Zanubrutinib vs ibrutinib in relapsed/refractory chronic lymphocytic leukemia and small lymphocytic lymphoma (R/R CLL/SLL): impact on health-related quality of life (HRQOL)

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ABSTRACT

Objectives: In the ALPINE study (NCT03734016), zanubrutinib, a potent and highly selective next-generation Bruton tyrosine kinase (BTK) inhibitor, was compared head-to-head with ibrutinib as treatment for patients with R/R CLL/SLL; zanubrutinib demonstrated superiority to ibrutinib in both progression-free survival and overall response rate and had a more favorable safety profile. In this analysis, we assessed HRQOL in patients treated with zanubrutinib and ibrutinib in the ALPINE study.

Methods: HRQOL was measured by EORTC QLQ-C30 and EQ-5D-5L at baseline, at cycle 1, and then every third 28-day cycle until end of treatment. Key patient-reported outcome (PRO) endpoints included global health status (GHS), physical and role functions, fatigue, pain, diarrhea, and nausea/vomiting. Descriptive analysis was conducted for all scales; a mixed models for repeated measures analysis using key PRO endpoints at the key clinical cycles of cycles 7 (6 months) and 13 (12 months) was performed to determine the least-squares (LS) mean change within treatment arms and LS mean change difference between treatment arms. Adjusted completion rates were calculated as the number of patients who completed the questionnaires at each cycle divided by the number still on treatment. Clinically meaningful was defined as a ≥5% mean change difference from baseline. For fatigue, nausea/vomiting, pain, and diarrhea, negative values indicate improvement.

Results: At data cutoff (August 8, 2022), a total of 652 patients were randomized to receive zanubrutinib (n=327) or ibrutinib (n=325); baseline characteristics were generally similar between arms, although the zanubrutinib arm had fewer male patients than the ibrutinib arm (65.1% vs 71.4%). At baseline, GHS, functional, and symptom scale scores were similar between arms. Treatment discontinuation due to adverse events was higher with ibrutinib (22.2%) than with zanubrutinib (15.4%), but adjusted PRO completion rates were high at cycles 7 and 13, respectively, in both the zanubrutinib arm (89.6% and 94.3%) and ibrutinib arm (87.7% and 92.3%). By cycle 7, GHS scores (LS mean change from baseline [95% CI]) improved in both zanubrutinib (8.18 [6.25-10.12]) and ibrutinib (5.18 [3.20-7.17]) treatment arms, with a significant difference between arms (LS mean change difference, 3.0 [95% CI, 0.23-5.77]; nominal *P*=.0338). By cycle 13, while both zanubrutinib (7.28 [5.41-9.15]) and ibrutinib (5.93 [3.97-7.89]) arms continued to showed improvement in GHS scores from baseline, the LS mean change difference between arms was no longer significant (1.34 [95% CI, −1.37 to 4.06]; nominal *P*=.3304). At cycles 7 and 13, respectively, patients in the zanubrutinib arm experienced clinically meaningful improvements in LS mean change (95% CI) for physical (6.55 [4.96-8.15] and 5.46 [3.87-7.04]) and role functioning (6.95

[4.85-9.06] and 6.81 [4.61-9.02]), pain (−5.06 [−7.21 to −2.91] and −5.18 [−7.38 to −2.97]), and fatigue (−12.54 [−14.47 to −10.60] and −11.13 [−13.19 to −9.08]), but the LS mean change difference between the arms was not significant (physical: 1.82 and 1.15; role: 0.63 and 1.80; pain: −1.43 and −2.43; fatigue: −1.91 and −0.35). Although patients in the zanubrutinib arm reported lower diarrhea scores (LS mean change [95% CI] of −2.11 [−3.80 to −0.42] at cycle 7 and −3.23 [−4.79 to −1.66] at cycle 13), the LS mean change difference (95% CI) between treatments was not significant: −1.59 (−4.01 to 0.84) at cycle 7 and −1.85 (−4.12 to 0.43) at cycle 13. Nausea/vomiting scores were maintained in both arms (zanubrutinib vs ibrutinib: −1.21 vs −0.92 at cycle 7 and −0.92 vs −0.40 at cycle 13), with no measurable difference between the arms at cycles 7 (−0.29) and 13 (−0.51). Visual analog scale scores showed greater improvement from baseline at both cycle 7 (7.92 vs 3.44) and cycle 13 (7.75 vs 3.92) with zanubrutinib vs ibrutinib treatment, respectively.

Conclusions: In ALPINE, patients with R/R CLL/SLL treated with zanubrutinib demonstrated improvement over those treated with ibrutinib on the QLQ-30 GHS/QOL scale at cycle 7 (6 months). Other endpoints continued to improve, suggesting that treatment with zanubrutinib positively influenced HRQOL and that HRQOL improved over time. As expected, given the generally good HRQOL at baseline in both arms, the differences between the arms were small and not significant.