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PB1877 ADJUSTING SURVIVAL DATA FOR TREATMENT CROSSOVER IN THE ELEVATE-TN TRIAL BY USING A HISTORICAL COHORT OF PATIENTS TREATED WITH CHEMOIMMUNOTHERAPY IN FRONT-LINE CHRONIC LYMPHOCYTIC LEUKEMIA

Topic: 06. Chronic lymphocytic leukemia and related disorders - Clinical

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Background: Acalabrutinib (A) is a next-generation Bruton tyrosine kinase inhibitor (BTKi) approved for chronic lymphocytic leukemia (CLL) treatment. ELEVATE-TN trial interim data (~47 months median follow-up [FU]) did not show survival benefit for A±obinutuzumab (O) versus chlorambucil+obinutuzumab (C+O) despite significantly superior progression-free survival (PFS). One explanation is C+O-to-A patient crossover (39%), which may have provided added overall survival (OS) benefit to the C+O arm.

Aims: We evaluated OS by adjusting for crossover using a historical C+O cohort.

Methods: The CLL11 trial demonstrated superior PFS and OS for C+O versus C and C+rituximab in first-line CLL prior to BTKi availability. Therefore, OS data for BTKi-naive C+O patients were digitized and compared with A±O from ELEVATE-TN. Individual patient datasets were used to plot Kaplan-Meier (KM) curves and calculate hazard ratios (HR) using Cox regression in R software. To validate our hypothesis (impact of crossovers on relative survival benefit), we compared 28-month FU data from ELEVATE-TN, where we observed lower OS HRs (non-significant) to CLL-11 data until that time period. The CLL11 and ELEVATE-TN trials enrolled patients with similar baseline characteristics; however, this analysis did not account for within-trial heterogeneity.

Results: There was a statistically significant reduction in risk of death with all 3 ELEVATE-TN treatments (47-month FU data) versus CLL-11 C+O: A+O versus $C+O_{CLL11}$ (HR=0.23 [95% CI=0.12-0.42, p<0.001]); A versus $C+O_{CLL11}$ (HR=0.43 [95% CI=0.27-0.70, p<0.001]); C+O versus $C+O_{CLL11}$ (HR=0.44 [95% CI=0.27-0.71, p<0.001]). In the additional analysis with 28-month FU data, comparing ELEVATE-TN arms with C+O from CLL-11, KM curves for C+O overlapped (HR=0.79 [95% CI=0.42-1.47], p>0.05), indicating no difference. However, HRs for A+O versus $C+O_{CLL11}$ (HR=0.39 [95% CI=0.18-0.84], p=0.02) and for A versus $C+O_{CLL11}$ (HR=0.48 [95% CI=0.24-0.99], p<0.05) were statistically significant.

Summary/Conclusion: The non-statistically significant OS for A±O versus C+O was likely due to treatment crossover. Conducting a treatment-switching analyses was challenging due to immature OS data; however, this analysis supports the hypothesis that crossover to A bolstered ELEVATE-TN C+O OS.