7045 POSTER

Preventive use of bisphosphonates against bone demineralisation promotes adjuvant anti-neoplasic effect on high risk prostate cancer patients

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Purpose: High-risk CaP demands multi-modal treatment to extend survival. Bisphosphonates was recently incorporated as an adjuvant element to prevent skeleton events and bone demineralization secondary from ADT regularly used in this subset of patients. The well-known in vitro anti-cancer effect may also delay tumor progression and metastasis development.
Material and Methods: One hundred-forty CaP with Gleason > 7 or = 7 with pattern 5 treated with definitive Radt or RRP were followed until metastasis developed. All of them received monthly IV clodronate as soon as PSA increased during the follow-up. Patients had had biochemical exams and semestral bone scintigraphy or image exams at pain sites. Cox's regression, Kaplan-Meier and log-rank test were applied with 5% significance.
Results: There was statistical difference in time to development of bone metastasis on those receiving clodronate in comparison to those not receiving it despite the primary treatment to the CaP ($p < 0.001$). Radt or RRP did not produced any difference on the time to metastasis development within the groups receiving or not the drug ($p = 0.98$). However, those not receiving clodronate presented metastasis appearance 7X faster than those receiving ($RR = 6.9 - p < 0.001$).
Conclusions: Clodronate significantly delayed the metastasis appearance on high-risk prostate cancer patients treated with definitive Radt or RRP that recurred during the oncological follow-up.

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Effectiveness of Carboplatin (C) plus weekly docetaxel (D) as second-line treatment for docetaxel-resistant, hormone-refractory prostate cancer (HRPC)

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Background: There is no standard chemotherapy for patients (pts) with docetaxel(D)-resistant, hormone-refractory prostate cancer (HRPC). While initial reports support the use of carboplatin (C) in combination with D as second-line treatment in these pts, the optimal regimen is still unknown.
Objective: Metastatic HRPC pts with serologic and/or radiographic evidence of progression on D were included in our single center, retrospective analysis. Intervention: Between February 2005 and April 2009, 38 pts received treatment with C AUC 5 q4wks in combination with D 35 mg/m^2 d1, d8, d15 q4wks.
Outcome measures: All pts were assessed for response rate (RR), progression free survival (PFS), and overall survival (OS).
Results: 35 pts were evaluable for response assessment. Median age was 68.5 years (range 56− 77) and median baseline performance status was ECOG 1 (range 0−3). The median number of prior therapies was 1 (range 1−3) with a median of 7 cycles of D therapy (range 3−34) administered. Median PSA at baseline was 244.3 ng/ml (range 12.33−6,446). Serum chromogranin A and neurone specific enolase (NSE) were elevated in 28/31 and 16/34 cases, respectively. The median follow-up was 7.5 months (range: 0−41) with a median number of 6 cycles DC administered (range: 1−39, total of 315 cycles). Treatment with DC elicited a PSA response (declines of $\geqslant$50%) in 18 of 35 pts (51.4%, 95% CI 33.9, 68.6%) and PSA stabilization in 9/35 pts (25.7%). 8/35 pts (22.8%) progressed without PSA response. 8 PSA responders (22.9%) had a maximal PSA reduction of >90%. The median duration of PSA response was 5.1 mo. (95% CI 3.9, 7.9 mo.). PFS was significantly longer in PSA responders vs. PSA non-responders (9.5 mo. vs 3.2 mo., $p < 0.0001$). 16 of 23 pts with measureable disease were evaluable for response assessment with 6 PR, 7 SD and 3 PD. 6 of 10 PSA responders had a PR and 4 SD, while 3/6 PSA non-responders had PD and 3 SD. At the time of analysis, 4 PSA responders and 11 PSA non-responders have died. Median OS of all patients was 12.9 mo. (95% CI 7.6, 21.7 mo.) with 19.8 mo. for PSA responders vs. 7.9 mo. for PSA non-responders ($p < 0.001$). The most common grade 3/4 toxicities were neutropenia in 12/38, anemia in 6/38 and thrombocytopenia in 4/38 pts. 19 of 38 pts received blood transfusions due to anemia. The most common grade 3−4 non-hematologic toxicities were bisphosphonate-induced osteonecrosis of the jaw in 6/31 cases with zoledronate treatment and thrombosis/embolism in 4/38 pts.
Conclusions: This retrospective analysis supports the usefulness of C plus weekly D chemotherapy as $\geqslant$second-line treatment in D-resistant PC patients.

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Exploration of the optimal dosimetric parameters to predict late rectal toxicity in external beam radiotherapy for prostate cancer

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Background: It is unclear whether the dose volume histogram (DVH) of the whole rectum or rectum wall are more accurate to predict rectal toxicity in external beam radiotherapy for prostate cancer. Furthermore, the rectal volume and position change often during a course of treatment. We studied the value of a correction factor for these volume changes to predict for late rectal toxicity.
Materials and Methods: We analyzed 100 patients treated with 70−76 Gy for primary prostate cancer. To adjust the DVH of the rectum for rectum volume changes during treatment, we calculated a "corrected" DVH. The correction factor was developed by Miralbell et al. (IJROBP 2003) and is a polynomial function correlating the initial rectal volume with the mean percentage of change in the rectal volume during treatment. A Cox Regression model was performed to analyze which DVH parameters influence late rectal toxicity grade 1−4 (Common Terminology Criteria Version 3.0). Factors included were the V40, V65 with and without the correction factor, mean and median dose to rectum and rectum wall as well as the prescribed dose to the prostate.
Results: Median follow up is 15 months (3−43 months). The majority of our patients (69%) had no late rectal toxicities, 22% had grade1and 2, 8% grade 3 and 1% grade 4. In the Cox Regression model only the V40 of the rectum ($p = 0.036$) and rectum wall (0.018) were significantly correlated with late rectal toxicity grade 1−4. The correction factor did not contribute to a better correlation.
Conclusion: The V40 of the rectum wall and that of the entire rectum are good predictors of late toxicity. The application of the correction factor for rectal volume changes during treatment did not improve the ability of DVH parameters to predict for late rectal toxicity.

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Elevated serum her2/neu in human prostate cancer and benign hyperplasia

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Background: Overexpression of the neu oncoprotein has been described in several tumor models including breast and prostate cancer. Her2/neu is a type I tyrosine kinase and a member of the ErbB receptor family. When overexpressed in the murine prostate, it causes the development of prostatic intraepithelial neoplasia, that progresses to adenocarcinoma. In the absence of androgens Her2/neu has been shown to confer growth advantage to prostate cancer cells.
Materials and Methods: The objectives of the study were twofold. First, to investigate serum Her2/neu expression in prostate cancer (CaP) in comparison to benign prostatic hyperplasia(BPH). Second, to determine whether Her2/neu expression correlates with Gleason score and PSA levels in prostate cancer. We have used ADVIA Centaur (Automated Hemilumine-scence system – Siemens) to determine serum Her2/neu levels. In addition, total and free PSA levels were analyzed in 45 patients: including 35 with CaP and 10 with BPH. Tumors were evaluated according to Gleason grading system and were sub-divided into 3 groups: well (Gleason grade 2−4), moderate (5−7) and poorly differentiated (8−10).
Results: Serum Her2/neu was overexpressed in 20/35 androgen-dependent CaP patients compared to 1/10 BPH patients. The levels of Her2/neu were higher in CaP patients with Gleason grade 5−7 (moderate differentiation). Serum PSA levels were significantly higher in the group of patients with elevated serum Her2/neu compared to patients with normal Her2/neu levels. The research is under development.
Conclusions: The findings of this study point to a different role of Her2/neu in prostate cancer with respect to PSA and emphasize the need to further explore their role in the setting of early diagnosis and treatment of prostate cancer. Her2/neu is not overexpressed in BPH compared to CaP.