Zanubrutinib + Obinutuzumab vs Last Prior Treatment in R/R Follicular Lymphoma: Growth Modulation Index From ROSEWOOD

Minoru Kanaya,[1] Judith Trotman,[2] Pier Luigi Zinzani,[3] Krimo Bouabdallah,[4] Shanmei Liao,[5] Laura Dima,[6] Dirk Weber,[7] Laurent Dumartin[6]

[1]Blood Disorders Center, Aiiku Hospital, Sapporo, Hokkaido, Japan; [2]Concord Repatriation General Hospital, University of Sydney, Concord, NSW, Australia; [3]Institute of Hematology "Seràgnoli", University of Bologna, Bologna, Italy; [4]Hôpital Haut-Lévêque, CHU Bordeaux, Pessac, France; [5]BeiGene (Shanghai) Co, Ltd, Shanghai, China; [6] BeiGene Medical Affairs, Paris, France; [7]BeiGene Switzerland GmbH, Basel, Switzerland

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Disclosures

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Name of LEAD PRESENTER: Minoru Kanaya		Institution or company/position: Blood Disorders Center, Aiiku Hospital	

	No	If yes, please specify the name of company, organization, your status.
employee or adviser of company and/or profit-making organization		Spouse (AbbVie)
profit of stock	x	
patent fee	x	
lecturer fee	x	
manuscript fee	x	
research expenses from company	x	
contributions or endowed chair	x	
fees of testimony, judgment, comment, etc.	x	
presents or other payment	x	
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Name of PRINCIPAL INVESTIGATOR: Pier Luigi Zinzani		Institution or company/position: Alfred Hospital and Monash University	

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profit of stock	x	
patent fee	x	
lecturer fee	x	
manuscript fee	x	
research expenses from company	x	
contributions or endowed chair	x	
fees of testimony, judgment, comment, etc.	x	
presents or other payment	x	
representative of organization for clinical study receiving research expenses from company	x	

Introduction

- FL is the second most common non-Hodgkin lymphoma[1]
- The phase 2 ROSEWOOD study (NCT03332017) compared efficacy and safety of ZO with O alone in patients with R/R FL who had received ≥2 prior lines of therapy[2]
  - Median PFS was longer with ZO (28.0 months; 95% CI, 16.1 months-NE) vs O (10.4 months; 95% CI, 6.5-13.8 months) (HR, 0.50; 95% CI, 0.33-0.75; *P*<.001) and compared favorably with the PFS of the last prior treatment (12.1 months)[2]
- The absence of a consensus standard of care in R/R FL and the heterogeneity of patient populations in trials limit indirect comparisons across different studies
- To overcome this challenge, the GMI considers each patient as their own control and evaluates treatment efficacy by comparing PFS durations with successive treatments

GMI, Growth Modulation Index; FL, follicular lymphoma; NE, not evaluable; O, obinutuzumab; PFS, progression-free survival; R/R, relapsed/refractory; ZO, zanubrutinib + obinutuzumab.

1. Carbone A, et al. *Nat Rev Dis Primers*. 2019;5:83-102; 2. Zinzani PL, et al. *J Clin Oncol*. 2023;41:5107-5117.

Study Design

- PFS was assessed by independent central review and defined in the ROSEWOOD study as the time from random assignment to the first documentation of progressive disease or death due to any cause, whichever occurred first[1]
- In this descriptive post hoc analysis, the efficacy of ZO in the sequence of treatments received by patients in the ROSEWOOD study was evaluated using the GMI clinical endpoint
- GMI was defined as the ratio of PFS_n/PFS_{n-1} for each patient[2-4]
  - A GMI of >1 indicated that the present treatment had extended the duration of PFS compared with the previous treatment[2-4]
  - A GMI of ≥1.33 is often used as a threshold for significant clinical activity[2-4]

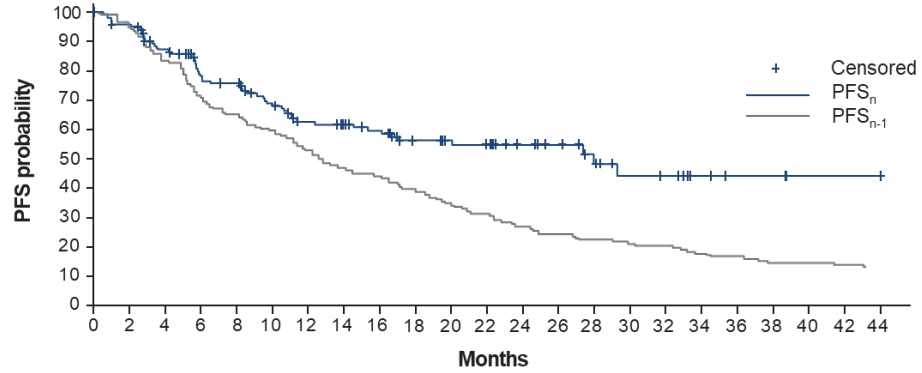
GMI, Growth Modulation Index; O, obinutuzumab; PFS, progression-free survival; PFS_n, PFS with the current treatment; PFS_n, PFS with the last prior treatment; POD24, progression of disease ≤24 months after starting first line of therapy; ZO, zanubrutinib + obinutuzumab.

1. Zinzani PL, et al. *J Clin Oncol*. 2023;41:5107-5117. 2. Penel N, et al. Ann Oncol. 2013;24:537-542; 3. Italiano A, et al. Cancers. 2020;12:3246-3255; 4. Cousin S, et al. Ann Oncol. 2013;24:2681-2685.

Median PFS With ZO Was Longer vs the Last Prior Treatment

- In ROSEWOOD, 145 patients were randomized to the ZO arm and 72 to the O arm
  - Patients with no PFS_{n-1} data available were excluded from the GMI analysis (ZO, n=5; O, n=3)

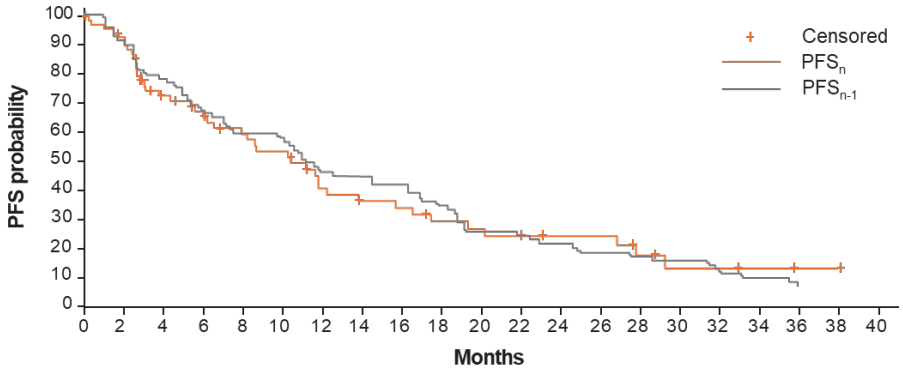
KM Curves of PFS_n and PFS_{n-1} in the ZO Arm



No. at risk

PFS_n	145	135	116	96	92	79	67	62	56	45	38	35	25	22	15	10	9	5	3	3	1	1	0
PFS_{n-1}	140	133	117	100	91	83	74	66	62	55	48	44	38	34	32	30	29	25	24	21	21	20	19

KM Curves of PFS_n and PFS_{n-1} in the O Arm



No. at risk:

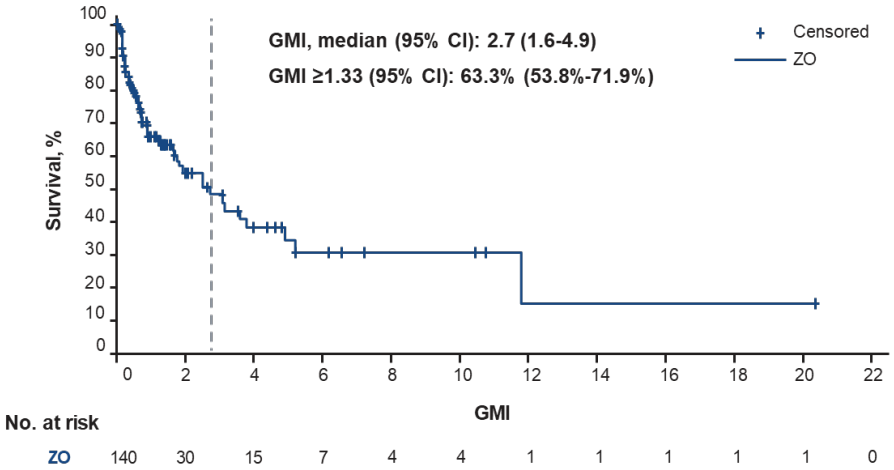
PFS_n	72	63	42	34	30	27	19	16	15	12	11	9	8	8	5	3	3	2	1	1	0	
PFS_{n-1}	69	63	54	47	41	40	32	31	29	24	18	17	15	13	12	11	9	7	6	5	5	

GMI, Growth Modulation Index; O, obinutuzumab; PFS, progression-free survival; PFS_n, PFS with the current treatment; PFS_n, PFS with the last prior treatment; POD24, progression of disease within 24 months of initiating the first line of therapy; ZO, zanubrutinib + obinutuzumab.

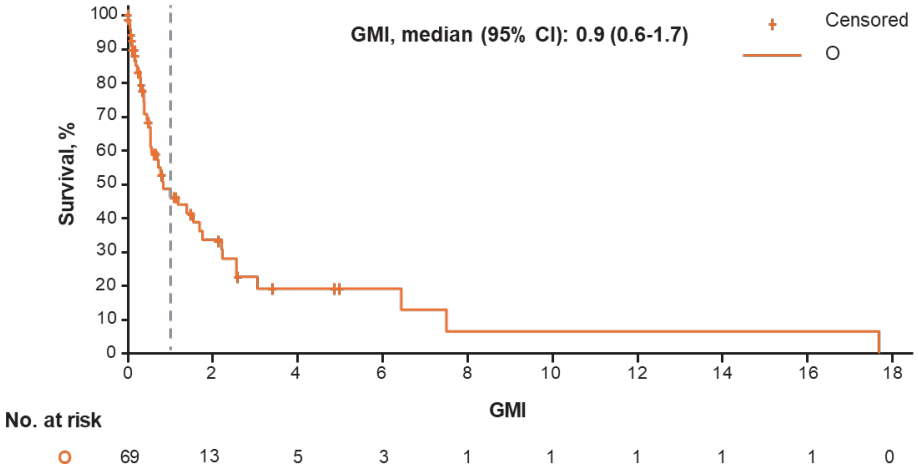
Most Patients Receiving ZO Had a Clinically Significant Improvement in PFS vs Their Last Prior Therapy

- In the ZO arm, 63.3% of patients (95% CI, 53.8%-71.9%) had a GMI of ≥1.33[a]

KM Analysis of GMI in the ZO Arm

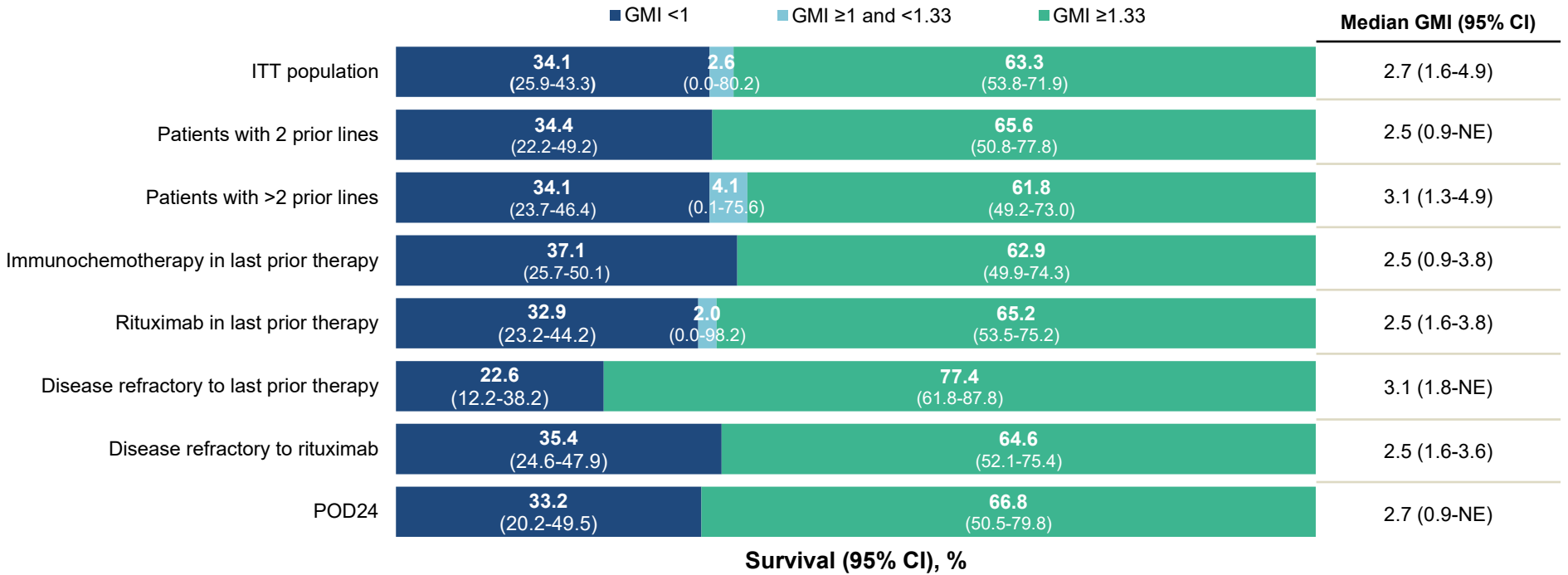


KM Analysis of GMI in the O Arm



[a] The GMI distribution, including the median and proportion in each GMI interval, was estimated using the Kaplan-Meier method; the 95% CIs for median GMI were estimated using the Brookmeyer-Crowley method; the 95% CIs for the proportion in each GMI interval were estimated using the Greenwood formula.
GMI, Growth Modulation Index; O, obinutuzumab; PFS, progression-free survival; ZO, zanubrutinib + obinutuzumab.

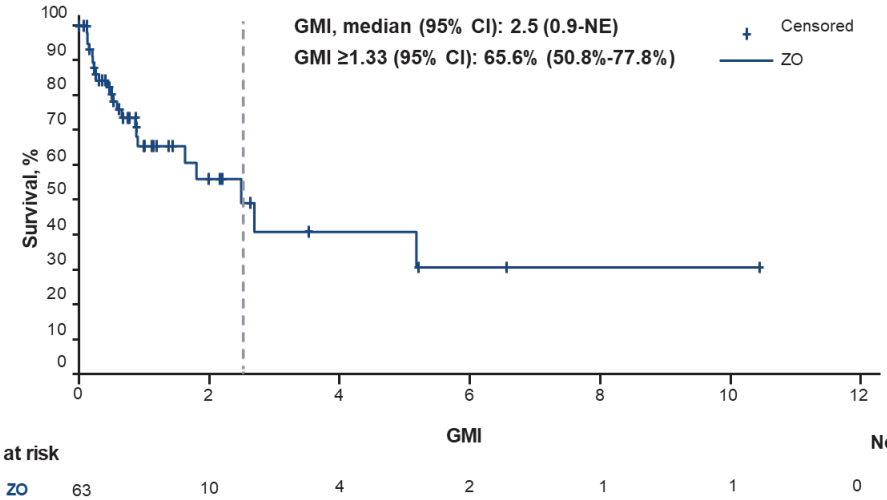
GMI Analysis Showed PFS Improvement Across Multiple Subgroups of Clinical Interest in the ZO Arm



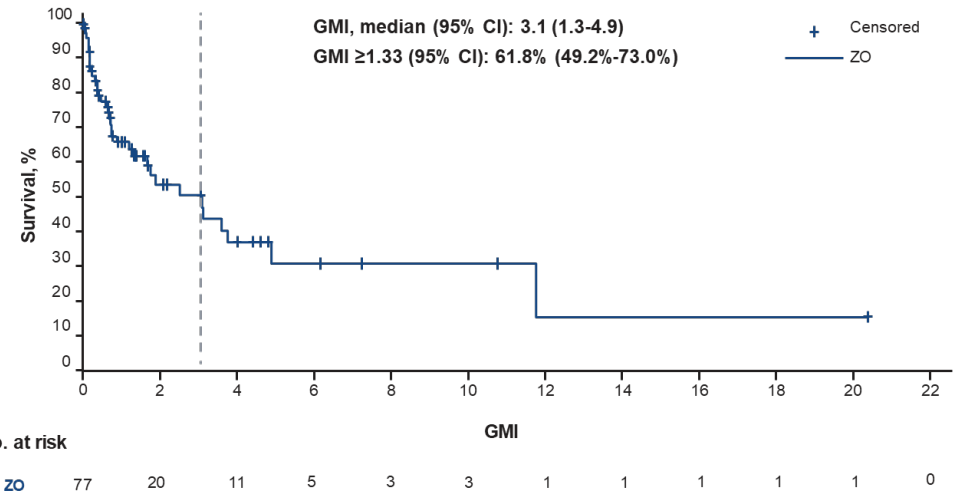
GMI, Growth Modulation Index; NE, not estimable; PFS, progression-free survival; POD24, progression of disease ≤24 months after starting first line of therapy; ZO, zanubrutinib + obinutuzumab.

With ZO, Patients Had Improved PFS Over Their Last Prior Treatment, Regardless of the Number of Prior Treatments

GMI in Patients With 2 Prior Lines of Therapy in the ZO Arm



GMI in Patients With >2 Prior Lines of Therapy in the ZO Arm



NE, not estimable; GMI, Growth Modulation Index; PFS, progression-free survival; ZO, zanubrutinib + obinutuzumab.

Conclusions

- This post hoc GMI analysis of data from ROSEWOOD allowed for the generation of comparative efficacy evidence for ZO in R/R FL using each patient as their own control
- The majority of patients with R/R FL receiving ZO had a significant improvement in PFS compared with the PFS with their last prior treatment, irrespective of the number of prior treatments
  - GMI was ≥1.33 in >60% of patients in the overall group and across multiple subgroups of clinical interest in the ZO arm
  - The median GMI of 2.7 in the ZO arm was more than double the 1.33 threshold for meaningful clinical activity compared with the last prior treatment
- These data further confirm the benefit of ZO as a novel treatment option for R/R FL

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Corresponding Author: Minoru Kanaya, minorukanaya0429@gmail.com