**Survival Outcomes Among Human Papillomavirus- Associated Oropharyngeal Squamous Cell Cancer Patients Treated with Upfront Surgery Versus Definitive Chemoradiation Therapy**

J.R. Kelly,1 Y. An,2 H.S.M. Park,1 W. Yarbrough,3 B.A. Burtness,4 and Z.A. Husain1;

*1Department of Therapeutic Radiology, Yale School of Medicine, New Haven, CT, 2Department of Therapeutic Radiology, Yale University School of Medicine, New Haven, CT, 3Yale University, New Haven, CT, 4Department of Medical Oncology, Yale University School of Medicine, New Haven, CT*

**Purpose/Objective(s):** Transoral robotic surgery (TORS) is associated with decreased morbidity compared to open surgery for early-stage oropharynx cancer. However, there is no prospective data comparing oncologic outcomes of primary surgery vs. definitive concurrent chemoradiation (CRT) in the management of human papillomavirus-associated oropharyngeal squamous cell carcinoma (HPV-A OPC). We therefore assessed the outcomes of both treatment strategies in presumed TORS- eligible patients in a large national sample.

**Materials/Methods:** The National Cancer Database was used to identify patients diagnosed with cT2 N1 or cT1-2 N2a-2b HPV-A OPC from 2010- 2013 who underwent treatment with either CRT or primary surgery +/- adjuvant therapy. Demographic and clinicopathologic predictors of treatment were analyzed by the chi-square test and logistic regression. Overall survival (OS) was evaluated using the Kaplan-Meier, log-rank test, multivariable Cox proportional hazard regression, and propensity score- matched analysis.

**Results:** We identified 3,168 patients, among whom 1,576 (49.8%) received CRT and 1,592 (50.2%) underwent primary surgery. Median follow-up was 32 months. Nine hundred seventy-two (61.0%) surgical patients received adjuvant CRT. On multivariable logistic regression, female sex, younger age, academic treatment facility, higher comorbidity index, and lower clinical T and N stages were associated with higher odds of receiving primary surgery. Three-year OS in the CRT cohort was 90.8% vs. 92.5% in patients receiving primary surgery (log-rank P = .92). On multivariable Cox regression, upfront surgery was not associated with improved OS when compared with CRT (hazard ratio [HR] 1.10, 95% confidence interval [CI] 0.84-1.43, P = .48). Increasing clinical T and N stage, older age, and non-private insurance were significantly associated with inferior OS. Lack of OS benefit with upfront surgery persisted in a subset analysis of patients with margin-negative resection, with a 3-year OS of 90.1% in patients undergoing CRT vs. 93.5% in primary surgery patients (log-rank P = .14). Propensity score-matching identified a cohort of 2,618 patients and redemonstrated similar OS (HR, 1.11; 95% CI 0.83- 1.49; P = 0.49).

**Conclusion:** Upfront surgery was not associated with improved OS compared to CRT in this patient cohort. The majority of surgical patients received trimodal therapy with adjuvant CRT. Efforts to improve patient selection in order to minimize the need for trimodal therapy are justified given the lack of observed survival benefit with surgery.