Rate of Atrial Fibrillation in Patients With B-Cell Malignancies Who Undergo Treatment With Zanubrutinib

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Introduction: Treatment of B-cell malignancies has been improved by effective inhibitors of B-cell receptor signaling, such as the first-generation Bruton tyrosine kinase inhibitor (BTKi), ibrutinib. Although ibrutinib has demonstrated efficacy, it has been associated with an increased risk for cardiovascular toxicities, such as atrial fibrillation (Afib).[1] Zanubrutinib is an irreversible, potent, next-generation BTKi designed to maximize BTK occupancy and minimize off-target inhibition.[2] Zanubrutinib has been generally well tolerated in clinical trials. This abstract reports the occurrence of Afib/flutter in ALPINE (NCT03734016), ASPEN (NCT03053440), and a larger pooled analysis of zanubrutinib trials.

Methods: This pooled analysis included patients with B-cell malignancies who were enrolled in 10 clinical studies of zanubrutinib, including ALPINE and ASPEN. The ALPINE study and ASPEN Cohort 1 comparing zanubrutinib with ibrutinib in patients with relapsed/refractory (R/R) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) or Waldenström macroglobulinemia, respectively, were also analyzed separately. Patients were evaluated through a blinded study for exposure-adjusted incidence rate (EAIR) of Afib, which was the pre-specified primary endpoint. To compare EAIR of Afib between zanubrutinib and ibrutinib, the difference of EAIR and the *P* value of the difference based on asymptotic normal distribution were also calculated.

Results: In the pooled analyses of 10 trials, 1550 patients received zanubrutinib as monotherapy, 938 had CLL/SLL (525 R/R CLL/SLL), and the median age was 67 years, with 61% of patients aged ≥65 years. Most patients were men (66%) and white (67%), with European Cooperative Oncology Group performance status of 0 or 1 (44.5% and 49.4%, respectively). Specifically, among patients enrolled in ALPINE, 5.8% (19/327; zanubrutinib) vs 5.8% (19/325; ibrutinib) had a history of Afib/flutter, whereas 1.9% vs 8.0% experienced a new Afib/flutter event. Among patients in ASPEN (Cohort 1), 10.8% (11/102; zanubrutinib) vs 8.1% (8/99; ibrutinib) had a history of Afib/flutter and 5.9% vs 22.4% experienced a new Afib/flutter event, respectively. The EAIR of Afib/flutter per 100 person-month was lower in both studies for zanubrutinib vs ibrutinib: 1) in ALPINE the EAIR was 0.16 for zanubrutinib and 0.79 for ibrutinib (*P* = 0.0003); 2) in ASPEN the EAIR was 0.19 for zanubrutinib and 0.86 for ibrutinib (*P* = 0.001). Afib rates in the pooled analyses were comparable to those observed with zanubrutinib in ALPINE and ASPEN.

Conclusions: Data from this analysis support the use of zanubrutinib as a treatment option for patients with B-cell malignancies, demonstrating reduced risk of Afib/flutter compared with ibrutinib.

References:

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