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(a supplement to the *Journal of Clinical Oncology*)

4606 General Poster Session (Board #G3), Sun, 2:00 PM - 6:00 PM

Comparative expression profiling with kinetic RT-PCR in paired fresh frozen and archived formalin-fixed, paraffin-embedded renal cell cancer and normal tissue. *G. Hennig, H. Paus, D. Atkins, S. Störkel; Bayer HealthCare AG, Leverkusen, Germany; HELIOS Clinic, Wuppertal, Germany*

Background: It would be a substantial progress if gene expression of tumor markers could be accurately analyzed on RNA isolated from formalin fixed paraffin-embedded (FFPE) tumor tissue which is routinely collected. To prove equivalence between fresh frozen and archived FFPE tissue RNA profiles, we quantified 12 different genes with kinetic RT-PCR in renal tumor and paired adjacent normal tissue archived for 8–14 years. **Methods:** We had access to a set of 32 clear cell renal cell cancers and its adjacent normal tissue (HELIOS Clinic, Wuppertal). Each sample existed as a FFPE tissue block and as paired fresh frozen tissue both stored over 8–14 years at RT or -80°C, respectively. RNA from FFPE tissue was isolated with a Bayer HealthCare internal silica bead-based isolation method. Each sample was analyzed with kinetic one-step RT-PCR for the gene expression of 3 housekeepers (RPL37A, GAPDH, CD63) and 9 candidate genes (EGFR, Her2/neu, Her3, Her4, EGF, TGFα, NRG1, HIF1α, VEGFα). **Results:** The comparative FFPE/fresh frozen expression data showed a good correlation over all data points (r = 0.87 for Ct values) and the tumor specific up- and down regulation of EGFR family genes and its ligands could be detected in both tissue types equally. We could clearly demonstrate the tumor specific up-regulation of EGFR (2-fold), TGFα (2-fold), VEGFα (4-fold) and down-regulation of EGF (60-fold), Her2/neu (4-fold), Her3 (2-fold) and Her4 (30-fold) in renal cell cancer for both tissue entities (fixed and fresh frozen). In addition a 3-dimensional Principal Component Analysis completely separated the renal tumor population from paired normal tissue in both tissue entities based on the differential gene expression. **Conclusions:** Here we demonstrate that a small set of genes from the EGFR family and their ligands is specifically up-/down-regulated in renal cell cancer tissue and therefore can be clearly distinguished from normal renal tissue. Furthermore, these data prove that the internal Bayer HealthCare isolation/kinetic RT-PCR detection protocol for RNA from FFPE tissue allows accurate retrospective expression profiling and validation of marker panels in archived tissue material stored for more than a decade.

4607 General Poster Session (Board #G4), Sun, 2:00 PM - 6:00 PM

Multicenter, randomized, phase III trial comparing radical retropubic prostatectomy with conventional external beam radiotherapy for localized prostate cancer: An interim report. *S. M. Di Stasi, A. Giannantoni, M. Valenti, L. Storti, F. Attisani, T. Palloni, E. A. Jannini, M. Bibas, G. Zampa; Tor Vergata University, Rome, Italy; University of Perugia, Perugia, Italy; University of L'Aquila, L'Aquila, Italy; Operative Unit of Urology, Sora (FR), Italy; S. Filippo Neri Hospital, Rome, Italy; S. Giacomo Hospital, Rome, Italy*

Background: We report the outcomes of a randomised trial comparing radical retropubic prostatectomy (RP) with conventional external beam radiotherapy (EBRT) in patients with clinically localized prostate cancer. **Methods:** Between January 1997 and September 2001, 137 patients with clinically localized diagnosed prostate cancer were randomly assigned to RP (n = 70) or EBRT (n = 67). Data collected at follow-up included evidence of clinical disease progression, survival rates and general and disease specific health-related quality of life. All data were measured by physical examination, digital rectal examination, PSA, annual TC and bone scan and questionnaire. Analysis was by intention to treat. **Results:** After a median follow-up of 67 months (range 24–88) 35 patients (32.8%) had evidence of biochemical disease progression, 22 (31.4%) in RP group and 23 (32.8%) in EBRT group respectively. The median time to biochemical failure was 55.5 months (range 1–86) in RP group and 56 (range 3–88) in EBRT group. A local progression was observed in 11 patients (15.79%) of RP group and 12 (17.9%) of EBRT group. The median time to local progression was 65 months (range 6–86) in RP group and 64 (range 6–88) in EBRT group. Distant metastases were observed in 4 patients (5.7%) in RP group and 6 (8.9%) in EBRT group. The median time to distant failure was 67 months (range 12–86) in RP group and 66 (range 12–88) in EBRT group. Death due to prostate cancer occurred in 3/70 of patients assigned to RP (4.3%) and in 1/67 of those assigned to EBRT (1.5%). A significant decrease in general HRQOL was evident only in the first month after RP ($p < 0.001$). At 2 years, patients undergoing RP report significantly worse urinary function ($p < 0.001$), but better bowel function than those treated with EBRT ($p < 0.001$). Sexual dysfunction was more prevalent in the RP than in the EBRT group (70.2% versus 61.2%). **Conclusions:** This interim analysis indicates that there was no significant difference between RP and EBRT in terms of clinical disease progression and survival rates in patients with clinically localized prostate cancer. However, additional larger sample size accrual and long-term follow-up data are warranted to confirm these results.

4608 General Poster Session (Board #G6), Sun, 2:00 PM - 6:00 PM

A phase II trial of docetaxel and samarium in patients with bone metastases from castration-refractory prostate cancer (CRPC) and a response or stabilization after induction docetaxel-estramustine. *A. Laplanche, P. Beuzeboc, J. Lumbroso, M. Di Palma, C. Theodore, D. Prapotnich, B. Escudier, J. Bouzy, V. Haddad, K. Fizazi; Institut Gustave Roussy, Villejuif, France; Institut Curie, Paris, France*

Background: Most patients (pts) with disseminated CRPC have bone metastases. Samarium is a radio-isotope with a high affinity to bone. Docetaxel is currently the standard of care in CRPC. We assess the efficacy of combining docetaxel and samarium as consolidation treatment after docetaxel-estramustine in pts with CRPC. **Methods:** This is a prospective, bi-center phase II trial. Pts with bone metastases from CRPC received docetaxel 70 mg/m^2 day 2 + estramustine 10 mg/Kg/day, day 1–5 (1 cycle every 3 weeks). Pts with a response or stabilization after 4 cycles were given consolidation therapy: docetaxel 20 mg/m^2/week x 6 weeks + samarium 1 injection during week 1 (37 MBq/Kg). Zoledronic acid was routinely used and was stopped 1 month before samarium infusion. This study used a Simon two-step design with a final target of 39 pts receiving the consolidation treatment. Biological responses were defined according to the working group criteria (Bubley, J Clin Oncol 1999). The primary endpoint was progression-free survival (PFS). **Results:** From 01/2004 to 12/2005, 43 pts were included in the trial and the accrual is over. Of the 39 pts currently fully evaluable after induction treatment, 28 (72%), 10 (26%) and 1 (3%) achieved a PSA response, stabilization, and progression, respectively. Of 30 pts currently evaluable after consolidation treatment, 20 (65%), 5 (16%) and 5 (16%) achieved a PSA response, stabilization, and progression, respectively. A pain response (defined as a decrease in pain intensity by at least 2/10 on a pain analog visual scale in pts with a baseline pain level ≥ 2/10) was achieved in 89% (16/18) after consolidation treatment. The consolidation docetaxel-samarium regimen was feasible with most pts experiencing a mild (grade 1–2) and rapidly reversible thrombocytopenia at week 5. Data on PFS and overall survival are pending. **Conclusions:** Combining docetaxel and samarium is feasible and well-tolerated. It yields a high PSA response rate and a major pain improvement in pts with bone metastases from CRPC.

4609 General Poster Session (Board #G7), Sun, 2:00 PM - 6:00 PM

Randomized phase II study comparing 4 monthly doses of ipilimumab (MDX-010) as a single agent or in combination with a single dose of docetaxel in patients with hormone-refractory prostate cancer. *E. Small, C. Higano, N. Tchekmedyian, O. Sartor, B. Stein, R. Young, J. Vestal, W. Moseley, S. Fischkoff, I. Lowy; University of California, San Francisco, San Francisco, CA; Seattle Cancer Care Alliance, Seattle, WA; Pacific Shores Medical Group, Long Beach, CA; Louisiana State University Health Sciences Center, New Orleans, LA; University Urological Research Institute, Providence, RI; Grand Strand Urology, Myrtle Beach, SC; Urology Associates of North Texas, Arlington, TX; San Diego Urology Research, San Diego, CA; Medarex, Inc., Bloomsbury, NJ*

Background: Ipilimumab is a fully human anti-CTLA-4 IgG1 monoclonal antibody that blocks CTLA-4 and augments immune responses. The current study evaluated the safety and activity of ipilimumab alone or with a single dose of docetaxel in hormone-refractory prostate cancer (HRPC). **Methods:** 43 chemotherapy naïve patients (pts) with HRPC, were treated; 23 were in arm A (ipilimumab at 3 mg/kg q 4 weeks × 4 doses) and 20 in arm B (ipilimumab as in Arm A and one dose of 75 mg/m^2 of docetaxel on day 1). **Results:** Six pts, 3 in each arm, demonstrated a decrease in PSA of > 50%. Three pts, 2 in arm A, and 1 in arm B had confirmed PSA responses with durations of 79+ days, 169+ days, and 280 days, respectively. There were no radiologic responses with these PSA responses. Thirty-six (84%) of the 43 pts experienced 1 or more adverse events considered to be related to treatment with ipilimumab. The most common adverse events included fatigue (44%), pruritus (26%), nausea (19%), rash (12%), constipation (12%), and weight loss (12%). Serious adverse events (SAEs) occurred in 18 patients (42%), who experienced 52 SAEs. The majority (42 out of 52, 81%) were judged by the Investigator to be unrelated or unlikely to be related to treatment with ipilimumab. Five of the 52 SAEs reported in 3 pts were considered to be possible immune breakthrough events (IBEs), associated with drug exposure and consistent with an immune-based mechanism of action. These were adrenal insufficiency (1), diarrhea, colitis, and melena (all in one patient) and colitis (1). One of these pts had a confirmed PSA response. **Conclusions:** Ipilimumab was well tolerated in this group of pts with HRPC. Three pts overall (6%) experienced an IBE, a phenomenon that has been correlated in other studies with efficacy. There were several confirmed responses as assessed by PSA, one of which was correlated with an IBE. There was no apparent enhancement of activity by coadministration of a single dose of docetaxel. Further studies exploring ipilimumab in prostate cancer are warranted, either as monotherapy at higher doses, or in combination with immune modulators or vaccines.