and emotional well-being – 17.5 vs 23.8. The difference between the two groups concerning emotional well-being will be tested for significance and the remaining items of the scale concerning cervix and gynaecological complaints are also under analysis.
**Conclusions:** General quality of life in cervix cancer survivors treated with chemoradiation isn't affected. Analysis of the specific part of our scale concerning gynaecological complaints will also be presented.

# Head and Neck Cancer

## *Oral presentations* (Mon, 24 Sep, 10.45–12.45)
## Head and neck cancer

**5500** ORAL

**Induction chemotherapy for larynx preservation. Updated results of the GORTEC 2000–01 randomized trial comparing docetaxel + cisplatinum + fluorouracil (TPF) versus cisplatinum + fluorouracil (PF)**

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**Background:** Induction chemotherapy (CT) with PF followed by RT in case of objective response is a standard alternative to total laryngectomy for patients with locally advanced larynx and hypopharynx cancer. Data have suggested that T may add to the efficacy of PF. The objective of this randomized phase III trial was to determine whether the addition of T to PF could increase the larynx preservation rate.
**Material and Methods:** Patients with larynx and hypopharynx cancer for whom surgical procedure required total laryngectomy were randomized to receive PF or TPF. Other inclusion criteria were: adequate organ function, WHO performance status 0 or 1, age between 18 and 70, signed informed consent. Treatment arms were: Arm 1 (PF): P: 100 mg/m$^2$/d1 and F: 1000 mg/m$^2$ continuous infusion (CI) d1 to 5, Arm 2 (TPF), T: 75 mg/m$^2$/d1, P: 75 mg/m$^2$/d1 and F: 750 mg/m$^2$ CI d1 to 5. 3 cycles with 21 days interval were planned. Patients with complete or partial response and who recovered normal larynx mobility received RT to a total dose of 70 Gy(35 f and 7 weeks). Non responders to the induction CT underwent total laryngectomy followed by RT. The primary endpoint was 3-year larynx preservation rate. To detect an absolute difference of 15% the sample size was 210 patients.
**Results:** 220 patients were randomized (108 to PF, 112 to TPF). Patients and T characteristics (age, sex, PS, primary site, TN) were well balanced. The TPF arm showed greater grade 3–4 alopecia (19% vs 2%) and neutropenia (57% vs 35%) while the PF arm showed greater grade 3–4 mucositis (9% vs 4%). Toxic death rate was not different (2%). Compliance to CT was better in the TPF arm. The specified treatment (according to the protocol) was delivered in 81.2% of patients in the TPF arm vs 67.4%. The overall response rate (T and N) was 82.8% in the TPF arm vs 60.8% ($p = 0.0013$). 60.6% of patients achieved a complete endoscopic response vs 46.7%. Larynx preservation was offered for 80% of patients in the TPF arm vs 57.6% in the PF arm. In a multivariate analysis, a high hemoglobin level (>14 gr/l) and a compliance to treatment >80% are associated with a better response rate. With a median follow up of 45 months the 3-year actuarial larynx preservation rate is 74% following TPF induction chemotherapy versus 51% using the PF regimen.
**Conclusion:** In advanced larynx and hypopharynx carcinomas, when it is used as induction chemotherapy, TPF regimen demonstrated significantly superior overall response rate compared to the PF regimen. Larynx preservation could be achieved for a higher proportion of patients. Results will be updated for the meeting and functionnal results will be presented.

**5501** ORAL

**Cetuximab plus platinum-based therapy first-line in recurrent and/or metastatic (R/M) squamous cell carcinoma of the head and neck (SCCHN): Efficacy and safety results of a randomized phase III trial (EXTREME)**

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**Background:** The epidermal growth factor receptor (EGFR) inhibitor, cetuximab, an IgG1 monoclonal antibody, is effective in the treatment of R/M SCCHN progressing on platinum-based therapy. This phase III trial assessed the efficacy, safety and QoL of cetuximab in combination with a standard platinum-based regimen in the first-line treatment of R/M SCCHN.
**Materials and Methods:** In this multicenter phase III trial, patients (pts) with stage III/IV R/M SCCHN, not suitable for local therapy, were randomized to receive a maximum of 6 three-weekly cycles of cisplatin (100 mg/m$^2$ IV on day 1) or carboplatin (AUC 5, day 1) and 5-FU (1000 mg/m$^2$/day continuous infusion over the first 4 days of each cycle) either in combination with cetuximab (initial dose 400 mg/m$^2$ then 250 mg/m$^2$ weekly) (Group A) or alone (Group B). Cetuximab was administered until disease progression or unacceptable toxicity. Randomization was stratified according to previous chemotherapy (CT) and Karnofsky performance status (KPS) <80 and ⩾80. The primary endpoint of the trial was overall survival time (OS). Secondary endpoints included response rate, progression-free survival time, safety and quality of life (QoL).
**Results:** 442 pts, from 80 sites in 17 European countries were randomized: Group A: 222 and Group B: 220. Pts were mainly male (399M/43F), with a median age of 57 years [range, 33–80], and a median KPS of 80 [range, 50–100]. The pharynx (47%) and the larynx (25%) were the most common primary tumor sites. Prior therapies included surgery, radiotherapy (RT), induction CT or concomitant CT with RT. The combination of platinum-based chemotherapy and cetuximab significantly prolonged OS: 10.1 months in Group A and 7.4 months in Group B ($p = 0.036$). At the date of 10 February 2006, an interim safety analysis on 429 pts revealed no increases in the incidence of grade 3/4 adverse events commonly known to be due to CT in the cetuximab and CT arm as compared to the CT alone arm. Grade 3/4 skin reactions and infusion reactions, present in Group A (3.3% and 2.3%, respectively) were not found in Group B.
**Conclusions:** The addition of cetuximab to platinum-based CT in the first-line treatment of R/M SCCHN significantly improved survival by over 2.5 months compared with CT alone. The addition of cetuximab did not modify the characteristic adverse event profile of platinum-based CT. Final analyses on efficacy, safety and QoL will be presented at the meeting.

**5502** ORAL

**Accelerated weekly concomitant boost postoperative radiation therapy combined to concomitantchemotherapy in patients with locally advanced head and neck cancer**

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**Background:** To assess the feasibility and efficacy of accelerated weekly 6 fractionated 66-Gy postoperative radiotherapy (PORT) using a single fraction regimen from Monday to Thursday and a concomitant boost in the Friday afternoon sessions combined with concomitant cisplatin chemotherapy (CT) in patients with locally-advanced head and neck cancer (LAHNC).
**Materials and Methods:** Between 2001 and 2006, 40 (m/f ratio: 35/5; median age: 60 years) patients with pT1-pT4 and/or pN0-pN3 LAHNC were included in this pilot study. Indications of PORT/CT were positive

surgical margins, 3 or more positive lymph nodes, or extranodal infiltration. Median interval between surgery and RT was 46 days (range: 24–112). RT consisted of 66 Gy (2 Gy/fr) in 5.5 weeks. Median RT duration was 39 days (range: 35−62). Five-field 3D conformal or intensity-modulated RT was performed in all patients according to the GORTEC/EORTC/RTOG guidelines. Concomitant cisplatin chemotherapy was planned at 100 mg/m$^2$ in days 1, 22, and 43 in all but one patient where carboplatin was chosen due to impaired renal function. Prophylactic percutaneous endoscopic gastrostomy was performed in 18 (45%) patients, and 3 (8%) patients required nasogastric feeding tube. Median follow-up was 37 months (range: 5−66).
**Results:** All but two patients received the planned total dose without unplanned interruption (66 Gy in 38, 64 Gy in 1, and 58 Gy in 1). According to the CTC/NCI v3.0 toxicity criteria, acute morbidity was acceptable: grade 3 mucositis in 10 (25%), grade 3 dysphagia in 9 (23%), grade 3 skin erythema in 5 (13%) patients. CT-related anemia was observed in 2 patients (grade 3 in 1, and grade 4 in 1), leukopenia in 4 patients (grade 3 in 2, and grade 4 in 2), and no grade 3 or 4 thrombocytopenia was observed. Grade 3 renal-function impairment was observed only in one patient. Median weight loss was 3.5 kg (range: 0−14.5). No treatmentrelated mortality was observed. Considering the late effects, grade 0, 1, or 2 xerostomia was observed in 9 (23%), 22 (55%), and 9 (23%) patients, respectively; grade 0, 1, and 2 edema in 25 (63%), 14 (35%), and 1 (3%) patients, respectively. Locoregional relapse was observed in 8 (20%) patients, and only 7 (18%) patients developed distant metastases. Median time to locoregional relapse was 6 months (range: 1−40). The 3-year overall, cause-specific, disease-free survival, and locoregional control rates were 65%, 69%, 64%, and 82%, respectively. Distant metastasis probability at 3 and 5 years was 19%. Univariate and multivariate analyses revealed that the only prognostic factor influencing the outcome was nodal status.
**Conclusions:** We conclude that reducing the overall treatment time using accelerated PORT/CT by weekly concomitant boost (6 fractions per week) combined to concomitant cisplatin chemotherapy is easily feasible with good locoregional and distant metastases control for patients operated with curative intent for LAHNC. Acute and late RT/CT-related morbidity is acceptable.

**5503** ORAL

**The predictive value of tumour thickness for cervical metastasis in squamous cell carcinoma of oral cavity: a meta-analysis of reported studies**

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**Background:** Cervical metastasis greatly impacts on survival in patients with carcinoma (SCC) of the oral cavity (OC). The significant occult nodal metastasis rate warrants consideration to elective neck treatment but controversy exists as to what patient groups will benefit from such interventions. In previous studies, tumor thickness (TT) appeared a strong predictor for nodal metastasis but no consensus exists on the optimal TT cutpoint (TTcp) for a clinical relevant risk of nodal involvement. To address this question, we conducted a meta-analysis.
**Methods:** All articles relating to TT and nodal involvement in OC were identified through searching OVID MEDLINE (1966−4th week of 2007) and EMBASE entries. Articles were also obtained by cross-reference from citations in relevant articles. Inclusion criteria comprised: SCC of OC; any T and N categories at inception; primary surgery only; a description of the true nodal status as either node Positive or Negative for specific ranges of TT. True nodal status was assessed by either pathologic positivity on immediate neck dissection (ND) or cases without ND where neck recurrence was identified after FU $\geqslant$ 2 years. Due to inconsistency in the upper boundary of each individual study, we calculated nodal detection proportions and 95% confidence interval (CI) (Clopper-Pearson method) according to an upper level for each TT category: <3 mm, <4 mm, <5 mm and <6 mm from pooled data. Differences between TTcp were tested using Logistic Regression with Generalized Estimating Equations.
**Results:** Two independent reviewers selected 16 eligible studies from 72 potential studies yielding a pooled total of 1136 patients for this study. The disease subsites were 46% oral tongue, 16% buccal mucosa, 12% floor of mouth and 22% lower lip. There are 4 studies TTcp set at 3 mm, 9 at 4 mm, 6 at 5 mm and 4 at 6 mm (4 studies had 2 TTcp, 1 study had 4 TTcp). For the overall group, the proportion of subsequent node detection was 5.3% (95% CI: 2.0−11.2), 4.5% (2.6−7.2), 16.6% (11.5−22.8), and 13.0% (9.7−16.9) for TT <3 mm, <4 mm, <5 mm and <6 mm respectively. The proportion of subsequent node detection for TT < 5 mm category increased significantly compared to TT < 4 mm category ($p = 0.05$).
**Conclusions:** When the TTcp of OC migrates from 4 mm to 5 mm, the risk of nodal metastasis increases significantly. We propose that the optimal "cutpoint" of tumor thickness is 4 mm. For tumors thicker than 4 mm, elective treatment of the neck should be considered.

**5504** ORAL

**Quantification of plasma Epstein-Barr virus DNA in patients with nasopharyngeal carcinoma: results of a prospective study**

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**Background:** Recently, quantification of plasma EBV DNA was shown to be useful for monitoring patients with nasopharyngeal carcinoma (NPC) and predicting the outcome of treatment. We designed a prospective study, to investigate the correlation between plasma EBV DNA levels and clinical status of the patients with NPC.
**Methods:** A total of 149 patients with NPC and healthy controls were enrolled between February 2004 and June 2006. The levels of circulating EBV DNA were measured in 3 NPC patient groups. Group A (35 patients): non-metastatic patients treated with curative intent and measurements were made at diagnosis and after treatment. Group B (82 patients): patients in remission with conventional follow-up examinations and measurements were made at follow-up. Group C (13 patients): patients with evident clinical/radiological local and/or distant relapse. Group D: 19 healthy volunteers were selected as control group.
**Results:** Group A: EBV DNA was detected quantitatively in plasma samples of 25 (71%) out of 35 patients at diagnosis. The median concentration of plasma EBV DNA at the time of initial diagnosis was 576 copies per milliliter (interquartile range, 41 to 15,599). The median EBV DNA concentration decreased to 0 copies per milliliter after the completion of treatment in all but four patients (3 with DM and 1 in clinical remission). Group B: During follow-up period, a quantitative increase in EBV DNA concentrations was detected in 8 (9.8%) out of 82 patients (range 0−13,731 copies/ml). The imaging of these patients revealed distant metastasis in 4, local/regional relapse in 3 and false positive in 1 patient. Group C: EBV DNA concentrations were measured quantitatively in seven (54%) of 13 patients with locoregional relapse or distant metastases. Group D: All healthy individuals have negative plasma EBV DNA.
**Conclusions:** This study showed that quantitative plasma EBV DNA can be detected in 71% of the NPC patients at diagnosis. The plasma EBV DNA levels were persistently undetectable or low in patients with clinical remission. These results suggest that quantitative analysis of plasma EBV DNA may be a useful clinical tool in the screening and monitoring of NPC patients.
This study is supported by Hacettepe University Scientific Research Project Unit with project number HUTF BAB 0401101007.

**5505** ORAL

**Large cohort dose-response analysis of parotid gland function after radiotherapy: IMRT versus conventional radiotherapy**

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**Background:** Five years after radiotherapy, approximately half of the head-and-neck cancer patients still complain of moderate or severe xerostomia. Intensity-modulated radiotherapy (IMRT) reduces the dose to the parotid glands and thereby the number of xerostomia complications. Data regarding doses that permit preservation of parotid gland function are conflicting and originate from relatively small patient groups. Aim of this study was to compare, in a large group of patients, the parotid gland dose-response curve after IMRT with that after conventional radiotherapy (CRT).
**Material and Methods:** A total of 221 patients treated with primary or postoperative radiotherapy for various head-and-neck malignancies were prospectively evaluated. Of these, 64 patients were treated with IMRT and 157 with CRT (of which 49 using 3D-conformal techniques). Stimulated parotid flow rates were measured before radiotherapy and 6 weeks, 6 months and one year after radiotherapy using Lashley cups. Parotid gland dose-volume histograms were derived from CT-based treatment planning. The $TD_{50}$ (the dose leading to a complication probability of 50%) was calculated using the normal tissue complication probability (NTCP) model proposed by Lyman and the mean dose to the parotid gland. A complication was defined as stimulated parotid flow rate <25% of the pre-radiotherapy flow rate.
**Results:** No difference was found between the $TD_{50}$ value for the IMRT and conventional treatment groups (Table 1). We found rather flat dose-response curves at one year after radiotherapy (slope $m = 0.44$ for the