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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Introduction: Zanubrutinib (ZANU) is a potent, highly selective, next-generation Bruton tyrosine kinase (BTK) inhibitor designed to maximize BTK occupancy and minimize off-target effects. In the ALPINE study (NCT03734016), ZANU demonstrated superior progression-free survival and overall response rate compared with ibrutinib (IBR) as treatment for R/R CLL/SLL and had a more favorable safety profile.

Aim: To assess HRQOL in patients (pts) treated with ZANU and IBR.

Material or Patients and Method: EORTC QLQ-C30 and EQ-5D-5L were used to measure patient-reported outcome (PRO) endpoints (global health status [GHS], physical and role functions, fatigue, pain, diarrhea, and nausea/vomiting) at baseline (BL), cycle (C) 1, and every third 28-day cycle until end of treatment. Descriptive analysis, using a mixed, repeated- measures model of key PRO endpoints at C7 (6 months) and C13 (12 months), was performed.

Results: Pts randomized to receive ZANU (n=327) or IBR (n=325) had similar baseline characteristics and similar GHS, functional, and symptom scale scores at BL. Adjusted PRO completion rates (the number of pts who completed the questionnaires at each cycle divided by those still on treatment) were high at C7 and C13 in both arms—89.6% and 94.3% (ZANU) and 87.7% and 92.3% (IBR), respectively—despite more pts discontinuing treatment due to adverse events with IBR vs ZANU (22.2% vs 15.4%). ZANU improved GHS scores compared with IBR at C7 (LS mean change difference, 3.0; 95% CI, 0.23-5.77; nominal *P*=0.0338) but not C13 (1.34; 95% CI, −1.37 to 4.06; nominal *P*=0.3304) (**Table**). Clinically meaningful improvements (mean change difference from BL of ≥5%) in physical and role functioning, pain, and fatigue at C7 and C13 were observed in the ZANU arm, as well as lower diarrhea scores, but the difference between arms was not significant. Nausea/vomiting scores were maintained in both arms, with no measurable difference. Visual analog scale scores showed greater improvement from BL at C7 (7.92 vs 3.44) and C13 (7.75 vs 3.92) with ZANU vs IBR, respectively.

Conclusions: In ALPINE, ZANU demonstrated improvement in GHS compared with IBR at C7 (6 months) in pts with R/R CLL/SLL. Improvement in other endpoints over time suggests that treatment with ZANU positively affected HRQOL; however, given the generally good HRQOL at BL in both arms, the differences between the arms were small and not significant.

Table. LS Mean Differences (95% CI) From Baseline Within and Between Treatment Arms

	Cycle 7 (6 months)			Cycle 13 (12 months)		
	Zanubrutinib (n=327)	**Ibrutinib (n=325)**		**Zanubrutinib (n=327)**	**Ibrutinib (n=325)**	
	Difference within the arm	Difference within the arm	**Difference between the arms**	Difference within the arm	Difference within the arm	**Difference between the arms**
GHS	8.18 (6.25 to 10.12)	5.18 (3.20 to 7.17)	3.00 (0.23 to 5.77)[a]	7.28 (5.41 to 9.15)	5.93 (3.97 to 7.89)	1.34 (−1.37 to 4.06)
Physical functioning	6.55 (4.96 to 8.15)	4.73 (3.08 to 6.38)	1.82 (−0.47 to 4.12)	5.46 (3.87 to 7.04)	4.31 (2.65 to 5.97)	1.15 (−1.15 to 3.44)
Role functioning	6.95 (4.85 to 9.06)	6.32 (4.14 to 8.50)	0.63 (−2.40 to 3.66)	6.81 (4.61 to 9.02)	5.01 (2.69 to 7.33)	1.80 (−1.40 to 5.00)
Fatigue[b]	−12.54 (−14.47 to −10.60)	−10.63 (−12.63 to −8.62)	−1.91 (−4.70 to 0.87)	−11.13 (−13.19 to −9.08)	−10.78 (−12.93 to −8.63)	−0.35 (−3.32 to 2.62)
Nausea/vomiting[b]	−1.21 (−2.03 to −0.38)	−0.92 (−1.77 to −0.07)	−0.29 (−1.48 to 0.89)	−0.92 (−1.94 to 0.10)	−0.40 (−1.47 to 0.66)	−0.51 (−1.99 to 0.96)
Pain[b]	−5.06 (−7.21 to −2.91)	−3.63 (−5.85 to −1.42)	−1.43 (−4.51 to 1.66)	−5.18 (−7.38 to −2.97)	−2.75 (−5.06 to −0.44)	−2.43 (−5.62 to 0.77)
Diarrhea[b]	−2.11 (−3.80 to −0.42)	−0.52 (−2.27 to 1.22)	−1.59 (−4.01 to 0.84)	−3.23 (−4.79 to −1.66)	−1.38 (−3.03 to 0.27)	−1.85 (−4.12 to 0.43)

Data cutoff: August 8, 2022; GHS, global health status;[a] Nominal $P<0.05$;[b] Negative values indicate improvement.