7049 POSTER

Early results of a phase II trial of second line chemotherapy with oxaliplatin (Ox) and capecitabine (Cp) in hormonorresistant metastatic prostate cancer

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Introduction: Docetaxel plus prednisone (DP) is the current standard of care in first line chemotherapy for metastatic hormone-refractory prostate cancer. However, there is no agent proven as effective after progression to standard DP therapy. Platins and capecitabine have shown activity in this setting. Here we present our early results of a phase II trial with the combination of Ox and Cp.
Patients and Methods: Between May 2004 and Feb 2009, 17 PS0–1 patients (pts) were included in this prospective, multi-centre trial. All pts had progressed to first line DP chemotherapy. Pts received Ox 100 mg/sqm on D1 and Cp 1000 mg/sqm/bid on days 1–14 every 21 days.
Results: A total of 94 cycles were administered; mean 5.5; range 3–8.3. Mean initial PSA was 561 ng/ml (27–4893). Mean postreatment PSA was 357 (range 3.2–2840). 10 of the treated pts presented with a PSA decrease compatible with biochemical response, 4 pts presents stable disease, and 3 pts presented progressive disease. In responding pts, mean PSA decrease was of 80% (range 50–99%). TTP was of 18.5 weeks (censored data). It is remarkable that 2 of the included pts progressed during DP therapy. No unexpected toxicity was observed. Only grade 3 toxicity reported was grade 3 anemia. 5 of the 17 pts presented grade 2 neuropathy.
Conclusions: Management of HRPC remains controversial. There is no standard treatment after DP progression. It is important to find well tolerated and active chemotherapy regimens for this situation. Platinum-based combinations, due to its lack of crossover resistance with antimicrotubule agents, could be a valid therapeutic alternative in this setting. Although ours is a small series, the results justify the study of this combination in a larger number of pts, to more precisely determine the effect of the combination and thus be able to evaluate the benefits that platinum-based combinations could bring to these pts, for whom there is no valid therapeutic alternative. We are still recruiting patients.

7050 POSTER

Evidence of psa decrease with fulvestrant acetate in androgen independent prostate cancer (AIPC) patients

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Introduction: Preclinical evidence supports the role of estrogen receptor (ER) signaling in prostate cancer. Fulvestrant (FVT) belongs to the SERD class of ER antagonists and has shown no estrogen-agonist activity in either preclinical or clinical studies. FVT binds competitively to the ER, inhibits receptor dimerization and reduces the ER half-life increasing protein turnover. ER are expressed prostate cancer established cell lines. Targeting the AR for down-regulation or degradation could be a useful approach for decreasing AR-dependent prostate cancer cell growth and for treating AIPC. This strategy has been proven in preclinical models. A potential dose-response co-relation has also been suggested for FVT.
Patients and Methods: Between June 2008 and February 2009, a total of 7 AIPC prostate cancer patients (pts) were treated inside a compassionate use treatment following the Spanish requierements. FVT was administered im, with a loading dose of 500 mg every 2 weeks during the first month, followed by 250 mg im monthly thereafter.
Results: Median baseline ECOG was 1 (0–2), median age was 73.7 years (range 54–83). Mean baseline PSA was 534 ng/ml (21–2462 ng/ml). Mean previously no. of hormonotherapy lines was 3.4 (range 2–5). Four pts had received chemotherapy, mean no. of lines was 1.75 (range 1–3). 5 of the treated pts presented with PSA decrease, mean 72.8% (range 40–99%). In 2 of the pts the PSA level increased despite the treatment with FVT. Time to treatment Failure was of 11.14 weeks (censored data). 3 of the pts that presented with PSA decrease, have developed biochemical failure. No relevant side effect has been recorded.
Conclusions: Under our knowledgement, this is the first treated cohort of AIPC pts that have presented with PSA decrease when treated with FVT. Our cohort is a heavily pretreated one, and the observed activity is exciting. Under our point of view it is justified to continue with the development of FVT in metastatic prostate cancer.

7051 POSTER

Clinical predictors of late gastrointestinal and genitourinary toxicity after three-dimensional conformal radiotherapy using seven coplanar fields to localize prostate cancer

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Background: Dose escalation of radiotherapy (RT) improves the treatment outcome of localized prostate cancer (LPC); however, late toxicity may limit the extent to which the dose may be escalated safely. This study estimated the late gastrointestinal (GI) and genitourinary (GU) toxicity after three-dimensional conformal RT (3DCRT) using seven coplanar fields for LPC and assessed the correlated clinical factors.
Material and Methods: At our institution, 88 LPC patients underwent 3DCRT between March 2004 and May 2007. The total dose was 74 Gy in 2 Gy daily fractions for each patient. The median patient age was 71 years (range 52–80). According to the National Comprehensive Cancer Network (NCCN) risk group classification, 6, 45, and 37 patients were low, intermediate, and high risk, respectively. There were 39, 34, and 15 patients at stages T1 to T3, respectively. Fifty-six patients were given androgen deprivation therapy (ADT). There was coexisting hypertension (HT) in 17 patients, diabetes mellitus (DM) in 10, and gastrointestinal (GI) disease in 12. Four patients had undergone previous abdominal surgery. Twelve patients were treated with anticoagulants/antiaggregants (A/A) for pre-existing vascular disease. The Radiation Therapy Oncology Group/European Organisation for Research and Treatment of Cancer (RTOG/EORTC) toxicity score was used to analyze late GI and GU toxicity of grade 2 or higher at 3 years. The relationships between the following variables and late GI and GU toxicity were accessed: NCCN risk, use of ADT, presence of HT or DM, A/A treatment, coexisting GI disease, and history of abdominal surgery.
Results: The median follow-up was 23 months (range 5–47 months). Late GI toxicity of grades 2 and 3 occurred in one patient each. Grade 2 late GU toxicity occurred in one patient. There was no grade 4 or higher late toxicity. Late GI and GU toxicity of grade 2 or 3 at 3 years occurred in 3 and 1.8% of the patients, respectively. In the univariate analysis, A/A treatment was correlated with grade 2 or 3 late GI toxicity and grade 2 late GU toxicity. Coexisting GI disease was significantly correlated with grade 2 or 3 late GI toxicity.
Conclusions: Coexisting GI disease was correlated with grade 2 or 3 late GI toxicity. A/A treatment appears to predict grade 2 or 3 late GI and GU toxicity.

Univariate analysis results for grade 2 or 3 late GI and GU toxicity (*P*-values)

Late GI toxicity	Late GU toxicity	
NCCN risk	0.25	0.67
ADT	0.76	0.25
HT	0.49	0.66
DM	0.068	0.75
A/A	0.0006	0.014
Coexisting GI disease	0.0005	0.75
Prior abdominal surgery	0.74	0.81

7052 POSTER

Comparison between Tomotherapy and 3D-CRT for localized prostate cancer in regard to integral dose

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Background: This study was designed to evaluate the three-dimensional conformal radiotherapy (3D-CRT) and intensity modulated RT by helical Tomotherapy (Tomo-IMRT) in regard to integral dose (ID) for treatment of localized prostate cancer.
Material and Methods: Fifteen radiation treatments plans using Tomo-IMRT (6MV) as well as 3D-CRT (Linac, 6 and 10 MV), were generated for patients with localized prostate cancer. The ID (mean dose × tissue volume) was calculated from dose-volume histogram. The total prescribed dose was an equivalent of 82 Gy (2 Gy daily fraction, EQD2) in 35 fractions for each patient.
Results: The percentage difference (PD) of mean ID of all planning target volumes (PTVs) between tomotherapy and 3D-CRT was (+0.073) and hence, the plans with both techniques were equivalent in the term of PTV

coverage. Compared with 3D-CRT, Tomo-IMRT reduced IDs to the rectum, the bladder and normal tissue (NT) by 14.8%, 6% and 16.7% respectively.
Conclusions: Tomotherapy is superior to 3D-CRT in regard to the delivery of high dose radiation and coverage of target volume while meeting the dose constrains of surrounding organs at risks and reduction of NTID. In our practice, helical tomotherapy is the IMRT-delivery of choice for treatment of localized prostate cancer.

7053 POSTER

Epirubicin, carboplatin and 5-fluorouracil as second-line chemotherapy in castration resistant prostate cancer

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Background: This single institution study evaluated epirubicin/carboplatin/5-fluorouracil (E-Carbo-F) as second-line chemotherapy for castration resistant prostate cancer (CRPC) progressing after docetaxel.
Methods: Men with CRPC who received at least 2 cycles of E-Carbo-F as second-line chemotherapy after first-line chemotherapy with docetaxel at University College London Hospital, were retrospectively identified. Patients treated with E-Carbo-F received epirubicin 50 mg/m^2 on day 1, carboplatin area under the curve (AUC) 5 on day 1 and 5-fluorouracil 440 mg/m^2 on days 1 and 15 in 28-day-cycle.
Results: The study included 20 patients with median age 68 years at the start of E-Carbo-F. Decline of prostate specific antigen (PSA) level of > 50% was observed in 6 patients (30%) and the median duration of PSA response was 5.5 months. Median time to PSA progression was 4.5 months (8 months in PSA responders and 2.5 months in non-responders). Median overall survival in those patients who died by the time of results evaluation (n = 14) was 15 months, while 6 patients were still alive with median length of follow-up 14.5 months. Response to first-line chemotherapy with docetaxel did not predict response to E-Carbo-F. The median number of E-Carbo-F treatment cycles was 6 (8 in PSA responders and 4 in non-responders). 13 patients were treated with full dose and 7 with reduced dose from the beginning (either carboplatin AUC 4 and full dose epirubicin and 5-fluorouracil, or all 3 agents reduced by 10−20%). 5 patients out of 20 required dose reduction during the course of treatment.
Conclusions: Carboplatin with epirubicin and 5-fluorouracil is an active regimen in men with CRPC, whose disease has progressed during or after docetaxel. Selection of patients with good performance status is required and individual adjustment of dose often needed.

7054 POSTER

High-dose-rate brachytherapy combined with external beam radiotherapy for localized prostate cancer: correlation between clinical and dosimetric parameters and the incidence of Grade 2 or worse rectal bleeding

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Background: Several investigations have revealed that the alpha/beta ratio for prostate cancer is atypically low, and that hypofractionated radiotherapy or high-dose-rate brachytherapy (HDR-BT) regimens using appropriate radiation doses are expected to improve the local control rate for localized prostate cancer. However, the increase in the total biological effective dose may cause an increase in the severity and incidence of normal tissue complications. The purpose of this study was to investigate if the clinical and dosimetric factors affected the incidence of Grade 2 or worse rectal bleeding after HDR-BT combined with external beam radiotherapy (EBRT).
Material and Methods: Between March 2001 and October 2007, 90 patients with localized prostate cancer were treated by HDR-BT combined with EBRT at Kochi Medical School Hospital. The fractionation schema for HDR-BT and EBRT was prospectively changed. The distribution of the fractionation schema used in the patients was as follows: 6 Gy × 3 (HDR-BT) + 2 Gy × 20 or 1.8 Gy × 25 (EBRT) in 16 patients (Group 1); 9 Gy × 2 + 2 Gy × 20 in 57 patients (Group 2); and 9 Gy × 2 + 3 Gy × 13 in 17 patients (Group 3). The median follow-up duration was 38 months (range 18−97 months). The toxicities were graded based on the National Cancer Institute-Common Terminology Criteria for Adverse Events v3.0.
Results: Six patients (7%) developed Grade 2 rectal bleeding. There were no patients with Grade 3 or worse rectal bleeding. All of those six patients belonged to Group 2 or 3. The more the prescribed biologically effective dose increased, the more the incidence of Grade 2 rectal bleeding increased. However, regarding the correlation with dosimetric factors, no significant differences were found in the average percentage of the entire rectal volume receiving 10%, 30%, 50%, 70%, and 90% of the prescribed radiation dose from both HDR-BT and EBRT between those with bleeding and those without in each Group. The presence of a history of the antiplatelet therapy was statistically significant risk factor for the occurrence of Grade 2 rectal bleeding.
Conclusions: A history of antiplatelet therapy was the statistically significant risk factor for the occurrence of Grade 2 rectal bleeding, although the rectal dose from both HDR-BT and EBRT was also associated with the risk of rectal bleeding.

Oral presentations (Tue, 22 Sep, 09:00−11:00)
Genitourinary malignancies − Renal and Other

7100 ORAL

High-dose sequential chemotherapy versus conventional-dose chemotherapy as first-line treatment for advanced poor prognosis germ-cell tumors: a multicenter Phase III Italian trial

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Background: Upfront high-dose chemotherapy for poor prognosis germ-cell tumors (GCTs) showed promising results in preliminary studies. We started a phase III randomized trial to assess the efficacy of high-dose sequential chemotherapy (HDS) followed by autologous hematopoietic stem-cells transplant (ASCT) over standard chemotherapy (CT).
Patients and Methods: IGCCCG poor prognosis GCT pts were randomly assigned to receive 4 cycles of PEB (cisplatin, etoposide, bleomycin) (arm A) or 2 cycles of PEB followed by a sequence of high-dose (HD) cyclophosphamide (7 gr/m^2), 2 courses of PEB with HD-VP16 2.4 gr/m^2 each and HD-carboplatin (AUC 25 mg/ml × min) rescued by ASCT (arm B). In both arms, post-CT surgery was planned on residual resectable masses. Primary endpoint (EP) was 2-yrs overall survival (OS). We planned to accrue 50 pts/arm to detect a 20% improvement in pts receiving HDS with an α of 5% and 80% power. Due to the prolonged accrual time and the results at interim analysis, the study was stopped anticipately.
Results: From 12/1996 to 04/2007, 89 pts were randomized: 46 in arm A and 43 in arm B. 84 pts (94%) were evaluable for response and outcome (43/41). 41 (95%) and 36 (88%) pts completed the program. Median follow-up was 50 mos (range 1−129). In an intent-to-treat analysis, major responses [complete responses (CR) + partial responses with normal markers (PRm-)] were 31 (67%) after PEB ± surgery while 30 (70%) after HDS ± surgery. OS and progression-free survival (PFS) at 2-yrs were not significantly different (66.8 vs 60.5% – Log-Rank p = 0.42 and 58.5 vs 55.8 – Log-Rank p = 0.94). 18 (39%) and 19 pts (44%) relapsed/progressed, respectively. 3/18 and 2/19 have been rescued by further conventional-dose salvages. Progressions occurred within a median time of 4 (1−8) and 5.5 (3−25) mos, respectively. Mean administered CDDP dose-intensity was significantly different between the 2 arms: 17.04 mg/m^2/w for arm A vs 20.62 mg/m^2/w for arm B ($p < 0.0001$ at unpaired t-test). At univariate analysis, no differences have been observed for primary EP between the 2 arms as for baseline markers level, tumor primitivity and sites of disease. There was one treatment-related death (arm A).
Conclusions: In our study, the administration of front-line HDS in poor prognosis GCTs did not improve treatment outcome. Novel treatment strategies are needed to improve results in this cohort of pts.