A Randomized Phase III Comparison of Standard-Dose (60 Gy) Versus High-dose (74 Gy) Conformal Chemoradiotherapy +/- Cetuximab for Stage IIIA/IIIB Non_Small Cell Lung Cancer. Preliminary Findings on Radiation Dose in RTOG 0617

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Purpose/Objectives: This report addresses the first objective of RTOG 0617; to compare the overall survival of patients (pts) treated with high-dose (HD)(74 Gy) versus standard-dose (SD)(60Gy) radiotherapy with concurrent chemotherapy.

Marterials/Methods: This Phase III Intergroup trial was planned to randomize 500 patients with Stage III NSCLC to 4 arms in a 2x2 design. Pts received HD (74 Gy) versus standard SD(60 Gy) radiation therapy +/- cetuximab. Concurrent chemotherapy (CT) included weekly paclitaxel (45 mg/m2) and carboplatin (AUC=2). Pts randomized to cetuximab received a 400 mg/m2 loading dose on Day 1 followed by weekly doses of 250 mg/m2. All pts were to receive consolidation chemotherapy. Stratification variables are RT technique (3D vs IMRT), Zubrod PS, PET staging, and histology (squam vs non-squam). Eligibility included biopsy-proven Stage IIIA/B NSCLC, PS 0-1, and FEV1≥1.2 L/sec. Exclusions included supraclavicular or contralateral hilar disease, ≥10% weight loss, or prior non-surgical therapy for NSCLC. The study was designed to detect a median overall survival improvement of 7 mos (24 vs 17 mos) in the HD radiation arms, with 80% power and a 1-sided alpha of 0.0125. These results reflect the initial planned interim analysis for overall survival.

Results: Between 11/2007 and 4/2011, 423 pts were accrued. The median follow up is 9.1 months. After 90 events, it was determined that the HD radiation arms had crossed the futility boundary. The HD radiation, as delivered in this trial, does not improve overall survival. The HD radiation arms were closed and the study remains open to 60 Gy with CT +/- cetuximab. The preliminary 1-yr OS rate is 74.8% (95%CI: 68.6, 80.0), with significant follow up remaining on the trial. Deaths are predominantly due to disease progression, as reported by institutions. There were 10 grade 5 adverse events attributed to protocol treatment (7 for HD and 3 for SD RT). There is no significant difference in treatment-related toxicity between the RT arms. Additional data on outcome and toxicity will be presented.

Conclusions: As delivered in RTOG 0617, 74 Gy is not associated with improved survival when compared to 60 Gy for treating unresectable Stage III NSCLC with concurrent weekly paclitaxel and carboplatin +/- cetuximab. Reported toxicity does not explain the early inferior survival with 74 Gy. The study remains open with SD RT at 60 with CT Gy +/- Cetuximab.

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