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 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) versus obinutuzumab monotherapy (O)[2]
  - Treatment with ZO demonstrated superior efficacy versus 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 versus 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 and mean difference between treatment arms[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 (3.1 vs. 2.0)

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.

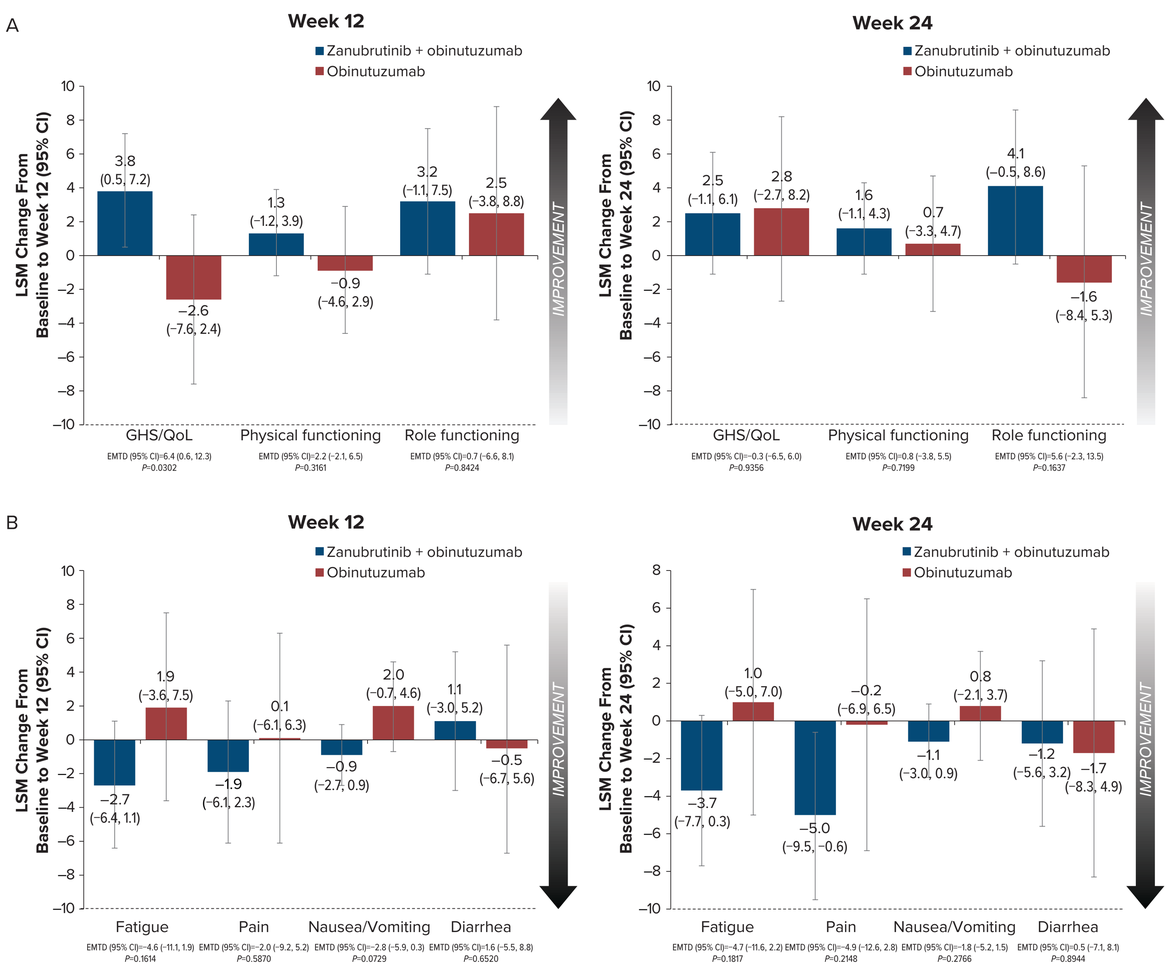
CONCLUSIONS

- In the ROSEWOOD trial, treatment with ZO was associated with better PROs compared with O in patients with R/R FL
- The differences in improvements in patients who received ZO versus 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 (**Figure 2**):
  - 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

Figure 2. MMRM Analysis of QLQ-C30 A) GHS/QoL and Functional and B) Symptom Domain Scores[a] for ZO vs O



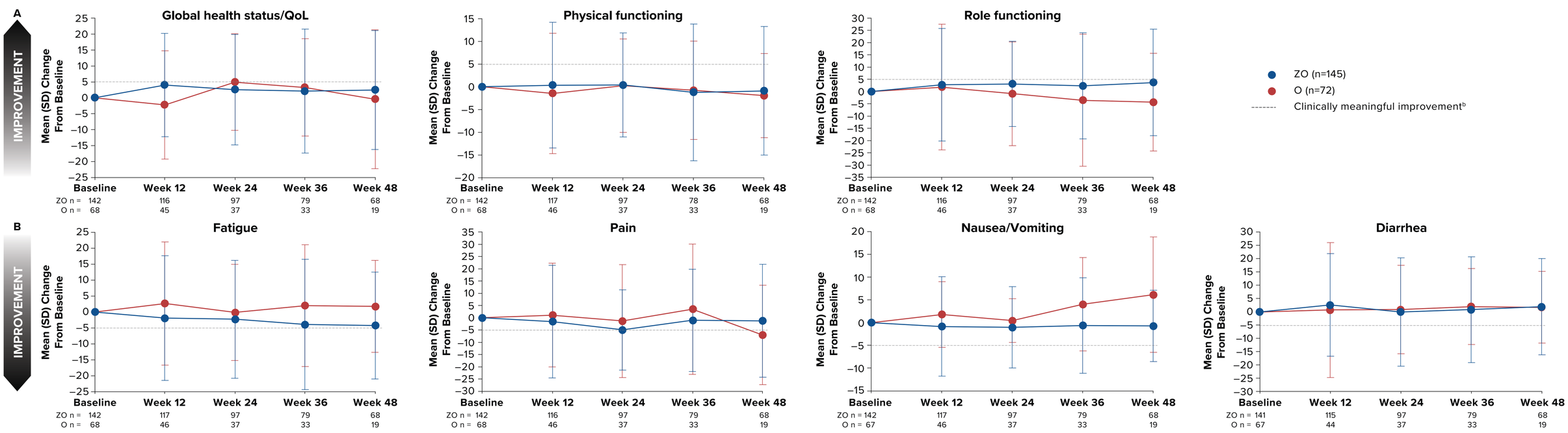
[a]Only patients with data at both baseline and each postbaseline visit were included in the summary statistics.
EMTD, estimated mean treatment difference; GHS, global health status; LSM, least squares mean; MMRM, mixed model for repeated measures; O, obinutuzumab; QLQ-C30, Quality of Life of Cancer Patients Questionnaire – Core 30; QoL, quality of life; ZO, zanubrutinib + obinutuzumab.

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

Domain	Week 12		Week 24		Week 36		Week 48	
	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 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.

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