**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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**Aim:** Assess HRQOL in patients treated with zanubrutinib vs ibrutinib.

**Method:** In the ALPINE study (NCT03734016), patients were randomized to zanubrutinib (n=327) or ibrutinib (n=325), and patient-reported outcome (PRO) endpoints (global health status [GHS], physical and role functions, fatigue, pain, diarrhea, and nausea/vomiting) were measured by EORTC QLQ-C30 and EQ-5D-5L at baseline, cycle 1, and every third 28-day cycle until end of treatment. Descriptive analyses using a mixed model for repeated measures of key PRO endpoints at cycle 7 (6 months) and cycle 13 (12 months) are presented.

**Results:** Patients had similar baseline characteristics and HRQOL at baseline. 15.4% of patients discontinued zanubrutinib due to adverse events vs 22.2% for ibrutinib. Adjusted PRO completion rates (the number of patients who completed the questionnaire divided by the number still on treatment) at cycles 7 and 13 were high with zanubrutinib (89.6% and 94.3%) and ibrutinib (87.7% and 92.3%). Zanubrutinib improved GHS scores vs ibrutinib at cycle 7 (least-squares mean change difference, 3.0; 95% CI, 0.23-5.77; nominal *P*=.0338) but not at cycle 13. Lower diarrhea scores and clinically meaningful improvements (≥5% mean change difference from baseline) in physical and role functioning, pain, and fatigue at cycles 7 and 13 were seen in the zanubrutinib arm (**Table**), but the difference between arms was not significant. Nausea/vomiting scores were maintained in both arms, with no measurable difference.

**Conclusion:** In ALPINE, patients with R/R CLL/SLL receiving zanubrutinib vs ibrutinib demonstrated improvement in GHS at cycle 7 (6 months). Improvement in other endpoints over time suggests that treatment with zanubrutinib positively affected HRQOL; however, given the generally good HRQOL at baseline in both arms, the differences between arms were small and not significant.

**Table. Least-Squares Mean Change (95% CI) From Baseline Within Treatment Arms**

| | Cycle 7 (6 months) | | Cycle 13 (12 months) | |
|---|---|---|---|---|
| | **Zanubrutinib** | **Ibrutinib** | **Zanubrutinib** | **Ibrutinib** |
| GHS | 8.18 (6.25-10.12) | 5.18 (3.20-7.17) | 7.28 (5.41-9.15) | 5.93 (3.97-7.89) |
| Physical functioning | 6.55 (4.96-8.15) | 4.73 (3.08-6.38) | 5.46 (3.87-7.04) | 4.31 (2.65-5.97) |
| Role functioning | 6.95 (4.85-9.06) | 6.32 (4.14-8.50) | 6.81 (4.61-9.02) | 5.01 (2.69-7.33) |
| Fatigue[a] | −12.54 (−14.47 to −10.60) | −10.63 (−12.63 to −8.62) | −11.13 (−13.19 to −9.08) | −10.78 (−12.93 to −8.63) |
| Nausea/vomiting[a] | −1.21 (−2.03 to −0.38) | −0.92 (−1.77 to −0.07) | −0.92 (−1.94 to 0.10) | −0.40 (−1.47 to 0.66) |
| Pain[a] | −5.06 (−7.21 to −2.91) | −3.63 (−5.85 to −1.42) | −5.18 (−7.38 to −2.97) | −2.75 (−5.06 to −0.44) |
| Diarrhea[a] | −2.11 (−3.80 to −0.42) | −0.52 (−2.27 to 1.22) | −3.23 (−4.79 to −1.66) | −1.38 (−3.03 to 0.27) |

Data cutoff: August 8, 2022; GHS, global health status; [a] Negative values indicate improvement.