

merits of adjuvant and neoadjuvant chemotherapy remain unproven. This study was performed to determine the feasibility and safety of induction chemotherapy with docetaxel, cisplatin and 5 FU (TPF) followed by concurrent chemoradiotherapy (CCRT) for advanced nasopharyngeal cancer (NPC).

**Methods:** Patients with metastatic or locoregionally advanced NPC were treated with 3 cycles of induction chemotherapy. Docetaxel (70 mg/m<sup>2</sup>) and cisplatin (75 mg/m<sup>2</sup>) were given on day 1, followed by 5 FU (1,000 mg/m<sup>2</sup>) as a continuous infusion for 4 days and repeated every 3 weeks. After induction chemotherapy, cisplatin was given at a dose of 100 mg/m<sup>2</sup> every 3 weeks with radiotherapy.

**Results:** Thirty patients were enrolled and 25 patients completed both induction treatment and the subsequent CCRT. Response to the induction TPF (N = 30) was as follows: five patients (16.7%) achieved a complete response (CR) and 23 patients (76.7%) a partial response (PR). At 6 weeks after CCRT (N = 25), 17 patients (68%) had a CR and eight patients (32%) a PR. The median progression free survival was 38.2 months and the 3-year overall survival was 79.6%. The main hematological toxicity was neutropenia and leucopenia. A greater than grade 3 neutropenia was observed in 20 patients (66.7%); febrile neutropenia developed in one patient (3.3%). The major non-hematological toxicities were asthenia, nausea and mucositis.

**Conclusions:** The results showed that this treatment was very effective with manageable toxicity in locally advanced, and distant metastatic NPC. In the near future a randomized phase III trial comparing TPF followed by CCRT versus CCRT alone will be started by the Radiotherapy Oncology Group for Head and Neck (GORTEC); the results of this future study will help determine specific treatment regimens for patients with advanced NPC.

8565

POSTER

#### **Surgery does not improve tonsil cancer patient's outcome in T2N1 stage compare to radiotherapy alone**

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Radiotherapy is a common treatment method for tonsil cancer patients. Patients with advanced loco-regional disease are treated primarily with surgery followed by additional radiotherapy. The aim of this project is to compare the results of radiotherapy alone with combination of radical surgery with radiotherapy for patients with tonsil cancer.

Between 1997 and 2000, 63 patients with tonsil cancer were treated in Institute of Oncology Gliwice. Patient's age ranged from 37 to 72 years, average 58 years. There were 14 (22%) men and 49 (78%). Whole group was homogenous in stage, all patients in T2N1. Majority 33 (52%) of patients were treated with combined treatment-surgery with additional radiotherapy (S+RT). Surgery procedure was performed in each case in the same manner: radical tonsillectomy and one side selective lymphangiectomy. Thirty (48%) of patients were treated only with radiotherapy alone (RT).

In all patients radiotherapy was delivered in 2 Gy fractions, 5 days a week. Tumour bed or primary tumour irradiation was carried out to the total dose of 60–74 Gy. Locoregional elective lymph nodes irradiation continued to the total dose of 50–66 Gy and 66–70 Gy was delivered to the metastatic lymph nodes. Total doses 70–74 Gy were used for radiotherapy as a sole modality, and 60–66 Gy for postoperative irradiation. In majority 23 of patients (70%) negative surgical margins were achieved, in remaining 10 patients (30%) positive margins were present. Operated patients at the beginning of radiotherapy were free of the disease. Statistical analysis includes 5-year Kaplan-Meier estimates of OS and LRC.

Overall 5-year OS and LRC were 52% and 50% respectively. During 5-year follow-up, there were 22 local relapses (35%) and 8 distant metastases (12%). The 5-year OS was higher in the RT group 58% than S+RT group but this difference was not significant (HR=1.8, p=0.12). Probability of loco-regional control was 67% in RT and 53% in S+RT groups, difference was close to significance (HR = 2.1, 0 = 0.08). There were 8 (26%) locoregional recurrences in RT group, 3 local and 5 regional, versus 14 (42%) in S+RT group, 10 local and 4 regional. Distant metastases in locoregional controlled patients were noted in 4 (23%) in RT and in 4 (12%) in S+RT group. Radiotherapy alone in patients with tonsil cancer was more effective than combined surgery with irradiation. Lower combined treatment efficacy may be related to higher local recurrence rate.

8566

POSTER

#### **Primary tumour site as a predictor of treatment outcome for definitive radiotherapy of advanced stage oral cavity cancers**

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**Purpose:** The purpose of this study was to evaluate the outcome of definitive radiotherapy (RT) for oral cavity cancers and to assess prognostic factors.

**Methods and Materials:** One hundred and fifteen patients with oral cavity cancers who received definitive RT from January 1995 to September 2007. Patient clinical stage distribution of stage III, IVA and IVB were 6%, 47% and 47%, respectively. The median dose of RT was 72 Gy (range, 62–76 Gy). Cisplatin-based chemotherapy was administered to 95% of patients. Eleven patients underwent salvage operation for RT-failure.

**Results:** In our cohort, 88 (76.5%) patients responded partially and 23 (20%) responded completely; of these, 18% and 57% experienced a durable effect of treatment. The 3-year overall survival (OS), disease-specific survival (DSS) and progression-free survival (PFS) was 22%, 27% and 25%, respectively. The 3-year PFS based on the primary tumor sites was as follows: group I (buccal, mouth floor and gum) 51%, group II (retromolar and hard palate) 18%, and group III (tongue and lip) 6% (P < 0.0001). The 3-year PFS for N0 patients was 41% and 19% for patients with N+ disease (P = 0.012). T stage and radiotherapy technique did not impact to survival. Patients underwent salvage surgery for RT failure demonstrated better 5-year OS and DSS (35% vs. 13%, P = 0.015 and 53% vs. 22%, P = 0.029, respectively).

**Conclusion:** Primary tumor site and neck stage are prognostic predictors in advanced stage oral cancer received radical radiotherapy. Primary tumor extension and radiotherapy technique did not influence survival. More aggressive treatment may be considered for unresectable disease.

8567

POSTER

#### **Nasopharyngeal carcinoma: prognostic factors and long-term outcomes with emphasis on radiotherapy techniques**

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**Background:** To evaluate long-term outcome after treatment of nasopharyngeal carcinoma (NPC) and determine the prognostic factors, with emphasis on radiation technique.

**Materials and Methods:** Retrospectively analyzed patients with NPC (n = 119) treated with curative intent in a single institute between 1982–2007. Stage IV, III and I-II (UICC 2002) were 40%, 35% and 25% respectively. Radiotherapy techniques were: 2D-RT (n = 52), 3D-CRT (n = 46) and IMRT (n = 19). Concomitant chemoradiation (CHRT) were given to 23 patients. The prescribed dose to tumour was 70 Gy. The locoregional recurrence (LRR), systemic failure, disease free survival (DFS), overall survival (OS) and prognostic factors were calculated using uni- and multivariate analysis.

**Results:** The 5-year actuarial LRR free survival, systemic failure free survival, DFS and OS were 57%, 72%, 46% and 38% respectively. The independent prognostic factors were: stage for all end points, pathological type and IMRT for LRR; 3D-RT, and IMRT for DFS; and finally age and CHRT for OS.

**Conclusions:** With regard to equally dose of 70 Gy for all patients the impact of radiation technique on the end points and superiority of IMRT compared to 3D-CRT can not be explain by radiation dose. These may be explained by the use of advanced imaging based on CT-MRI-PET scanning for preparation of an IMRT plan.

8568

POSTER

#### **Prophylactic swallowing exercises during and after radiotherapy for head and neck cancer - results of phase I trial**

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**Background:** Dysphagia is a common and severe side effect after radiotherapy (RT) for head and neck cancer (HNC). Alterations of all structures and functions of the throat have been described. At the same time structures important for swallowing are often tumour embedded or close to target areas, making swallowing sparring RT an uncertain strategy with respect to both efficacy and safety. Therefore, we wanted to examine the effect of prophylactic swallowing exercises in HNC patients. The current reports concerns the phase I feasibility study.

**Materials and Methods:** HNC patient scheduled for radical radiotherapy were included. They were examined with videofluoroscopy (VF) and answered EORTC C30 and H&N35 quality of life questionnaires (QLQ) as well as questions regarding the exercises (diary). The patients were instructed in exercises for the pharyngeal constrictor, tongue, jaw, suprahyoid muscles and oesophageal sphincter and to perform the exercise program 3 times daily or as frequent as possible. VF was performed before RT and two, five and 11 months after RT. Compliance, the swallowing scale of the QLQ, and the usefulness of the diary were the primary endpoints.

**Results:** 10 males with cancer of the pharynx (5), larynx (3) and oral cavity (2) with a median age of 59 years were included. All patients had some dysphagia at inclusion. Patient-reported tube dependency peaked at 14 days after therapy (38%) and reached 0% at 8 months. Patients stated complete adherence to the exercise protocol at 11% of encounters. At least one exercise a day for all organs was carried out for 100%, 75% and 66% of patients after 1, 3 and 5 weeks of therapy, respectively and 83%, 85%, 50%, 60% and 50% at 14 days, 2, 5, 8 and 11 months after therapy, respectively. Adherence to the instructions and swallowing capability could not be predicted from pre-RT variables. During and shortly after radiotherapy there was a tendency that pain limited the conduction of exercises. Later the tendency was reversed.

**Conclusions:** The exercises were uncomfortable during radiotherapy and compliance only moderate. Support from the therapists is crucial for an opportunity to build a relation to the patient that promoted the adherence to the protocol. We will continue to a randomized phase II study with VF changes as the primary endpoint.

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8569

POSTER

#### Neoadjuvant chemotherapy plus concomitant chemoradiotherapy in head and neck cancer: late toxicity and impact on quality of life

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**Background:** head and neck tumors and their treatment may negatively affect patient's quality of life (QoL). The aim of this study is the evaluation of the impact of neoadjuvant chemotherapy (NACT) followed by chemoradiation therapy (CRT) on QoL and psychological functioning of patients with oral and oropharyngeal tumors.

**Methods:** the population was composed by 36 patients affected by advanced oral cavity and oropharynx tumors, who underwent NACT, followed by concomitant CRT. In order to evaluate the late effects of RT we used the RTOG-EORTC late radiation morbidity score plus the DISCHE morbidity recording scheme; we also applied a visual analogue scale to evaluate dysphonia, dysphagia and dysmorphia. Psycho-oncological assessment included: HADS, MADRS, MINI MAC, EORTC QoL HN 35.

**Results:** the late toxicity evaluation demonstrates that salivary glands function, subcutaneous fibrosis, dysphagia and dysphonia are the most relevant and severe damages. Low levels of anxiety and depression were observed; the profile underscores the prevalence of active coping styles (fighting spirit, fatalism, respect to negation, anxiety and desperation). Patients with severe dysphagia (Dische 3-4) showed higher levels of depression: dysphagia influences the perceived global health (GH) and QoL, with effects on fatigue, physical and social functioning. It further determines problems in relationship (sexuality, social eating and contacts). Taste impairment was associated to lower perceived GH and QoL, with higher scores of depression. Dryness of mouth determines impairment in some aspects of QoL, such as social eating and contact, although without effects on emotional scores and perceived GH and QoL.

**Discussion:** NACT followed by CRT could result in a heavy addictive effect, strongly affecting nutrition. Depressive traits seems to be sub evaluated by auto-report instruments. However, late side effects of treatments, such as dysphagia, are clearly associated to impairment in perceived QoL and global health, and to a higher risk of psychological complains.

8570

POSTER

#### Body mass index (BMI) – simple tool for prediction and prognosis in patients with locoregionally advanced head and neck carcinomas (LA HNSCC)

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Changes in nutritional status are common in patients (pts) with HNSCC. Some data have pointed out that 5% of weight loss in 6 months before initial

treatment for LA HNSCC, was an independent predictor of poor disease specific survival in men. On the other hand obesity because of high energy intake (alcohol) might also negatively influence final outcomes. In our work we evaluate the correlation between initial BMI (weight kg / height m<sup>2</sup>), therapeutic response to neoadjuvant chemo and overall survival (OS) in pts with LA HNSCC treated with combined chemoradiotherapy.

During the period Jan. 2003–Oct. 2006, a total of 69 pts (N = 69, two pts being females) with T3-T4a, b; N1-N2b; M0 tumors (AJCC, 6-th ed. 2002) has been treated this way. Median age was 54 yrs (range 36–71 yrs) with ECOG status 1 (range 0–2). Two pts had primaries in epipharynx, 30 pts in oropharynx, 29 pts in hypopharynx, and 8 pts in larynx. All received PF regimen enhanced with Cytarabine (CAR) as a Platinum potentiator. Pts had been given 500 mg/m<sup>2</sup> of CAR (D1), 750 mg/m<sup>2</sup> of 5FU as a continuous infusion (D1-D5), and CDDP 120 mg/m<sup>2</sup> (D1) for 3 cycles, and then proceeded to radiotherapy with concomitantly applied CDDP 100 mg/m<sup>2</sup> (D2, D23, D44). Before radiotherapy, all of them were evaluated for response. Based on BMI, pts were categorized as overweight (BMI ≥ 25; 27% pts), normal weight (18.5 ≤ BMI < 25; 57% pts), and underweight (BMI < 18.5; 16% pts). Forty seven pts (68%) achieved response rate (CR+PR), 18 pts (26%) had stabilisation (SD) and four of them (6%) had progressed.

Responders had significantly higher values of initial BMI than non responders (Man-Whitney test; p < 0.01). In normally weighted, BMI positively correlates with response (OR = 15; p > 0.0018) and the same is true in overweighted pts (OR = 16.9; p < 0.00335). Underweighted pts had also significantly poorer OS compared to normally weighted (log rank test: p = 0.003) and overweighted (log rank test: p = 0.001). Between normally and overweighted pts such difference has not been observed (log rank test: p = 0.648).

In conclusion, we propose pretreatment nutritional assessment using BMI in this population pts which might in addition to TNM staging help in better and more sophisticated treatment planning.

8571

POSTER

#### Correlation of p53 and PCNA expression with the invasion and prognosis of oral squamous cell carcinoma

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**Background:** Abnormalities in cell cycle-controlling genes are important in the malignant transformation and proliferation of tumors. Among these genes, the tumor suppressor gene p53 is most notable, and its mutations provide an indicator of tumor progression and prognosis. This study examined the expression of p53 and PCNA at the invasive front of oral squamous cell carcinomas by immunohistochemical staining, and investigated the relationship of these proteins to clinicopathological findings. Moreover, the relationships between the expression of these protein at the invasive front and survival rates were examined.

**Methods:** Fifty-nine biopsy specimens of oral squamous cell carcinoma were examined by immunohistochemical staining. p53 labeling index (p53-LI) and PCNA labeling index (PCNA-LI) were examined at the invasive front of tumors.

**Results:** None of the indices correlated significantly with the clinical findings. In highly invasive carcinoma, p53-LI and PCNA-LI were increased and co-expression. Patients with p53 and PCNA co-expression had a worse prognosis than other expression combination.

**Conclusions:** It is significant to detect p53-LI and PCNA-LI at the invasive front of oral squamous cell carcinoma in the examination of tumor cell characteristics.

8572

POSTER

#### Therapeutic results of TPF chemotherapy prior to definitive radiochemotherapy for advanced nasopharyngeal cancer

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This is a clinical study conducted to evaluate the toxicity and efficacy of TPF chemotherapy of docetaxel, cisplatin, and fluorouracil prior to definitive radiochemotherapy in patients with advanced epithelial carcinoma of the nasopharynx.

**Patients and Methods:** Eligible patients with good performance status (ECOG 0–2) who had stage III/IV, or unresectable local recurrent diseases and no distant metastases were assigned to receive TPF chemotherapy. Intravenous infusion of 75 mg/m<sup>2</sup> of docetaxel and 75 mg/m<sup>2</sup> of cisplatin on day 1 followed by continuous intravenous instillation of 1000 mg/m<sup>2</sup>/day