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Treatment Burden Among Patients Aged 75 Years or Older with Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma (CLL/SLL)

Authors: Daniel A. Ermann[1], Aseel Alsouqi,[2] Xiaoliang Wang,[3] Dong Yuan,[3] Rhys Williams,[3] Erlene K. Seymour,[3] Derrick van Beuge,[3] Joanna M. Rhodes[4]

Affiliations: [1]Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT, USA; [2]The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [3]BeOne Medicines, Ltd, San Carlos, CA, USA; [4]Rutgers Cancer Institute, New Brunswick, NJ, USA

CONTEXT: Novel therapies have improved survival outcomes in patients with CLL; however, evidence in older patients is limited due to low trial enrollment.

OBJECTIVE: Describe treatment burden in patients aged ≥75 years at diagnosis who received first-line CLL therapy between Jan 2011-Oct 2025.

METHODS: This retrospective, observational study used the US Flatiron Health database. Patients were followed from first line until the earliest of next treatment/second-line start, end of follow-up, death, or study end. Primary outcome was probability of starting next treatment using the cumulative incidence function, including death as a competing risk, in overall patients, by age group, del(17p)/*TP53* status and IGHV status. Secondary outcomes included most common first-line treatment by time period and age group, and Richter transformation frequency.

RESULTS: In 3234 patients, median age at diagnosis was 79 years (75-79, n=1901 [59%]; 80-84, n=1215 [38%]; ≥85, n=118 [4%]); 60% were male; 73% were non-Hispanic White; 27% and 33% had ECOG performance status of 0 and 1, respectively; 13% had del(17p)/*TP53* mutation, and 14% had unmutated IGHV. Median time from diagnosis to first line was 10.4 months (IQR, 1.7-29.5). Median follow-up was 24.7 months (IQR, 8.9-48.1) with decreasing follow-up with increasing age (75-79 years, 35.8 months; 80-84 years, 16.2 months; ≥85 years, 1.7 months). Second-line therapy frequency increased over time (6 months, 12.4% [95% CI, 11.3-13.6]; 24 months, 28.5% [26.8-30.1]; 48 months, 37.9% [36.1-39.8]; 96 months, 46.5% [44.2-48.6]) and did not plateau. Second-line therapy was more frequent in patients aged 75-79 years (53.3% [95% CI, 50.3-56.1]) vs ≥80 years (34.4% [31.4-37.4]), and among patients not tested for del(17p)/*TP53* during follow-up (48.4%) vs those testing positive (42.0%) or negative (46.8%). Results were similar by IGHV status until ≥60 months. Most common first-line treatment since 2014 overall and across age groups was Bruton tyrosine kinase inhibitor monotherapy. Richter transformation occurred in 55 patients (1.7%); 52.3% died during follow-up (median age, 85 years).

CONCLUSIONS: Treatment burden in patients aged ≥75 years at CLL diagnosis increases over time, with increasing likelihood of receiving second-line therapy with longer follow-up, emphasizing the importance of longitudinal treatment sequencing when choosing front-line treatment for older patients.