Health-related quality of life (HRQoL) in patients with relapsed/refractory follicular lymphoma (R/R FL) treated with zanubrutinib + obinutuzumab versus obinutuzumab monotherapy: the ROSEWOOD trial

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ABSTRACT

Introduction: Zanubrutinib is a potent and highly selective next-generation BTK inhibitor designed to maximize BTK occupancy and minimize off-target effects.[1] In the phase 2 ROSEWOOD study (NCT03332017), zanubrutinib plus obinutuzumab (ZO) demonstrated superior efficacy and a manageable safety profile compared with obinutuzumab monotherapy (O) as treatment for patients with heavily pretreated R/R FL. [2] Here, we report HRQoL outcomes from the ROSEWOOD trial.

Materials and methods: Patient-reported outcomes (PROs) were secondary endpoints and assessed using the European Organisation for Research and Treatment of Cancer Quality of Life of Cancer Patients Questionnaire–C30 (EORTC QLQ-C30) and European Quality of Life 5-Dimensions 5-Levels (EQ-5D-5L). Patients completed questionnaires at baseline (cycle 1 day 1, before the first dose of study drug), then every 12 weeks for 2 years, every 24 weeks for the next 2 years, and then annually until disease progression, death, or withdrawal of consent. Compliance rates were calculated as the number of patients who completed questionnaires vs. the number expected to complete questionnaires at each visit in each arm. Descriptive analyses, including change over time, were performed on EORTC QLQ-C30 domains and EQ-5D-5L visual analog scale (VAS) scores. A mixed model for repeated measures (MMRM) analysis was performed using predefined PRO endpoints (the most relevant disease and treatment related scales) at the 2 predefined key clinical cycles, weeks 12 and 24. The PRO endpoints included the EORTC QLQ-C30 global health status (GHS)/quality of life (QoL), physical and role functioning domains, and fatigue, pain, nausea/vomiting, and diarrhea symptom domains. Clinically meaningful change was defined as ≥5-point mean difference from baseline. [3]

Results: A total of 217 patients were randomized to ZO (n=145) and O (n=72); baseline demographics and disease characteristics were well balanced between the arms. The median (range) duration of study treatment was 12.2 (0.5–44.1) and 6.5 (0.1–28.7) months, respectively. Compliance rates for PRO assessments in both arms were ≥80% at week 12, and ≥84% at week 24. By week 24, patients in the ZO arm had better overall outcomes particularly in role functioning, fatigue, pain, and nausea/vomiting (**Table**). There were no observable differences between the arms in EQ-5D-5L VAS scores (3.1 vs 2.0).
MMRM analyses revealed clinically meaningful differences from baseline to week 24 for ZO vs O in role functioning (least squares mean difference [95% CI]: 5.6 [-2.3, 13.5]), fatigue (-4.7 [-11.6, 2.2]), and pain (-4.9 [-12.6, 2.8] points).

Conclusions: In the ROSEWOOD trial, ZO was associated with improved HRQoL in patients with R/R FL. In particular, patients who received the ZO had greater improvements in fatigue, pain symptoms, and role functioning, than those who received O monotherapy. These findings suggest that zanubrutinib contributed clinically meaningful benefits to patient HRQoL when added to obinutuzumab.

Table: Results of MMRM Analysis of QLQ-C30 Domain Scores for ZO vs O

	Week 12		Week 24	
Domain	**LSM difference (95% CI)**	***P*-value**	**LSM difference (95% CI)**	***P*-value**
Functional[a]				
Global health status/ QoL	6.4 (0.6, 12.3)	0.0302	–0.3 (–6.5, 6.0)	0.9356
Physical functioning	2.2 (–2.1, 6.5)	0.3161	0.8 (–3.8, 5.5)	0.7199
Role functioning	0.7 (–6.6, 8.1)	0.8424	5.6 (–2.3, 13.5)	0.1637
Symptoms[b]				
Fatigue	–4.6 (–11.1, 1.9)	0.1614	–4.7 (–11.6, 2.2)	0.1817
Pain	–2.0 (–9.2, 5.2)	0.587	–4.9 (–12.6, 2.8)	0.2148
Nausea/Vomiting	–2.8 (–5.9, 0.3)	0.0729	–1.8 (–5.2, 1.5)	0.2766
Diarrhea	1.6 (–5.5, 8.8)	0.652	0.5 (–7.1, 8.1)	0.8944

[a]Positive value favors ZO.
[b]Negative value favors ZO.
LSM, least squares mean; MMRM, mixed model for repeated measures; O, obinutuzumab; QLQ-C30, Quality of Life of Cancer Patients Questionnaire – Core 30; QoL, quality of life; ZO, zanubrutinib + obinutuzumab.