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

Authors: Barbara Eichhorst,[1] Nicole Lamanna,[2] Susan M. O'Brien,[3] Constantine S. Tam,[4] Lugui Qiu,[5] Keri Yang,[6] Ken Wu,[6] Tommi Salmi,[7] Gisoo Barnes,[6] and Jennifer R. Brown[8]

Affiliations: [1]Department of Internal Medicine, University of Cologne, Center for Integrated Oncology Aachen, Bonn, Cologne, Duesseldorf, Cologne, Germany; [2]Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY, USA; [3]Chao Family Comprehensive Cancer Center, University of California, Irvine, CA, USA; [4]The Alfred Hospital, Melbourne, Victoria, Australia; Monash University, Melbourne, Victoria, Australia; [5]National Clinical Medical Research Center for Blood Diseases and State Key Lab for Experimental Hematology, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China; [6]BeiGene USA, Inc., San Mateo, CA, USA; [7]BeiGene International, GmbH, Switzerland; [8]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA

Introduction: Zanubrutinib (zanu) is a potent and 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 superiority to ibrutinib (ibr) in both progression-free survival (PFS) and overall response rate and a more favorable safety profile in R/R CLL/SLL. The purpose of this analysis was to assess health-related quality of life (HRQOL) in patients (pts) treated with zanu and ibr. Results from the data cutoff related to recent PFS analysis (8 Aug 2022) are reported here.

Methods: HRQOL was measured by EORTC QLQ-C30 and EQ-5D-5L at baseline, cycle 1, and every 3rd 28-day cycle until end of treatment. Key pt-reported outcome (PRO) endpoints included global health status (GHS), physical and role functions, fatigue, pain, diarrhea, and nausea/vomiting. Descriptive analysis was conducted on all the scales; a mixed-model repeated-measure analysis using key PRO endpoints at the key clinical cycles of cycles 7 (6 months) and 13 (12 months) was performed. Adjusted completion rates were defined as the number of pts who completed the questionnaires at each cycle divided by number still on treatment. Clinically meaningful was defined as a ≥5% mean change difference from baseline.

Results: A total of 652 pts were randomized to receive zanu (n=327) or ibr (n=325); baseline characteristics were generally similar between arms, although the zanu arm had fewer males vs ibr arm (65.1% vs 71.4%). At baseline, GHS, functional, and symptom scales scores were similar between arms. Although more ibr-treated pts discontinued treatment due to adverse events vs zanu(22.2% vs 15.4%), adjusted PRO completion rates were high at cycles 7 and 13 in both the zanu (89.6% and 94.3%) and ibr arm (87.7% and 92.3%), respectively. By cycle 7, GHS scores were improved with zanu vs ibr and by cycle 13, the difference in GHS scores from baseline was no longer significant (Table). Pts in the zanu arm experienced clinically meaningful improvements in physical and role functioning as well as pain and fatigue at cycles 7 and 13, but the difference between arms was not significant. Although pts in the zanu arm reported lower diarrhea scores, the difference between treatments was not significant. Nausea/vomiting scores were maintained in both arms with no measurable difference. VAS scores showed greater improvement from baseline at both cycle 7 (7.92 vs 3.44) and cycle 13 (7.75 vs 3.92) of treatment with zanu vs ibr, respectively.

Conclusions: In ALPINE, pts with R/R CLL/SLL treated with zanu demonstrated improvement vs ibr in the QLQ-C30 GHS/QoL scale at cycle 7. Other endpoints continued to improve, suggesting treatment with

zanu positively affected and improved HRQOL over time. As expected, given the generally good HRQOL at baseline 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, 10.12)	5.18 (3.20, 7.17)	**3.00 (0.23, 5.77)***	7.28 (5.41, 9.15)	5.93 (3.97, 7.89)	1.34 (-1.37, 4.06)
Physical functioning	6.55 (4.96, 8.15)	4.73 (3.08, 6.38)	1.82 (-0.47, 4.12)	5.46 (3.87, 7.04)	4.31 (2.65, 5.97)	1.15 (-1.15, 3.44)
Role functioning	6.95 (4.85, 9.06)	6.32 (4.14, 8.50)	0.63 (-2.40, 3.66)	6.81 (4.61, 9.02)	5.01 (2.69, 7.33)	1.80 (-1.40, 5.00)
Fatigue[a]	-12.54 (-14.47, -10.60)	-10.63 (-12.63, -8.62)	-1.91 (-4.70, 0.87)	-11.13 (-13.19, -9.08)	-10.78 (-12.93, -8.63)	-0.35 (-3.32, 2.62)
Nausea/vomiting[a]	-1.21 (-2.03, -0.38)	-0.92 (-1.77, -0.07)	-0.29 (-1.48, 0.89)	-0.92 (-1.94, 0.10)	-0.40 (-1.47, 0.66)	-0.51 (-1.99, 0.96)
Pain[a]	-5.06 (-7.21, -2.91)	-3.63 (-5.85, -1.42)	-1.43 (-4.51, 1.66)	-5.18 (-7.38, -2.97)	-2.75 (-5.06, -0.44)	-2.43 (-5.62, 0.77)
Diarrhea[a]	-2.11 (-3.80, -0.42)	-0.52 (-2.27, 1.22)	-1.59 (-4.01, 0.84)	-3.23 (-4.79, -1.66)	-1.38 (-3.03, 0.27)	-1.85 (-4.12, 0.43)

Data cutoff: 08 August 2022.

*Nominal *P* value <0.05.

[a]Negative values indicate improvement.

ICML 2023