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Offline position correction based on implanted markers gives in clinical practice an adequate coverage of the prostate and base of seminal vesicles, comparable to the planned dose

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Background: To determine the best position correction protocol for prostate radiotherapy using repeat CT scans and daily electronic portal imaging (EPI).
Material and Methods: We analysed 350 EPIs and 117 repeat CT scans from ten prostate cancer patients who were treated with curative intent: 77 Gy to the prostate bed and 70 Gy to the base of the seminal vesicles (SV). Before treatment, 4 gold markers were implanted in the prostate. Intensity modulated radiotherapy plans were made with an 8 mm margin. To determine the total received dose, while taking organ motion (including rotations) into account, CT scans were acquired in treatment position daily during the first week and weekly thereafter. For position verification, we performed daily EPI using orthogonal fields. From these portal images we determined the shift in bony anatomy and markers. With these data we simulated various position correction protocols: online and offline based on the position of the markers and the bony anatomy. These corrections only contained translations, because rotations cannot be corrected for. Using the original beam set-up, the dose distribution was recalculated on the repeat CT scans to determine the daily variation of the dose. From these dose distributions the accumulated dose on the prostate and the SV was determined for the different simulated position correction protocols.
Results: In case of no setup corrections, the standard deviations (SD) of the systematic displacements were 1.5 mm in left-right direction, 2.8 mm in anterior-posterior direction and 3.5 mm in the craniocaudal direction. The corresponding SD of the random displacements were 2–2.8 mm in each direction. The average D99% of the prostate over all patients is above 73.15 Gy (95% of the prescribed dose) for all protocols, even using skin alignment only. However, when looking at individual patient data, on- and offline marker based positioning gave the highest coverage of the prostate. The D99% of these cases were all above 74 Gy and within 1% of the planned dose. For the SV the D99% is for all individual patients above 66.5 Gy (95% of the prescribed dose) for the online and offline marker position correction protocol. For the other correction protocols the D99% is lower in individual patients.
Conclusion: Using repeat CT scans to include anatomical variation and the actual displacements on the linac, we found that offline position verification with gold markers aimed for adequate treatment of the prostate and base of seminal vesicles is satisfactory using an 8mm margin.

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Phase II study with pharmacodynamic evaluation of docetaxel-prednisone (DP) in combination with metronomic cyclophosphamide (CTX) and celecoxib (C) as first line treatment in castration resistant prostate cancer (CRPC)

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Background: DP has become the standard of care for CRPC, moreover, low-dose metronomic antiangiogenic CTX and C have demonstrated a significant activity in preclinical and clinical studies without relevant toxicities. Integrating MTD chemotherapy with a metronomic schedule could be of interest in advanced prostate cancer patients.
Materials and Methods: Patients (pts) with CRPC received D 60 mg/sqm iv day 1 every 3 weeks up to 12 cycles and from day 2 continuously: P 5 mg po BID, CTX 50 mg po daily and C 200 mg po BID. Primary objective was the percentage of pts free of progression at 6 months; secondary were: PSA levels decrease $\geqslant$ 50%, objective responses (RECIST), toxicities (NCI-CTC criteria) survival and pharmacodynamic evaluations.
Results: To date 34 pts have been enrolled. Main pts characteristics were: median age 72 years (52–79 years), median PS 0 (0–2), median baseline PSA level 36 ng/ml (2.5–1309 ng/ml); main sites of disease: bone 26 pts (76%), lymphnodes 9 pts (26%), liver 1 pt (3 %). Thirty-four pts were evaluable for toxicity whereas 29 for PSA response (1 pt abandoned the study due to allergic reaction after first D administration, 1 pt had measurable disease only without expressing PSA and 3 pts did not receive at least 12 weeks of treatment). Median number of D cycles delivered was 11 (1–12) and median duration of metronomic CTX plus P and C was 237 days (21–874 days). Main grade 3 side-effects were: neutropenia (2 pt; 6%), thrombocytopenia, diarrhoea, stomatitis, dyspnea, peripheral oedema and onycholysis (1 pt; 3%). One pt required C permanent discontinuation due to skin rush. Grade 4 toxicity have been observed in only 1 pt (3%) that experienced a D allergic reaction. The rate of pts free of progression at 6 months was 85%. Overall 22 pts (76%) showed a PSA decrease $\geqslant$ 50% and 26 pts (90%) showed any PSA decrease from baseline (range: 4–99% decrease). Eight pts were evaluable according to RECIST criteria: we observed 1 CR, 2 PR, 4 SD and 1 PD. The median time to PSA progression was 7.6 months (range 1–26 months).
Conclusions: DP plus metronomic CTX and C was a feasible and tolerable regimen. Preliminary activity was also interesting. The evaluation of plasma levels of thrombospondin-1 (TSP-1), VEGF, sVEGFR-2, VE-cadherin mRNA and the expression of TSP-1 and VEGF in peripheral blood mononuclear cells, as potential surrogated markers of antiangiogenic activity of the combination, is ongoing.

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Clinical, biochemical (PSA) and radiographic benefit with sunitinib as a single agent in metastatic chemoresistant and hormone-refractory prostate cancer (HRPC) patients

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Background: Sunitinib is an oral multi-target tyrosine-kinase inhibitor of VEGFR (1, 2, 3), PDGFR (α, β), RET, KIT and FLT-3. VEGFR and PDGFR have been correlated with disease progression and poor prognosis in HRPC. There is no standard therapy for HRPC previously treated with docetaxel. Preliminary results of a phase II study presented at ASCO 2008 suggested single-agent activity and PSA decline in this patient population
Methods: Patients (pts) with highly resistant and castrated HRPC patients with rising PSA were consecutively treated under a compassionate use named-patient based with sunitinib due to no other therapeutic approved options are available. All pts were propose to receive a daily dose of sunitinib 37.5 mg continuous dose with no rest. One cycle was defined as a 3-wk period. Treatment continued until disease progression, toxicity or investigator/patient decision. Pts were evaluable every 6 wks until 4th cycle and then every 12 wks. Primary endpoint was response rate by decline in PSA >50% or measurable disease. PSA was monitored every 4 weeks.
Results: 19 pts with a median age of 73 (61–81) yrs were treated between May 08 and April 09. Median PS (ECOG) was 2; Pts had received a median of 3 previous therapy lines for the hormonorefractory setting. Baseline median PSA was 280 ng/ml (range 26–2908). Gleason score was 7 in 63% and 8–10 in 32%. Pts received a median number of 4 cycles (1.3–13.3+). Disease was measurable in 63%, and 84% were evaluable by rising PSA. 1 PR (5%) was achieved by RECIST and 10 pts (52%) had SD; median PFS was 3.5 m. PSA declined > 50% in 3/19 (16%)and 26% of pts had stable PSA. At this report 9 patients remain on study and 10 are off study (9/10 due to progressive disease and 1 for toxicity). The most common adverse events were asthenia (21% G3), diarrhea (5% G3), anemia (only G1 and 2), hand-foot syndrome (16% G3) and thrombopenia (only G1 and 2). No G4 drug-related events were seen.
Conclusion: Hints of activity with sunitinib were seen in a very highly treated population of pts with refractory to docetaxel HRPC. Tolerability was acceptable. Ongoing randomized studies should confirm the sunitinib efficacy in advanced prostate cancer.

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Oral vinorelbine as a fixed-weekly schedule in taxanes-refractory advanced HRPC. A single institution experience

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Background: Vinorelbine (VRL) has been shown to be active in hormone-refractory prostate cancer (HRPC). Oral formulation of VRL represents a significant advance in the treatment of advanced cancer. The recommended doses are 60–80 mg/m^2(d1–8 q3wks). We evaluated