

IN PURSUIT OF *YOUR CURE.*[®]

How do I treat R/R DLBCL in a deserted island

Alvaro Alencar

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@SylvesterCancer



Disclosures

- AdBoard
 - Genentech, Lilly, Amgen, TG Therapeutics, Incyte, BeiGene, Janssen, Epizyme, SeaGen, Kite, ADC Therapeutics
- Research Funding
 - Lilly, Incyte, BeiGene, BostonGene, ONO Therapeutics

R/R DLBCL

- Decreasing role of cytotoxic therapy
 - Chemorefractory
 - Impact on cell health and marrow function
- Bispecific antibodies, CAR-T cell therapy
- CRS, ICANS
 - Multispecialty teams
 - Inpatient monitoring
 - Prompt management of acute toxicity

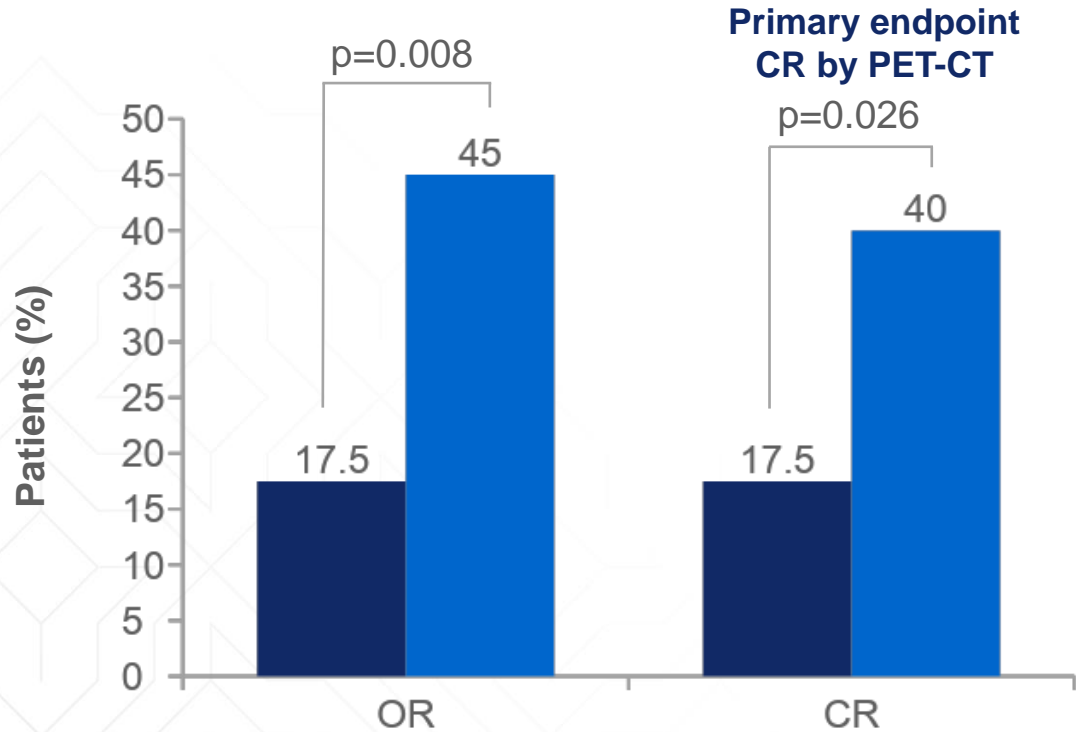
Alternative approach to R/R DLBCL

- Polatuzumab vedotin
 - ADC to CD79b delivering monomethyl auristatin E (MMAE)
 - Bendamustine, rituximab
- Tafasitamab
 - anti-CD 19 Fc-enhanced monoclonal antibody
 - Lenalidomide
- Loncastuximab tesirine
 - humanized anti-CD19 ab conjugated to a pyrrolobenzodiazepine dimer toxin (PBD)

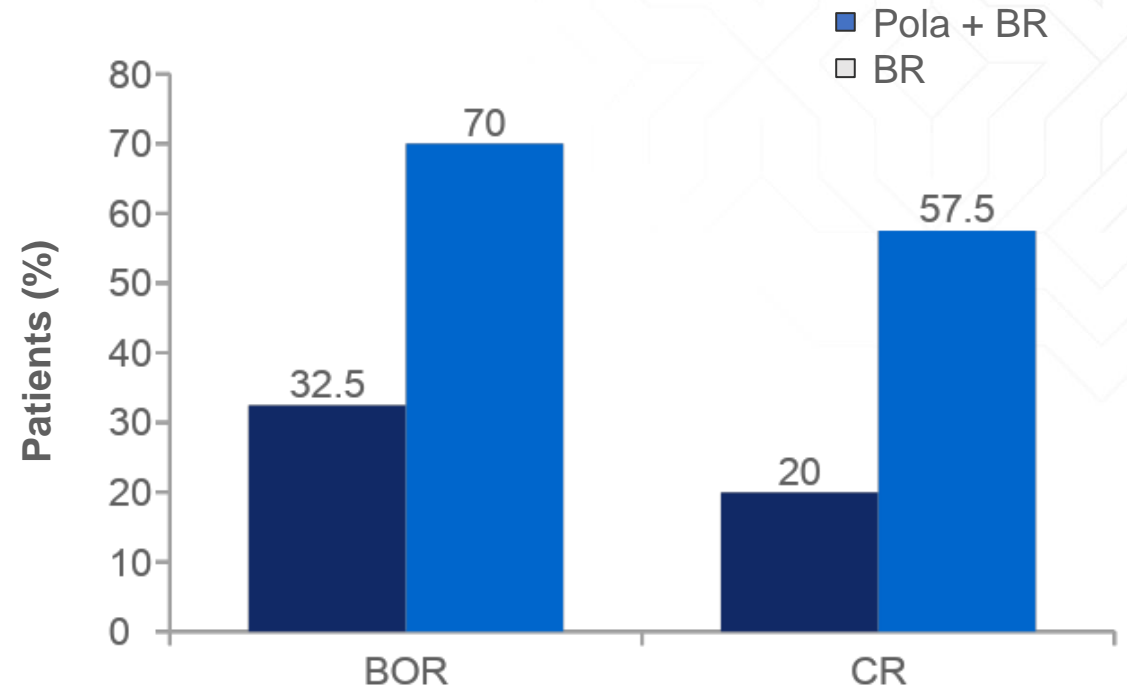
Polatuzumab vedotin

Polatuzumab + BR – phase 2

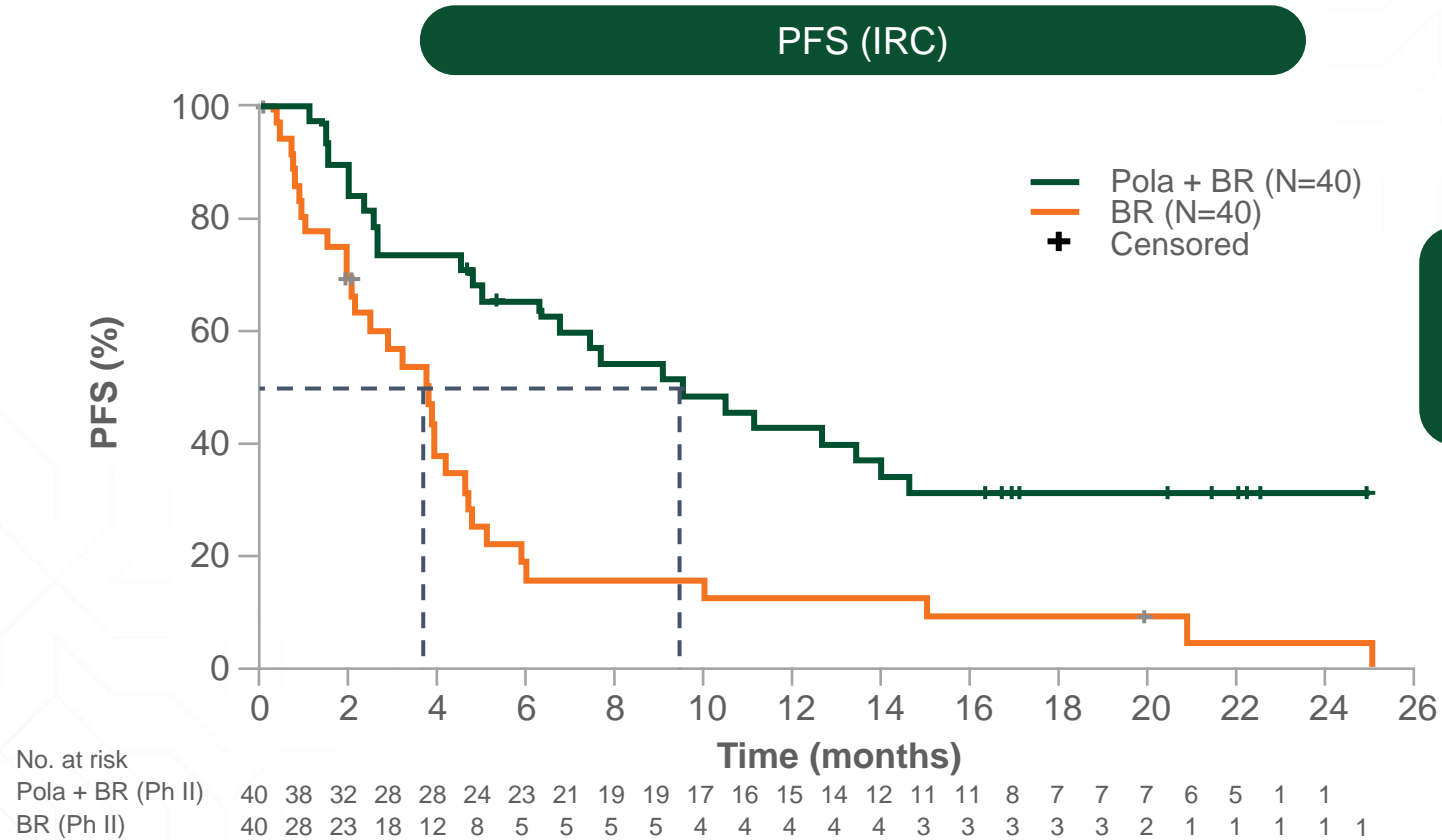
Response at EOT (IRC)*



BOR and CR (INV)

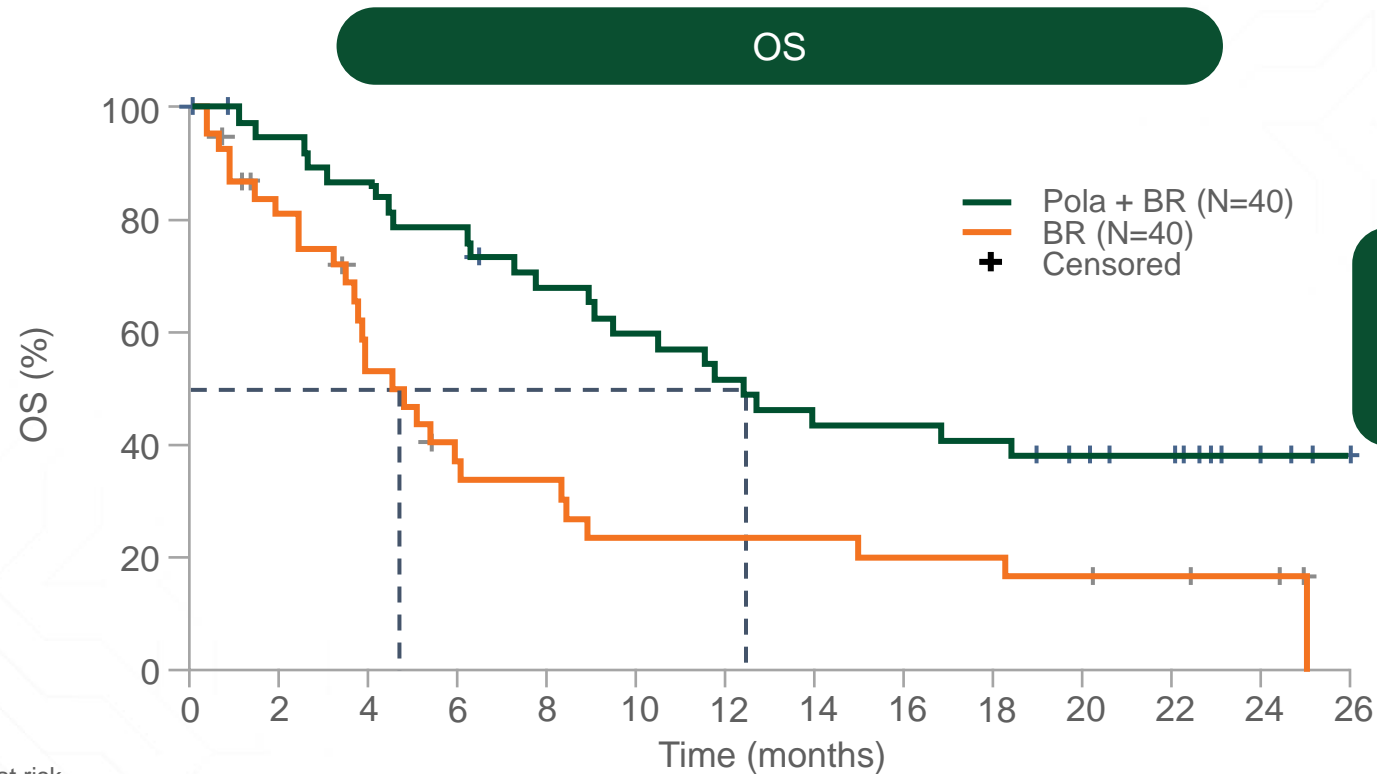


Polatuzumab + BR – phase 2



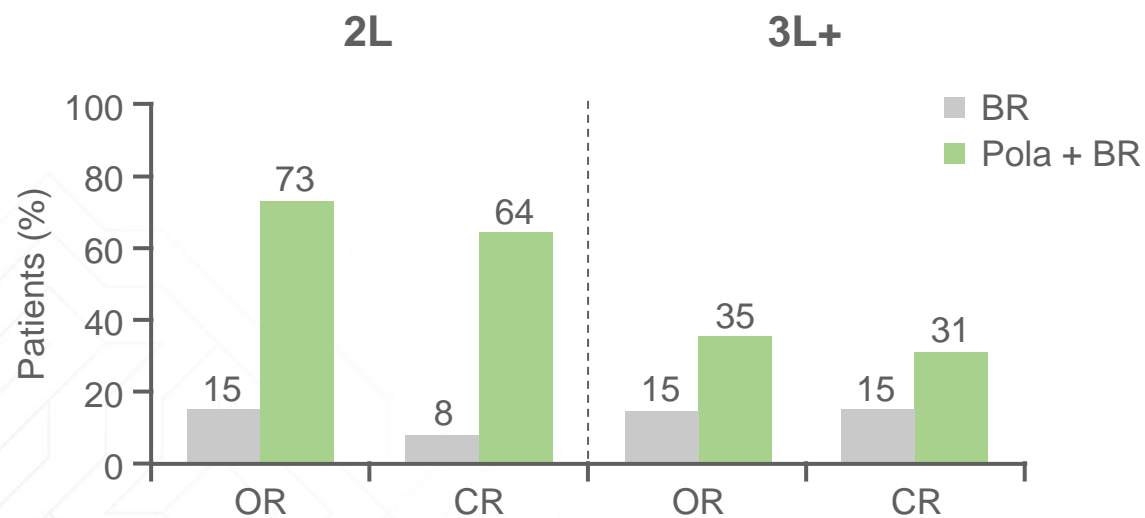
Pola + BR vs BR:
Median PFS 9.5 vs 3.7 months
HR, 0.36 (95% CI: 0.21–0.63)
P-value (log-rank) = 0.0002

Polatuzumab + BR – phase 2

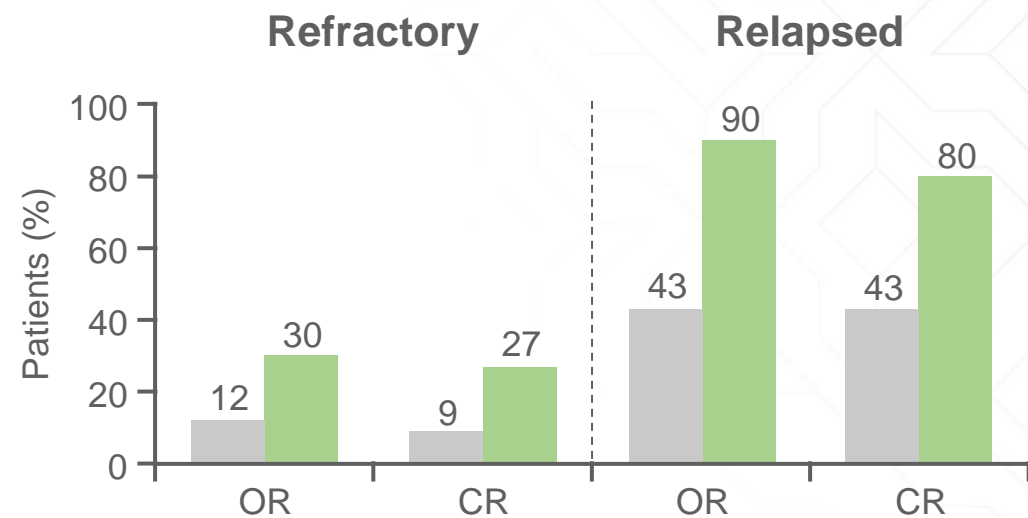


Time (months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26
No. at risk	40	38	36	34	33	30	30	27	25	24	22	21	19	17
Pola + BR (Ph II)	40	33	27	25	17	15	11	10	10	7	7	7	7	7
BR (Ph II)	40	33	27	25	17	15	11	10	10	7	7	7	7	7

Polatuzumab + BR – phase 2



IRC (EOT)	2L		3L+	
	BR (n=13)	Pola + BR (n=11)	BR (n=27)	Pola + BR (n=29)
Median PFS, mo (95% CI)	3.7 (1.5–5.1)	11.1 (10.4–NR)	2.0 (1.5–2.8)	6.0 (4.0–7.6)
Median OS, mo (95% CI)	5.9 (3.9–8.4)	NR (10.5–NE)	3.8 (3.2–8.9)	11.5 (8.9–NE)

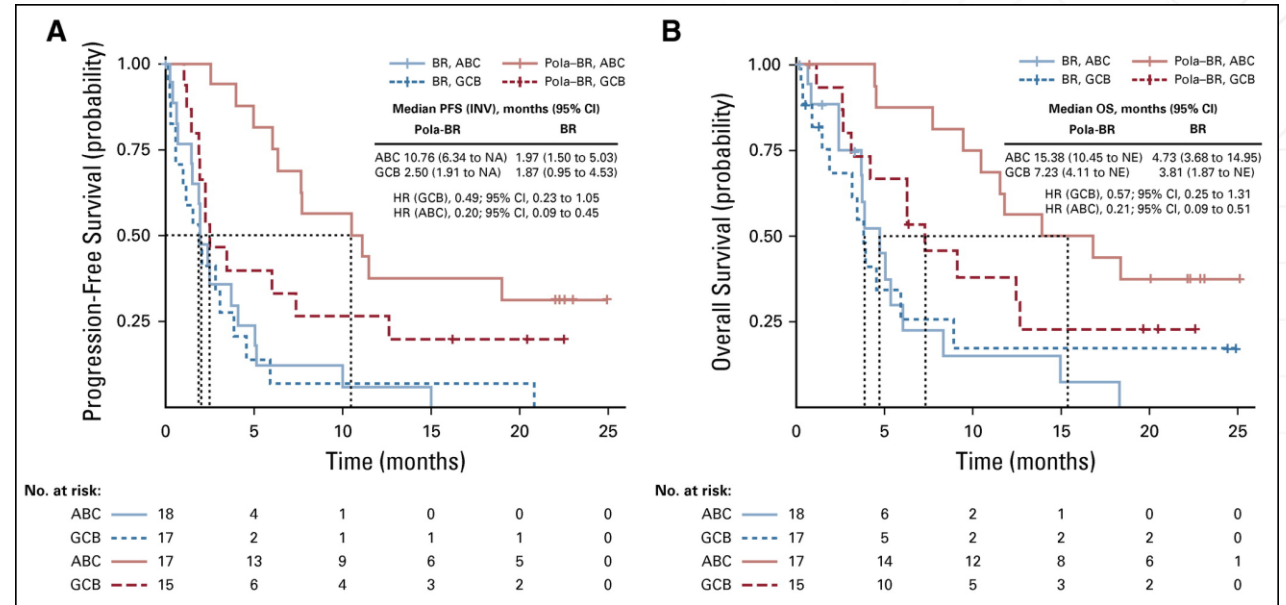
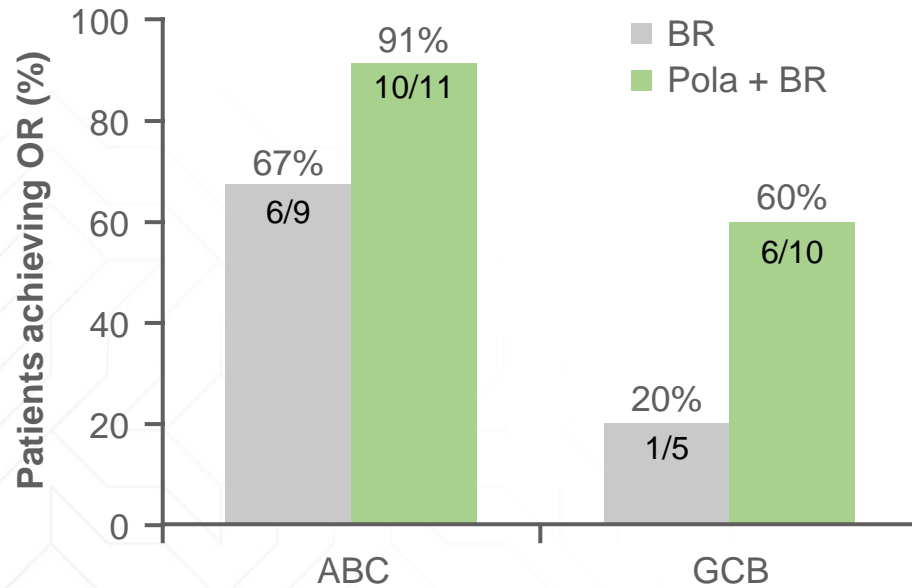


IRC (EOT)	Refractory		Relapsed	
	BR (n=33)	Pola + BR (n=30)	BR (n=7)	Pola + BR (n=10)
Median PFS, mo (95% CI)	1.9 (1.1–2.8)	6.0 (3.5–7.4)	5.1 (2.5–10.0)	11.1 (10.4–NE)
Median OS, mo (95% CI)	3.8 (3.2–5.3)	11.5 (7.2–12.4)	NR (NE–NE)	NR (6.0–NE)

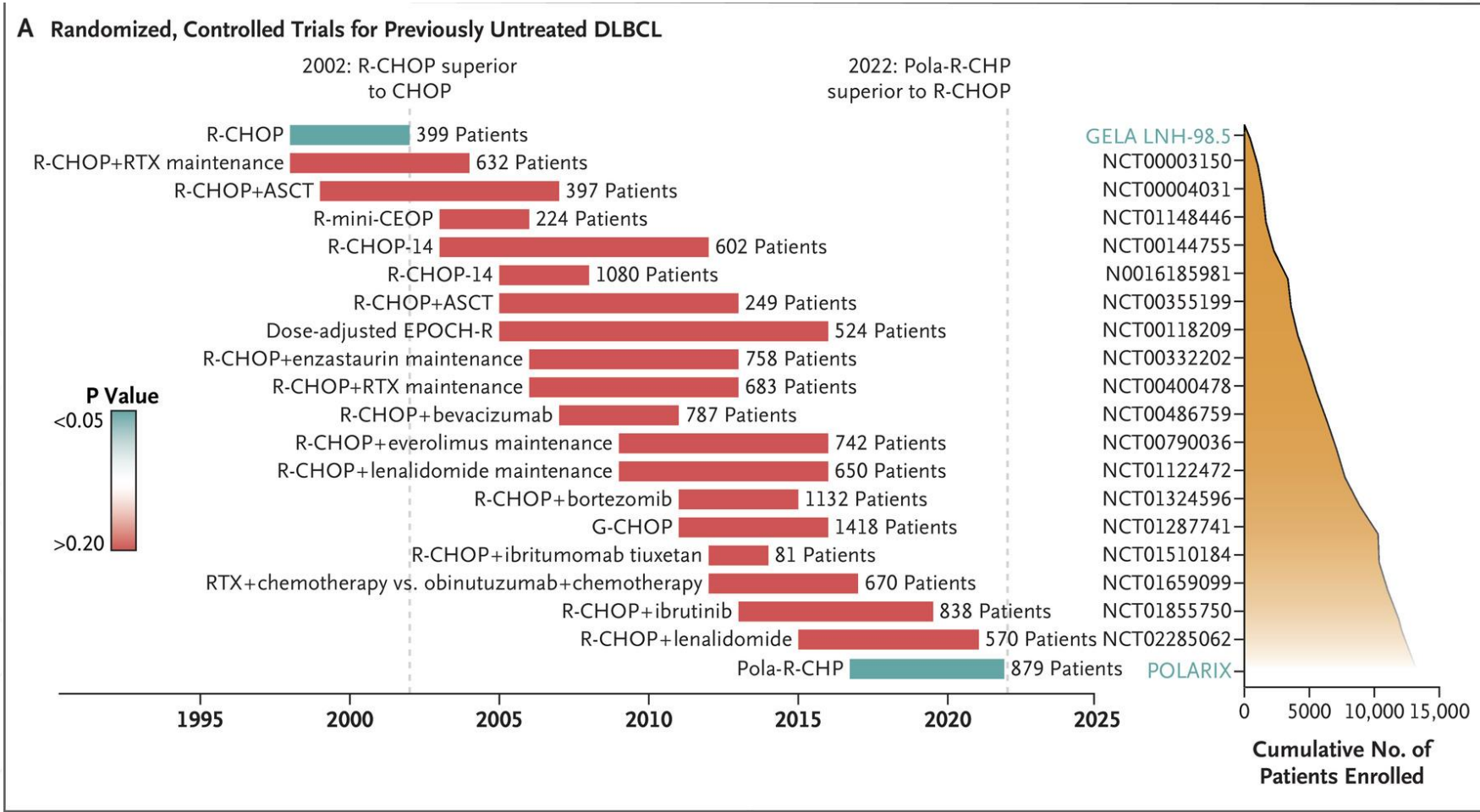
Polatuzumab + BR – phase 2

Adverse Event	Pola-BR (n = 39)*		BR (n = 39)*	
	All Grades, No. (%)	Grades 3-4, No. (%)	All Grades, No. (%)	Grades 3-4, No. (%)
Blood and lymphatic system disorders				
Anemia	21 (53.8)	11 (28.2)	10 (25.6)	7 (17.9)
Neutropenia	21 (53.8)	18 (46.2)	15 (38.5)	13 (33.3)
Thrombocytopenia	19 (48.7)	16 (41.0)	11 (28.2)	9 (23.1)
Lymphopenia	5 (12.8)	5 (12.8)	0	0
Febrile neutropenia	4 (10.3)	4 (10.3)	5 (12.8)	5 (12.8)
GI disorders				
Diarrhea	15 (38.5)	1 (2.6)	11 (28.2)	1 (2.6)
Nausea	12 (30.8)	0	16 (41.0)	0
Constipation	7 (17.9)	0	8 (20.5)	1 (2.6)
General disorders and administration site conditions				
Fatigue	14 (35.9)	1 (2.6)	14 (35.9)	1 (2.6)
Pyrexia	13 (33.3)	1 (2.6)	9 (23.1)	0
Metabolism and nutrition disorders				
Decreased appetite	10 (25.6)	1 (2.6)	8 (20.5)	0
Peripheral neuropathy				
Peripheral neuropathy†	17 (43.6)	0	3 (7.7)	0

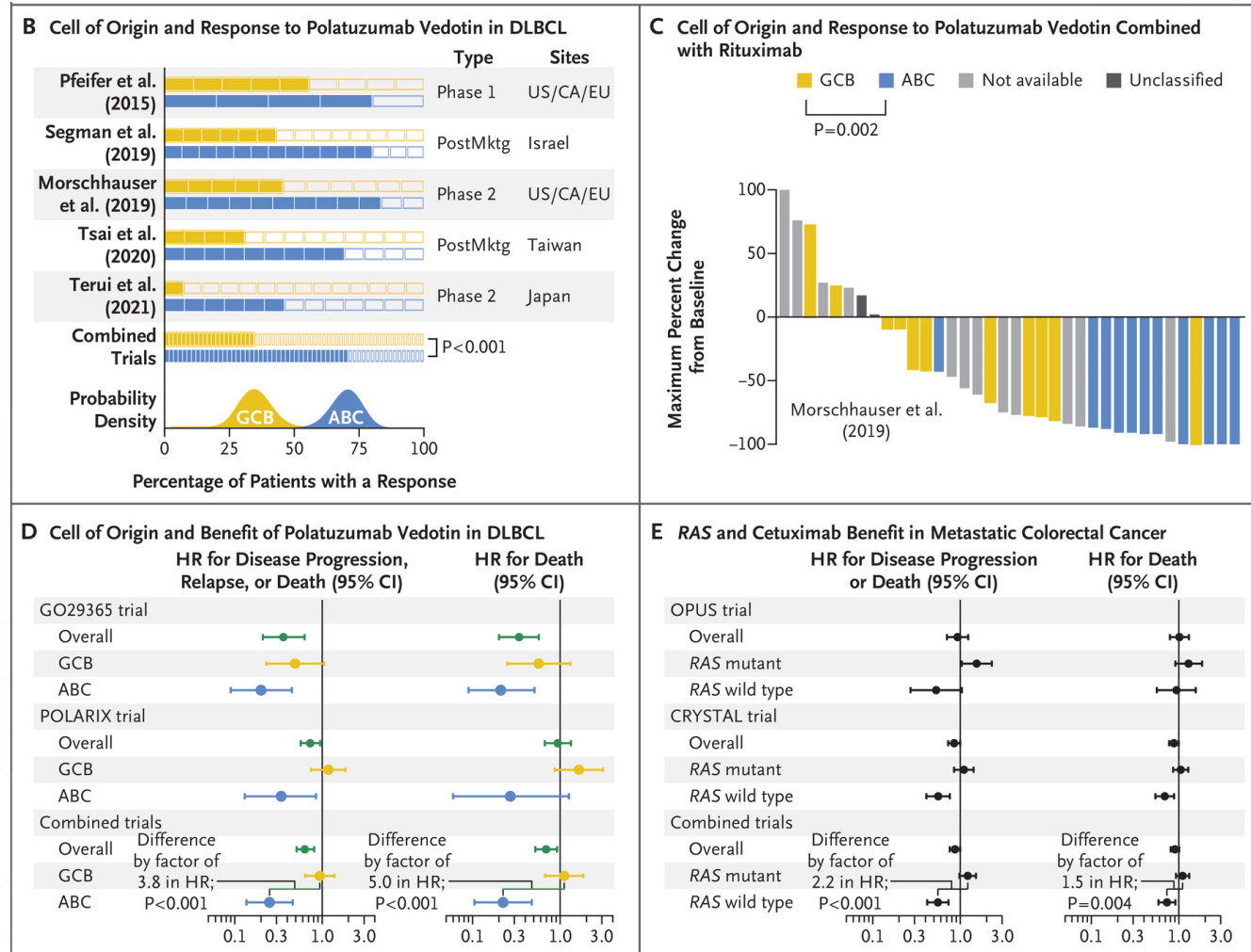
Polatuzumab + BR – phase 2



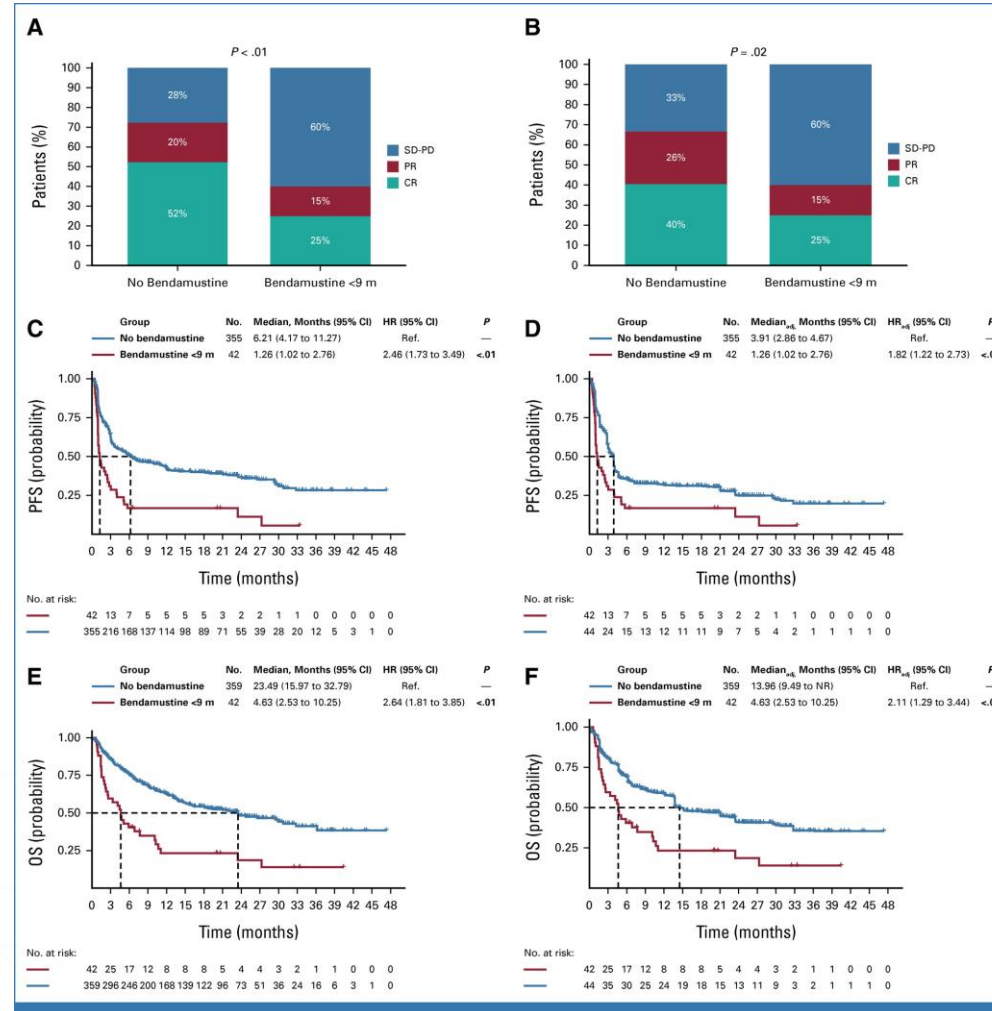
Polatuzumab in POLARIX



Polatuzumab in POLARIX



Bendamustine and CAR-T

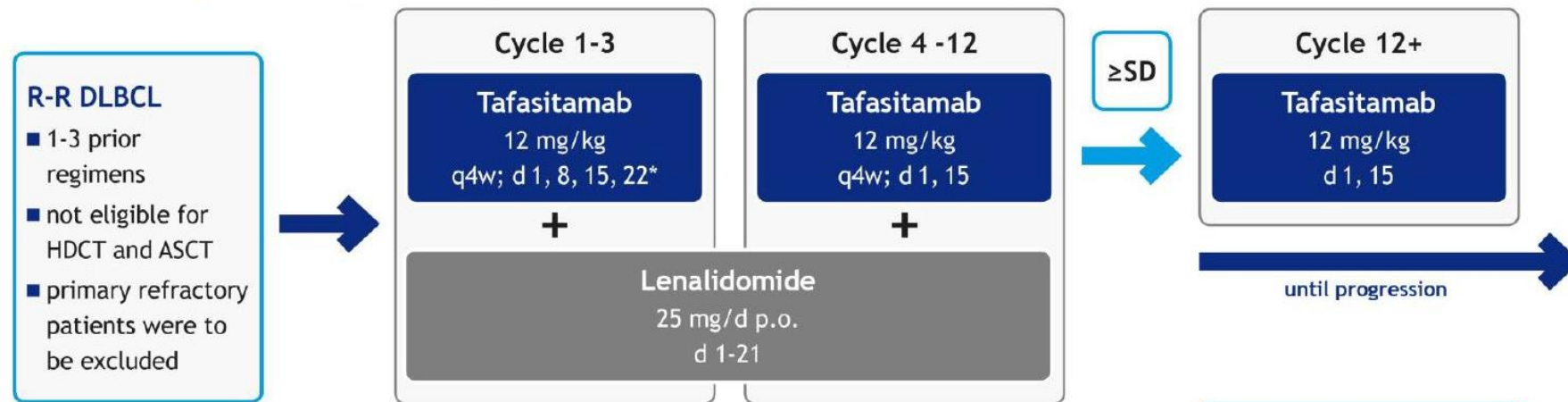


Tafasitamab

L-MIND – Tafasitamab + Lenalidomide

L-MIND: Study Design

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

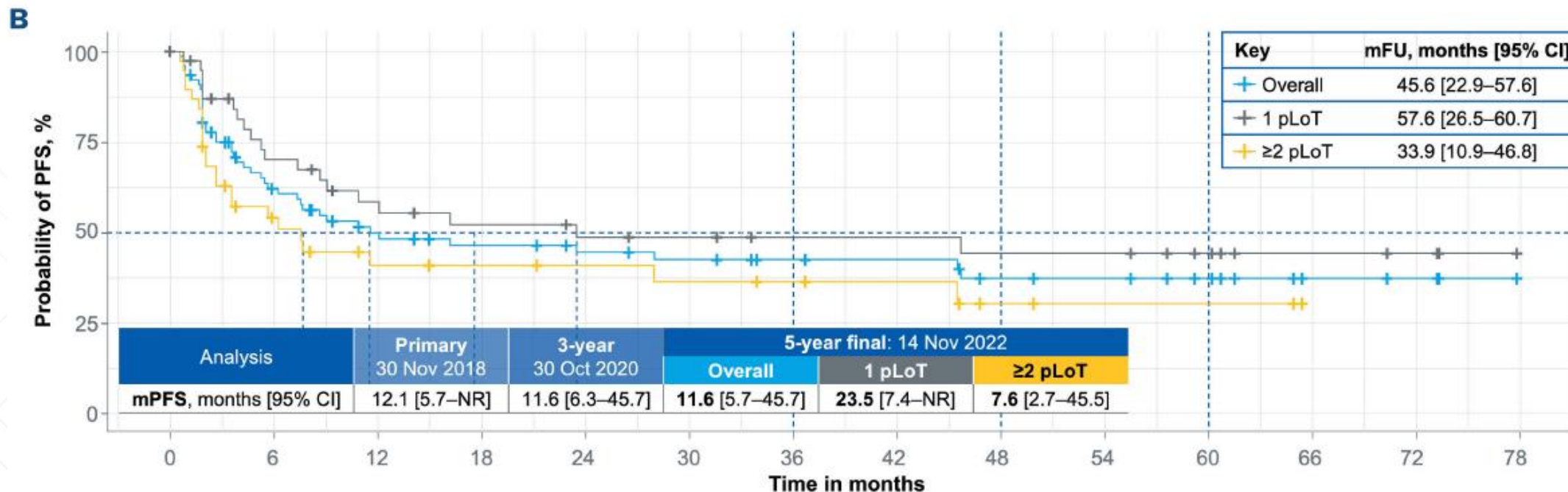


Characteristic	Specification	n=81 (%)
Sex	Male Female	44 (54) 37 (46)
Age [years]*	median (range)	72 (41-86)
Risk (IPI)*	0-2 3-5	40 (49) 41 (51)
Ann Arbor Stage*	I-II III-IV	20 (25) 61 (75)
Elevated LDH*	Yes No	45 (56) 36 (44)
Prior Lines*	median 1 2 3 4	2 40 (49) 35 (43) 5 (6) 1 (1)
Primary Refractory	Yes No	15 (18) 66 (82)
Refractory to last prior therapy*	Yes No	36 (44) 45 (56)

L-MIND – Tafasitamab + Lenalidomide

	Primary analysis	3-year follow-up	Final 5-year data	5-year data in patients with 1 PLOT (n = 40)	5-year data in patients with ≥2 PLOT (n = 40)
Data cut-off date	30-Nov-18	30-Oct-20	14-Nov-22	14-Nov-22	14-Nov-22
Best ORR, n (%) [95% CI]	48 (60.0) [48.4-70.9]	46 (57.5) [45.9-68.5]	46 (57.5) [45.9-68.5]	27 (67.5) [50.9-81.4]	19 (47.5) [31.5-63.9]
CR rate, n (%) [95% CI]	34 (42.5) [32.0-54.0]	32 (40.0) [29.2-51.6]	33 (41.3) [30.4-52.8]	21 (52.5) [36.1-68.5]	12 (30.0) [16.6—46.5]
PR rate, n (%) [95% CI]	14 (17.5) [10.0-28.0]	14 (17.5) [9.9-27.6]	13 (16.3) [8.9-26.2]	6 (15.0) [5.7-29.8]	7 (17.5) [7.3-32.8]
Median DOR, months [95% CI]	21.7 [21.7-NR]	43.9 [26.1-NR]	NR [33.8-NR]	NR [9.1-NR]	NR [26.1-NR]
Median PFS, months [95% CI]	12.1 [5.7-NR]	11.6 [6.3-45.7]	11.6 [5.7—45.7]	23.5 [7.4-NR]	7.6 [2.7-45.5]
Median OS, months [95% CI]	NR [18.3-NR]	33.5 [18.3-NR]	33.5 [18.3-NR]	NR [24.6-NR]	15.5 [8.6-45.5]

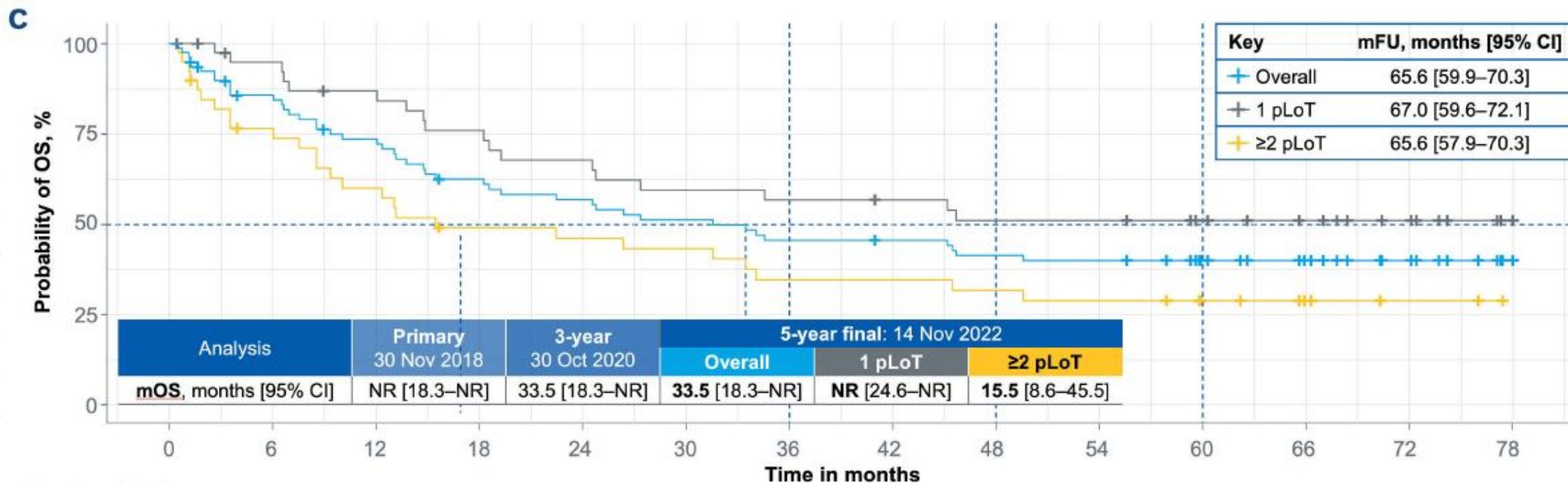
L-MIND – Tafasitamab + Lenalidomide



Number at risk:

	0	6	12	18	24	30	36	42	48	54	60	66	72	78
Overall	80	42	30	26	23	21	18	17	13	12	9	4	3	0
1 pLoT	40	25	19	16	14	13	11	11	10	10	7	4	3	0
≥2 pLoT	40	17	11	10	9	8	7	6	3	2	2	0	0	0

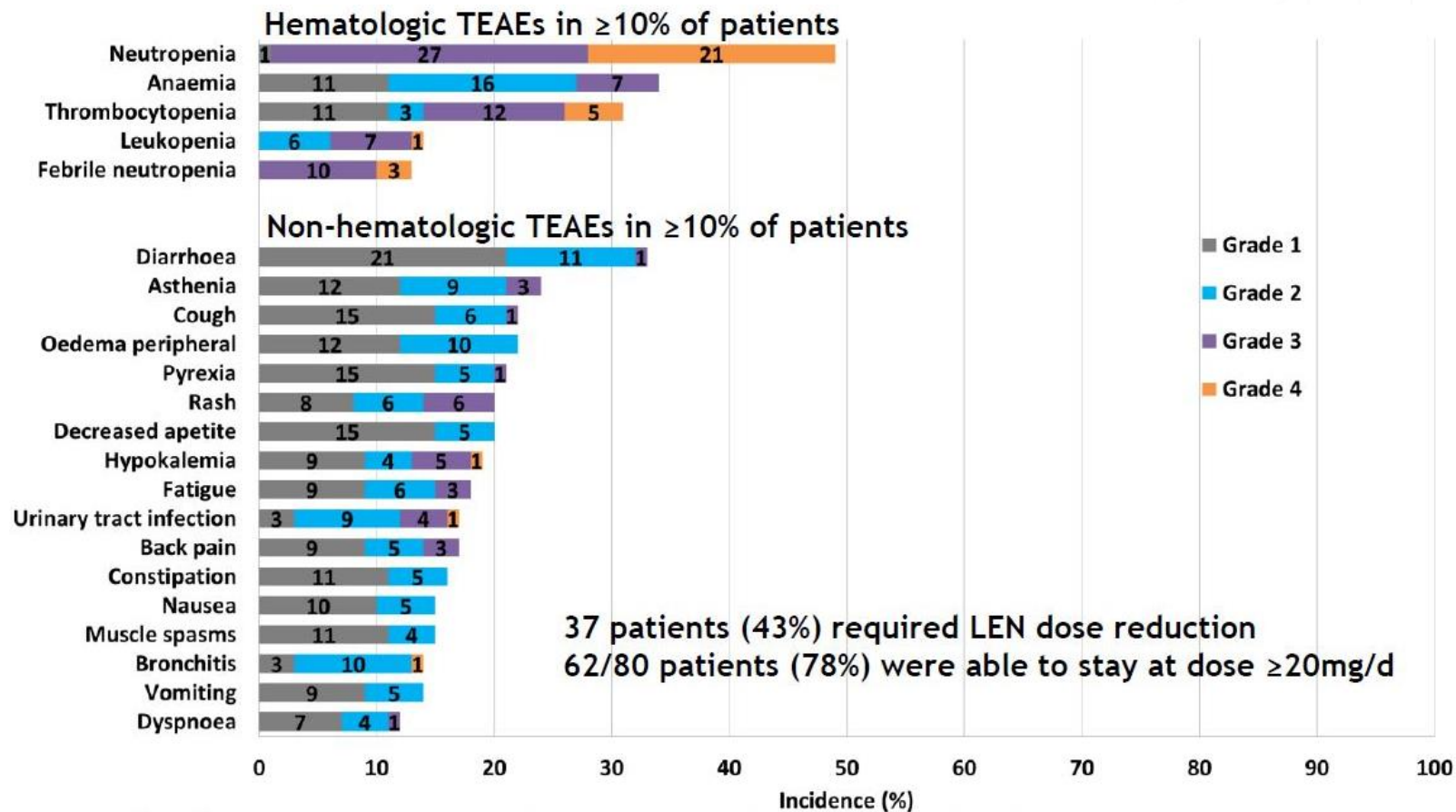
L-MIND – Tafasitamab + Lenalidomide



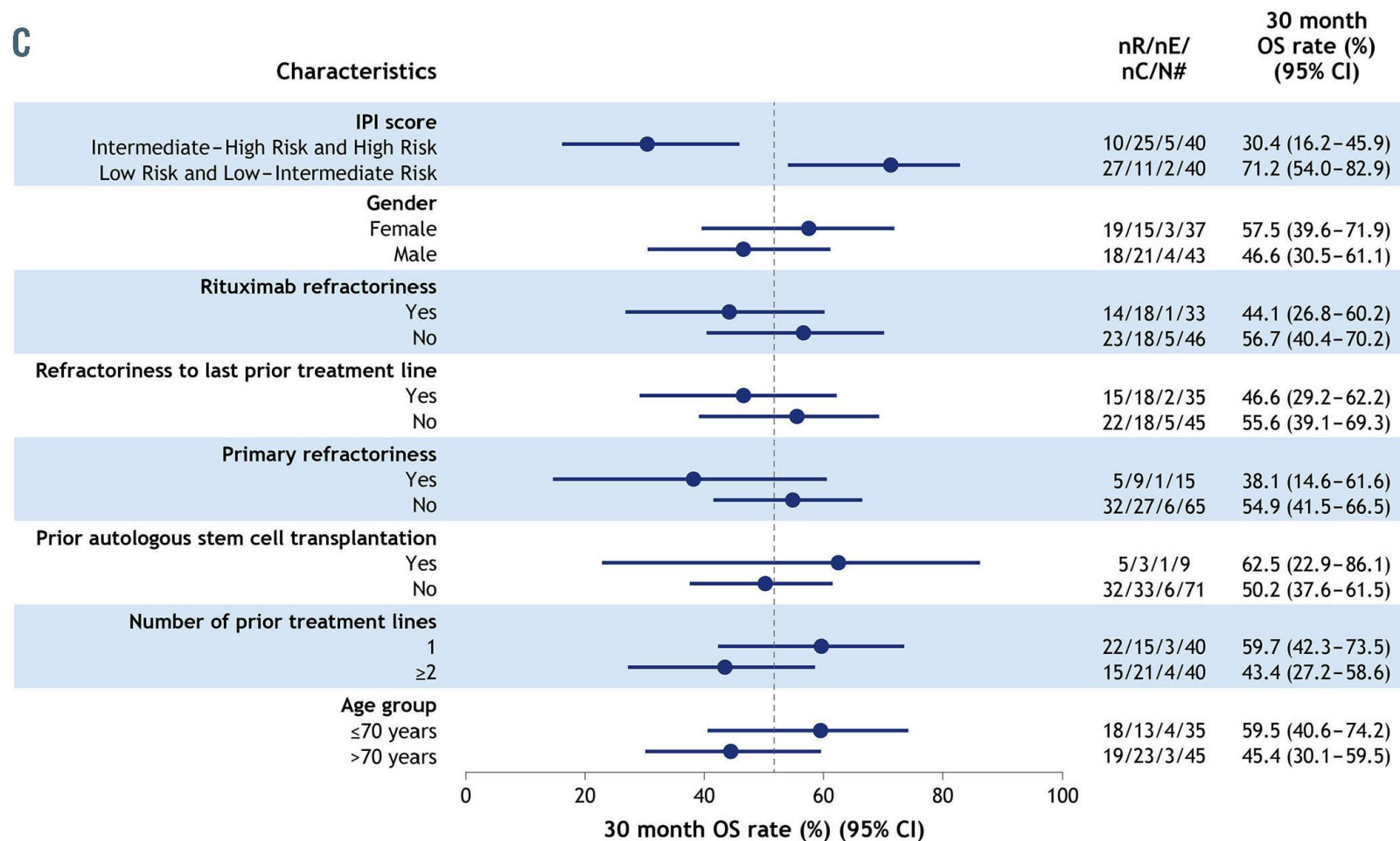
Number at risk:

	0	6	12	18	24	30	36	42	48	54	60	66	72	78
Overall	80	64	54	45	41	37	33	32	29	28	21	15	9	1
1 pLoT	40	36	32	28	25	22	21	20	18	18	14	11	7	1
≥2 pLoT	40	28	22	17	16	15	12	12	11	10	7	4	2	0

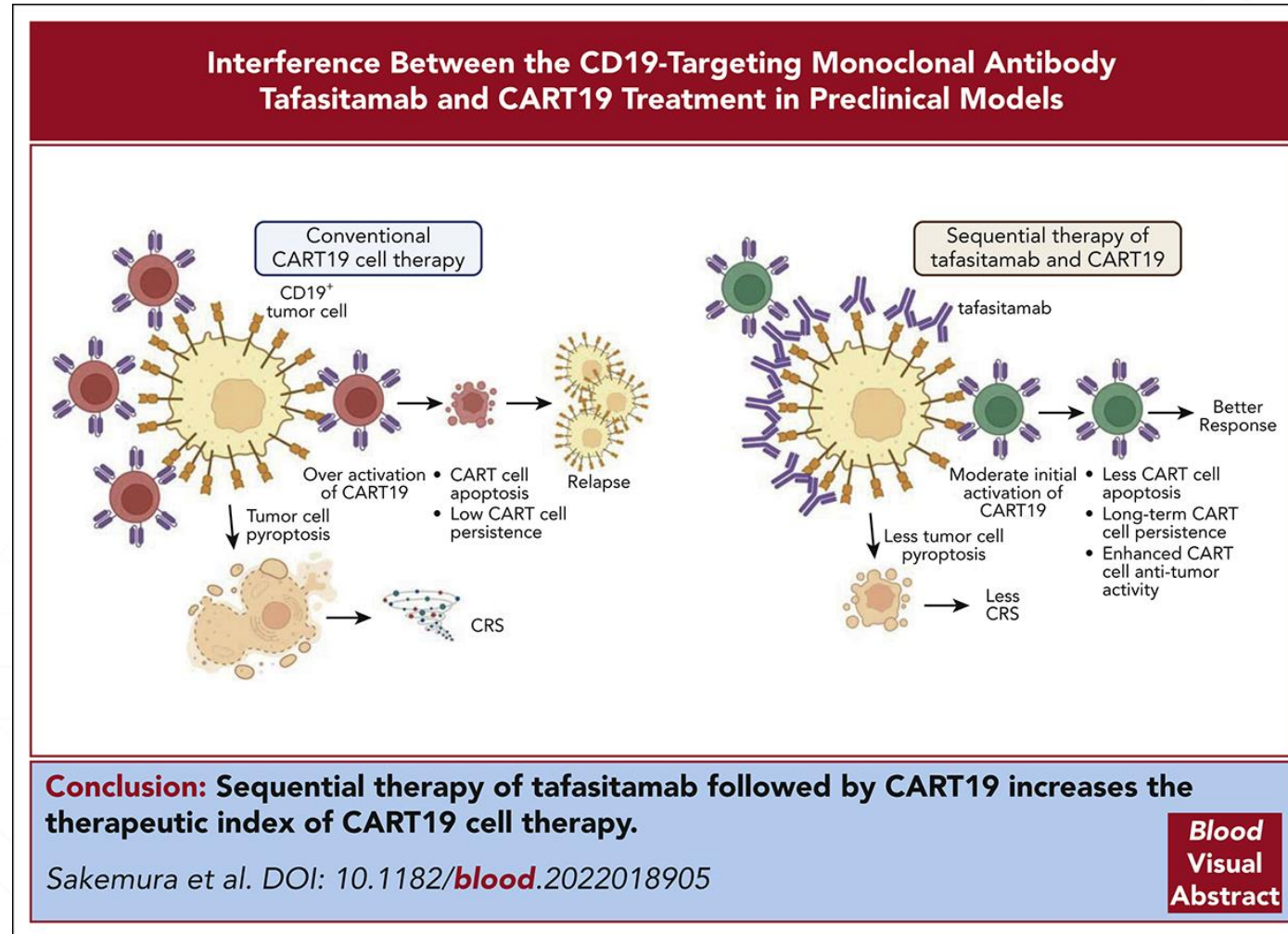
L-MIND – Tafasitamab + Lenalidomide



L-MIND – Tafasitamab + Lenalidomide

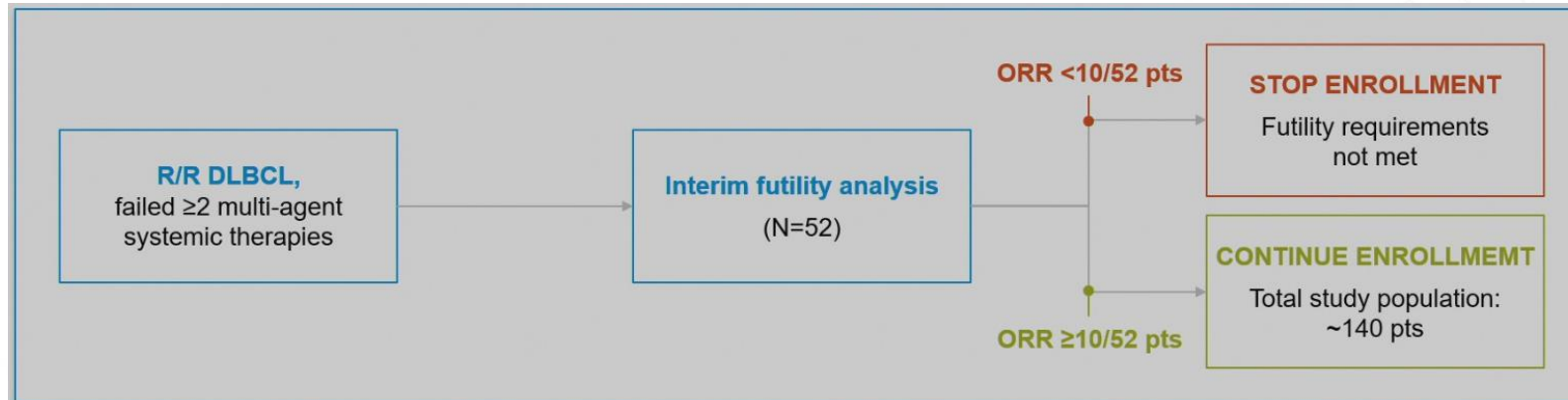


Tafasitamab and CAR-T



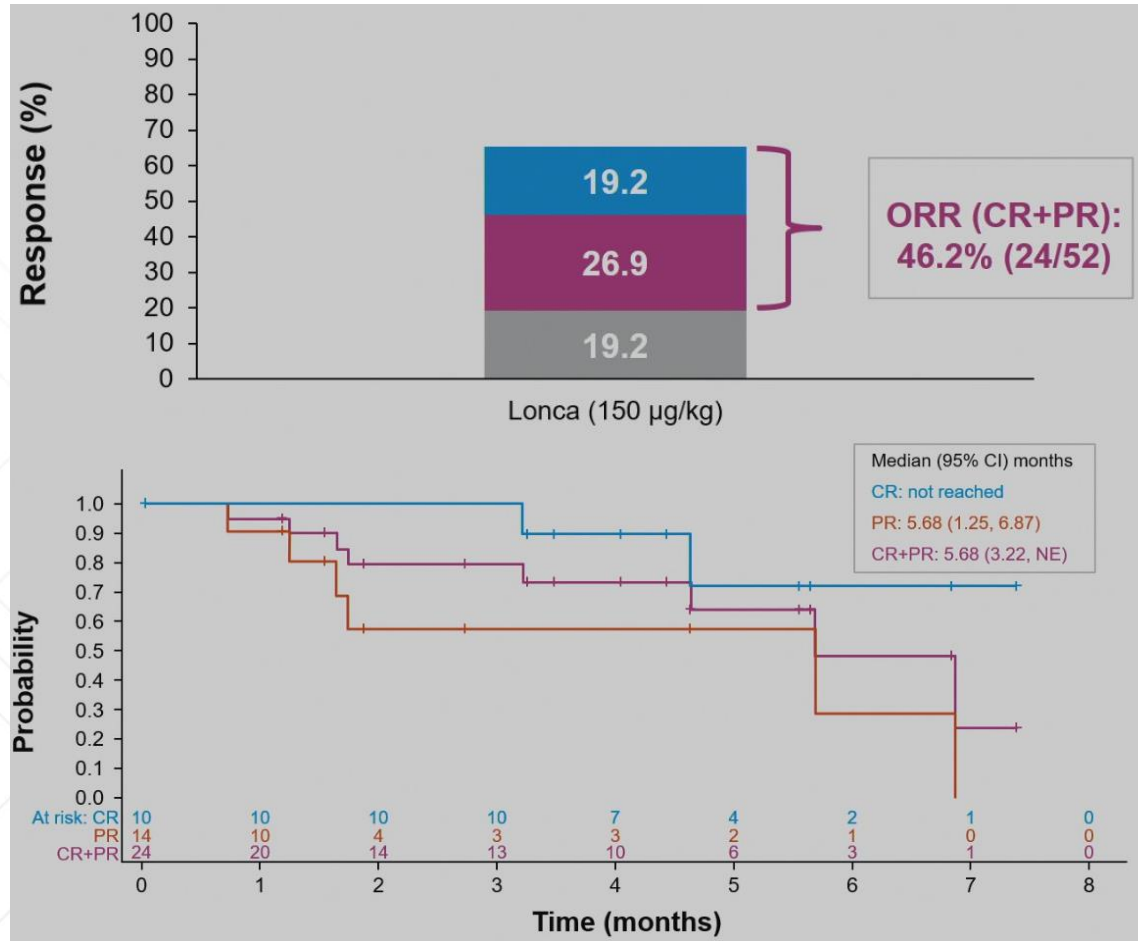
Loncastuximab tesirine

Loncastuximab – phase 2



Patient characteristics		Total (N=52)	Patient treatment history		Total (N=52)
Sex, n (%)	Male	38 (73.1)	First-line systemic therapy response, n (%)	Relapsed	32 (61.5)
	Female	14 (26.9)		Refractory	16 (30.8)
Race, n (%)	White	48 (92.3)	Other*	4 (7.7)	
	Black/African American	2 (3.8)	Last-line systemic therapy response, n (%)	Relapsed	17 (32.7)
	Asian	1 (1.9)		Refractory	28 (53.8)
	Other	1 (1.9)	Other*	7 (13.5)	
Age, years, median (min, max)		63 (24, 84)	No. of previous systemic therapies, median (min, max)		3 (2, 7)
Histology, n (%)	DLBCL	45 (86.5)	Prior stem cell transplantation, n (%)	Allogeneic	11 (21.2)
	Double/triple hit	3 (5.8)		Autologous	9 (17.3)
	Transformed disease	8 (15.4)	Both	1 (1.9)	
	Follicular	7 (13.5)			
	Richter's	1 (1.9)			
	HGBCL	4 (7.7)			
PMBCL	3 (5.8)				
Stage, n (%)	I-II	14 (26.9)			
	III-IV	38 (73.1)			

Loncastuximab – phase 2



Non-hematological TEAEs (reported in ≥20% patients) (N=52)		
Preferred term, n (%)	Grade 1–2	Grade ≥3
GGT increased	14 (26.9)	13 (25.0)
Pyrexia	18 (34.6)	-
Cough	15 (28.8)	-
Hypokalemia	12 (23.1)	3 (5.8)
Nausea	15 (28.8)	-
ALP increased	13 (25.0)	1 (1.9)
Fatigue	12 (23.1)	2 (3.8)
Vomiting	11 (21.2)	-

Hematological TEAEs (reported in ≥20% patients) (N=52)		
Preferred term, n (%)	Grade 1–2	Grade ≥3
Platelet count decreased*	26 (50.0)	11 (21.2)
Neutrophil count decreased*	12 (23.1)	17 (32.7)
Anemia	8 (15.4)	6 (11.5)

Loncastuximab – LOTIS-2

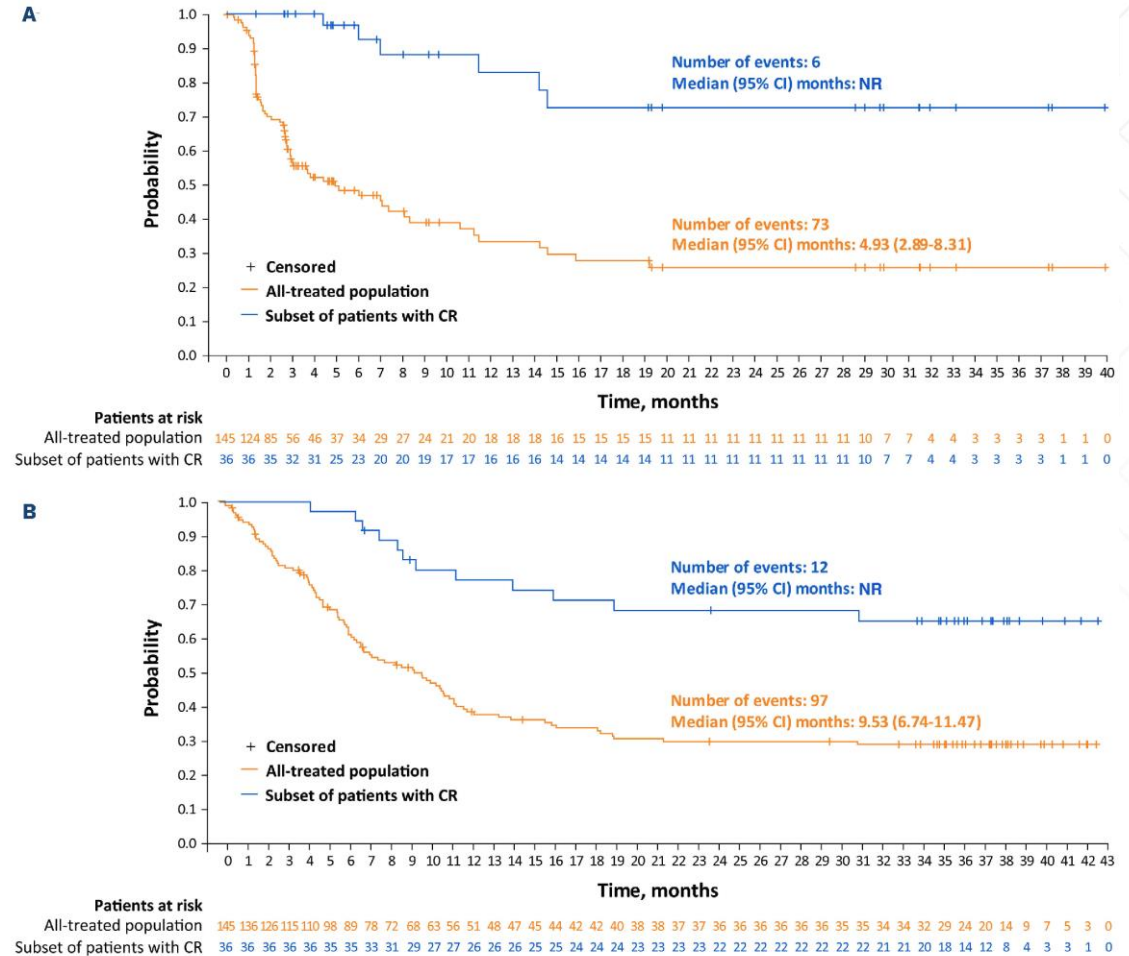
- N= 145
 - Median f/u 7.8 months [range, 0.3-42.6]

- ORR 70 of 145 (48.3%)
 - CR 36 (24.8%)

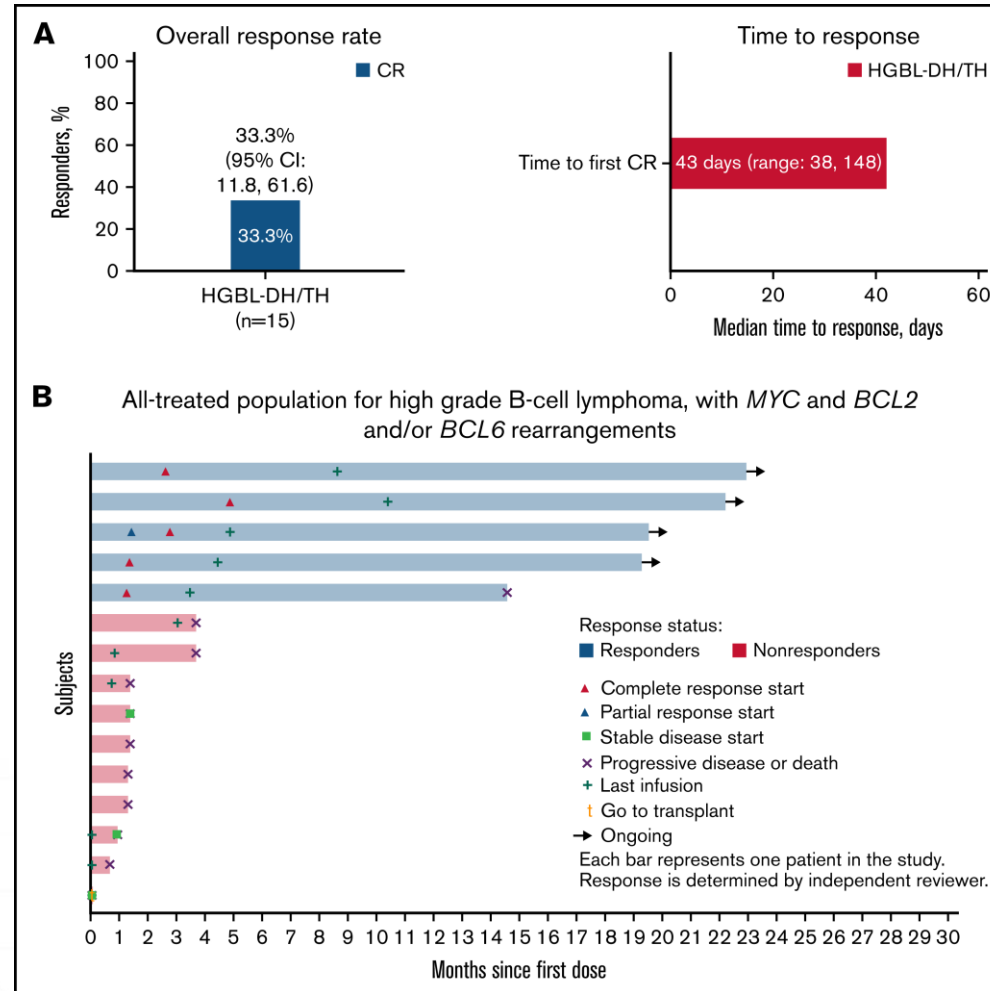
- median OS 9.5 months
- median PFS 4.9 months

- Gr3+ AE
 - neutropenia 26%
 - thrombocytopenia 18%
 - incr GGTP 17%

- SAE 39%



Loncastuximab – LOTIS-2



Summary

- “easier” agents may provide some disease control
- Polatuzumab
 - May have decreasing role in R/R
 - Question of COO
 - Good bridging
 - Avoid benda
- Tafasitamab
 - Likely better in lower risk presentations
 - Well tolerated
- Loncastuximab
 - Activity even in higher risk
 - Well tolerated

Thank you

