**Long-Term Results of RTOG 0617: A Randomized Phase 3 Comparison of Standard Dose Versus High Dose Conformal Chemoradiation Therapy +/- Cetuximab for Stage III NSCLC**

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**Purpose/Objective(s):** RTOG 0617 had two primary objectives; to compare standard-dose (SD) (60 Gy) versus high-dose (HD) (74 Gy) chemoradiation therapy and to determine the efficacy of the EGFR anti- body cetuximab for Stage III NSCLC. Mature 5-year follow-up data are reported.

**Materials/Methods:** This phase III randomized trial used a 2 x 2 factorial design with radiation dose as one factor and cetuximab as the other factor, with a primary endpoint of overall survival. Overall and progression-free survival rates were estimated using the Kaplan-Meier method and the survival rates compared using the log-rank test. Cox proportional hazards models were used to evaluate the impact of treatment and other factors on overall and progression-free survival. Local, regional, and distant failure rates were estimated using the cumulative incidence method, and Fine-Gray models were used to evaluate the impact of treatment and other factors on these rates.

**Results:** Five hundred forty-four patients were accrued and 496 were eligible for analysis. Median follow-up for surviving patients is 5.1 years with an interquartile range of 4.6-6 years. Patient, tumor, and treatment characteristics are described in the primary manuscript. With respect to RT randomization, there were 3 Grade 5 adverse events in the SD arm and 9 in the HD arm (one additional since primary report with GI bleed). Treatment-related grade 3+ dysphagia and esophagitis occurred in 3.2% and 5.0% in the SD arm versus 12.1% and 17.4% in the HD arm, respectively (P<0.0001). There remains no statistical difference in overall pulmonary toxicity, with Grade 3+ events occurring in 20.6% and 19.3%, respectively. Median overall survival is 28.7mo vs 20.3mo (P = 0.0072) for SD vs HD arms, respectively. 5-year OS and PFS rates are 32.1% vs 23% (P = 0.004) and 18.3% vs 13% (P = 0.055), respectively, favoring the SD arm. Factors impacting OS on multivariable analysis were radiation dose favoring SD, tumor location, institution accrual volume, esophagitis/dysphagia, PTV, and heart V5. Local, regional and distant failure patterns are 38.2% vs 45.7% (P = 0.068), 35.7% vs 38.4% (P = 0.5), and 52.3% vs 57.6% (P = 0.3). The use of cetuximab confers no benefit. The prior signal of cetuximab benefit in patients with higher H-scores is no longer apparent.

**Conclusion:** Sixty Gy with concurrent chemotherapy should remain the standard of care, with an OS rate amongst the highest reported in the literature for Stage III NSCLC. Cetuximab, an antibody to EGFR, had no effect on OS.