⩾1.4 mg/dL, respectively; or any doubling of the baseline serum creatinine. Risk factor analysis was conducted using multivariate Poisson regression to adjust for varying patient observation periods.
Results: Among the 122 eligible patients, the mean observation period was 422.3 days, with an average ZA treatment period of 367.2 days (mean 10.7 infusions per patient). The mean age at the first ZA infusion was 70.1 years. About 59% of the patients discontinued ZA treatment, 21% of whom due to renal complications. Twenty-nine patients (23.8%, 95% confidence interval: 16.2%-31.3%) had renal impairment during treatment, and the risk of renal impairment increased with an extended duration of ZA therapy (<6 months: 22.5%; ⩾12 months: 23.5%; ⩾24 months: 31.3%). Risk factor analysis found that a significantly greater risk of renal impairment ($p < 0.05$) was associated with: increasing age at ZA initiation (relative risk [RR] = 1.1 per additional year), cigarette smoking (RR = 2.1), a history of prior renal disease (RR = 4.6), hypercalcemia (RR = 4.0), benign prostate hyperplasia (BPH) (RR = 3.0), diabetes mellitus (DM) (RR = 2.9), and treatment with anti-hypertensives (RR = 2.6).
Conclusions: In a naturalistic clinical setting, nearly one-quarter of the ZA-treated patients experienced renal impairment; this renal risk is much higher than previously reported in clinical trials. The risk of renal impairment increases with ZA treatment duration. Older age, smoking, antihypertensive therapy, and a history of renal disease, hypercalcemia, BPH or DM are also associated with an increased renal toxicity risk in ZA-treated HRPC patients.

811 ORAL

ASCENT: A double-blinded randomized study of DN-101 (high-dose calcitriol) plus docetaxel vs. placebo plus docetaxel in androgen-independent prostate cancer (AIPC)

T. Beer[1], C. Ryan[1], P. Venner[2], D. Petrylak[3], G. Chatta[4], J. Ruether[5], K. Chi[6], A. Arroyo[7], F. Clow[7]. [1]*Oregon Health & Science University, Medicine/Hematology Oncology, Portland, OR, USA;* [2]*Cross Cancer Institute, Edmonton, Canada;* [3]*Columbia Presbyterian Medical Center, New York, NY, USA;* [4]*University of Pittsburgh, Medicine/Hematology Oncology, Pittsburgh, USA;* [5]*University of Calgary, Tom Baker Cancer Center, Calgary, Canada;* [6]*British Columbia Cancer Agency, Medical Oncology, Vancouver, Canada;* [7]*Novacea, Inc., Medical Oncology, South San Francisco, CA, USA*

Background: High doses of 1.25-dihydroxycholcalciferol enhance the antitumor activity of multiple classes of chemotherapy in preclinical cancer models and showed encouraging Phase 2 results in combination with docetaxel for the treatment of AIPC. DN-101 is a new high-dose oral formulation designed to conveniently and reliably deliver the high 1.25-dihydroxycholcalciferol concentrations required for cancer therapy.
Methods: Patients with progressive castrate metastatic prostate cancer, no prior chemotherapy, and adequate organ function received weekly docetaxel 36 mg/m^2 iv for 3 weeks of a 4-week cycle with either 45 μg DN-101 or placebo orally 1 day prior to 36 mg/m^2 docetaxel.
Results: 250 patients were randomized 1:1 at 48 sites in the US and Canada. Baseline characteristics were similar for both arms. Any grade 3/4 adverse event occurred in 58% of DN-101-treated patients and 70% of placebo-treated patients. Most common grade 3/4 toxicities in the DN-101 and placebo-treated arms were neutropenia (10% vs. 8%), fatigue (8% vs. 16%), infection (8% vs. 13%) and hyperglycemia (6% vs. 12%). PSA response within 6 months (the primary endpoint) occurred in 58% of DN-101 patients and 49% of placebo patients ($p = 0.16$). Overall, PSA responses were seen in 63% of DN-101 patient and 52% of placebo patients ($p = 0.07$). The median survival for DN-101 treated patients has not been reached and is estimated at 23.5 months. The observed median survival was 16.4 months in placebo treated patients. With the specified adjustment for baseline characteristics of performance status and hemoglobin, therapy with DN-101 was associated with a statistically significant survival benefit (HR 0.67, $p = 0.035$).
Conclusions: The addition of weekly DN-101 did not increase the toxicity of weekly docetaxel with trends suggesting improved safety by several parameters. The trend favoring DN-101 plus docetaxel over placebo plus docetaxel for PSA response did not reach statistical significance, however, in a secondary endpoint of overall survival, DN-101 therapy was associated with a substantial improvement in overall survival that was statistically significant in a prospectively planned multivariate analysis that adjusted for baseline characteristics.

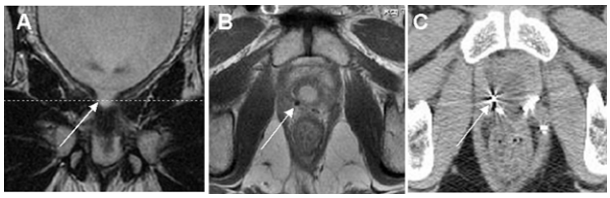
Poster presentations (Wed, 2 Nov)
Genitourinary cancer

812 POSTER

Measuring the accuracy of ultrasound-guided fiducial marker placement in reference to prostatic anatomy using MRI: Implications for high-precision radiotherapy

C. Menard[1], A. Bayley[1], A. Toi[2], K. Wiltshire[1], A. Kirilova[1], T. Rosewall[1], C. Catton[1], P. Chung[1], M. Gospodarowicz[1], M. Haider[2]. [1]*Princess Margaret Hospital, University of Toronto, Department of Radiation Oncology, Toronto, Canada;* [2]*Princess Margaret Hospital, University of Toronto, Department of Diagnostic Radiology, Toronto, Canada*

Background: Techniques in high precision external beam radiotherapy for prostate cancer are increasingly integrating the use of internal fiducial markers. Literature supports their role 1) as surrogates to prostate gland position during daily online image-guidance, 2) as common landmarks in multi-modality image registration, and 3) as a strategy to mark the location of the prostatic apex and/or urethral anastomosis otherwise invisible on treatment planning CT images. In order to determine the validity of the latter strategy, we sought to measure the spatial accuracy of ultrasound-guided marker placement in reference to anatomical boundaries using MRI.
Methods: Twenty patients with prostate cancer underwent trans-rectal ultrasound-guided placement of a gold fiducial marker approximately 1 week prior to CT simulation and investigational MRI examination. Twelve patients with a new diagnosis of prostate cancer had a marker placed immediately above the prostate apex. MRI examination consisted of axial GRE and T2-FSE images (slice thickness 2 mm). The distance between the Z MRI coordinate of the fiducial marker (identified on GRE images) and the visualized prostatic apex (identified on T2-FSE images) was measured and compared to the reported distance measured on ultrasound at the time of placement. Eight patients destined to receive adjuvant or salvage radiotherapy after radical prostatectomy had a marker placed immediately lateral to the urethral anastomosis under ultrasound-guidance. MRI examination consisted of 3 mm axial FRFSE proton density (B) and coronal T2-weighted FSE (A) image acquisitions. The distance between the Z MRI coordinate of the anastomosis (identified on the coronal images as a distinct signal change between urethral sphincter and bladder junction-A) and the fiducial marker (identified on axial FRFSE images-B) was measured.



Results: The difference between the reported and measured distance from the fiducial marker to the prostate apex ranged from 0–3 mm, with a mean error of 1.42 mm (SD 1.16 mm). The distance between the fiducial marker and the post-prostatectomy urethral anastomosis ranged from 0–6 mm, with a mean error of 3 mm (SD 2.77 mm). In both instances, the mean error lies within that expected from slice-thickness volume averaging on axial MRI and CT image.
Conclusion: Fiducial markers can be accurately placed in reference to prostatic anatomy using trans-rectal ultrasound guidance, and are valid surrogate anatomical markers of the prostate apex and post-prostatectomy urethral anastomosis in CT-based target definition. In those instances where MRI is not available for treatment planning, a margin of 2–3mm accounting for the error introduced by slice-thickness volume averaging may be considered.

813 POSTER

Longitudinal evaluation of quality of life and rectal toxicity in patients with conformal radiation therapy for prostate cancer

H. Geinitz[1], F. Zimmermann[1], C. Scholz[1], N. Prause[1], C. Winkler[1], M. Keller[2], R. Busch[3], M. Molls[1]. [1]*Klinik fuer Strahlentherapie, Technische Universitaet Muenchen, Muenchen, Germany;* [2]*Psychosoziale Nachsorgeeinrichtung, Chirurgische Universitaetsklinik, Heidelberg, Germany;* [3]*Institut fuer Medizinische Statistik, Technische Universitaet Muenchen, Muenchen, Germany*

Background: To prospectively evaluate quality of life (QoL) and rectal toxicity in patients with conformal radiation therapy (CRT) for localized prostate cancer.