**Survival Impact of Increasing Time to Treatment Initiation for Head and Neck Cancer in the United States**

*C.T. Murphy, T.J. Galloway, E. Handorf, L. Wang, R. Mehra, D. Flieder, and J.A. Ridge*

**Purpose/Objective(s):** To estimate the survival impact from increasing time to treatment initiation (TTI) for patients with head and neck squamous cell cancer (HNSCC) in the United States.

**Materials/Methods:** Using the National Cancer Database (NCDB), we examined patients treated with curative therapy for the following HNSCC sites: oral tongue, oropharynx, larynx, and hypopharynx. TTI was defined as the number of days from diagnosis to initiation of definitive treatment with surgery or radiation, or either modality in combination with chemotherapy. We excluded unknown TTI, TTI>365 days, distant metastases, in situ disease, palliative treatment, and patients without Charlson Comorbidity Index. We used Kaplan Meier methods to estimate overall survival (OS) and determined the effect of TTI on OS with Cox proportional hazard regression models (MVA), controlling for confounding covariates. Interaction testing explored combined effects on OS between TTI and covariates. Using recursive partitioning analyses (RPA), we identified optimal TTI thresholds predicting OS based on randomly selected training and validation sets and repeated this process 1000 times to ensure robustness of selected thresholds.

**Results:** A total of 51,655 patients met inclusion criteria. On MVA, longer TTI predicted worse OS for both 61 to 90 days (HR = 1.13 95% CI 1.08-1.19) and >90 days (HR = 1.29, 95% CI = 1.21-1.38) when compared to TTI <30 days. The combined effects model demonstrated significant interaction and higher risk of death for stage I-II compared to stage III-IV as TTI increased (P < .001). TTI of 67 days appeared as the optimal threshold on the training RPA with statistical significance confirmed in the validation set (P < .001) and was identified as the optimal threshold in 54% of repeated simulations. Overall, 96% of simulations validated 2 optimal TTI thresholds predicting OS with ranges of 46 to 52 days and 62 to 67 days. Median OS for TTI <52 days versus 53 to 67 days versus >67 days was 71.9 months (95% CI = 70.3-73.5) versus 61 months (95% CI = 57-66.1) versus 46.6 months (95% CI 42.8-50.7), respectively (P < .001). In the most recent year with available data (2011), 9.6% of all patients had TTI >67 days, 25% had TTI >46 days, and 40% treated with chemoradiation at academic facilities had TTI >46 days. Treatment at academic (HR = 0.93 95% CI = 0.89-0.97) or comprehensive cancer facilities (HR = 0.96 95% CI = 0.92-1.0) improved OS when compared to community facilities. Transitioning care from one facility to another between diagnosis and treatment similarly improved OS (HR = 0.96 95% CI = 0.93-0.98).

**Conclusion:** One in 4 patients with HNSCC experienced treatment delays in 2011. Patients with TTI >46 to 52 days have increased risk of death that is most consistently detrimental beyond 60 days. The deleterious effect of prolonged TTI currently impacts survival in the United States.