

Methods: Over the last 5 years we investigated 87 patients for the pO₂-status of cervical cancer (age 34-80 yrs). All patients were treated with curative intent and the same treatment schedule. The pO₂-measurements were done using polarographic needle probes and the Eppendorf-device. The microvessel density was determined in pretreatment biopsies immunohistologically using a CD31-antibody.

Results: The median- pO₂ for all 87 patients was 15 mmHg pooled over 4 measured tracks, so the threshold for classification was set to 15 mmHg. We found only a marginal effect of the pretreatment pO₂ in the 3-year-survival (52 +9% vs. 69 + 8% p =0,15). Measurements of oxygenation after 11 fractions revealed no changes of pO₂ if the group of patients was analyzed as a whole group. The analysis of the pO₂-changing after 11 fractions can be classified in 4 groups of pO₂-modification: 1. a level >15mmHg at both measured points; 2. a level <15mmHg at both measured points 3. an increased or a decreased pO₂ after 11 fractions. In a Cox-model - adjusted to stage -the best clinical results were obtained for patients with a well-oxygenated tumor independent of the time of high pO₂-level, the worst results are shown in patients with persistent hypoxic cancers. In 46/87 patients the vascular density prior to therapy was evaluated. Tumors with a persisting low pO₂ showed a significantly higher vessel count in comparison to the 3 other groups (p<0,001).

Conclusions: Our investigation demonstrated that tumor hypoxia is linked to angiogenesis. This supports the use of hypoxic-modifying strategies.

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POSTER DISCUSSION

Erythropoietin enhances radiation treatment efficacy in patients with pelvic malignancies. final results of a randomized phase III study

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Purpose: To determine the efficacy and safety of the subcutaneous administration of recombinant human erythropoietin (EPO) to patients with pelvic malignancies receiving radiotherapy(RT).

Patients and Methods: 385 patients underwent conventional RT with 2 Gy daily fraction/5days/week to a total dose of 50-60 Gy +/- EPO 10000U daily 5 times per week. All patients received iron supplements. Primary endpoints were weekly haemoglobin increase and local tumor control. Secondary endpoints were safety, disease free survival and overall survival.

Results: There were no significant differences between the two groups for age, Hb levels before RT, site and stage of disease(P>0.1). The mean Hb levels during RT in the EPO group were 12.9±2.6g/dL versus 10.6±2.5 g/dL in the control group. The mean weekly increase of Hb was 0.54g/dL in the EPO group versus 0.17g/dL in the control group. The 4 year disease free survival was 85.3% in the EPO group versus 67.2% in the control group(p=0.0008). No EPO related side effects were observed.

Conclusion: EPO can be safely administered and improves significantly the local tumor control in patients with pelvic malignancies undergoing RT.

Genitourinary cancer

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POSTER DISCUSSION

The importance of implant dose on biochemical outcome following I-125 prostate brachytherapy

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Purpose: To determine the effect of implant dose as assessed by CT based post-implant dosimetry on biochemical outcomes following I-125 brachytherapy for prostate cancer.

Methods: 234 patients were treated from 1991 to 1999 with I-125 brachytherapy without hormonal therapy or external beam irradiation for T1-T2 prostate cancer. All patients had Gleason scores < 7. Presenting PSA ranged from 1.3 to 189 (median 6.8). Clinical stage was T1b-T2a in 173 patients and T2b-T2c in 61 patients. All patients were implanted using a real-time ultrasound guided technique. One month post-implant, all patients underwent CT based dosimetric analysis. Implant dose was defined as D90 (dose delivered to 90% of the prostate on dose volume histogram). D90 values ranged from 15 to 256 Gy (median 163 Gy). All values conformed to

TG43 guidelines. PSA failure rates were calculated with actuarial methods using the ASTRO definition. Follow-up from date of implant to last seen ranged from 24 to 119 months (median 47).

Results: Implant dose had a significant effect on freedom from PSA failure (FFPF) rates. Patients with D90 values of < 140 Gy (71), 140 - < 160 Gy (97), 160 - < 180 (100) and > or equal to 180 Gy (97) had FFPF rates at 7 years of 63%, 85%, 95% and 88%, respectively (p=0.0025). Overall, patients with D90s > or equal to 140 Gy had a FFPF rate at 7 years of 90% versus 63% for those with D90s < 140 Gy (p=0.0003). In addition, pretreatment PSA also significantly affected PSA failure with FFPF rates at 7 years of 82%, 83% and 24% for PSA levels of < or equal to 10, >10-20 and > 20, respectively (p=0.0001). A dose response cutpoint of 140 Gy was seen in both patients with initial PSA < or equal to 10 (190) and those with PSA > 10 (44), p=0.001 and p=0.04, respectively. The median follow-up was 48 months and 46 months for patients with D90 < 140 Gy and > or equal to 140 Gy, respectively. A multivariate analysis testing the effect of dose, PSA, score and stage on FFPF rates found dose to be the most significant predictor of outcome with p values of <0.0001, 0.03, 0.31 and 0.58, respectively.

Conclusions: Implant dose is the most significant predictor of PSA failure following I-125 prostate brachytherapy. Based on this analysis, optimal D90 values from the post-implant CT analysis should be > or equal to 140 Gy. Current data reveal no significant improvements with values > 180 Gy.

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POSTER DISCUSSION

Inhibition of 20S Proteasome results in serum IL-6 and PSA decline in patients (pts) with Androgen-Independent Prostate Cancer (AIPCa) treated with the Proteasome Inhibitor PS-341

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Purpose: Assessing surrogate markers of NFkappaB activity in patients with androgen-independent prostate cancer(AIPCa) treated with proteasome inhibitors is of great importance for drug development. Preclinical studies indicate that PS-341, a specific proteasome inhibitor, inhibits NFkappaB, which is implicated in the progression of PCa in bone and resistance to therapy. Serum IL6 concentration can serve as a surrogate of NFkappaB activity.

Methods: We studied 43 pts [age: 64 (45-78), PS:0/1: 43] with metastatic AI PCa treated on a Phase I trial of PS-341, administered intravenously weekly x 4 every 6 wks over 14 dose levels (0.13-1.6 mg/m²) for evidence of anti-tumor activity, serial serum (s) IL-6 concentration (by ELISA) and 20S proteasome inhibition (20S-PI). 20S-PI is measured ex vivo in peripheral blood (PB) using a fluorogenic substrate.

Results: 4/15 pts with 45-55% 20S-PI (0.75-1.21 mg/m²) and 16/18 pts with > 70% 20S-PI (1.32-1.6 mg/m²) had serum available for analysis. Patients with 45-55% 20S-PI had 40% suppression in median sIL-6 but no change in PSA slope or concentration, while pts with >70% 20S-PI had 80% decline in median sIL-6 with parallel decline in PSA slope (63% of pts) and PSA concentration (19% of pts). We also observed radiographic partial response (PR) in 2 patients.

Conclusions: Our data demonstrate a dose dependent decline in sIL-6 and PSA slope and concentration in pts treated with weekly PS-341. The biologic effect occurs within a tolerable dose range of PS-341. This data suggests that weekly PS-341 may be active in prostate cancer and supports the view that its action may be mediated through the inhibition of NFkappaB.

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POSTER DISCUSSION

Pronounced radiosensitization of estramustine phosphate in the treatment of locally advanced prostate cancer

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Purpose: Since the potential of Estramustine phosphate (EMP) as tumor radiosensitizer has been shown extensively by us and others in animal models, a clinical study was designed to test the hypothesis that EMP would preferentially enhance the anti-tumor effects of radiation therapy for the treatment of prostate cancer. A prospective phase II trial was carried out to determine whether the combined EMP and external beam radiotherapy (EBRT) would increase the tumor control rate of locally advanced prostate cancer with no enhanced normal tissue toxicity.

Methods: Between January 1991 and March 2000, 75 patients (pts), stage T2 through stage T4, were entered into the study. Forty-seven (63%)