echelon lymph node drainage) and CTV2 (residual lymph node regions). A total of 60 Gy/30 fractions was delivered to the periphery of CTV1 and 50–54 Gy/25–30 fractions to the CTV2. Treatments were delivered over six weeks, 5 days/week.
There were 23 stage III/IV, seven stage II and three stage I patients. Nine patients received concomitant, weekly platinum based chemotherapy.
Results: At the time of this analysis, Mar/2005, and a median follow-up of 33.3 months, there were seven locoregional and one distant failures. Three patients died of disease and two of other causes.
The 3-year OS was 90%. The 2 and 3-year DFS was 84 and 73%, respectively. The locoregional control (LRC) was 84 and 78% at two and three years, respectively.
Treatments were well tolerated. Seventeen patients had grade III acute toxicity, 11 patients with mucositis/pharyngitis, and 6 with dermatitis. Grade IV acute toxicity occurred in three patients. Late toxicity was limited to grade I/II in 12 patients. One patient had grade IV laryngeal edema requiring a temporary tracheostomy.
Conclusion: Dose escalation by means of dose painting of the H/N SCCa can safely and effectively be delivered using IMRT. Our preliminary results are encouraging and comparable, if not better, to most randomized dose escalation trials. We believe that, dose painting to escalate the dose needs further evaluation in a randomized fashion.

1019 POSTER

Radiotherapy alone versus radiotherapy with amifostine 3 times a week versus radiotherapy with amifostine 5 times a week: a prospective randomised study in squamous cell head and neck cancer

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Background: Xerostomia is an important side effect of radiotherapy in the head and neck region. To increase the therapeutic index of radiotherapy, it could be worthwhile to enhance selectively the radioresistance of normal tissues. The aim of this study was to investigate whether non-daily (3 times/week) intravenous administration of amifostine, a selective radioprotector, is as effective as daily intravenous administration in reducing the incidence of grade II or higher xerostomia.
Material and methods: 91 patients treated with bilateral irradiation for squamous cell head and neck cancer were randomly assigned to receive radiotherapy alone (AMI-0: 30 patients) versus amifostine 200 mg/m^2 intravenously 3 times/week before irradiation (AMI-3: 31 patients) versus amifostine 200 mg/m^2 intravenously 5 times/week before irradiation (AMI-5: 30 patients). Acute and late xerostomia according to RTOG criteria and quality of life (QoL; EORTC QLQ-C30 and QLQ-H&N35) were assessed at baseline, 6 weeks, 6, 12, 18 and 24 months.
Results: Grade $\geqslant$2 late xerostomia according to the RTOG-criteria differed significantly at 6 months, but not after longer time intervals (AMI-0 74% vs. AMI-3 67% vs. AMI-5 52%, ($p = 0.03$)). No significant differences between treatment arms were found for acute xerostomia or acute mucosal toxicity. During follow up, patient-rated xerostomia was significantly worse among the AMI-0 cases (mean difference score (MDS) 52) compared to AMI-3 (MDS 25) and AMI-5 cases (MDS 29)($p = 0.01$). No significant differences were observed for other QoL dimensions. The 2-year locoregional control rate was comparable for all study arms (AMI-0: 79% vs. AMI-3: 67% vs. AMI-5: 83% ($p = 0.31$)) as was the 2-year overall survival (AMI-0: 70%; AMI-3: 58% and AMI-5 84% ($p = 0.26$)). The most frequently reported side effect of amifostine was nausea and vomiting, which was however mild in most cases, i.e. grade 2 or more toxicity was observed in only 4 patients. However, 28% of the patients discontinued amifostine administration before the end of radiotherapy, mostly because of nausea and vomiting.
Conclusions: In this prospective randomised study, patient-rated xerostomia was significantly less among patients that received amifostine. No difference was noted between amifostine 3 times/week as compared to daily administration. For late xerostomia according to the RTOG criteria, a temporary effect was noted at 6 months, which disappeared thereafter.

1020 POSTER

Squamous cell carcinoma of buccal mucosa treated with free-flap based radical surgery and neck dissection

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Background: To analyze the survival and prognostic factors for survival in patients with squamous cell carcinoma of the buccal mucosa (BSCC) treated with free-flap based radical surgery and neck dissection.
Methods: Between February 1996 to July 2002, 161 consecutive untreated BSCC patients who received free-flap based radical surgery were enrolled. In all, 108 (67%) had advanced BSCC (pathologic stage [pS] III and IV). Most patients (154; 96%) had neck dissection (ND), and 41% of these had pathologic neck node metastases. Post-operative radiation therapy (RT) was scheduled for those who had at least one pathologic finding (i.e., pT4 or nodal positive, or margin $\leqslant$4 mm). Adjuvant concomitant chemo-radiotherapy (CCRT) was given in patients with extra-capsular spreading (ECS).
Results: The 5-year local, local regional control, overall, disease–free, and disease-specific survivals were 85%, 76%, 68%, 69%, and 76%, respectively. The 5-year overall survival was 100% in pathologic stage I, 78% in stage II, 69% in stage III, and 56% in stage IV ($p = 0.033$). The 5-year disease specific survival (DSS) was 100%, 86%, 76%, and 64% in pS I, II, III and IV, respectively ($P = 0.01$). By multivariate analyses, the independent risk factors for local regional control and DSS were pathologic nodal status and differentiation. Pathologic nodal status and pathological overall stage were significant prognostic factors of local control.
Conclusions: Good tumor control and survival can be observed in most patients treated with free-flap based radical surgery and neck dissection.

1021 POSTER

Comparison of Cumulative Incidence (CI) and Kaplan-Meier (KM) estimates on late normal tissue outcome in the presence of competing risks: Evidence from CHART (Continuous Hyperfractionated Accelerated Radiotherapy) Head and Neck Study

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Background: Cumulative incidence (CI) and the Kaplan-Meier (KM) estimates are the two estimators used to quantify the late side effects over time in the presence of competing risks. The aim of this study was to estimate and compare the properties of the two estimators for late morbidity over time for different prognostic groups.
Material and Methods: Three late morbidity endpoints were studied, dryness of the mouth, laryngeal oedema and subcutaneous fibrosis. In each patient, the time to first failure was recorded, or, in patients without any of the events, the time of the last follow up was used as input data for the analysis. KM analysis was performed in two ways: (1) KM (1st) estimate: For each patient the type of first event and time to first event were used as input data. (2) KM (any) estimate: For each patient the event of interest whether it was the first event or not was used as input data. KM (1st) and KM (any) and CI estimates were analysed using SPSS. The estimates were compared in early versus advanced T stage disease among 360 node negative (No) patients in the CHART arm where locoregional failure was the competing event.
Results: The CI estimates were lower for advanced T stage group for all three endpoints when compared to early T stage group. The most striking difference was noticed for dryness of mouth. The CI estimate indicated that there was 9% less dryness of mouth in patients with T3–4 disease. KM (any) rates were very close to KM (1st) rates for the dryness of mouth and the laryngeal oedema endpoints. For subcutaneous fibrosis and oedema rates KM (any) estimate was higher than the KM (1st) estimate and this difference was more pronounced in T3–4 disease. The results are shown at the table below.
Conclusion: Without a comprehensive understanding of the assumptions of KM method, the clinical interpretations must be made with caution. The KM and the CI methods should be used as complementary analyses. The natural behaviour of the tumour site and the competing events under study

should be clearly understood by clinicians before applying any of these methods.

Morbidity at 5 years	CHART N_0 T1–2			CHART N_0 T3–4		
	KM (1^{st}) (SE)	KM (any) (SE)	CI (SE)	KM (1^{st}) (SE)	KM (any) (SE)	CI (SE)
Dryness of mouth	56 (0.05)	55 (0.04)	0.46 (0.04)	0.55 (0.05)	52 (0.05)	0.37 (0.04)
Subcutaneous fibrosis and oedema	0.23 (0.04)	0.32 (0.04)	0.19 (0.03)	0.28 (0.05)	0.43 (0.05)	0.18 (0.03)
Laryngeal oedema	0.49 (0.04)	0.50 (0.05)	0.42 (0.04)	0.55 (0.05)	52 (0.05)	39 (0.04)

1022 POSTER

Patterns of local-regional recurrence in patients with head and neck cancer treated by parotid-sparing IMRT

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Background: To analyze the patterns of local-regional recurrence in patients with head and neck cancer treated by parotid-sparing intensity-modulated radiation therapy (IMRT).
Methods: Forty-one patients with pharyngeal squamous cell carcinomas were treated by IMRT between 2000 and 2004. The mean age of the patients was 59 years old with a range from 35 to 81 years old. There were 15 nasopharyngeal cancers (NPC), 14 oropharyngeal cancers (OPC), and 12 hypopharyngeal cancers (HPC). Clinical stage (UICC, 2002) was stage I; 2, II; 10, III; 6, IVa; 20, or IVb; 3. For 20 patients with OPC or HPC, unilateral (n = 15) or bilateral (n = 5) neck dissection was performed before IMRT. All patients were treated with whole-neck RT to 46–50 Gy/23–25 fractions by IMRT, followed by boost IMRT to the high-risk clinical target volume to a total dose of 60 to 70 Gy in 30 to 35 fractions (median, 68 Gy). A median follow-up period was 17 months with a range of 3 to 47 months. Twenty-nine patients were treated with concurrent chemo-radiotherapy using cisplatin (60–80 mg/m^2 x 2–3) for 13 NPCs or weekly docetaxel (15 mg/m^2) for 16 OPCs or HPCs.
Results: By IMRT, mean doses to the contralateral and ipsilateral parotid glands could be reduced to 24.0±6.2 Gy and 30.3±6.6 Gy, respectively. Recurrence or persistent tumors in the primary site was noted in 8 patients (20%). Recurrence was noted from the center of gross tumor volume (GTV) in 4 of the 12 HPCs and 2 of the 14 OPCs, while recurrence from the planning target volume (PTV) margin was noted in 2 of the 15 NPCs. Both of the NPCs had T4 tumors, and recurrence or persistent tumor was noted at the posterior edge of the clivus or at the anterior wall of the sphenoid sinus. Residual or recurrence of neck lymph nodes was noted in 5 patients (12%), including 2 patients with neck nodes recurrence after salvage surgery for recurrent primary tumors. In 2 patients with NPCs, PTV delineation for the neck nodes was insufficient, and recurrences were noted at the posterior chain nodes and at the nodes near the parotid gland. As both the primary site and neck nodes recurrence were noted in one patient, the PTV marginal recurrence was noted in three (7%) NPCs. In three of the four marginal recurrences, keen review of the pretreatment MRI of the patients showed the involved nodes or the extension of the primary tumor at the edge of the PTV.
Conclusions: In some patients with head and neck cancer, local–regional recurrences after IMRT can be related to the insufficient delineation for the PTV. Keen evaluation of the pretreatment MRI is essential for the treatment planning of IMRT.

1023 POSTER

Phase II study of capecitabine (X) plus reirradiation in patients (pts) with recurrent squamous cell carcinoma of the head and neck (SCCHN)

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Background: X has shown substantial activity in SCCHN [Pivot et al. 2004] and is replacing 5-FU as the backbone of chemotherapy in a wide range of solid tumours, particularly colorectal cancer, in both the metastatic and adjuvant setting. In addition, X has a unique survival benefit in breast cancer. There is substantial data to support using X in chemoradiation [Dunst et al. 2004]. This study evaluated the therapeutic impact and safety profile of reirradiation with concurrent oral X in SCCHN.
Materials and methods: Pts with locally advanced unresectable SCCHN who had prior radiation therapy (with or without chemotherapy) received X 450 mg/m^2 twice daily, 7 days a week. Radiation therapy was delivered as a standard fractionated regimen (2 Gy/day, 5 fractions/week) up to a total dose of 50–70 Gy. The cumulative (life-time) dose within overlapping fields was not to exceed 120–130 Gy.
Results: Currently, 12 male pts have completed treatment. Baseline characteristics were as follows: median age 56 (42–72), ECOG PS 0/1 3/9. Six pts had previous chemoradiation followed by radical resection; 4 had surgery and postoperative radiotherapy; 2 had concomitant chemoradiation (accelerated and hyperfractionated). Six pts experienced locoregional recurrences, 4 developed secondary primaries, and 2 had a regional lymph node relapse. The median time since prior radiation therapy was 38 months. Efficacy (as evaluated by WHO criteria): 3 pts had a complete response (25%); stable disease was observed in 8 pts, and tumour progression immediately after therapy was observed in 1 pt. Median duration of local control and median survival will be presented at the meeting. The most frequently observed toxicity was mucositis, which was grade 3 in only 2 pts; grade 1 or 2 skin reaction was seen in 8 pts. There was no evidence of systemic toxicity or myelosuppression, probably due to the very low dose of X. Radiation therapy was completed without delay in all pts, and X was prematurely interrupted in 1 pt due to mucositis grade 3.
Conclusions: Our preliminary data suggest that X chemoradiation is a well-tolerated and effective treatment modality for previously irradiated pts with SCCHN. Based on available data, a higher dose of X should be feasible and potentially more effective. Earlier use of X in SCCHN could also be evaluated.

1024 POSTER

Do smokers really have more fun?

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Background: Smoking is an important etiologic factor in the development of head and neck cancer. Smoking during radiotherapy influences survival and smoking after therapy, influences the recurrence rate and rate of second cancers. Many patients believe that “smokers have more fun” and thus better quality of life.
Materials and methods: A cross sectional quality of life and morbidity study was performed using EORTC C30 and H&N35 as well as the DAHANCA morbidity scoring system. The patients were attending follow up after single modality treatment with either radical radiotherapy (N = 83) or surgery (N = 33) for cancer of the larynx (N = 44), pharynx (N = 34) or oral cavity (N = 38). No data on social- or economical status or comorbidity were accessible.
Results: Fifty-two of 114 patients, with available smoking information, were registered as self reported smokers at follow up. Smoking status was not significantly correlated with any of the tumour or patient related endpoints registered on the DAHANCA forms including age, sex, tumour site, stage, time since therapy or therapy. Nevertheless smokers invariable have the lowest function scores and the highest symptoms scores in both DAHANCA and EORTC QLQ except fibrosis and HN Weight gain. This difference was significant in 20 of the 33 QoL scales, but none of the morbidity scores. The difference was apparent in both general endpoints (physical function, cognitive function, fatigue, nausea/vomiting, dyspnoea, appetite loss, constipation, diarrhoea and financial problems) and organ specific endpoints (HN pain, swallowing, senses, social eating, dry mouth, coughed, nutritional supplement, feeding tube, and weight loss). When dividing the non-smokers (N = 62) in patients admitting to smoke during initial therapy (N = 48) and never smokers (N = 14) a “dose” dependent effect could be seen with smokers having more symptoms than former smokers that had more symptoms than never smokers. The difference was significant between present and never smokers in 10 items, between former and present smoker in 10 items and between former and never smokers in 2 items.
Conclusion: Smokers had a significantly reduced score of many items of the EORTC C30 and H&N35 quality of life questionnaires. Smoking was not correlated with any of the disease, patients or treatment related factors registered. There was a clear tendency towards a dose effect with previous smokers constituting an intermediate group between present-smokers and never-smokers. These findings support the recommendation that head and neck cancer patients should quit smoking and indicate that there could be an immediate benefit to the patient’s health related quality of life of smoking cessation since former smokers did better than current smokers.