Efficacy of Zanubrutinib Versus Acalabrutinib in the Treatment of Relapsed or Refractory Chronic Lymphocytic Leukemia (R/C LL): A Matching-Adjusted Indirect Comparison (MAIC)

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Abstract

Zanubrutinib, a second-generation Bruton’s tyrosine kinase inhibitor (BTKi), is approved by the U.S. Food and Drug Administration (FDA) for the treatment of relapsed or refractory (R/R) chronic lymphocytic leukemia (CLL). This retrospective MAIC compared the efficacy of zanubrutinib in the ALPINE trial of patients with advanced CLL with del(17p) or del(11q), with Acalabrutinib in the ASCEND phase III trial of R/R CLL. The primary endpoint was progression-free survival (PFS) over 42 months. Results were robust across multiple sensitivity analyses.

METHODS

Population

The ALPINE study included 327 patients with R/R CLL with del(17p) or del(11q). The ASCEND study included 243 patients with R/R CLL. The MAIC was based on individual patient data (IPD) from the ALPINE and ASCEND trials, and unadjusted and adjusted analyses were performed using matching, reweighting, and adjusting for variables. The MAGT and MAAT were reconstructed from the digitized Kaplan-Meier curves, reported in the ALPINE and ASCEND trials, respectively.

RESULTS

The adjusted analysis showed improved PFS vs rituximab in the ALPINE trial. The adjusted hazard ratio (HR) was 0.50 (95% CI, 0.25-0.92) for zanubrutinib vs acalabrutinib. Two weighted logistic regression models were used to estimate the impact of COVID-19 on treatment efficacy. The sensitivity analysis indicated that the impact of COVID-19 was not statistically significant.

CONCLUSIONS

Zanubrutinib is a promising treatment option for patients with R/R CLL with del(17p) or del(11q). The adjusted analysis showed improved PFS vs rituximab in the ALPINE trial. The weighted logistic regression models showed that the impact of COVID-19 was not statistically significant. The MAIC findings are robust across multiple sensitivity analyses.

Keywords: Chronic lymphocytic leukemia, Zanubrutinib, Acalabrutinib, Progression-free survival, Matching-Adjusted Indirect Comparison, COVID-19.