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Treatment de-intensification in HPV-associated squamous cell carcinoma of the head and neck (SCCHN)

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Objectives: Recent chemo radiation studies in HPV-associated head and neck cancer have resulted in high rates of tumor control compared no traditional tobacco-associated cancers, but significant long term toxicities. This has resulted in strategies to deintensify treatment in Cooperative Group studies, but the appropriate combination of treatments and verification of specification of risk factors is still controversial.

Methods & Results: E2399 was phase II trial of chemoradiation, induction paclitaxel/carboplatin followed by paclitaxel/70Gy for organ preservation in locally advanced oropharynx and hypopharynx cancers, as was the first to prospectively reveal a statistically significant improvement in response rate and survival (95% vs 62% at 2 yrs) in HPV+/p16+ patients. As a follow-up phase II trial, E1308 evaluated chemo-responsiveness in p16+ oropharynx cancer using 3 cycles of cisplatin, paclitaxel, and cetuximab; if a cCr was obtained, reduced-dose 54Gy/cetuximab was delivered; patients with <cCR were treated with cetuximab and 69.3Gy. cCR to induction was 71%. PFS at 2 yrs was 80% for 54Gy IMRT vs. 65% for patients treated with full dose IMRT. Non bulky (T1-T3) and minimal smokers (<10 pk-years) had the best outcomes with 2-year PFS of >90%. Only one grade >3 late toxicity was observed (gr 3 hypomagnesemia at 30 months). RTOG subset analysis in patients enrolled on R0129 and R0522 showed similarly improved PFS and OS (55% vs. 28% at 2 yrs) in p16+ patients, and efforts to decrease RT dose are ongoing in follow-up studies. Minimally invasive surgical strategies (ECOG 3311) are prospectively evaluating adjuvant dose-de intensification or even observation based on pathologic findings.

Discussion: Smoking status and TNM stage are crucial selection criteria for deintensification chemo radiation and minimally invasive surgical strategies in p16+ SCCHN. The appropriate combination and intensity of each treatment modality is under investigation in Cooperative Groups.

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