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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INTRODUCTION

- Zanubrutinib is a potent and highly selective next-generation BTK inhibitor designed to maximize BTK occupancy and minimize off-target effects[1]
- ROSEWOOD (BGB-3111-212; NCT03332017), an open-label, multicenter, randomized phase 2 study of adult patients with heavily pretreated R/R follicular lymphoma (FL), compared outcomes associated with zanubrutinib plus obinutuzumab (ZO) vs obinutuzumab monotherapy (O)[2]
  - Treatment with ZO demonstrated superior efficacy vs O, and had a manageable safety profile[2]
- HRQoL was measured via patient-reported outcomes (PROs), and was a secondary endpoint within the trial. The current analysis evaluated HRQoL in patients with R/R FL who received ZO or O in the ROSEWOOD trial

METHODS

Design and Patients

- In the ROSEWOOD trial, patients were randomized 2:1 to receive ZO or O
  - Zanubrutinib 160 mg was orally administered twice daily
  - Obinutuzumab 1000 mg was administered intravenously on days 1, 8, and 15 of cycle 1 (28 days per cycle), day 1 of cycles 2–6, then once every 8 weeks for up to 20 total infusions (2-year maintenance)
  - The drugs were administered until progressive disease or unacceptable toxicity
- Eligible patients were at least 18 years of age and had measurable grade 1, 2, or 3a FL without transformation to aggressive B-cell lymphoma, and had received ≥2 prior systemic therapies for FL including anti-CD20 antibody and an alkylating agent, but excluding prior BTK inhibitor

Assessments and Analyses

- PROs were assessed for all patients randomized to a treatment arm using the European Organisation for Research and Treatment of Cancer Quality of Life of Cancer Patients Questionnaire – Core 30 (EORTC QLQ-C30) and European Quality of Life 5-Dimensions 5-Levels (EQ-5D-5L) visual analog scale (VAS)
- 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
- Scores and changes from baseline for all the domains of EORTC QLQ-C30 and EQ-5D-5L VAS were analyzed descriptively
- The predefined PRO endpoints (the most relevant disease and treatment related scales) were global health status (GHS)/quality of life (QoL), physical functioning, and role functioning and symptoms of fatigue, pain, nausea/vomiting, and diarrhea measured via EORTC QLQ-C30
  - Predefined key clinical cycles were weeks 12 and 24; clinically meaningful change was defined as mean change of ≥5 points from baseline[3]
- A mixed model for repeated measures (MMRM) analysis was used to compare the changes in PRO endpoints from baseline to the key clinical cycles
  - *P*-values were generated for descriptive purposes only as the analysis was not powered to determine statistical significance

RESULTS

- Baseline demographics and disease characteristics were well balanced between the ZO (n=145) and O (n=72) treatment arms
  - The median (range) duration of study treatment was 12.2 (0.5 to 44.1) months in the ZO arm and 6.5 (0.1 to 28.7) months in the O arm
- QLQ-C30 and EQ-5D-5L VAS scores were well balanced between treatment arms at baseline (**Table 1**)
  - Compliance rates for PRO assessments in both arms were ≥80%, ≥84%, ≥85%, and ≥77% at weeks 12, 24, 36, and 48, respectively

Descriptive Analysis Results

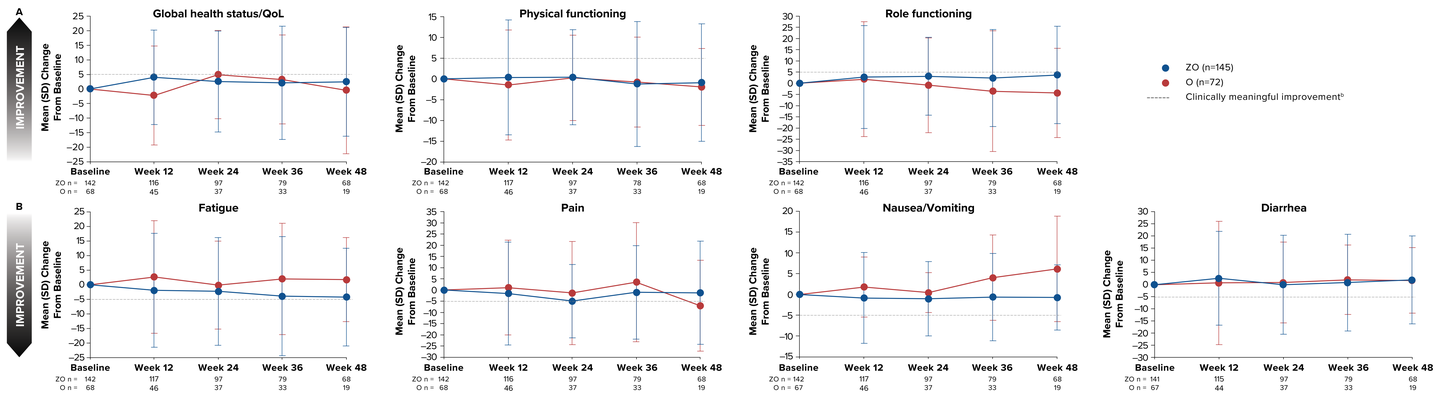
- The changes from baseline through week 48 in EORTC QLC-C30 domain scores are shown in **Figure 1** and **Table 2**
  - Patients in the ZO arm had larger improvements in role functioning and symptoms of fatigue
  - Nausea/vomiting was maintained in the ZO arm whereas worsening occurred in the O arm
  - There was no noticeable difference between arms in physical functioning, pain, or diarrhea
- EQ-5D-5L VAS scores showed no noticeable difference between treatment arms through week 48 (**Figure 2**)

Table 1. Mean (SD) PRO Scores at Baseline

	ZO (n=145)	O (n=72)
EORTC QLQ-C30 domains		
Global health status/QoL	69.4 (21.8)	68.9 (20.2)
Physical functioning	81.7 (19.6)	78.4 (22.1)
Role functioning	78.1 (26.2)	79.2 (29.7)
Fatigue	30.0 (22.6)	30.1 (24.6)
Pain	19.5 (24.5)	19.6 (24.8)
Nausea/Vomiting	4.6 (10.7)	2.7 (9.4)
Diarrhea	8.7 (19.0)	10.9 (22.0)
EQ-5D-5L VAS	74.4 (19.3)	74.1 (17.7)

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life of Cancer Patients Questionnaire – Core 30; EQ-5D-5L, European Quality of Life 5-Dimensions 5-Levels; O, obinutuzumab; PRO, patient-reported outcomes; QoL, quality of life; VAS, visual analog scale; ZO, zanubrutinib + obinutuzumab.

Figure 1. Change From Baseline Through Week 48 in QLQ-C30 Scores for (A) Functional and (B) Symptomatic Domains[a]



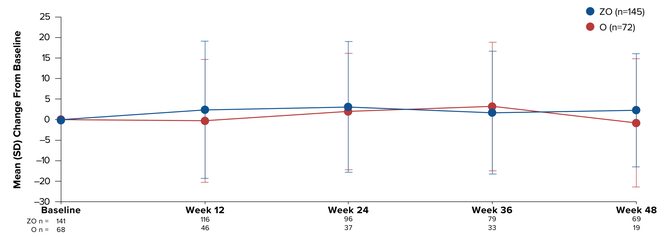
[a]Only patients with data at both baseline and each post-baseline visit were included in the summary statistics for change from baseline.
[b]Defined as a ≥5-point change from baseline.
O, obinutuzumab; QLQ-C30; Quality of Life of Cancer Patients Questionnaire – Core 30; QoL, quality of life; ZO, zanubrutinib + obinutuzumab.

Table 2. Mean (SD) Change From Baseline in EORTC QLC-30 Domain Scores Through Week 48[a]

	Week 12		Week 24		Week 36		Week 48	
Domain	**ZO**	**O**	**ZO**	**O**	**ZO**	**O**	**ZO**	**O**
Global health status[b]	4.0 (16.2)	–2.2 (17.0)	2.6 (17.4)	5.0 (15.1)	2.1 (19.5)	3.3 (15.3)	2.5 (18.7)	–0.4 (21.8)
Functional domains[b]								
Physical functioning	0.4 (13.8)	–1.4 (13.3)	0.4 (11.4)	0.3 (10.3)	–1.2 (15.0)	–0.8 (10.8)	–0.9 (14.1)	–1.9 (9.3)
Role functioning	2.7 (22.9)	1.8 (25.6)	3.1 (17.4)	–0.9 (21.1)	2.3 (21.6)	–3.5 (26.9)	3.7 (21.7)	–4.4 (19.9)
Symptoms[c]								
Fatigue	–1.9 (19.6)	2.7 (19.3)	–2.3 (18.5)	–0.2 (15.1)	–3.9 (20.4)	2.0 (19.1)	–4.2 (16.7)	1.8 (14.5)
Pain	–1.6 (22.9)	1.1 (21.2)	–5.0 (16.3)	–1.4 (23.0)	–1.1 (20.9)	3.5 (26.6)	–1.2 (23.1)	–7.0 (20.3)
Nausea/Vomiting	–0.9 (10.9)	1.8 (7.2)	–1.0 (8.9)	0.5 (4.8)	–0.6 (10.5)	4.0 (10.2)	–-0.7 (7.9)	6.1 (12.7)
Diarrhea	2.6 (19.3)	0.8 (25.4)	0.0 (20.4)	0.9 (16.6)	0.8 (20.0)	2.0 (14.3)	2.0 (18.1)	1.8 (13.5)

[a]Only patients with data at both baseline and each postbaseline visit are included in the summary statistics for change from baseline.
[b]Positive value denotes improvement.
[c]Negative value denotes improvement.
EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life of Cancer Patients Questionnaire – Core 30; O, obinutuzumab; ZO, zanubrutinib + obinutuzumab.

Figure 2. Change from Baseline Through Week 48 in EQ-5D-5L VAS Score[a]



[a]Only patients with data at both baseline and each postbaseline visit were included in the summary statistics.
EQ-5D-5L, European Quality of Life 5-Dimensions 5-Levels; O, obinutuzumab; VAS, visual analog scale; ZO, zanubrutinib + obinutuzumab.

CONCLUSIONS

- In the ROSEWOOD trial, treatment with ZO was associated with better HRQoL outcomes compared with O in patients with R/R FL
- The differences in improvements in patients who received ZO vs O were clinically meaningful short-term (week 12) in GHS/QoL and fatigue and long-term (week 24) in fatigue and pain symptoms, and role functioning
- These findings, along with the primary clinical outcomes, suggest that zanubrutinib + obinutuzumab for treatment of patients with R/R FL is associated with higher clinical and HRQoL benefits than treatment with obinutuzumab alone

MMRM Results

- Results of MMRM analyses showed clinically meaningful differences between treatment arms in function and symptoms (**Table 3**):
  - At week 12, differences in GHS/QoL and fatigue were clinically meaningful between ZO and O arms
  - At week 24, differences in role functioning, fatigue, and pain were clinically meaningful between ZO and O arms

Table 3. 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[b]				
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)	0.5870	–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)	0.6520	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.

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