CRPC by patient subgroups (ClinicalTrials.gov; NCT00286091; Sponsored by Amgen Inc).
Methods: Men with non-metastatic CRPC at high-risk for bone metastasis (PSA value ⩾8.0 ng/mL and/or PSA doubling time ⩽10.0 months) were randomized 1:1 to receive either monthly subcutaneous denosumab 120 mg or placebo. Calcium and vitamin D supplements were encouraged. Enrollment began February 2006; primary analysis cut-off was July 2010, when >660 men had bone metastasis or died. The primary endpoint was time to first bone metastasis or death from any cause, i.e. bone metastasis-free survival. Here we assessed time to bone metastasis-free survival by patient subgroup including baseline PSA risk group (a) dual risk factors: PSA ⩾8.0 ng/mL + PSA doubling time ⩽10.0 months vs (b) single risk factor: PSA <8.0 ng/mL + ⩽10.0 months or ⩾8.0 ng/mL + >10.0 months, Gleason score (2−7 or 8−10), age (<75 years old or ⩾75 years), ethnicity (white or other), and geographic location (North America, Europe, or rest of world).
Results: 1432 men were enrolled; 716 in each arm. Denosumab significantly increased median bone metastasis-free survival by 4.2 months compared with placebo (29.5 and 25.2 months, respectively; Hazard Ratio [HR] 0.85 [0.73–0.98], $P = 0.03$). This benefit on bone metastasis-free survival was consistently observed among all patient subgroups (range of HRs 0.79–0.95). Denosumab also delayed time to symptomatic bone metastasis (0.67 [0.49–0.92]; $P = 0.01$). Primary results including efficacy and safety have been presented previously (Smith et al, AUA 2011).
Conclusion: Denosumab significantly prolonged bone metastasis-free survival compared with placebo among all men, with consistent results observed among subgroups of disease and demographic variables. This is the first large, clinical trial to demonstrate that targeting of the bone microenvironment significantly delays onset of bone metastases.

7004 ORAL

Pain Outcomes in a Randomized Phase 3 Clinical Trial of Denosumab Vs Zoledronic Acid (ZA) in Patients With Solid Tumours and Bone Metastases

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Background: Bone metastases in patients with advanced cancer commonly cause pain and can lead to skeletal-related events (SREs). Denosumab is a fully human monoclonal antibody against RANK Ligand that delayed or prevented SREs more effectively than ZA in patients with solid tumours and bone metastases in a randomized phase 3 clinical trial (Henry D et al, *J Clin Oncol*. 2010. Abstr 9133). We present here the pain outcomes for patients with solid tumours. Patients with breast or prostate tumours were not enrolled in the trial (sponsored by Amgen Inc., ClinicalTrials.gov identifier NCT00330759).
Methods: Eligible patients received 120 mg of denosumab SC or 4 mg of ZA IV every 4 weeks in a randomized, multinational, double-blind, double-dummy trial. Patient-reported pain was assessed with the Brief Pain Inventory (0: no pain-10: pain as bad as can be imagined) at baseline (BL), day 8, and before each monthly visit. Analgesic use was assessed by the 8-point Analgesic Quantification Algorithm (AQA). Analyses included time to moderate/severe pain (>4 points), proportion of patients with no/mild pain (0−4) at BL reporting moderate/severe pain by visit, time to clinically significant worsening of pain (⩾2-point increase from BL), time to clinically significant improvement in pain (⩾2 point decrease from BL), and proportion of patients shifting from no or low analgesic use (AQA ⩽ 2) at BL to strong opioid use (AQA ⩾ 3) by visit.
Results: At BL, mean worst pain scores were 4.9 points (SD=2.8) for the denosumab group (N = 799) and 5.2 points (SD=2.9) for the ZA group (N = 797). Patients with no/mild pain at BL (n = 596) experienced a delay in median time to moderate/severe pain with denosumab treatment (144 days) compared with ZA treatment (112 days) (HR 0.81, CI: 0.66−1.0, $P = 0.0499$). The proportion of patients with no/mild pain at BL reporting moderate/severe pain on study was lower at each visit with denosumab treatment than with ZA treatment. Denosumab-treated patients also experienced a delay in clinically significant worsening of pain compared with ZA-treated patients (median: denosumab 143 days, ZA 119 days; HR 0.86, CI: 0.74–0.99, $P = 0.0392$). The time to clinically significant improvement in pain was similar between treatment groups. Compared with ZA, a lower proportion of patients receiving denosumab shifted from low or no analgesic use to strong opioid use at each visit.
Conclusion: In patients with solid tumours, denosumab delayed the time to increased pain severity compared with ZA. Also, a lower proportion of patients receiving denosumab required increased analgesic use over time.

Poster Discussion Presentations (Mon, 26 Sep, 11:00−12:00)

Genitourinary Malignancies − Prostate Cancer

7005 POSTER DISCUSSION

PSA Measurement at the Fifth Week of Radiotherapy Is an Independent Predictor of Failure in Intermediate Risk Prostate Cancer Patients

R. de Crevoisier[1], T. Messai[2], P. Wibault[2], A. Bridier[2], P. Blanchard[2], J.D. Ospina[3], M. Bakkour[2], A. Bossi[2]. *[1]Centre Eugène Marquis INSERM642, Ille et vilaine, Rennes, France; [2]Gustave-Roussy, Ile de France, Villejuif, France; [3]INSERM 642, Ile et Vilaine, Rennes, France*

Background: The objective was to identify early predictor of recurrence during exclusive radiotherapy for intermediate risk prostate cancer patients.
Material and Methods: A total of 240 patients of median age 71 years (range: 50−83 years) received exclusive external beam radiotherapy (EBRT) for intermediate prognostic group prostate cancer (D'Amico classification). T stages were: stage 1 (45%) and stage 2 (55%). Gleason scores were: scores ⩽6 (57%) and score 7 (43%). Mean pre-treatment PSA (PSA0) value was 11 ng (range: 1.4−20). All the patients received a total dose of 70 Gy in 7 weeks, either in 2.0 Gy/fraction, 5 fr/week (n = 53) or 2.5 Gy/fr, 2.0 Gy/ week (n = 187). PSA was also measured at the fifth week after treatment started (PSA5). Cox regression and log-rank test were used to analyze the impact of the following variables on biochemical failure (BF: nadir + 2 ng/ml) and clinical failure (CF) (metastases): T stage, Gleason score, PSA0, PSA5, PSA ratio (PSA5/PSA0) and dose/fraction.
Results: Median follow-up was: 58 months (range: 6–235). Five year BF and CF rates were 28% (95% CI: 23%-33%) and 5.5% (95% CI: 2%-9%), respectively. Median PSA5 was 8 ng (range: 0.8−30) and median PSA ratio was 0.72 (range: 0.14−3.7).
In univariate analysis, PSA5 was found significant on BF ($p < 0.01$; odds ratio =1.13). Neither the PSA0, PSA ratio as continuous variable, T stage, the Gleason score and the dose/fr were found as predictors for BF. PSA ratio >0.8 increased significantly the risk of BF($p = 0.01$; odds ratio =2.0). In multivariate analysis, PSA ratio >0.8 remained the only predictor of BF ($p = 0.03$; odds ratio =2.3).
As there are only 13 events of CF, multivariate analysis was not feasible. In univariate analysis, neither the PSA0, PSA ratio as continuous variable, T stage nor the Gleason score were found as predictors for CF. However, PSA5 ($p = 0.01$; odds ratio =1.13) as well as PSA ratio >0.8 had a significant impact on CF (logrank test: $p = 0.04$).
Conclusions: PSA measured at 5th week of radiotherapy and PSA ratio (PSA5/PSA0) can be use as simple early predictor of recurrence among intermediate risk prostate cancer patients receiving exclusive radiotherapy. "Bad responders" (PSA ratio >0.8) could receive "intensified" treatment like androgen deprivation combined with high dose radiotherapy.

7006 POSTER DISCUSSION

Predictive Models of Rectum Toxicity in Prostate Cancer Radiotherapy

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Background: In case of prostate 3D conformal radiotherapy (3DCRT): - To identify patients and treatment predictors of rectal toxicity; - To compare the performance of different Normal Tissue Complication Probability (NTCP) models for predicting rectal toxicity.
Materials and Methods: A total of 439 patients (pts) received 3DCRT for localized prostate cancer to a median total dose of 78 Gy (range: 70 to 80 Gy), 2 Gy/fraction. Pts were selected based on the availabilityof dose-volume histograms (DVH). Median age was 67 years (45−78). History of abdominal or pelvic surgery, anticoagulant therapy (ACT) and diabetes were observed in 30%, 15% and 6% of pts, respectively. Tumour prognostic groups (D'Amico classification) were: good (7%),medium (65%)