Materials and Methods: Median follow-up of 110 months.

Purpose/Objective: We studied the effect of a higher dose on tumor control for localized prostate cancer in a randomized trial with a median follow-up of 110 months.

Materials and Methods: Patients with T1b-T4 prostate cancer were included in the period 1997-2003 (n=664) and randomized between 78 Gy (n=333) and 68 Gy (n=331). Primary endpoint was biochemical and/or clinical failure (BCF) according the guidelines of the American Society for Therapeutic Radiology and Oncology (ASTRO) (3 consecutive rises). Secondary endpoints were BCF using the Phoenix definition (Table) and OS. Explorative subgroup analyses were performed.

Results: Estimated freedom from BCF at 10 years according ASTRO was 45.9 % and 38.4 % for 78 Gy and 68 Gy, respectively (Log Rank, p=0.046). CF and OS were similar in both arms (Table). LF as a first event was significantly less observed in the 78 Gy arm (14 versus 27 events, p=0.036). Figure. At the current update, 205 patients were deceased (104 in the 78 Gy arm), including 88 patients with PCRD (44 cases in both arms). Subgroup analysis for BCF showed a greater benefit for patients with PSA ≥ 10 ug/L compared to <10 ug/L (p=0.01 for heterogeneity). Within the subgroup PSA ≥ 10 ug/L, estimated freedom from BCF at 10 years (ASTRO) was 41.7 % for the 78 Gy arm and 30.0 % for the 68 Gy arm (p=0.008). For the subgroup PSA < 10 ug/L, these numbers were 54.4 % and 52.6 %, respectively (p=0.9).

Table. Failures and overall survival at 5 years and 10 years with 1SE (Kaplan-Meier method).

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>78 Gy (%)</th>
<th>68 Gy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free from Failure with Phoenix definition</td>
<td>66.9 (2.6)</td>
<td>61.9 (2.6)</td>
</tr>
<tr>
<td>Free from Clinical Failure</td>
<td>77.1 (2.3)</td>
<td>76.5 (2.4)</td>
</tr>
<tr>
<td>Free from Local Failure</td>
<td>97.6 (0.9)</td>
<td>94.3 (1.3)</td>
</tr>
<tr>
<td>Overall Survival</td>
<td>86.3 (1.0)</td>
<td>84.2 (2.0)</td>
</tr>
</tbody>
</table>

Conclusions: For the first time, a significant difference in LF is demonstrated in a randomized trial. However, despite significant differences in BCF and LF, no significant differences in CF and OS were observed after a median follow-up of 110 months. More follow-up is needed to identify possible effects for these endpoints. Probably only subgroups of the trial population truly benefit from a higher local dose in terms of prolonged OS.

Purpose/Objective: Bone metastases from renal cell carcinoma (RCC) are common and often less responsive to palliative radiotherapy (RT) than metastases from other tumors. Sorafenib is a multi-targeted tyrosine-kinase inhibitor that improves progression-free survival in metastatic RCC. There is pre-clinical evidence to indicate that sorafenib also improves the effectiveness of RT. The purpose of this study was to examine the efficacy and toxicity of sorafenib in patients with RCC receiving palliative RT for painful bone metastases.

Materials and Methods: Twelve patients with RCC and bone metastases were accrued to a phase I/II prospective study of RT and sorafenib. An index lesion was identified in each patient and treated to a dose of 30 Gy in 10 daily fractions. Sorafenib 200 mg or 400 mg per day was administered beginning one week before RT until at least nine weeks after RT. Patients who responded to sorafenib were eligible to continue beyond 12 weeks. Pain scores were evaluated using the Brief Pain Inventory (BPI). 18F-FDG PET imaging was performed at baseline (prior to any treatment) and four weeks after treatment to assess metabolic response. Standardized uptake values
SUV were compared using linear-mixed modeling at baseline and at four weeks after RT for target and non-target lesions.

Results: Eleven patients were eligible for analysis. There were 13 target lesions in 12 irradiated target lesions and 12 non-target lesions (treated with sorafenib alone). Two patients experienced severe toxicity: one developed hand-foot syndrome and another died during treatment from unrelated causes. There were no severe side effects directly attributable to the combination of RT and sorafenib. The BPI mean ‘present’ pain scores at baseline, 2 weeks, and 12 weeks were 3.9, 1.6, and 1.6 respectively (p = 0.07 for 7 weeks vs. baseline; p = 0.13 for 12 weeks vs. baseline). There was a significant difference in the metabolic response of target lesions versus non-target lesions (p = 0.002). For target lesions, SUV values decreased after RT and sorafenib (p = 0.003). However, for non-target lesions, there was a trend towards an increase in SUV (p = 0.09). Only two patients required re-irradiation of a previously treated index lesion.

Conclusions: The combination RT and sorafenib is feasible and well tolerated as a treatment for palliation of painful bone metastases in patients with metastatic RCC. Both the treatment and PET results suggest that RT provides additional palliative benefit in this patient population and should be considered even in those receiving tyrosine-kinase inhibitors like sorafenib.

OC-0055

Linac based SBRT for prostate cancer in 5 fractions: Preliminary report of a Phase II study with FFF delivery

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Purpose/Objective: To assess urinary (GU) function and toxicity in patients treated with image-guided proton therapy (PT) for early- and intermediate-risk prostate cancer and to analyze the impact of pretreatment urinary obstructive symptoms on urinary function after PT.

Materials and Methods: Two prospective trials accrued 171 prostate cancer patients from August 2006 to September 2007. Low-risk patients received 78 cobalt gray equivalent (CGE) in 39 fractions and intermediate-risk patients received 78 to 82 CGE. Median follow-up was 5 years. The International Prostate Symptom Score (IPSS) and GU toxicities (per CTCAE v3.0 and v4.0) were documented prospectively.

Results: Five transient GU events were scored Gr 3 per CTCAE v4.0, for a cumulative late GU toxicity rate of 2.9% at 5 years. There were no Gr 4 or 5 events. On multivariate analysis (MVA), the only factor predictive of Gr ≥2 GU toxicity was pretreatment IPSS severity (p = 0.044). Patients with pretreatment IPSS of 15 had a significant improvement in median IPSS at 5 years compared to baseline (p = 0.001). Patients with pretreatment IPSS of <15 had a 3-point decline (deterioration) in IPSS. Patients with IPSS ≤15 had a stable median IPSS of 6 before treatment and at 6 months.

Conclusions: Urologic toxicity at 5 years with image-guided PT has been uncommon and transient. Patients with pretreatment IPSS of <15 had stable urinary function 5 years after PT, but patients with 15-25 showed substantial improvement (decline) in median IPSS, a finding not explained by initiation or dose adjustment of alpha blockers. This suggests that PT provides a minimal toxicity and effective treatment for low and intermediate prostate cancer patients, including those with significant pretreatment GU dysfunction (IPSS ≥15).

OC-0052

Late toxicity in the randomized phase III Dutch Hypofractionation Trial for prostate cancer patients (HYPRO).

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Purpose/Objective: Accumulating evidence demonstrates the sensitivity of prostate cancer to fractionation, estimating a low α/β ratio. This suggests a significant therapeutic benefit of hypofractionation, delivering a higher biological dose to the prostate without increasing toxicity. To test this hypothesis a randomized multicenter phase III Hypofractionation Trial was performed in The Netherlands. Here we report on the first results of late toxicity.

Materials and Methods: Between April 2007 and January 2011, 820 men with localized prostate cancer were included. They were randomly assigned to a standard fractionation (SF) arm of 39x2 Gy (5 fractions a week), or a hypofractionated (HF) arm of 19x3.4 Gy (3 fractions a week). Primary endpoints were relapse-free survival (RFS) and toxicity scores. The late toxicity scores were measured twice a year. After finishing the course (RC) patients were evaluated using RTOG/ECRC criteria. The highest grade scored in the follow-up was considered.

Results: To each fractionation arm 410 patients were randomly assigned. The median follow-up was 27 months (range 2.3-57 months). A grade ≥ 2 late gastrointestinal toxicity (GI) after finishing the RC was reported by 15% of the patients treated with SF and by 20% of the