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Natalizumab Treatment for Multiple Sclerosis in Clinical Practice

Dinah Thyerlei, Lynda Hillman, Valerie Woolvett, Dora Krasucki, Annette Wundes, Seattle, WA

OBJECTIVE: To describe clinical and MRI outcome after treatment with natalizumab for up to 3.5 years. **BACKGROUND:** Natalizumab, an alpha4 integrin antagonist, is indicated for use in relapsing multiple sclerosis (MS), but can cause rare severe side effects (PML, other infections). With the recent increase of PML cases reported in late 10/2009, possible association with previous immune suppression and duration of natalizumab treatment is discussed. **DESIGN/METHODS:** Retrospective observational study of 169 consecutive MS patients treated with natalizumab at the University of Washington. Clinic progression, MRI and laboratory monitoring including antibody-positivity, side effects and causes for discontinuation were evaluated. **RESULTS:** To date, 169 patients received 1–41 monthly infusions (mean 18.7); an overall total of 3126 infusions. 59 patients have been treated for >2 years. Patients had failed multiple (1–4) disease-modifying therapies before; a single patient was treatment-naïve. Clinical disease progression was seen in 11 patients, 8 of them continued natalizumab. Annual follow-up MRI in almost all patients was unchanged. Eight patients with positive anti-natalizumab antibodies demonstrated either hypersensitivity reaction (n=6) or disease progression (n=2). Two (1%) patients developed shingles while on natalizumab. Thirty patients (17.7%) discontinued natalizumab due to patient's decision (no benefit/too high risk), hypersensitivity reaction, disease progression, side effects or intended pregnancy. **CONCLUSIONS/RELEVANCE:** In our cohort natalizumab was found to be very effective in stabilizing the course of disease in the majority of patients. So far, we have not observed any severe side effects. Updated information, in particular in light of recent new PML cases and possibly increased PML risk with previous immune suppression and treatment duration, will be presented.

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Use of Glatiramer Acetate during Pregnancy: Offering Women a Choice

Aaron E. Miller, Jennifer L. Reardon, New York, NY

OBJECTIVE: To determine the willingness of women to use glatiramer acetate (GA) during attempted conception and throughout pregnancy and to assess outcomes of pregnancy in women remaining on GA. **BACKGROUND:** MS frequently affects women who desire pregnancy. Those taking disease-modifying agents face a dilemma. If they discontinue medication prior to attempting to conceive, they will lose drug protection. However, continuing medication may have risks to the fetus. Because GA has a Category B rating, we have prospectively suggested that women consider remaining on GA while attempting conception and during pregnancy. **DESIGN/METHODS:** Women contemplating pregnancy were counseled about the pros and cons of remaining on GA while attempting to conceive and during pregnancy. They were told (1)they would have no protection from MS while off medication. (2)pregnancy is associated with lower relapse rate compared to non-pregnancy periods. (3)relapse rate is higher during the post-partum period, and (4)resumption of medication immediately after delivery might not be adequately protective during that more vulnerable period. The term "Category B pregnancy rating" was explained and the difficulty of knowing whether GA was truly safe was emphasized. Patients then decided whether to continue GA. **RESULTS:** 35 women were counseled about the potential use of GA during pregnancy. Only 8 patients initially discontinued GA; 4 remained on GA, but discontinued when pregnant. Among the 23 women who remained on GA, 27 pregnancies have occurred; 18 resulted in normal children and 3 are ongoing. One minor congenital anomaly required no intervention. Two pregnancies were terminated because of Trisomy 21 fetuses, thought unrelated to GA. One ectopic pregnancy and 3 other miscarriages occurred (2 in one patient after IVF). **CONCLUSIONS/RELEVANCE:** Most women offered the option of remaining on GA for pregnancy choose to continue the medication. These results in a limited number of patients suggest that GA may be safely continued during pregnancy.

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Immunological Response to Glatiramer Acetate in MS Patients after Different Pretreatments – The CopImmunoNet Study

Nina Kleiner, Tjalf Ziemssen, Dresden, Germany

OBJECTIVE: To investigate the immunological response to the MS immunomodulator glatiramer acetate (GA) in MS patients starting de novo on whether the immunological and so probably the clinical response to GA is altered by different pretreatments (IFN, MX, NA). As antigen-based therapy, GA is believed to develop its treatment effects by the induction of specific immunological changes ranging from altered monocyte function over modified T cell function up to GA-specific antibodies. As some MS treatments are limited regarding their duration (MX, probably NA), it is of high clinical interest what are the immunological effects of different MS pretreatments on the following GA treatment. **DESIGN/METHODS:** As a prospective multicenter trial (CopImmunoNet Trial), 32 patients starting de novo on GA, 19 patients switching from IFN to GA, 5 patients deescalating from MX to GA and 4 patients switching from NA to GA were assessed over 1 years by an extensive immunological protocol in combination with detailed clinical analysis. Proliferation and cytokine production (3H thymidine and CFSE) of PBL to GA and tetanus toxoid as well as GA-specific-antibodies were analyszed at various timepoints. **RESULTS:** There were no significant differences regarding the decrease of proliferation to GA over time in all patients starting on GA which could be first seen 3 months after starting GA. TH1-TH2 shift was present in all patients at month 6 irrespective the different pretreatments. Analysis of serum antibodiesto GA did not demonstrate significant differences between the different groups. All patients did clinically well. **CONCLUSIONS/RELEVANCE:** From the immunological point, GA seems to be useful platform drug which can be used independent of different pretreatments (IFN, NA, MX) as no immunological differences were seen between patients started de novo on GA and patients switched on GA. **Supported by:** TEVA Pharma/Sanofi Aventis Germany.

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Development and First Evaluation of the New Patient Management and Documentation System MSDS 3D for Patients with Multiple Sclerosis

Tjalf Ziemssen, Fabian Kratzsch, Marco Eulitz, Raimar Kempcke, Nina Kleiner, Dresden, Germany

OBJECTIVE: To develop and evaluate a new Multiple Sclerosis patient management software and hardware MSDS 3D for guideline-based management and ducumentation of MS patients. **BACKGROUND:** Multiple Sclerosis Documentation System (MSDS) has been developed as standard MS documentation system in Germany since 2001 to generate data for the German MS registry. Up to now, there has been no interface to patient and nurse data for multidimensional evaluation (fatigue, depression, QoL, treatment management). As MS treatment protocols get more and more complicated with implementation of new drugs, MSDS 3D was developed to change the solely documentation to a patient management system according current guidelines. **DESIGN/METHODS:** In addition to the local hardware running MSDS, a touch-screen and internet-based module (interface to patient's mobile phone) was developed for this project using ABS-VO technology to add patient's and nurse's data using this interface. Special treatment and study modules were developed with a defined visit schedule and mandatory examinations which are documented and visualized by MSDS. Other reports eg. from neuroradiologists, ophthalmologists are implemented using the MSDS internet server. A touch screen terminal was developed for collecting patient's data. **RESULTS:** In a pilot version, MSDS 3D was tested in 100 representative patients by physicians and nurses. MSDS 3D touch screen and internet based patient module was well accepted by the patients and the physicans. As not only documentation, but patient management was provided by this software, quality of patient management was significantly improved and standardized. **CONCLUSIONS/RELEVANCE:** A first step of multidimensional documentation and patient management of MS patienrs was taken by the development and first evaluation of MS patients. There is the need not only by a softeware-guided documentation, but standardized patient management according the MS guidelines. Further studies (Repabo, X-Scale) are on the way to implement the MS management software in clinical studies and daily clinical practice.

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Intellectual Enrichment Lessens the Negative Impact of Brain Atrophy on Cognition in Multiple Sclerosis

James F. Sumowski, Glenn R. Wylie, Nancy Chiaravalloti, John DeLuca, West Orange, NJ

OBJECTIVE: To determine whether lifetime intellectual enrichment lessens the negative impact of brain disease on cognitive status in persons with Multiple Sclerosis (MS). That is, whether cognitive reserve protects MS patients from cognitive decline. **BACKGROUND:** About 50% of MS patients develop cognitive impairment, especially slowed information processing and learning / memory dysfunction. MRI markers of MS disease progression (i.e., brain atrophy) are relatively weak predictors of cognitive status. This indirect relationship between MS disease and cognition may be explained by the protective effect of lifetime intellectual enrichment, which