Publishing Title: **A Phase III Trial To Test Accelerated Versus Standard Fractionation In Combination With Concurrent Cisplatin For Head And Neck Carcinomas (rtog 0129): Report Of Efficacy And Toxicity.**

Author Block: K. Ang[1], T. Pajak[2], D. Rosenthal[1], F. Nguyen-Tan[3], C. Lu[1], H. Kim[4], R. Axelrod[5], C. Silverman[6], R. Weber[1], *[1]M.D. Anderson Cancer Center, Houston, TX, [2]RTOG, Philadelphia, PA, [3]CHUM Hopital Notre Dame, Montreal, QC, Canada, [4]Wayne State University Medical Center, Detroit, MI, [5]Thomas Jefferson University Hospital, Philadelphia, PA, [6]University of Louisville, Louisville, KY*

Abstract Body:

Purpose: A phase III trial was completed to test the efficacy-toxicity of combining cisplatin with an accelerated concomitant boost (AFX-C) versus standard fractionation (SFX) in locally advanced head and neck carcinoma (LA-HNC).

Material & Methods: Patients had stage III-IV carcinoma of the oral cavity, oropharynx, hypopharynx, or larynx, Zubrod performance status (PS) 0-1 and good hematologic, hepatic, and renal functions. Prescribed radiation (RT) were 72 Gy/42 F/6 W and 70 Gy/35 F/7 W for AFX-C and SFX and cisplatin doses were 100 mg/m^2 q3W for 2 and 3 cycles, respectively. Acute RT reactions (≤90 days from start of RT) and chemotherapy toxicities were scored using CTC 2.0 and late complications by RTOG/EORTC Scheme. Endpoints were estimated using Kaplan-Meier method and compared with a log-rank test or by cumulative incidence method with a Gray's test.

Results: From 7/'02 to 5/'05, 743 cases were entered; 721 were analyzable (360 - AFX-C; 361 - SFX). Two arms were balanced by site (oropharynx: 60%-60%; larynx: 27%-25%; others: 13%-15%), stage (IV: 78%-79%), PS (0: 59%-57%), and age (median: 55-56 years), etc. Compliance rates to RT per protocol or minor variation were 93% and 96% in the AFX-C and SFX arms, respectively, and to cisplatin were 88% and 69%. At analysis, 418 patients were alive with median follow up of 4.8 (0.3-6.5) years. Twelve and 7 cases died of any cause ≤30 days of therapy completion (p=0.26); 1 and 2 other deaths were therapy related in AFX-C and SFX, respectively. No differences were observed in overall survival (5-Y: 59% vs. 56%; HR: 0.90, 0.72-1.13; p=0.18), disease-free survival (45% vs. 44%; p=0.42), local-regional failure (31% vs. 28%; p=0.76), or metastasis (18% vs. 22%; p=0.06). There were also no differences in the overall grade 3-4 acute mucositis (33% vs. 40%) and worst grade 3-4 late toxicity (26% vs. 21%). Feeding tube rates were 22% and 25% pretreatment, 67% and 69% at therapy end, 28 and 29% at 1 year, respectively, but declined later to 5-15%. Exploratory multivariate analyses showed that patients receiving SFX and ≥160 mg/m^2 of cisplatin had better survival than those receiving less doses (HR: 0.44; 0.27-0.73) but there was no striking trend in the SFX subset between patients receiving 240-300 and 160-210 mg/m^2 of cisplatin (HR: 0.87; 0.59-1.28), in the 160-210 mg/m^2 subset between those receiving AFX-C and SFX (HR: 0.88; 0.60-1.29), or in HPV/p16+ oropharyngeal carcinoma (HR: 0.90; 0.51-1.42).

Conclusion: First analysis of this trial showed that, when combined with concurrent cisplatin, AFX-C did not improve outcome or increase late toxicity in patients with LA-HNC. No effect by HPV/p-16 status was detected and the benefit of the third cisplatin cycle appeared minimal.