target tumor (the most symptomatic tumor) responses achieved a single, pre-selected primary treatment goal (e.g., improved wound care, better pain control) versus 15% of nonresponders. Pharmacokinetic studies showed peak plasma levels of total and free platinum 10- to 20-fold lower after intratumoral administration of CDDP/epi gel than reported for systemic cisplatin therapy. Patients treated with CDDP/epi gel experienced few of the side effects typically reported with intravenous cisplatin.

Conclusion: CDDP/epi injectable gel significantly reduces tumor burden, ameliorates tumor symptoms, and provides a new therapeutic option for managing patients with solid tumors such as HNSCC.

372 POSTER

Elective lymph node dissection following hyperfractionated accelerated radio-(chemo-)therapy for advanced head & neck cancer

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Purpose: The two years results of a German multicentre randomized trial showed that accelerated chemoradiation with MMC/5-FU to 70.6 Gy is more effective than accelerated radiation to 77.6 Gy alone at equivalent levels of acute and late radiation morbidity (abstracts ECCO10 and ASTRO 2000). Frequency, histopathology and impact on local tumour control of additive elective lymph node dissection were analysed.

Methods: Between 2/1996-8/2000 at T*bingen University 41 randomized patients plus 50 none-randomized patients with stage III/IV head&neck cancer were treated according to this protocol. Six to nine weeks after completion of accelerated (chemo)radiation an elective lymph node dissection was performed, if the primary tumour was in complete remission and clinical plus computed tomography proved residual lymph node disease. Nineteen of 39 patients with residual node disease underwent uni- or bilateral elective node dissection, the remaining patients had residual primary tumours, clinical detoriation or refused neck dissection. After elective node dissection one haematoma required additional surgical intervention and prolonged secondary wound healing was observed.

Results: After a median actuarial follow up of 24 months, 1 and 2 year overall survival was 81% and 64%, and loco-regional tumour control 64% and 56%, respectively. Three year loco-regional tumour control in randomized patients was 49% compared to 47% in non-randomized patients (log rank p=.78). Two-years loco-regional tumour control in stage cT4cN0 was 73% compared to 52% in cT2-4 cN1-3 tumours. Subgroup analysis of patients with involved nodes revealed a 2-year loco-regional tumour control in 58% (19/29 pat.) with complete remission of neck disease, 63% (12/16 pat.) with residual neck disease and elective node dissection versus 33% (12/23 pat.) without further treatment (p=.007). Restriction to patients with complete remission of the primary tumour revealed a 2-year loco-regional tumour control in 60% (16/22 pat.) with complete remission of neck disease, 75% (10/12 pat.) with residual neck disease and elective node dissection versus 33% (4/6 pat.) without further treatment (p=.08)

Histopathological examination showed viable tumour in 8 of 19 patients.

Conclusions: Elective node dissection of residual neck disease 6 to 9 weeks after completion of hyperfractionated accelerated radio-(chemo-)therapy contributed to loco-regional tumour control in advanced head&neck cancer.

373 POSTER

The hazard of ceiling effect for acceleration of postoperative radiotherapy of squamous cell head and neck cancer

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Purpose: To analyze the probability of loco-regional tumor control (TCP) in postoperative radiotherapy for squamous cell head and neck cancer (PRT) as a function of the average dose-intensity (DI) of radiation course.

Material/methods: The analysis included 942 patients in various locations and stages who were treated in Center of Oncology, Gliwice between 1980 and 1998. Mean total radiation dose, dose per fraction, overall radiation treatment time (OTT), and the interval surgery-radiotherapy were 62,4 Gy 2,1 Gy, 46 days and 62 days respectively. The heterogeneity in DI (mean 9.8 Gy/week, Std ±1.4) resulted both from unplanned treatment gaps and the diversity in dose/time prescription. Mathematical modeling of the relationship DI-TCP-dose has followed a statistical analysis of the clinical data.

Results: The data show that, for a given level of radiation dose, the relationship DI-TCP is non-linear, and increase in DI from 6 to 12 Gy/week results in steep increase in TCP, unlike increase in DI over 12 Gy/week, which brings only modest further improvement in local control. The same effect is predicted from theoretical modeling, which incorporates the effect of heterogeneity in radiosensitivity, repopulation, and subclinical tumor burden. For total radiation doses of 50 Gy or less such ceiling effect may appear at tumor cure levels below 80%.

Conclusion: The gain from shortening of OTT (and/or from increase in DI) is smaller than therapeutic lose from equivalent protraction of PRT. Clinical data on split-course therapy, or unplanned treatment gaps should not be used for prediction of gain from accelerated treatments.

374 POSTER

Recombinant human erythropoietin (r-HuEPO) corrects anemia and prevents transfusion during induction and concurrent chemotherapy during head and neck cancer (HNC) treatment

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The etiology of anemia in HNC is multifactorial, and can be caused by poor nutrition, low endogenous erythropoietin production, poor erythropoietin response, radiation and chemotherapeutic agents, and inflammation. We have previously reported preliminary toxicity and efficacy results of two sequential multi-institutional phase II taxane-based chemoradiation trials in locally-advanced HNC. This is a report describing the concurrent use of r-HuEPO in ameliorating treatment-induced anemia.

Eligibility: Previously untreated stage 3 or 4 squamous cell carcinoma of the larynx, hypopharynx, or base of tongue; no metastatic disease; good organ system function. Treatment: all 42 patients received induction chemotherapy with paclitaxel (P) 135 mg/m2 and carboplatin (CB) AUC 7.5 every 21d x 3 cycles. Patients with PR or CR at the primary site then received definitive RT (70-74 Gy in daily 2 Gy fxs) with concurrent P-based chemotherapy. Concomitant regimen 1 consisted of weekly P 30 mg/m2 q7d plus cisplatin 75 m2 d1, 22, and 43 (n=20). Regimen 2 consisted of weekly P 30 mg/m2 and weekly CB AUC 1 x 7 doses (n=22). All 42 patients were treated sequentially. Results: It was noted that 3 of the first 6 patients (50%) developed a moderate to severe anemia and required transfusions during chemoradiation to keep hemoglobin (Hgb) * 10 gm/dl. Thereafter, the treatment protocol was amended and all subsequent patients (n=36) received weekly r-HuEPO 40,000U in addition to induction and concurrent chemotherapy. Only 6 of 36 (15%) required transfusion after the addition of r-HuEPO. Median pre-treatment Hgb level in all 42 patients was 13.1 gm/dl, and was not different between groups. Without r-HuEPO, median end-treatment Hgb was 10.6 gm/dl. With the addition of weekly r-HuEPO end-treatment Hgb was 13.2 gm/dl, despite receiving fewer transfusions.

Conclusion: The use of weekly r-HuEPO 40,000U significantly reduced the need for transfusions and maintained hemoglobin throughout aggressive induction chemotherapy and concurrent chemoradiation in locally-advanced HNC patients. We are currently gathering long-term data to determine if maintaining a higher Hgb during treatment with r-HuEPO positively affects QOL and tumor control.

375 POSTER

Investigation of molecular targets for therapy in salivary glands carcinoma

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Purpose: Patients with recurrent and/or metastatic salivary glands carcinoma (SGC) respond poorly to chemotherapy. The availability of new selective drugs targeting receptors or molecular pathways warrants the conduct of studies assessing tumor-associated molecular alterations that will eventually drive new tailored therapeutic approaches in SGC.

Methods: Histologic types were: adenoid cystic carcinoma (ACC, n = 27), adenocarcinoma (ADC, n = 7), salivary duct carcinoma (SDC, n = 9), myoepithelial carcinoma (n = 5), mucoepidermoid carcinoma (n = 2), acinic cell carcinoma (n = 1) and undifferentiated salivary gland carcinoma (n = 1). The expression of estrogen (ER), progesterone (PgR), androgen (AR), and epidermal growth factor 1 (EGFR) and 2 (HER2) receptors was investigated by immune-histochemistry (IHC) on formalin-fixed archival