Treatment burden among patients (pts) aged 75 or older with chronic lymphocytic leukemia and small lymphocytic lymphoma (CLL/SLL)

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Background: CLL is the most common leukemia among adults in the US, with median age at diagnosis of 70 y and median age at death of 82 y. Novel therapies have improved survival outcomes among pts with CLL; however, evidence in older pts is limited due to low clinical trial enrollment.

Aims: This study describes treatment burden, defined as likelihood of receiving next line of therapy, among pts aged ≥75 y overall and by subgroups.

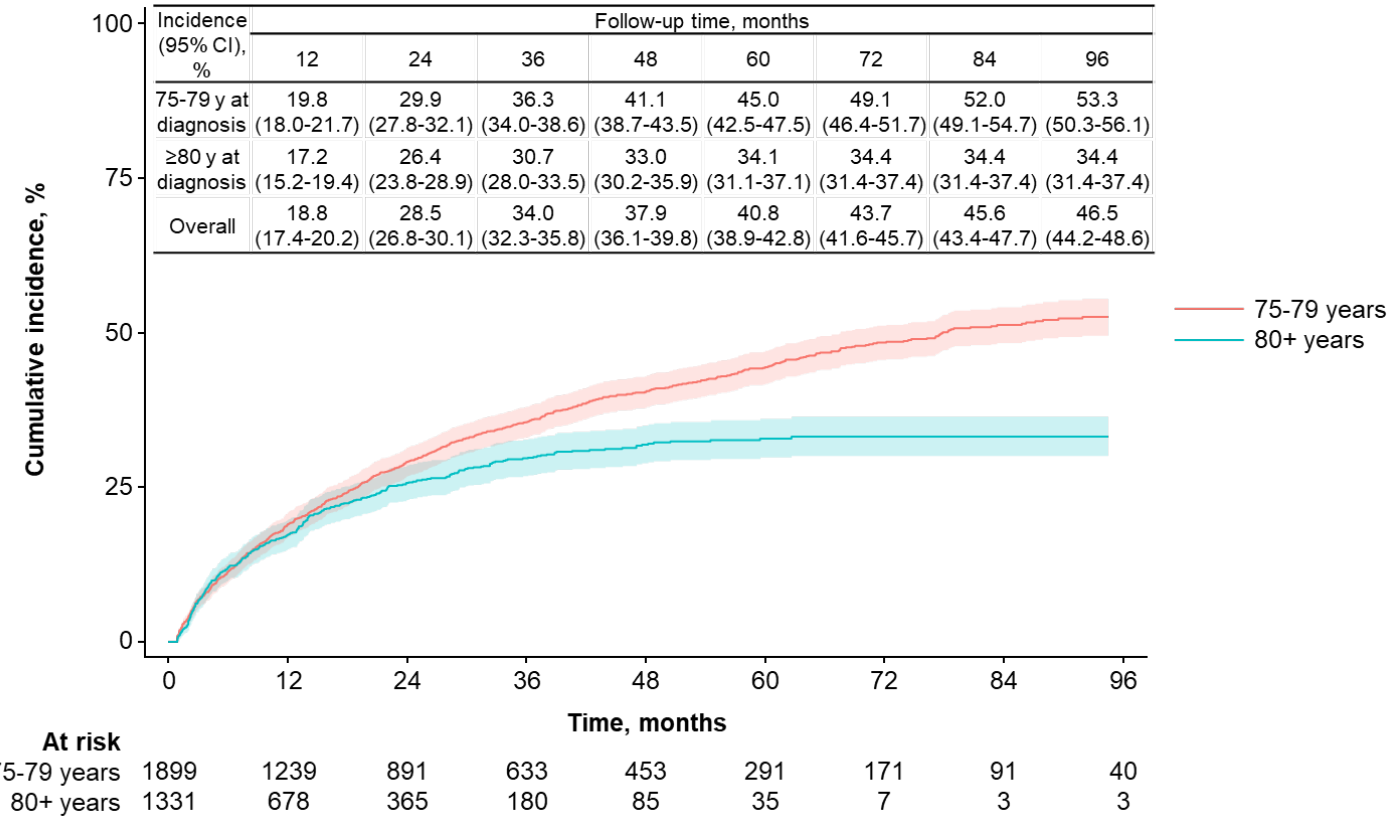
Methods: This retrospective, observational cohort study utilized the US nationwide Flatiron Health electronic health record–derived, deidentified database. Pts were included if they were aged ≥75 y at diagnosis and had received first-line (1L) therapy for CLL between Jan 2011-Oct 2025. Primary outcome was the cumulative probability of starting next treatment, including death as a competing risk. Pts were followed from 1L until the earliest of next treatment/second-line (2L) start, end of follow-up, death, or study end. Cumulative incidence function was used to summarize overall pts, age groups (75-79, ≥80 y), del(17p)/*TP53* status (positive, negative, not tested) and immunoglobulin heavy chain variable region (IGHV) status (unmutated, mutated, not tested). Secondary outcomes included a descriptive summary of the most common 1L treatment by time period and age group, and frequencies of Richter transformation during follow-up.

Results: In total, 3234 pts were included, with a median age of 79 y at diagnosis; 60% were male, and 73% were non-Hispanic White. Overall, 27% and 33% had baseline Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 and 1, respectively; 13% had del(17p)/*TP53* mutation, and 14% had unmutated IGHV. Median time from diagnosis to 1L treatment was 10.4 mo (IQR, 1.7-29.5). Among all pts, 1901 (59%) were aged 75-79 y at diagnosis, 1215 (38%) were 80-84 y, and 118 (4%) were ≥85 y. Overall median follow-up was 24.7 mo (IQR, 8.9-48.1) with decreasing follow-up observed across increasing age strata (median 35.8 mo in 75-79 y, 16.2 mo in 80-84 y, and 1.7 mo in ≥85 y). Using competing-risk analysis, the probability of receiving 2L increased through the follow-up period: 12.4% (95% CI, 11.3-13.6) at 6 mo, 28.5% (26.8-30.1) at 24 mo, 37.9% (36.1-39.8) at 48 mo, and 46.5% (44.2-48.6) at 96 mo, and did not plateau. The likelihood of receiving 2L was higher in pts aged 75-79 y with 53.3% (95% CI, 50.3-56.1) of pts receiving 2L by the end of follow-up compared with

34.4% (95% CI, 31.4-37.4) in pts aged ≥80 y (Figure). The likelihood of receiving 2L was also consistently higher among those not tested for del(17p)/*TP53* during follow-up (positive subgroup, 42.0%; negative subgroup, 46.8%; not tested at 96 mo, 48.4%). The results were similar by IGHV mutation status until 60 months or later. For secondary outcomes, Bruton tyrosine kinase inhibitor monotherapy was the most common 1L treatment since 2014 overall and across age groups. In addition, 55 pts (1.7%) had Richter transformation and 52.3% of patients died during follow-up (median age at death, 85 y).

Summary/Conclusion: The treatment burden for pts aged ≥75 y at CLL diagnosis continues to increase throughout a pt's journey, with more than half receiving next treatment among pts aged 75-79 (majority of pts in this elderly cohort) and over one-third among pts aged ≥80 y. The data also suggest it would continue to increase with longer follow-up. These results emphasize the need to consider longitudinal treatment sequencing when choosing front-line treatment for most older pts.

Figure. Cumulative Incidence of Next Treatment by Age Groups



Incidence (95% CI), %	Follow-up time, months							
	12	24	36	48	60	72	84	96
75-79 y at diagnosis	19.8 (18.0-21.7)	29.9 (27.8-32.1)	36.3 (34.0-38.6)	41.1 (38.7-43.5)	45.0 (42.5-47.5)	49.1 (46.4-51.7)	52.0 (49.1-54.7)	53.3 (50.3-56.1)
≥80 y at diagnosis	17.2 (15.2-19.4)	26.4 (23.8-28.9)	30.7 (28.0-33.5)	33.0 (30.2-35.9)	34.1 (31.1-37.1)	34.4 (31.4-37.4)	34.4 (31.4-37.4)	34.4 (31.4-37.4)
Overall	18.8 (17.4-20.2)	28.5 (26.8-30.1)	34.0 (32.3-35.8)	37.9 (36.1-39.8)	40.8 (38.9-42.8)	43.7 (41.6-45.7)	45.6 (43.4-47.7)	46.5 (44.2-48.6)

At risk									
75-79 years	1899	1239	891	633	453	291	171	91	40
80+ years	1331	678	365	180	85	35	7	3	3