OPTIMA—A Phase II Trial of Induction Chemotherapy Response-Stratified RT Dose and Volume De-escalation for HPV+ Oropharynx Cancer: Efficacy, Toxicity, and HPV Subtype Analysis

(Abstract 5)

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Purpose/Objective(s): This prospective phase II de-escalation study used induction chemotherapy to identify favorable HPV+ oropharyngeal cancer (OPC) pts, including those with high-risk tumors, and applied significantly lower radiation or chemoradiation doses than previously reported. We herein report an updated analysis with p16 IHC and HPV PCR genotyping.

Materials/Methods: Pts with HPV+ OPC were classified as low-risk (≤T3, ≤N2B, ≤10 PYH) or high-risk (T4 or ≥N2C or >10 PYH). Pts received 3 cycles of carboplatin and nab-paclitaxel induction. Low-risk pts with ≥50% response received low-dose radiotherapy alone to 50Gy (RT50). Low-risk pts with 30-50% response OR high-risk pts with ≥50% response received low-dose chemoradiotherapy to 45Gy (CRT45). All other (=poor response) pts received regular-dose chemoradiotherapy to 75 GY (CRT75). All pts also received de-escalated RT volumes limited to the first echelon of uninvolved nodes. RT50 was delivered in 2Gy/fx once daily whereas CRT arms used paclitaxel, 5-FU, hydrea, and 1.5Gy twice daily RT every other week. Primary site biopsy and neck dissection were performed only after de-escalated treatment (RT50, CRT45) for pathologic confirmation. The primary endpoint was 2-year PFS. Secondary endpoints included pathologic complete response (pCR) rate and toxicity.

Results: 62 pts were enrolled; p16 IHC was positive in all cases. Confirmatory HPV DNA PCR showed HPV16 in 94.9%, HPV18 in 1.7%, and HPV33 in 3.4%. 28 pts (45.2%) were low-risk and 34 pts (54.8%) were high-risk. 71.4% of low-risk pts received RT50 and 21.4% received CRT45. 70.6% of high-risk pts received CRT45. The pCR rate was 94.7% after RT50 and 89.3% after CRT45. Median follow-up is 1.5 years. The 2-year PFS and OS were both 100% for low-risk pts, and 93.5% and 97.0% for high-risk pts. A single in-field failure occurred in a high-risk pt 11 months after treatment with CRT45 and was surgically salvaged. Acute toxicity was significantly improved including grade ≥3 mucositis (15.8% RT50, 46.4% CRT45, 60.0% CRT75, p=.033) and grade ≥3 dermatitis (0% RT50, 21.4% CRT45, 30.0% CRT75, p=.056). Long-term PEG-tube dependency was also significantly improved (1-year rate: 0% RT50, 3.5% CRT45, 9.1% CRT75, p<.0001).

Conclusion: The use of 50Gy limited-field RT alone in low-risk HPV+ pts or 45Gy CRT in high-risk HPV+ pts with favorable response to induction chemotherapy resulted in excellent pCR and survival outcomes with reduced acute and late toxicity rates; long-term follow-up is ongoing.