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Final Analysis of the Randomized Phase 2 ROSEWOOD Study of Zanubrutinib + Obinutuzumab vs Obinutuzumab Monotherapy in Patients With Relapsed/Refractory Follicular Lymphoma

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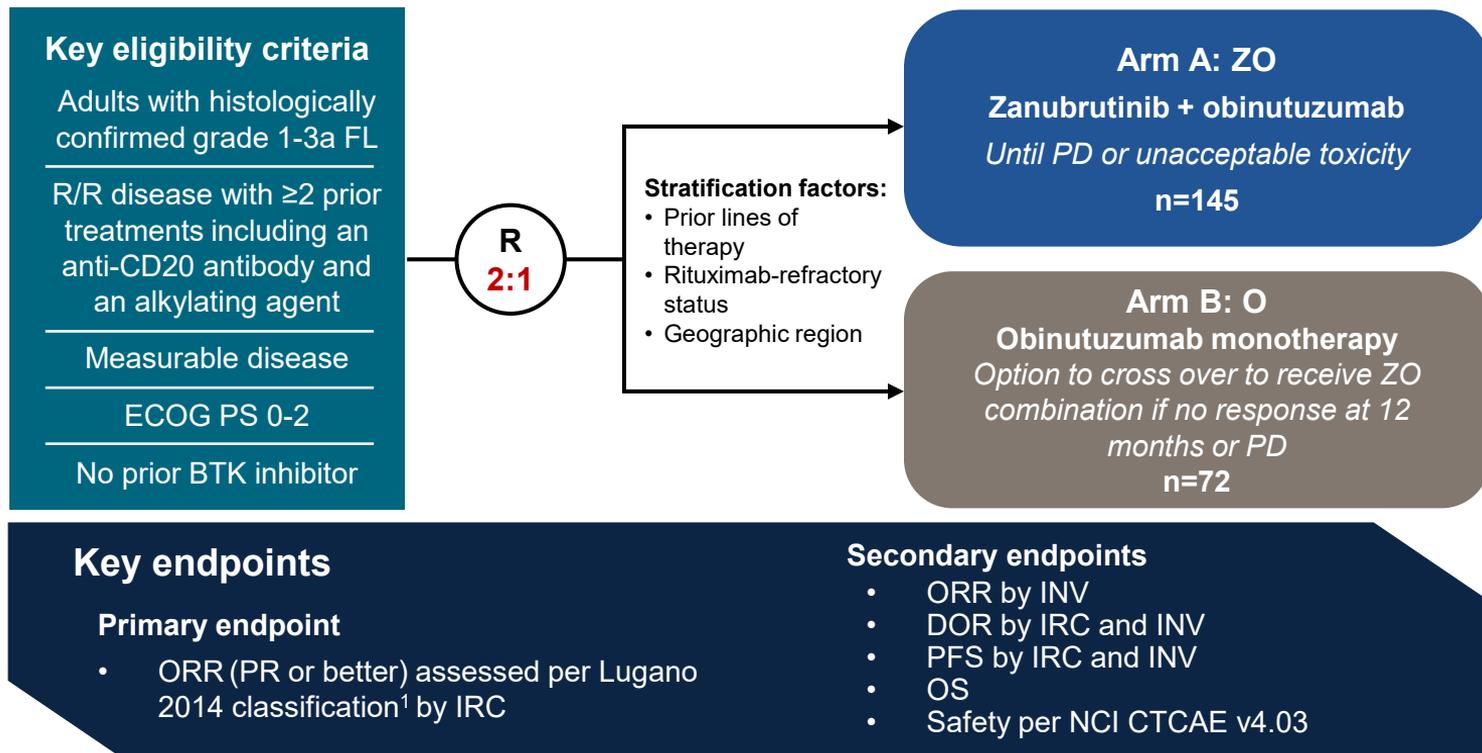
Introduction

- Treatment advances have improved outcomes in FL; however, many patients experience multiple relapses, highlighting a need for new therapies¹
- Zanubrutinib, a potent and selective, next-generation BTK inhibitor designed for complete and sustained BTK occupancy, is approved in multiple countries for various B-cell malignancies²⁻⁴
- ROSEWOOD (NCT03332017) is a phase 2 study of zanubrutinib and obinutuzumab (ZO) combination therapy vs obinutuzumab monotherapy (O) in patients with R/R FL who had received ≥ 2 prior lines of therapy⁵
- A previous analysis (median follow-up of 20.2 months) showed a significantly improved ORR per independent review committee (IRC) with ZO vs O⁵
- Here, we report the final analysis of ROSEWOOD with a median follow-up of 34.6 months

BTK, Bruton tyrosine kinase; FL, follicular lymphoma; IRC, independent review committee; O, obinutuzumab monotherapy; ORR, overall response rate; R/R, relapsed/refractory; ZO, zanubrutinib + obinutuzumab.

1. Ghione P, et al. *Haematologica*. 2023;108(3):822-832; 2. Guo Y, et al. *J Med Chem*. 2019;62(17):7923-7940; 3. Brukinsa (zanubrutinib). Prescribing information. BeOne Medicines, Ltd; 2023; 4. Brukinsa (zanubrutinib). Summary of product characteristics. BeOne Medicines, Ltd; 2024; 5. Zinzani PL, et al. *J Clin Oncol*. 2023;41(33):5107-5117.

ROSEWOOD: A Global, Randomized, Open-Label, Phase 2 Study



BTK, Bruton tyrosine kinase; CD, cluster of differentiation; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; INV, investigator; IRC, independent review committee; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; O, obinutuzumab; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; R, randomized; R/R, relapsed/refractory; ZO, zanubrutinib + obinutuzumab.

1. Cheson BD, et al. *J Clin Oncol.* 2014;32(27):3059-3068.

Baseline Characteristics

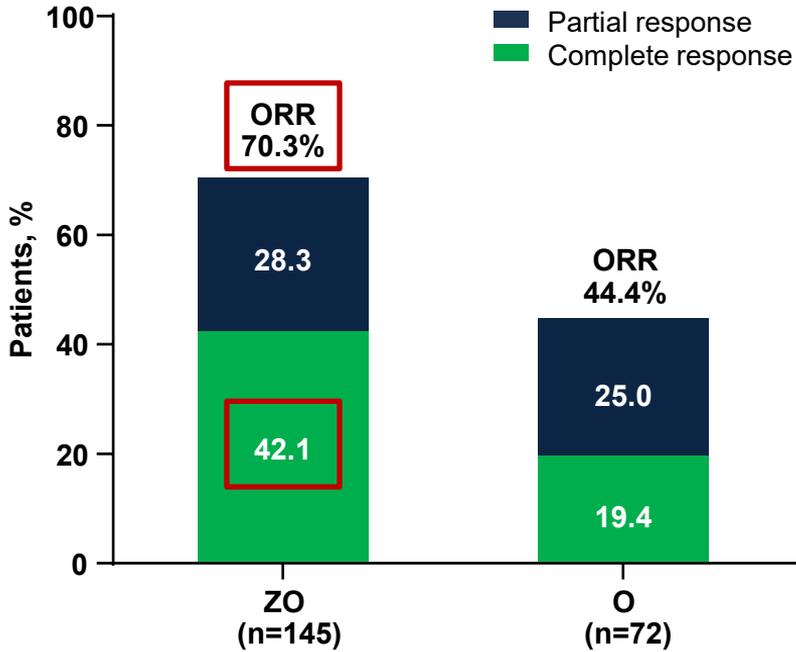
- 217 patients from 127 sites in 17 countries/regions were randomized between November 2017 and June 2021
 - 214 received treatment with ZO (n=143) or O (n=71)
- As of December 31, 2024, median study follow-up was 34.6 months (range, 0.1-69.7 months)

Characteristic	ZO n=145	O n=72
Age, median (range), years	63.0 (31-84)	65.5 (32-88)
Male, n (%)	75 (51.7)	33 (45.8)
Race, n (%)		
White	92 (63.4)	47 (65.3)
Asian	30 (20.7)	17 (23.6)
Not reported	23 (15.9)	8 (11.1)
ECOG PS \geq1, n (%)	59 (40.6)	41 (57.0)
High FLIPI score (\geq3), n (%)	77 (53.1)	37 (51.4)
Ann Arbor stage III-IV, n (%)	119 (82.1)	60 (83.3)
Bulky disease (\geq7 cm), n (%)	23 (15.9)	12 (16.7)
Bone marrow involvement at screening, n (%)	39 (26.9)	26 (36.1)
High tumor burden per GELF criteria, n (%)	83 (57.2)	40 (55.6)
High LDH level ($>$ULN), n (%)	49 (33.8)	29 (40.3)

Characteristic	ZO n=145	O n=72
No. of lines of prior therapy, median (range)	3 (2-11)	3 (2-9)
2-3, n (%)	104 (71.7)	54 (75.0)
$>$ 3, n (%)	41 (28.3)	18 (25.0)
Refractory to rituximab, n (%)	78 (53.8)	36 (50.0)
Refractory to most recent line of therapy, n (%)	47 (32.4)	29 (40.3)
POD24, n (%)	51 (35.2)	30 (41.7)
Prior therapy, n (%)		
Anti-CD20 mAb	145 (100)	72 (100)
Prior immunochemotherapy	143 (98.6)	71 (98.6)
Cyclophosphamide	136 (93.8)	68 (94.4)
Anthracyclines	118 (81.4)	57 (79.2)
Bendamustine	79 (54.5)	40 (55.6)
Prior stem cell transplant	32 (22.1)	13 (18.1)

ECOG PS, Eastern Cooperative Oncology Group performance status; FLIPI, Follicular Lymphoma International Prognostic Index; GELF, Groupe d'Etude des Lymphomes Folliculaires; LDH, lactate dehydrogenase; mAb, monoclonal antibody; O, obinutuzumab; POD24, progression of disease \leq 24 months after starting frontline therapy; ULN, upper limit of normal; ZO, zanubrutinib + obinutuzumab.

ORR per IRC With ZO Was Higher Compared With O

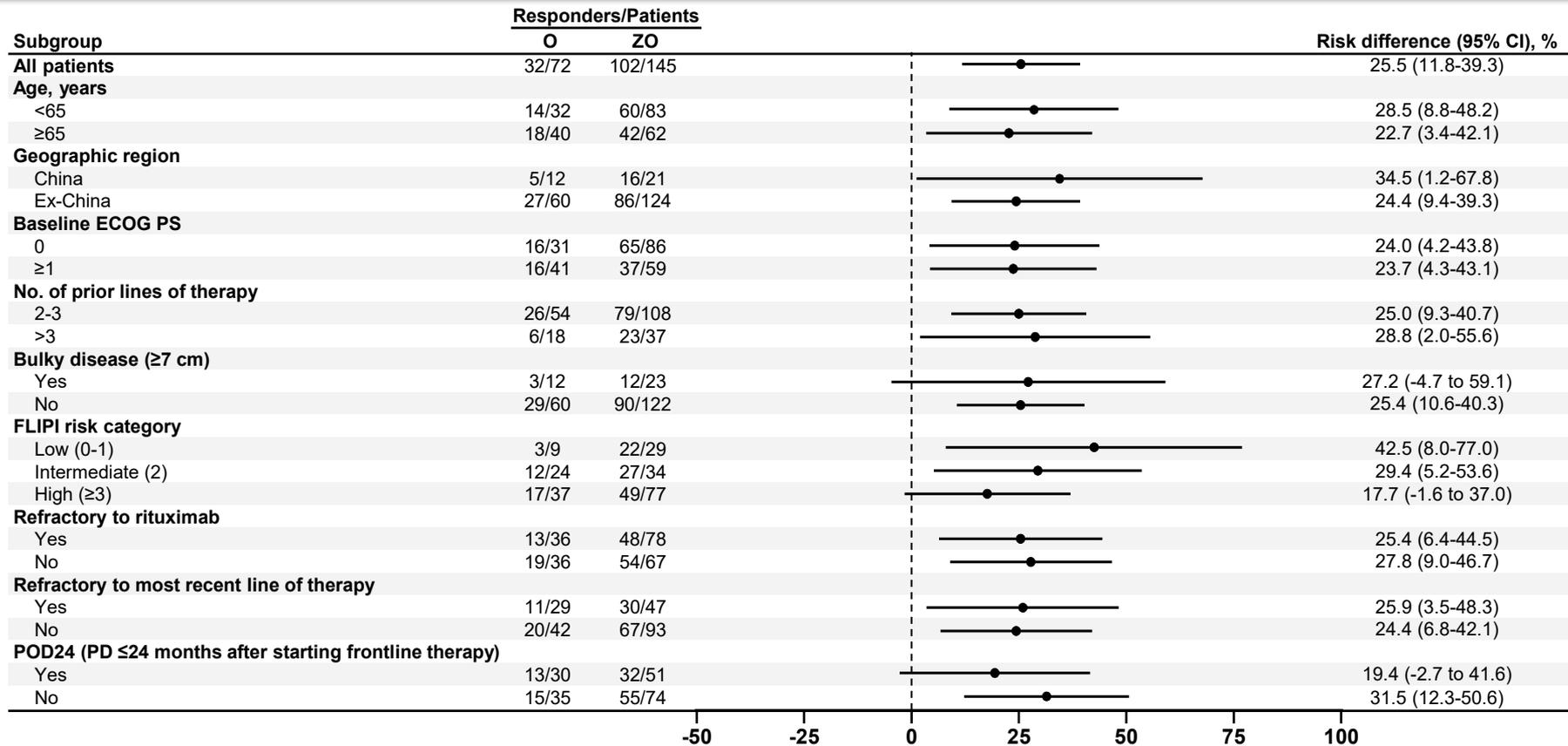


	ZO (n=145)	O (n=72)
Overall response rate, n (%)	102 (70.3)	32 (44.4)
95% CI	62.2-77.6	32.7-56.6
Risk difference (95% CI), %	25.5 (11.8-39.3)	
2-sided P value ^a	.0003	
Complete response rate, n (%)	61 (42.1)	14 (19.4)
95% CI	33.9-50.5	11.1-30.5
2-sided P value ^a	.0009	
Other responses, n (%)		
Stable disease	21 (14.5)	14 (19.4)
Indeterminate due to zanubrutinib hold	1 (0.7)	0
Non-progressive disease ^b	6 (4.1)	9 (12.5)
Progressive disease	13 (9.0)	16 (22.2)
Discontinued prior to first assessment/NE	2 (1.4)	1 (1.4)

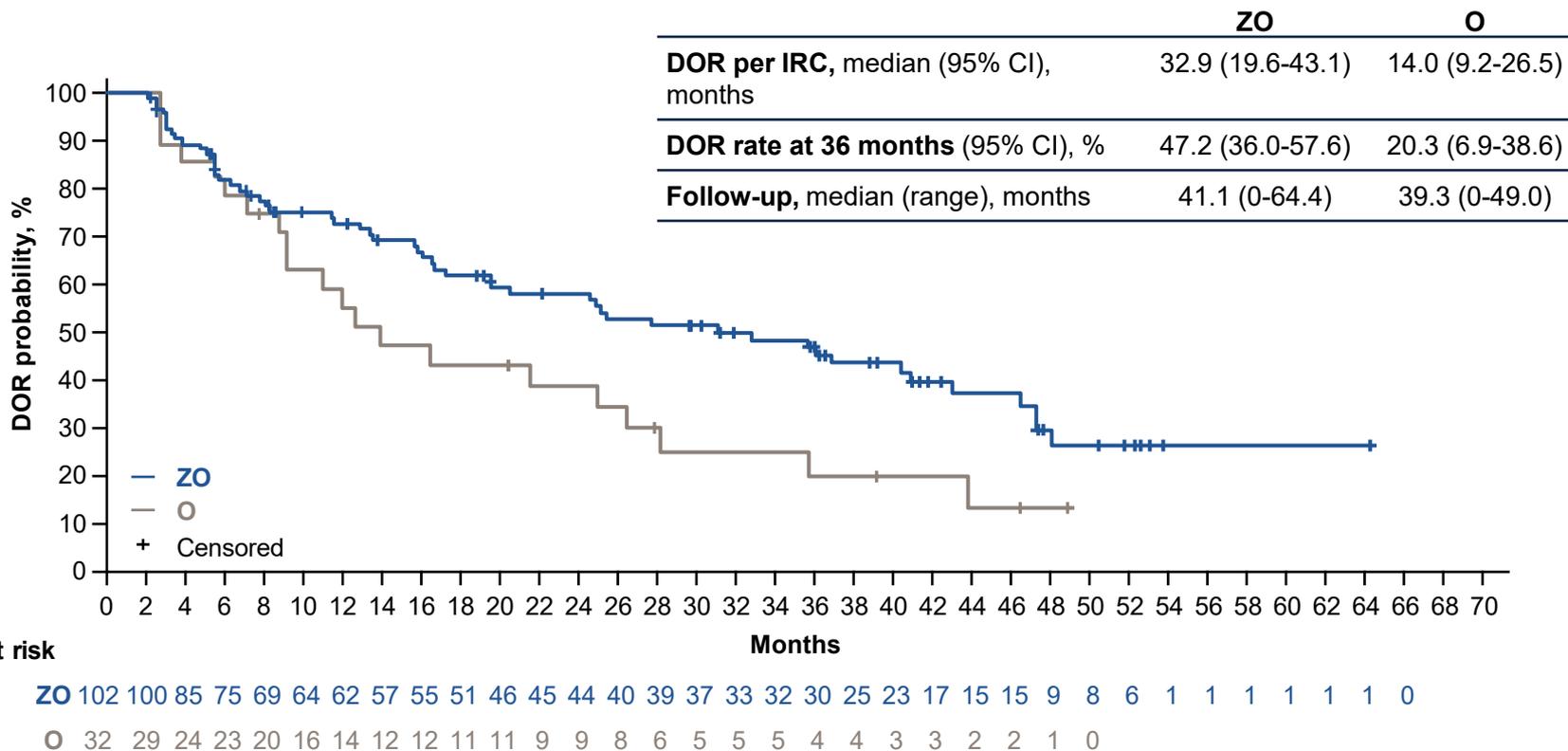
- ORRs per INV were similar to ORRs per IRC (ZO, 68.3%; O, 43.1%)

^aP value is descriptive. ^bDefined as PET assessment missing or not evaluable, and CT assessment showed no progressive disease. CT, computed tomography; INV, investigator; IRC, independent review committee; O, obinutuzumab; ORR, overall response rate; PET, positron emission tomography; ZO, zanubrutinib + obinutuzumab.

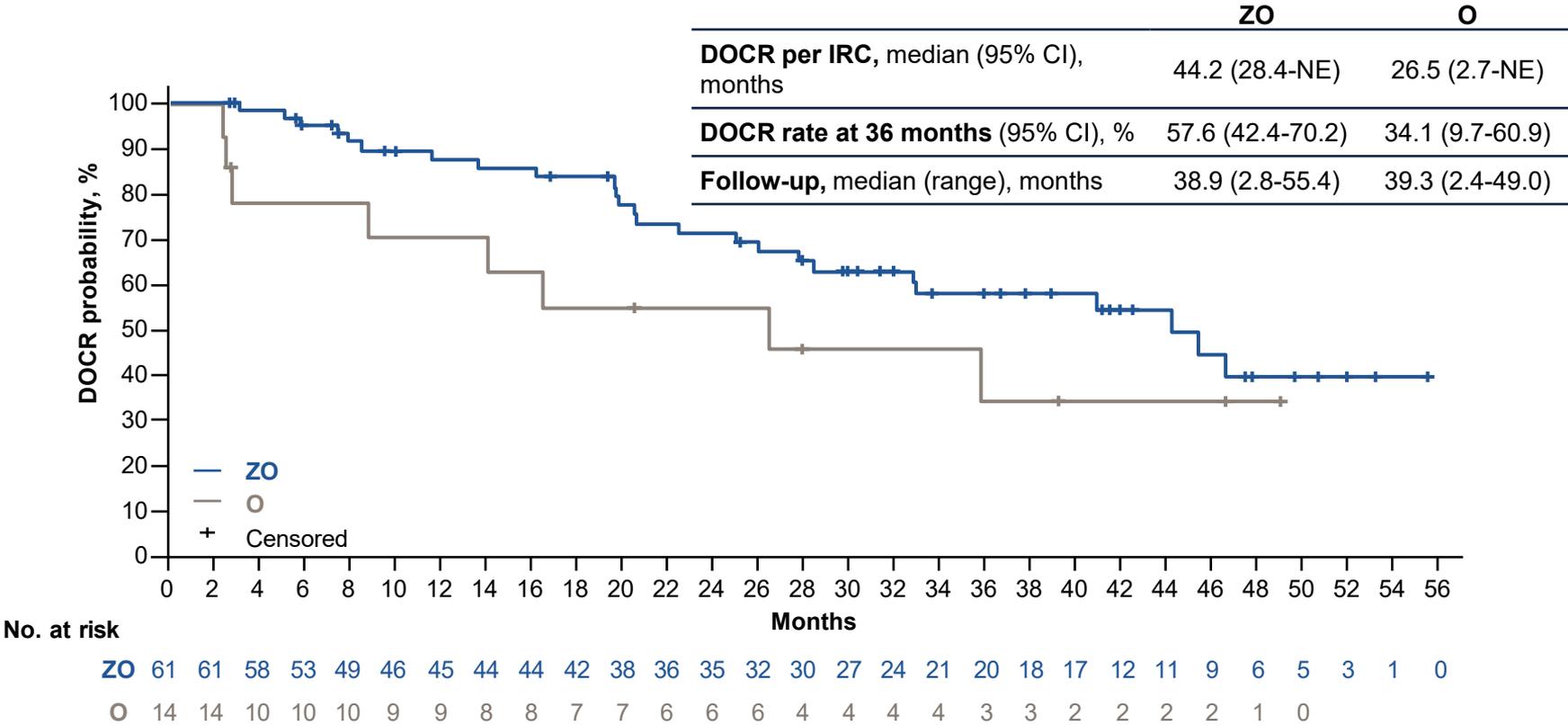
ORR Benefit With ZO Over O Consistent Across Subgroups



Duration of Response Was Longer in the ZO Arm

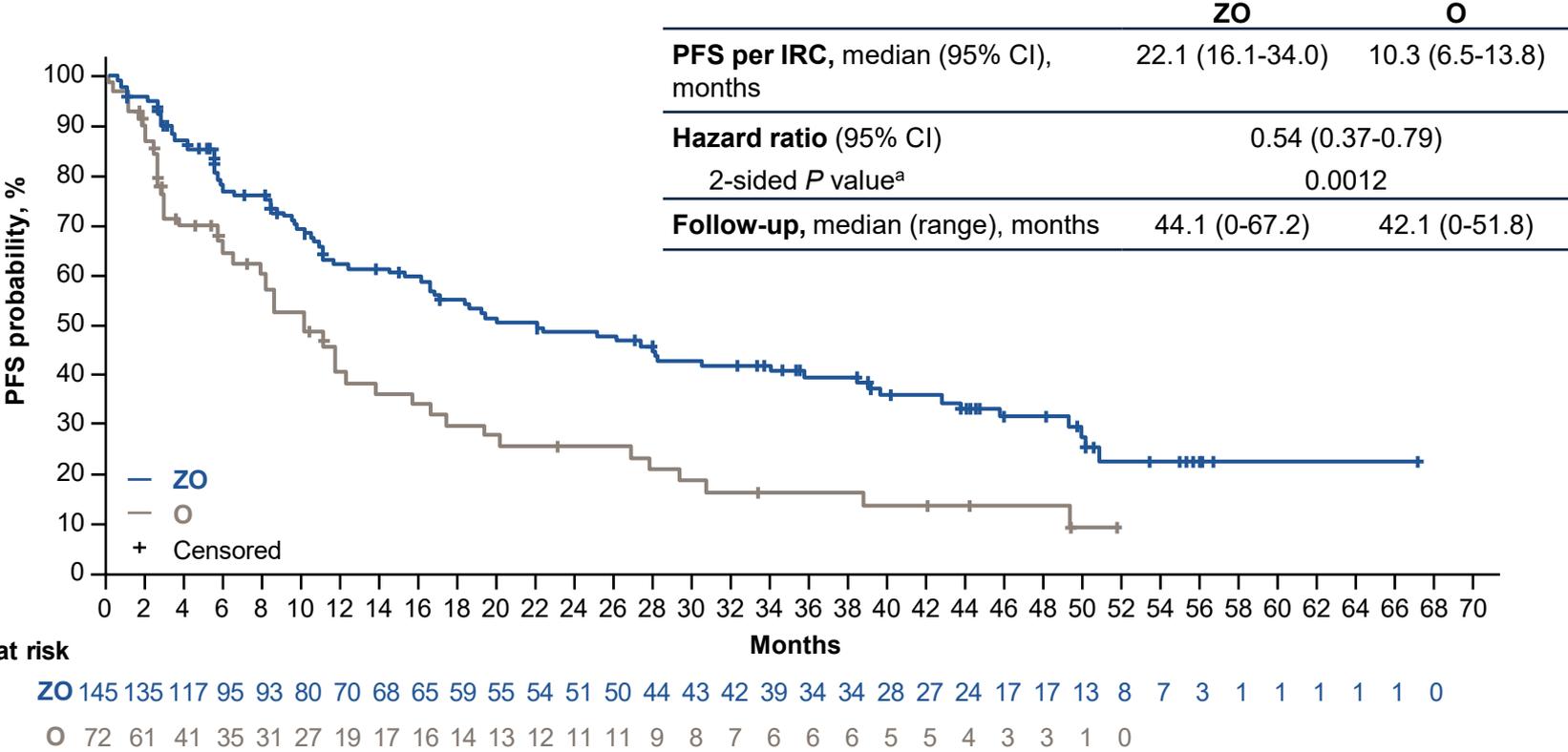


Complete Responses Were Durable



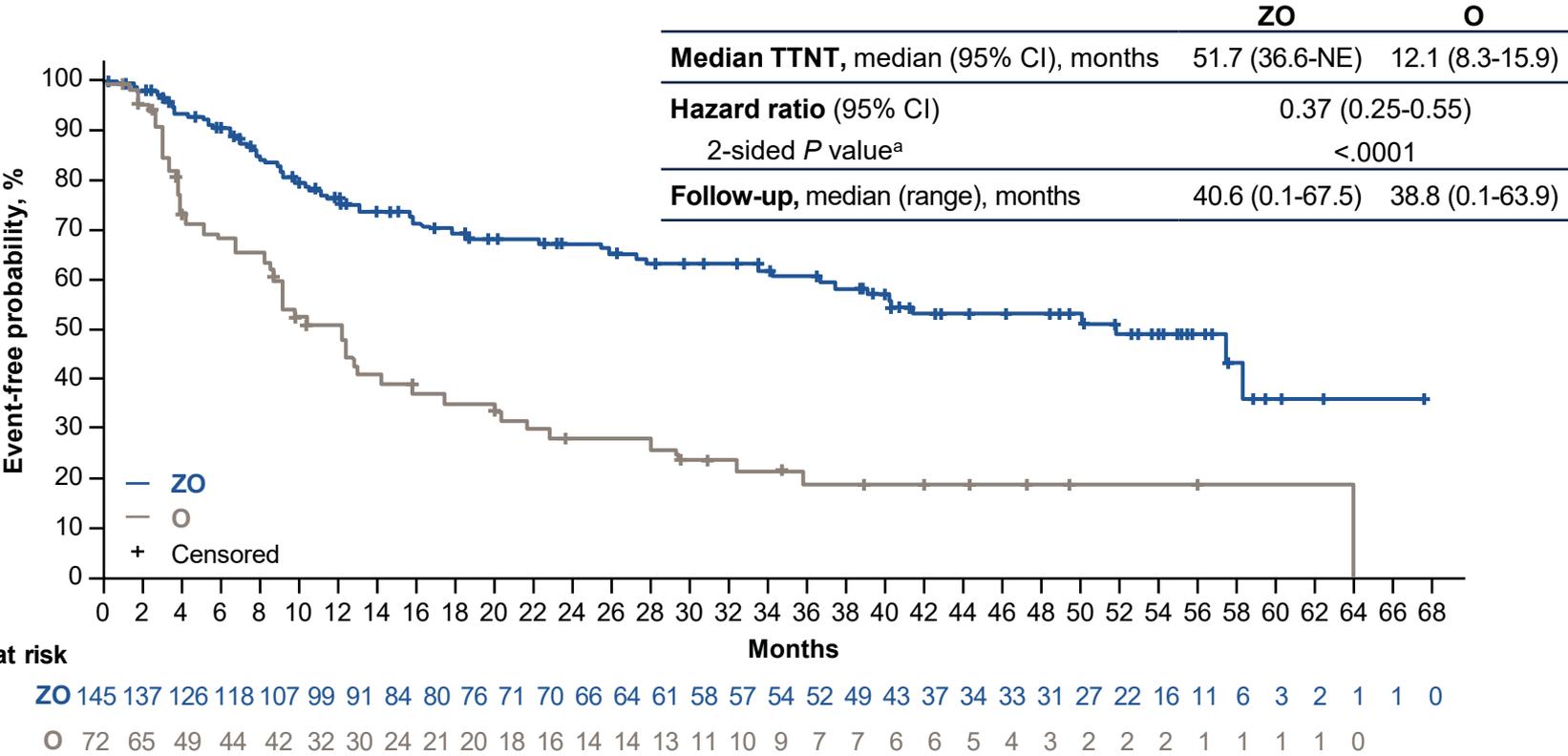
DOCR, duration of complete response; IRC, independent review committee; O, obinutuzumab; NE, not estimable; ZO, zanubrutinib + obinutuzumab.

PFS per IRC Was Longer in the ZO Arm



^aP value is descriptive.
 IRC, independent review committee; O, obinutuzumab; PFS, progression-free survival; ZO, zanubrutinib + obinutuzumab.

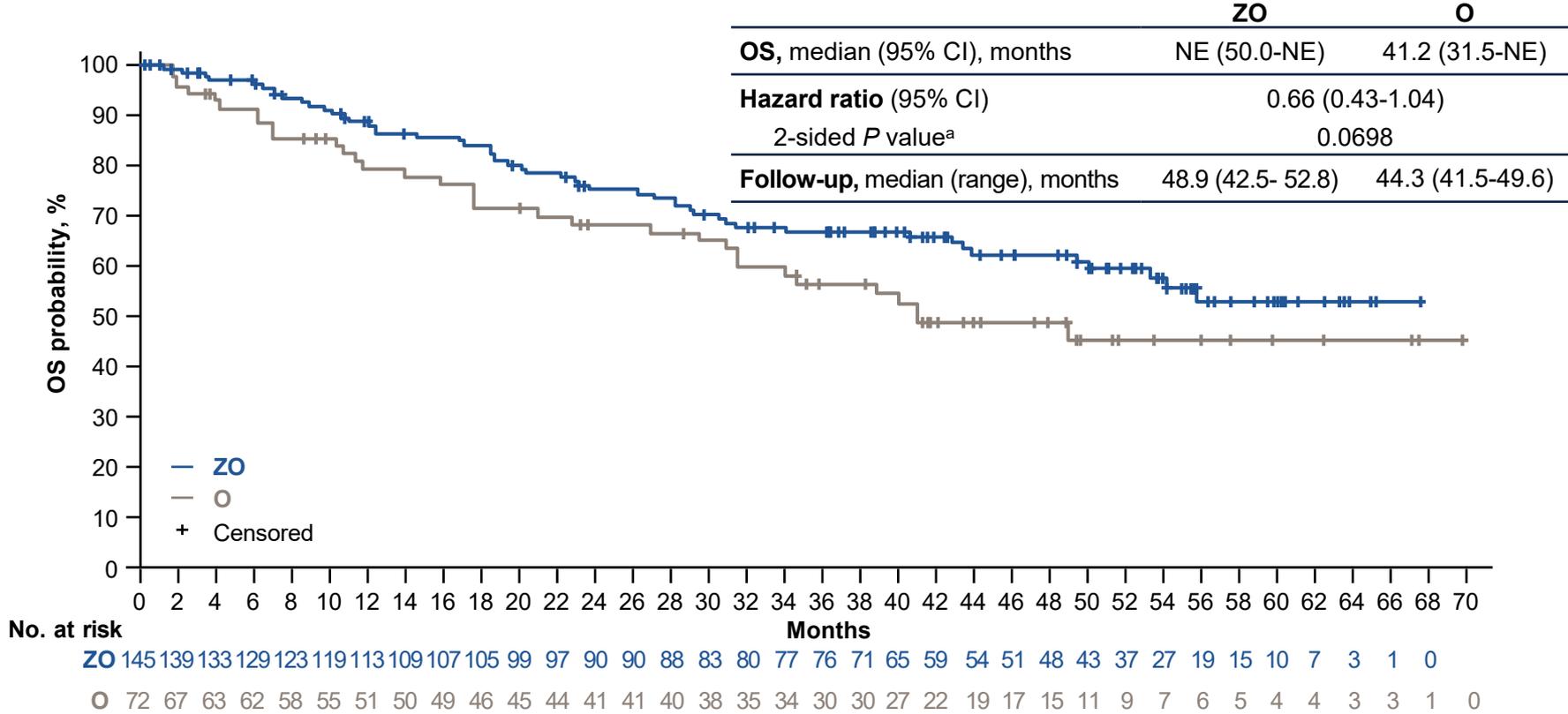
Time to New Anticancer Therapy Was Longer in the ZO Arm vs the O Arm



^aP value is descriptive.

TTNT, time to new anticancer therapy or crossover; NE, not estimable; O, obinutuzumab; ZO, zanubrutinib + obinutuzumab.

Overall Survival



^aP value is descriptive.

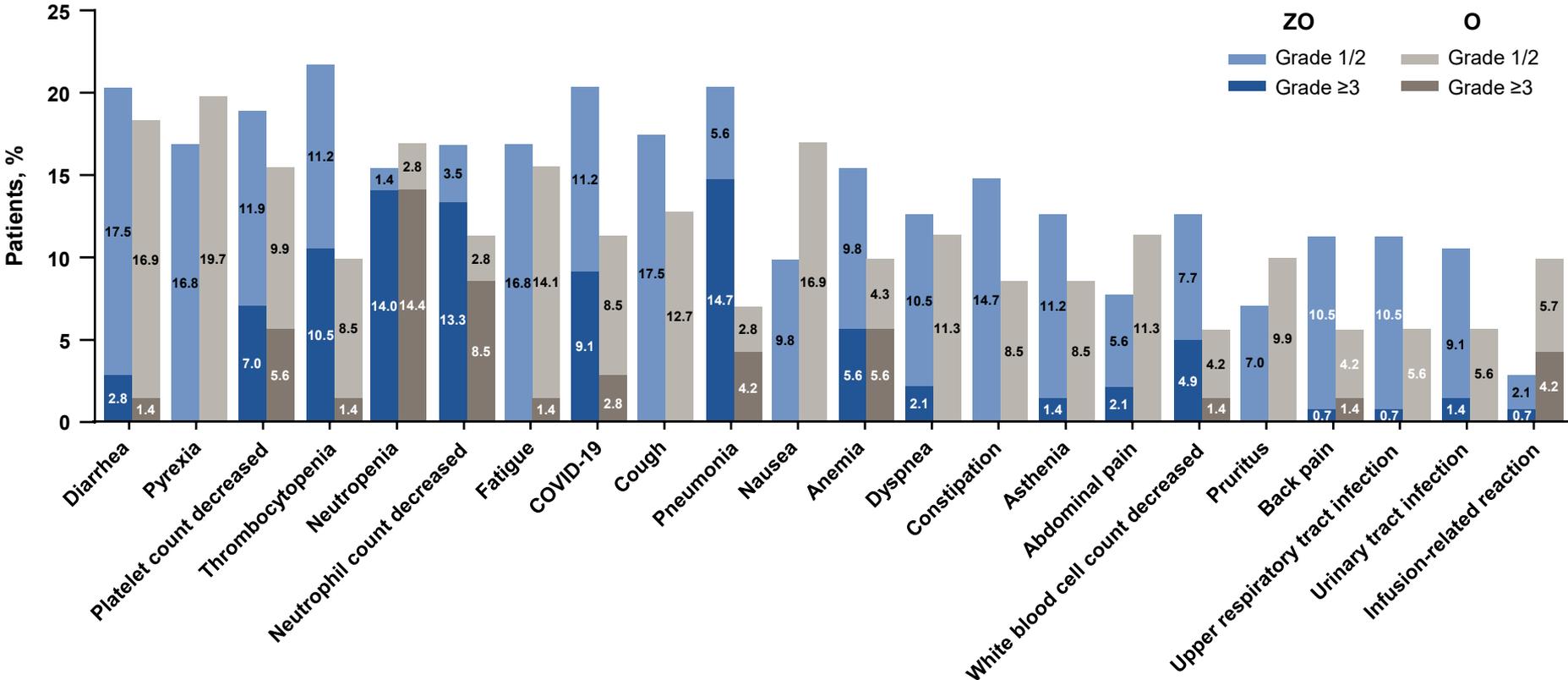
NE, not estimable; O, obinutuzumab; OS, overall survival; ZO, zanubrutinib + obinutuzumab.

Safety Summary

- With a longer median duration of exposure (ZO, 12.4 months; O, 6.5 months), the incidence of TEAEs and treatment-related TEAEs was generally higher in the ZO arm vs the O arm

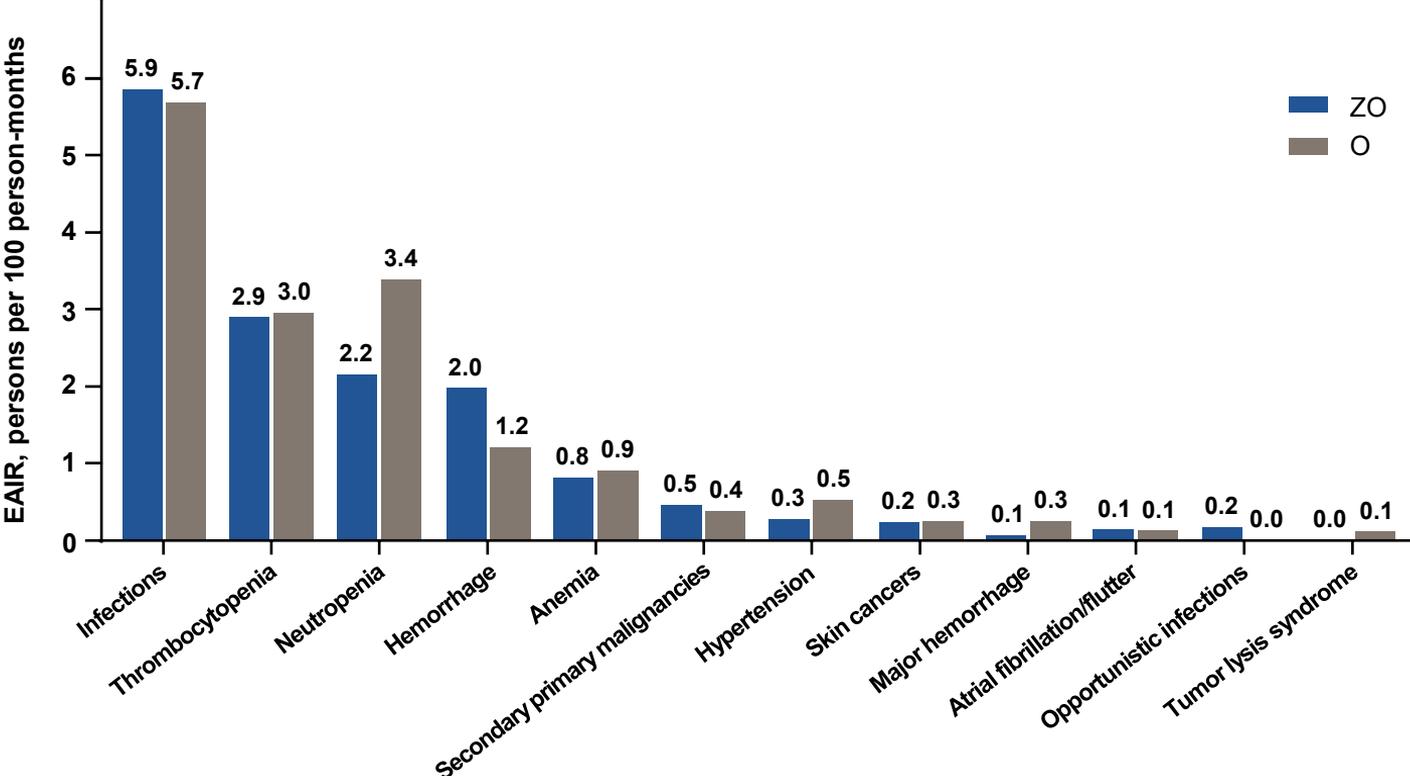
n (%)	ZO n=143	O n=71
Any TEAE	137 (95.8)	65 (91.5)
Any treatment-related TEAE	110 (76.9)	49 (69.0)
Grade ≥3	103 (72.0)	34 (47.9)
Treatment-related grade ≥3	62 (43.4)	19 (26.8)
Serious	75 (52.4)	22 (31.0)
Treatment-related serious	29 (20.3)	8 (11.3)
Leading to death	15 (10.5)	7 (9.9)
Treatment-related leading to death	2 (1.4)	1 (1.4)
Leading to treatment discontinuation	31 (21.7)	9 (12.7)
Treatment-related leading to treatment discontinuation	14 (9.8)	3 (4.2)

TEAEs Were Generally Consistent With the Known Safety Profiles of Zanubrutinib and Obinutuzumab



O, obinutuzumab; TEAE, treatment-emergent adverse event; ZO, zanubrutinib + obinutuzumab.

Exposure-Adjusted Incidence Rates (EAIRs)^a for TEAEs of Special Interest Were Comparable Between Arms



^aEAIR is calculated as the number of patients experiencing the event divided by the total exposure time from the first dose date to the first event date, or from the first dose date to the treatment-emergent period end date if there was no event.

EAIR, exposure-adjusted incidence rate; O, obinutuzumab; TEAE, treatment-emergent adverse event; ZO, zanubrutinib + obinutuzumab.

Final Analysis of ROSEWOOD: Conclusions

- The favorable risk-benefit profile of ZO in heavily pretreated patients with R/R FL was sustained
- Compared with O monotherapy, combination treatment with ZO demonstrated substantially
 - higher ORR and CR rate
 - longer DOR and PFS
- ZO had a manageable, consistent safety profile, with no new safety signals
- With a long median follow-up (34.6 months), these data support the potential benefit of ZO as a novel combination therapy for patients with R/R FL
- To further evaluate ZO in patients with R/R FL with ≥ 1 prior line of therapy, the phase 3 MAHOGANY study (NCT05100862) comparing ZO vs lenalidomide + rituximab is ongoing

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