7009 POSTER

Proton radiotherapy for patients with prostate cancer

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Background: Proton radiotherapy (PRT) is a sophisticated treatment modality for prostate cancer. The purpose of this study is to examine clinical results of prostate cancer treated with PRT.
Materials and Methods: From Apr 2003 to Oct 2004, 290 males aged 48−85 (average 69) with histologically-proven cT1−3N0M0 prostate cancer (1997 UICC TNM) received PRT. Clinical T stage was classified T1a/T1b/T1c/T2a/T2b/T3a/T3b as 2/3/112/79/38/36/20. Initial prostate specific antigen (PSA) level was distributed 1.2 to 222 (mean 17.8 ng/ml). Patients were stratified into three prognostic risk groups: Group A patients had a T1-T2a, PSA < 20 ng/ml, and the percentage of positive prostate biopsies (PPPB) <50%; Group B: T2b-T3, or 20 ng/ml⩽ PSA < 50 ng/ml, or PPPB ⩾50 %; and Group C: PSA>50 ng/ml irrespective of T factor. Eighty-three of 170 patients (49%) in group A received PRT with neoadjuvant androgen ablation (NAA) for 6 months, while 100 of 101 (99%) in group B were treated by NAA followed by PRT. All of 19 in group C were treated by NAA, PRT and adjuvant androgen ablation. PRT was planned with a 3D planning system using bilateral 2 fields; patients received 74 GyE (gray equivalent, using a relative biologic equivalence factor of 1.1) of protons (190 to 230 MeV) at 2.0 GyE per fraction. GI and GU toxicity was scored according to the RTOG/EORTC Late Morbidity Grading Scale. Overall survival (OS) and biochemical disease free survival rate were calculated by Kaplan-Meier and Log-rank test. Multivariate analysis was examined by Cox proportional hazards model.
Results: Five patients died from other disease including brain tumor, gall bladder cancer, cerebral hemorrhage, bronchitis, and pneumonia, in the follow-up period ranging from 53 to 72 months (median 62). Biochemical disease free survival/OS rates at 5 years was 88.2%/96.5% in all cases and was 97.6%/96.4%, 83.8%/97.0%, 52.1%/94.7%, in the group A, B, C, respectively. According to MSKCC risk criteria, 5 year biochemical disease free survival rates in favorable (n = 62)/intermediate (n = 106)/unfavorable (n = 116) were 98.2%/94.8%/76.3%, respectively. T factor, Gleason score, PPPB, PSA, HIBMC, MSKCC risk group were significant in univariate analysis for PSA failure and initial PSA is only prominent in the multivariate analysis. The GI toxicity rates of G0/G1/G2/G3 were 91.0%/4.8%/4.1%/0%, and the GU toxicity rates of G0/G1/G2/G3 were 85.5%/7.9%/5.5%/1.0%, respectively.
Conclusions: Our proton radiotherapy showed excellent OS and biochemical disease free survival rates in patients with prostate cancer with minimum late morbidities.

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The role of previous abdominal surgery in the development of late rectal bleeding in prostate cancer patients treated with 3D-CRT: specific constraints and nomogram prediction

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Purpose: To discuss the role of specific types of abdominal surgery (SURG) before radiation therapy (RT) as a risk factor for late rectal bleeding (lrb) in prostate cancer patients (pts) and to build a nomogram for the prediction of G2−3 lrb.
Methods: 718 pts accrued in AIROPROS 0102 trial with a complete follow-up of 36 mos are here analysed. Previous multivariate logistic analysis (MVA) (Fiorino et al IJROBP 08) showed lrb as highly correlated with V75 Gy, SURG (OR = 2.24), acute G2−3 lower gastro-intestinal (LGI) toxicity and androgen deprivation (AD). This work focuses on pts who underwent SURG before RT to clarify if a different dose-volume relationship is present and to evaluate the possible role and weight of different abdominal surgeries (rectum-sigma resection, kidney resection, cholecystectomy or appendectomy) on lrb. A nomogram for SURG pts was developed based on MVA modeling.
Results: 28/718 (3.9%) G2 and 24/718 (3.3%) G3 lrb were registered. In the subgroup of pts previously submitted to SURG (n = 69; 8 G2-G3 lrb), V70 Gy was found to be highly correlated with lrb (continuous variable, OR=1.10, p = 0.012) while V70 Gy was of minor importance in the population of pts who did not undergo SURG prior to RT. A cut-off V70 Gy = 20% was found to be a useful constraint for SURG pts. When considering the kind of surgery, cholecystectomy was found to be highly correlated with lrb: OR = 4.3 and p = 0.006 (G2−3 lrb) and OR = 5.4 and p = 0.01 (G3 lrb). In MVA, G2−3 lrb was correlated to appendectomy (OR = 2.5, p = 0.13), cholecystectomy (OR = 6.1, p = 0.002), AD (protective factor, OR = 0.57, p = 0.09) and V75 Gy (continuous variable, OR = 1.063, p = 0.004). G3 lrb was mainly correlated to appendectomy (OR = 5.2, p = 0.07) and cholecystectomy (OR = 4.2, p = 0.038). The inputs in the SURG nomogram for estimation of G2−3 lrb were: AD (protective factor), V70 Gy and the nomogram estimated G2−3 LGI toxicity probability (estimation made using the nomogram published in Valdagni et al IJROBP 08).
Conclusions: This analysis highlights previous SURG as the best predictor of lrb. For these pts an impairment of the repair capacity of the rectum due to regional (neurological? vascular? inflammatory?) effects might be hypothesized. V70 Gy was highly correlated with lrb for the group of SURG pts. Among the different types of SURG, cholecystectomy (and secondarily appendectomy) plays the major role in the risk of lrb. A nomogram for SURG pts was developed aiming to support radiation oncologists in the prediction of lrb.

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A double-blind, randomised dose-response phase II, multicentre study of radium-223 for the palliation of painful bone metastases in castration refractory prostate cancer patients

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Background: Alpharadin (radium-223) is a novel alpha pharmaceutical in development for treatment of bone metastases. This new generation bone seeker delivers high linear energy transfer a-particle irradiation with extremely short range, thus sparing bone marrow. These characteristics generate highly localized radiation zones which may inhibit tumour progression and induce pain relief. The aim of the study was to investigate if there is a pain relieving effect and a dose-response relationship after a single dose of Alpharadin.
Materials and Methods: 100 castration-refractory prostate cancer patients with painful bone metastases were randomised in a double-blind dose-ranging study to receive one out of four dose levels: 5, 25, 50 or 100 kBq/kg b.w. of radium-223. Median age, baseline PSA and baseline patients' diary Visual Analogue Score (VAS) were 70 years, 149 μg/L and 42 mm, respectively. The primary efficacy endpoint was Pain Index (PI) based on a combination of the change in diary pain rating (VAS scale) and the change in analgesic consumption during a 16 weeks period. Pain and physical function were also measured using BPI (Brief Pain Inventory). Bone-ALP and safety were assessed.
Results: At 8 weeks after injection there were 50, 50, 60 and 74% responders (including both pain response and stable disease) in the four dose levels: 5, 25, 50 or 100 kBq/kg b.w., respectively. Within each dose group, for the responders, a significant pain relieving effect was observed in the patients' diary VAS score. Median decrease were −15, −30, −26 and −22 mm and the p values were 0.01, 0.001, 0.0005 and <0.0001 respectively. The pain response improved gradually from 2 to 8 weeks, with the best effects in the highest dose group. 33 % of the patients in the 5 and 25 kBq/kg groups had increased use of analgesic (non-responders) compared to 10 % of the patients in the two highest dose groups after 4 weeks. Improvements in BPI pain severity and functional interference index confirmed progressive improvements up to 8 weeks. A significant reduction was seen in bone-ALP for the highest dose level (p < 0.0001 at week 4). The haematological toxicity was generally mild and not clinically significant.
Conclusions: A single dose of Alpharadin exhibits a pain palliative effect, with the most prominent effects documented for the highest dose level, both on pain relief and reduced bone-ALP. Alpharadin was well tolerated and confirmed the benign side effect profile seen in other studies.
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