Un nuovo anticorpo anti-CD19

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Disclosures (1): PIER LUIGI ZINZANI

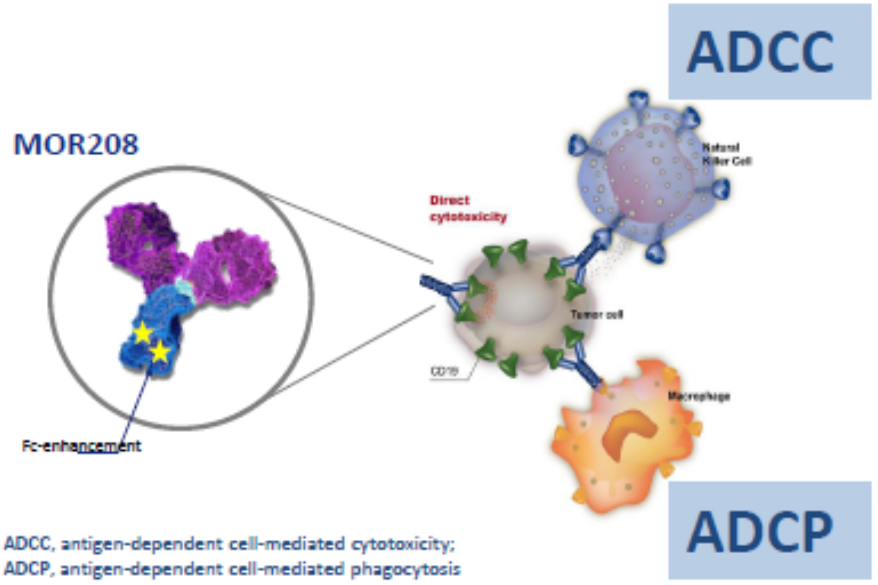
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Secura Bio						X	
Celltrion					X	X	
Gilead					X	X	
Janssen-Cilag					X	X	
BMS					X	X	
Servier					X	X	
Sandoz						X	
MSD			X		X	X	
TG Therap.					X	X	

Disclosures (2): PIER LUIGI ZINZANI

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Takeda					X	X	
Roche					X	X	
Eusapharma			X		X	X	
Kyowa Kirin					X	X	
Novartis			X		X	X	
ADC Therap.						X	
Incyte					X	X	
Beigene					X	X	

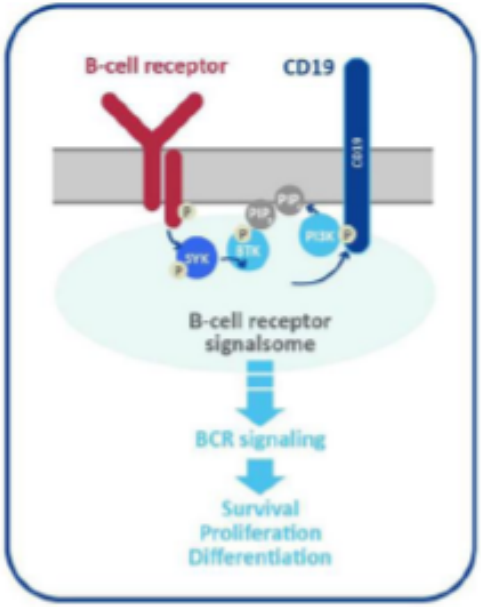
MOR208: An Enhanced CD19 Antibody

- **MOR208** is an Fc-enhanced monoclonal antibody that targets CD19
- Fc-enhancement of MOR208 leads to a potentiation of **ADCC** and **ADCP**
- MOR208 induces **direct cytotoxicity**



ADCC, antigen-dependent cell-mediated cytotoxicity;
ADCP, antigen-dependent cell-mediated phagocytosis

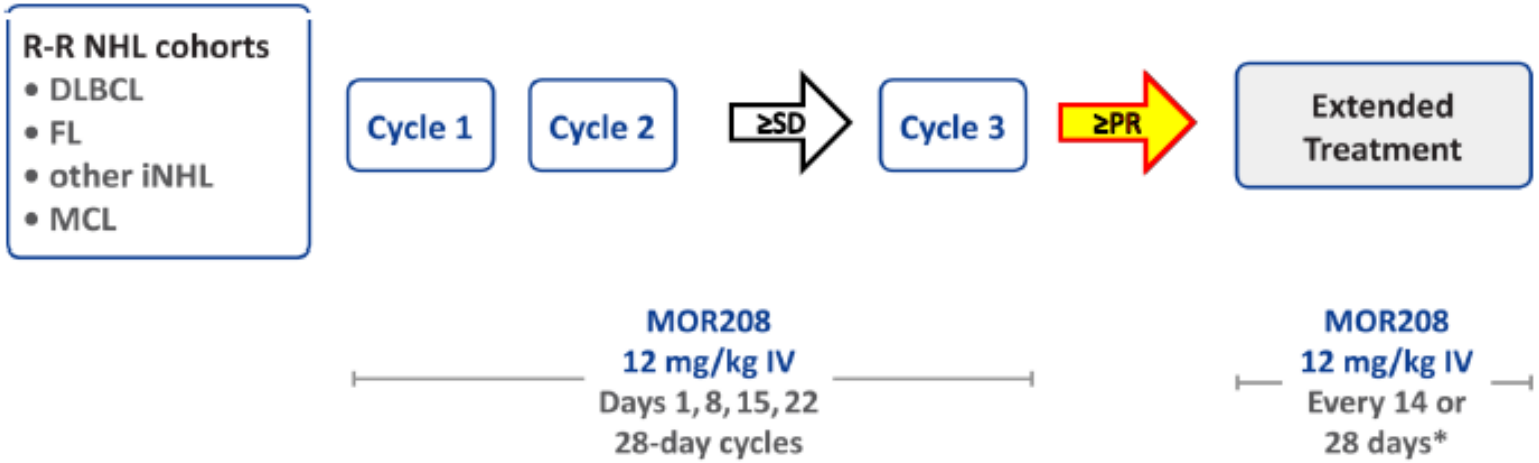
Direct cytotoxicity



Katz B-Z et al Leukemia & Lymphoma 2014
Fujimoto M, et al. Immunity 2000

Phase II a: MOR208 in R-R NHL – study design

Multicentre study with 2-stage design (NCT01685008)



Primary objective

- ORR

Secondary objective

- DoR & PFS
- Safety and tolerability
- Pharmacokinetics and pharmacodynamics

Excluding Patients with SD from further therpy
Leeds to underestimation of MOR-208 efficeacy
- Especially in iNHL

Jurczak W and Zinzani PL, *Ann Oncol* 2018

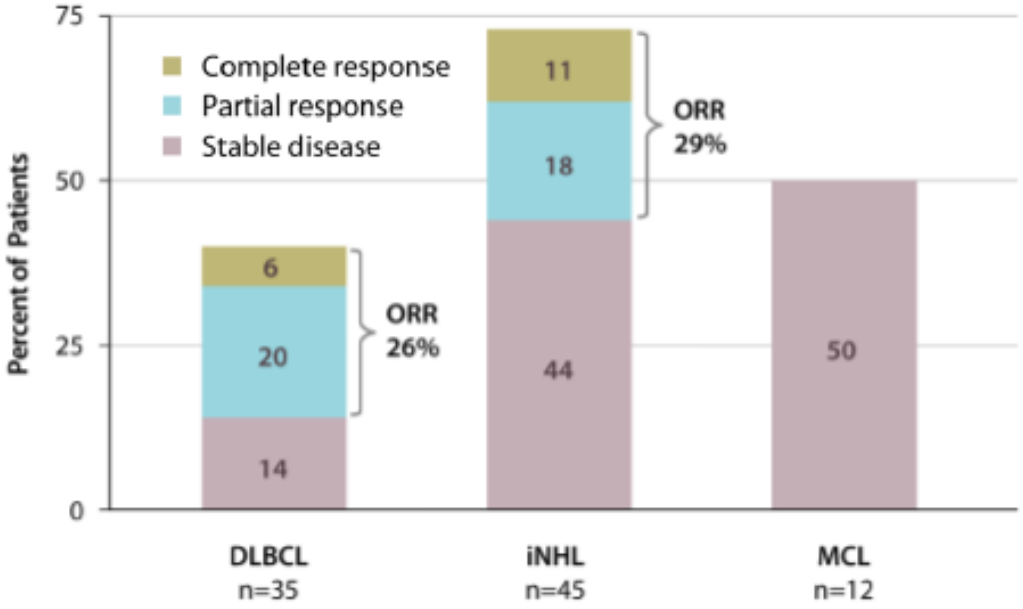
Phase II a: MOR208 in R-R NHL – Baseline Characteristics

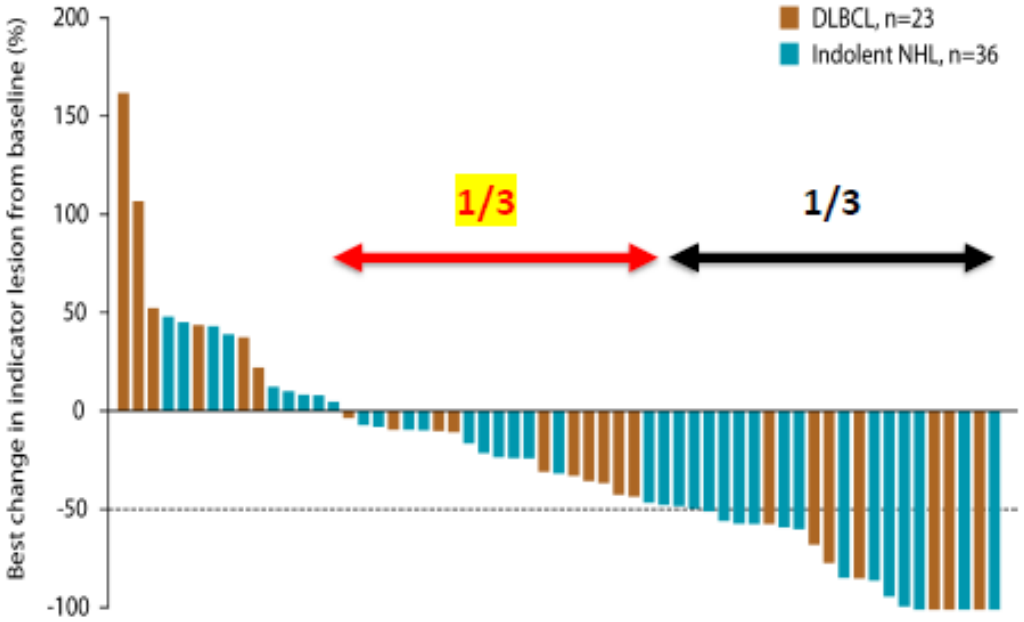
Characteristic, n (%)		DLBCL n=35	iNHL* n=45	MCL n=12	Total n=92
Age, years	Median	71	66	64.5	66.5
Sex	Male	24 (69)	21 (47)	11 (92)	56 (61)
Ann Arbor stage	I-II	4 (11)	5 (11)	1 (8)	10 (11)
	III-IV	30 (86)	40 (89)	11 (92)	81 (88)
	Missing	1 (3)	0	0	1 (1)
ECOG PS	0-1	34 (97)	43 (96)	11 (92)	88 (96)
	2	1 (3)	2 (4)	1 (8)	4 (4)
Prior lines of therapy	1	12 (34)	16 (36)	3 (25)	31 (34)
	2	8 (23)	6 (13)	1 (8)	15 (16)
	≥3	15 (43)	23 (51)	8 (67)	46 (50)
Rituximab refractory	Yes	24 (69)	22 (49)	6 (50)	52 (57)
Last rituximab dose	<6 months	14 (40)	6 (13)	1 (8)	21 (23)
Prior stem cell transplantation	Yes	4 (11)	8 (18)	1 (8)	13 (14)

*Includes follicular lymphoma and other indolent NHLs
Data are n (%) unless otherwise stated. Rituximab refractory was defined as patients who demonstrated less than a partial response or response lasting less than 6 months to a prior rituximab-containing regimen

Jurczak W and Zinzani PL, *Ann Oncol* 2018

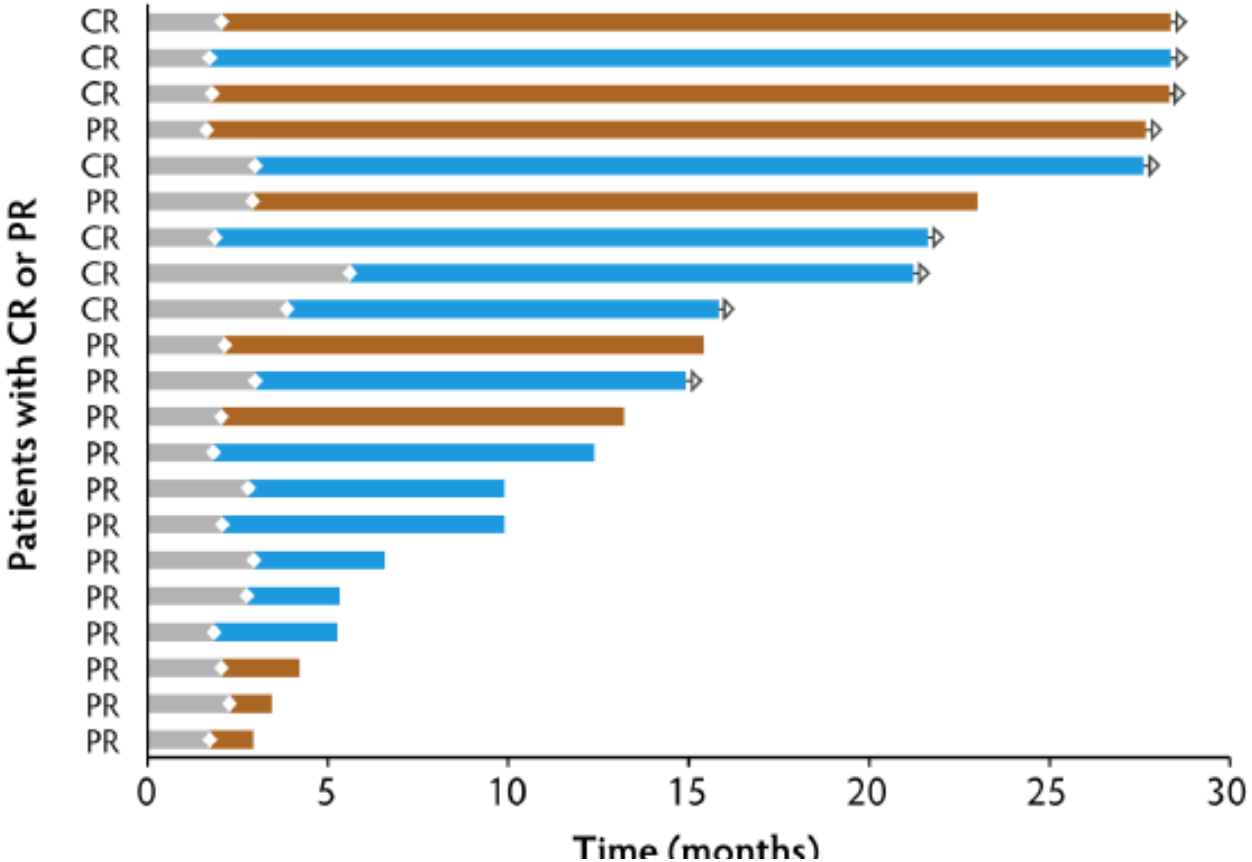
Phase II a: MOR208 in R-R NHL – Best Overall Response Rate





Jurczak W and Zinzani PL, *Ann Oncol* 2018

Phase II a: MOR208 in R-R NHL –Duration of Response



Duration of response

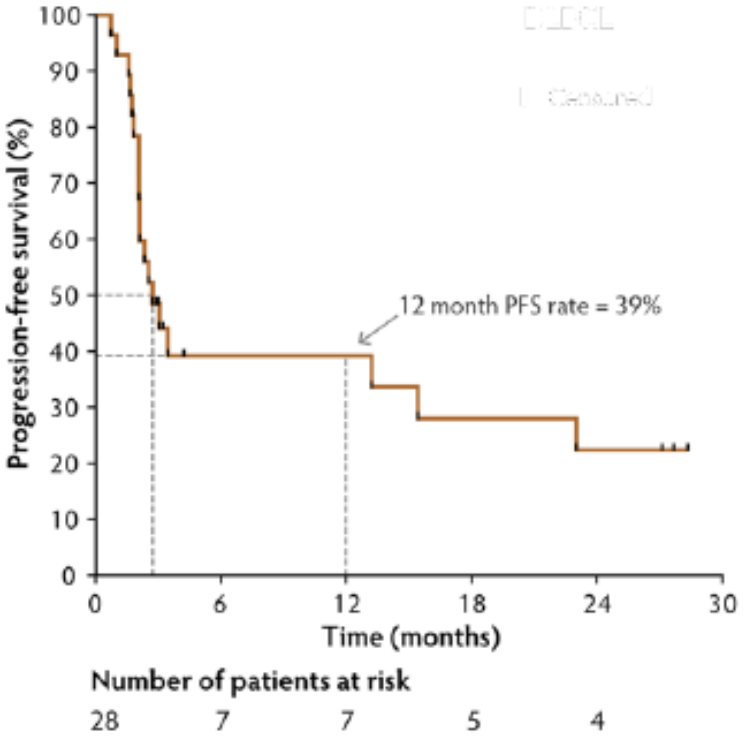
- DLBCL, n=9
- Indolent NHL,* n=12
- Ongoing response, n=9
- Time to response, n=21

- 3 DLBCL patients still in remission, longest DoR >26 months, ongoing
- 6 iNHL patients still in remission, longest DoR >26 months, ongoing
- **Median DoR 20.1 months in DLBCL and not reached in iNHL**

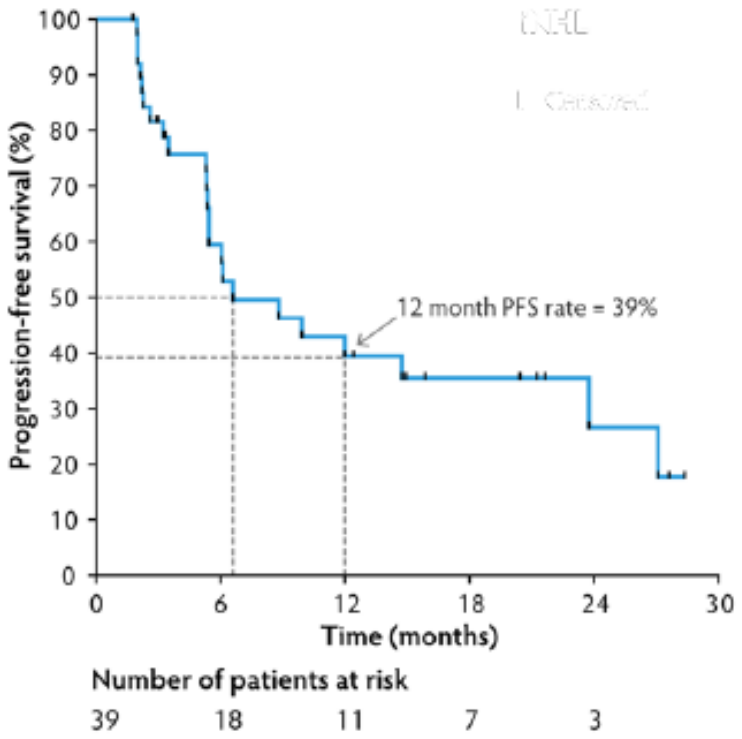
Jurczak W and Zinzani PL, *Ann Oncol* 2018

Phase II a: MOR208 in R-R NHL – PFS

DLBCL



iNHL subtypes



Jurczak W and Zinzani PL, *Ann Oncol* 2018

Phase II a: MOR208 in R-R NHL – AE Profile

Grade ≥3 TEAEs,* n (%)	DLBCL n=35	iNHL† n=45	MCL n=12	Total n=92
Any‡	19 (54)	14 (31)	4 (33)	37 (40)
Hematological¥				
Neutropenia	6 (17)	2 (4)	0	8 (9)
Thrombocytopenia	2 (6)	1 (2)	1 (8)	4 (4)
Anemia	3 (9)	0	0	3 (3)
Non-Hematological¥				
Dyspnea	2 (6)	1 (2)	1 (8)	4 (4)
Pneumonia	3 (9)	0	0	3 (3)
Fatigue	1 (3)	1 (2)	0	2 (2)
Hypokalemia	1 (3)	1 (2)	0	2 (2)
Infections and Infestations#	5 (14)	1 (2)	0	6 (7)
Infusion-related, n (%)	**DLBCL n=35**	**iNHL† n=45**	**MCL n=12**	**Total n=92**
Any	4 (11)	5 (11)	2 (17)	11 (12)
Grade 1/2	4 (11)	4 (9)	2 (17)	10 (11)
Grade 4	0	1 (2)	0	1 (1)

There were no treatment-related deaths

Jurczak W and Zinzani PL, *Ann Oncol* 2018

MOR208 Single Agent in R/R NHL

MOR208

Showed encouraging single-agent activity in R-R DLBCL and R-R iNHL for further development:

- **ORR: 26% in DLBCL and 29% in iNHL**
- **Target lesion shrinkage also observed in patients with stable disease** (5/6 DLBCL and 14/17 iNHL)
- Efficacious in patients with **rituximab-refractory disease**

MOR208

Is able to induce **long-lasting responses** in DLBCL and iNHL

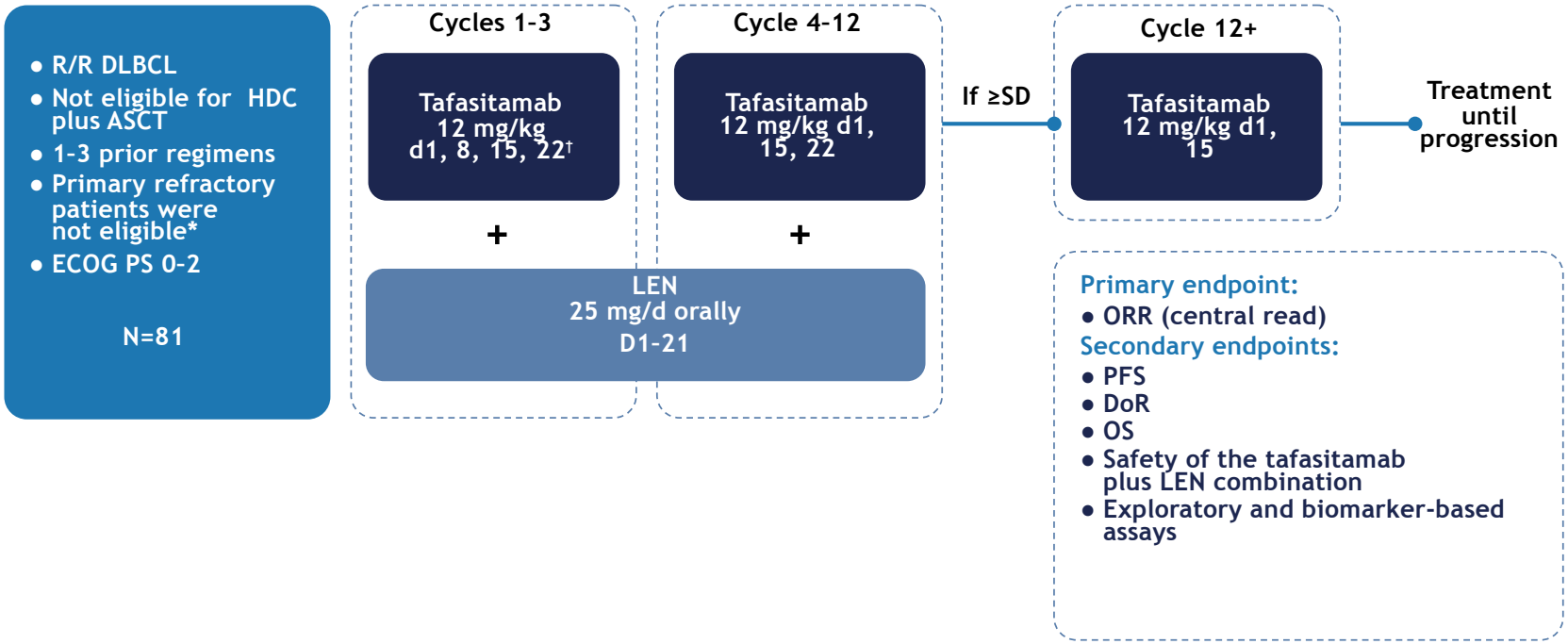
- **12 month PFS rate: 39%** in DLBCL and iNHL
- Longest responses: five iNHL and one DLBCL patient are on treatment for more than 4 years

MOR208

- **Well tolerated**, also in long-term treatment

Jurczak W and Zinzani PL, *Ann Oncol* 2018

L-MIND: Trial design



- *Primary refractory is defined as no response to, or progression/relapse during or within 6 months of frontline therapy.
- †A loading dose of tafasitamab was administered on Day 4 of Cycle 1. ASCT, autologous stem cell transplantation; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HDC, high-dose chemotherapy; IRC,independent review committee; LEN, lenalidomide; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed or refractory; SD, stable disease.

- 1. Salles G, et al. Lancet Oncol 2020;21(7):978-88.

L-MIND: Patient characteristics

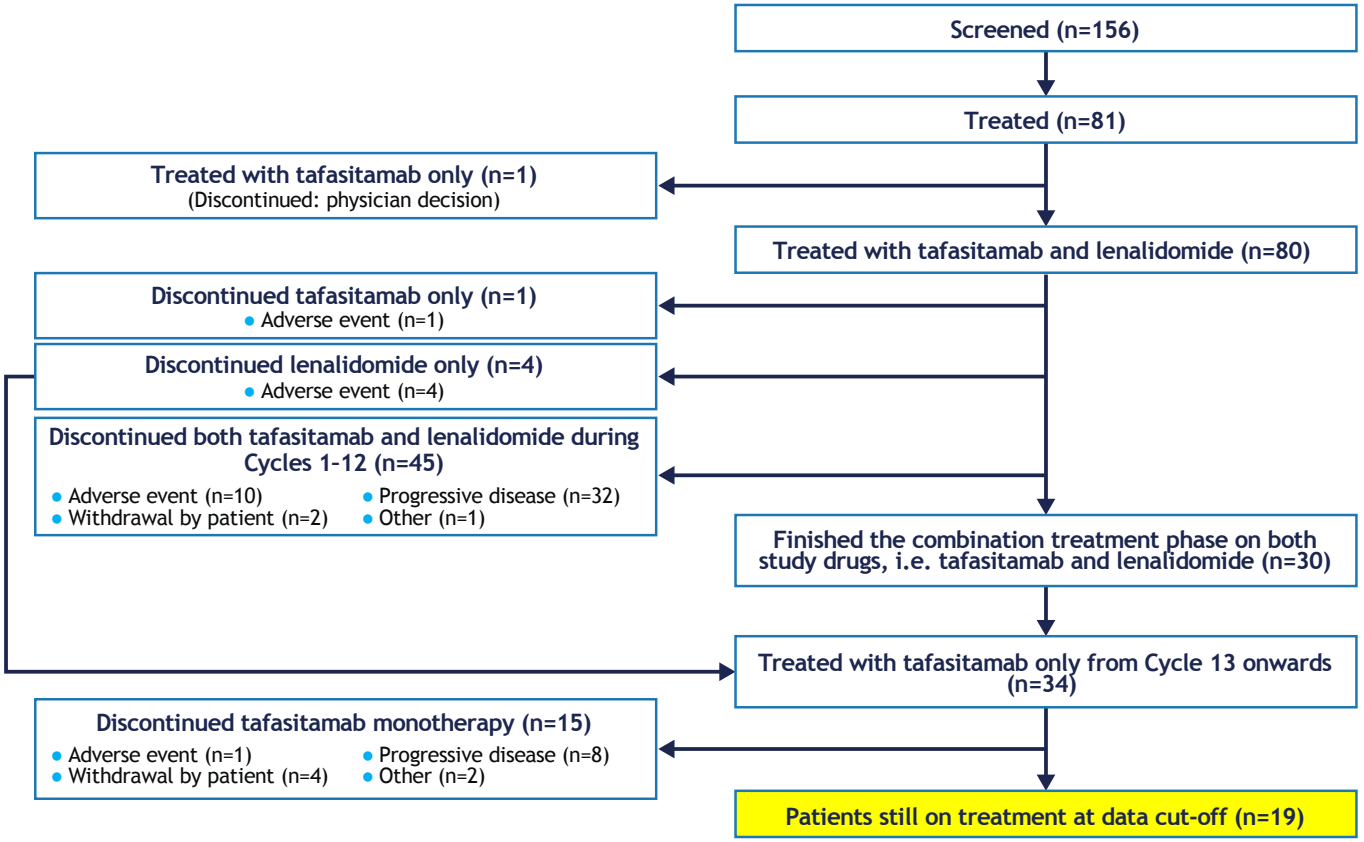
Characteristic	Specification	N=81
Age, years*	Median (range)	72 (41-86)
Sex, n (%)	Male	44 (54)
	Female	37 (46)
Ann Arbor stage, n (%)*	I-II	20 (25)
	III-IV	61 (75)
Risk (IPI), n (%)*	0-2	40 (49)
	3-5	41 (51)
Elevated LDH, n (%)*	Yes	45 (56)
	No	36 (44)
Prior lines, n (%)*	Median	2
	1	40 (49)
	2	35 (43)
	3	5 (6)
	4	1 (1)

Characteristic	Specification	N=81
Primary refractory, n (%)*	Yes	15 (19)†
	No	66 (81)
Refractory to previous therapy line, n (%)*	Yes	36 (44)
	No	45 (56)
Prior ASCT, n (%)	Yes	9 (11)
	No	72 (89)
Cell of origin (by IHC), n (%) (Centrally assessed—Hans algorithm)	GCB	37 (46)
	Non-GCB	20 (25)
	Unknown	24 (30)

- *At study entry. †Primary refractory patients had a DoR to 1 prior line of therapy of 3–6 months.
- ASCT, autologous stem-cell transplant; GCB, germinal center B-cell–like; IHC, immunohistochemistry; IPI, International Prognostic Index; LDH, lactate dehydrogenase; SCT, stem cell transplant.

- 1. Salles G, et al. Lancet Oncol 2020;21(7):978-88.

L-MIND: Patient disposition after ≥35 months f-up



- Adapted from Maddocks K, et al. Poster presented at ASH 2020. Abstract 3021.

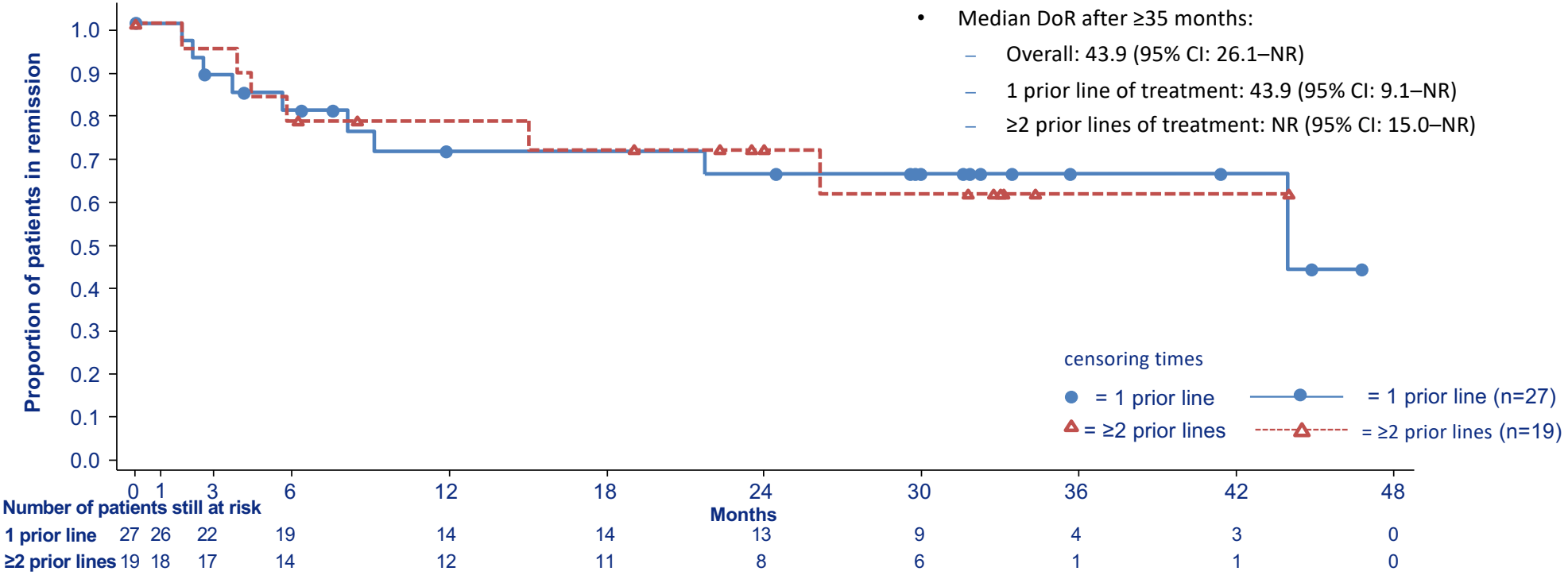
Primary endpoint: Best objective response rate (IRC)

Tafasitamab plus LEN	1 prior treatment (N=40)	≥2 prior treatments (N=40)	Overall (N=80)
Best objective response, n (%)			
CR	19 (47.5)	13 (32.5)	32 (40.0)
PR	8 (20.0)	6 (15.0)	14 (17.5)
SD	7 (17.5)	6 (15)	13 (16.3)
PD	5 (12.5)	8 (20.0)	13 (16.3)
NE*	1 (2.5)	7 (17.5)	8 (10.0)
ORR, n (%) [95% CI][†]	27 (67.5) [50.9–81.4]	19 (47.5) [31.5–63.9]	46 (57.5) [45.9–68.5]

- *No valid post-baseline response assessments. [†]Two-sided 95% Clopper-Pearson exact method based on a binomial distribution.CI, confidence interval; CR, complete response; IRC, independent review committee; LEN, lenalidomide; NE, not evaluable; ORR, objective response rate; PD, disease progression; PR, partial response; SD, stable disease.

- Nowakowski G, et al. ASCO 2020 (Abstract 8020)

DoR by number of prior treatment lines



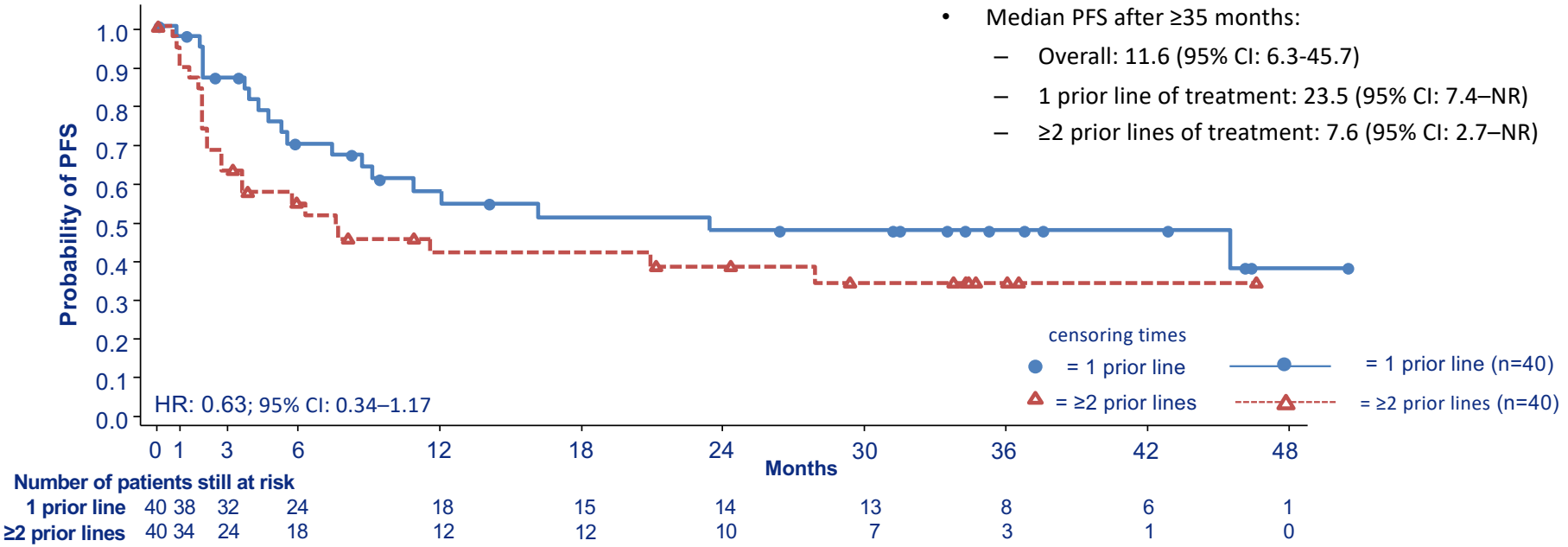
- Median DoR after ≥35 months:
  - Overall: 43.9 (95% CI: 26.1–NR)
  - 1 prior line of treatment: 43.9 (95% CI: 9.1–NR)
  - ≥2 prior lines of treatment: NR (95% CI: 15.0–NR)

	1 prior line (n=40)	≥2 prior lines (n=40)	All patients (n=80)
12-month DoR, % (95% CI)	70.8 (48.0, 85.0)	77.8 (51.1, 91.0)	73.7 (57.4, 84.5)
18-month DoR, % (95% CI)	70.8 (48.0, 85.0)	71.3 (44.0, 87.0)	70.9 (54.2, 82.4)
24-month DoR, % (95% CI)	65.7 (42.6, 81.4)	71.3 (44.0, 87.0)	67.9 (51.0, 80.1)
36-month DoR, % (95% CI)	65.7 (42.6, 81.4)	61.1 (31.0, 81.3)	64.3 (46.8, 77.4)

- CI, confidence interval; DoR, duration of response; NR, not reached;

Duell J, *ICML* 2021

PFS by number of prior treatment lines



- Median PFS after ≥35 months:
  - Overall: 11.6 (95% CI: 6.3-45.7)
  - 1 prior line of treatment: 23.5 (95% CI: 7.4–NR)
  - ≥2 prior lines of treatment: 7.6 (95% CI: 2.7–NR)

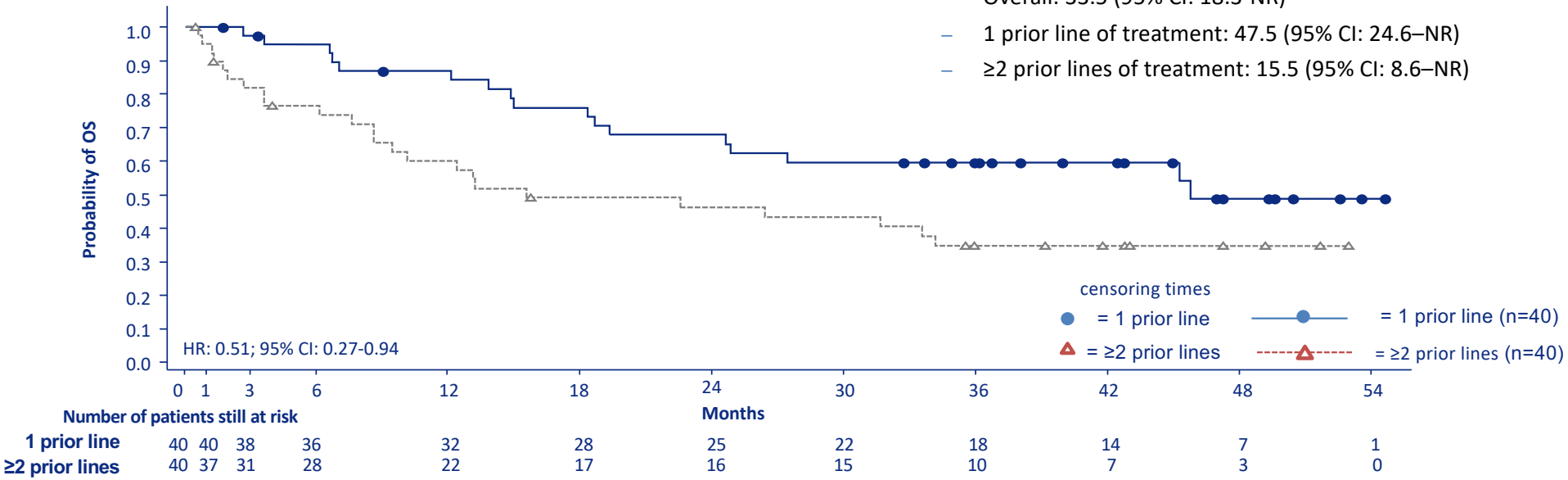
	1 prior line (n=40)	≥2 prior lines (n=40)	All patients (n=80)
12-month PFS, % (95% CI)	57.8 (39.9, 72.2)	421 (25.7, 57.7)	50.0 (37.8, 61.0)
18-month PFS, % (95% CI)	51.2 (33.4, 66.5)	42.1 (25.7, 57.7)	46.6 (34.5, 57.9)
24-month PFS, % (95% CI)	47.8 (30.2, 63.4)	38.6 (22.6, 54.5)	43.1 (31.1, 54.5)
36-month PFS, % (95% CI)	47.8 (30.2–63.4)	34.3 (18.6–50.7)	41.1 (29.1, 52.7)

- CI, confidence interval; HR, hazard ratio; NR, not reached; PFS, progression free survival.

Duell J, *ICML* 2021

OS by number of prior treatment lines

- Median OS after ≥35 months:
  - Overall: 33.5 (95% CI: 18.3-NR)
  - 1 prior line of treatment: 47.5 (95% CI: 24.6–NR)
  - ≥2 prior lines of treatment: 15.5 (95% CI: 8.6–NR)

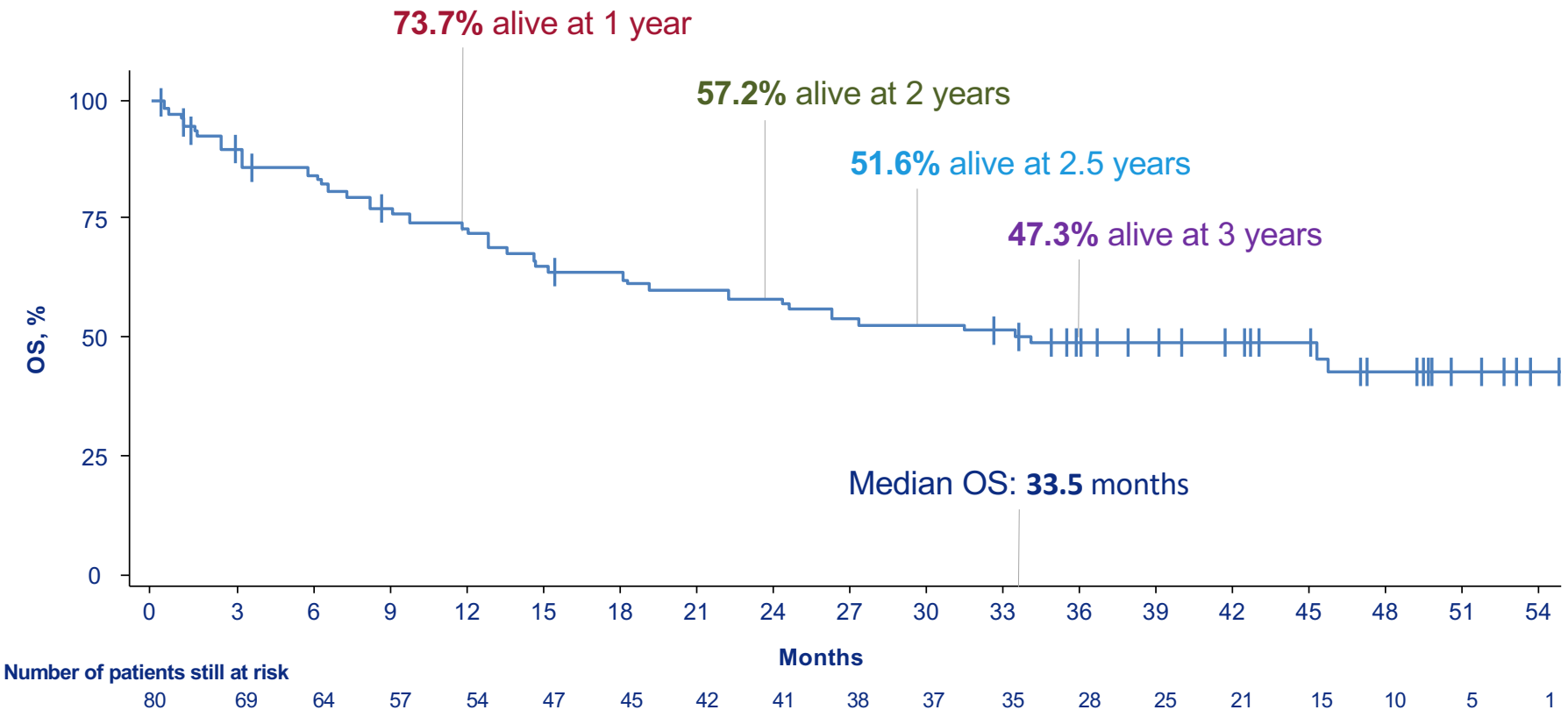


	1 prior line (n=40)	≥2 prior lines (n=40)	All patients (n=80)
12-month OS, % (95% CI)	86.9 (71.3, 94.3)	60.1 (42.8, 73.8)	73.7 (62.2, 82.2)
18-month OS, % (95% CI)	76.0 (59.0, 86.8)	49.2 (32.5, 63.9)	62.8 (50.8, 72.6)
24-month OS, % (95% CI)	67.9 (50.4, 80.3)	46.3 (29.8, 61.3)	57.2 (45.1, 67.5)
36-month OS, % (95% CI)	59.7 (42.3, 73.5)	34.7 (19.9, 50.1)	47.3 (35.5, 58.2)

- CI, confidence interval; CR, complete response; NR, not reached; OS, overall survival; PR, partial response..

Duell J, *ICML* 2021

Patients alive after 3 years of follow-up



- OS, overall survival

Duell J, *ICML* 2021

Favorable safety profile of tafasitamab + LEN followed by extended tafasitamab monotherapy

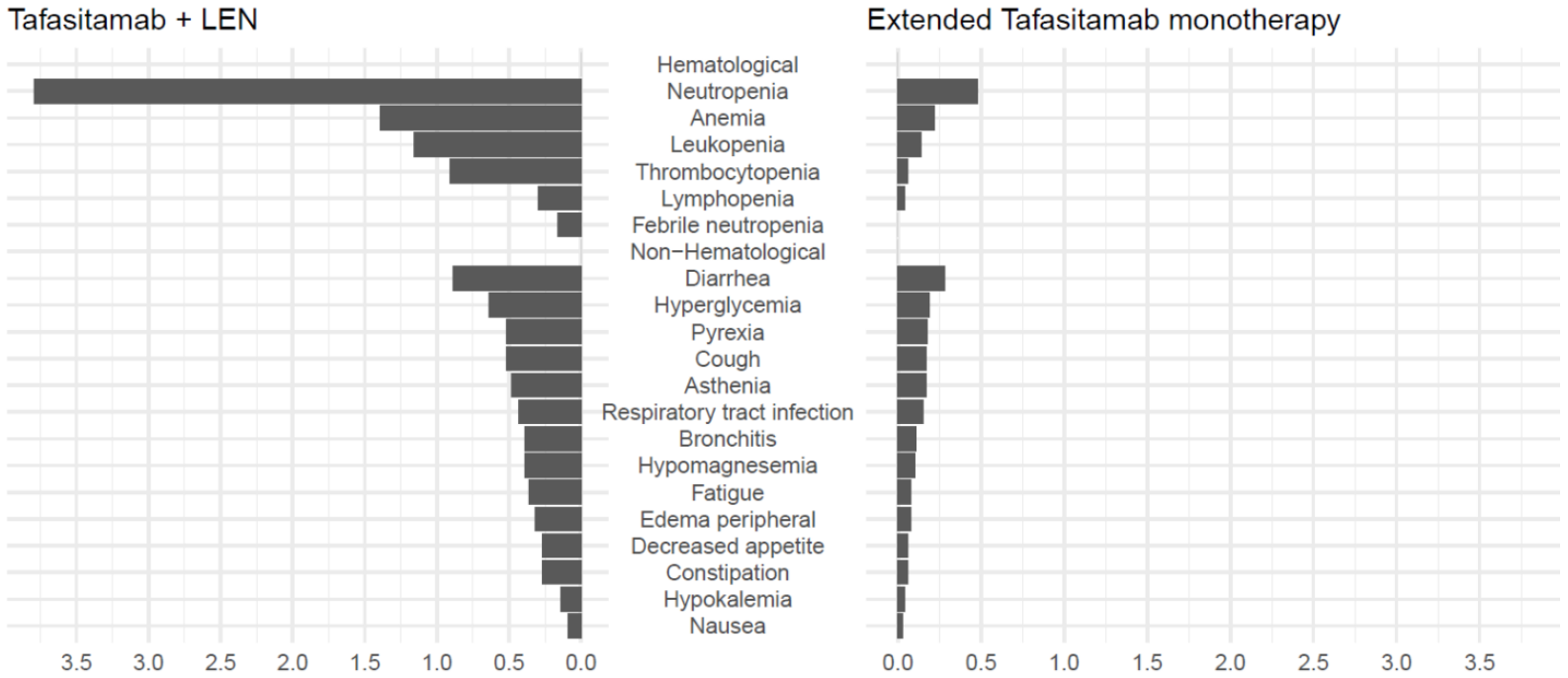
- No unexpected toxicities or new safety signals were reported from the updated analyses

Event	All Grades (≥10%) All patients N=81	Grade ≥3 (>1 patient) All patients N=81
Hematologic TEAEs, n (%)		
Neutropenia	41 (50.6)	40 (49.4)
Anemia	30 (37.0)	6 (7.4)
Thrombocytopenia	25 (30.9)	14 (17.3)
Non-hematologic TEAEs, n (%)		
Diarrhea	29 (35.8)	1 (1.2%)
Asthenia	20 (24.7)	2 (2.5%)
Cough	22 (27.2)	1 (1.2%)

- TEAE, treatment emergent adverse events.

Duell J, *ICML* 2021

Summary of hematological and non-hematological TEAEs (any Grade) count by patient-years of exposure to tafasitamab



- LEN, lenalidomide; TEAE, treatment emergent adverse event.

- 1. Salles G, et al. Lancet Oncol 2020;21(7):978-88.

Summary

- Updated analyses with 3-year follow-up confirm the potential of tafasitamab + LEN followed by tafasitamab monotherapy in achieving durable remission and survival benefit
  - Median DoR was 43.9 months across the full analysis set and was comparable regardless of number of prior therapies
  - Median OS was 33.5 months across the full analysis set and was 47.5 months in patients with one prior therapy
- Tafasitamab plus LEN conferred longer PFS and OS in patients who received with 1 vs ≥2 prior lines of therapy
- Decreased burden of TEAEs during extended tafasitamab monotherapy suggests a good tolerability profile for the extended tafasitamab treatment until progression, leading to durable remission
- These data demonstrate the clinical benefit of this chemotherapy-free regimen as a SoC in patients with R/R DLBCL who are ineligible for ASCT, especially those who have received 1 prior line of treatment

- CR, complete response; LEN, lenalidomide NR, not reached; OS, overall survival; SoC, standard of care; PFS, progression free survival; TEAE, treatment emergent adverse events.