selection of patients who might avoid unnecessary cancer treatments that are associated with serious sequelae.

854 POSTER

Chemotherapy vs. radiotherapy in clinical stage CSA and B1/B2 seminomatous testicular tumours: the two institutions experience

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Background: Radiotherapy (RT) applied to retroperitoneal and ipsilateral pelvic nodes represent standard treatment in CSA and B1/B2 seminomatous testicular tumours (STT), promising results have been reported with chemotherapy (CHT). The aim of the prospective non-randomized study was to analyze the survival, relapses, acute and late side effects following RT and CHT.
Material and methods: Between 1982 and 2003, 456 patients (pts) in CSA and B1/B2 STT were divided into 2 groups according to primary tumour treatment. Group A (1997–2003) CSA (n = 177): 170 pts received 2 cycles of CHT with carboplatin (CBDCA). CS B1/B2 (n = 17) underwent induction CHT (platinum (P) and etoposide (E)). Complete response (CR) to CHT was defined as complete radiographic resolution of metastasis or a <3 cm stable residual mass (rm). Partial response (PR) to CHT was defined as >3 cm stable rm followed by delayed selective consolidation with retroperitoneal lymph adrenalectomy. Group B (1982–1997), 286 pts (247 in CSA and 39 in CS B1/B2) received RT in majority of pts by linear accelerator (8 pts were treated using Co unit), applied to retroperitoneal and ipsilateral pelvic nodes. The prescribed dose at midplane was 30 Gy/18 fractions.
Results: Group A – after median follow-up (mfu) of 4 years all pts in CSA are alive and free of disease (afd). 1 pt (0.6%) relapsed in the retroperitoneal nodus at 28 months (m) and achieved CR with PE CHT. All pts in CS B1/B2 entered in CR following PE CHT (2 pts with RM <3 cm). 1 pt relapsed at 12 m in retroperitoneal lymph nodes and achieved CR with salvage CHT. All pts are afd after mfu of 55 m. Group B – after mfu of 10 years afd are 98% and 91% in CSA and B1/B2, respectively. Relapses were registered in 14 pts (4.9%) within mfi of 10 m. 9 (64.3%) relapsing pts achieved CR with CHT and/or RT: 7/10 in CSA and 2/4 in CS B1/B2. 7 pts died (4 of STT, 3 of intercurrent disease). 7 pts developed second malignancy within mfi of 160 m (lung 3 pts, non-Hodgkin lymphoma 1 pts, bladder 1 pts, opposite testis 2 pts)
Conclusions: Orchidectomy followed by RT for CSA and B1/B2 seminoma resulted in an excellent survival and low rate of complications and relapses. CBDCA CHT appear to be an acceptable alternative approach in CSA STT: application is easy, side effects are mild, relapse rate and late sequels are lower than after RT. However, primary CHT in CSA + B1/B2 STT necessitate long term follow-up studies in order to determine more precisely late events.

855 POSTER

Differences in degree and duration of bone protection with intravenous bisphosphonates in prostate cancer patients receiving androgen deprivation therapy (adt): results of a placebo-controlled trial

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Background: Although androgen deprivation therapy (ADT) is the gold standard of treatment for hormone-refractory prostate cancer (HRPC), the associated bone demineralization increases the risk of osteoporosis, osteopenia, and related skeletal fractures. Because of their beneficial effects on bone turnover, bisphosphonates have been investigated as a potential treatment to maintain bone integrity in such patients.
Methods: This prospective, placebo-controlled study included 97 men who were randomly assigned to 1 of 3 treatment groups after undergoing androgen ablation (LHRH-agonist therapy or orchiectomy). The treatment groups included: monthly intravenous (IV) clodronate infusions (n = 39); monthly IV zoledronate infusions (n = 27), or no bone protection (control; n = 34). Efficacy evaluations included PSA, serum testosterone, x-ray, bone scintigraphy, and dual-energy x-ray absorptiometry (DEXA) scans with densitometry performed every 6 months. Patients were followed for a minimum of 36 months.
Results: The average patient age was 63 years. Bisphosphonate treatment maintained bone mineral density to a greater extent than the control, with clodronate providing greater protection against osteopenia than zoledronate. The average time to development of osteopenia after ADT was 6 months in the control group, vs 24 months and 18 months in the IV clodronate and IV zoledronate groups, respectively. Likewise, the average time to develop osteoporosis was 24 months in the control group, compared with 28.3 months and 28.5 months in the IV clodronate and IV zoledronate groups, respectively.
Conclusions: Bisphosphonates should become the standard of care to maintain bone integrity in those patients receiving ADT for the treatment of HRPC. In this study, IV clodronate provided greater protection against osteopenia than IV zoledronate.

856 POSTER

Prostate size and the effect of hormonal manipulation

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Background: To evaluate prostate gland length and volume in a large population of men diagnosed with localized prostate cancer. Furthermore, to assess the effect of hormonal manipulation (HM), specifically the difference between luteinizing hormone releasing hormone (LHRH) agonist therapy alone (LHRH) compared to total androgen blockade (TAB).
Materials and methods: 3370 men with presumed organ confined prostate cancer underwent I^{125}/Pd^{103} prostate brachytherapy (PB) at a single institution from October 1997 through January 2003. Prior to PB, transrectal ultrasound prostate sagittal and transverse image based volume studies (VS) were performed at least once on all patients. A B-K medical systems ultrasound machine and biplanar probe was used for each VS. 363/3370 (10.8%) patients required a repeat VS specifically because they were considered suboptimal candidates for PB secondary to excessive prostate volume. Subsequently, this group was subjected to HM for the purpose of decreasing prostate size (cytoreduction) in preparation to PB. 313/363 (86.2%) of these patients were given cytoreduction with LHRH while 50/363 (13.8%) patients received TAB. TAB consisted of biclutamide 50 mg p.o. q day times 3 months in addition to LHRH 7.5 mg depot IM q 1 month $\times$ 3. After three months of cytoreductive therapy, a repeat VS was performed.
Results: The mean sagittal length and prostate volume for the entire group of 3370 patients was 38.6$\pm$6.5 mm and 41.9$\pm$18.4 cm^3, respectively. The mean prostate volume for the 313 patients who received LHRH only and the 50 patients who received TAB prior to any hormonal manipulation was 70.1$\pm$19.8 cm^3 and 76.9$\pm$24.5 cm^3, respectively. The mean prostate volume for the 313 patients who received LHRH only and the 50 patients who received TAB after receiving hormonal manipulation was 49.4$\pm$16.0 cm^3 and 49.7$\pm$16.6 cm^3, respectively. There was a significant difference in the mean percent decrease in prostate volume for those receiving LHRH versus TAB (28.9%$\pm$14.6% vs. 34.1%$\pm$14.2% (p = 0.022)).

Table 1: Prostate size results

Patient group	Original		Repeat	
(# patients)	Sagittal length (mm) (mean$\pm$SD)	Prostate volume (cm^3) (mean$\pm$SD)	Sagittal length (mm) (mean$\pm$SD)	Prostate volume (cm^3) (mean$\pm$SD)
All (3370)	38.6$\pm$6.5	41.9$\pm$18.4	N/A	N/A
LHRH (313)	47.2$\pm$6.8	70.1$\pm$19.8	41.1$\pm$6.6	49.4$\pm$16.0
TAB (50)	47.8$\pm$6.9	76.9$\pm$24.5	40.9$\pm$5.8	49.7$\pm$16.6

Conclusions: Whether for therapeutic benefits or strictly for prostate cytoreduction, the use of HM remains prevalent prior to PB. Controversy has existed regarding the use of LHRH versus TAB. This study strongly suggests that patients undergoing TAB experience a significantly higher reduction in overall prostate volume than those who receive LHRH agonist alone.

857 POSTER

Weekly paclitaxel plus carboplatin in patients with metastatic transitional cell carcinoma of the urothelium who failed MVAC: Phase II trial

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Backgrounds: Though MVAC is one of the standard care for *transitional cell carcinoma* (TCC), this regimen might be toxic for pretreated or elderly pts. There is no standard salvage treatment for pts who failed MVAC. Paclitaxel(P) is active agent for TCC and Carboplatin(C) has synergistic activity with P. P plus C is safely manageable and effective regimen for ovarian or lung cancer. Weekly administration of P plus C can be not only less toxic treatment for these pretreated pts but also more

effective treatment with sustained cumulative exposure and dose-dense drug delivery.
Methods: From May 2003 to May 2005, 34 pts of TCC who failed MVAC entered to this phase II study. Weekly P (80mg/m2) and C (AUC2) were administered on day 1, 8, 15, 22, 29, 36 and repeated every 7 weeks until progression or intolerable toxicity (maximum 18 cycles). Platinum-free interval (PFI) was defined as the interval from the last MVAC to the start of weekly P plus C.
Results: Pts' characteristics were as follows. Median age was 65.5 (53–80). 13 pts (38%) were 70 y.o. or older. Median PS was 1 (0–3). 25 pts (74%) had visceral metastasis. Median PFI was 4.4 months (1.5–106). Among assessable 31 pts, 2 complete and 8 partial responses were observed (overall response rate 32.3%, 95% CI 15.8–48.7%). The relations between PFI and tumor response were as follows: <6 months; 23.5% (4/17) and ⩾6 months; 42.9% (6/14), respectively (p = 0.43). Median progression-free and overall survivals were 3.7 and 10.3 months, respectively. Elderly pts obtained almost equal response rates (<70 y.o; 31.5% (6/19), ⩾70 y.o; 33.3% (4/12)) and median overall survivals(<70 y.o; 10.2 months, ⩾70 y.o; 17.1 months). One pt whose PS was 3 died from sepsis within 1 month from the last cycle of chemotherapy. Grade 3–4 CTC-toxicities were as follows: anemia; 35%, thrombocytopenia; 0%, neutropenia; 50%, febrile neutropenia: 9%. Most common non-hematological toxicities were alopecia (⩾Grade 1; 72%), neurotoxicity (Grade 1; 59.3%, Grade 2; 9.4%, ⩾ Grade 3; 0%), nausea and vomiting (Grade 1; 34%, Grade 2; 6%, Grade 3; 3%) and diarrhea (Grade 1; 13%, Grade 2; 3%, Grade 3; 3%).
Conclusions: Weekly P plus C was tolerable and active for TCC who failed MVAC. This regimen was less toxic and deserves further evaluation especially for elderly pts with TCC. We are planning the next trial to assess this regimen as the first-line treatment for elderly TCC pts with comprehensive geriatric assessment.

858 POSTER

Alpha and beta CTX urine levels in patients with prostate cancer

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Degradation products of type I collagen can be measured by CrossLaps (CTX) immunoassays, providing an index of bone resorption. The CTX epitope EKAHDGGR comprises a DG-motif susceptible to post-translational modifications. In newly synthesized collagen this motif is in the native form denoted alpha CTX, but converts to an isomerized form (beta CTX) during ageing of bone. Other markers of bone resorption including serum N-telopeptide are elevated in prostate cancer.
For this study, alpha and beta CTX levels were analyzed in serial urines of prostate cancer patients using the respective Nordic Bioscience ELISA. Urines were obtained from patients who participated in a multicenter placebo-controlled trial of pamidronate vs placebo (JCO 21, pp: 4277, 2003). Baseline urine samples were available from 147 patients with advanced disease; 43.5% were terminated early due to disease-related outcomes including death and unsatisfactory therapeutic effect. In this study we correlated urine marker levels with time to skeletal-related events (TTSRE), and also a composite endpoint defined as either TTSRE or early discontinuation from the trial. Serial urine samples were available from a smaller subset of patients due to the early termination.
Median alpha CTX levels were 1.77 (range 0.2–31.9 μg/mmol) and beta CTX levels were 5.26 (range 0.01–86.7 μg/mmol). There was no control data available for males with castrate levels of sex hormones, so control data was used from postmenopausal females. The 95 percentile cutoff (determined for control women who were post-menopausal for less than 5 years) was 2.4 μg/mmol for alpha CTX and 9.62 μg/mmol for beta CTX. Using these cutoffs, 33.1% of patients had elevated alpha CTX levels and 26.5% had elevated beta CTX levels. Patients with elevated baseline urine beta CTX levels had significantly shorter time to the composite end point (Log rank p-value = 0.03), but alpha CTX did not. The change in alpha and beta CTX levels between baseline and 9 weeks after treatment was also analyzed for those patients who had elevated urine marker levels at baseline. Those patients with >50% decrease in alpha CTX urine levels had a significantly longer TTSRE and time to composite endpoint, but no association was seen with change in urine beta CTX.
In conclusion, serial alpha CTX urine levels deserve further evaluation in patients with prostate cancer.

859 POSTER

Bone alkaline phosphatase is predictive of prostate cancer-related outcome in metastatic hormone-refractory prostate cancer

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Background: Bone alkaline phosphatase (BALP), a biochemical marker of osteoblastic activity in metastatic hormone-refractory prostate cancer (HRPC), is associated with sclerotic bone metastases. BALP may be of value as a surrogate for progressive disease in prostate cancer; however, dynamic measures of BALP have not been evaluated as predictors of outcome in men with metastatic HRPC. A large, randomized, double-blind, placebo-controlled study of 10 mg atrasentan (Xinlay™) versus placebo was conducted in patients with metastatic HRPC. Time to disease progression (TTP) was the primary endpoint for the study and was defined by radiographic and clinical events and confirmed by independent radiology and oncology review. In addition, the majority of patients in the study reported new metastatic bone pain, the cardinal symptom of metastatic prostate cancer. The objective of this analysis was to evaluate the predictive value of increasing BALP on disease-related outcome (disease progression and bone pain) in patients receiving placebo.
Material and methods: Data from 369 patients randomized to placebo who had BALP values at both baseline and week 4 were divided into 2 groups: increased or decreased BALP from baseline at week 4. TTP, time to bone pain reported as an adverse event (TTBP), and time to death were compared between the two BALP groups using Kaplan-Meier and Cox proportional hazards methodologies.
Results: At week 4, 64.8% of the patients recorded an increased BALP from baseline and 35.2% a decrease in BALP. TTP and TTBP were significantly shorter for patients with rising BALP (log-rank p < 0.001 and log-rank p = 0.002, respectively). The median TTP was 85 days for those with an increased BALP at week 4 compared to 117 days for those with a decreased BALP. The hazard associated with an event of disease progression or time to the first adverse event of bone pain was decreased by 40% (95%-CI = 0.470, 0.769) and 38% (95%-CI = 0.456, 0.843) for patients with a BALP decrease at week 4. There was no significant difference in survival between the 2 groups.
Conclusions: These data demonstrate that a rising BALP at week 4 in patients with metastatic HRPC is associated with early disease progression and early onset of metastatic bone pain. Prospective trials will be required to determine if serial BALP measurements are predictive of disease-related outcome in HRPC.

860 POSTER

Diagnostic and prognostic value of serum TRACP 5b, MMP-2, MMP-9, and tALP in patients with advanced prostate cancer

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Background: Skeletal metastases are a significant problem in prostate cancer (PC) patients. Tartrate-resistant acid phosphatase isoform 5b (TRACP 5b) is a specific parameter of osteoclast activity and bone resorption in cancer patients. Matrix metalloproteinases (MMPs) MMP-2 and MMP-9 are gelatinases, which have been shown to be associated with poor prognosis in patients with cancer. We evaluated TRACP 5b, MMP-2 and MMP-9 in relation to the standard analyte total alkaline phosphatase (tALP) as markers of skeletal metastases and as predictors for survival in advanced PC.
Material and methods: The sera were collected from 35 PC patients with (BM+) diagnosed skeletal metastases and from 49 PC patients without (BM−) radiological evidence of skeletal metastases. Non-fasting serum samples were collected and stored in −70ºC before analysis. Total ALP was determined using a standard laboratory method (Roche Diagnostics). Serum TRACP 5b activity was measured using an in-house immunoassay system. Quantitative analysis of serum MMP-2 and MMP-9 was performed using a commercial ELISA System (Amersham Biosciences, UK). The diagnostic accuracy of the markers was evaluated by ROC curve analysis. The diagnostic sensitivity and specificity were determined at the cut-off level with the highest diagnostic accuracy in the ROC analysis, and these cut-off levels were used in Kaplan-Meier survival analyses for the markers.
Results: Mean values of TRACP 5b and tALP were significantly higher in BM+ group than in BM-group (p < 0.0001), whereas no such difference was observed for MMP-2 or MMP-9. Total ALP showed the highest area under the curve (AUC = 0.98), followed by TRACP 5b (AUC = 0.82) and MMP-9 (AUC = 0.62). The best combination of sensitivity (91%) and specificity (100%) for tALP was reached with cut-off point = 227 U/L, for TRACP