Patients & Methods: Between 1993 and 1994, 59 patients with advanced inoperable SCC H & N were allocated to radiation (RT) or RT with chemotherapy (RCT). 27 pts received accelerated RT. Primaries were located in the hypopharynx (26), oropharynx (15) and in the oral cavity (14). Fresh frozen specimens were used for Ki-67 labeling index (L.I.) and flow cytometry (FCM). Routinely processed parraffin embedded sections were stained using monoclonal antibody MIB-1. Feulgen staining was used for image cytometry (ICM). Prognostic impact on RFS was evaluated for T and N integer score (TANIS), different treatment modalities, age, grading, typing, MIB-1 L.I., Ki-67 L.I., ploidy, SPF and 5c-ER

Results: Median follow-up was 345 days (89–891 d). Survival and RFS were 39% and 31% at 2 years, respectively. In univariate analysis, MIB-1 (L.I. < Median: 57% RFS; L.I. ≥ Median: 11% RFS, p = 0.017); MIB-1 L.I. without accelerated patients (L.I. < Median: 57% RFS; *L.I.* ≥ Median 9% RFS; p = 0.006); ploidy (diploid: 38% RFS; peritriploid: 35% RFS; tetraploid: 10% RFS; p = 0.04); remission quality (CR @ 3 mos: 57% RFS vs. PR/NC @ 3 months: 0%, p < 0.001) and TANIS (TANIS 5: 48% RFS; TANIS 6: 36% RFS; TANIS 7: 0% RFS; p = 0.0341). In a multivariate Cox regression analysis including MIB-1, TANIS and ploidy, only MIB-1 was an independent prognostic factor (p = 0.0051).

Conclusion: After RT/RCT of SCC H & N remission @ 3 mos, TANIS and MIB-1 are prognostic factors.

840 POSTER

Carboplatin as part of each fraction of treatment: Potential for improvement upon hyperfractionated irradiation in advanced head and neck cancer

A. Villar, J.C. Martinez, L. de Serdio, M.D. Perez, C. Fuentes, E. Espiñeira, J. Gil-Curbelo, L. Cejas, R. Hernandez, J.A. Saavedra. *Hospital Nuestra Señora de la Candelaria, Santa Cruz de Tenerife, Spain*

Purpose: To investigate if modulation with carboplatin shows potential for improvement upon the EORTC hyperfractionated irradiation trial in advanced head and neck cancer.

Methods: From february 1993 to January 1996 49 patients (3 Stage 3, 46 Stage 4) were treated with a regimen composed of 2 fractions a day. Each fraction consisted of 115 cGy preceded by 5 mg/m2 of carboplatin. Treatment was administered 5 days a week up to total doses of 350 mg/m2 of carboplatin + 8050 cGy in 7 weeks. There were 13 hypopharynx, 25 oropharynx, 4 oral cavity, 3 nasopharynx, 1 maxillary antrum and 3 cervical masses of unknown primary tumour. 39 patients presented with N+ (37% of N3, 63% of the nodes being fixed).

Results: 82% of patients tolerated treatment exactly as scheduled and 100% received the planned radiation dose. Local toxicity was similar to that reported in the EORTC trial. No renal, otic or neurotoxicity were observed. Hematological toxicity was moderate. 47/49 (96%) CR and 2/49 (4%) PR were achieved for an overall response rate of 100%. After mean follow-up of 30 months (12–45) the actuarial local control and disease-free survival are 73 and 59% respectively. The actuarial control of the nodes is 94%.

Conclusions: This schedule is very effective, shows potential for improvement upon the EORTC hyperfractionated trial, and merits investigation in multicentric clinical trials.

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Carboplatin (CBDCA) + radiotherapy (RT) vs RT in inoperable stage III–IV head and neck (HN) carcinoma

M. Airoldi[1], R. Orecchia[2], P. Gabriele, G.L. Sannazzari, G. Beltramo, M.G. Ruo Redda, C. Bumma[1]. *[1]Medical Oncol. S. Giovanni A.S.; [2]Radiother. Dep. Turin Univ., Turin, Italy*

In attempt to improve results in pts with inoperable stage III–IV SCC-HN we administered CBDCA (45 mg/m2 d. 1–5 of the 1, 3, 5, 7 wk) concurrently with RT (70 G y/7 wk). From 11/92, 160 pts were enrolled; 156 are evaluable for response and toxicity. Pts were males (90%) and females (10%) with a median age of 52 yrs (45–71) and PS1 (0–2). Site: oral c. (30) orophar. (85), hypoph. (22), larynx (19). Stage: III = 22%; IV = 78%; 45% had N2–3. RT (76 pts) and RT + CBDCA (80 pts) group were well balanced according to PS, site, stage, Nstatus. 18/76 pts (23%) treated with RT achieved a CR vs 32/80 (40%) (p < 0.05). Median RT dose: 67 in RT; 66 in CBDCA + RT; CBDCA relative D.I. of 0.90. There was a prevalence of leukopenia in CBDCA pts; 3 yrs O.S. = 12.5% RT vs 35% (p < 0.01);

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Prognostic significance of monoclonal antibody MIB-1 in early stage larynx carcinoma

Th. Betten[1], H.E. Eckel[1], R. Hake[2], J. Thiele[2]. *[1]Dept. of Otorhinolaryngology; [2]Dept of Pathology, University of Cologne, Germany*

Purpose: To compare MIB-1 labeling index to clinical staging, histological grading and clinical outcome in early stage larynx carcinoma with regard to its prognostic value.

Methods: The tumor specimens obtained during primary surgical treatment of 21 patients with locoregional recurrences and of 26 recurrence free patients after endolaryngeal laser partial laryngectomy were examined for the detection of Ki67 antigen by standard immunohistochemical procedures with MIB-1 monoclonal antibody. Staining results were compared to clinical staging, histological grading and clinical outcome.

Results: MIB-1 staining occurred in 88% of the tumors. The percentage of positive nuclei varied between 8.5 and 35.4 (median 20.1; mean 22.02) for the recurrence group and between 2.6 and 29 3 (median 7.6; mean 9.95) for the control group. There was no significant correlation between expression of the antigen and tumor staging but between tumor grading and staining. Recurrent tumors had in average a more than double labelling index of MIB1 than non recurrent ones (p = 0.0001). Only 47.6% of patients with an above median labeling index were recurrence free after the first year compared to 87.7% in the below median group (p = 0.0005).

Conclusion: MIB-1 labeling index can provide useful prognostic information in early stage larynx carcinoma. Patients with a high MIB-1 labeling index seem to have a shorter recurrence free interval than patients with a low MIB-1 labeling index.

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Phase II study of vinorelbine (NVB) in patients with metastatic and/or recurrent squamous cell carcinoma of the head and neck (SCCHN)

M. Degardin, Ph. Bastit, F. Rolland, J.P. Armand, B. Chevallier, M. Van Glabbeke[1], J. Boudillet[2], P. Tresca[2]. *Cappelaere on behalf of EORTC-ECSG; [1]EORTC Data Center; [2]Pierre Fabre Oncologie, France*

Aim: To assess the efficacy and safety of NVB in patients (pts) with metastatic and/or locoregional recurrent SCCHN untreated by chemotherapy (CT) and with lesions outside previously irradiated fields.

Methods: The following eligibility criteria were required: histologically documented SCCHN; at least one bidimensionally measurable lesion, PS ≤ 2 (WHO), normal haematological, renal and hepatic functions, neo-adjuvant CT is allowed with 6 months wash out time, written informed consent. From March 1995 to December 1996, 28 pts were included; data are currently available on 21 pts. Main characteristics were: sex M/F 18/3, median age 54 (38–71), PS: 0 (0–2). The sites of primary tumour included oral cavity (2), oropharynx (9), hypopharynx (7), larynx (3), and the sites of metastases were: lung, liver, lymph nodes. Prior treatment: surgery (9), radiotherapy (18), neoadjuvant CT (3). **Treatment:** NVB was given at 30 mg/m^2 weekly until progression or unacceptable toxicity. If the absolute granulocyte count on day 8 was ≤1,000/μl or another toxicity of CALGB grade 3–4 occurred, the treatment was postponed for one week or until recovery.

Results: The overall response rate was 15% (CI: 3.2–37.9%): 3 partial responses in 20 evaluable pts. The duration of responses was: 20.16 and 18+ weeks. All responses were seen in lung metastases and in lymph nodes. The treatment was generally well tolerated, 22 of 152 administered cycles were delayed for haematological toxicity. Tolerance was analysed on all included pts, data are available on 21 pts. Neutropenia CALGB toxicity grade 3–4 was seen in 13 pts (54%). No severe mucositis, no nausea/vomiting and no case of severe neurotoxicity were recorded. The median number of treatment was 6 cycles and the median dose intensity 83.53% (56.7–100%).

Conclusion: Present data demonstrate a moderate activity and a good tolerance of NVB with our schedule for pts with metastatic and/or recurrent SCCHN.