Poster 304

Zanubrutinib Plus Obinutuzumab vs Obinutuzumab in Patients With Relapsed/Refractory Follicular Lymphoma: Updated Analysis of the ROSEWOOD Study

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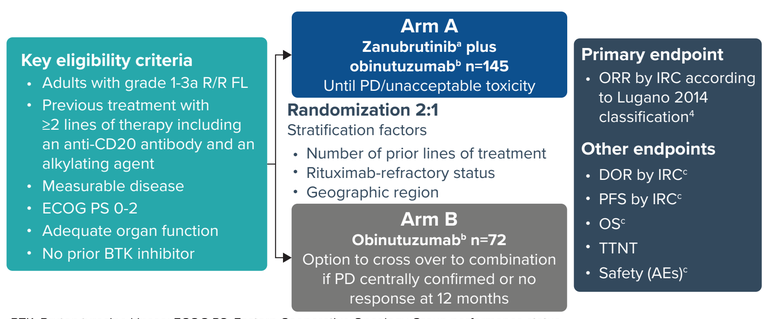
BACKGROUND

- Follicular lymphoma (FL) is the second most common non-Hodgkin lymphoma subtype worldwide[1]
- In a phase 1b/2 study that included patients with relapsed/refractory (R/R) FL, the combination of zanubrutinib plus obinutuzumab was generally well tolerated, with an objective response rate (ORR) of 72% and a complete response rate of 39%[2]
- The phase 2 ROSEWOOD trial (BGB-3111-212; NCT03332017) examined zanubrutinib plus obinutuzumab vs obinutuzumab monotherapy in patients with R/R FL who had received ≥2 prior lines of therapy
- In the previously reported primary analysis, the trial met its primary endpoint, with significant improvement in the ORR with zanubrutinib plus obinutuzumab vs obinutuzumab (68.3% vs 45.8%, respectively; *P*=.0017)[3]
- Here we report an updated analysis of the ROSEWOOD trial with a median follow-up of 20.2 months

METHODS

- ROSEWOOD was a global study that assessed the efficacy and safety of zanubrutinib plus obinutuzumab vs obinutuzumab (**Figure 1**)

Figure 1. Study Design



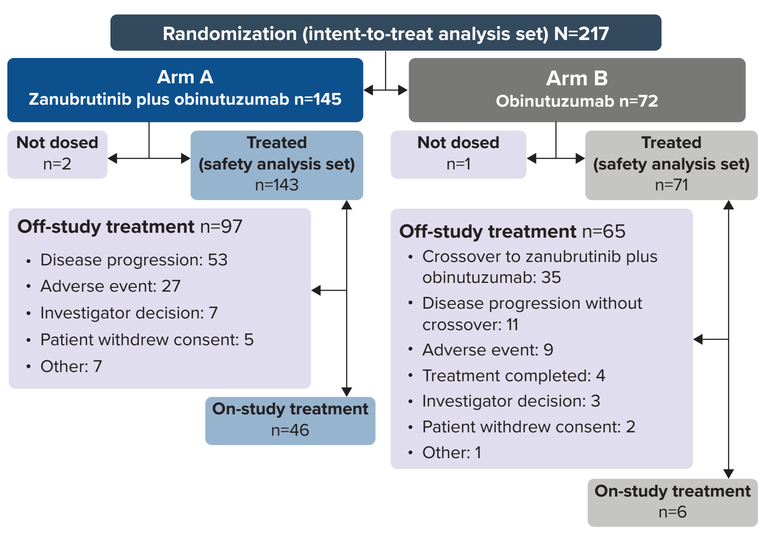
BTK, Bruton tyrosine kinase; ECOG PS, Eastern Cooperative Oncology Group performance status.
[a] Zanubrutinib was given orally at 160 mg twice daily. [b] Obinutuzumab was given intravenously at 1000 mg in both arms on days 1, 8, and 15 of cycle 1, day 1 of cycles 2 to 6, and then every 8 weeks up to 20 doses maximum. [c] Secondary endpoint.

RESULTS

Patients

- A total of 217 patients from 127 sites in 17 countries/regions were randomized between November 2017 and June 2021 (**Figure 2**)
- Median follow-up for this analysis was 20.2 months

Figure 2. Patient Disposition



- Baseline characteristics are shown in **Table 1**

Table 1. Patient Characteristics

Characteristic	Zanubrutinib + obinutuzumab (n=145)	Obinutuzumab (n=72)
Age, median (range), years	63.0 (31-84)	65.5 (32-88)
ECOG PS ≥1, n (%)	59 (40.6)	41 (57.0)
FLIPI score ≥3, n (%)	77 (53.1)	37 (51.4)
Ann Arbor stage III-IV, n (%)	119 (82.1)	60 (83.3)
Bulky disease (≥7 cm), n (%)	23 (15.9)	12 (16.7)
High LDH level (>ULN), n (%)	49 (33.8)	29 (40.3)
High tumor burden per GELF criteria, n (%)	83 (57.2)	40 (55.6)
No. of prior lines of therapy, median (range)	3 (2-11)	3 (2-9)
Refractory to rituximab, n (%)	78 (53.8)	36 (50.0)
Refractory to most recent line of therapy, n (%)	47 (32.4)	29 (40.3)
PD ≤24 months after starting first line of therapy, n (%)	50 (34.5)	30 (41.7)
Prior therapy, n (%)		
Immunochemotherapy	143 (98.6)	71 (98.6)
Anthracyclines	118 (81.4)	57 (79.2)
Cyclophosphamide	136 (93.8)	68 (94.4)
Bendamustine	79 (54.5)	40 (55.6)

ECOG PS, Eastern Cooperative Oncology Group performance status; FLIPI, Follicular Lymphoma International Prognostic Index; GELF, Groupe d'Etude des Lymphomes Folliculaires; LDH, lactate dehydrogenase; ULN, upper limit of normal.

Treatment Exposure

- In the zanubrutinib plus obinutuzumab arm, median duration of zanubrutinib exposure was 12.2 months (range, 0.5-44.1 months)
  - 56.7% of patients received ≥12 cycles
  - Median relative dose intensity was 98.9% (range, 30.7%-100%)
  - Median number of obinutuzumab infusions was 11 (range, 3-20)
- In the obinutuzumab arm, median exposure was 6.5 months (range, 0.1-28.7 months)
  - Median number of infusions was 9 (range, 3-20)

Efficacy

- At the median study follow-up of 20.2 months, the difference in the ORR by independent review committee (IRC) was 22.7% (95% CI, 9.0%-36.5%) in favor of zanubrutinib plus obinutuzumab (**Table 2**)

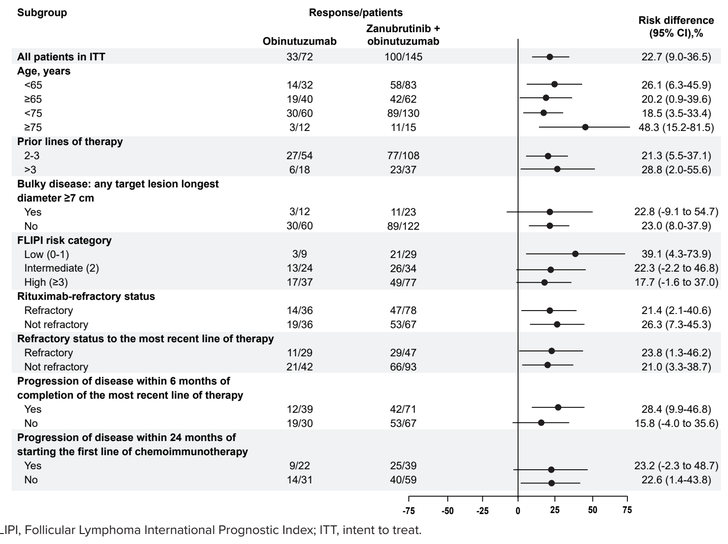
Table 2. Efficacy Outcomes

Endpoint	Zanubrutinib + obinutuzumab (n=145)	Obinutuzumab (n=72)	2-sided *P* value
ORR by IRC (95% CI), %	69.0 (60.8-76.4)	45.8 (34.0-58.0)	.0012
CR	39.3	19.4	.0035
PR	29.7	26.4	–
DOR by IRC			
Median (95% CI), mo	NE (25.3-NE)	14.0 (9.2-25.1)	–
18-month DOR rate (95% CI), %	69.3 (57.8-78.2)	41.9 (22.6-60.1)	–
DOCR by IRC			
Median (95% CI), mo	NE (26.5-NE)	26.5 (2.7-NE)	–
18-month DOCR rate (95% CI), %	87.4 (73.8-94.2)	51.1 (21.0-74.9)	–

DOCR, duration of complete response; NE, not estimable.

- Across prespecified subgroups of patients, zanubrutinib plus obinutuzumab showed consistent benefit over obinutuzumab (**Figure 3**)

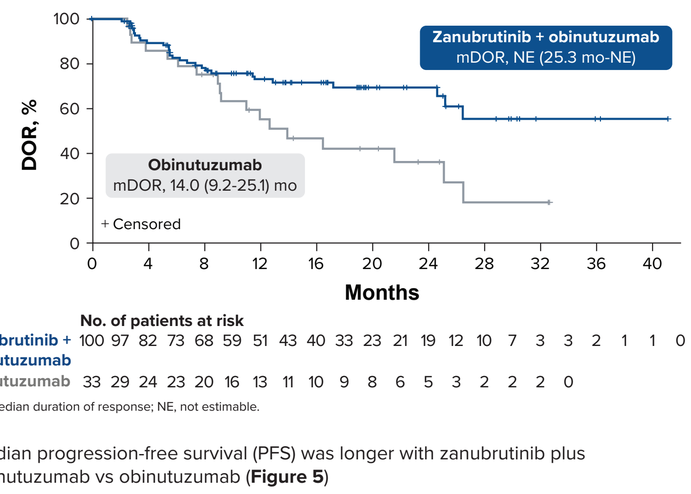
Figure 3. ORR by IRC in Predefined Subgroups



FLIPI, Follicular Lymphoma International Prognostic Index; ITT, intent to treat.

- Median duration of response by IRC was 14.0 months with obinutuzumab and was not reached in the zanubrutinib plus obinutuzumab arm (**Figure 4**)

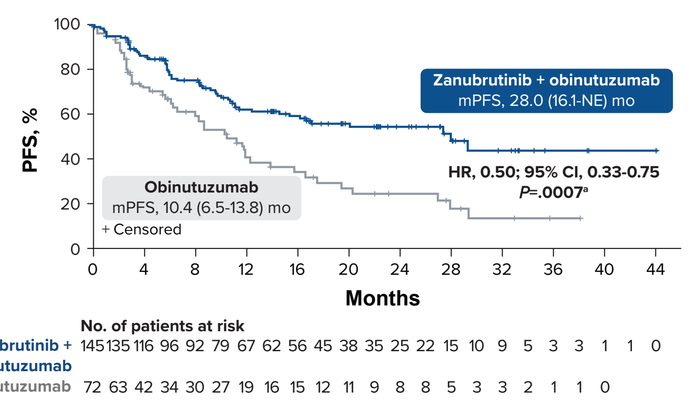
Figure 4. Duration of Response by IRC



mDOR, median duration of response; NE, not estimable.

- Median progression-free survival (PFS) was longer with zanubrutinib plus obinutuzumab vs obinutuzumab (**Figure 5**)

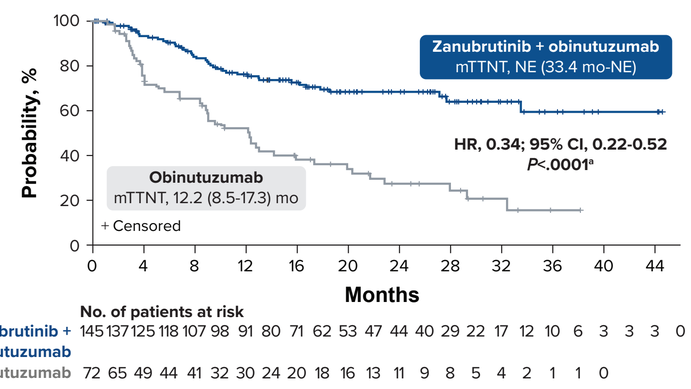
Figure 5. Progression-Free Survival by IRC



mPFS, median progression-free survival; NE, not estimable.
[a] Descriptive 2-sided *P* value.

- Time to next antilymphoma treatment (TTNT) was prolonged with zanubrutinib plus obinutuzumab (**Figure 6**)

Figure 6. Time to Next Antilymphoma Treatment



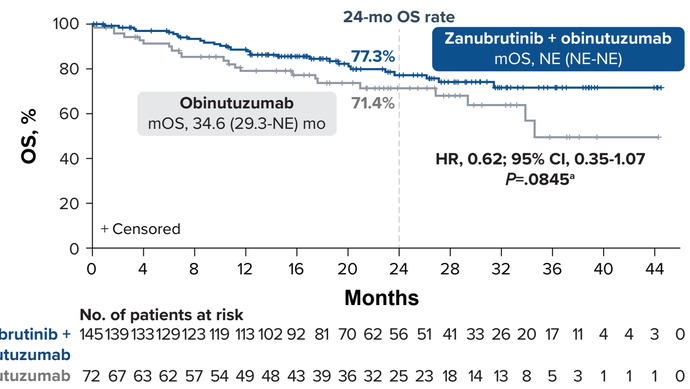
mTTNT, median time to next antilymphoma treatment; NE, not estimable.
[a] Descriptive 2-sided *P* value.

- The estimated overall survival rate at 24 months was numerically higher with zanubrutinib plus obinutuzumab vs obinutuzumab (**Figure 7**)

CONCLUSIONS

- In the ROSEWOOD study, zanubrutinib plus obinutuzumab demonstrated meaningful efficacy and a manageable safety profile in heavily pretreated patients with R/R FL
- This longer follow-up analysis provides evidence of the significant complete response rate, with longer PFS and TTNT, with zanubrutinib plus obinutuzumab vs obinutuzumab
  - A consistent benefit was observed across key prespecified subgroups
- The combination of zanubrutinib and obinutuzumab demonstrates a favorable risk-benefit profile and may represent a potential novel combination therapy for patients with R/R FL
- A phase 3 study of zanubrutinib plus obinutuzumab in patients who previously received ≥1 line of systemic therapy is now underway (MAHOGANY; NCT05100862)

Figure 7. Overall Survival



mOS, median overall survival; NE, not estimable.
[a] Descriptive 2-sided *P* value.

Safety

- There were no unexpected safety findings with zanubrutinib plus obinutuzumab (**Figure 8**; **Table 3**)
  - Among common nonhematologic treatment-emergent adverse events (TEAEs) of any grade, pyrexia and infusion-related reactions occurred more frequently with obinutuzumab (>5% difference vs zanubrutinib plus obinutuzumab)
- Exposure-adjusted incidence rates for TEAEs of special interest are given in **Figure 9**
  - Incidences of atrial fibrillation and hypertension were low and similar in both treatment arms
  - Two patients in each arm reported major hemorrhage

Figure 8. Common Nonhematologic TEAEs (Any Grade)

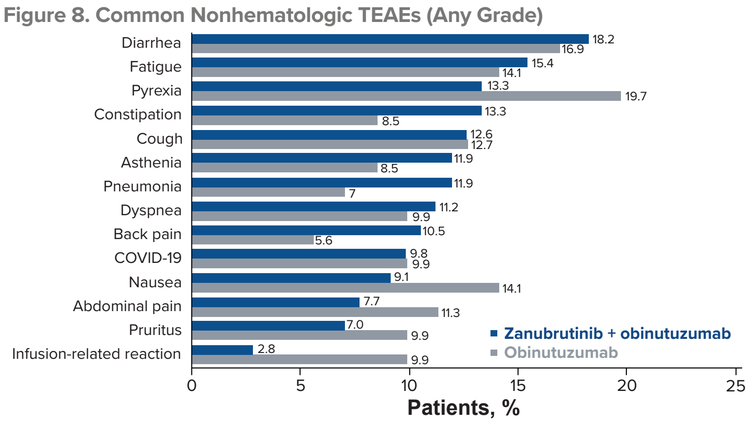
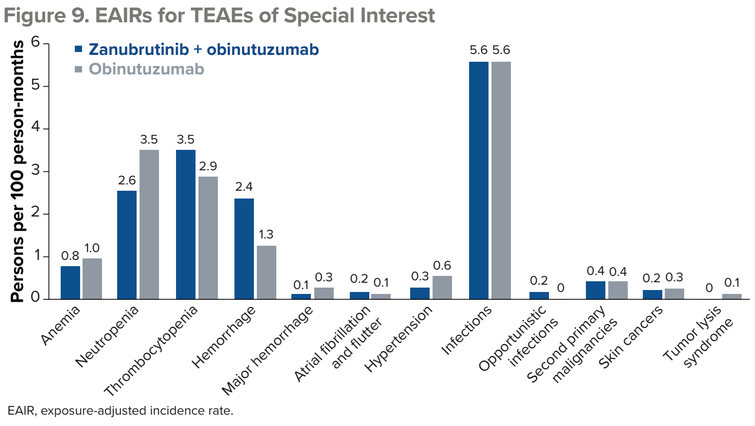


Table 3. Selected Grade ≥3 Nonhematologic TEAEs

n (%)	Zanubrutinib + obinutuzumab (n=143)	Obinutuzumab (n=71)
Pneumonia	14 (9.8)	3 (4.2)
COVID-19	8 (5.6)	2 (2.8)
COVID-19 pneumonia	5 (3.5)	2 (2.8)
Diarrhea	4 (2.8)	1 (1.4)
Febrile neutropenia	3 (2.1)	1 (1.4)
Atrial fibrillation	2 (1.4)	0 (0)
Infusion-related reaction	1 (0.7)	3 (4.2)
Hypertension	1 (0.7)	1 (1.4)

Figure 9. EAIRs for TEAEs of Special Interest



EAIR, exposure-adjusted incidence rate.

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DISCLOSURES

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