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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BACKGROUND AND OBJECTIVE

Zanubrutinib is a second-generation, covalently linked, irreversible inhibitor of Bruton’s tyrosine kinase (BTK) with a target engagement profile across wild-type and select BTK-mutated (D422E, L265P, and S476C) chronic lymphocytic leukemia (CLL) patients. Acalabrutinib is a third-generation, covalently linked, irreversible BTK inhibitor that is approved in the United States and the European Union for the treatment of patients with relapsed or refractory (R/R) CLL.

METHODS

In this indirect comparison, we compared the efficacy of zanubrutinib with acalabrutinib in a post hoc analysis of the ALPINE (N=327) and ASCEND (N=254) trials. The study was sponsored by Regeneron, Sanofi, and Genentech, and the MAIC methodology was followed. The ALPINE and ASCEND trials enrolled patients with R/R CLL, and both studies included a control arm of patients receiving bendamustine.

Efficacy outcomes compared include complete response (CR), partial response (PR), and overall survival (OS) as the primary end points. The tests were performed using the WinNonlin software (v22.2). The data were matched using propensity score methods and the ESS=184.8. The MAIC methodology was used to compare the efficacy and safety of zanubrutinib versus acalabrutinib as an indirect comparison.

RESULTS

Table 1 shows the baseline characteristics of the zanubrutinib and acalabrutinib populations. The baseline characteristics between the two groups were well balanced. The Kaplan-Meier curves for PFS and OS are presented in Figure 1A and 1B, respectively. The ESS for PFS and OS was 184.8.

CONCLUSIONS

This indirect comparison demonstrated a significant HR for PFS and OS in favor of zanubrutinib compared with acalabrutinib. The study is consistent with the previous findings of the ALPINE and ASCEND trials.

LIMITATIONS

The study is based on the data from two randomized controlled trials. The findings should be interpreted with caution, and additional studies are needed to confirm the results.

REFERENCES