

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 LYMPHOXYTIC LEUKEMIA

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

Priyanka Gaitonde¹, Bengt Liljas¹, Bob Shaw², Paulo Miranda¹

¹ AstraZeneca, Gaithersburg, United States; ² AstraZeneca, Cambridge, United Kingdom

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.

Copyright Information: (Online) ISSN: 2572-9241

© 2022 the Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the European Hematology Association. This is an open access Abstract Book distributed under the Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) which allows third parties to download the articles and share them with others as long as they credit the author and the Abstract Book, but they cannot change the content in any way or use them commercially.

Abstract Book Citations: Authors, Title, HemaSphere, 2022;6:(S3):pages. The individual abstract DOIs can be found at <https://journals.lww.com/hemasphere/pages/default.aspx>.

Disclaimer: Articles published in the journal HemaSphere exclusively reflect the opinions of the authors. The authors are responsible for all content in their abstracts including accuracy of the facts, statements, citing resources, etc.