**Early-Stage, Low-Grade Follicular Lymphoma: How Much Evidence Do We Need to Adopt Radiation Therapy as the Primary Treatment?**

*J. Vargo, B.S. Gill, G. Balasubramani, and S. Beriwal*

**Purpose/Objective(s):** Despite international practice guidelines endorsing radiation therapy as the preferred initial management, treatment approaches vary for early-stage, low-grade follicular lymphoma. To provide additional data on survival outcomes for the various management approaches in the context of modern therapy, we engaged the population-based data in the National Cancer Data Base (NCDB). We hypothesized that the utilization of radiation therapy was decreasing, and that decreasing radiation therapy utilization in favor of alternative management strategies may lead to a survival decrement.

**Materials/Methods:** A NCDB retrospective cohort study of 35,961 patients with nodal and extra-nodal stage IeII, grade IeII follicular lymphoma diagnosed from 1998-2012. Univariate and multivariate analyses were performed to identify sociodemographic, treatment, and tumor characteristics predictive of overall survival and treatment utilization. Propensity-adjusted Cox proportional hazards ratios for survival in treatment with follicular lymphoma were used.

**Results:** Of the included 35,961 follicular lymphoma patients, 63% had stage I disease, 79% were without extra-nodal disease, and 61% were older than 60 years. Radiation therapy utilization decreased from 37% in 1999 to 24% in 2012 (P < .0001) with corresponding significant increases in observation (34% in 1998 to 44% in 2012, P < .0001) and single-agent chemotherapy (5.4% in 1999 to 11.7% in 2006, P = .01). Decreases in radiation therapy utilization was associated with increasing age, female gender, African American race, increasing comorbidity score, treatment at an academic/research program, stage II disease, presence of B-symptoms, absence of extranodal disease, receipt of

chemotherapy, and increasing year of diagnosis. The median follow-up was 58 months (interquartile range: 28-93). Patients receiving radiation therapy had a 5-year and 10-year overall survival of 86% and 68% versus 74% and 54% for those not receiving radiation therapy (P < .0001). Conversely, utilization of chemotherapy had no significant impact on survival, P = .43. Observed patients had a 5-year and 10-year overall survival of 74% and 52% versus 80% and 62% for patients receiving any initial therapy, P < .0001. On propensity-adjusted Cox multivariate analysis, radiation therapy remained independently associated with improved overall survival (hazard of death 0.54, 95% CI = 0.47-0.63, P < .0001).

**Conclusion:** Radiation therapy improves overall survival for early-stage follicular lymphoma. Despite lower radiation therapy dose, smaller treatment fields, and now two large population-based analyses showing radiation therapy improves overall survival, radiation therapy utilization has continued to decrease to a nadir of 24% in 2012. With a lack of randomized evidence and these striking findings, physicians should strongly reconsider excluding radiation therapy outside of clinical trials.