PATIENT-REPORTED OUTCOMES FROM A PHASE 3 RANDOMIZED STUDY OF ZANUBRUTINIB VERSUS BENDAMUSTINE PLUS RITUXIMAB (BR) IN PATIENTS WITH TREATMENT-NAÏVE (TN) CLL/SLL

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Background: Zanubrutinib is an oral, highly selective, next-generation Bruton tyrosine kinase (BTK) inhibitor. In cohort 1 of the phase 3 SEQUOIA trial (BGB-3111-304; NCT03336333), efficacy and safety of zanubrutinib and BR were compared in adult patients (pts) with TN chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) without del(17p).
Aims: Here, we report the health-related quality of life (HRQoL) outcomes from an interim analysis of the SEQUOIA trial.
Methods: Patient-reported outcomes (PROs) were secondary endpoints and assessed using the EORTC QLQ-C30 and EQ-5D-5L VAS. Patients completed these questionnaires at baseline, every 12 weeks for 96 weeks, and then every 24 weeks until disease progression, death, or withdrawal from study. The PRO endpoints included global health status (GHS), physical and role functions, and symptoms of fatigue, pain, diarrhea, and nausea/vomiting, measured by QLQ-C30, with critical clinical cycles of Weeks 12 and 24. Descriptive analyses were performed on all questionnaire responses, and a mixed model for repeated measures was performed on the PRO endpoints at Weeks 12 and 24. **Results:** Baseline demographics and disease characteristics between the zanubrutinib (n=241) and BR (n=238) arms were similar. Across all pts, adjusted completion rates for PROs (# of pts who completed the questionnaire at each cycle divided by # of pts expected to complete the questionnaires) were high (~80%) at Weeks 12 and 24. Compared with pts who received BR, pts treated with zanubrutinib experienced greater improvements in HRQoL at Weeks 12 and 24 as reported on the QLQ-C30 (**Table**). By Week 24, significant improvements were observed with zanubrutinib vs BR in GHS, physical functioning, role functioning as well as greater reductions in diarrhea, fatigue, and nausea/vomiting. Per EQ-5D-5L VAS, comparable improvements from baseline between zanubrutinib and BR in the health status were observed at Weeks 12 (4.3 vs 3.5) and 24 (4.5 vs 4.9), respectively.
Image:

	Week 12 LS Mean Difference* (95% CI)	*P*-value	Week 24 LS Mean Difference* (95% CI)	*P*-value
Global Health Status	0.7 (-3.3, 4.7)	0.73	4.9 (0.9, 9.0)	**0.017**
Functional domains				
Physical functioning	1.0 (-1.9, 3.9)	0.51	3.8 (0.8, 6.7)	**0.012**
Role functioning	4.4 (-0.5, 9.4)	0.080	4.8 (-0.2, 9.7)	**0.061**
Symptoms				
Diarrhea	-1.7 (-5.4, 2.0)	0.36	-6.2 (-10, -2.5)	**0.0012**
Fatigue	-3.7 (-8.1, 0.7)	0.97	-4.5 (-8.9, -0.1)	**0.047**
Nausea/vomiting	-3.9 (-6.5, -1.3)	**0.0035**	-4.2 (-6.8. -1.6)	**0.0015**
Pain	4.7 (0.1, 9.3)	**0.047**	0.4 (-4.3, 5.1)	0.87

*LS mean difference between zanubrutinib and BR arms.

Summary/Conclusion: In the SEQUOIA trial, zanubrutinib was associated with significant improvements in HRQoL in pts with TN CLL/SLL without del(17p), as indicated by the PRO endpoints of the GHS, physical and role functions, and greater reductions in symptoms of fatigue, diarrhea and nausea/vomiting compared with BR