17TH ULTMANN
CHICAGO LYMPHOMA SYMPOSIUM

THE UNIVERSITY OF CHICAGO
MEDICINE & BIOLOGICAL SCIENCES

17TH INTERNATIONAL ULTMANN CHICAGO LYMPHOMA SYMPOSIUM

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Disclosure

Jason Westin

I have the following relevant financial relationships to disclose:

Consultant for: **Novartis, BMS, Kite/Gilead, Genentech, Astra Zeneca, Morphosys, Curis, Amgen**

Speaker's Bureau for: NA

Grant/Research support from: **Novartis, BMS, Kite/Gilead, Genentech, Astra Zeneca, Morphosys, Curis, Amgen, 47, Unum**

Stockholder in: NA

Honoraria from: NA

Employee of: NA

I will discuss the following off label use and/or investigational use in my presentation: loncaT

References

Non-Immunotherapy Options for R/R DLBCL

Jason Westin, MD, MS, FACP
Director, Lymphoma Clinical Research
MD Anderson Cancer Center

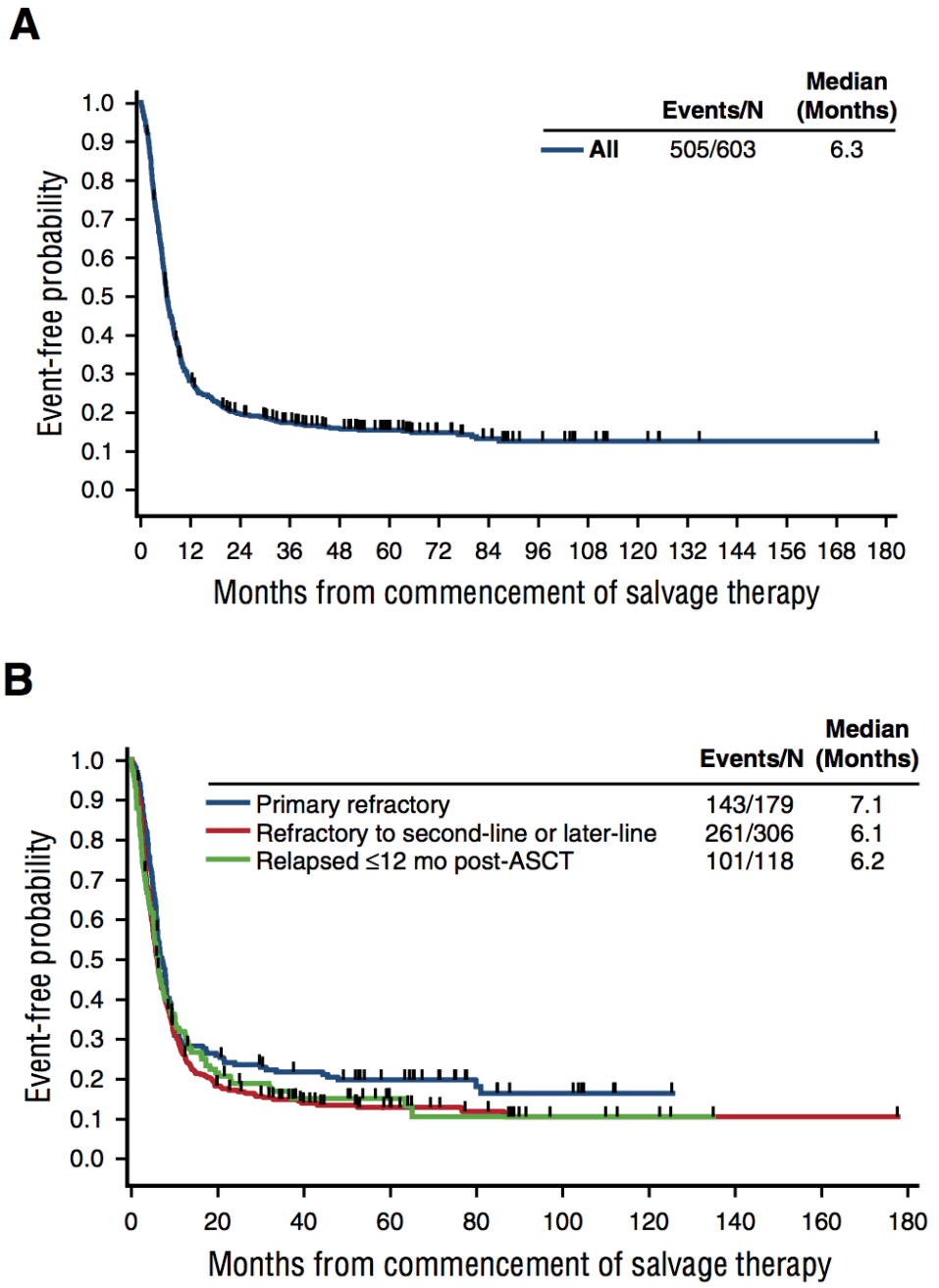
Outline

- Unmet need
- Antibody-drug conjugate
- Monoclonal Ab
- Small Molecules
- Novel combinations
- Future directions

References

Unmet Need

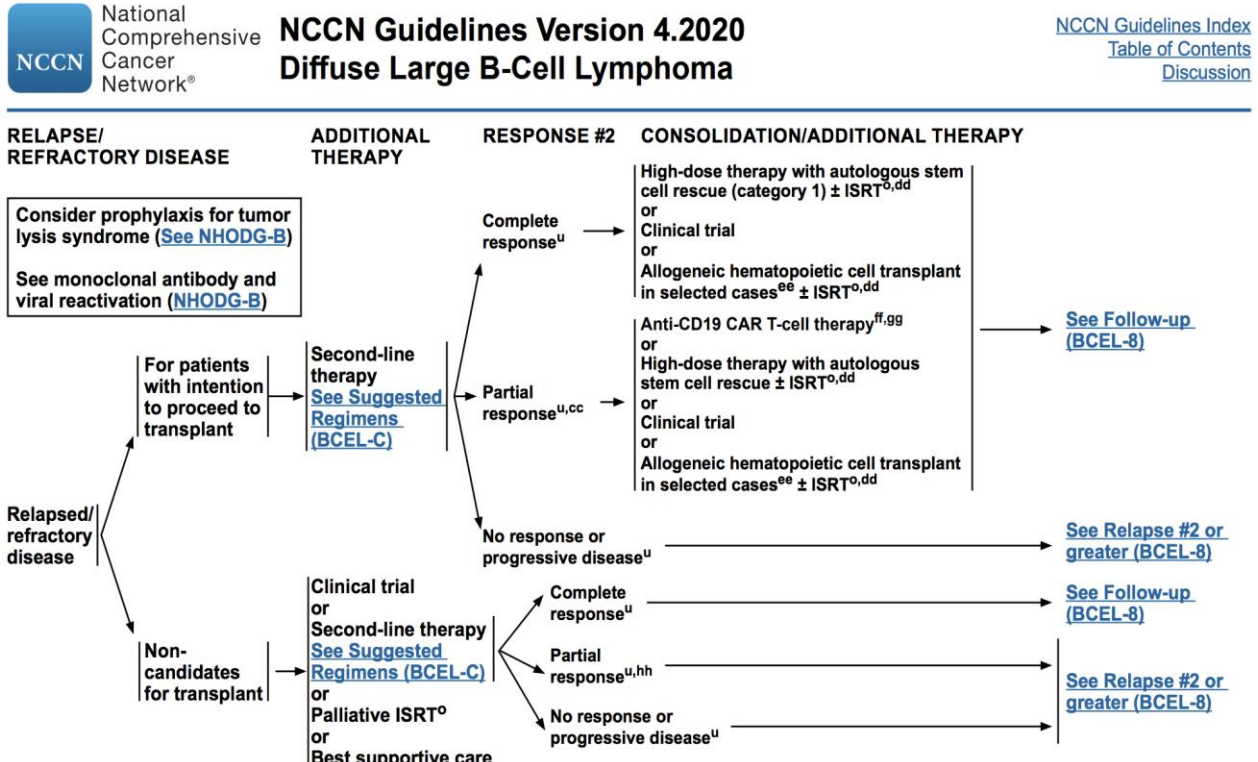
- ~30,000 new DLBCL diagnoses/year in US
- 2/3 cured with 1L therapy
- Of 10,000 with R/R DLBCL:
  - Half eligible for AutoSCT = 5000
  - Half of those respond = 2500
  - Half of those have durable response = 1250
- Of 8750 not cured with 2L chemo, ~20% getting CAR T-cell
- ~7000 R/R DLBCL patients each year need new approaches

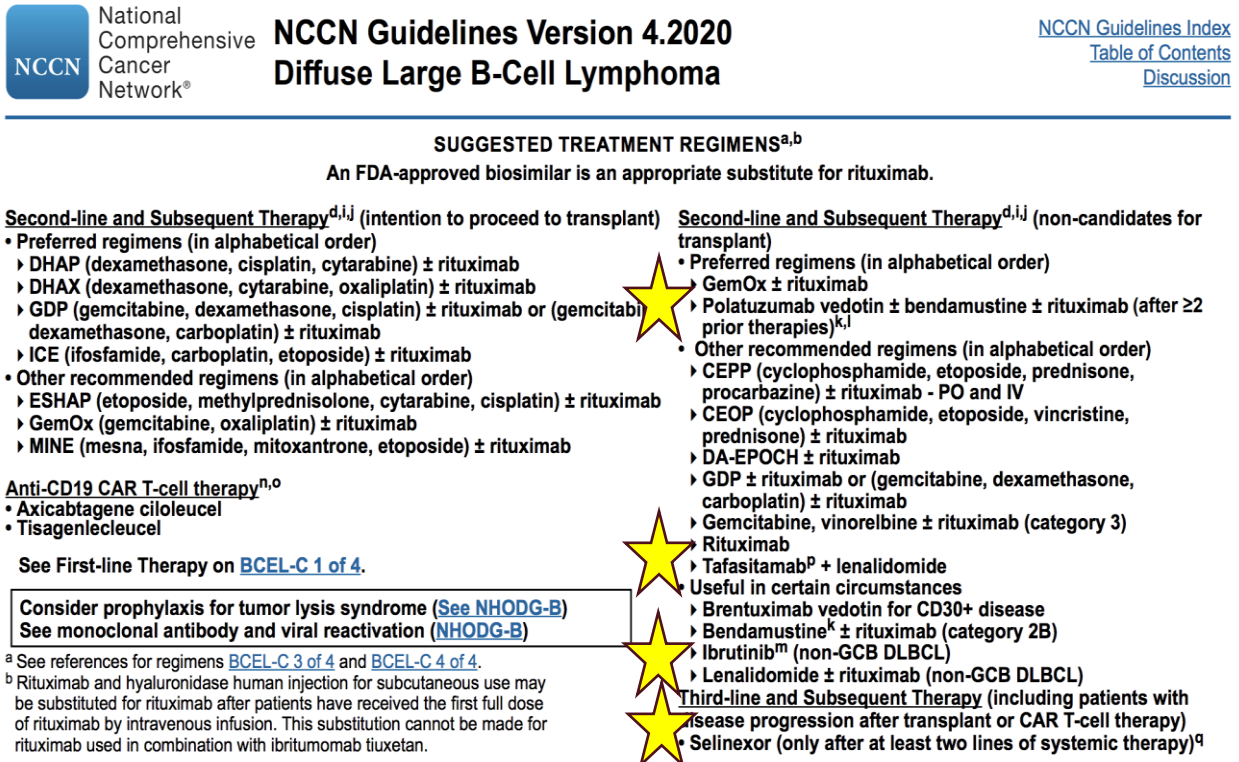


References Crump, … Westin, et al, Blood, 2017, Vol 130, Number16

Unmet Need

- The standard approach for 'non-immunotherapy options' historically have been palliative, not curative
- Chemotherapy regimens often used in a chemotherapy resistant disease





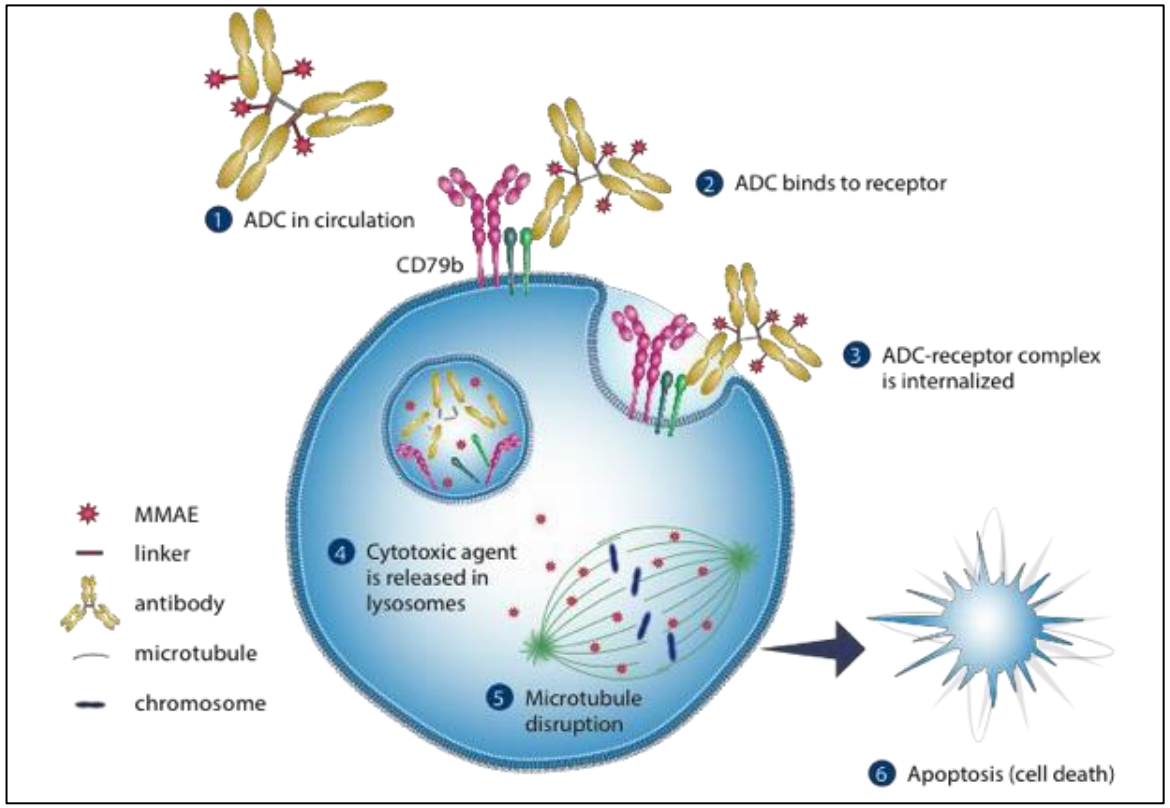
Non-Immunotherapy Non-Chemotherapy Options

- Polatuzumab
- Tafasitamab + Lenalidomide
- Ibrutinib + Lenalidomide
- Selinexor

References

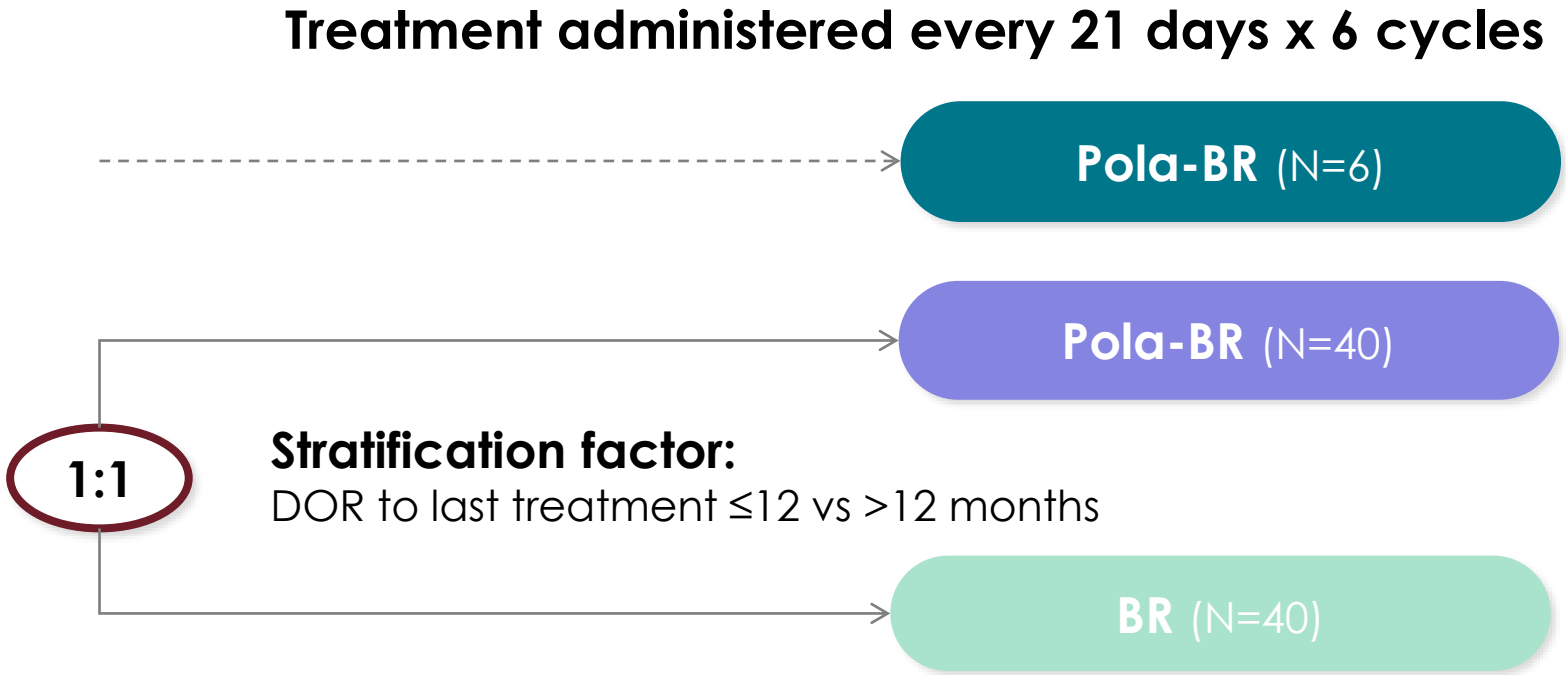
Antibody Drug Conjugates

- Brentuximab Vedotin (CD30)
- Polatuzumab Vedotin (CD79b)
- Loncastuximab Tesirine (CD19)*



References Sehn L, et al. ASH 2019. 1. Sehn L, et al. JCO 2019. DOI: 10.1200/JCO.19.00172 [Epub ahead of print].

Polatuzumab Vedotin Plus BR in R/R DLBCL: Updated Results of a Phase 1b/2 Randomized Study



Key eligibility criteria

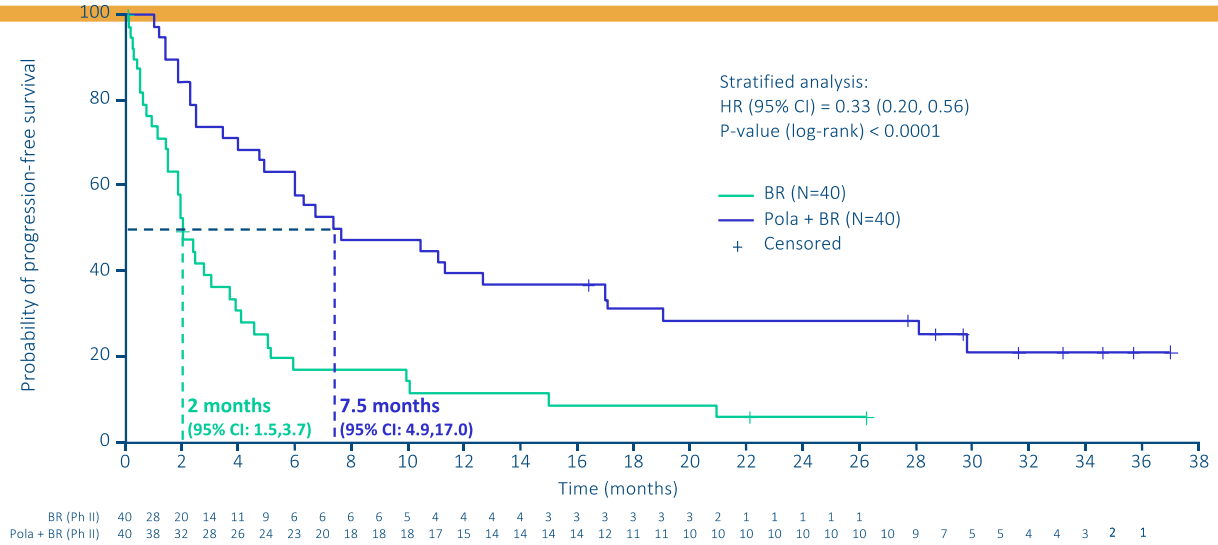
- DLBCL with ≥1 prior therapy
- HSCT ineligible (prior auto-HSCT >100 days from C1D1 allowed)
- Excluded: FL grade 3b, transformed iNHL, CNS lymphoma
- Excluded: prior allogeneic HSCT

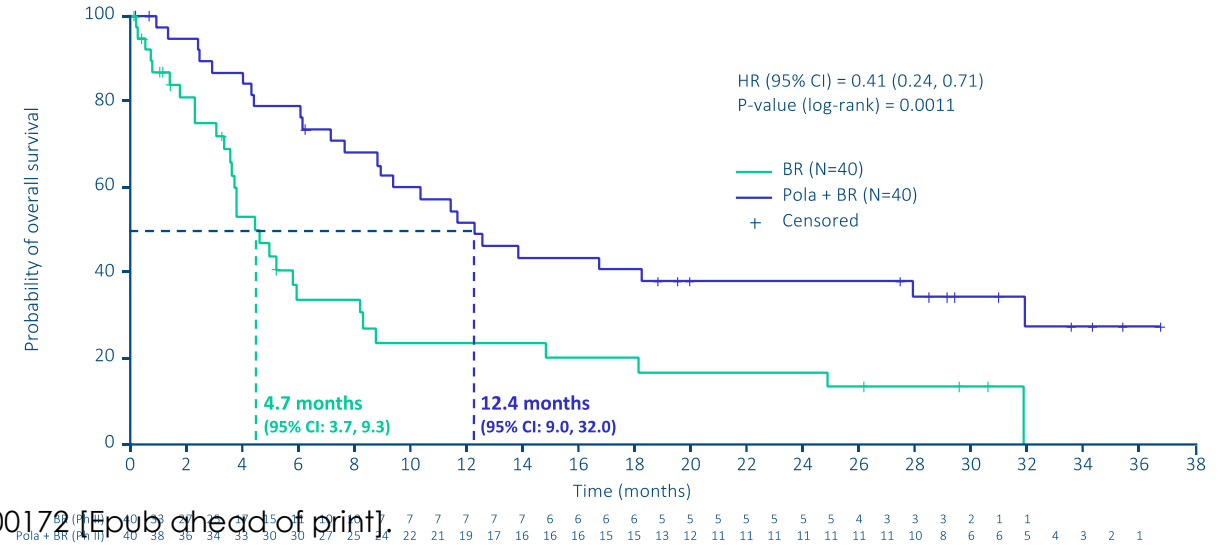
- **Polatuzumab vedotin:** 1.8 mg/kg, day 2 in cycle 1 then day 1 in each subsequent cycle
- **Rituximab (R):** 375 mg/m^2 day 1 in each cycle
- **Bendamustine (B):** 90 mg/m^2 days 2-3 in cycle 1, then day 1-2 in each subsequent cycle

References Sehn L, et al. ASH 2019. 1. Sehn L, et al. JCO 2019. DOI: 10.1200/JCO.19.00172 [Epub ahead of print].

Polatuzumab-BR: Efficacy

INV-Assessed Updated Efficacy Outcomes[a]	Phase 1b	Phase 2 Randomized	
	Pola-BR (N=6)	BR (N=40)	Pola-BR (N=40)
Median DOR, mo[b,c] (95% CI)	44.6 (NE, NE)	**4.1** (2.6, 12.7)	**12.7** (5.8, 27.9)
HR (95% CI)	-	**0.42** (0.19, 0.91); *P*=0.0245	
Median PFS, mo (95% CI)	24.3 (1.8, 46.7)	**2.0** (1.5, 3.7)	**7.5** (4.9, 17.0)
HR (95% CI)	-	**0.33** (0.2, 0.56); *P*<0.0001	
Median OS, mo (95% CI)	NE (5.6, NE)	**4.7** (3.7, 8.3)	**12.4** (9.0, 32.0)
HR (95% CI)	-	**0.41** (0.24, 0.71); *P*=0.0011	

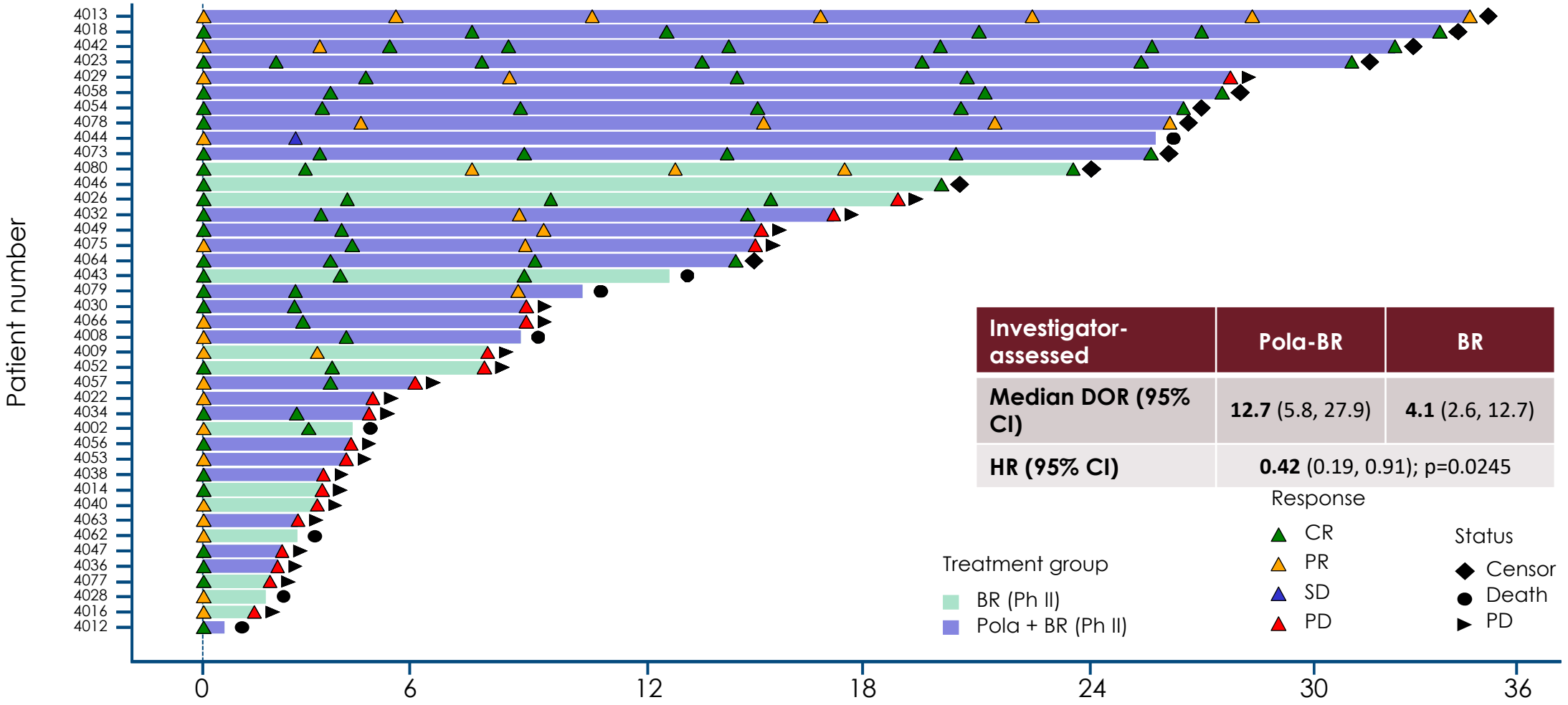




NE: Not estimable.
[a]HR and p-values based on stratified analysis.
[b]All responding patients: pola-BR n=28; BR n=13.
[c]Median DOR (95% CI) by INV after censoring for consolidative therapy: pola-BR 10.3 months (5.8, NE); BR: 3.3 months (2.6, 18.9).
Sehn L, et al. ASH 2019.

References Sehn L, et al. ASH 2019. 1. Sehn L, et al. JCO 2019. DOI: 10.1200/JCO.19.00172 [Epub ahead of print].

Polatuzumab-BR: Phase 2 Randomized DOR (INV-Assessed)



Investigator-assessed	Pola-BR	BR
Median DOR (95% CI)	**12.7** (5.8, 27.9)	**4.1** (2.6, 12.7)
HR (95% CI)	**0.42** (0.19, 0.91); p=0.0245	

References Sehn L, et al. ASH 2019.

Polatuzumab + BR: Phase 2 Trial Results

Response Rate and Duration of Response

End of Treatment Response by IRC	Pola + BR (N=40)	BR (N=40)	Hazard Ratio
ORR	45.0%	17.5%	-
CR	40.0%	17.5%	-
PR	5.0%	0%	-
mDoR, mo (IRC) *(95% CI)*	12.6 (7.2, NE)	7.7 (4.0, 18.9)	0.47 (0.19, 1.14) p=not significant

Safety Results

Adverse Events	Pola + BR (n=39)	BR (n=39)
Neutropenia (Grade 3-4)	46.2%	33.3%
Thrombocytopenia (Grades 3-4)	41.0%	23.1%
Peripheral neuropathy	43.6%	7.7%
Diarrhea	38.5%	28.2%

IRC, independent review committee; mDoR, median duration of response; NE, not evaluable.

References

Sehn LH et al. *J Clin Oncol.* 2020;38(2):155-165.

Polatuzumab works – but with Bendamustine?

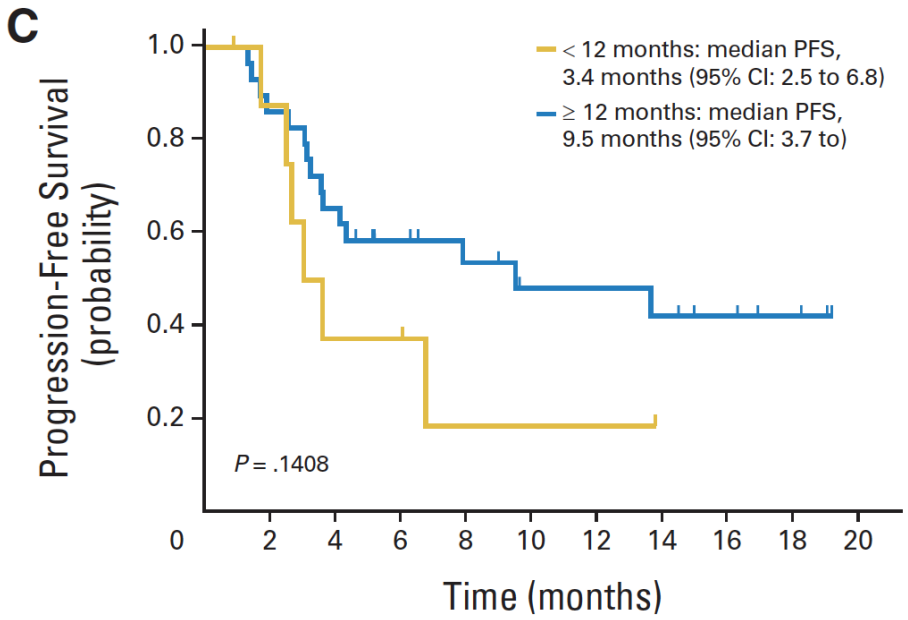
Multicenter Phase II Study of Bendamustine Plus Rituximab in Patients With Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Ken Ohmachi, Nozomi Niitsu, Toshiki Uchida, Seok Jin Kim, Kiyoshi Ando, Naoki Takahashi, Naoto Takahashi, Naokuni Uike, Hyeon Seok Eom, Yee Soo Chae, Takashi Terauchi, Ukihide Tateishi, Mitsuaki Tatsumi, Won Seog Kim, Kensei Tobinai, Cheolwon Suh, and Michinori Ogura

Table 3. Treatment Response to Bendamustine Plus Rituximab

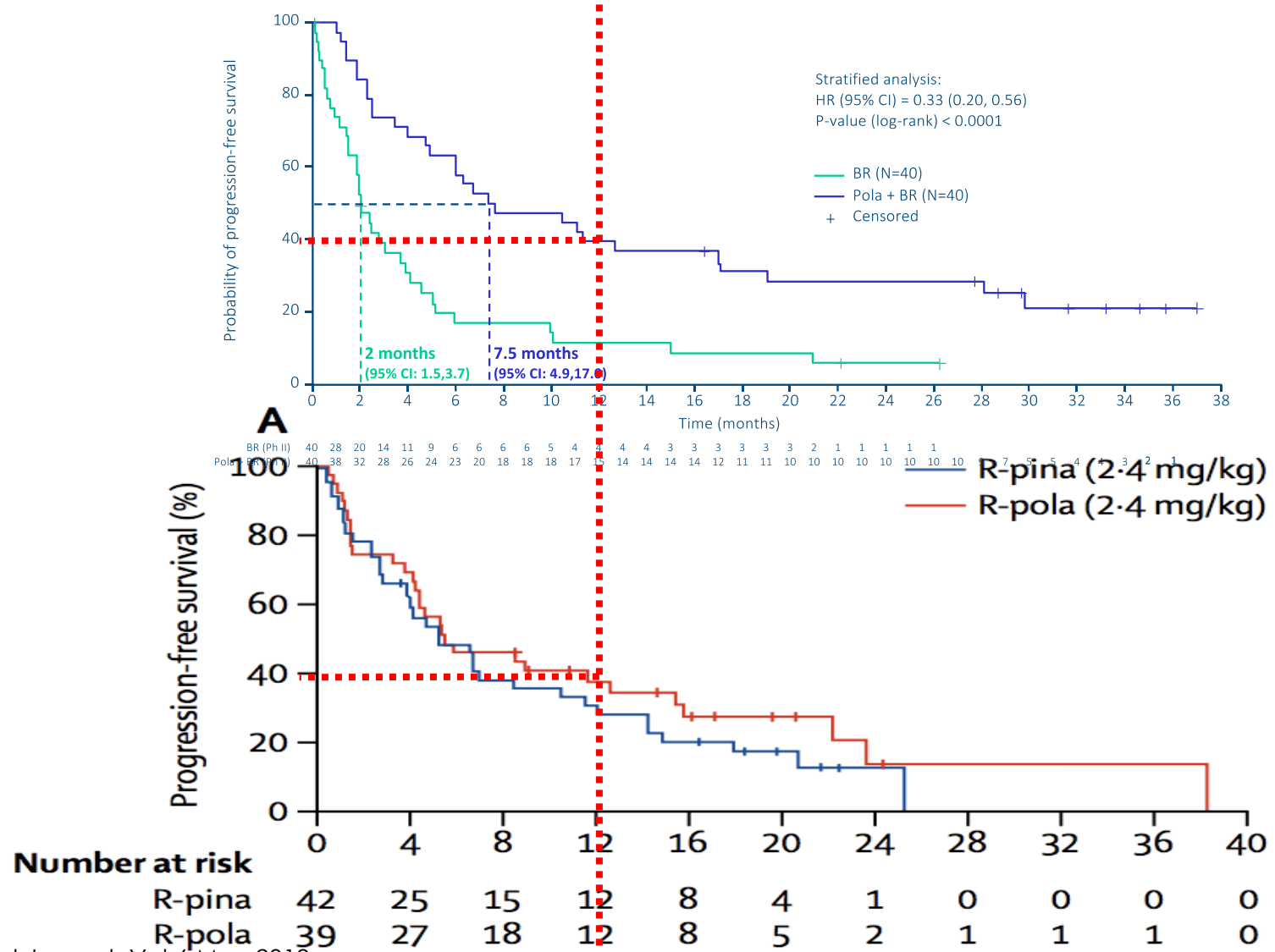
		Tumor Response										ORR		CR Rate	
		CR		PR		SD		PD		NE					
Variables	No.	No.	%	No.	%	No.	%	No.	%	No.	%	%	95% CI	%	95% CI
No. of patients	59	22	37.3	15	25.4	10	16.9	10	16.9	2	3.4	62.7	49.1 to 75.0	37.3	25.0 to 50.9
Age, years (P = 1.000 with respect to the ORR)															
≥ 65	37	14	37.8	9	24.3	6	16.2	7	18.9	1	2.7	62.2	44.8 to 77.5	37.8	22.5 to 55.2
< 65	22	8	36.4	6	27.3	4	18.2	3	13.6	1	4.5	63.6	40.7 to 82.8	36.4	17.2 to 59.3
No. of prior regimens (P = .027, 1 *v* 2, 1 *v* 3, 2 *v* 3 with respect to the ORR)															
1	38	16	42.1	12	31.6	3	7.9	5	13.2	2	5.3	73.7	56.9 to 86.6	42.1	26.3 to 59.2
2	13	4	30.8	3	23.1	4	30.8	2	15.4	0	0.0	53.8	25.1 to 80.8	30.8	9.1 to 61.4
3	8	2	25.0	0	0.0	3	37.5	3	37.5	0	0.0	25.0	3.2 to 65.1	25.0	3.2 to 65.1
Relapse after ASCT	8	3	37.5	2	25.0	2	25.0	1	12.5	0	0.0	62.5	24.5 to 91.5	37.5	8.5 to 75.5
Elapsed time since prior treatment, months (P = .036 with respect to the ORR)															
< 12	9	0	0.0	4	44.4	1	11.1	2	22.2	2	22.2	44.4	13.7 to 78.8	0	0 to 33.6
≥ 12	29	16	55.2	8	27.6	2	6.9	3	10.3	0	0.0	82.8	64.2 to 94.2	55.2	35.7 to 73.6
Lactate dehydrogenase (P = .060 with respect to the ORR)															
< ULN	26	13	50.0	7	26.9	4	15.4	2	7.7	0	0.0	76.9	56.4 to 91.0	50.0	29.9 to 70.1
≥ ULN	33	9	27.3	8	24.2	6	18.2	8	24.2	2	6.1	51.5	33.5 to 69.2	27.3	13.3 to 45.5

Abbreviations: ASCT, autologous stem-cell transplantation; CR, complete response; NE, not evaluated; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; ULN, upper limit of normal.



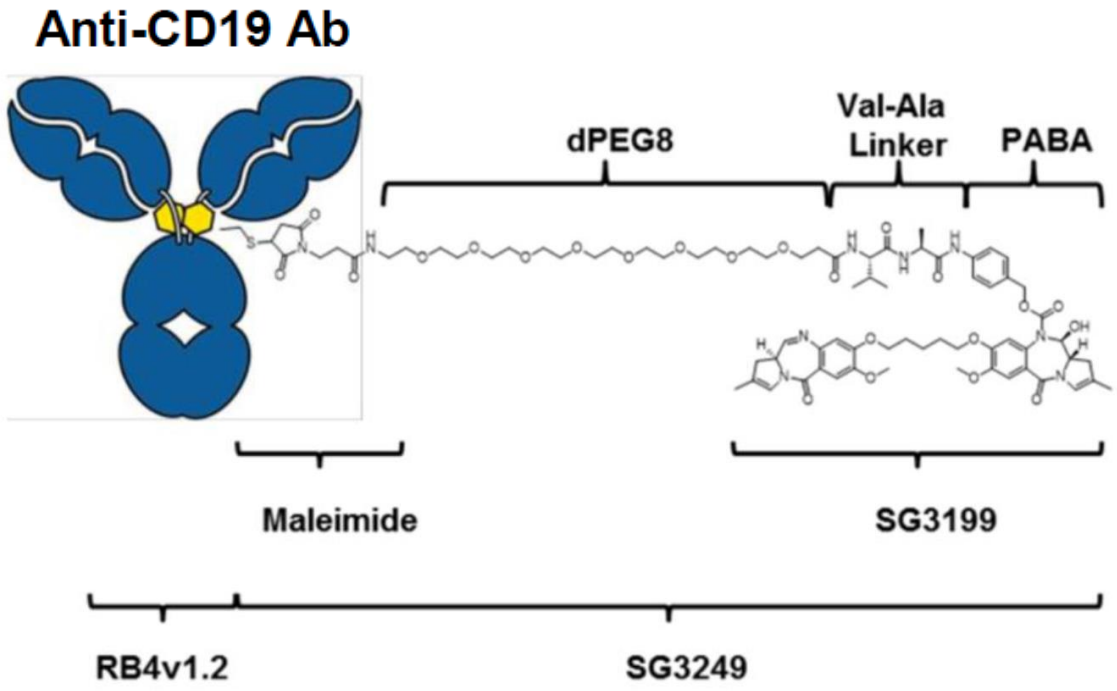
References JCO 2013, 31:2103-2109

What if the trial was BR vs PBR vs PR?



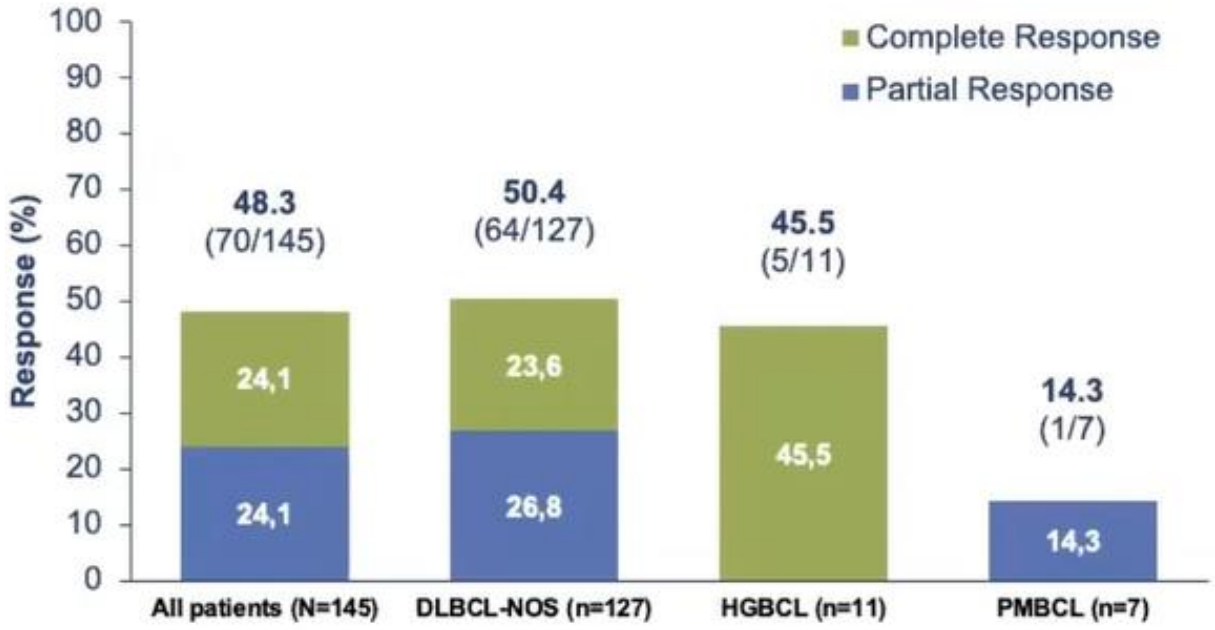
References Morschhauser et al, Lancet, Vol 6 May 2019

Loncastuximab Tesirine (ADCT-402)



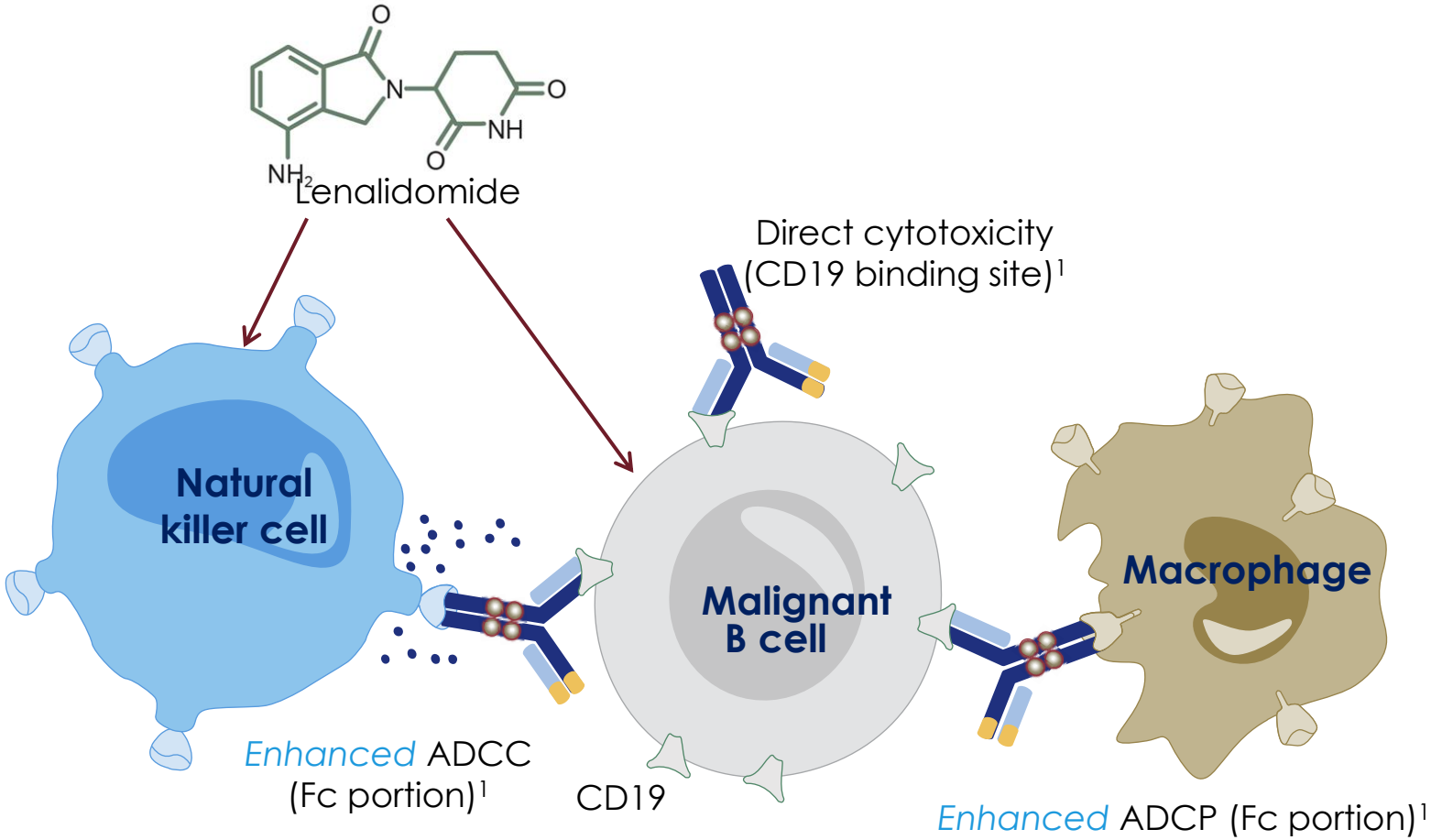
Loncastuximab tesirine comprises a humanized anti-CD19 Ab stochastically conjugated to a potent PBD dimer toxin[1]

Loncastuximab tesirine binds to CD19 antigen on the tumor cell surface

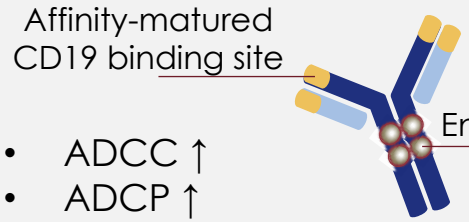


References Zammarchi F, et al. *Blood*. 2018;131:1094–105., Carlo-Stella C, et al. EHA 2020. Abstract P426-4.

Tafasitamab (MOR208) and Lenalidomide (LEN)



Tafasitamab (Fc-enhanced, anti-CD19 mAb)[1–3]



- ADCC ↑
- ADCP ↑
- Direct cell death
- Encouraging single-agent activity in patients with R/R DLBCL and iNHL

Lenalidomide[4,5]

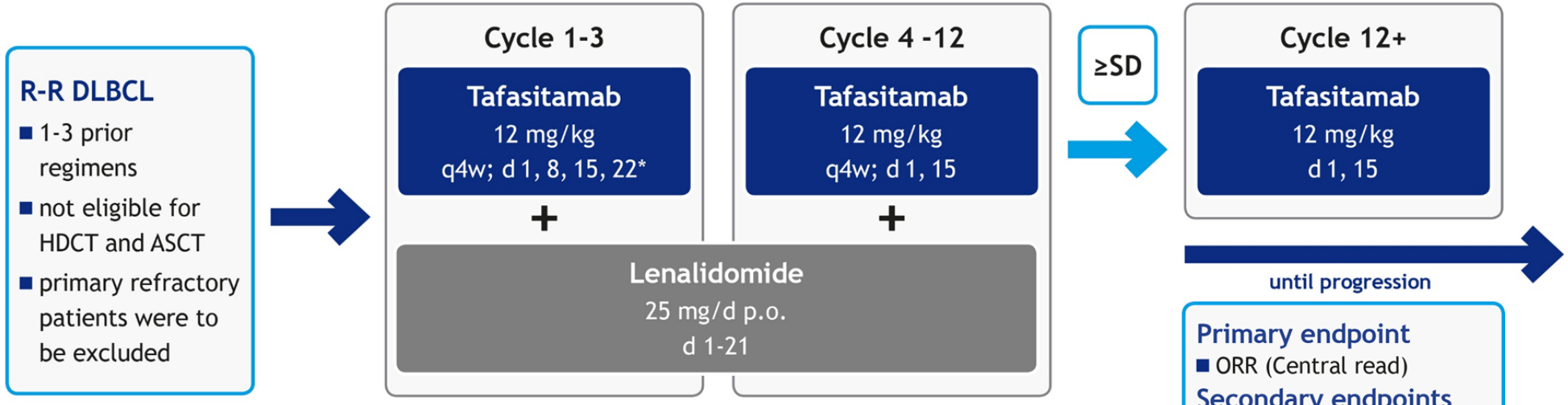
- T-cell and NK-cell activation/expansion
- Direct cell death
- Well-studied as an anti-lymphoma agent, alone or in combination

ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; iNHL, indolent non-Hodgkin's lymphoma; NK-cell, natural killer cell.

References 1. Horton HM et al. *Cancer Res* 2008;68(19):8049–57; 2. Woyach JA et al. *Blood* 2014;124(24):3553–60; 3. Jurczak W et al. *Ann Oncol* 2018;29(5):1266–72; 4. Witzig TE et al. *Ann Oncol* 2015; 26(8):1667–77; 5. Czuczman MS et al. *Clin Cancer Res* 2017;23(15):4127–37.

L-MIND Study Design

Phase 2, single-arm, open-label, multicenter study (NCT02399085)



*A loading dose of tafasitamab was administered on day 4 of cycle 1

- Sample size suitable to detect ≥15% absolute increase in ORR for tafasitamab/LEN combination versus LEN monotherapy at 85% power, 2-sided alpha of 5%
- Mature data: primary endpoint analysis with data cut-off of Nov 30, 2018; minimum follow-up 12 months, median follow-up 17.3 months

References Salles et al. ICML 2019. #124.

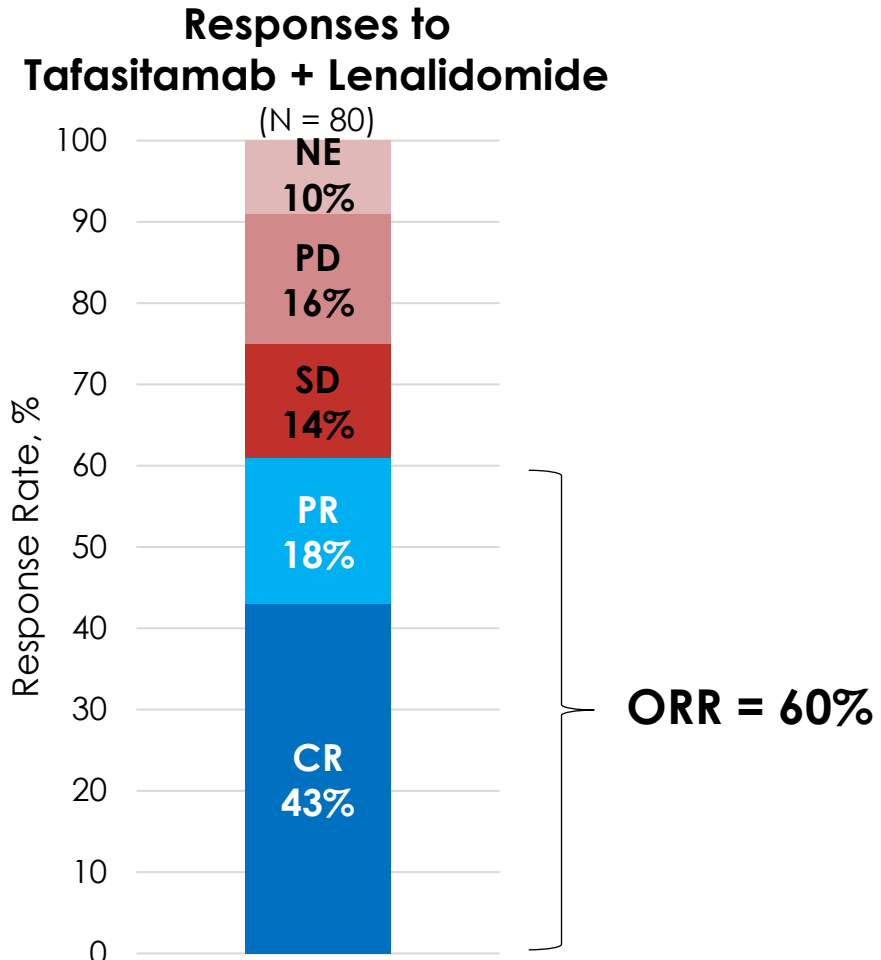
L-MIND: Baseline Characteristics

Characteristic	Specification	N = 81
Age, years	Median	72 (62-76)
Sex, n (%)	Male	44 (54%)
Ann Arbor stage at screening, n (%)	III or IV	61 (75%)
IPI score at screening, n (%)	0-2 (low and low-intermediate risk) 3-5 (intermediate-high and high risk)	40 (49%) 41 (51%)
Lactate dehydrogenase concentrations at screening, n (%)	Elevated Within reference range	45 (56%) 36 (44%)
Previous lines of systemic therapy , n (%)	Median (range) 1 2 >3	2 (1-4) 40 (50%) 35 (43%) 6 (7%)
Primary refractory, n (%)	Yes	15 (19%)
Refractory to most recent previous therapy, n (%)	Yes	36 (44%)
Previous ASCT, n (%)	Yes	9 (11%)
Cell of origin by immunohistochemistry, n (%)	Germinal center B cell Non-germinal center B cell Unknown	38 (47%) 21 (26%) 22 (27%)

References

IPI, International Prognostic Index.
Salles G, et al. *Lancet Oncol*. 2020;21(7):978-988.

L-MIND: Objective Response Rate (Primary Endpoint)



IRC-assessed response[a]	Patients treated with tafasitamab plus lenalidomide (N = 80) n (%, 95% CI)
Best objective response[a]	
Complete response	34 (43%; 32-54)
Partial response	14 (18%; 10-28)
Stable disease	11 (14%; 7-23)
Progressive disease	13 (16%; 9-26)
Not evaluable	8 (10%; 4-19)
PET-confirmed complete response	30/34 (88%; 73-97)
Objective response (CR + PR)	48 (60%; 48-71)
Disease control (CR + PR + SD)	59 (74%; 63-83)

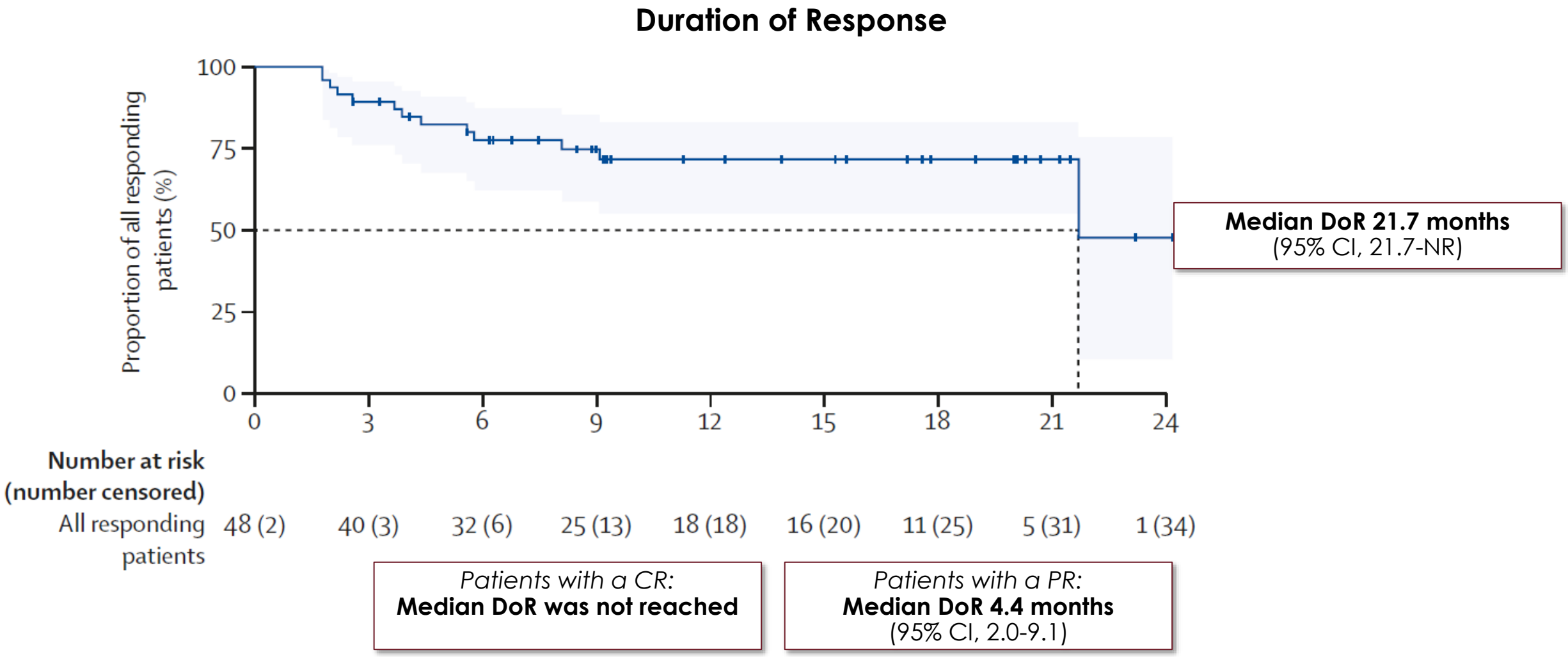
[a] Best objective response according to independent radiology committee or clinical review committee.

PET, positron emission tomography.

References Salles G, et al. *Lancet Oncol*. 2020;21(7):978-988.

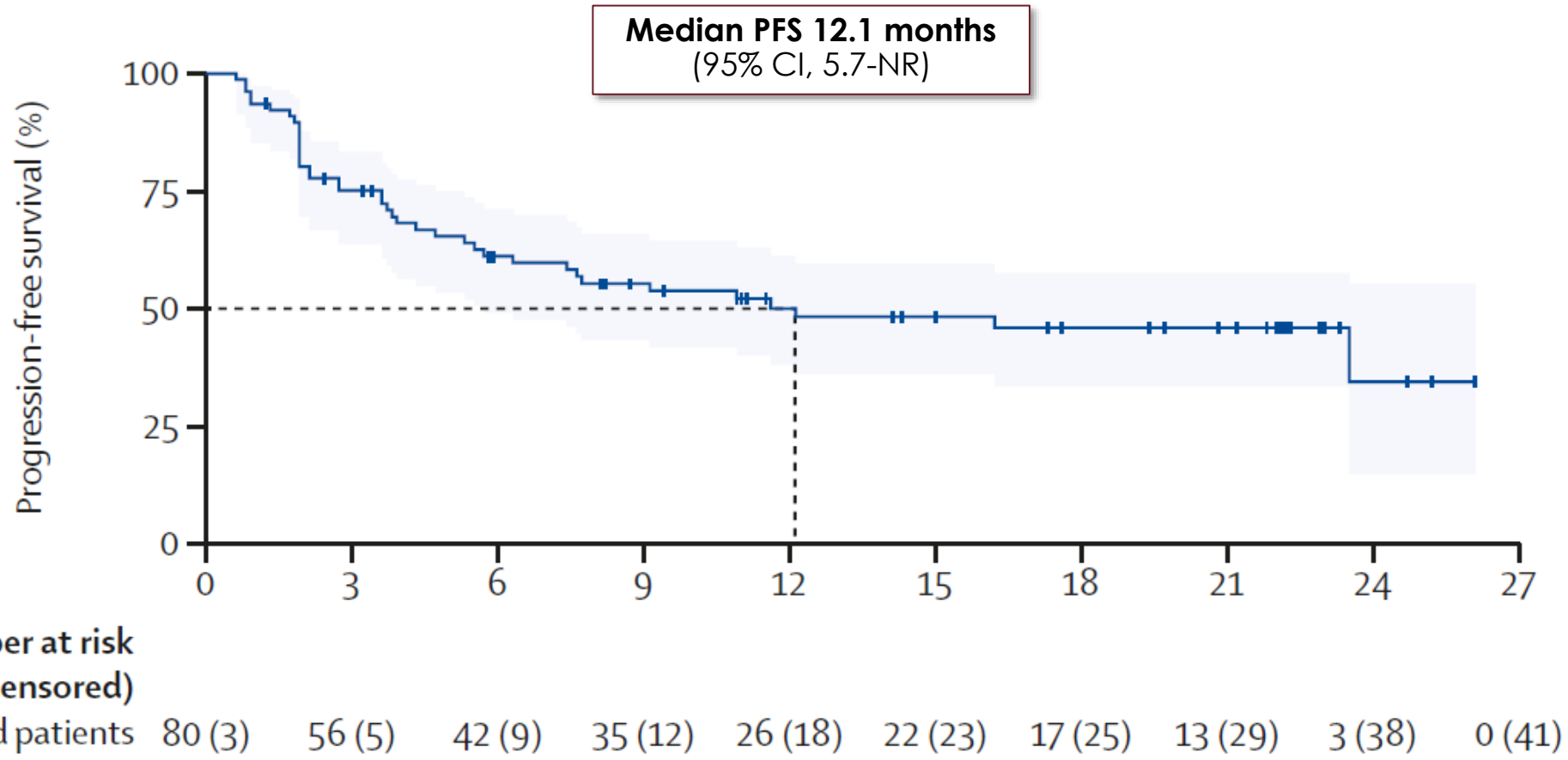
19

L-MIND: Duration of Response



References Salles G, et al. *Lancet Oncol*. 2020;21(7):978-988.

L-MIND: Progression-Free Survival[a]



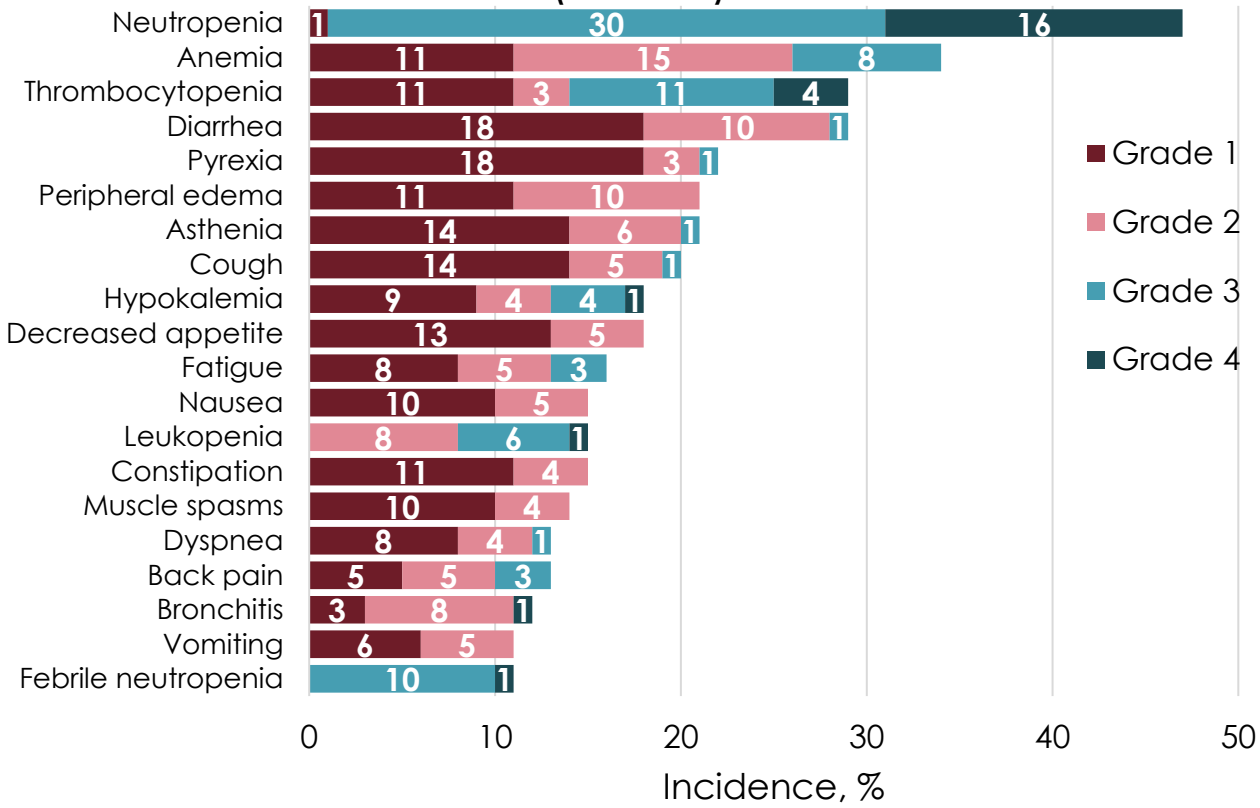
[a] Median follow-up of 17.3 months.

References Salles G, et al. *Lancet Oncol*. 2020;21(7):978-988.

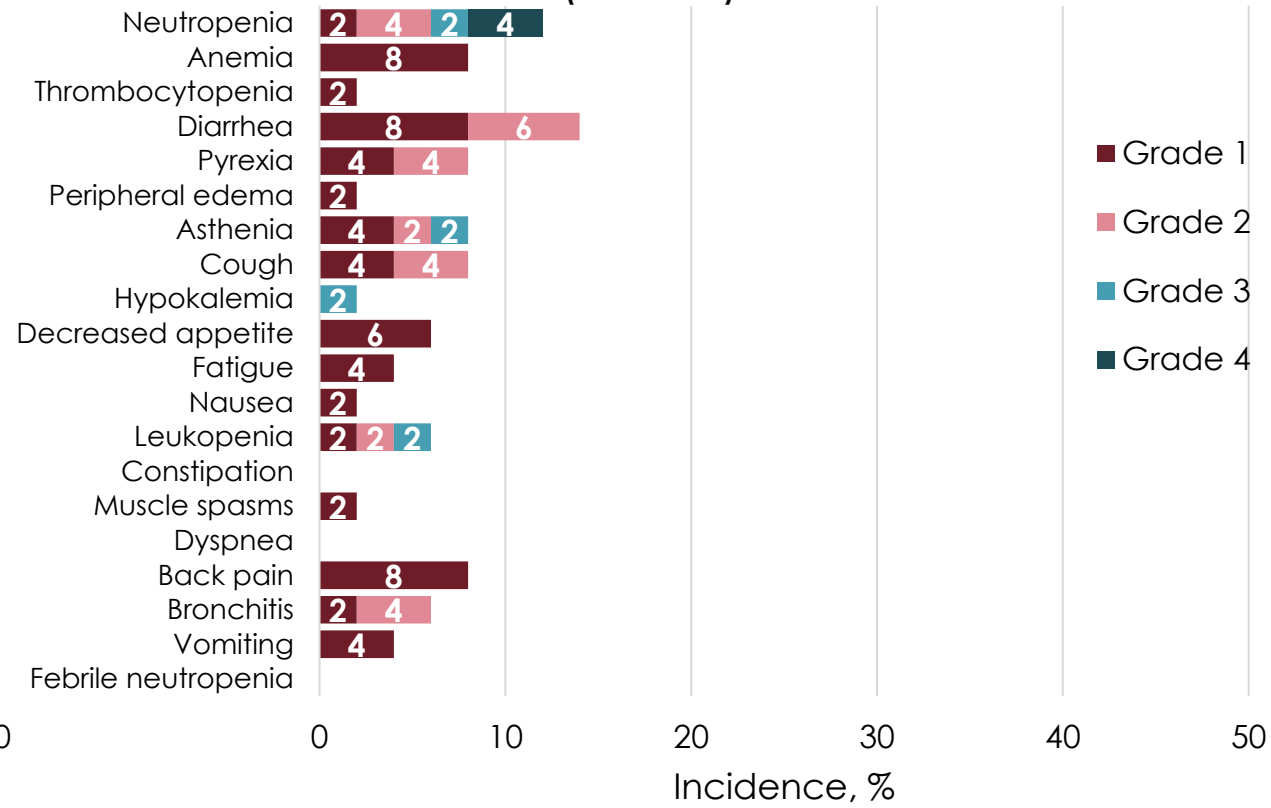
21

L-MIND: Safety by Treatment Phase

AEs During Cycles 1-12
Before discontinuation of lenalidomide
(N = 80)



AEs During Tafasitamab Monotherapy
After discontinuation of lenalidomide
(N = 51)



TEAEs, treatment-emergent adverse events.

References Salles G, et al. *Lancet Oncol*. 2020;21(7):978-988.

22

Tafasitamab works, but with Lenalidomide?

Response Rates Based on IRAC Assessment (IWRC 1999)[a]
(mITT Population)

	Overall		Immunohistochemis GCB		
	Len $n = 51$	IC $n = 51$	Len $n = 23$	IC $n = 25$	Len $n = 28$
ORR, *n* (%)	14 (27.5)	6 (11.8)	6 (26.1)	3 (12.0)	8 (28
[95% CI][b]	[15.9–41.7]	[4.4–23.9]	[10.2–48.4]	[2.5–31.2]	[13.2–4
P value[c]	0.079		0.279		
PFS, weeks	13.6	7.9	10.1	9.0	15.
HR (95% CI)	0.64 (0.41–0.99)		0.82 (0.43–1.57)		0.5
P value	0.041		0.550		
OS, weeks	31.0	24.6	30.0	24.9	32.
HR (95% CI)	0.91 (0.59–1.41)		1.23 (0.65–2.34)		0.
P value	0.673		0.526		

[a]mITT population; defined as all randomized patients who had confirmed DLBCL an
[b]Exact CI based on binomial distribution.
[c]*P* value derived from the Fisher exact test.

	All patients[a] (n = 45) n (%)	DLBCL (n = 32) n (%)
ORR, % (n)	15 (33%)	9 (28%)
CR	10 (22%)	7 (22%)
PR	5 (11%)	2 (6%)
SD	11 (24%)	9 (28%)
PD	15 (33%)	12 (37%)
Unevaluable	4 (9%)	2 (6%)

ABC, activated B-cell; IC, investigator's choice; IRAC, independent response assessment committee; IWRC, international workshop response criteria; mITT, modified intent-to-treat.

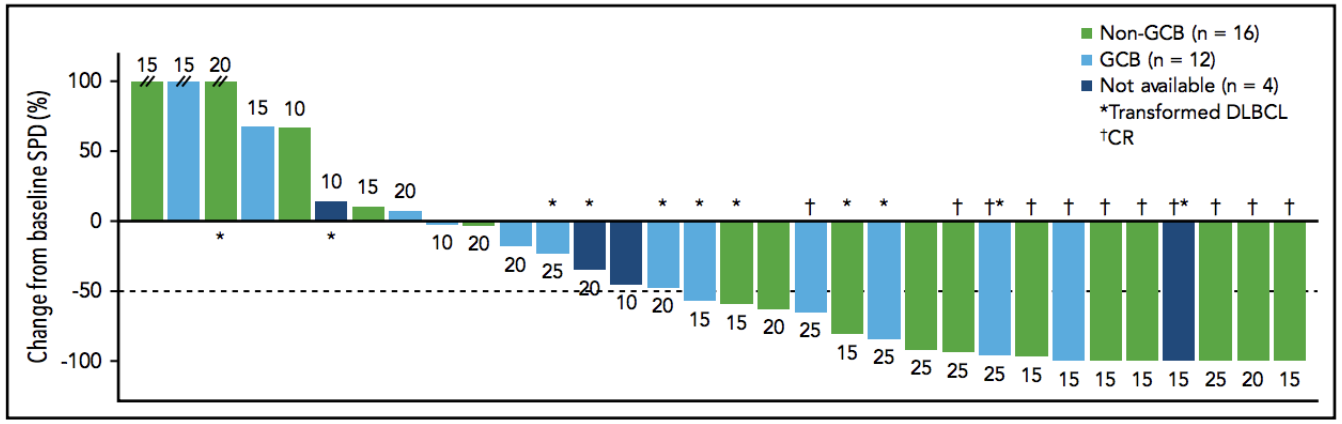
References Czuczman MS, et al. *Clin Cancer Res* 2017;23(15):4127–37., Wang M, et al. Leukemia. 2013;27:1902-1909.

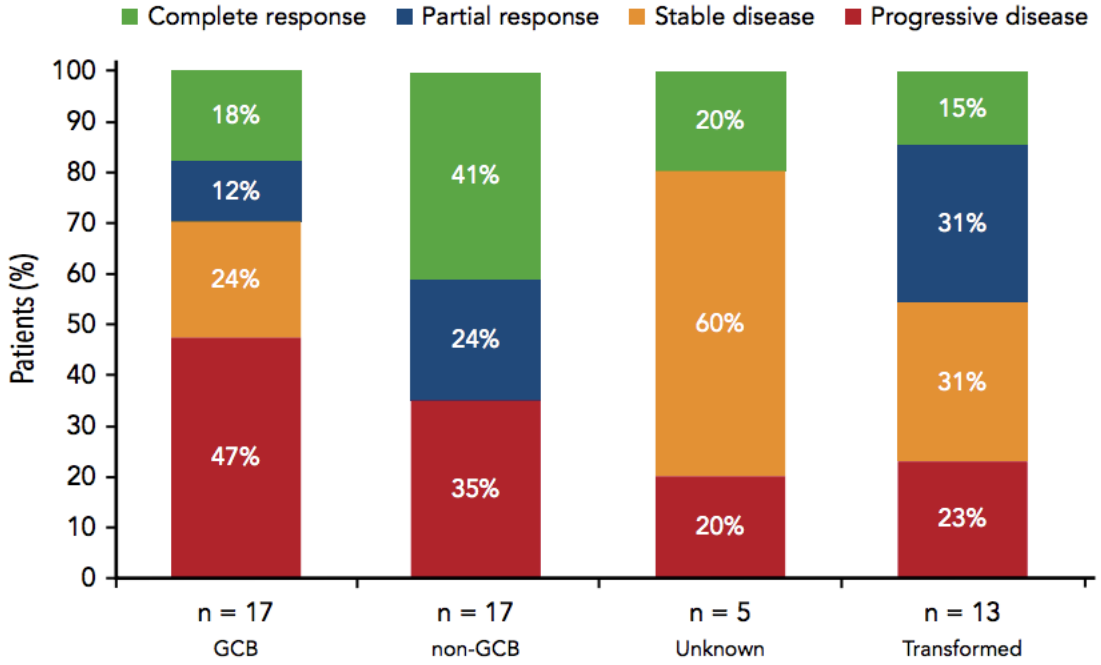
Lenalidomide + Ibrutinib + Rituximab in R/R DLBCL

CLINICAL TRIALS AND OBSERVATIONS

Ibrutinib plus lenalidomide and rituximab has promising activity in relapsed/refractory non–germinal center B-cell–like DLBCL

Andre Goy,[1] Radhakrishnan Ramchandren,[2] Nilanjan Ghosh,[3] Javier Munoz,[4] David S. Morgan,[5] Nam H. Dang,[6] Mark Knapp,[7] Maria Delioukina,[8] Edwin Kingsley,[9] Jerry Ping,[10] Darrin M. Beaupre,[10] Jutta K. Neuenburg,[10] and Jia Ruan[11]

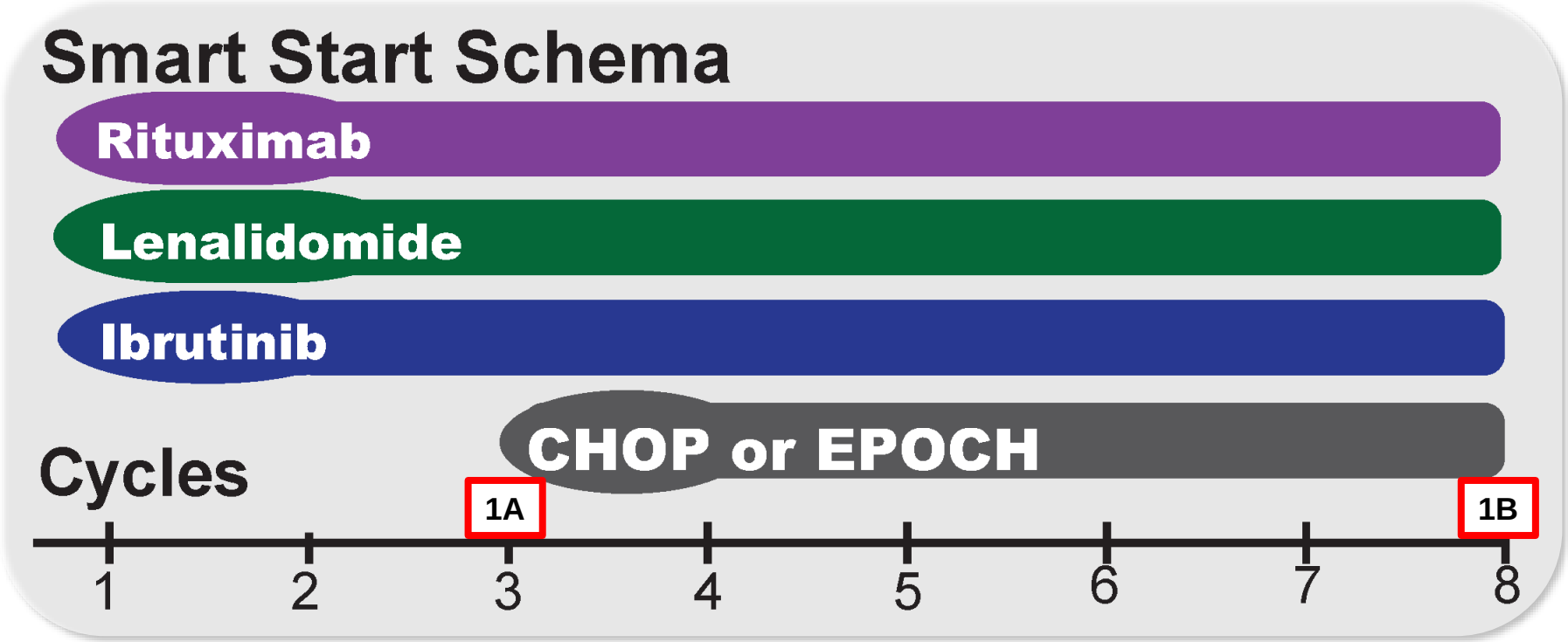




References Goy et al, Blood 2019, Vol 134, Number 13

Lenalidomide + Ibrutinib + Rituximab in 1L DLBCL

- Phase II, single arm, single center, investigator-initiated trial



- Primary Objectives
  - 1A: To determine the ORR at the end of 2 cycles of RLI alone
  - 1B: To determine the CR rate at the end of RLI x 2 + RLI combined with chemotherapy x 6

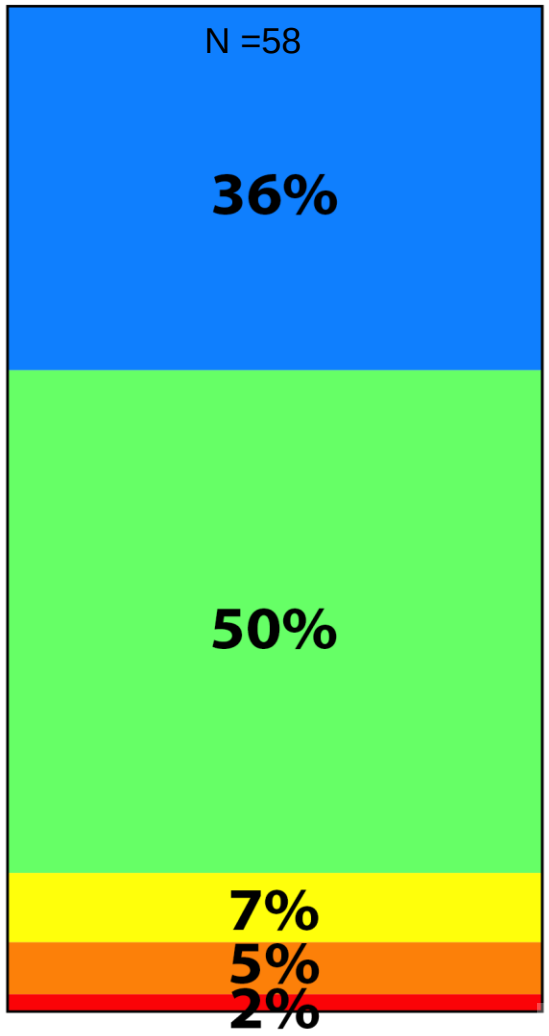
References

Jason Westin – Smart Start Trial

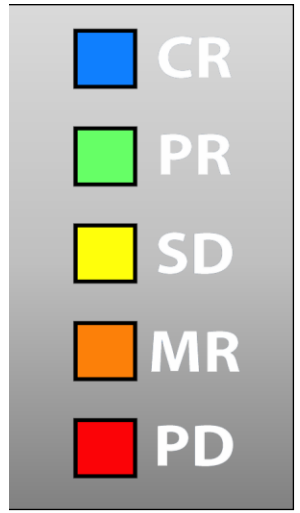
Overall Response

RLI 2 Cycles

1A



1B



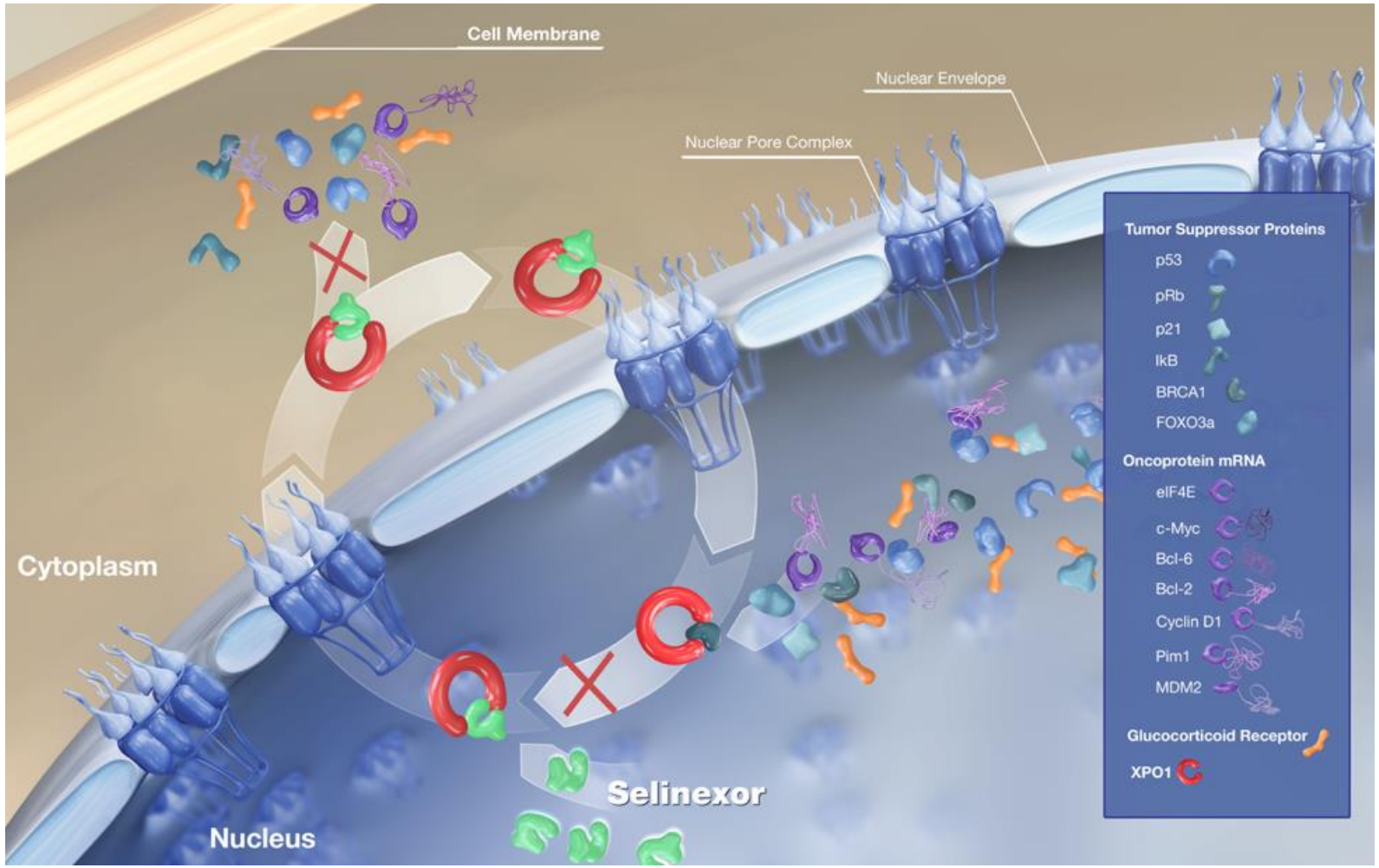
ITT ORR 98%
1 scan and off therapy
CR 92.3% (n=52)
PR 5.8% (n=3)
PD 1.9% (n=1)

OFF Study
2 WC

1 WC
1 PD

1 Death in PR

Selinexor



Select Targets	Outcome
TP53	Tumor suppressor
IkB	Inhibitor of NFkB signaling pathway
FOXO	Tumor suppressor (upregulate factors which inhibit cell proliferation)
CDKN1 A/1B	Inhibitors of cell cycle progression
eIF4E	Regulates passage of mRNA of a number of oncoproteins (MYC, Cyclin D1)

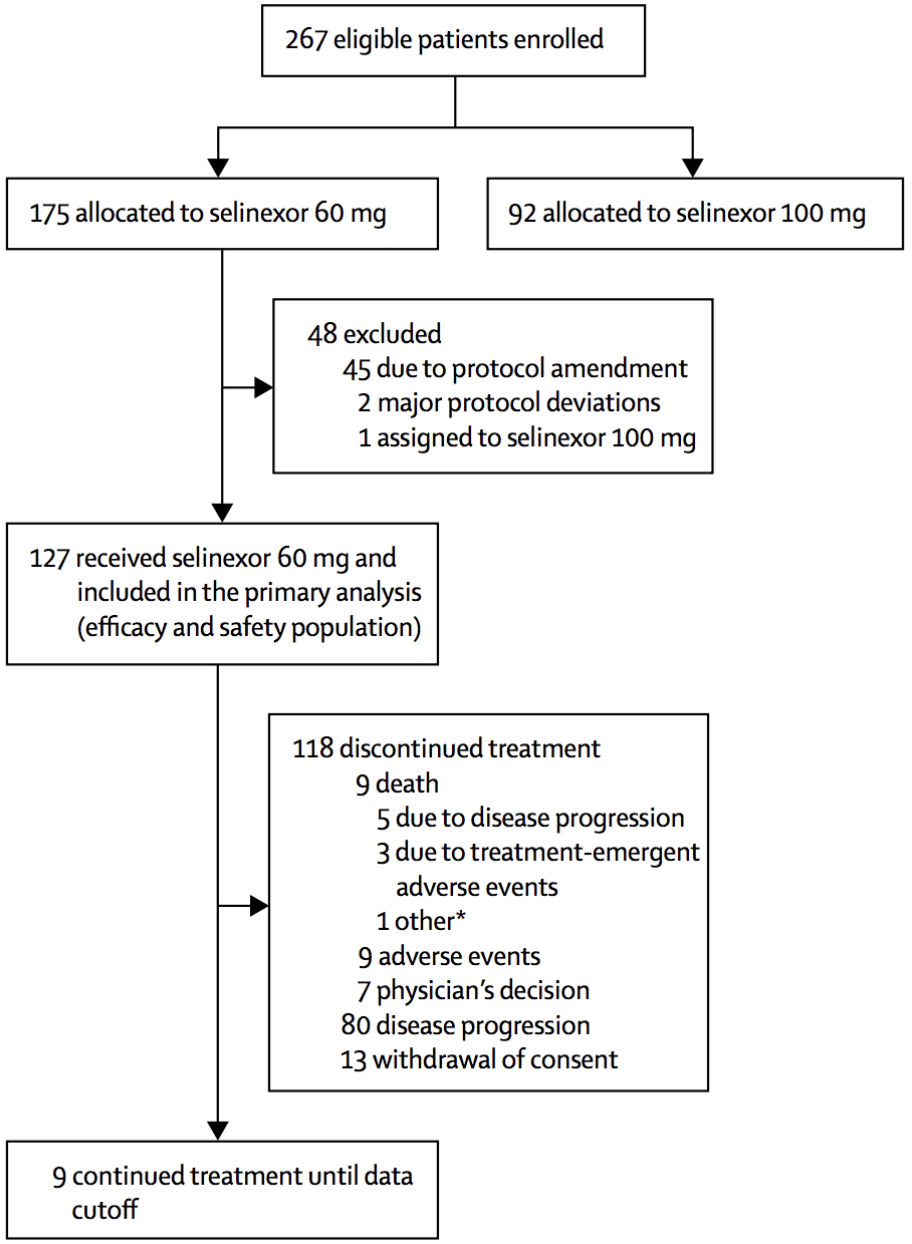
References

Selinexor

Selinexor in patients with relapsed or refractory diffuse large B-cell lymphoma (SADAL): a single-arm, multinational, multicentre, open-label, phase 2 trial

Nagesh Kalakonda, Marie Maerevoet*, Federica Cavallo, George Follows, Andre Goy, Joost S P Vermaat, Olivier Casasnovas, Nada Hamad, Josée M Zijlstra, Sameer Bakhshi, Reda Bouabdallah, Sylvain Choquet, Ronit Gurion, Brian Hill, Ulrich Jaeger, Juan Manuel Sancho, Michael Schuster, Catherine Thieblemont, Fátima De la Cruz, Miklos Egyed, Sourav Mishra, Fritz Offner, Theodoros P Vassilakopoulos, Krzysztof Warzocha, Daniel McCarthy, Xiwen Ma, Kelly Corona, Jean-Richard Saint-Martin, Hua Chang, Yosef Landesman, Anita Joshi, Hongwei Wang, Jatin Shah, Sharon Shacham, Michael Kauffman, Eric Van Den Neste, Miguel A Canales*

- Patients whose most recent systemic anti-DLBCL therapy induced a partial response or complete response had to have at 60 days or more elapsed since the end of that therapy.
- All other patients, had to have at least 14 weeks (98 days) elapsed since the end of their most recent systemic anti-DLBCL therapy



References Lancet Hematology 2020, Vol 7, Issue 7, E511-522

Selinexor Against Diffuse Aggressive Lymphoma (SADAL): Open-Label, Phase 2 Study Design

Key eligibility criteria

- Patients with de novo or t-DLBCL
- R/R DLBCL
- Not eligible for ASCT or post ASCT
- 2-5 prior treatment regimens
- Platelet count >75,000/mm^3
- CrCl <30 mL/min – excluded

Oral Selinexor
60 mg BIW
Days 1, 3 – 28 day cycle

Treatment until PD or intolerable toxicity

Response assessed every 8 weeks per *Cheson 2014*

mITT Population for all Analysis and Safety
(≥Protocol Version 6 patients)

Objectives

- **Primary Endpoint**: Overall response rate (ORR): Independent Central Radiological Review (ICRR); Lugano Classification (2014)
- **Secondary Endpoints**: Duration of response (DOR), Overall survival (OS), Safety

Modified Intent to Treat (mITT) Population: All patients who were randomized to the **60 mg Arm**

References Kalakonda N, et al. ICML 2019. Follows G, et al. EHA 2020. Maerevoet M, et al. EHA 2020. Zijlstra JM, et al. EHA 2020.

SADAL: Patient and Disease Characteristics

Patient Characteristics, n (%)		(N=127)
Median age, years (range)		67 (35-87)
Age distribution	<70 years	70 (55)
	≥70 years	57 (45)
Sex	Female	52 (41)
	Male	75 (59)
ECOG PS	0	55 (43)
	1	58 (46)
	2	13 (10)
	3	1 (0.8)
CrCl, mL/min	<30	2 (1.6)
	30 - <60	32 (25)
	≥60	93 (73)
LDH > 2xULN	Yes	16 (13)
	No	108 (85)
	Missing	3 (2.4)

Disease Characteristics, n (%)		(N=127)
Median time since last disease progression event, weeks (range)		7.9 (1.9-406.3)
Disease type	De novo DLBCL	94 (74)
	Transformed DLBCL	31 (24)
	Missing	2 (1.6)
DLBCL histology	GCB	59 (47)
	Non-GCB	63 (50)
	Not-classified	5 (3.9)
Double or triple expressor		26 (21)
Prior regimens	Median (range)	2 (2-5)
	2	75 (59)
	≥3	52 (41)
Previous autologous stem-cell transplant		38 (30)
Refractory to last prior therapy[a]		91 (72)
Progressed <1 year of first DLBCL therapy[b]		66 (52)
R/R <1 year post last SCT		21 (17)

[a]Defined as best response of <PR, or progressive disease within 6 months (if not ASCT) or 12 months if ASCT from the most recent systemic treatment regimen.
[b]Progressed during or within 1 year of the end of their first systemic treatment for DLBCL.

References Kalakonda N, et al. ICML 2019. Follows G, et al. EHA 2020. Maerevoet M, et al. EHA 2020. Zijlstra JM, et al. EHA 2020.

SADAL: Response Rates

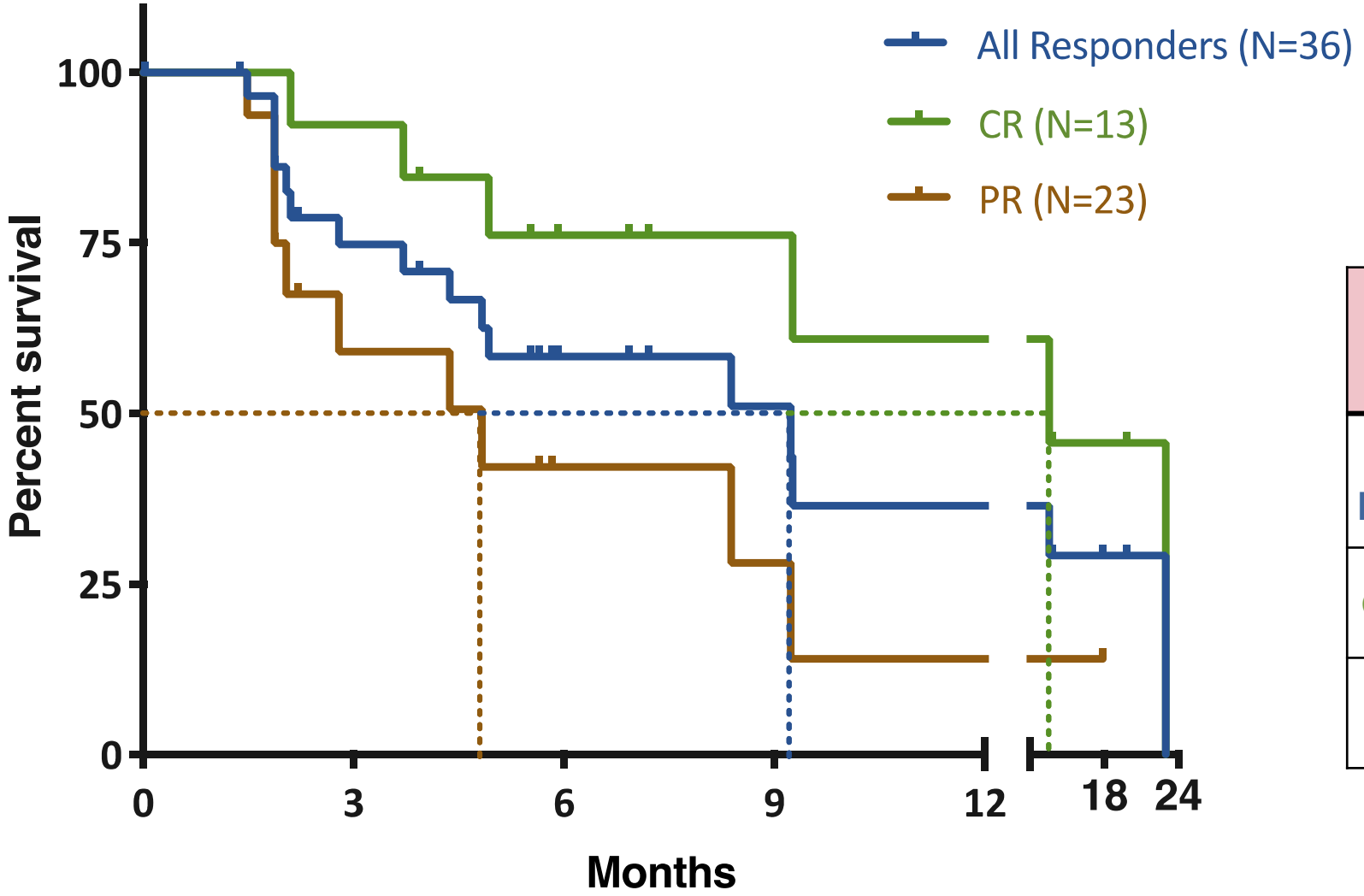
Response and DOR (N=127)	Response per IRC, n (%)[a]	Median DOR per IRC, months (95% CI)[c]
ORR[b] [95% CI]	36 (28.3) [20.7, 37.0]	9.3 months (4.8, 23.0)
CR	15 (11.8)	23.0 months (10.4, 23.0)
PR	21 (16.5)	4.4 months (2.0, NE)
SD	11 (8.7)	N/A
PD/NE	80 (63.0)	N/A

- Median time to response: 1.8 months (range: 1.5 – 6.4)

[a]Responses were adjudicated according to the Lugano 2014 Criteria by an Independent Radiologic Committee (IRC) and confirmed by an Independent Oncologist Reviewer. The Deauville criteria (a 5-point scale) was used to grade response using PET-CT. PET-CT results were prioritized over CT results. [b] Includes CR + PR. [c] Median follow up 11.1 months

References: Kalakonda N, et al. ICML 2019. Maerevoet M, et al. EHA 2020. Zijlstra JM, et al. EHA 2020.

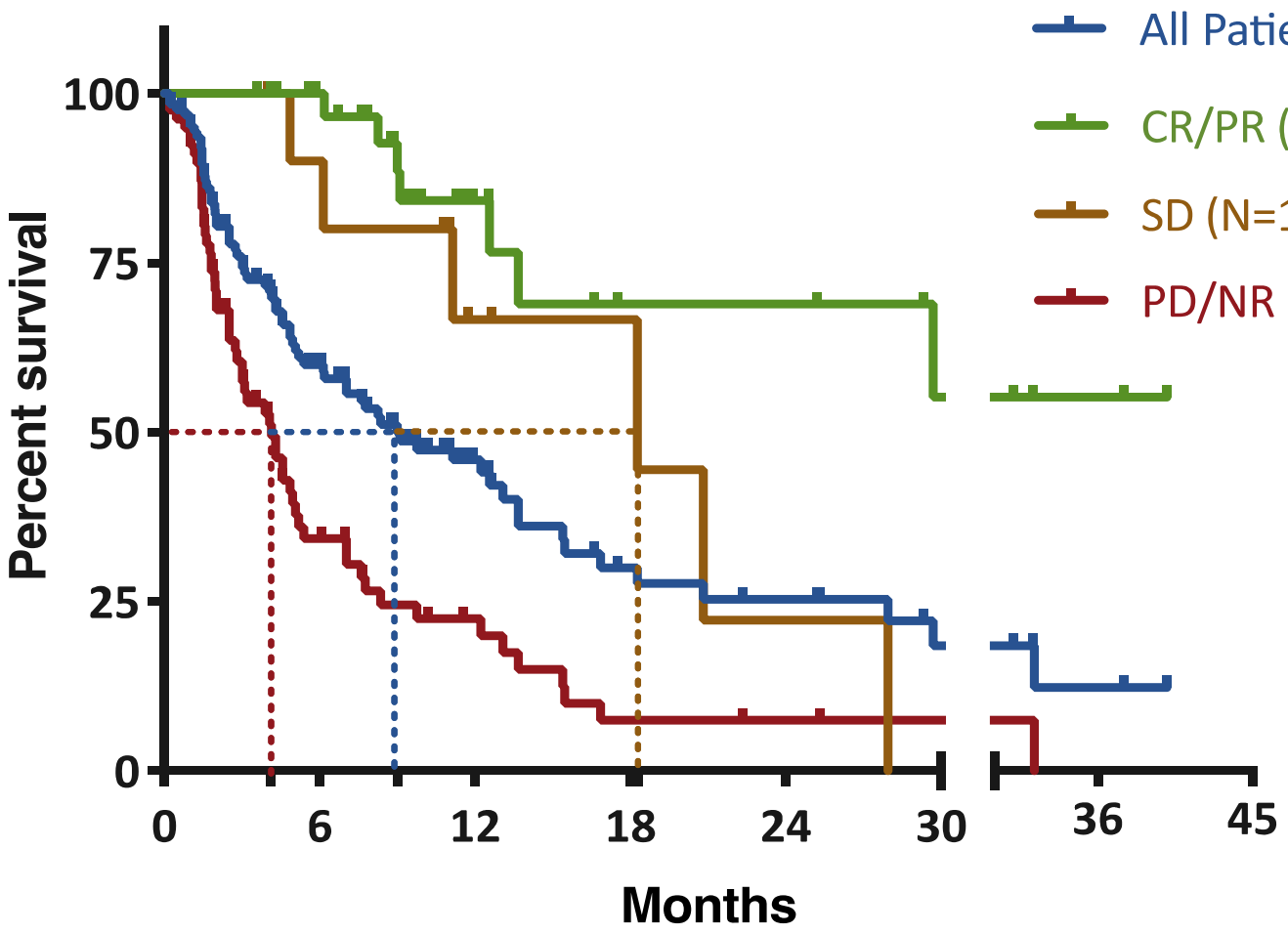
SADAL: Duration of Response (DOR)



Category	Median DOR (months)	95% CI
All Responders	9.3	(4.8 – 23.0)
CR Patients	23.0	(9.3 – 23.0)
PR Patients	4.4	(2.0 – NE)

References Kalakonda N, et al. ICML 2019. Maerevoet M, et al. EHA 2020. Zijlstra JM, et al. EHA 2020.

SADAL: Overall Survival (OS)



Category	Median OS (months)	95% CI
All Patients	9.1	(6.2 – 13.7)
CR/PR Patients	Not Reached	(13.7 – NE)
SD Patients	18.3	(11.1 – 28.0)
PD/NR Patients	4.3	(3.0 – 5.2)

References: Kelakonda N, et al. ICML 2019. Maerevoet M, et al. EHA 2020. Zijlstra JM, et al. EHA 2020.

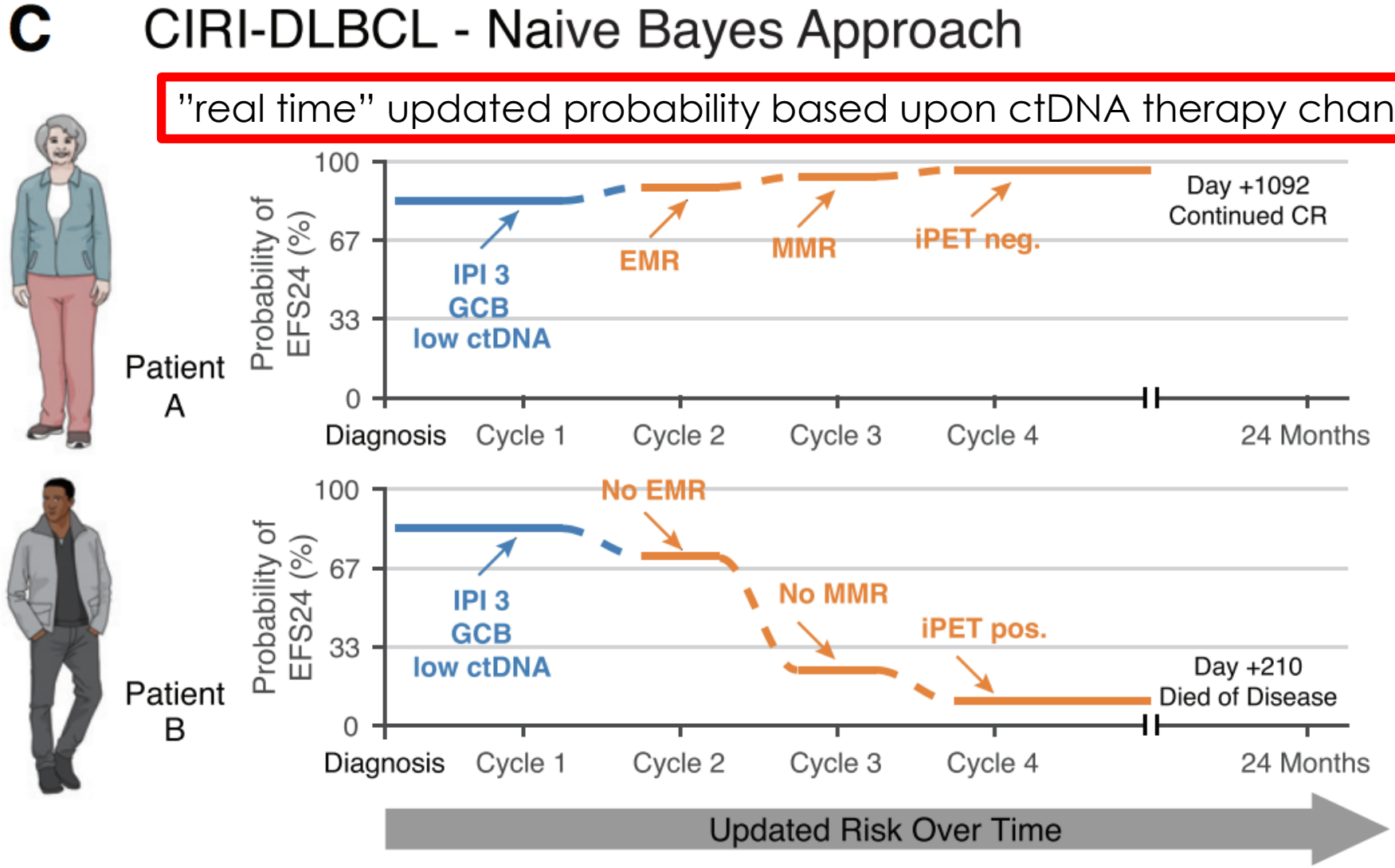
SADAL: Treatment-Related Adverse Events

Treatment-Related AEs, n (%)		Selinexor 60 mg BIW mITT Population (N=127)				
		Grade 1	Grade 2	Grade 3	Grade 4	Total
Hematologic	Thrombocytopenia	6 (4.7)	10 (7.9)	35 (27.6)	15 (11.8)	66 (52.0)
	Anemia	3 (2.4)	18 (14.2)	16 (12.6)	1 (0.8)	38 (29.9)
	Neutropenia	1 (0.8)	6 (4.7)	17 (13.4)	9 (7.1)	33 (26.0)
Gastrointestinal	Nausea	31 (24.4)	28 (22.0)	8 (6.3)	--	67 (52.8)
	Anorexia	20 (15.7)	19 (15.0)	5 (3.9)	--	44 (34.6)
	Vomiting	25 (19.7)	6 (4.7)	2 (1.6)	--	33 (26.0)
	Diarrhea	14 (11.0)	8 (6.3)	4 (3.1)	--	26 (20.5)
	Dysgeusia	12 (9.4)	3 (2.4)	--	--	15 (11.8)
	Constipation	10 (7.9)	4 (3.1)	--	--	14 (11.0)
Constitutional	Fatigue	19 (15.0)	17 (13.4)	12 (9.4)	--	48 (37.8)
	Asthenia	5 (3.9)	11 (8.7)	3 (2.4)	--	19 (15.0)
	Weight Loss	10 (7.9)	17 (13.4)	--	--	27 (21.3)

- No related grade 5 AEs were reported in the mITT population
- Side effects were generally reversible and managed with dose modifications and/or standard supportive care

References Kalakonda N, et al. ICML 2019.

Future Directions



References Kurtz et al, Westin, Alizadeh, Cell 2019

Conclusions

- Although CAR T-cell is a game changer, Non-Immunotherapy approaches for R/R DLBCL patients show promise
- Polatuzumab, Tafasitamab + Lenalidomide, and Selinexor recently approved by the FDA
- Clinical trials remain the best weapon

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