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