Acute esophageal reactions from proton beam therapy and concurrent chemotherapy for non-small cell lung cancer (NSCLC): Reduction in incidence and severity despite higher doses

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Purpose and Objective(s): To assess the incidence and severity of acute esophageal reactions from concurrent chemotherapy and 3-dimensional proton beam therapy (PBT) in the context of previous results with concurrent chemotherapy and 3-dimensional photon therapy (XT) for NSCLC.

Materials and Methods: Twenty-five consecutive patients with NSCLC (stages IIB [1], IIIA [8], IIIB [8], IV [2], post-operative recurrent [6], underwent PBT and concurrent chemotherapy with curative intent on IRB approved protocols. Chemotherapy was platinum-based in all patients, most frequently carboplatin/paclitaxel (16 patients). There were 16 males/9 females ranging in age from 49 to 81 years (median 67 years). Histopathologic diagnosis was squamous cell carcinoma in 9 and non-squamous in 16 patients. All patients were evaluable for acute (< or = 90 days from first treatment) reactions. Toxicity was based on NCI common toxicity criteria vs. 3.0. XT comparisons were based on published data from our institution (215 patients) (Wei X et al, Int J Radiat Oncol Biol Phys 2006)

Results: Total doses with PBT ranged from 63 cobalt-gray equivalent (CGE) (using RBE of 1.1 vs. cobalt gamma rays) to 74 CGE (60-69.6 Gy with XT) in 33 to 37 fractions (30-58 fractions with XT). The median total dose was 74 CGE vs. 63 Gy for XT. Acute esophageal reactions were observed in 60% of PBT patients (200 of 215/93% with XT). Seven (28%) of patients had grade 2 esophageal reactions (97 of 215/45.1% with XT). Four (16%) of patients had grade 3 esophageal reactions (43 of 215/20.0% with XT). No patient had a grade 4 reaction (1of 215/0.5% with XT).

Conclusions: Proton beam therapy permitted higher total doses (17%-+) with concurrent chemotherapy yet were associated with reduced esophageal reactions compared with 3-dimensional conformal photon therapy.

Consolidation chemotherapy with monthly Paclitaxel and Cisplatin (PC) or observation after concurrent chemoradiation for locally advanced non-small cell lung cancer (NSCLC): Randomized phase II study

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Background: Concurrent chemoradiotherapy (chemoRT) is the preferred treatment for patients with unrespectable stage III NSCLC. Limited safety information is available on the use of concurrent docetaxel, carboplatin and thoracic RT. We report the safety information on the initial 100 patients (pts) treated with this chemoRT as part of an ongoing US randomized web-based phase III trial (D0410) evaluating the role of erlotinib/placebo following this concurrent chemoRT treatment. The sample size is 400 pts and the primary endpoint is progression-free survival.

Methods: Pts with unrespectable pathologically confirmed stage III NSCLC are randomized to receive either erlotinib 150 mg or placebo orally daily for 2 years following concurrent chemoRT with docetaxel 20 mg/m², carboplatin AUC=2 intravenously weekly for 6 wks with thoracic RT of at least 61 Gy in 33 fractions over 6.5 weeks. The planned total lung volume exceeding 20 Gy (V20) was less than 32%. Only the chemoradiation safety information is being reported. This data is reviewed by an independent safety and data monitoring committee.

Results: Pt characteristics; 59% males, median age 69 years (range 38 to 86), 21% adenocarcinoma, 48% squamous cell, 94% ECOG PS0-1, 49% stage IIIA, 15% weight loss ≥ 10%. Of 600 planned chemotherapy treatments, 500 were administered (93 wk 1, 86 wk 2, 83 wk 3, 82 wk 4, 80 wk 5, 76 wk 6). There were 27 chemotherapy dose reductions; most commonly for esophagitis (8), neutropenia (5), renal dysfunction (3), hypersensitivity (2). There were no treatment-related deaths. There were 28 grade 3 and 3 grade 4 treatment-related adverse events. The most common grade 3/4 events were esophagitis (7), fatigue (3), dysphagias (2), odynophagia (2), neutropenia (1), thrombocytopenia (1), dermatitis (1).

Conclusions: This concurrent chemoradiation regimen appears to be safe. Enrollment to the phase III trial continues. There is a planned interim efficacy evaluation at 150 events (deaths or disease progression). Funded in part by Sanofi-Aventis, Genentech, and OSI Pharmaceuticals.