La rivoluzione terapeutica nel **linfoma** e nel **mieloma**

Napoli, Royal Hotel Continental • 14–15 Maggio 2026

FCL
Il prossimo futuro: BTKi, nuovi anticorpi, nuove COMBO

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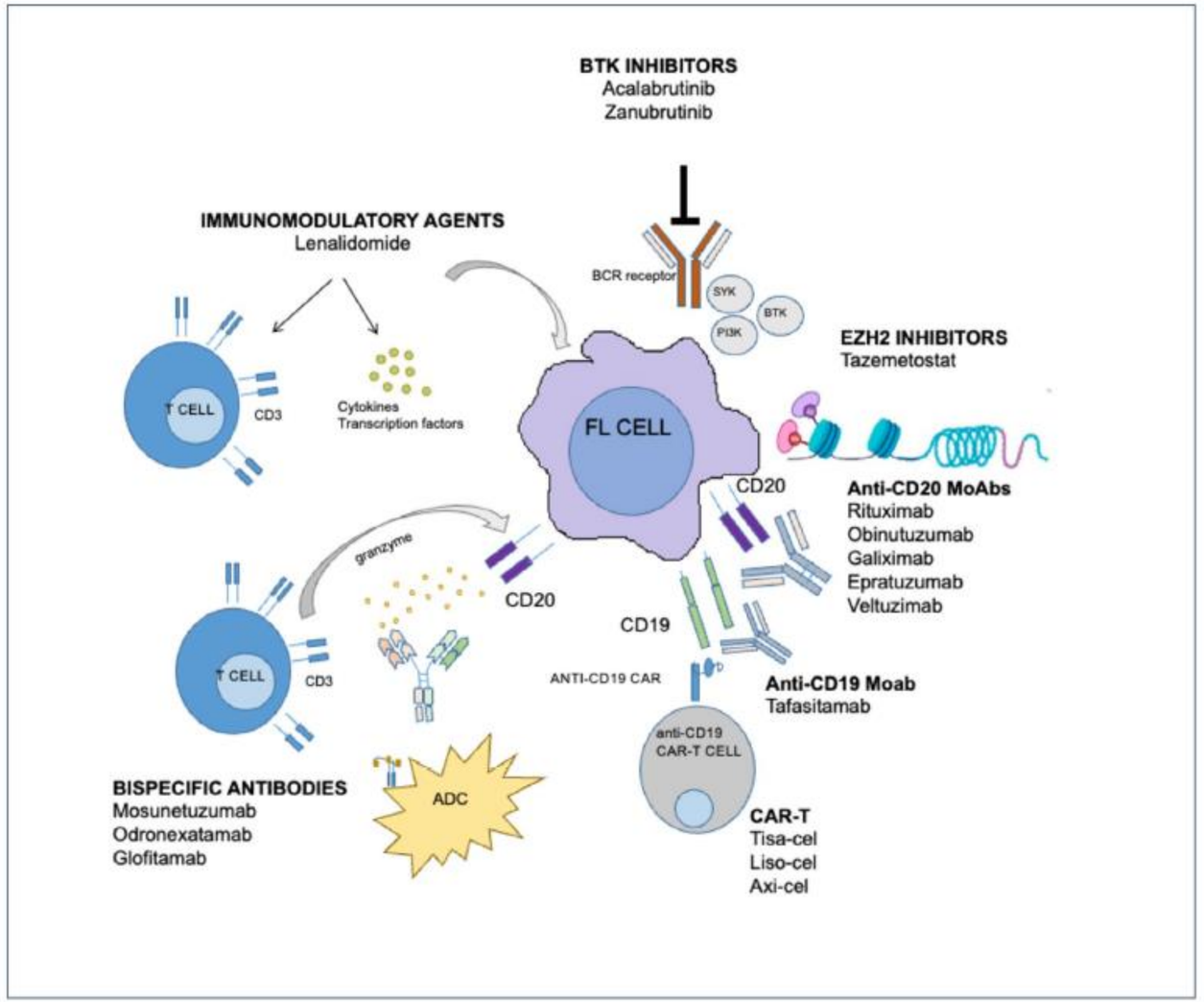
Disclosures of Massimo Gentile

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Menarini					x		
AbbVie,					x	x	
AstraZeneca					x	x	
GSK					x	x	
Beone					x	x	
J&J			x		x	x	
Pfizer						x	
Sanofi					x	x	

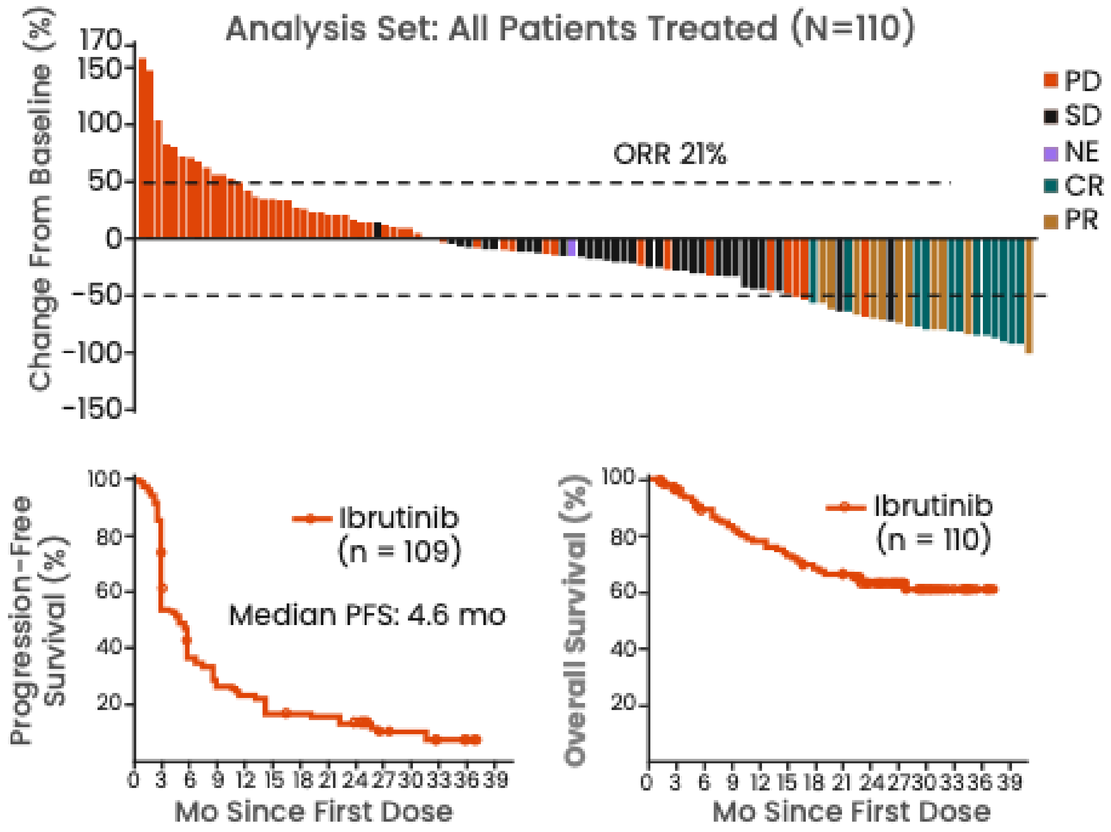
The main chemo-free strategies currently available



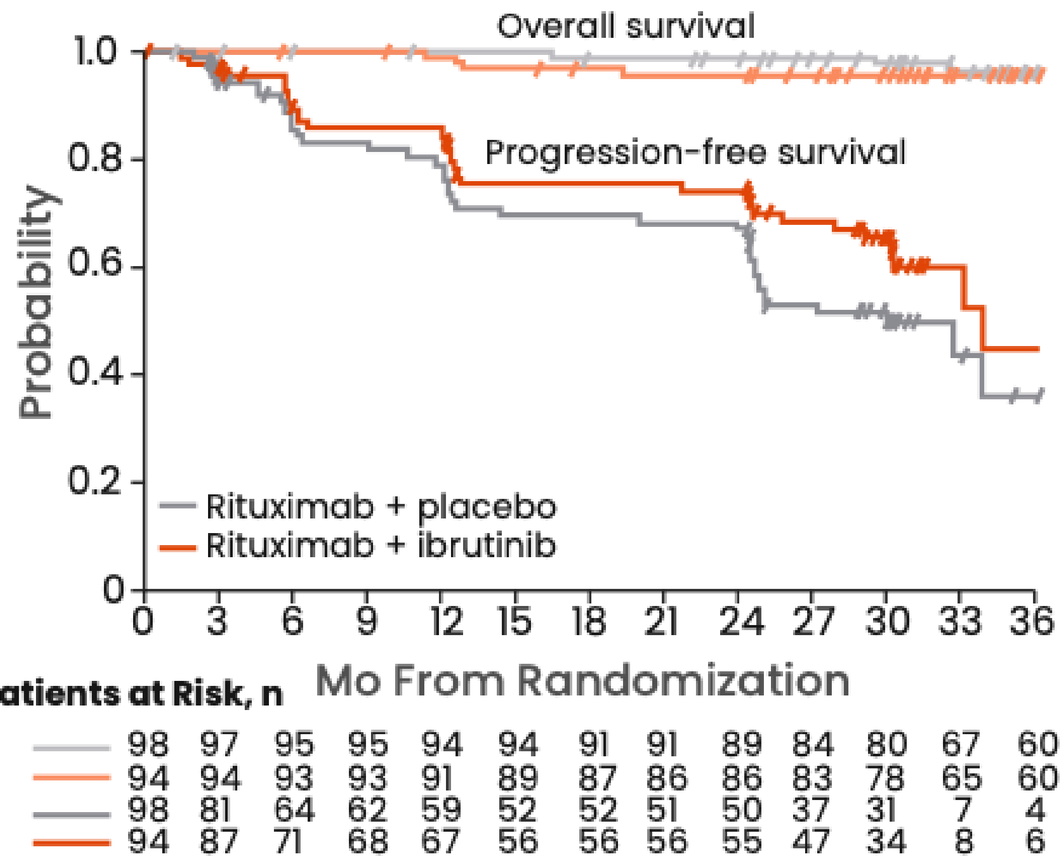
Martino EA & Gentile M; EJH 2026

Ibrutinib ± Rituximab in FL

DAWN Phase II: Ibru in R/R FL



SAKK 35/14 in 1L FL



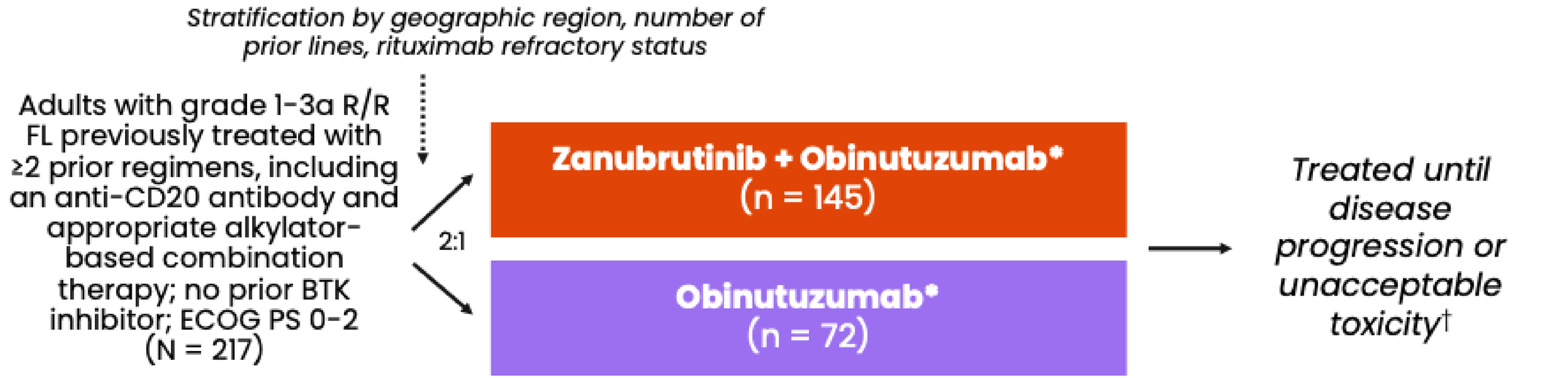
Patients at Risk, n

	98	97	95	95	94	94	91	91	89	84	80	67	60
	94	94	93	93	91	89	87	86	86	83	78	65	60
	98	81	64	62	59	52	52	51	50	37	31	7	4
	94	87	71	68	67	56	56	56	55	47	34	8	6

Gopal. JCO. 2018;36:2405. Ostenstad. Haematol Oncol. 2023;41:117.

ROSEWOOD: Next-Generation BTK Inhibitor Zanubrutinib With Obinutuzumab in R/R FL

Global, randomized, open-label phase II trial



*Zanubrutinib dosed at 160 mg PO BID. Obinutuzumab dosed at 1000 mg IV on Days 1, 8, 15 of cycle 1 and Day 1 of cycles 2-6, then Q8W to ≥20 doses. †Patients assigned to obinutuzumab with centrally confirmed PD or no response at 12 mo could cross over to receive combination therapy.

- **Primary endpoint:** IRC-assessed ORR according to Lugano classification
- **Key secondary endpoints:** investigator-assessed ORR, CR, DoR, PFS, OS, safety

Zinzani. JCO. 2023;41:5107.

ROSEWOOD: Response

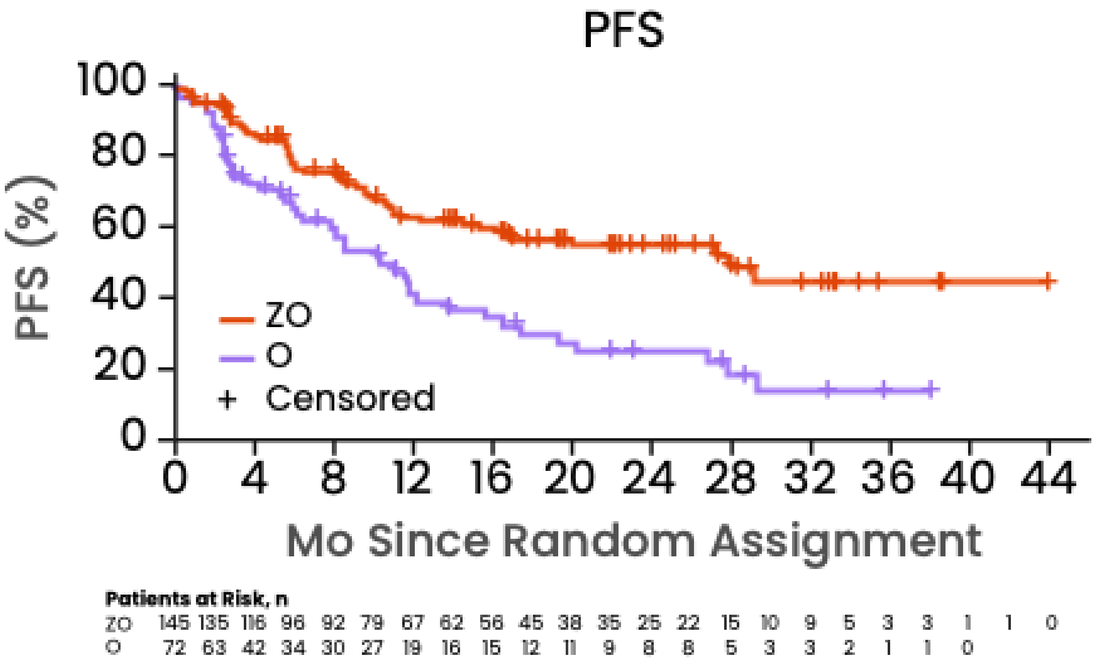
Response by IRC	Zanubrutinib + Obinutuzumab (n = 145)	Obinutuzumab (n = 72)	*P* Value
ORR, %	69	46	.001
Best overall response, n (%)			
• CR	57 (39)	14 (19)	.004
• PR	43 (30)	19 (26)	--
Median DoR, mo (95% CI)	NE (25.3-NE)	14.0 (9.2-25.1)	--

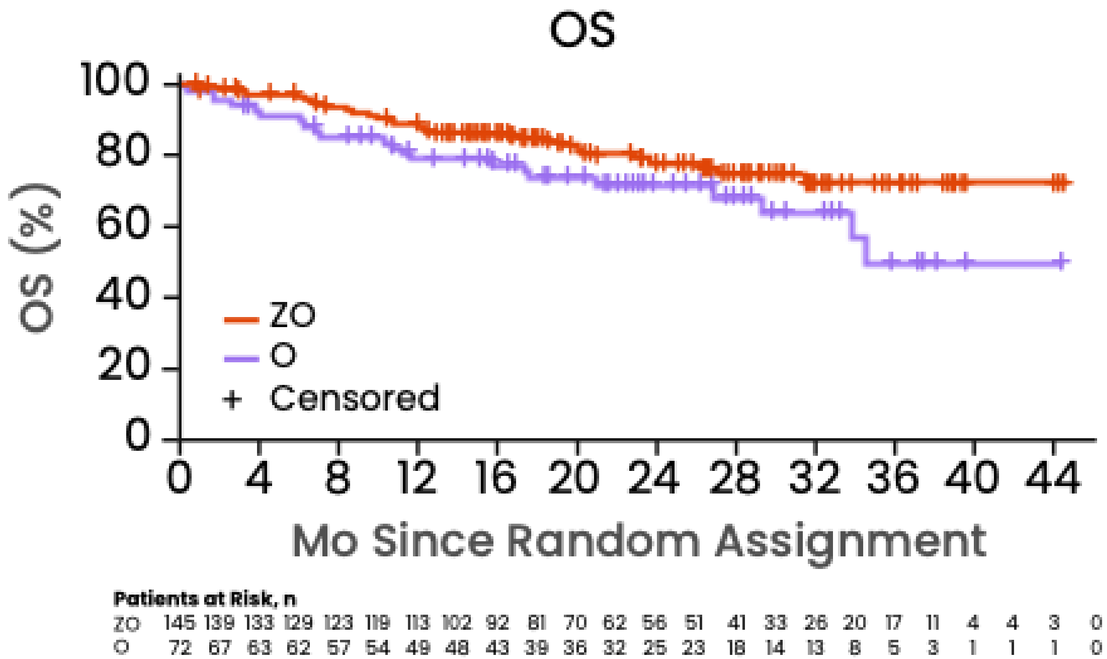
Median follow-up: 20.2 mo

- Combination with improved ORR vs obinutuzumab across most patient subgroups, except in patients with bulky disease
- 34 patients in the obinutuzumab arm crossed over to receive zanubrutinib and obinutuzumab after PD, and in 1 patient, crossover to receive zanubrutinib and obinutuzumab occurred after SD with ≥12 mo follow-up

Zinzani. JCO. 2023;41:5107.

ROSEWOOD: PFS and OS





hazard ratio, 0.50 [95% CI, 0.33 to 0.75]; P < .001

Zinzani. JCO. 2023;41:5107.

ROSEWOOD: Any-Grade and Grade ≥3 TEAEs and AEs of Special Interest

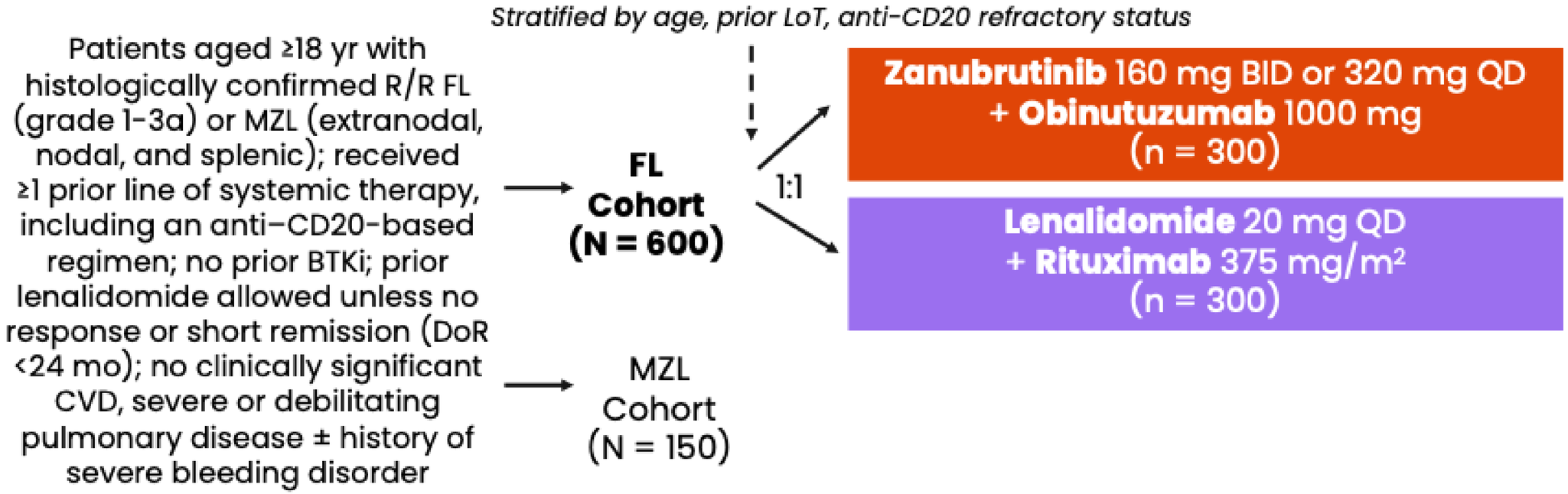
AE, n (%)	Zanubrutinib + Obinutuzumab (n = 143)		Obinutuzumab (n = 71)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
≥1 TEAE	135 (94)	90 (63)	64 (90)	34 (48)
Thrombocytopenia	51 (36)	22 (15)	17 (24)	5 (7)
Neutropenia	42 (29)	35 (24)	20 (28)	16 (23)
Diarrhea	26 (18)	4 (3)	12 (17)	1 (1)
Fatigue	22 (15)	0 (0)	10 (14)	1 (1)
Constipation	19 (13)	0 (0)	6 (8)	0 (0)
Pyrexia	19 (13)	0 (0)	14 (20)	0 (0)
Cough	18 (13)	0 (0)	9 (13)	0 (0)
Pneumonia	17 (12)	14 (10)	5 (7)	3 (4)
Asthenia	17 (12)	1 (1)	6 (8)	0 (0)
Dyspnea	16 (11)	3 (2)	7 (10)	0 (0)
Back pain	15 (10)	1 (1)	4 (6)	1 (1)
Anemia	16 (11)	7 (5)	7 (10)	4 (6)
COVID-19	14 (10)	8 (6)	7 (10)	2 (3)

Any-Grade AESI, n (%)	Zanubrutinib + Obinutuzumab (n = 143)	Obinutuzumab (n = 71)
Atrial fibrillation	4 (3)	1 (1)
Hypertension	5 (3)	4 (6)
Bleeding	40 (28)	9 (13)
Major hemorrhage	2 (1)	2 (3)
Infections	79 (55)	29 (41)

Zinzani. JCO. 2023;41:5107.

MAHOGANY: Zanubrutinib or Lenalidomide in Combination With an Anti-CD20 mAb in R/R FL or MZL

Ongoing international, open-label, randomized phase III study



Primary endpoint: PFS by BIRC

Key secondary endpoints: PFS by INV, ORR and DoR by BIRC and INV, OS

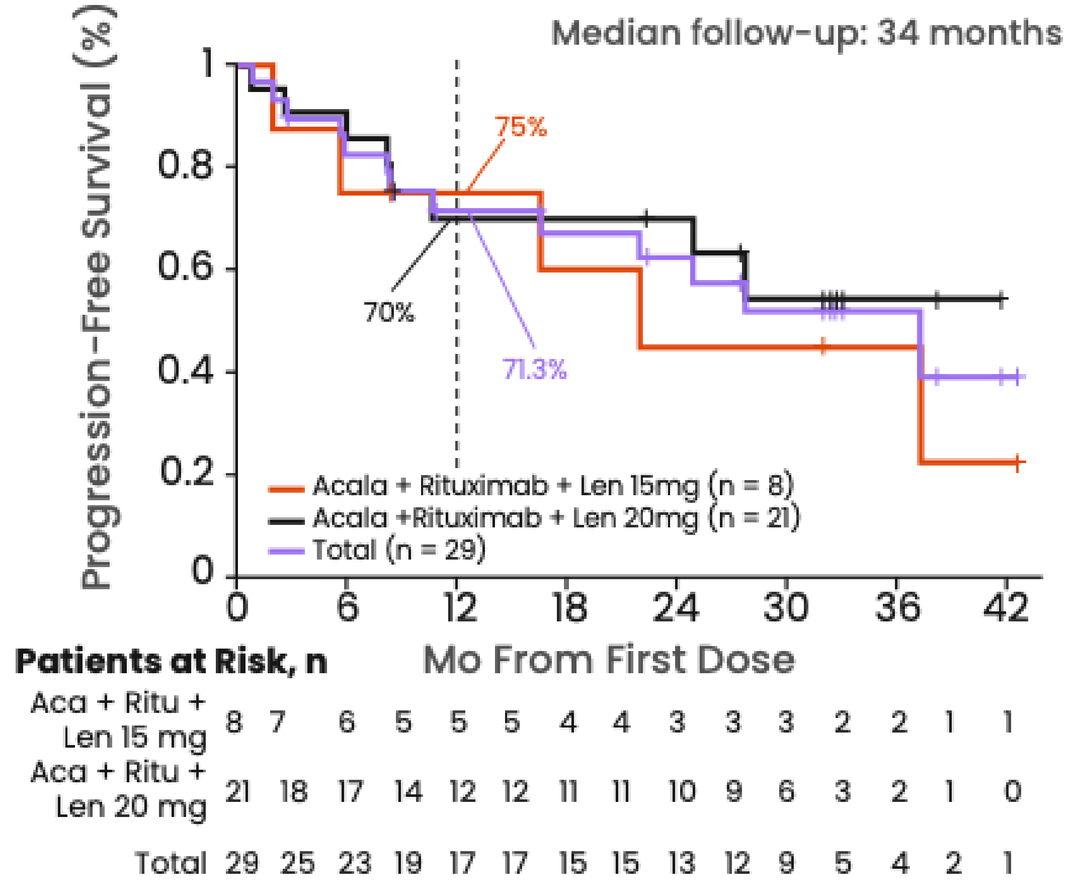
Sehn. ICML 2023. Abstr 994. NCT05100862.

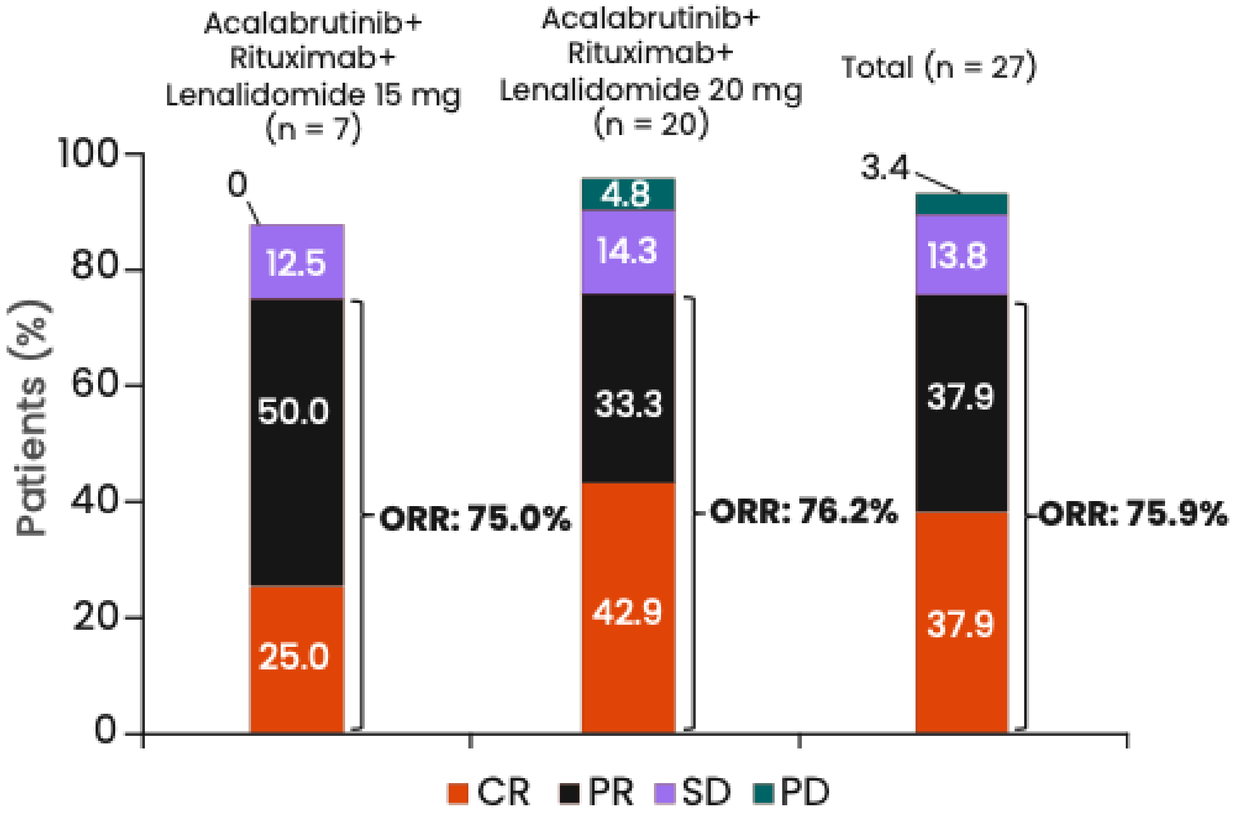
Phase Ib Open-Label ACE-LY-003: Acalabrutinib + R² in R/R FL

Subgroup	Acalabrutinib + Rituximab + Lenalidomide 15 mg (n = 8)	Acalabrutinib + Rituximab + Lenalidomide 20 mg (n = 21)	Total (N = 29)
Median age, yr (range) • Age ≥65 yr	65 (51-76) 4 (50.0)	64 (44-75) 10 (47.6)	64 (44-76) 14 (48.3)
Male, n (%)	7 (87.5)	15 (71.4)	22 (75.9)
White, n (%)	7 (87.5)	17 (81.0)	24 (82.8)
Tumor bulk, n (%) • ≥5 cm • ≥10 cm	 2 (25.0) 1 (12.5)	 11 (52.4) 1 (4.8)	 13 (44.8) 2 (6.9)
FLIPI score, n (%) • Low (0-1) • Intermediate (2) • High (3-5)	 2 (25.0) 4 (50.0) 2 (25.0)	 6 (28.6) 8 (38.1) 7 (33.3)	 8 (27.6) 12 (41.4) 9 (31.0)
BM involvement, n (%)	3 (37.5)	7 (33.3)	10 (34.5)
Extranodal disease, n (%)	6 (75.0)	14 (66.7)	20 (69.0)
High tumor burden per GELF criteria, n (%)	4 (50.0)	16 (76.2)	20 (69.0)
LDH >ULN, n (%)	1 (12.5)	6 (28.6)	7 (24.1)
Prior systemic regimens, median n (range)	2.0 (1-2)	1.0 (1-5)	1.0 (1-5)

Strati. Br J Haematol. 2025;206:887.

Acalabrutinib + R² in R/R FL: PFS and Response





Strati. Br J Haematol. 2025;206:887.

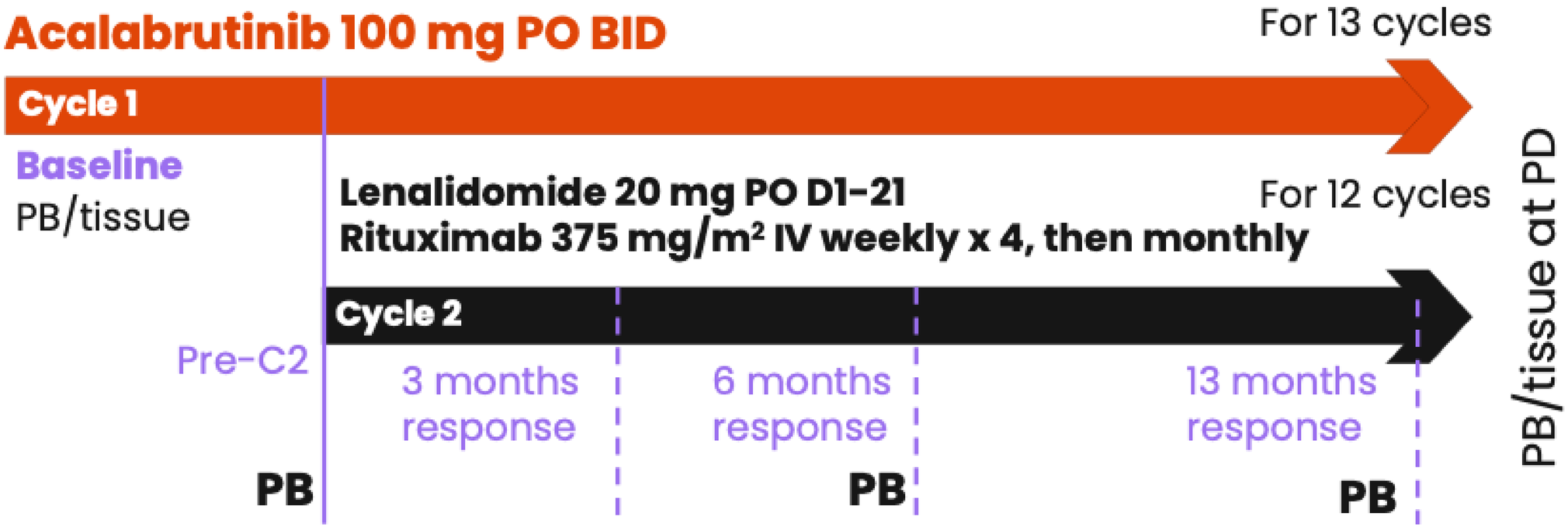
Acalabrutinib + R² in R/R FL: Treatment-Emergent AEs

TEAE, n (%)	Acalabrutinib + Rituximab + Lenalidomide 15 mg (n = 8)		Acalabrutinib + Rituximab + Lenalidomide 20 mg (n = 21)		Total (N = 29)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Neutropenia	1 (12.5)	1 (12.5)	14 (66.7)	10 (47.6)	15 (51.7)	11 (37.9)
COVID-19 pneumonia	0	0	4 (19.0)	4 (19.0)	4 (13.8)	4 (13.8)
Rash	2 (25.0)	0	5 (23.8)	2 (9.5)	7 (24.1)	2 (6.9)
Thrombocytopenia	1 (12.5)	0	2 (9.5)	2 (9.5)	3 (10.3)	2 (6.9)
Atrial fibrillation	1 (12.5)	0	1 (4.8)	1 (4.8)	2 (6.9)	1 (3.4)
Anemia	2 (2.5)	1 (12.5)	2 (9.5)	0	4 (13.8)	1 (3.4)
Thrombocytopenia	1 (12.5)	0	4 (19.0)	2 (9.5)	5 (17.2)	2 (6.9)
Hemorrhage	1 (12.5)	0	11 (52.4)	0	12 (41.4)	0
Hepatotoxicity	0	0	2 (9.5)	0	2 (6.9)	0
Hypertension	0	0	2 (9.5)	0	2 (6.9)	0
Infections	5 (62.5)	2 (25)	15 (71.4)	10 (47.6)	20 (69)	12 (41.4)
Pneumonitis	0	0	0	0	0	0
Second primary cancers	0	0	1 (4.8)	1 (4.8)	1 (3.4)	1 (3.4)
Tumor lysis syndrome	0	0	1 (4.8)	1 (4.8)	1 (3.4)	1 (3.4)

The incidence of grade ≥3 serious TEAEs was 37.5% and 52.4% in the lenalidomide 15-mg and 20-mg cohorts, respectively

Strati. Br J Haematol. 2025;206:887.

Frontline Acalabrutinib + R² for Patients With Advanced Stage FL With High Tumor Burden

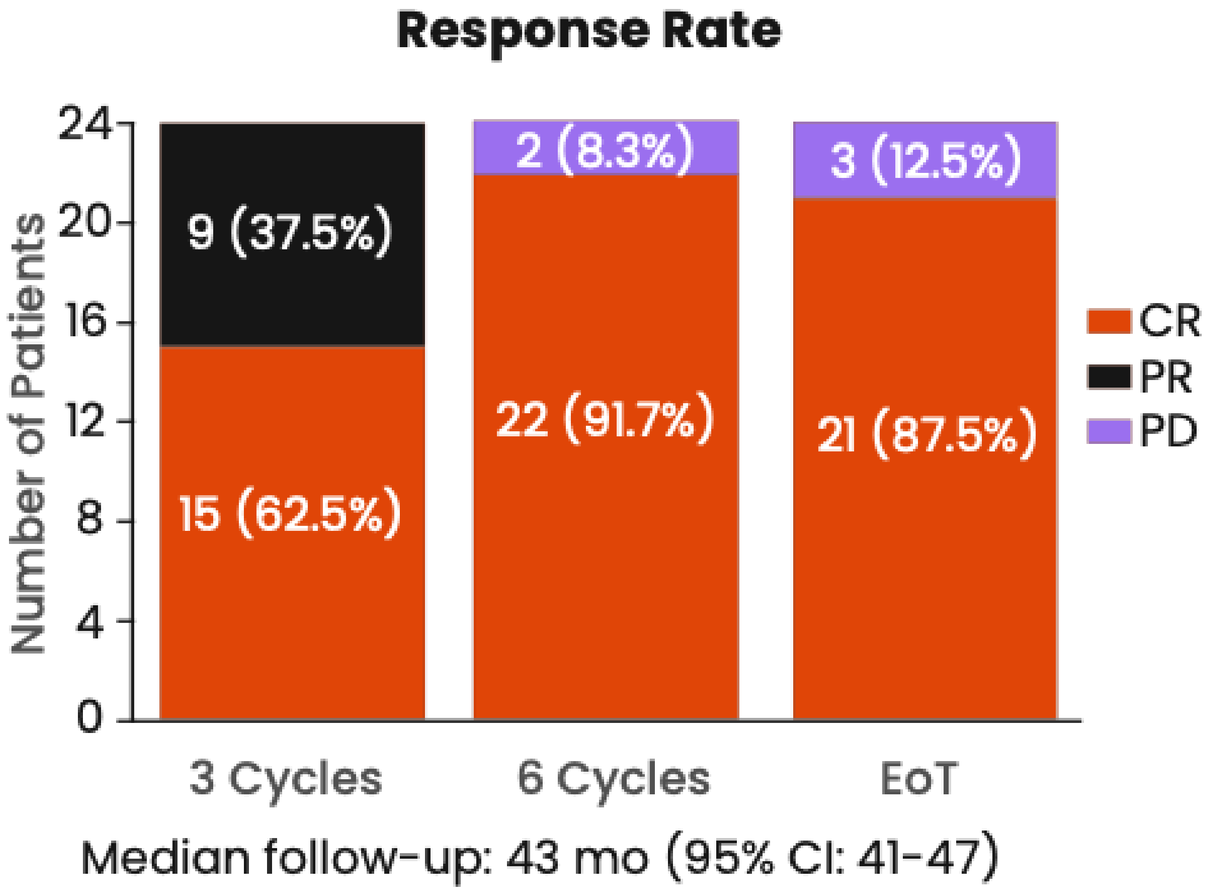


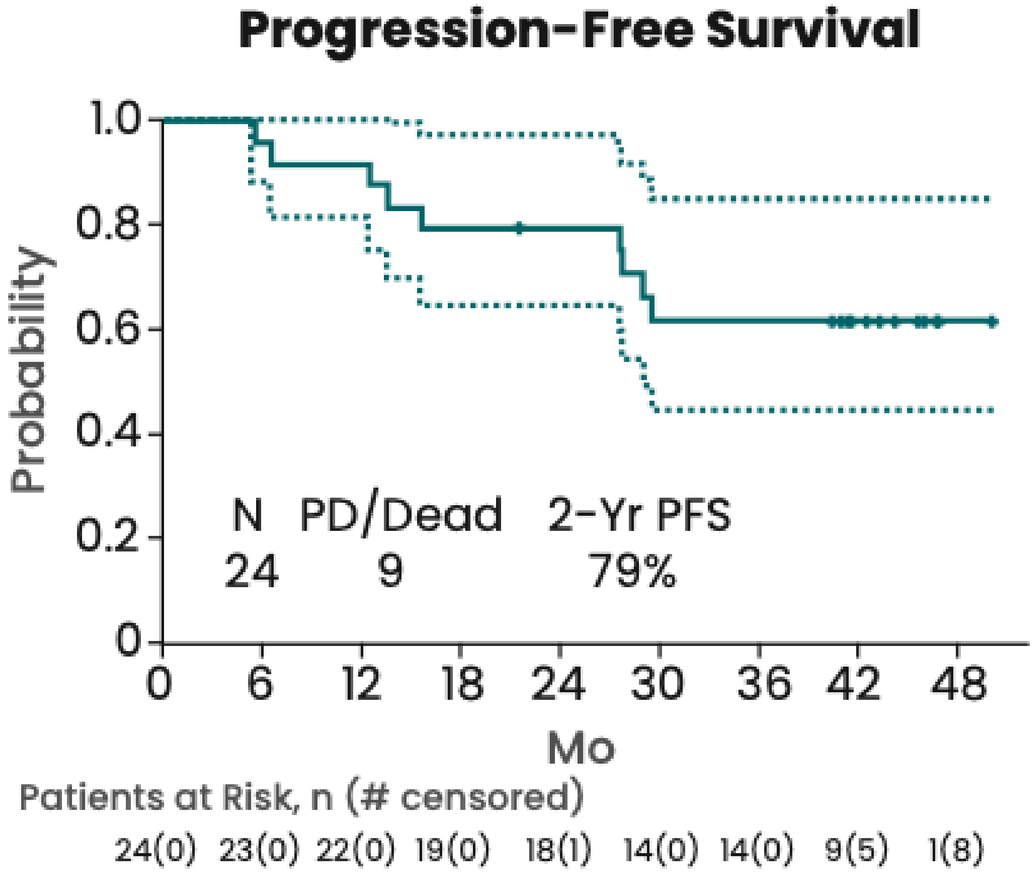
The primary endpoint was best CR rate;
The secondary endpoints were ORR, duration of response measured as CR at 30 months, POD24 rate, PFS, OS and safety.

Strati. Nat Commun. 2025;16:7300.

Frontline Acalabrutinib + R^2: Efficacy

Best ORR was 100% and best CR rate was 92%.





Strati. Nat Commun. 2025;16:7300.

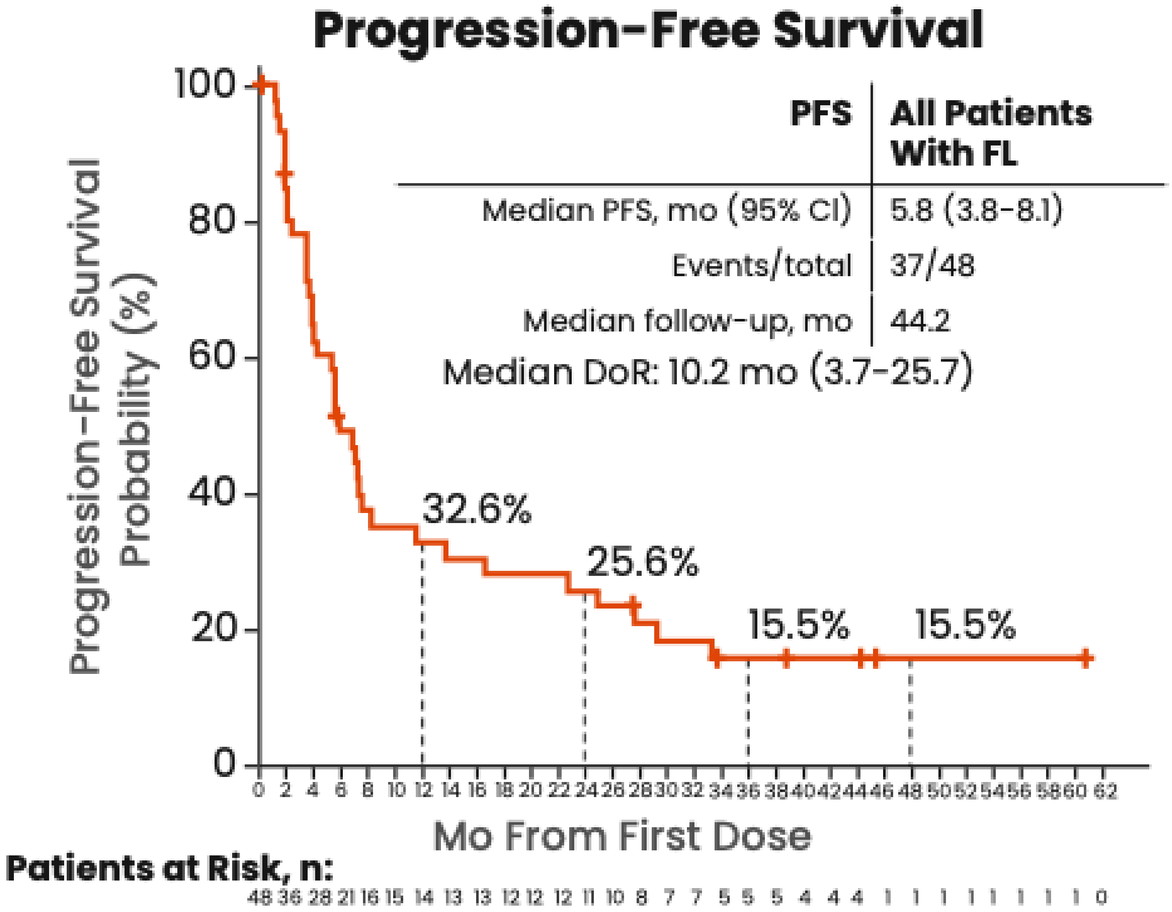
Pirtobrutinib in Patients with R/R FL

Patients with R/R FL: N=48

- Median age: 64.5 y (range 37-85)
- Median prior lines of therapy: 3 (range 1-12)
- Pirtobrutinib: 200 mg once daily

Response, %	Patients With FL (n = 48)
ORR	52.1
Best Response, n (%)	
CR	8 (16.7)
PR	17 (35.4)
SD	11 (22.9)
PD	11 (22.9)
NE	1 (2.1)

Median follow-up: 40.5 mo



Shah. Blood Advances. 2025;[Epub].

Safety of Pirtobrutinib in Patients With R/R FL (n = 48)

AE, %	All-Cause AEs (≥15%)		TRAEs	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Diarrhea	29.2	2.1	8.3	0
Fatigue	25.0	4.2	14.6	0
Nausea	22.9	2.1	12.5	2.1
Arthralgia	18.8	0	8.3	0
Back pain	18.8	0	0	0
Neutropenia	16.7	14.6	10.4	8.3
AE of Interest, %	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**
Infections	56.3	18.8	12.5	0
Rash	14.6	2.1	8.3	2.1
Bruising	10.4	0	2.1	0
Hemorrhage	6.3	0	2.1	0
Hypertension	6.3	2.1	0	0
Atrial fibrillation/flutter	2.1	0	2.1	0

Median time on treatment: 7.6 mo (0.6-63); dose reductions in 4 patients (8.3%) and discontinuations in 2 patients (4.2%) due to TEAS

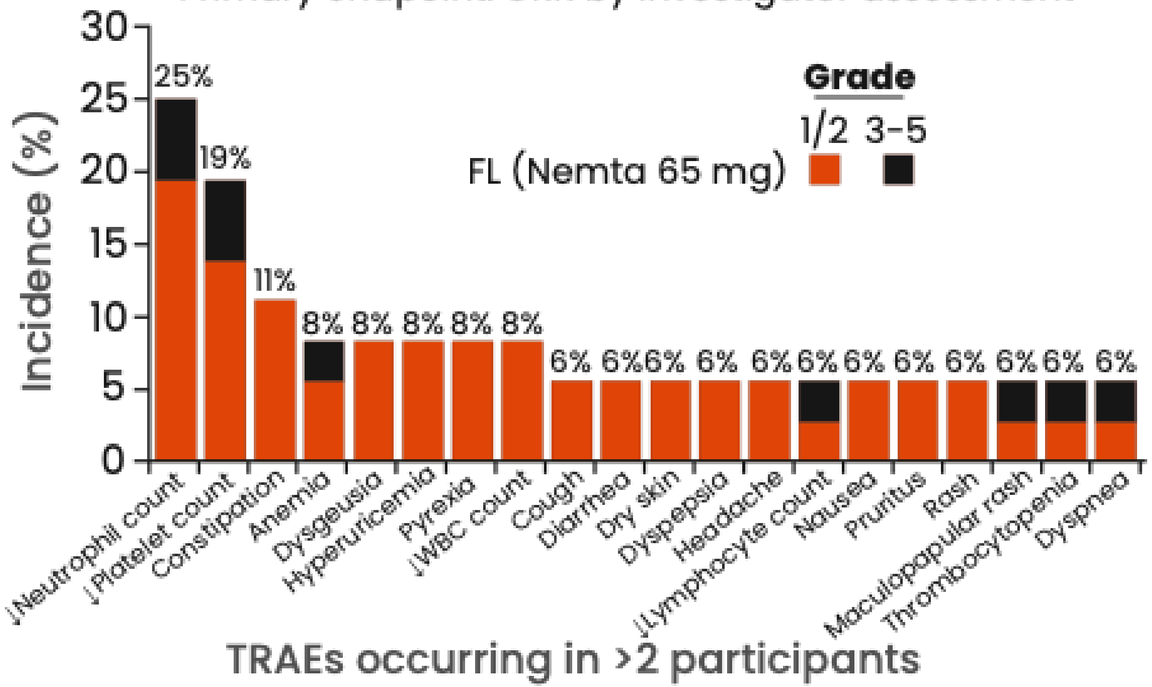
Shah. Blood Advances. 2025;[Epub].

Phase II BELLWAVE-003: Nemtabrutinib in R/R FL

BELLWAVE-003 trial design

Cohort G: R/R FL to CIT and IMiDs (n = 36) → Nemtabrutinib 65 mg QD until toxicity, PD, or withdrawal

Primary endpoint: ORR by investigator assessment



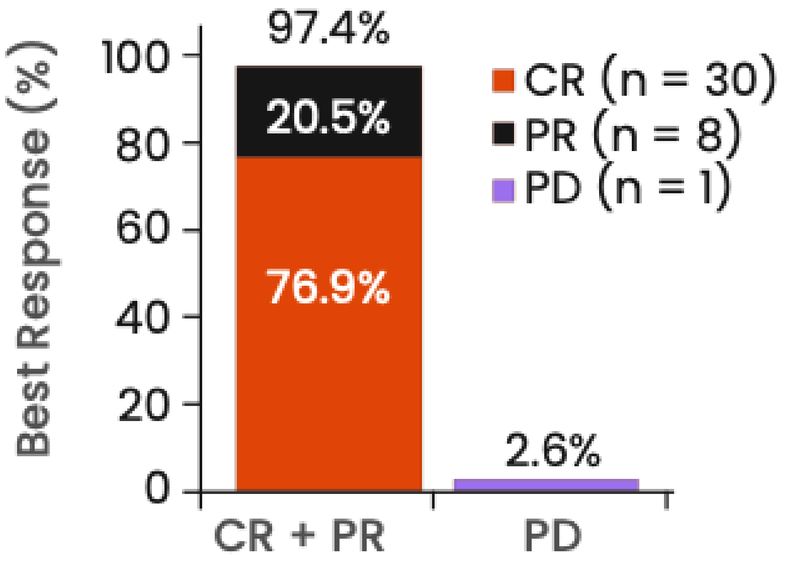
Response	N = 29
ORR, % • CR • PR	41 3 38
SD, %	21
PD, %	24
Not assessed/tx discontinued, %	14
Median DoR, mo	5.8
PFS	
Median PFS, mo • 6-mo PFS, %	5.5 34

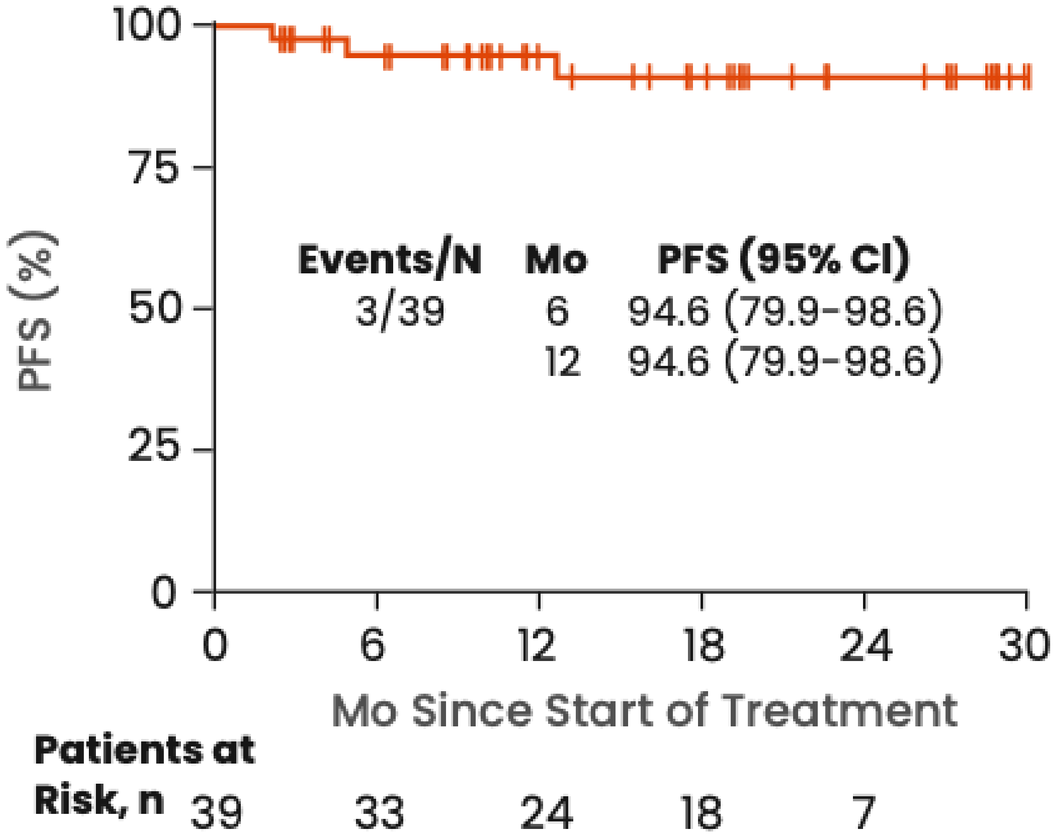
Jurczak. ASH 2024. Abstr 1634. NCT04728893.

Loncastuximab Tesirine + Rituximab in R/R FL

Response adapted design, up to 39 wk of treatment

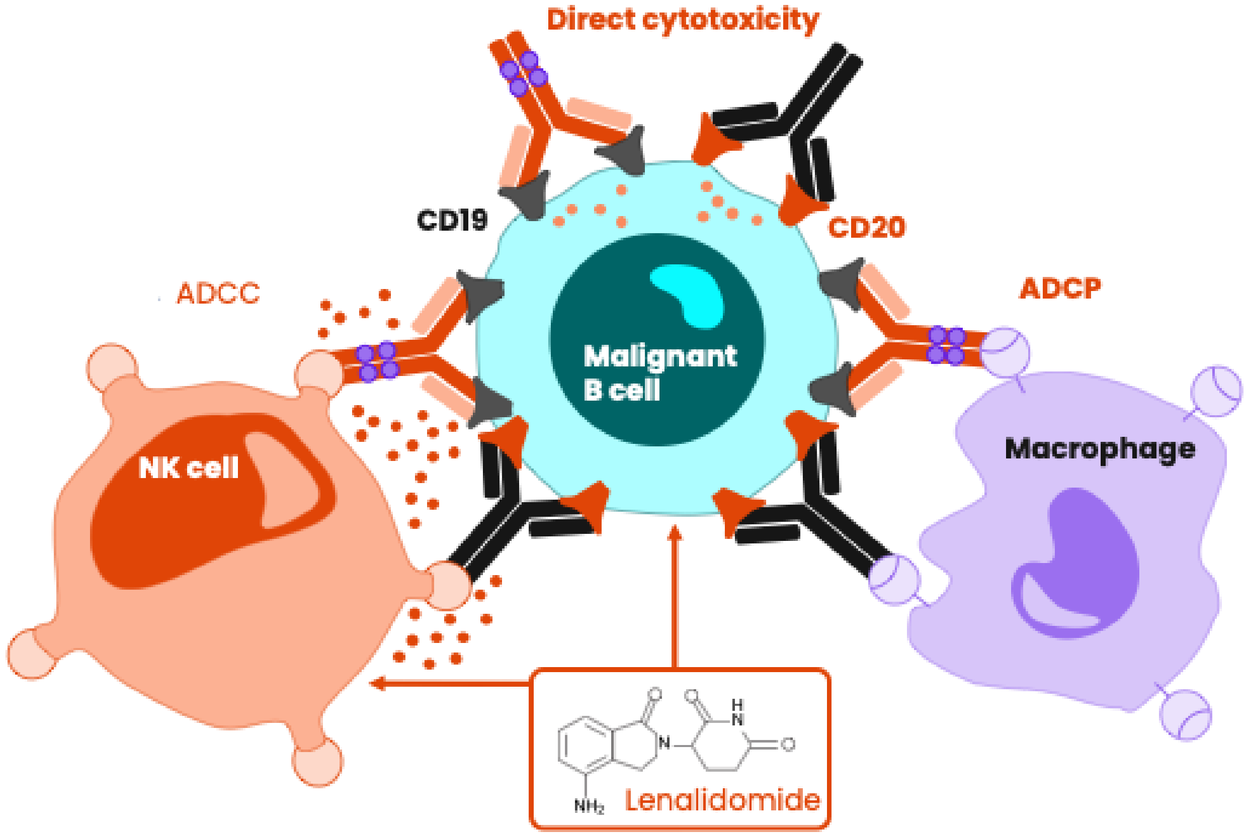
Median follow-up: 18 mo





Alderuccio. Lancet Haematol. 2025;12:e23.

inMIND: Evaluated the Efficacy and Safety of Adding Tafasitamab to Len + R in Patients With R/R FL or MZL



Tafasitamab (Fc-Modified, Anti-CD19 mAb)

Affinity-matured CD19-binding site

Modified Fc portion

- ADCC
- ADCP
- Direct cytotoxicity

Rituximab (Anti-CD20 mAb)

- ADCC
- ADCP
- Direct cytotoxicity
- CDC

Targeting CD19 and CD20 together with lenalidomide immunomodulation

Adapted from Dull. Ther Adv Hematol. 2021:12:20406207211027458. Cheson. Blood Cancer J. 2021;11:68.

InMIND: Tafasitamab + R² vs R² Alone in R/R FL or MZL

Global, double-blind, placebo-controlled, randomized phase III trial

- Tafasitamab: Fc-engineered humanized anti-CD19 mAb

Stratification: FL: POD24 (yes vs no), refractory to anti-CD20 tx (yes vs no), prior lines tx (<2 vs ≥2)
MZL: prior lines tx (<2 vs ≥2)

Adults with R/R FL (grade 1-3a) or MZL previously treated with ≥1 anti-CD20 mAb; no prior R²; ECOG PS 0-2 (Planned N = 618; FL, 528; MZL, 60-90) (N = 654)

12 cycles

Tafasitamab 12 mg/kg IV* + **Rituximab†/Lenalidomide‡**

Placebo IV§ + **Rituximab†/Lenalidomide‡**

→ *5-yr follow-up*

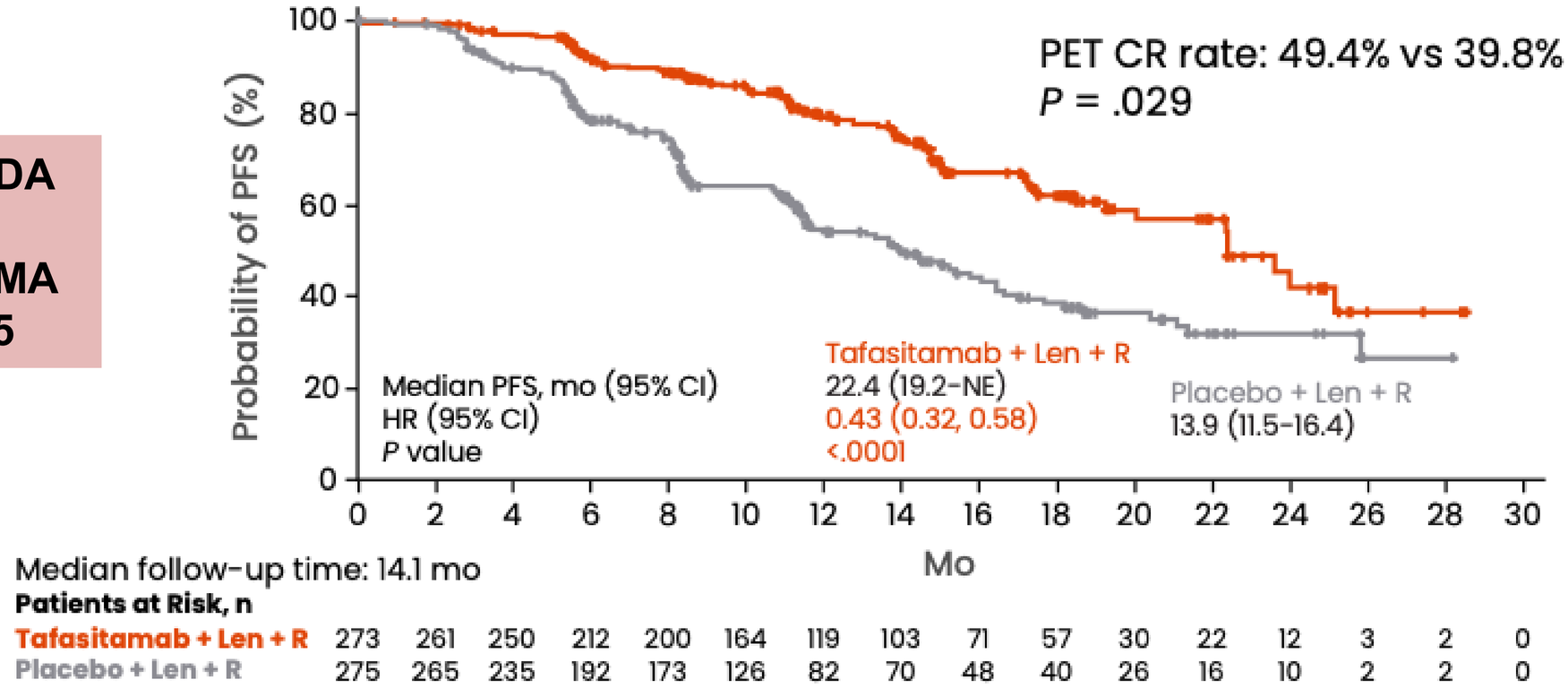
*Tafasitamab given Days 1, 8, 15, 22 of cycles 1-3 and Days 1, 15 of cycles 4-12 on 28-day cycle.
†Rituximab dosed at 375 mg/m² IV; given on Days 1, 8, 15, 22 of cycle 1, then Day 1 of cycles 2-5.
‡Lenalidomide dosed at 20 mg PO QD given on Days 1-21 for 12 cycles. §Placebo given as 0.9% saline solution IV.

- **Primary endpoint:** PFS by investigator per Lugano 2014 criteria in FL population
- **Key secondary endpoints:** PFS in overall population, PET/CR at EOT and OS in FL population

Sehn. ASCO 2022. Abstr TPS7583. NCT04680052.

inMIND: PFS by Investigator Assessment (Primary Endpoint)

Approvazione FDA
Giugno 2025
Approvazione EMA
Dicembre 2025

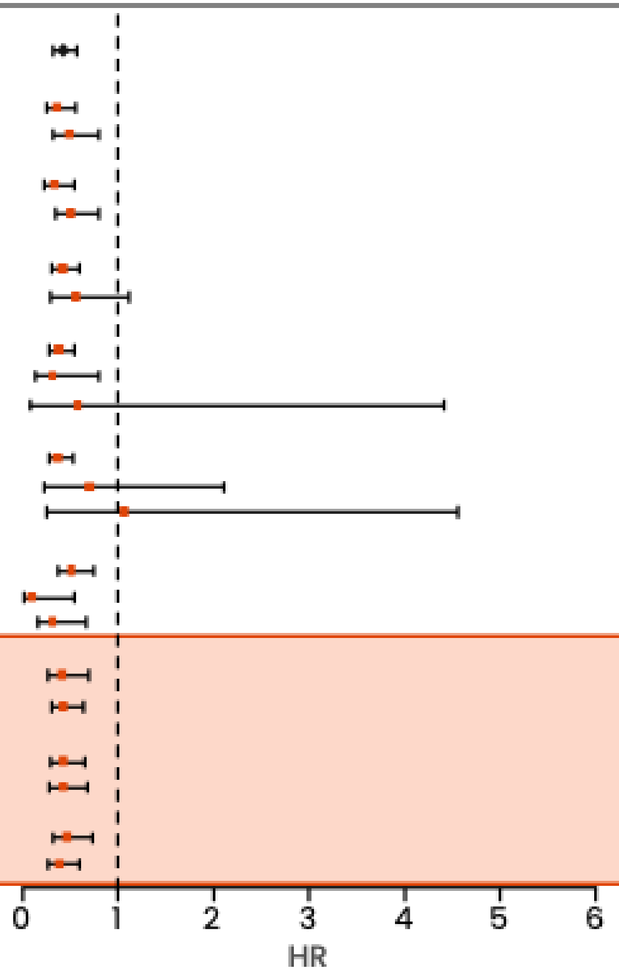


Significant improvement in PFS was observed with tafasitamab

Sehn. ASH 2024. Abstr LBA-1.

inMIND: Prespecified Subgroup Analysis of PFS

Subgroup	Tafasitamab + Len + R # Events/# Patients Censored	Placebo + Len + R # Events/# Patients Censored	HR (95% CI)
Subgroup			
All patients	75/198	131/144	0.43 (0.32-0.58)
Sex			
Male	40/110	78/71	0.38 (0.26-0.56)
Female	35/88	53/73	0.51 (0.33-0.80)
Age group 1			
<65 yr	29/108	69/70	0.35 (0.23-0.55)
≥65 yr	46/90	62/74	0.53 (0.35-0.80)
Age group 2			
<75 yr	55/164	102/119	0.44 (0.31-0.61)
≥75 yr	20/34	29/25	0.58 (0.30-1.12)
Race			
White	61/158	106/113	0.40 (0.29-0.55)
Asian	11/29	21/21	0.34 (0.14-0.81)
Other/missing	3/11	4/10	0.60 (0.08-4.41)
Ethnicity			
Not Hispanic or Latino/a	62/166	112/114	0.39 (0.28-0.53)
Hispanic or Latino/a	8/23	10/14	0.71 (0.24-2.10)
Other/missing	5/9	9/16	1.07 (0.25-4.56)
Geographic region			
Europe	52/124	88/105	0.53 (0.38-0.76)
North America	8/30	11/13	0.12 (0.02-0.55)
Rest of the world	15/44	32/26	0.33 (0.16-0.68)
POD24			
Yes	29/56	52/36	0.43 (0.27-0.69)
No	46/142	79/108	0.45 (0.31-0.65)
Refractory to prior anti-CD20			
Yes	45/73	68/47	0.44 (0.30-0.65)
No	30/125	63/97	0.44 (0.28-0.68)
Number of prior lines			
1 line	36/110	61/86	0.48 (0.32-0.74)
≥2 lines	39/88	70/58	0.41 (0.28-0.61)



Sehn. ASH 2024. Abstr LBA-1.

inMIND: Grade ≥3 TEAEs and Dose Modifications

Grade 3/4 TEAE, n (%)	Tafa + Len/R (n = 274)	Placebo + Len/R (n = 272)	Total (N = 546)
Neutropenia	109 (39.8)	102 (37.5)	211 (38.6)
Pneumonia	23 (8.4)	14 (5.1)	37 (6.8)
Thrombocytopenia	17 (6.2)	20 (7.4)	37 (6.8)
Decreased neutrophil count	16 (5.8)	18 (6.6)	34 (6.2)
Anemia	12 (4.4)	16 (5.9)	28 (5.1)
COVID-19	16 (5.8)	6 (2.2)	22 (4.0)
COVID-19 pneumonia	13 (4.7)	3 (1.1)	16 (2.9)

Dose Interruptions or Discontinuations due to TEAEs	Tafa + Len/R (n = 274)	Placebo + Len/R (n = 272)
Tafasitamab or placebo, n (%)		
• Delay or interruption	203 (74)	190 (70)
• Discontinuation	30 (11)	18 (7)
Len		
• Discontinuation, n (%)	39 (14)	31 (11)
• Median relative dose intensity, %	86	87

Sehn. ASH 2024. Abstr LBA-1.

inMIND: CD19 Expression

Central lab assessment of CD19 expression in screening biopsy demonstrated:

- 86% of patients had 100% CD19-positive cells
- 14% of patients had a median of 50% CD19-positive cells (range 10%–85%); n = 2 CD19-negative patients in placebo arm

23/24 posttreatment samples remained CD19 positive, including 7 of 8 samples from patients who received tafa + Len + R

- 1 sample from a patient receiving tafa + Len + R who achieved a PR was CD19 negative (initially had 80% CD19-negative tumor cells at screening)

CD19 Expression at End of Treatment or Follow-up

Sample	Tafasitamab + Len + R (n = 273)	Placebo + Len + R (n = 275)
Total samples, n	13	19
Lymphoma detected, n	8	16
CD19 positive, n/N	7/8	16/16

Reinke. EHA 2025. Abstr PF1006. Sehn. ICML 2025. Abstr 028.

EPCORE FL-1: Epcoritamab + R² vs R² in Patients With R/R FL

Global, multicenter, open-label phase III study

Adults (≥18 yr) with body scan and histologically confirmed R/R FL grade 1-3 or grade 4 with no evidence of histologic aggressive transformation; at least 1 systemic PLOT; CrCl ≥50mL/min; ECOG 0-2

→ **Epcoritamab IV** 48 mg for 12 cycles
Rituximab IV 5 cycles
Lenalidomide IV 12 cycles

→ **Rituximab IV** 5 cycles
Lenalidomide IV 12 cycles

→ *Until 12 cycles of therapy, disease progression, or meets off-treatment criteria*

Primary endpoints: ORR, and PFS as assessed by IRC per Lugano criteria

Key secondary endpoints: CRR, BOR, OS, MRD

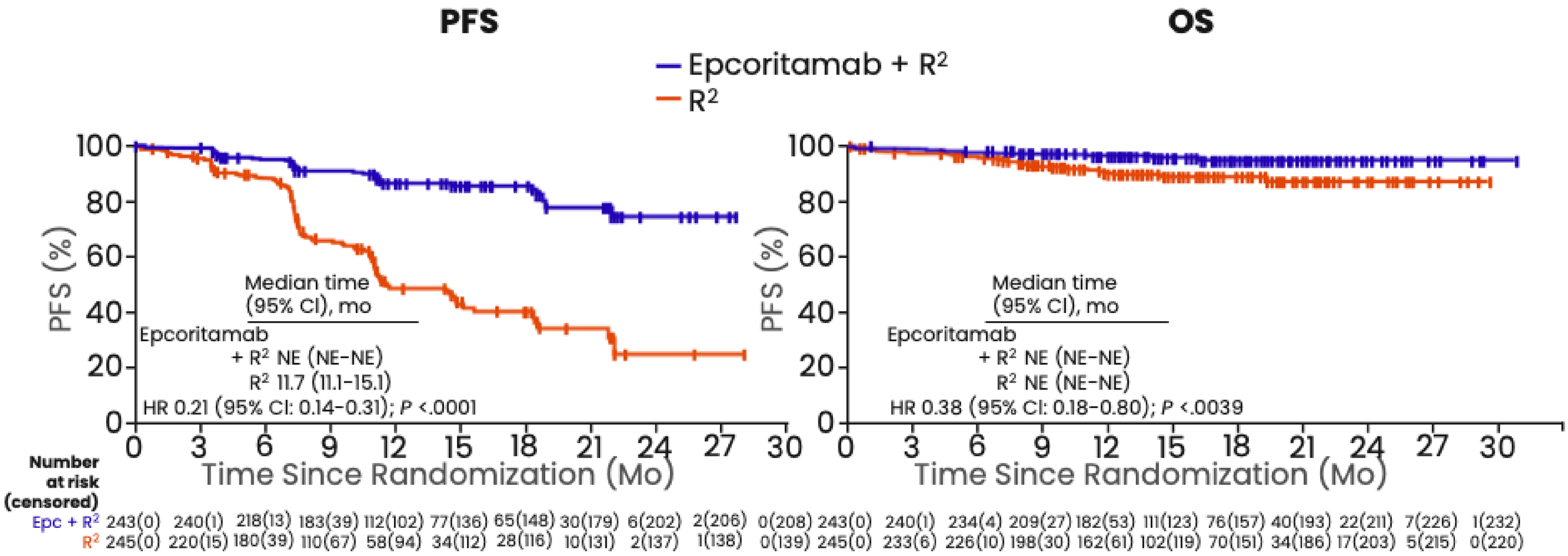
Falchi. Lancet. 2025;S0140-6736:25:02360-8.

EPCORE FL-1: Efficacy With Epcoritamab + R^2 vs R^2 in Patients With R/R FL

	Epcoritamab + R^2 (n = 243)	R^2 (n = 245)
Median follow-up, mo, median (95% CI) [IQR]	14·8 (13·96–16·23) [12·0–19·3]	14·6 (13·57–15·64) [10·2–18·6]
Overall response rate, n (% [95% CI])	**231 (95% [92–97])**	**194 (79% [74–84])**
Complete response, n (% [95% CI])	**201 (83% [77–87])**	**122 (50% [43–56])**
Partial response	30 (12%)	72 (29%)
Stable disease	1 (<1%)	17 (7%)
Progressive disease	7 (3%)	16 (7%)

Falchi. Lancet. 2025;S0140-6736:25:02360-8

EPCORE FL-1: PFS and OS With Epcoritamab + R² vs R² in Patients With R/R FL



Falchi. Lancet. 2025;S0140-6736:25:02360-8

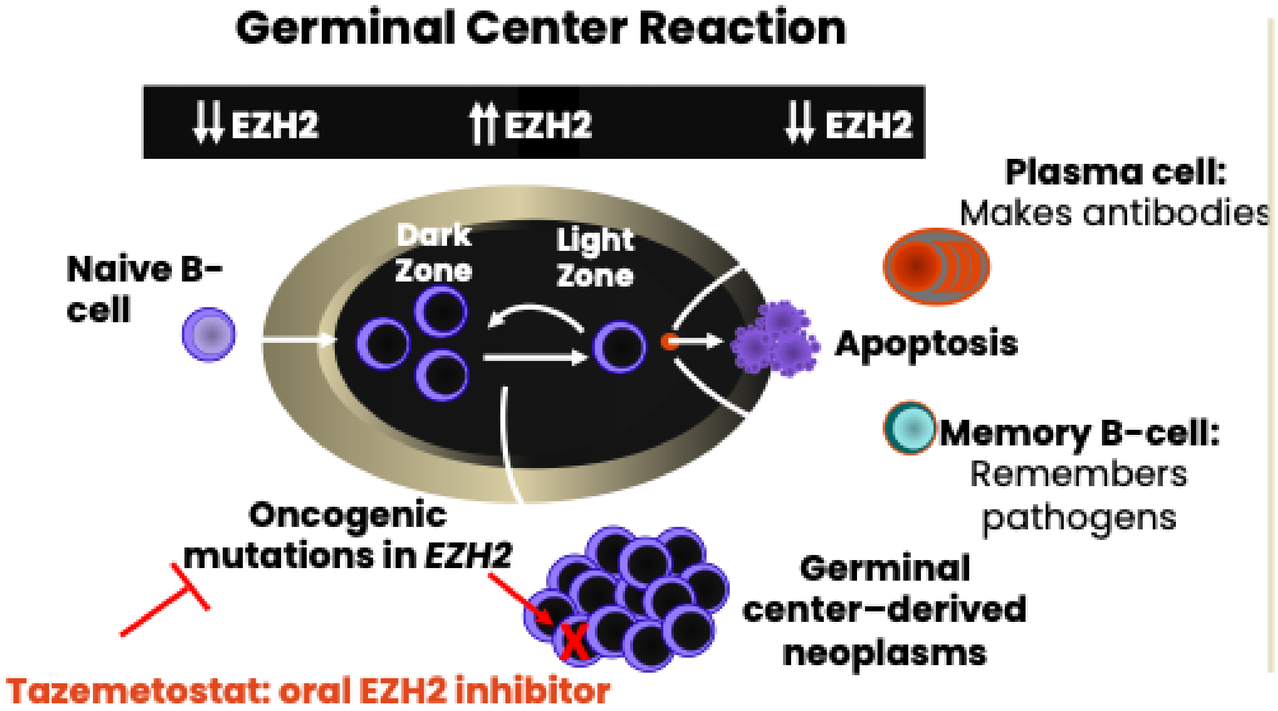
On November 18, 2025, the FDA approved epcoritamab + R² for R/R FL based on the results of the EPCORE FL-1 trial. The trial demonstrated superiority of PFS and ORR in the epcoritamab arm (PFS HR: 0.21; *P* <.0001; ORR: 89% vs 74%)*

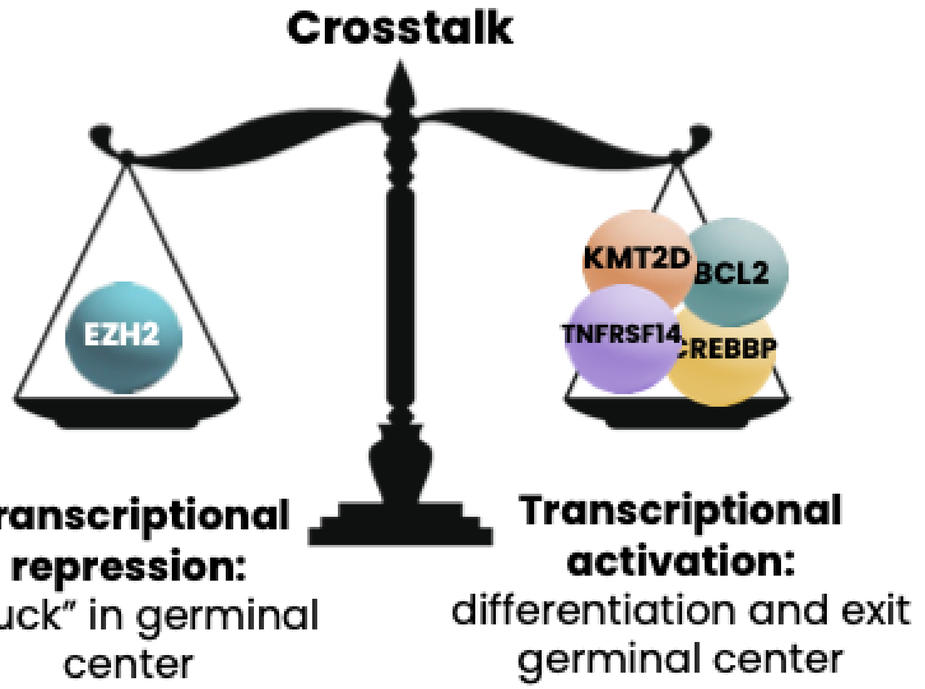
EPCORE FL-1: Safety and Adverse Events

n (%)	Epcoritamab + R² (n = 243)		R² (n = 238)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any adverse event	242 (>99)	219 (90)	235 (99)	161 (68)
Adverse event related to study drug	236 (97)	203 (84)	213 (90)	129 (54)
Serious adverse event	135 (56)	--	69 (29)	--
Adverse event leading to treatment discontinuation	46 (19)	--	29 (12)	--
Epcoritamab	21 (9)	--	--	--
Rituximab	7 (3)	--	12 (5)	--
Lenalidomide	45 (19)	--	29 (12)	--
Adverse event of special interest				
Infections	188 (77)	81 (33)	125 (53)	37 (16)
Neutropenia	180 (74)	167 (69)	123 (52)	100 (42)
CRS	85 (35)	0	1 (<1)	0
Anemia	68 (28)	19 (8)	41 (17)	11 (5)
Thrombocytopenia	67 (28)	23 (9)	44 (18)	15 (6)
Pyrexia	58 (24)	1 (<1)	33 (14)	3 (1)
Rash	58 (24)	19 (8)	53 (22)	9 (4)
COVID-19	54 (22)	7 (3)	32 (13)	4 (2)

Falchi. Lancet. 2025;S0140-6736:25:02360-8.

Follicular Lymphoma and *EZH2*: Tazemetostat





EZH2: an epigenetic regulator of gene expression and cell fate decisions

- In normal B-cell biology, EZH2 regulates germinal center formation
- *EZH2* mutations can lead to oncogenic transformation by locking B-cells in germinal state and preventing terminal differentiation

Gan. Biomark Res. 2018;6:10. Béguelin. Cancer Cell. 2013;23:677. Tazemetostat PI.

Tazemetostat in R/R FL: A Phase II Study

Open label, multicohort, single-arm phase II study conducted at 38 sites across NA, Europe, Australia (data cutoff for efficacy: August 9, 2019; for safety: May 24, 2019)

SCREENING: *Central testing of archival tissue for* EZH2 *hot spot activating mutations*

Adults with R/R FL (grade 1-3b) with measurable disease per IWG-NHL following ≥2 prior systemic treatments (including ≥1 anti-CD20–based regimen); transformed FL allowed; tumor tissue for *EZH2* mutation testing; life expectancy ≥3 mo; ECOG PS 0-2 (N = 99)

Cohorts

- **Mutant *EZH2*** (n = 45)
- **Wild-type *EZH2*** (n = 54)

Tazemetostat 800 mg BID → *Treatment continues until PD or withdrawal*

Response assessment by 2007 IWG-NHL criteria Q8W.

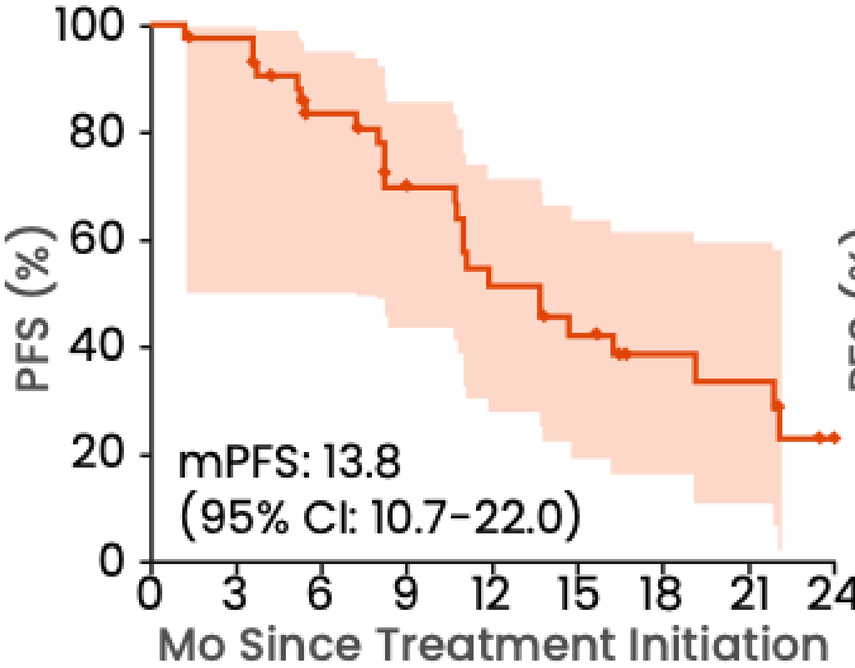
- **Primary endpoint:** ORR
- **Secondary endpoints:** DoR, PFS, safety/tolerability

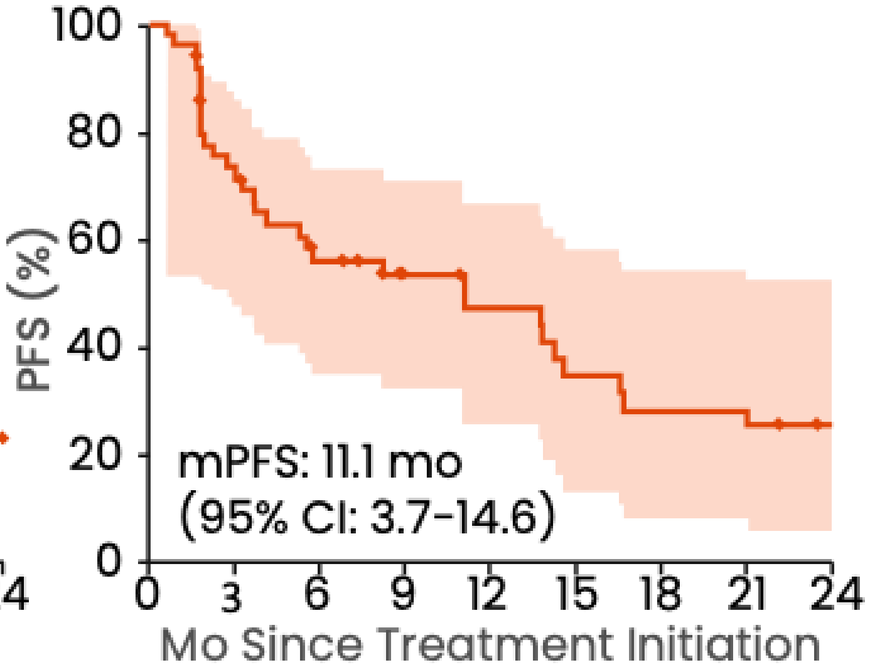
Morschhauser. Lancet Oncol. 2020;21:1433. NCT01897571.

Tazemetostat in R/R FL: ORR and PFS by IRC

Response by IRC	Mutant (n = 45)	WT (n = 54)
ORR, n (%)	31 (69)	19 (35)
• CR, n (%)	6 (13)	2 (4)
• PR, n (%)	25 (56)	17 (31)
SD, n (%)	13 (29)	18 (33)
PD, n (%)	1 (2)	12 (22)

High concordance between IRC- and INV-assessed response rates.





Approved by FDA for adults with *EZH2*mut+ R/R FL after ≥2 prior systemic therapies or any adult with R/R FL without alternative treatment options

Morschhauser. Lancet Oncol. 2020;21:1433. Tazemetostat PI.

Tazemetostat in R/R FL: Safety (ITT)

TEAEs, %	All TEAEs (N = 99)		Treatment-Related TEAEs (N = 99)	
	All Grades*	Grade ≥3	All Grades	Grade ≥3
Nausea	23	0	19	0
Diarrhea	18	0	12	0
Alopecia	17	0	14	0
Cough	16	0	2	0
Asthenia	15	3	13	1
Fatigue	15	2	11	1
URTI	15	0	1	0
Bronchitis	15	0	3	0
Abdominal pain	12	1	2	0
Headache	12	0	5	0
Vomiting	11	1	6	0
Back pain	11	0	0	0
Pyrexia	10	0	2	0
Anemia	9	5	7	2
Thrombocytopenia	5	5	5	3
Neutropenia	3	4	3	3

Morschhauser. Lancet Oncol. 2020;21:1433.

Tazemetostat was generally well tolerated

- 8% discontinued due to TEAEs
- 9% had a dose reduction due to TEAEs
- 27% had a dose interruption due to TEAEs
- Low rate of grade ≥3 treatment-related TEAEs

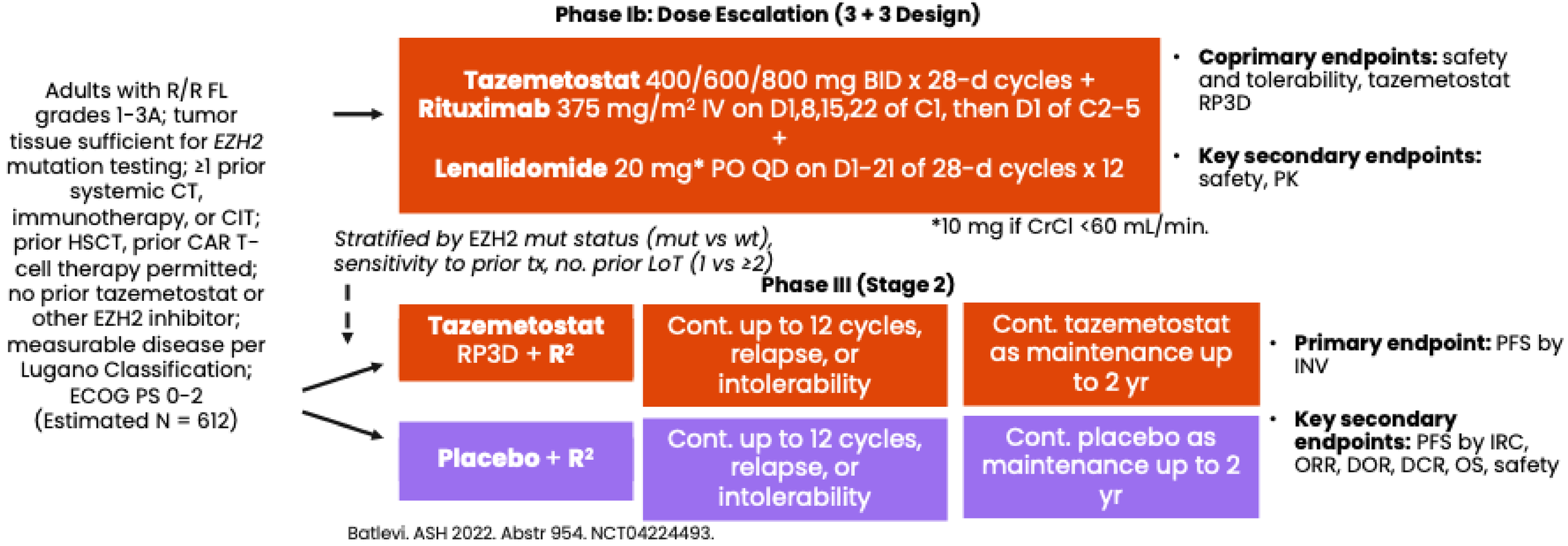
No treatment-related deaths

*Occurring in ≥10% of patients.

Phase Ib/III SYMPHONY-1: Study Design

Phase Ib safety run-in analysis (stage 1) of international, double-blind, randomized phase Ib/III trial

- Stage 2: phase III design comparing tazemetostat at RP3D + R² vs placebo + R² in patients with R/R FL
- Stage 3 (to be executed if stage 2 futility analysis finds that efficacy fails in overall population but is promising for *EZH2*-mutated subpopulation): in patients with *EZH2*-mutated R/R FL



Batlevi. ASH 2022. Abstr 954. NCT04224493.

FDA Alerts Health Care Providers and Patients about Increased Risk of New Blood Cancers with Tazverik (tazemetostat) Use; Sponsor to Voluntarily Withdraw Product from Market

An increased incidence of hematologic SPMs among people taking Tazverik was observed in the study, “SYMPHONY-1.” In this study, as of March 6, 2026, 18 out of 318 (5.7%) patients treated with Tazverik developed hematologic SPMs, compared to no reported events among patients in the control arm.

Based on these findings, enrollment on the SYMPHONY-1 trial should be stopped and that all patients receiving Tazverik should discontinue treatment immediately. Shortly thereafter, the sponsor, Ipsen, notified FDA of their plans to discontinue Tazverik treatment for patients in the clinical study and withdraw Tazverik from the U.S. market. All expanded access programs for Tazverik will be discontinued as well.

Conclusions

- The number of therapeutic options for patients with R/R FL is increasing
- It is important to consider patient characteristics, disease behavior, prognostic indicators, goals of therapy, and patient preferences before treatment selection
- It is also important to consider response type and duration of response to last therapy
- For optimal treatment sequencing:
  - Weigh benefit vs toxicity
  - Biomarkers to guide treatment selection are greatly needed