⩾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)

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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

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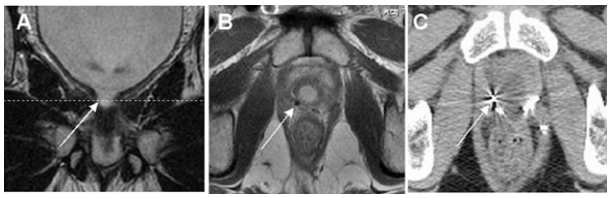
Background: Techniques in high precision external beam radiotherapy for prostate cancer are increasingly integrating the use of internal fiducial markers. Literature supports their role 1) as surrogates to prostate gland position during daily online image-guidance, 2) as common landmarks in multi-modality 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

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

Material and methods: 110 patients were entered onto the study: 78 (71%) received definitive CRT with a median dose of 70 Gy to the prostate (64.8–74 Gy) and 32 (29%) received adjuvant CRT after radical prostatectomy with a median dose of 59.4 Gy (55.9–64.8 Gy). QoL, rectal toxicity, and fecal continence were assessed before CRT, during CRT at 40 Gy and 60 Gy and 8 weeks and 12 months after CRT. The following standardized questionnaires were used: the EORTC quality of life questionnaire C30, the prostate cancer module QLQ-PR25, an 8-item rectal toxicity score (RT-TOX), and the Wexner fecal continence score.
Results: Global QoL did not change significantly during CRT, 8 weeks after treatment the values were above the baseline ($p = 0.013$). The following QoL scores significantly deteriorated during therapy and then returned to the baseline after CRT: role functioning, fatigue, diarrhoea, urinary symptoms, and sexual activity. Emotional functioning improved during and after therapy and the 2- and 12-months-values were significantly above the baseline. PR-25 fecal symptoms, RT-TOX and the fecal continence score significantly increased during CRT. All three scores recovered slightly 8 weeks after CRT without reaching baseline levels and subsequently deteriorated again one year after treatment. RT-TOX and the fecal continence score correlated inversely with global quality of life 12 months after CRT ($\rho = -0.48$ and $\rho = -0.31$, respectively, $p<0.001$). Neither neoadjuvant hormonal therapy nor treatment indication (definitive vs. adjuvant CRT) was associated with RT-TOX, fecal continence or global quality of life.
Conclusions: A decrease in quality of life parameters during CRT is mostly transient and affects only a limited number of QoL domains. Especially global quality of life does not deteriorate during or after treatment. The PR-25 fecal symptom score, the rectal toxicity score and the fecal continence score display a similar time course: following a slight improvement 8 weeks after treatment the scores deteriorate again 12 months after CRT probably reflecting the onset of chronic toxicity. Impaired fecal continence, although mostly mild, must be regarded as an acute as well as a late side effect of CRT.

814 POSTER

Impact of percent positive biopsies on biochemical outcome in prostate cancer patients treated with external beam radiotherapy with or without androgen deprivation

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Background: The primary objective of this study is to identify the prognostic factors for biochemical outcome in patients with prostatic adenocarcinoma treated with external beam radiotherapy (EBRT) with or without androgen deprivation (AD) and to investigate the impact of positive biopsy core percentage in different risk groups.
Material and methods: Between 1998 and 2003, 333 patients diagnosed with prostate cancer were treated with definitive EBRT in the Radiation Oncology Departments of Metropolitan Hospital and Marmara University. Median age was 71 years (range 44–85); 74% had clinically localized (T1–2), 26% had locally advanced (T3) disease. Gleason scores were below 7 in 48%, 7 in 39%, and over 7 in 13%. Pretreatment PSA levels were below 10 ng/ml in 50%, between 11–20 ng/ml in 25%, and over 20 ng/ml in 25%. Perineural invasion (PNI) was present in 31%. Distribution of patients due to risk factors according to D'Amico was as low risk in 21%, intermediate risk in 34%, and high risk in 45%. Of the patients 18% were treated with a 4 field conventional technique, whereas 82% were treated with 4–6 conformally shaped fields. Median prostate dose defined to the periphery was 72 Gy (range 59.4–76 Gy). Androgen deprivation was given to 78% of the patients. Percentage of positive biopsy cores was calculated as number of positive cores in biopsy materials divided by total core numbers. Biopsies from seminal vesicles and nodules were excluded. The median number of cores was 8 (range 6–26). Percentage of positive cores were <33% in 34% of patients, between 33%-67% in 39%, and ⩾67% in 27%. Patients were evaluated every 3–6 months after the completion of radiotherapy. Median number of post-RT PSA counts per patient was 8 (range 3–32). Biochemical failure was defined using the ASTRO consensus definition. Potential risk factors like Gleason score, T stage, initial PSA level, PNI, time on AD, radiation dose, percent of positive biopsies and risk groups were evaluated.
Results: After a median follow-up of 35 months (range 12–91 months), the 5-year biochemical control (BC), prostate cancer-specific survival, and overall survival rates were 83%, 98%, and 88%, respectively. The 5-year BC according to risk groups were 85% for low risk, 88% for intermediate risk, and 79% for high risk patients. For the entire cohort high GS ($p = 0.0042$), high risk group ($p = 0.0281$) and higher percent positive core biopsies ($p = 0.0342$) were significant predictors of reduced biochemical control. In the intermediate risk group BC was 90% vs 74% in the patients with <67% positive cores and >67% positive cores, respectively ($p = 0.036$). On multivariate analysis the only independent predictor for PSA failure was percent positive biopsies.
Conclusions: This trial demonstrated especially in the intermediate risk group that high percent positive biopsies could be an early indicator of biochemical relapse. Those patients may be evaluated as having high risk disease.

815 POSTER

Androgen deprivation for cytoreduction prior to interstitial brachytherapy for early-stage prostate cancer is associated with an increased risk of urinary morbidity

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Background: We previously demonstrated that biculatumide monotherapy (BT) has similar cytoreductive efficacy when compared with luteinizing hormone-releasing hormone analogue monotherapy (LHRHa). Here we assess the impact of androgen deprivation (AD) given for prostate volume reduction prior to brachytherapy on acute and chronic urinary morbidity following implant.
Materials and methods: Between May 1998 and January 2004, 81 patients received AD for the sole purpose of cytoreduction prior to interstitial brachytherapy. 56 patients received a median 3 months of LHRHa (leuprolide 7.5 mg per month or goserelin 3.6 mg per month) and 25 patients received a median 3 months of BT (bicalutamide 50 mg per day). Prostate volume was measured prior to initiating hormonal therapy and then intraoperatively by a single ultrasonographer (CK). Events recorded were:
1. The incidence of urinary retention requiring prolonged catheterization (greater than 1 week)
2. The need for surgical intervention to relieve urinary obstruction
3. The occurrence of long-term incontinence (>6 months) following surgical intervention.

Outcomes were compared to those for a control group of 81 patients who were matched 1:1 based on similar prostate volume (within 1 cc) at the time of implant, but who had not received AD. Median follow-up for all patients was 41 months (range 11–66 months).
Results: Median percent reduction in prostate volume after AD was 30%. There were no statistical differences in urinary morbidity between patients receiving LHRHa and BT. Prolonged catheterization was required significantly more often for patients receiving AD when compared to volume-matched controls (27% vs. 9%, $p = 0.02$). Surgical intervention was required significantly more often for patients receiving AD when compared to volume-matched controls (9% vs. 4%, $p = 0.03$). Long-term incontinence occurred in 3 (4%) out of the 7 patients that had received AD and subsequently required surgical intervention. Long-term incontinence occurred in 1 (1%) out of the 3 patients that had not received AD and subsequently required surgical treatment.

	AD	No. AD	*P*
Median Volume at Implant (cc)	34.0	34.1	0.99
Prolonged Catheterization	27%	9%	0.02
Surgical Intervention	9%	4%	0.03
Urinary Incontinence	4%	1%	0.03

Conclusions: The use of AD for cytoreduction was associated with a significantly increased incidence of prolonged catheterization, need for surgical intervention, and occurrence of long-term incontinence when compared with patients implanted at similar volumes who did not receive AD. This suggests that patients who achieve smaller prostate volumes through the use of AD maintain an increased risk for urinary complications and should be counseled accordingly prior to implant.

816 POSTER

Tolerance of elderly patients (⩾75years) to prostate external beam radiotherapy or brachytherapy

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Purpose: To investigate if patients ⩾75yr are at higher risk of developing toxicity from prostate external beam radiotherapy (EBRT) or brachytherapy