Postoperative Adjuvant Stereotactic Body Radiotherapy (SBRT) ± Cetuximab Following Salvage Surgery in Previously-Irradiated Head-and-Neck Cancer

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PURPOSE:

• Locoregional recurrence remains primary failure pattern following salvage surgery for previously-irradiated head-and-neck cancer (rHNC).
• Randomized trials have suggested a complementary role for adjuvant chemotheraphy and conventional re-irradiation at the expense of significant increases in toxicity.
• We hypothesized that adjuvant SBRT ± cetuximab may improve tumor control for high-risk rHNC following salvage surgery compared to a wait-and-see approach while reducing the treatment-related toxicity of conventional CT/Re-RT.

BACKGROUND:

• While there are no randomized data to test the benefits of salvage surgery after prior irradiation, for patients who have surgical resection, surgical resection represents the currently accepted standard of care for rHNC.
• Even patients with resectable rHNC are at high-risk for subsequent failure (67% overall failure rates). In patients with close or positive surgical margins following salvage surgery, recurrence rates of nearly 100% have been reported (see Table 3).
• Phase III data from Janot et al, provides level 1 evidence that re-irradiation improves local control albeit with the expense of significant toxicity (see Table 3).
• Initial phase I dose-escalation study established the safety of SBRT up to 44 Gy in 5 fractions for unresectable rHNC (Heron et al).
• Recent prospective data suggested that cetuximab + SBRT may improve tumor control without significant increases in re-irradiation toxicity for unresectable rHNC (Comet et al).
• While there is growing evidence for SBRT in unresectable rHNC, there is limited data in the adjuvant setting following salvage surgery.

MATERIALS/METHODS:

• Retrospective review (2005-2011) of 35 patients with high-risk features (positive surgical margins or extra-nodal extension) following macroscopic complete (RO/R1) salvage surgery treated with adjuvant SBRT ± cetuximab
• Patient characteristics are outline in Table 1
• SBRT consisted predominately of 40-44Gy in 5 fractions over 1-2 weeks with concurrent cetuximab (n=7) administered at 400mg/m² day -7 + 250mg/m² days 0 and +8.
• Dose was prescribed to the clinical treatment volume (CTV), which was the tumor bed/high-risk region as defined by head and neck oncologist (CTV=PTV).
• Toxicity was physician recorded, plus prospectively collected University of Washington Quality-of-Life-Revised surveys.

RESULTS:

• All patients completed adjuvant SBRT at a median of 62 days (range: 15-168) following salvage surgery. Figure 1 is example of an SBRT plan. The median SBRT treatment volume was 23.1cc (range: 2.5-166).
• At a median follow-up of 16 months (range: 2-69), the 1-year and 2-year locoregional (LC), distant control (DC), DFS, and OS were 58/48%, 88/75%, 57/43%, and 71/56%, respectively (see Figure 2).
• There were no significant differences in tumor control or survival by treatment volume (>25cc), cetuximab, histology (squamous vs. non-squamous) or reason for adjuvant therapy (compromised/positive margins or extra-nodal extension).
• As outlined in Table 2, the rates of acute and late severe (≥ grade 3) toxicity were low at 0% and 12%, respectively.
• PR-QoL was preserved across all head-and-neck specific domains throughout the duration of survey follow-up (see Figure 3). Specific domains of speech (p=0.028) and anxiety (p=0.017) showed significant improvement comparing UW-QoL retrospectively compared to historical results ± cetuximab ± re-irradiation ± chemotherapy.

CONCLUSIONS:

• Adjuvant SBRT ± cetuximab was well-tolerated with promising oncologic outcomes compared to historical results with salvage surgery alone (see Table 3).
• Overall rates of acute/late grade 3+ toxicity were low and when combined with preserved PR-QoL, compares favorably to prior series using conventional re-irradiation ± chemotherapy.
• Future prospective trials should evaluate adjuvant SBRT ± cetuximab vs. a wait-and-see approach for rHNC with high-risk features following salvage surgery.