was 81% and 73% for 180 mg and 90 mg BI 655066 arms vs 40% for UST. Body weight had little impact on efficacy for BI 655066. At Week 20, 90% and 76% of BI 655066 patients (180 mg and 90 mg, respectively) achieved PASI 90 vs 55% for UST; and 62% and 51% of BI 655066 patients had complete clearing of lesions (PASI 100) vs 25% of UST patients. Clinical responses were sustained at high levels beyond Week 36 for the 180 mg and 90 mg BI 655066 dose groups. In patients with PsA, there was a greater decrease in pain at Week 12 observed with BI 655066 (180 mg and 90 mg, pooled) vs UST (68% vs 57%). AEs were similar between treatment arms with no dose–response relationship noted for any AE. Seven patients with serious AEs were reported (four in the 18 mg and two in the 90 mg BI 655066 arms, and one in the UST arm); all were considered unrelated to study medication or procedures. Selective blockade of IL-23 by BI 655066 demonstrates superior efficacy with a sustained duration of response, and a more rapid onset, compared with blockade of IL-12/23 by UST, further supporting the central role for IL-23 in psoriasis pathogenesis.

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Selective blockade of IL-23p19 with BI 655066 is associated with significant improvement in QoL outcomes compared with ustekinumab in patients with moderate-to-severe plaque psoriasis

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Psoriasis is a chronic, immune-mediated, inflammatory disease that has a considerable negative impact on patient quality of life (QoL). BI 655066, a humanized IgG1 monoclonal antibody that selectively inhibits the p19 subunit of IL-23, has demonstrated superiority to ustekinumab in the proportion of patients who achieved Psoriasis Area and Severity Index (PASI) 90 at Week 12 (Papp K et al. AAD Annual Meeting, 2015). Here, we assess the effect of BI 655066 compared with ustekinumab on health-related QoL in patients with moderate-to-severe plaque psoriasis (NCT02054481). In this multicenter, randomized, double-blind (within BI 655066 dose groups) Phase II study, 166 patients were assigned to receive subcutaneous injections of BI 655066 at three different dose regimens (18 mg single injection, 90 mg or 180 mg at Weeks 0, 4, and 16) or ustekinumab (45 mg or 90 mg, based on body weight, at Weeks 0, 4, and 16). Dermatology Life Quality Index (DLQI) and the EuroQol-5D (EQ-5D) were completed at Weeks 0, 12, 24, and 48. The median percentage changes from baseline in DLQI total score (analyzed descriptively and by the van Elteren test) were compared with ustekinumab at Weeks 12 and 24. The proportion of patients achieving a DLQI score of 0 or 1 was also assessed. The EQ-5D index score was analyzed descriptively. BI 655066 results are reported for the pooled 90 mg and 180 mg arms. At baseline, the median DLQI score was 13.0 for patients randomized to BI 655066, compared with 16.0 for those randomized to ustekinumab. Mean EQ-5D index score was 0.7 in both treatment arms. At Week 12, the median percentage improvement in DLQI score was greater for patients receiving BI 655066 than for those receiving ustekinumab (100% vs 90.6%, respectively; $P = .0304$). The proportion of patients with a DLQI score of 0 or 1 at Week 24 was 80% for BI 655066 patients compared with 61% for ustekinumab patients. At Week 12, BI 655066 patients were observed to have a ~50% greater improvement in mean EQ-5D index score compared with ustekinumab patients (0.5 vs 0.2, respectively). This was sustained at Week 24. In patients with moderate-to-severe plaque psoriasis, selective blockade of IL-23 by BI 655066 demonstrated superior efficacy and provides significant improvement in QoL outcomes compared with ustekinumab.

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Single transition from adalimumab to ABP 501: Evaluation of immunogenicity in a phase 3 study in subjects with moderate to severe plaque psoriasis

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Background and objectives: ABP 501 is being developed as a biosimilar candidate to adalimumab, a fully human recombinant monoclonal antibody and has the same amino acid sequence as adalimumab. Antibodies to adalimumab are associated with lower serum adalimumab concentration. Here we report results of immunogenicity evaluation after single transition from adalimumab to ABP 501 in a phase 3 study of subjects with moderate to severe plaque psoriasis.

Methods: In this double-blind, active-controlled study subjects were randomized (ABP 501: n = 175; adalimumab: n = 175) to receive study treatment subcutaneously 80mg on week 1/day 1 and 40mg at week 2 and every 2 weeks thereafter. At week 16, subjects with ≥PASI 50 remained on study for up to 52 weeks and were rerandomized in a blinded fashion such that all subjects initially randomized to ABP 501 continued on ABP 501 (group A/A); those on adalimumab either continued on adalimumab (group B/B) or switched to ABP 501 (group B/A). Immunogenicity was assessed for each sample at weeks 1,4,16,20,32,52 using validated electrochemiluminescent assays for ABP 501 and adalimumab: a sample was considered positive if either assay was positive. Noninferiority (NI) was evaluated by comparing the upper bound of 95% CI of the difference in incidence of developing antidrug antibodies (ADAs) with a margin of 21.7%.

Results: Through week 16, incidence of binding ADAs was 55.2% in ABP 501 and 63.6% in adalimumab groups; upper bound of 95% CI (-18.2%, 2.0%) fell within NI margin of 21.7%. Incidence of neutralizing ADAs was 9.8% and 13.9% respectively. After single transition from adalimumab to ABP 501, at week 20 incidence of binding ADAs was 60.5%, 69.6% and 66.2% for groups A/A, B/B and B/A; 95% CI for difference between groups A/A and B/B was (-19.6%, 4.5%) and between groups B/A and B/B was (-16.5%, 11.3%); both upper bounds fell within the NI margin. Incidence of neutralizing ADAs was 9.9%, 13.9% and 14.3%. ADA incidence at week 52 was 68.4%, 74.7% and 72.7% in the groups A/A, B/B and B/A; 95% CI for difference between groups A/A and B/B was (-15.7%, 7.6%) and between groups B/A and B/B was (-13.5%, 13.0%); both upper bounds fell within the NI margin. Incidence of neutralizing ADAs was 13.8%, 20.3% and 24.7%.

Conclusions: Incidence of ADAs was similar and comparable between ABP 501 and adalimumab before and after rerandomization. Single transition to ABP 501 did not result in altered or increased immunogenicity over 52 weeks.

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Six-year interim results from the ESPRIT 10-year postmarketing surveillance registry of adalimumab for moderate to severe psoriasis

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Introduction: ESPRIT, a 10-year (yr) international observational registry, is prospectively evaluating long-term effectiveness and safety of adalimumab (ADA) in patients (pts) treated for moderate/severe plaque psoriasis (NCT00799877). Interim safety and effectiveness over the first 6-yrs of the registry are reported.

Methods: ESPRIT enrolled pts continuing ADA treatment from a current prescription or previous study participation. The All-Treated Population (All-Rx) received at least 1 ADA dose in the registry, including a subgroup of pts initiating ADA within 4 weeks of entering the registry (New-Rx). Pts are evaluated 3 and 6 months (mos) postenrollment, then every 6 mos up to 10 yrs. The as-observed effectiveness parameter was Physician's Global Assessment (PGA). A standardized mortality ratio of <1.0 indicates the observed number of deaths was below expected in an age, sex, country-matched population. Incidence rates (IR) for all treatment-emergent adverse events (All-TEAEs) are reported as events/100 pt yrs of total exposure, occurring from initial through last ADA dose, excluding AEs during treatment interruptions.

Results: From 26 Sept 2008 through 30 Nov 2014, 6056 pts were enrolled and dosed (All-Rx), including 2559 (42.3%) New-Rx. Median registry exposure was 993 days for All-Rx and 881 days for New-Rx (range 1-2257 days/group). 1057 (17.5%) All-Rx and 566 (22.1%) New-Rx discontinued the registry; most frequent reason was lost to follow-up (8.2% and 10.9%, respectively). For All-Rx at baseline, 57.7% were male; median age was 47 yrs (range 18-94 yrs) and median weight was 87 kg (range 41-252 kg). The IR for All-TEAEs (All-Rx) was: overall 21.8; malignancies 0.9 (melanoma <0.1, lymphoma <0.1, nonmelanoma skin cancer 0.6); cardiovascular-related (cerebrovascular accident 0.1, congestive heart failure <0.1, myocardial infarction 0.1); serious infections 1.0, opportunistic infections excluding oral candidiasis and TB <0.1, active TB <0.1, TB conversion <0.1. Standard mortality ratio was 0.28 [95% CI: 0.19, 0.40]. Pts achieving PGA 'clear' or 'minimal' at 12, 24, 36, 48, 60, 72 mos of treatment were 2615/4586 (57.0%), 2277/3896 (58.4%), 1618/2774 (59.4%), 1206/1907 (63.2%), 440/704 (62.5%), 20/36 (55.6%), respectively.

Conclusions: No new safety signals were observed with ADA treatment during this interim. Observed number of registry treatment-emergent deaths was below that expected. As-observed effectiveness remained stable through 72 mos.

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