**Treatment Selection and Survival Outcomes in Early-Stage Peripheral T-Cell Lymphomas: Does Anaplastic Lymphoma Kinase Mutation Impact the Benefit of Consolidative Radiation Therapy?**

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**Purpose/Objective(s):** With the role of consolidative radiotherapy (RT) controversial in the more common aggressive B-cell lymphomas such as diffuse large B-cell lymphoma, the role of RT is even less substantiated in uncommon peripheral T-Cell lymphomas. Anaplastic lymphoma kinase (ALK) mutation sub-categorizes peripheral T-cell lymphomas, with ALK+ having a distinctly favorable prognosis. We hypothesize that consolidative RT improves overall survival in peripheral T-cell lymphomas irrespective of ALK status.

**Materials/Methods:** We identified 3,670 stage I-II peripheral T-cell lymphoma patients treated with multi-agent chemotherapy alone or multi-agent chemotherapy plus RT between 1998 and 2012 from the National Cancer Database. Primary cutaneous anaplastic large cell lymphoma was excluded. Binary logistic regression analyses were used to identify factors predictive of treatment selection. Survival was estimated using the Kaplan-Meier method. Multivariable Cox regression analyses were performed to account for potential confounding imbalances, including propensity-score and 6-month conditional landmark.

**Results:** Of the included 3,670 patients, 60% were ALK+, 51% were stage II, 28% had extra-nodal disease, and 44% were older than 60 years. Use of combined modality decreased from 44% in 1998 to 24% in 2012 for all patients, 31% to 24% for ALK-, and 47% to 24% for ALK+, P < 0.01. The median RT dose was 36 Gy [interquartile range (IQR): 30.6-41.4] for all patients, ALK-, and ALK+; IMRT was used in 7%. Chemotherapy was initiated at a median of 27 days (IQR: 14-44); and RT was initiated at a median of 140 days (IQR: 105-176) from diagnosis. Treatment selection was significantly influenced by income, age, stage, and B-symptoms; with no difference by ALK status. Median follow-up was 38 months (IQR: 32-78). Estimated 5-year overall survival was 57% (95% CI 55-59%) for all patients, 52% (95% CI 49-54%) for multi-agent chemotherapy alone, and 66% (95% CI 63-69%) for combined modality therapy, P < 0.01. 5-year overall survival was 44% (95% CI 41-47%) for ALK- versus 65% (95% CI 63-67%) for ALK+, P < 0.01; irrespective of ALK status RT on univariate was associated with improved overall survival 38%(95% CI = 35-42%) versus 56% (95% CI = 51-61%) for ALK- and 61% (95% CI = 58-64%) versus 72% (95% CI 69- 75%) for ALK+, P < 0.01. After adjusting for immortal-time and indication bias, combined modality was associated with better overall survival than multi-agent chemotherapy alone for ALK- patients (HR = 0.69, 95% CI = 0.52-0.92, P = 0.01); no significant difference was noted for ALK+ (HR = 1.01, 95% CI = 0.74-1.38, P = 0.97) or all patients (HR = 0.83, 95% CI = 0.67-1.02, P = 0.08). Sensitivity analyses excluding time-biased and incomplete covariates confirmed the improved overall survival associated with RT in ALK- patients.

**Conclusion:** Combined modality therapy is associated with improved overall survival for ALK- peripheral T-cell lymphomas; ALK+ subgroups have a more favorable prognosis which may decrease the benefit of consolidative RT.