up in the 2005 analysis to gather current data from the study sites. With a minimum follow up through December 1, 2008, data on survival, progression free survival and other factors were gathered and analyzed by summary statistics.
Results: The initial demographics, therapy and toxicity were previously reported. Data of 85% of 501 subjects randomized to either TPF or PF treatment on TAX 324 was collected. With a median follow up of 71 months and a minimum of 5 years, the overall survival in the TPF group was significantly longer than in the PF group (HR 0.74; 95% CI 0.58−0.94; p = 0.013). Median survival was 71 and 30 months respectively, and mortality was reduced 24% in the TPF arm compared with PF. At 5 years 52% and 42% of the TPF and PF patients are alive (p = 0.06). Subset analysis showed that the median survival was improved across all sites with TPF. Median survival was not reached in patients with oropharyngeal tumor locations who were treated with TPF while it was 68 months in the PF group (HR 0.71, 95% CI 0.5−1.97; p = 0.07). The complete data set including the rate of tracheostomy and enteral feeding tube dependence among survivors will be presented at the meeting.
Conclusion: The benefit of induction chemotherapy with TPF is significantly superior to PF beyond 5 years and has been maintained at essentially the same level of impact as in the 2 year follow up. These data support the long term efficacy of TPF and sequential therapy in the management of appropriate patients with locally advanced head and neck cancer.

8503 ORAL

Final report of NPC-9901trial on therapeutic gain and late toxicities attributed to concurrent-adjuvant chemotherapy for T1−4N2−3M0 nasopharyngeal carcinoma

A.W.M. Lee[1], S.Y. Tung[2], D.T.T. Chua[3], R.K.C. Ngan[4], R. Chappell[5], R. Tung[6], C.W. Choi[7], L. Siu[8], J.T. Lau[9], W.H. Lau[4]. *[1]Pamela Youde Nethersole Eastern Hospital, Department of Clinical Oncology, Hong Kong, China; [2]Tuen Mun Hospital, Department of Clinical Oncology, Hong Kong, China; [3]Queen Mary Hospital, Department of Clinical Oncology, Hong Kong, China; [4]Queen Elizabeth Hospital, Dept. of Clinical Oncology, Hong Kong, China; [5]University of Wisconsin Medial School, Dept. of Biostatistics, Madison, USA; [6]Hong Kong Cancer Fund, Department of Service, Hong Kong, China; [7]University of Hong Kong, Dept. of Community Medicine, Hong Kong, China; [8]Princess Margaret Hospital, Ontario Cancer Institute, Toronto, Canada; [9]Chinese Universtiy of Hong Kong, Center for Epidemiology and Biostatistics, Hong Kong, China*

Purpose: The NPC-9901 Trial aims to evaluate the therapeutic ratio achieved by concurrent–adjuvant chemoradiotherapy (CRT) for regionally advanced nasopharyngeal carcinoma (NPC). This is the first trial with long term data on late toxicities in addition to survival rates.
Patients and Methods: Eligible patients with non-keratinizing NPC staged T1−4N2−3M0 were randomly assigned to radiotherapy (RT) alone or CRT. Both arms used the same RT technique and dose in line with the policy adopted by individual centers, all patients were treated with conventional fractionation to a total dose $\geqslant$ 66 Gy. Those in the CRT arm were given the Intergroup-0099 Regimen of cisplatin 100 mg/m^2 every 3 weeks for 3 cycles in concurrence with RT, followed by 3 adjuvant cycle of cisplatin 80 mg/m^2 and 5-fluorouracil 1000 mg/m^2/day for 96 hours every 4 weeks. All analyses were based on intention-to-treat principle.
Results: From March 1999 to January 2004, 348 patients have been accrued: 176 were randomized to RT and 172 to CRT. The median follow-up was 5.9 years. The 2 arms were well-balanced in all prognostic factors and RT parameters. The tumor control and late toxicity rates were listed in the attached Table.
Conclusions: Long term data confirmed that CRT could achieve significant improvement in progression-free survival due largely to improvement in locoregional control, but the benefits in distant control and overall survival did not reach statistical significance. No significant excess in overall late toxicity rate (Grade $\geqslant$3) was observed.

Comparison of Chemoradiotherapy versus Radiotherapy alone

Endpoint	Comparison of actuarial rate by log-rank test		Independent significance of CRT by multivariate analyses	
	5-year rate (%)	*P* value	Hazard Ratio (95% CI)	*P* value
Loco-regional control	88 *vs* 78	0.005	0.45 (0.25, 0.79)	0.006
Distant control	74 *vs* 68	0.319	0.82 (0.56, 1.21)	0.32
Failure-free rate	67 *vs* 55	0.014	0.66 (0.47, 0.92)	0.015
Progression-free survival	62 *vs* 53	0.035	0.72 (0.53, 0.98)	0.036
Overall survival	69 *vs* 64	0.188	0.79 (0.57, 1.12)	0.189
Late toxicity (Grade $\geqslant$3)	30 *vs* 21	0.205	1.29 (0.87, 1.93)	0.206

8504 ORAL

Induction chemotherapy (IC) followed by concomitant chemoradiotherapy (CCRT) versus CCRT alone in patients with locally advanced nasopharyngeal carcinoma (LA-NPC) – a randomized phase II study of the Hellenic Cooperative Oncology Group

G. Fountzilas[1], E. Ciuleanu[2], A. Kalogera-Fountzila[1], G. Karayannopoulou[1], M. Bobos[1], E. Samantas[1], S. Lambaki[1], D.V. Skarlos[1], K.T. Kalogeras[1], T. Ciuleanu[3]. *[1]Hellenic Cooperative Oncology Group, Data Office, Athens, Greece; [2]Cancer Institute Ion Chiricuta, Department of Radiation Therapy, Cluj, Romania; [3]Cancer Institute Ion Chiricuta, Department of Medical Oncology, Cluj, Romania*

Background: CCRT is considered standard treatment in LA-NPC. The role of IC when followed by CCRT in improving locoregional control remains controversial.
Patients and Methods: 141 eligible patients with LA-NPC were randomized to either 3 cycles of IC with cisplatin (175 mg/m^2), epirubicin (75 mg/m^2) and paclitaxel (75 mg/m^2) (CEP) every 3 weeks followed by definitive radiotherapy (70 Gy) and concomitant weekly cisplatin (40 mg/m^2) (group A, 72 patients) or CCRT alone (group B, 69 patients). For the present analysis, p16, MAP-Tau and ERCC1 protein expression were assessed centrally in tissue microarrays by immunohistochemistry in 107 tumors. EBER status was investigated by in situ hybridization.
Results: 66 patients (92%) in group A received 3 cycles of IC. Totally, 89% of patients (86% in group A vs 93% in group B, p = 0.718) completed treatment as planned. The two groups were balanced in terms of age, gender, PS, stage, and histology (WHO). Overall response rate (ORR), the primary endpoint, was 78% in both groups. Complete response rate was 57% in group A and 52% in group B (p = 0.614). Most frequently reported severe toxicities included neutropenia (3% vs 6%), leukopenia (24% vs 29%), thrombocytopenia (17% vs 1%, p = 0.005), nausea/vomiting (20% vs 19%) stomatitis (30% vs 38%), dysphagia (15% vs 6%), and weight loss (25% vs 26%). After a median follow-up of 31 months, 26 patients progressed (10 vs 16) and 28 (12 vs 16) died. 1-year PFS rate was 84% and 70% in groups A and B, respectively (p = 0.006). p16, MAP-Tau and ERCC1 protein expression was reported in 4%, 44% and 49%, respectively. EBER positivity was recorded in 67 out of 76 patients (88%) with type III, 18 out of 22 patients (82%) with type II and 3 out of 9 patients with type I histology (p = 0.001). No biological marker was associated with tumor response.
Conclusions: ORR with the CEP regimen followed by CCRT is not superior compared to CCRT alone in patients with LA-NPC. None of the biological markers investigated was of predictive value. Follow-up is continued to obtain further information on the type of progression and survival.

8505 ORAL

RapidArc for locally advanced head and neck cancer – first clinical results

M. Bieker[1], P. Doornaert[1], M.R. Vergeer[1], W. Verbakel[1], S. Senan[1], B. Slotman[1]. *[1]VU Medical Center, Radiotherapy, Amsterdam, The Netherlands*

Background: Volumetric modulated arc radiotherapy is of upcoming interest instead of classical standard IMRT for treating locally advanced head and neck squamous cell carcinoma (HNSCC). For the first time we present clinical data regarding acute toxicity for a cohort of 40 patients (pt) treated with RapidArc (RA, Varian Medical Systems) with a simultaneous integrated boost (SIB) technique.
Material and Methods: From June 2008 until March 2009 40 pt with HNSCC completed RA treatment with curative intend. Primary tumor was located in the oropharynx (60%), hypopharynx and larynx (22.5%), nasopharynx (10%), paranasal sinus (5%) and nasal cavity (2.5%). Thirty pt were staged as AJCC stage III or higher, 10 pt were staged as I or II. Concurrent systemic therapy (cisplatin, cetuximab) was applied in 22 cases. Dose prescription was set at 70 Gy (2 Gy/fraction) for the primary tumor an pathological lymph nodes deliver as a SIB. The elective lymph nodes recieved a dose of 54.25 Gy (1.55 Gy/fraction) in an accelerated scheme (6 times a week, total treatment time 6 weeks) or 57.75 Gy (1.65 Gy/fraction) in a conventional setting (5 times a week, total treatment time 7 weeks). All patients were treated with two complementary arcs to optimize PTV homogeneity (Verbrakel et al, IJROBP 2009). Acute toxicity was recorded weekly according to RTOG Radiation Morbidity Scoring Criteria for dermatitis (D), mucositis (M), xerostomia (X), dysphagia (D) and laryngitis (L) and analyzed by the end of therapy. Results were compared retrospectively with recently published data from our patients treated using 7 field IMRT with sliding window technique (Vergeer et al, IJROBP 2009).
Results: All patients completed treatment as planned. S,M,D,L grade 3 or higher appeared in 32.5% and 12.3% (RA/IMRT), 30% and 18%, 50% and

54.8%, 20% and 13.7%. Xerostomia grade 2 appeared in 72.5% and 49.3% (RA/IMRT) of all cases. For all results, there was no statistically sigificant difference ($p \geqslant 0.05$, Mann-Whitney). Treatment could be delivered within 4 minutes, compared to more than 10 minutes for conventional IMRT.
Conclusion: Deliver rotational radiotherapy with SIB using RA is a quicker approach to irradiate complex volumes in patients with locally advanced HNSCC with acute toxicity comparable to conventional IMRT. RA has become our standard treatment approach for locally advanced HNSCC.

8506 ORAL

Cisplatin dose intensity correlates with outcome in patients with locally advanced head and neck squamous cell carcinoma receiving concurrent cisplatin based chemoradiation: a multi-institutional experience

R. Granata[1], G. Pond[2], J. Kim[3], L.L. Siu[3], P. Olmi[4], E. Orlandi[4], P. Bossi[1], L.D. Locati[1], L. Licitra[1]. *[1]Fondazione IRCCS "Istituto Nazionale dei Tumori", Head and Neck Cancer Medical Oncology Unit, Milan, Italy; [2]Ontario Clinical Oncology Group and McMaster University, Statistics, Toronto, Canada; [3]Princess Margaret Hospital University of Toronto, Clinical Oncology, Toronto, Canada; [4]Fondazione IRCCS "Istituto Nazionale dei Tumori", Radiotherapy, Milan, Italy*

Background: A standard treatment option for patients with locally-advanced head and neck squamous cell cancer (LA-HNSCC) consists of concomitant cisplatin (CDDP) and radiation (RT). However the optimal dose and scheduling of CDDP is still controversial. To date, the significance of giving the full intended dose of CDDP (300 mg/m^2) on cancer-control has not been evaluated prospectively. To this end, we retrospectively evaluate 301 LA-HNSCC patients treated with chemoradiation (CRT).
Methods: the study population consists of 301 non-nasopharynx LA-HNSCC patients treated with primary CRT between January 2002 and September 2008 both in our Institution and at Princess Margaret Hospital in Toronto, Canada. Only patients that received CDDP and concomitant full dose of RT were included. The data collected consisted of patients and, tumor characteristics, CDDP and RT delivery details, toxicity, overall survival (OS) and disease-free survival (DFS).
Results: median age: 57; male: 77%; ECOG performance status 0: 67%; 0 comorbidities: 36%; oropharynx tumors: 60%; T3: 24%; T4: 30%; N2a: 6%; N2b: 32%. Of 301 patients, 278 (92%) received 70/72 Gy and 13 (4%) received 66 Gy, mainly due to the use of intensity-modulated radiation therapy with simultaneous integrated boost technique (IMRT-SIB). Of all, 94 (31%) patients received full-dose CDDP. The 2-year OS and DFS were respectively 83% and 70%. In multivariate analyses. Poorer ECOG-PS was significantly associated with decreased OS ($p < 0.001$). Conversely, oropharynx tumors were associated with better OS ($p = 0.004$). No prolongation of overall RT duration was significantly associated with improved OS ($p < 0.001$). Full-dose CDDP significantly increased overall DFS ($p = 0.009$). Interestingly, full-dose CDDP CT was associated with better local and regional DFS ($p = 0.005$), but not with distant DFS.
Conclusions: in patients with LA-HNSCC, full dose CDDP is associated with better DFS rates. Our data confirm that the dose of CDDP plays an important role in this patients' category. Whether CDDP based neoadjuvant can compensate for the suboptimal dose of CDDP in the concomitant phase is still to be demonstrated.

Poster presentations (Tue, 22 Sep, 09:00−12:00)
Head and neck cancer

8507 POSTER

The EGFRvIII variant in squamous cell carcinomas of the head and neck: Expression and correlation with clinico-pathological parameters in 675 patients from the randomised DAHANCA 6/7 study

J.G. Eriksen[1], P. Lassen[2], J. Overgaard[2]. *[1]Odense University Hospital, Department of Oncology, Odense, Denmark; [2]Aarhus University Hospital, Department of Experimental Clinical Oncology, Aarhus, Denmark*

Background: The Epidermal Growth Factor Receptor (EGFR) is frequently overexpressed in squamous cell carcinomas of the head and neck (HNSCC). Genomic rearrangements can give rise to modified variants like EGFRvIII, which is a truncated receptor formed by a 267 amino-acid in-frame deletion. EGFRvIII has only sparsely been studied in HNSCC and the constitutively activation of this receptor may account for the relatively low response rates to EGFR-inhibitors. The aim of the present study was to describe the expression of EGFRvIII and correlate this with wtEGFR expression and clinical parameters.
Material and Methods: Formalin-fixed paraffin embedded tissue-blocks from 675 patients is at present available and evaluated for the expression of wtEGFR and EGFRvIII. All patients were randomised to primary radiotherapy 5 or 6 fx/week, 2 Gy/fx, in total 66−68 Gy. wtEGFR was visualised using a well known commercial antibody, whereas the antibody against EGFRvIII is relatively new but is specific for the variant receptor when tested by western blot. Expression of wtEGFR was evaluated on a 4-grade scale and the data was dichotomised into high or low expression by the cut-point 50% of positive tumour staining. EGFRvIII is at present only evaluated as a positive or negative staining. Expression was correlated to patient- and tumour characteristics and when the full cohort of up to 800 patients is evaluated, then outcome data will be analysed.
Results: EGFRvIII was present in 267 (40%) of the tumours, with a non-uniform staining pattern. Expression was evenly distributed in the larynx and pharynx (37 and 40%) and in 51% of the tumours of oral origin and expression of EGFRvIII was inversely correlated wtEGFR ($p = 0.001$). In contrast to wtEGFR, the expression of EGFRvIII was not more frequent in low differentiated tumours compared to well differentiated HNSCC. No other correlations with patient or tumour characteristics were observed.
Conclusions: This is by far the largest clinical study of EGFRvIII in head and neck cancer. The variant is expressed in 40% of the tumours in a heterogeneous pattern not related to the expression of wtEGFR. When the full cohort is evaluated, outcome data will be analysed and presented at the meeting.
Presented on behalf of the Danish Head and Neck Cancer group (DAHANCA)

8508 POSTER

Preliminary results of the randomized phase II TREMPLIN study: TPF Induction chemotherapy followed by radiotherapy plus cisplatin or cetuximab

Y. Pointreau[1], J.L. Lefebvre[2], F. Rolland[3], M. Alfonsi[4], A. Baudoux[5], C. Sire[6], D. de Raucourt[7], E. Bardet[8], C. Tuchais[9], G. Calais[10]. *[1]Henry Kaplan Center University Hospital Tours, Radiotherapy Department, Tours, France; [2]Oscar Lambret Center, Chirurgie Cervico-Faciale, Lille, France; [3]Rene Gauducheau Center, Medical Oncology, Nantes, France; [4]Clinique Sainte Catherine, Radiotherapy, Avignon, France; [5]clinique Sainte Elisabeth, Radiotherapy, Namur, Belgium; [6]Lorient Hospital Center, Radiotherapy, Lorient, France; [7]François Baclesse Center, Surgery, Caen, France; [8]Rene Gauducheau Center, Radiotherapy, Nantes, France; [9]Paul Papin Center, Radiotherapy, Angers, France; [10]Henry Kaplan Center University hospital Tours, Radiotherapy, Tours, France*

Background: induction chemotherapy (ICT) followed by radiotherapy (RT) or concurrent chemoradiotherapy (CRT) in case of objective response were a standard alternative to total laryngectomy and indicated for larynx preservation (LP) strategy. Data have suggested that cetuximab may add to improve the efficacy of radiotherapy in head and neck cancer. Docetaxel-based ICT was the most effective schedule. The objective of this phase II randomized trial was to compare the 3 months larynx preservation rate after TPF induction regimen followed by radiotherapy plus either cisplatin or cetuximab.
Material and Methods: the French GORTEC-GETTEC group initiated a randomized phase II study in previously untreated patients (pts) for whom surgical procedure required total laryngectomy. Eligible pts received 3 cycles of ICT (docetaxel and cisplatin both 75 mg/m^2 on day 1 and 5-FU 750 mg/m^2/day on days 1−5). In case of response $\geqslant$50% pts were randomized to receive either in arm A: RT (70 Gy) with cisplatin (100 mg/m^2 on days 1, 22 and 43 of RT) or in arm B: Cetuximab (400 mg/m^2 week 0 and 250 mg/m^2 on the first day of the 7 weeks of RT). Pts with response <50% had surgery. Primary endpoint was LP 3 months after treatment, secondary endpoints were larynx function preservation at 18 months, quality of function and tolerance to treatment.
Results: from March 2006 to April 2008 (end of accrual), 153 pts with stage III-IV larynx/hypopharynx cancer were enrolled in the study and could start ICT. Patients and T characteristics (age, sex, PS, primary site, TN) were well balanced. Of them 74 % could receive the planned ICT while the others had either reduced dosages or less than 3 cycles. Toxic deaths occurred in 2 pts (1.3%). Of the 149 evaluable pts after ICT, 22 were non-responders (15%), 4 pts were withdrawn from the study, 7 pts had ICT-related toxicity precluding any further cisplatin and 116 pts could be randomized (60 in arm A and 56 in arm B). 58 patients started RT + cisplatin ant 55 RTE + cetuximab. The 3 months LP rates were not statistically different (92% in arm A and 98% in arm B). In arm A, 43 % of pts could receive the full CRT protocol versus 71 % in arm B. In arm A 50% of pts had cisplatin-related toxicity (definitive in 52% the cases) while in arm B 26 % of patients had cetuximab-related toxicity (definitive in only 1 case). There was no CRT treatment-related death.
Conclusion: TPF-ICT followed by RT with concurrent cetuximab appeared more manageable than concurrent cisplatin with the same LP rate 3 months