IMRT group and m = 0.46 for the CRT group) suggesting there is no distinct threshold dose.

Table 1. Mean dose in Gy (95% confidence interval) to the parotid gland leading to a complication probability of 50% (TD_{50}). N represents number of glands.

	6 weeks post-RT		6 months post-RT		1 year post-RT	
	Dose	N	Dose	N	Dose	N
All patients	30 (26−32)	319	34 (30−36)	254	40 (37−44)	220
CRT	32 (28−35)	222	36 (32−39)	181	40 (36−45)	168
IMRT	26 (18−29)	97	28 (20−34)	73	39 (34−48)	52

Conclusion: This large cohort dose-volume response analysis of parotid gland function shows no difference in NTCP curve between IMRT and conventional radiotherapy. One year after radiotherapy, a dose of 40 Gy results in a 50% complication probability.

5506 ORAL

Factors predicting prolonged percutaneous tube feeding in patients treated with hyperfractionated accelerated radiation therapy for advanced head and neck cancer

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Purpose/Objective: Swallowing dysfunction requiring the placement of percutaneous tubes for feeding and fluid supplementation can be prolonged for patients undergoing aggressive curative radiation for head and neck cancer (HNC). This analysis describes the incidence of and factors predicting the requirement for prolonged tube feeding in patients treated on a phase-II accelerated radiation dose escalation protocol.
Materials and Methods: Patients with stage III&VI HNC (n = 171) were enrolled in a prospective radiation dose escalation study between 1998 and 2003. Three sequential dose levels of 60, 62 and 64 Gy were delivered in 40 fractions bid over 4 weeks with non-IMRT techniques. Percutaneous tubes were inserted in 131 patients. For the first dose level, tubes were inserted as needed; prophylactic insertion was used routinely for subsequent dose levels. Tubes were removed when swallowing function had recovered enough to permit sufficient oral intake. Time between tube insertion and removal or last follow-up with the tube still in place was calculated for each patient. Kaplan-Meier rates of tube dependence were calculated for the entire group. The influence of patient (age, gender, smoking, alcohol), tumour (stage, site, recurrence), and treatment (dose, technique, field size) factors on tube dependence was examined with log rank and Cox proportional hazards models.
Results: The rate of tube dependence at 1 year post insertion was 22% for all patients. On univariate analysis, the following factors predicted for increased one year rates of tube dependence: age ($\leqslant$58 = 12% vs >58 = 32%, p < 0.0001), recurrence (no = 16% vs yes = 41%, p = 0.0058), high dose field size ($\leqslant$69 cm^2 = 12% vs >69 cm^2 = 31%, p = 0.0008), dose (60 Gy = 0% vs 62 Gy = 15% vs 64 Gy = 24%, p = 0.065), T category (T1/2 = 15% vs T3 = 22% vs T4 = 24%, p = 0.067), alcohol (no = 18% vs yes = 43%, p = 0.075) and smoking (no = 14% vs yes = 42%, p = 0.12). Gender, primary site (oropharynx vs hypopharynx vs larynx), N category and treatment technique did not have an effect. On multivariate analysis only age and relapse were significant (p = 0.0014 and p = 0.003 respectively).
Conclusions: Actuarial rates of tube dependence in HNC patients treated with this aggressive accelerated radiation regimen are significant. Age greater than 58 and the presence of recurrent disease were the strongest independent predictors of tube dependence, however other factors should be considered when informing patients of the risk of this complication.

5507 ORAL

A phase 2 study of axitinib (AG-013736; AG) in patients (pts) with advanced thyroid cancers

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Background: AG is a potent small molecule inhibitor of VEGFR 1, 2 and 3. The efficacy and safety of AG was examined in pts with advanced thyroid cancers in a single-arm, multi-center study. Increased concentrations of plasma VEGF and decreased concentrations of soluble VEGFR2 and/or VEGFR3 have been observed after treatment with VEGFR inhibitors, and the relationship between clinical response and soluble protein was also explored.
Methods: 60 pts with metastatic or unresectable locally advanced thyroid cancer refractory to, or not suitable candidates for, ^{131}iodine (^{131}I) treatment, with measurable disease received AG (starting dose 5 mg orally BID). The primary endpoint was response rate (RR) by RECIST criteria. A Simon 2-stage minimax design was used (α = 0.1; β = 0.1; null RR = 5%; alternative RR = 20%). Samples were collected at baseline and q8wks to assess pharmacological modulation of plasma VEGF, soluble VEGFR2, VEGFR3 and KIT.
Results: Median age was 59 yrs (26−84), 35 (58%) were male. Histological subtypes included papillary: 29 pts (48%); follicular: 15 pts (25%), including 11 (18%) with Hurthle cell variant; medullary: 12 pts (20%); anaplastic: 2 pts (3%), and other/unknown: 2 pts (3%). 53 pts (88%) had prior surgery, 42 (70%) had prior ^{131}I treatment, 27 (45%) had prior external beam radiation, and 9 (15%) had prior chemotherapy. Partial response by investigator was achieved in 13 pts (22%, CI: 12.1, 34.2), with 31−68% maximum tumor regression and duration of response (DOR) of 1−16 months. 30 pts (50%) have stable disease with a DOR of 4−13 months and 13−67% maximum tumor regression in 28 pts. Response assessments are ongoing. Treatment duration range is 6–670 days with 38 pts currently on study. Median PFS has not been reached with a median follow up of 273 days. The most common treatment-related adverse events were fatigue (37%), proteinuria (27%), stomatitis/mucositis (25%), diarrhea (22%), hypertension (20%) and nausea (18%). Plasma VEGF increased by approximately 2.8-fold after 3 days of AG treatment. AG therapy decreased soluble VEGFR2 and VEGFR3 by 32 and 35%, respectively compared with baseline. In contrast, a relatively modest decrease in soluble KIT of 13% was observed (although statistically significant).
Conclusions: AG has substantial anti-tumor activity in advanced thyroid cancer and demonstrated pharmacodynamic activity as a selective VEGFR inhibitor. A global pivotal trial testing AG in doxorubicin-refractory thyroid cancer is ongoing.

Poster presentations (Tue, 25 Sep, 09:00−12:00)

Head and neck cancer

5508 POSTER

Efficacy of BIBW 2992, a potent irreversible inhibitor of EGFR and HER2, in models of head and neck cancer

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Background: EGFR is highly expressed in approximately 90% of head and neck squamous cell carcinomas (HNSCC). Cetuximab, a monoclonal antibody targeting EGFR, has demonstrated clinical benefit in HNSCC patients in combination with radiotherapy (locally advanced disease). More recently, a high incidence of EGFR mutations resulting in a deletion in the extracellular domain (EGFRvIII) has been reported in HNSCC. BIBW 2992 is a potent inhibitor of both EGFR (IC50 = 0.5 nM) and HER2 (IC50 = 14 nM) receptor tyrosine kinase activity with high selectivity against a panel of more than 50 other kinases. In vivo studies in nude mice have shown excellent single-agent efficacy in xenograft models of human breast, gastric, ovarian and vulvar carcinomas. BIBW 2992 demonstrated encouraging results in phase I studies and is currently in phase II clinical trials.