

Afr. (including one total laryngectomy (TLE) for severe haemorrhage of a radiation ulcer). Mild laryngeal oedema was noticed in 35%, 22% and 38%, and persisting swallowing complaints were seen in 14%, 12%, and 9% for Cfr., HAfr., and Afr., resp. For patients receiving TLE for local recurrence, fistulae were seen in 14% (2/14), 29% (2/7), and 50% (3/6) after Cfr., HAfr., and Afr., resp.

**Conclusion:** In the Afr. schedule accelerated fr. started in week 3 and in the HAfr. schedule in week 4. This may account for the increased late toxicity in the Afr. schedule. Reducing treatment time by 2 weeks without reduction of total dose didn't result in increased toxicity using the HAfr. schedule.

368

POSTER

### Interleukin-18 is constitutively expressed in head and neck squamous cancer cells

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**Purpose:** An imbalance of immunoregulatory factors is believed to contribute to immunosuppression associated with human head and neck squamous cell carcinomas (SCCHN). Interleukin (IL)-18 is a potent cytokine which promotes monocyte, macrophage and T helper 1 responses through induction of Interferon (IFN)-gamma by activated T cells. The aim of the present study was to define the production of IL-18 by SCCHN and its possible role in modulating the immune responses.

**Methods:** Expression of IL-18 in untreated and 5-fluorouracil (5-FU)-treated PCI4A and PCI13 SCCHN cell lines was analyzed by reverse transcription polymerase chain reaction (RT-PCR), flow cytometry, western blot and ELISA.

**Results:** We found that both PCI4A and PCI13 SCCHN cell lines express IL-18 at the mRNA as well as at the protein level. However, the protein is expressed intracellularly and predominantly released as unprocessed form (kDa 24). After exposure to 5-FU, an adjuvant therapeutic agent of choice for advanced SCCHN treatment, in both cell lines bioactive form of IL-18 was detected together with the inactive form.

**Conclusions:** The failure of SCCHN cells to process IL-18 raises the question of the role of the caspase 1/ICE in these cells. Experiments are now in progress to answer this question. However, these preliminary results suggest that 5-FU treatment promotes the processing of IL-18 in SCCHN cells, inducing the release of the active form of the cytokine that potentially can elicit an in vivo protective anti-tumor effects.

369

POSTER

### Hemoglobin change, not hemoglobin concentration, has the predictive value in postoperative radiotherapy for locally advanced laryngeal cancer

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**Purpose:** Hemoglobin (Hb) concentration has an established prognostic value in radiotherapy alone for head and neck cancer. In our previous study, however, we could not confirm its value in a heterogeneous group of patients treated with postoperative radiotherapy (pRT) (Radiother. Oncol. Vol.56, Supl.1, p.158, abst. 598). The aim of this study was to investigate the predictive value of Hb concentration and Hb change in a subset of patients with advanced laryngeal cancer.

**Material and Methods:** Medical records of 690 patients with squamous laryngeal cancer treated with pRT in Centre of Oncology in Gliwice, Poland between 1980 and 1995 were reviewed for the analysis. The mean age of patients was 54 years. Male-female ratio was 9:1. There was considerable heterogeneity in total dose of pRT (20-72 Gy), fraction dose (1.5 - 2.5 Gy), overall treatment time, and Hb concentration (median-13.2). Median time from surgery to RT was 56 days. The data on locoregional tumour control were analysed using Cox proportional hazard regression model.

**Results:** A univariate analysis has shown that high Hb concentration at the end of pRT, and its increase during the course of irradiation were significantly related to longer recurrence-free survival, but Hb concentration after surgery was not significant. A multivariate analysis has shown that only change in Hb concentration during the course of irradiation appeared significant. A logistic analysis of a dose-response relationship suggest that a decrease in Hb concentration of 1 mg% could be compensated by an increase in radiation dose of 5 Gy, or by shortening of radiation treatment time by 8 days.

**Conclusion:** Hb change (but not Hb concentration) appears to be an important predictor of treatment outcome for patients with advanced laryngeal

cancer treated with PRT. This shows a potential for treatment strategies aiming in increase and/or prevention of decrease in Hb concentration after surgery and during radiation treatment course.

370

POSTER

### Parotid gland function following radiotherapy for head and neck cancer: dose/volume effects

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**Purpose:** To study the radiation tolerance of the parotid glands as a function of dose and volume irradiated.

**Methods:** 108 patients treated with radiotherapy for various malignancies in the head and neck region were prospectively evaluated. Lashley cups were used to collect stimulated parotid flow rate before, 6 weeks, 6 months and 1 year after radiotherapy. Parotid gland dose volume histograms were derived from CT based treatment planning. The normal tissue complication probability (NTCP) model proposed by Lyman was fit to the data. A complication was defined as stimulated parotid flow rate < 25% of the pre-radiotherapy flow rate.

**Results:** Size of the parotid gland, gender, age, tobacco and alcohol consumption, and tumour characteristics were not correlated with pre-radiotherapy parotid flow. A considerable variability in parotid output was found with a range of 0.03 to 1.66 ml/min (mean 0.34 ml/min). Reduction in post-radiotherapy flow rate correlated significantly with mean parotid dose. The NTCP model parameter TD50 (the dose to the whole organ leading to a complication probability of 50%) was found to be 31, 35 and 39 Gy at 6 weeks, 6 months and 1 year post-radiotherapy respectively. The volume dependency parameter n was around 1, which means that the mean parotid dose correlates best with the observed complications. There was no steep dose/response curve (m=0.45 at 1 year post-radiotherapy). No threshold dose was found.

**Conclusions:** A linear correlation between post-radiotherapy flow ratio and parotid gland dose and a strong volume dependency was shown. Recovery of parotid gland function was shown 6 months and 1 year after radiotherapy. Planning attempts should be made to achieve a mean parotid dose at least below 39 Gy.

371

POSTER

### Treatment of advanced head and neck squamous cell carcinoma (HNSCC) with intratumoral cisplatin/epinephrine (CDDP/epi) injectable gel: Phase III multicenter studies

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**Purpose:** Therapeutic options for patients with advanced HNSCC are limited. We evaluated CDDP/epi gel for local tumor control and symptom relief in two identical Phase III placebo-controlled trials. This novel drug, designed for direct intratumoral administration, achieves high, sustained tumoral cisplatin concentrations with minimal systemic toxicity.

**Methods:** Adult patients with recurrent or refractory, histologically confirmed HNSCC were enrolled, stratified by tumor volume (up to 20 cubic cm), and randomized 2:1 to receive CDDP/epi gel (IntraDose Injectable Gel, Matrix Pharmaceutical, Inc.) or placebo gel. Maximum of 6 weekly intratumoral injections given in 8-wk period. Dose: 0.25 mL CDDP/epi gel per cubic cm tumor, up to 10 mL total. Patients with disease progression could crossover from the blinded to open-label study.

**Results:** 178 patients were evaluable. Most had been treated with multiple modalities: 89% of tumors were in a previously irradiated field. 19 patients (227 tumors) were treated with CDDP/epi gel; 59 patients (88 tumors) with placebo gel. Combined results from the two trials confirmed significant objective tumor responses (CR + PR) in these intensively pre-treated patients with poor prognoses: 29% (35/119), including 19% CR (23/119) for CDDP/epi gel, versus 2% (1/59) for placebo (p < 0.001). The response rate (CR + PR) for patients who previously had been treated with systemic cisplatin or carboplatin was 29% versus 30% for patients who were platinum naïve. Patients who crossed over from placebo to active drug treatment had a 27% (11/41) response rate. Tumor response and patient benefit were significantly associated (p=0.006): 47% of patients with