tumors showing higher AI had longer overall survival but the difference was not statistically significant. No significant correlation was found between AI and gender, age, site of disease and tumor grade as well as with topoisomerase IIa, p21 and p27 expression.

Conclusions: Our findings indicate that apoptosis is mainly related with advanced stage of disease and wild type p53 protein and does not seem to play an important role to the overall survival of the patients with head and neck cancer.

648 PUBLICATION

Phase II study of paclitaxel (P) twice a week as a radiosensitizer, after paclitaxel-carboplatin (C) induction chemotherapy (IC) in stage IIId–IV head and neck carcinoma (HNC)

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To assess the tolerance and efficacy of combined fractionated radiotherapy (RT) with P, after IC, 29 patients (pts) with unresectable HNC were enrolled at a phase II study from 09.97 to 11.98. IC consisted of two courses of P 175 mg/m^2 and C AUC 6, every 21 days. 66.6 Gy were delivered 4 weeks after the IC (1.8 Gy daily, 5 fractions per week, one week rest at 45 Gy) to a volume encompassing the primary tumor and regional lymph nodes. Concurrent CT consisted of P 20 mg/m^2 over 1 hour twice a week. Characteristics of the pts were: median age 56 years (range 43 to 75), WHO performance status of 0–2 (11 PS0, 12 PS1, 6 PS2), primary site was: oropharynx 15, hypopharynx 12, larynx 2. All pts presented with AJCC stage III or IV. 29 pts received two cycles of IC and were evaluable for toxicity and response. The response was 52% (3 CR, 12 PR, 12 NC, 2 PD). The toxicity following IC was hematological with 4G1 and 1G2 anemia, 8G1–2 and 2G3–4 leucopenia, 1G2 thrombopenia. 19 pts completed the chemoradiotherapy (CRT), median (range) total dose of RT was 65.7 Gy (63–68, 8 Gy). 11 pts required interruption during RT (2–5 weeks). The median duration of RT was 9.3 (7–12) weeks. One patient did not receive CRT due to early progression and 9 pts are still under RT. All the 19 pts experienced mucositis (5G2, 14G3) and 9 required hospitalization. 12 CR (64%) and 2 PR (11%) were achieved. Median duration of response was 11+ months (range 6+–12+ months. This combined treatment is highly effective in poor prognosis unresectable HNC. The main toxicity (mucositis) is manageable.

649 PUBLICATION

A phase III study of concurrent radiotherapy with carboplatin or weekly paclitaxel in patients with advanced squamous cell head and neck cancer (SCHNC)

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Introduction: Patients (pts) with advanced SCHNC have poor prognosis. Chemotherapy (CT) and Radiotherapy (RT) given concurrently increase local-regional control and survival rates compared with RT alone. From 5/98 we started a phase III study of the activity and toxicity of Chemoradiotherapy using Carboplatin or Taxol in the CT arm. We report our preliminary results of this study.

Methods: Thirty six pts with advanced (stage III and IV), inoperable SCHNC received RT to the primary and lumph nodes 1.8–2 Gy/day, 5 fractions/week, total 65/72 Gy. During RT, Carboplatin 400 mg/m$_2$ day 1, 22, 43 was administered in 19 pts (mean age 59.8 years) and Taxol 80 mg/m$_2$ weekly (as 1-hour infusion) in 17 pts (mean age 55.1 years). The two groups were similar with respect to age, sex, stage, PS of the pts, differentiation and site of primary tumor.

Results: 28 pts (77.8%) achieved a remission (CR:16, PR:12 pts). In the Carboplatin group we observed 12 responses (63.2%) with 6 CR (31.6%) and 6 PR (31.6%) and in the Taxol group 16 responses (94.1%) [$p < 0.05$] with 10 CR (58.8%) and 6 PR (35.3%). Grade III/IV neutropenia occurred in 3 pts of the Carboplatin group and 5 of the Taxol group and grade III/IV stomatitis in 2 and 4 pts respectively.

Conclusions: Weekly Taxol given concurrently with RT seems to be safe and more active than Carboplatin/RT in pts with advanced SCHNC. Updated results about survival will be presented.

650 PUBLICATION

Prognostic value of hematocrit level in radiotherapy of laryngeal cancer

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Purpose: The evaluation of importance of pre-treatment hematocrit level in radiotherapy of laryngeal cancer.

Material and Methods: In the group of 295 laryngeal cancer patients treated by definitive radiation therapy pre-treatment level of hematocrit was scored. The impact of hematocrit level on results of treatment was assessed using proportional hazard (Cox) regression and the logistic regression.

Results: In analysed group of patients median of pre-treatment hematocrit level was 42% (range 30%–52%). Logistic regression model and the proportional hazard regression showed that tumour control probability (TCP) was 0.2 and 0.8 for hematocrit level 30% and 52%, respectively ($p < 0.0002$). When both haemoglobin and hematocrit were introduced to model, hematocrit had lower p-value.

Conclusion: In radiotherapy of laryngeal cancer pre-treatment hematocrit level significantly affect TCP.

651 PUBLICATION

Phase II studies using electroporation therapy in patients with recurrent head and neck cancer: A safe and active treatment approach

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Electroporation is a process which temporarily increases the permeability of cell membranes, therefore enhancing the intracellular delivery of locally injected substances. Two Phase II studies were conducted in patients with recurrent or refractory head and neck cancer following standard curative therapy and who were not candidates for salvage therapy. A total of 41 patients were enrolled in two multicenter trials to evaluate the patient response of intratumoral (IT) administration of bleomycin or Electroporation Therapy (EPT), defined as IT bleomycin with electroporation. Patient responses were evaluated over 12 weeks by direct measurement of lesions as well as CT/MRI studies. Of the 41 patients enrolled, 31 had failed two or more prior treatment modalities, i.e. surgery, radiation, and/or chemotherapy. In protocol EPT-97-01, 23 patients were treated with IT bleomycin alone and crossed over to EPT (n = 15) if progressive disease occurred. In protocol EPT-97-02, 18 patients received EPT only. The significant side effects related to EPT therapy were necrosis of the tumors and overlying skin in cervical lesions associated with cellulitis [7%] and bleeding [12%] requiring increased wound care. No deaths attributable to the therapy were reported. In 33 patients who completed therapy receiving EPT there was a 64% objective response rate durable over 12 weeks. In summary, Electroporation Therapy is an efficient, safe, and well tolerated method of treating symptomatic recurrences of head and neck cancer that warrants further investigation.

652 PUBLICATION

Head and neck cancer: Pretreatment and midtreatment PO_2 levels

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Purpose: In vitro studies have shown that fully hypoxic cells are 3 times more radioresistant than fully oxygenated cells. Accordingly, clinical studies have proven that pretreatment tumor hypoxia is an essential factor in predicting local tumor control, survival and the rate of metastases. In this ongoing study we compare pretreatment tumor pO2 levels with measurements taken during nonsurgical treatment when the size of the cervical metastatic node has decreased by 50%.

Methods: Using the Eppendorf pO2 histograph we measured pO2 levels in metastic lymph nodes of so far 10 patients with head and neck SCC who were being treated with nonsurgical management.

Results: A mean of 72.6 measurements per session was taken from each lymph node. The median tumor pO2 measurement fell from a mean of 13.9 ± 8.0 mm Hg to 7.3 ± 9.9 mm Hg Even more dramatic, however, was the substantial increase in the percentage of values less than 5 mm Hg, a rise from 29% to 52%.

Conclusions: While there is variability both in the pretreatment tumor pO2 and in the change in pO2 during treatment, there appears to be a

decrease in the overall oxygenation of the tumors. The dramatic increase in very low oxygen measurements may reflect selective survival of radio- or chemoresistant hypoxic tumor cells.

653 PUBLICATION

Concurrent cisplatin and concomitant boost accelerated radiotherapy (CBAR) in advanced head and neck (H&N) cancer

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Purpose: To evaluate feasibility and efficacy of concurrent cisplatin and CBAR in advanced H&N cancer.

Methods: Forty one previously untreated patients with unresectable squamous cell H&N cancer were enrolled between 3/95–9/98, 36 (88%) of whom had IV stage disease. Primary and subclinical disease was irradiated to 54 Gy in 30 fractions for 5.5 weeks, with two daily fractions during the first two days. Gross tumour was boosted during the last 2.5 weeks to 72 Gy with a second daily fraction of 1.5 Gy. Continuous I.V. infusion of Cisplatin 20 mg/m^2/24 h was administered for 5 consecutive days in I and V week of the basic treatment. The median follow-up for the surviving patients was 19 months (range, 4–45). The median dose and treatment duration were 72 Gy (range, 67–74) and 41 days (range, 36–47). Ten patients (24%) did not have a second chemotherapy course.

Results: Grade 3 (RTOG) dysphagia (12%), weight loss (average 9%), grade 3–4 mucousitis (66%) and grade 3 myelosuppresion (5%) were the most important acute side effects. Two of the patients died during 2 months following the treatment. Soft tissue necrosis was observed in 3 patients (7%), 4–10 months after treatment. The tumour response was impressive: 85% (33/41) CR. The 2-year actuarial loco-regional control was 60% and the overall survival was 53%.

Conclusions: Although longer follow-up is needed for a definitive evaluation, we conclude that this schedule is feasible and appears to be effective.

654 PUBLICATION

The efficacy of Xialine in patients with xerostomia resulting from radiotherapy for head and neck cancer (a pilot study)

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Objectives: The aim of the study was to evaluate the changes in subjective sensations due to xerostomia, and quality of life (QoL) before and after use of Xialine, a xanthan gum-based saliva substitute, in patients with xerostomia as a result of radiation therapy in the head and neck area.

Methods: The effect of Xialine was evaluated by the EORTC questionnaires QLQ-C30 and the QLQ-H&N35 in a double-blinded, placebo-controlled, cross-over design in 30 patients with xerostomia. Seventy-five percent of the volume of the parotid glands received at least 50 Gy or more during previous radiation therapy. Patients received Xialine or placebo for one week, followed by a wash-out period of one week and another week placebo or Xialine. The composition of the placebo was similar to Xialine, but did not contain xanthan gum.

Results: After administration of Xialine a decrease of problems with speech and 'smell and taste' was noted (−7 and −6 respectively on a 0–100 scale), while a minimal decrease with regard to these endpoints was noted after placebo (−1 and −2). Global QoL increased with 4 on the same scale after Xialine, while a reduction of 3 was noted after placebo. Although not statistically significant in this small group, these changes were regarded as clinically relevant. Xerostomia in general decreased with Xialine as well as with placebo to approximately the same degree (−17 versus −16). No differences between Xialine and placebo were noted with regard to other domains.

Conclusion: problems with speech, 'taste and smell' and the global QoL in patients with xerostomia resulting from radiation therapy for head and neck cancer. A larger study will be initiated to confirm the trends observed in this pilot.

655 PUBLICATION

Prognostic impact of the steroid receptor level in head and neck cancer

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Purpose: The aim of our study was to investigate steroid receptor contents and expression of Bcl2 in head and neck cancer (HNSCC) and to compare them with known predictors of outcome as age, tumor size, differentiation and lymph node status.

Methods: Oestrogen and progesterone receptor contents of tissue samples of 61 HNSCC and the neighbouring healthy mucosa were determined by radio ligand assay as well as Bcl2 levels of 46 of the same tumors by Western blot analysis.

Results: We found that steroid receptor positivity was significantly more common in tumour tissues than in the healthy mucosa for both receptors ($p < 0.05$). The rate of tumour free survival was significantly higher in oestrogen receptor positive cases ($p < 0.05$). There was a positive correlation between Bcl2 and oestrogen receptor content and between Bcl2 and lymph node status. However, there was no relationship between tumor size, differentiation and survival.

Conclusions: Our results suggest that oestrogen receptor positivity might be of prognostic value in HNSCC as well, but we could not prove the independent prognostic impact of Bcl2 expression.

656 PUBLICATION

Supracricoid partial laryngectomy in advanced laryngeal cancers

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Purpose: Supracricoid partial laryngectomy (SCPL) has been shown satisfactory oncological outcome and postoperative functional results. In this study we evaluated the efficacy of this procedure as a primary surgical modality in advanced laryngeal cancers and the functional results according to the type of the surgery for the successful functional rehabilitation.

Mehtods: Thirty nine patients with laryngeal cancers were managed by this procedure between 1993 and 1999, and the tumors were glottic and supraglottic in origin in 32 and 7 patients, respectively. To evaluate the efficacy of this procedure in locally advanced cancer, sixteen patients monitered for at least more than one year and over than T2b stage were reviewed. For the functional evaluation, voice parameters were analyzed by CSL program and swallowing analysis was performed by modified barium swallow test.

Results: Local recurrence was found in 4 (25%) cases and all of them was pathologically T4. Among them 2 patients were successfully managed by salvage operation but 2 patients showed distant metastasis. Voice parameters were different from normal speaker, but the patients were allowed for the social interaction successfully. Normal deglutition was achieved in 38 patients, but one patients had total laryngectomy because of intractable aspiration. Aspiration was associated with faulty backward tilting and improper position of epiglottis and inadequate movement of base of tongue. Silent aspiration was observed more frequently in extended procedures and delayed decannulation cases.

Conclusion: The SCPL could be considered as a primary surgical modality in selected advanced laryngeal cancers with good oncologic and functional results.

657 PUBLICATION

Neoadjuvant cisplatin (P) 5-fluoracilo (5-FU) and radiation therapy (RT) for organ preservation in squamous cell carcinoma of the head and neck: A single institutional experience

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The use of neoadjuvant Cisplatin – 5-Fluoracil followed by radiation therapy is an effective method for organ preservation in squamous cell carcinoma of the head and neck. We developed a phase II study with P 100 mg/m^2 over 3 hours d1, 5FU 1000 mg/m^2 over 24 hours d1–5, followed by (XRT) 60–70 Gy, as preservation organ strategy. Tumor response assesment was done after the 2nd cycle and after the end of neoadjuvant treatment. Between february 92 and november 97, 56 patients (pts) were admitted to the trial.