

Materials/Methods: Eligibility criteria included T3-4 primary squamous cell HNC with or without cervical lymphadenopathy. Patients with distant metastases were excluded. Patients randomized to HFRT received 75 Gy in 1.25 Gy/fraction twice daily while those randomized to HFRT+CT received 1.25 Gy/fraction twice daily to 70 Gy. Concurrent cisplatin 12 mg/m²/day and 5-FU 600 mg/m²/day were administered over five days during the first and sixth weeks of radiotherapy. Patients with \geq N2 presentations and a complete primary tumor response underwent neck dissection 6–8 weeks after the completion of radiotherapy. Survival curves were estimated by the Kaplan-Meier method. The Cox-Mantel test was used to compare survival distributions between the HFRT and HFRT+CT groups.

Results: Median follow-up is now 113 months for surviving patients. Most enrolled patients had primary tumors of the oropharynx (45%), hypopharynx (20%) or larynx (16%) with either T3-4 (88%) or N2-3 disease (53%). Patients receiving HFRT+CT achieved superior 10 year loco-regional control (LRC) and failure free survival (FFS) compared with HFRT alone (Figs. 1, 2 and Table 1). There was a trend towards improved cause specific survival (CSS). Freedom from distant failure (FFDF) did not significantly differ with HFRT+CT versus HFRT alone.

Conclusions: HFRT+CT improved 10 yr FFS and LRC compared with HFRT alone. There is a strong trend towards improved 10 yr CSS. The superiority of HFRT with concurrent CT over HFRT alone has since been confirmed in other phase 3 trials.

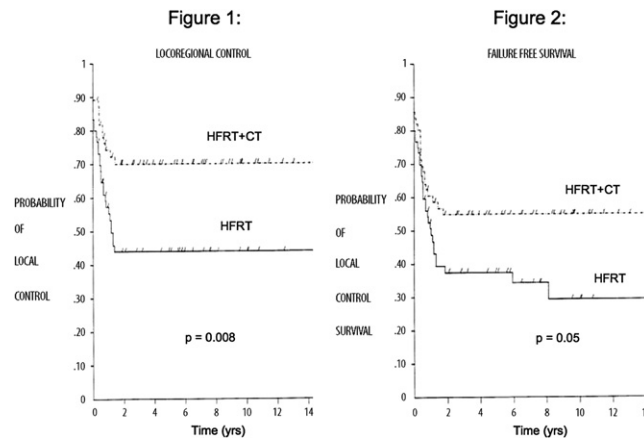


Table 1: Outcome with HFRT versus HFRT + CT

	HFRT (%)	HFRT + CT (%)
10 year LRF	44	70, $p = 0.008$
10 yr FFDF	57	81, $p = 0.2$
10 yr FFS	30	55, $p = 0.05$
10 yr CSS	32	57, $p = 0.07$

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21 A Phase III Trial to Compare Standard Versus Accelerated Fractionation in Combination With Concurrent Cisplatin for Head and Neck Carcinomas (RTOG 0129): Report of Compliance and Toxicity

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Purpose/Objective(s): A phase III trial was conducted to compare the relative toxicity and efficacy of combining the standard fractionation (SFX) versus an accelerated regimen by concomitant boost (AFX-C) with concurrent cisplatin. Frequent inquiries triggered this first analysis focusing on compliance and toxicity of treatments.

Material/Methods: From July 2002 to June 2005, 743 patients with stage III or IV carcinoma of the oral cavity, oropharynx, hypopharynx, or larynx and having Zubrod performance status of 0–1 and adequate hematologic, hepatic, and renal functions were enrolled. A total of 723 were analyzable, of whom 361 received SFX + cisplatin and 362 received AFX-C + cisplatin. The distribution between the 2 arms was balanced in patient age (median: 56–55.5 years), gender (male: 85%–80%), performance status (Zubrod 0: 57%–59%; 1: 43%–41%), primary site (oropharynx: 60%–60%; larynx: 25%–27%; others: 15%–13%), and AJCC stage (IV: 79%–78%). The radiation doses prescribed were 70 Gy/35 F/7 W and 72 Gy/42 F/6 W for the SFX and AFX-C arms, respectively. Cisplatin, 100 mg/m², was given iv q3W, for 3 and 2 courses, respectively. Acute RT toxicities (\leq 90 days from start of RT) and systemic effects at any time were scored using CTC version 2.0 and late RT complications using the RTOG/EORTC Scheme.

Results: Radiotherapy was delivered according to the protocol or with acceptable minor variation in 96% and 92% of patients on the SFX and AFX-C arms, respectively. For cisplatin, 68% on SFX arm received all 3 planned cycles whereas 87% on the AFX-C arm received both planned cycles. Table 1 summarizes the acute toxicity and late morbidity observed after a median follow-up of 2.0 years for all patients and 2.4 years for living patients. The proportions of patients with feeding tube were 25% and 22% before therapy, 68% and 67% at the end of treatment, and 30% and 27% at 1 year from therapy for the 2 arms, respectively. No statistically significant difference was detected for any toxicity endpoint. *From all causes up to 30 days after completion of treatment. ^bDefinitely or probably related to treatment.

Conclusions: The first analysis of this phase III trial revealed that the compliance to the combination of AFX-C and concurrent cisplatin was high and that this regimen did not result in higher acute toxicity or subacute morbidity relative to SFX plus cisplatin. The efficacy analysis will take place when the predetermined number of cancer related events is reached.

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22 Phase II Randomized Trial of Surgery Followed by Chemoradiation Plus Cetuximab for High-Risk Squamous Cell Carcinoma of the Head and Neck (RTOG 0234)

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Purpose/Objective(s): The RTOG has completed enrollment in a randomized phase II trial to examine the safety and feasibility of combining concurrent chemoradiation with cetuximab (anti-EGFR mAb) in the postoperative treatment of H&N cancer patients with high-risk pathologic features. Patients received 60 Gy and weekly cetuximab over 6 weeks with either weekly cisplatin (30 mg/m²) or weekly docetaxel (15 mg/m²).

Materials/Methods: This trial enrolled 238 subjects between April 2004 and December 2006 for an average monthly accrual of 7.6. To ensure a minimum of 6 month follow up beyond treatment completion, only those subjects enrolled on or before June 30, 2006 were included for this report yielding a total of 147 evaluable cases. All subjects had pathologic stage III or IV squamous cell carcinoma of the H&N with high-risk pathologic features following gross total resection including either microscopically positive resection margins, two or more metastatic neck nodes, or extracapsular tumor extension.

Results: Adverse events and treatment delivery parameters were reviewed. One patient (1.5%) on the cisplatin arm died of treatment-related causes. Seven patients (10.6%) on the cisplatin arm and 8 patients (9.9%) on the docetaxel arm experienced Grade 4 adverse events. Grade 3–4 mucositis of the oral cavity, pharynx, or larynx was experienced by 36.4% of patients on the cisplatin arm and 32.1% of patients on the docetaxel arm. The acute grade 4/5 non-hematologic toxicity rate (within 90 days from start of RT) was 10.6% on the cisplatin arm and 6.2% on the docetaxel arm. Study chair review of radiation therapy has been completed for 133 of 147 (90.5%) subjects with 95.5% scored as acceptable or minor variation. Study chair review of systemic treatment has been completed for 139 of 147 (94.6%) subjects with 87.1% scored as per protocol. Tolerable treatment was defined as receiving $\geq 90\%$ of the protocol radiation dose; $\geq 95\%$ of the cetuximab loading dose; ≥ 4 weeks of cetuximab with at least 95% of protocol dose and ≥ 4 weeks of cisplatin or docetaxel with at least 95% of protocol dose. Forty-six of 66 patients (69.7%) on the cisplatin arm, and 66/81 (81.5%) on the docetaxel arm met all of these criteria.

Conclusions: RTOG 0234 is the first completed randomized study to examine the safety and feasibility of two distinct H&N chemoradiation regimens combined with cetuximab. This preliminary review of treatment toxicity and tolerance suggests that concurrent triple therapy (radiation, cisplatin or docetaxel, and cetuximab) is safe and feasible under the conditions tested. Indeed, the Grade 4–5 non-hematologic acute toxicity rate of up to 10.6% compares favorably with the estimated rate of approximately 15% from RTOG prior experience in the same H&N patient setting using radiation plus high-dose cisplatin (RTOG 9501). Additional follow up data will be available for the 2007 ASTRO meeting.

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23 Phase II Multi-Institutional Study of IMRT \pm Chemotherapy for Nasopharyngeal Carcinoma (RTOG 0225): Preliminary Results

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Purpose/Objective(s): To assess the feasibility/toxicity of a multi-center trial of IMRT \pm chemotherapy (CTH) for nasopharyngeal cancer (NPC).

Materials/Methods: Patients with NPC, WHO I-III, stages I-IVB requiring radiation (RT) were eligible. Patients having $>T2a$ disease and/or + node(s) also received concurrent + adjuvant CTH. Target definition/delineation, dose prescription, and dose volume constraints for both targets/critical tissues were described in the protocol. The doses delivered to the planning target volumes of primary tumor/involved nodes (PTV₇₀) and subclinical disease (PTV_{59.4}) were 70 Gy and 59.4 Gy, delivered simultaneously in 33 fractions. Central quality assurance (Q/A) was performed for all centers and all patient treatment plans. Primary endpoint was to determine the ability to implement IMRT for NPC across multi-centers (defined as ≤ 9 major variations of the first 57 patients); secondary endpoints were to assess the acute/late toxicities + the rate of xerostomia at one year, and to test the hypothesis that a potential reduction of RT side effects on salivary flow will increase patient compliance to combined therapy.