State of the Art in Non-Hodgkins Lymphoma

A Focus on DLBCL

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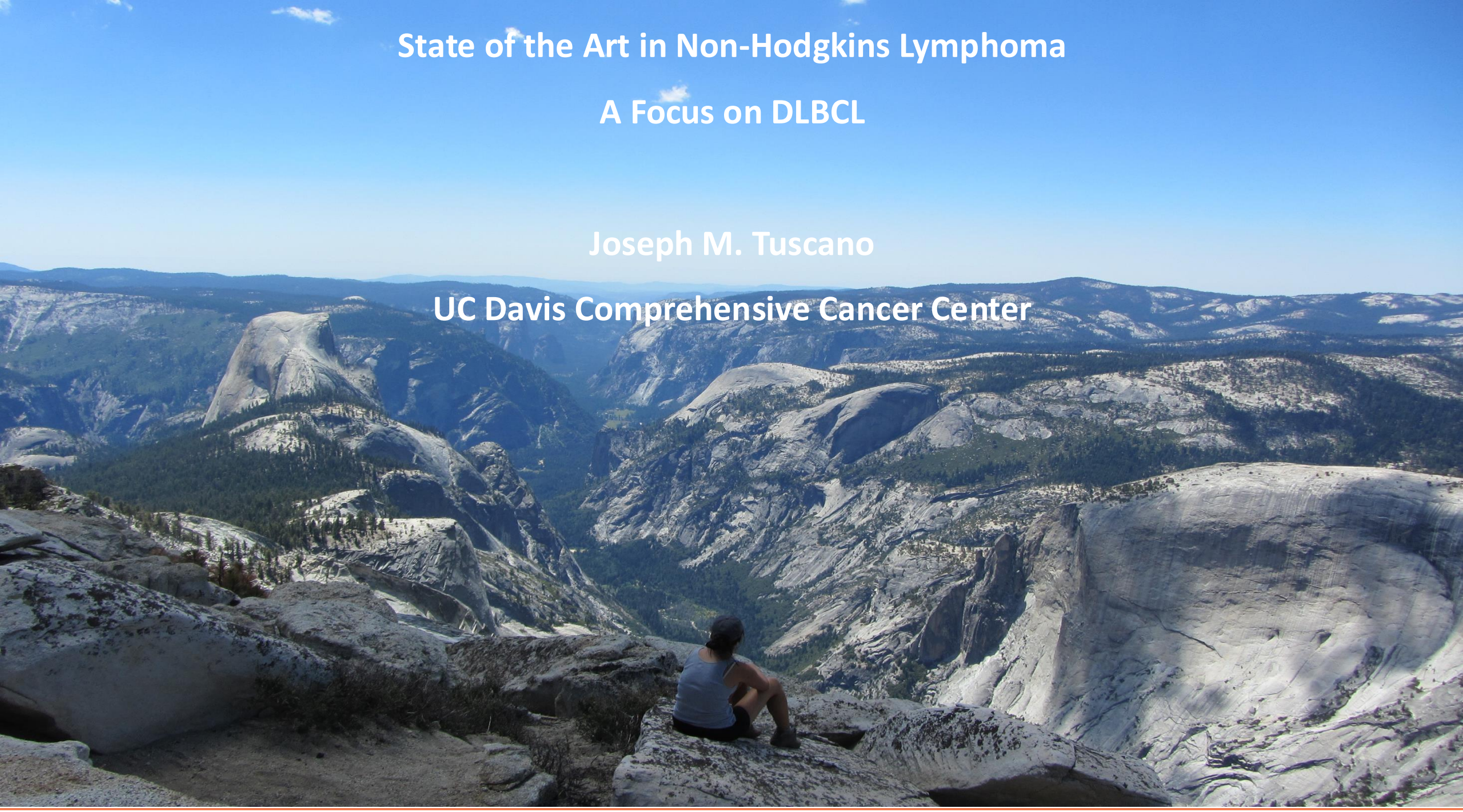
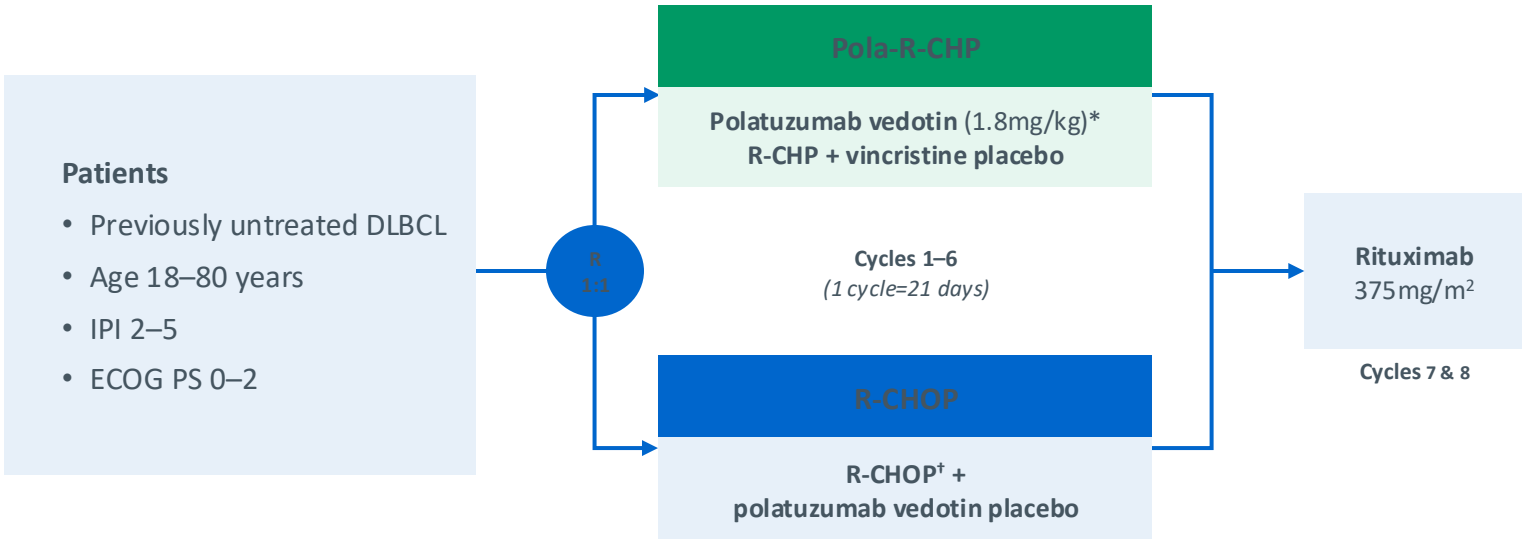


Objectives

- Previously untreated DLBCL
- Relapsed/Refractory DLBCL
- CAR-T
- Bispecifics
- Novel combinations
- Quick update on Mantle Cell Lymphoma

Previously Untreated DLBCL

Phase 3 POLARIX Study: Polatuzumab Vedotin + R-CHP Versus R-CHOP for Newly Diagnosed DLBCL—Study Design



Stratification factors

•IPI score (2 vs 3–5)

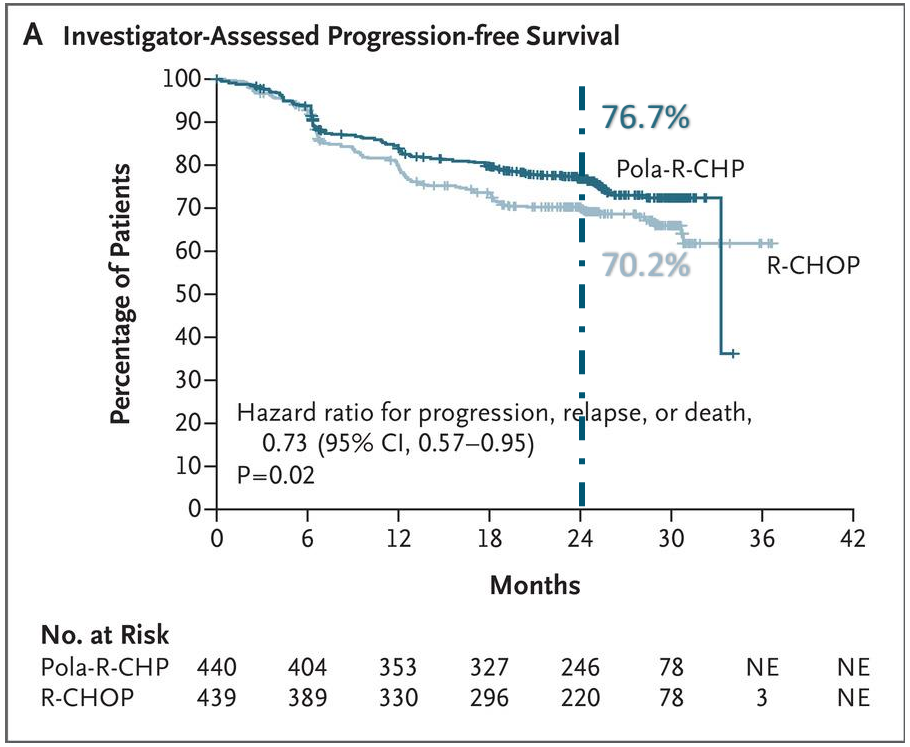
•Bulky disease (<7.5 vs ≥7.5cm)

•Geographic region (Western Europe, US, Canada, & Australia vs Asia vs rest of world)

- Primary endpoint: PFS (INV)
- Secondary endpoints: EFS, CR at EOT, DFS, OS, safety

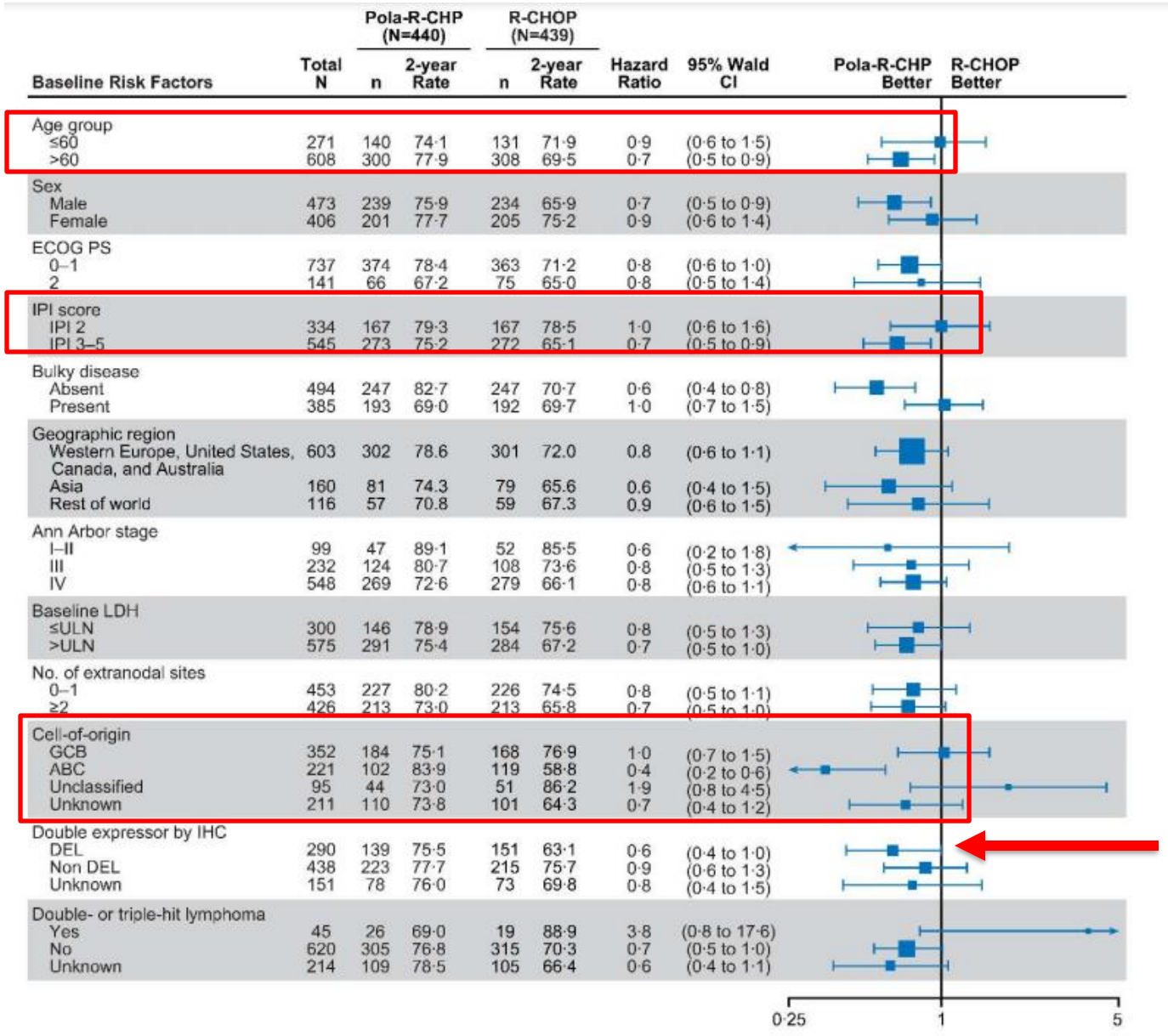
Median follow up, 28.2 mo; data cut off: 28 JUN 2021.

Tilly H, et al. *N Engl J Med*. 14 Dec 2021. Tilly H, et al. ASH 2021 LBA1.



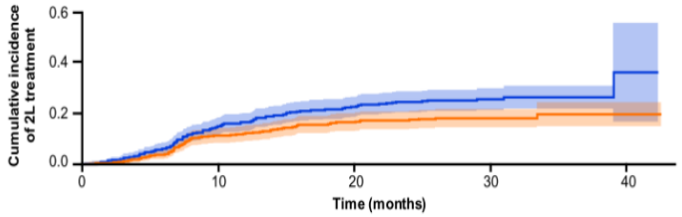
- 27% reduction in risk of progression, relapse or death with Pola-R-CHP

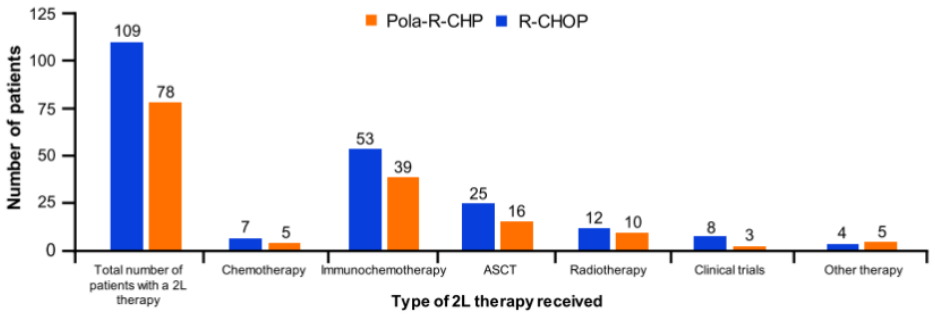
Median follow up, 28.2 mo; data cut off: 28 JUN 2021.
Tilly H, et al. *N Engl J Med*. 14 Dec 2021. Tilly H, et al. ASH 2021 LBA1.



Boissard F, et al. ASH 2022. Abstract 2958.

Pola_R-CHP results in a reduction in the need for subsequent therapy





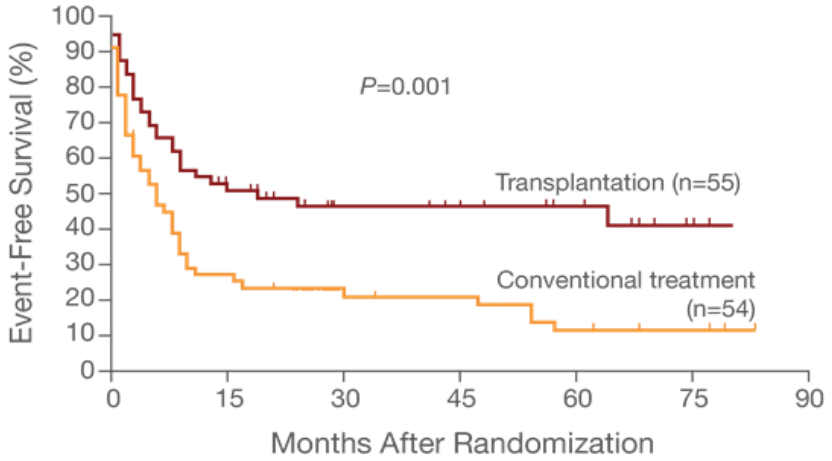
Most of this benefit is in high IPI/non-GCB/ABC

Boissard F, et al. ASH 2022. Abstract 2958.

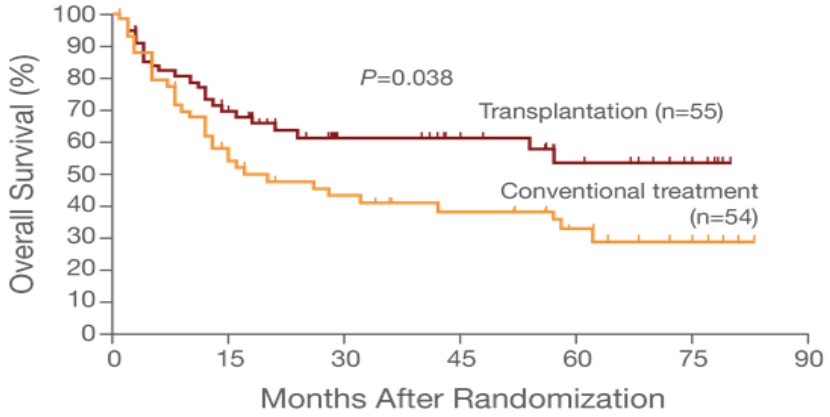
Salvage Therapy for Relapsed or Refractory DLBCL

Standard of Care for Chemosensitive R/R DLBCL is ASCT

Event-Free Survival[1]



Overall Survival[1]



- 20% to 50% of patients will relapse or be refractory to R-CHOP, depending on IPI[2]
- 30% to 40% of patients will respond to salvage chemotherapy and proceed to ASCT[2]
  - Relative equivalency with intensive salvage regimens
- 50% will relapse after ASCT[2]

1. Philip T, et al. *N Engl J Med.* 1995;333(23):1540-1545. 2. Crump M, et al. *Blood*. 2017;130(16):1800-1808.

CAR T-Cell Therapy With Relapse< 12 Months

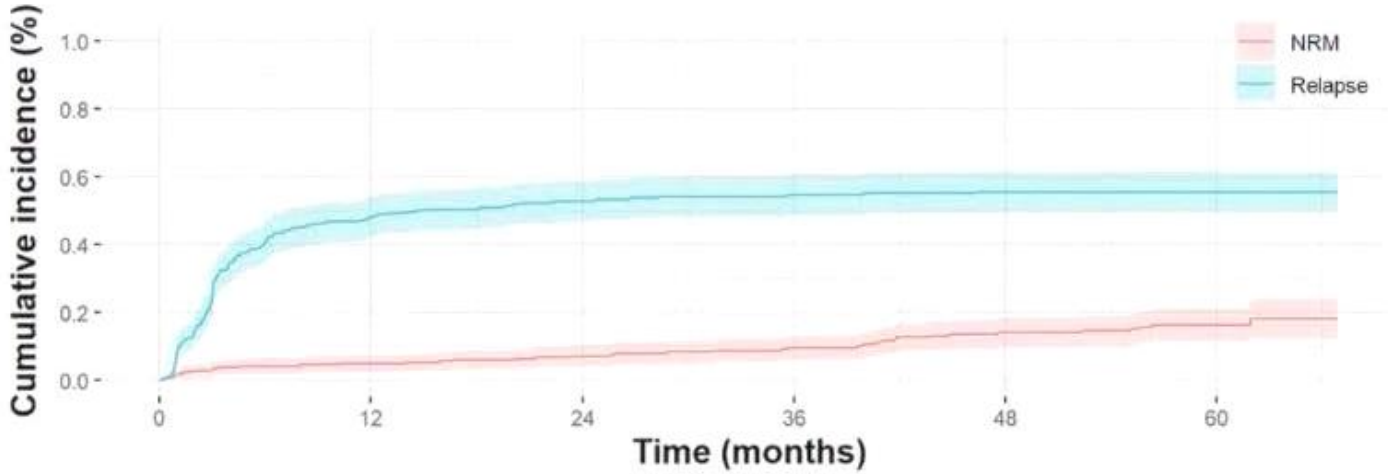
	ZUMA-7[1]		BELINDA[2,a]		TRANSFORM[3,b]	
	Axi-cel (n=180)	SOC (n=179)	Tisagenlecleucel (n=162)	SOC (n=160)	Liso-cel (n=92)	SOC (n=92)
Primary end point	EFS	EFS	EFS after wk 12	EFS after wk 12	EFS	
Median age (range), y	58 (21–80)	60 (26–81)	59.5 (19–79)	58 (19–77)	60 (53.5-67.5)	58.0 (42-65)
Eligibility	R/R at ≤12 mo, ASCT-eligible; no impending organ compromise	R/R at ≤12 mo, ASCT-eligible; no impending organ compromise	R/R at ≤12 mo, ASCT-eligible	R/R at ≤12 mo, ASCT-eligible	Adults with aggressive NHL* R/R ≤12 mo, ASCT eligible, LVEF > 50%	
Bridging therapy	Glucocorticoids only (36% received)	NA	Chemotherapy optional (83% received)	NA	Chemotherapy optional	NA
Disease status at study entry, %						
Refractory to any therapy / relapsed / prior ASCT	0	73 / 27 / NA	66 / 34 / NA	67 / 33 / NA	73 / 27 / NA	
Clinical outcomes						
Median follow-up, mo	25	25	10	10	6.2	6.2
Response, %	83	50	46	43	86	48
CR, %	65	32	28	28	74	43
mEFS, mo (%95 CI)	8.3 (4.5-15.8)	2.0 (1.6-2.8)			52.6 (42.3-62.9) 18-mo	20.8 (12.2-29.5) 18-mo
EFS, HR (95% CI); P value	0.40 (0.31–0.51); P<0.0001		1.07 (0.82-1.40); P=0.61		0.349 (0.229-0.530); P <.0001	
PFS, %	24-mo, 46	24-mo, 27	NR	NR	18-mo, 58.2	18-mo, 28.8

OS Benefit for Axi-Cel-Westin et al 2023

1. Locke FL, et al. *N Engl J Med*. 2022;7:640-654. 2. Bishop MR, et al. *N Engl J Med*. 14 DEC 2021. 3. Kamdar. ASH 2021. Abstract 91.

Five-Year Outcomes of Patients With Large B-Cell Lymphoma Treated with Standard-of-Care Axicabtagene Ciloleucel: Results from the US Lymphoma CAR-T Cell Consortium (Spiegel JY, et al. ASH 2023)

- Standard of care cohort (n = 298)
  - 43% ZUMA-1 ineligible comorbidities
- 5-year cumulative risk of the following:
  - Relapse 55.2%
    - 151 total progression events (13% after 1-year)
    - Last progression 46.4 months post infusion
  - NRM 16.2%
    - 40 NRM events
- Non-relapse mortality overall 16.5%, highlighting the need for better post–CAR-T management strategies (anti-infectives and vaccination) to maximize CAR-T benefit



Axil-Cel or Liso-Cel are NCCN Preferred for Second Line R/R DLBCL that have relapsed w/in 12 Months

But are there alternatives?

Autologous Transplant (auto-HCT) Is Associated with Improved Clinical Outcomes Compared to CAR-T Therapy in Patients (pts) with Large B-Cell Lymphoma (LBCL) Achieving a Complete Remission

ASH 2023 abstract #781

Table-1: Selected baseline characteristics

	CAR-T	auto-HCT	P-value
Age, years	64	59	0.14
Extra-nodal disease	58%	63%	0.37
Refractory disease to first-line	29%	20%	0.22
Prior lines of therapy, n	3	2	**<0.01**
Early treatment failure (within 12 months)	72%	58%	**0.02**
Elevated LDH before treatment	37%	31%	**0.04**
high-grade B-cell lymphoma with MYC and BCL2 or BCL6 rearrangement	14%	27%	**0.03**

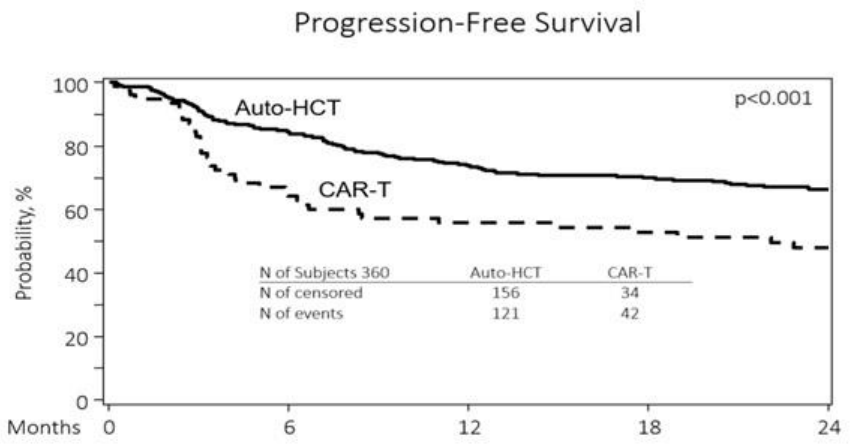


Figure-1: PFS in pts with LBCL who received auto-HCT vs. CAR-T while in CR

Abstract 781 ASH 2023, Mazyar Shadman, MD, MPH[1,2], *Kwang Wooahn, PhD*[3*], *Manmeet Kaur*[4*], *Mohamed A. Kharfan-Dabaja, MD, MBA*[5], *Alex F. Herrera, MD*[6], *Craig S Sauter, MD*[7] *and Mehdi Hamadani, MD*[8]

Zuma-7-Only ~ 30% responded in the ASCT group and those that made it to transplant had a statistically equivalent DOR when compared to Axi-cel (Locke et al NEJM Sup fig 4)

Chemosensitivity matters!

CAR T can still be used for Auto-HCT failures-Reverse is not true

Key Data on Currently Approved Noncellular R/R DLBCL Regimens

No head-to-head studies have been conducted, and direct comparisons cannot be made between these studies

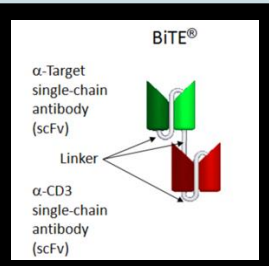
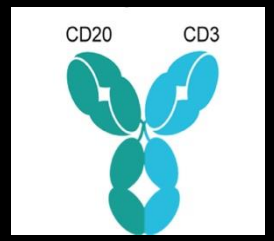
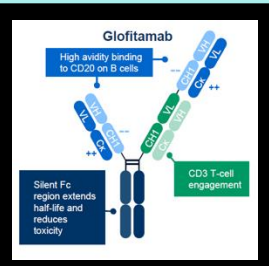
Agents	Study Name Trial Design	ORR	CR	Median OS	Median PFS
Epcoritamab[1,a]	EPCORE NHL-1 Phase 2, single arm	63%	39%	NR	4.4 mo (IRC)
Glofitamab[2]	NP30179 Phase 2, single arm	52%	39%	11.5 mo (INV)	4.9 mo (IRC) 3.8 mo (INV)
Lonca-T[3]	LOTIS-2 Phase 2, single arm	48%	24%	9.9 mo	4.9 mo
Pola-BR[4]	GO 29365 Phase 1/2, single arm	63%	50%	12.4 mo (IRC)	9.5 mo (IRC)
Selinexor[5]	SADAL Phase 2, single arm	28%	12%	9.1 mo	2.6 mo
Tafa + Len[6]	L-MIND Phase 2, single arm	60%	43%	NR	12.1 mo (IRC)

[a] Includes patients with LBCL.

1. Thieblemont C, et al. *J Clin Oncol.* 2022;41(12):2238-2247. **2.** Dickinson MJ, et al. *N Engl J Med*. 2022;387(24):2220-2231. **3.** Caimi PF, et al. *Lancet Oncol*. 2021;22(6):790-800. **4.** Sehn LH, et al. *J Clin Oncol*. 2020;38(2):155-165. **5.** Kalakonda N, et al. *Lancet Haematol*. 2020;7(7):e511-e522. **6.** Salles G, et al. *Lancet Oncol*. 2020;21(7):978-988.

Bispecific AntiBodies

Bispecific Antibodies in Non-Hodgkin Lymphomas

The Original: Proof of Concept	Newer Therapies	
Blinatumomab[1]	Epcoritamab[2]	Glofitamab[3]
		
CD3 (scFV) × CD19 (scFV)	DuoBody- CD3 × CD20 BsAb	CD3 (Fab) × CD20 (Fab x2) Fc BsAb

Key Bispecific Antibodies in 3L DLBCL: Efficacy and Safety

	Study Phase	Study Population	Clinical Trial	ROA	Sample Size	Median Prior LOT	Efficacy: ORR, CR, mDOR/DoCR	Safety All CRS	Safety Grade ≥3 CRS	Safety Other
Epcoritamab[1,2] [Hospitalization required for 24h after dose on C1 D15]	P1/2	Patients with R/R DLBCL and B-NHL after anti-CD20 treatment	NCT03625037 (EPCORE NHL-1)	SUBQ	DLBCL=46	3 (2-4)	68% ORR, 45% CR (dose 12-60 mg)	59%	0%	Neurological: 6%
					LBCL=157	3 (2-11)	63.1% confirmed ORR by IRC, mDOR 12 mo	49.7%	2.5% (Gr 3)	Pyrexia: 23.6% Neutropenia: 21.7%
Glofitamab[4,5] [Pretreatment with obinutuzumab required]	P2	Patients with R/R DLBCL after at least 2 prior systemic therapy	NCT03075696 (NP30179)	IV	DLBCL=155	3 (2-7)	52% ORR, 39% CR	63%	4%	Grade ≥3 NEs: 3%

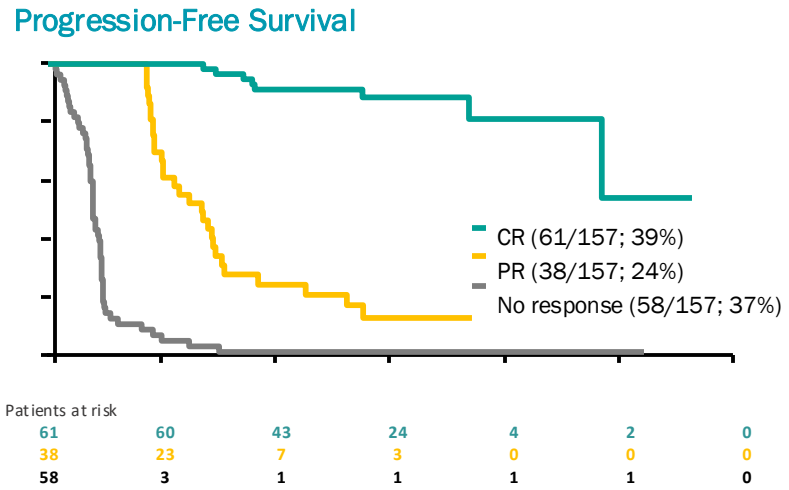
Epcoritamab and glofitamab have been approved by the FDA for use in R/R DLBCL; mosunetuzumab is not approved by the FDA or other regulatory authorities for use in DLBCL.
This table is for illustration only and side-by-side data should be interpreted with great caution.

1. Hutchings M, et al. *Lancet*. 2021;398(10306):1157-1169. **2.** Thieblemont C, et al. *J Clin Oncol*. 2023;41(12):2238-2247.
3. Bartlett N, et al. *Blood Adv.* 2023:2022009260. **4.** Dickinson MJ, et al. *N Engl J Med*. 2022;387(24):2220-2231. **5.** Dickinson MJ, et al. ASCO 2022. Abstract 7500.

EPCORE NHL-1 Phase 2 Study of Epcoritamab in Patients with R/R LBCL: Overall Response, PFS, and OS[1,2,3]

Best overall response by IRC[a]	LBCL (N=157)
Overall response, n (%) [95% CI]	99 (63.1) [55.0-70.6]
Complete response, n (%) [95% CI]	61 (38.9) [31.2-46.9
Partial response, n (%)	38 (24.2)
Stable disease, n (%)	5 (3.2)
Progressive disease, n (%)	37 (23.6)

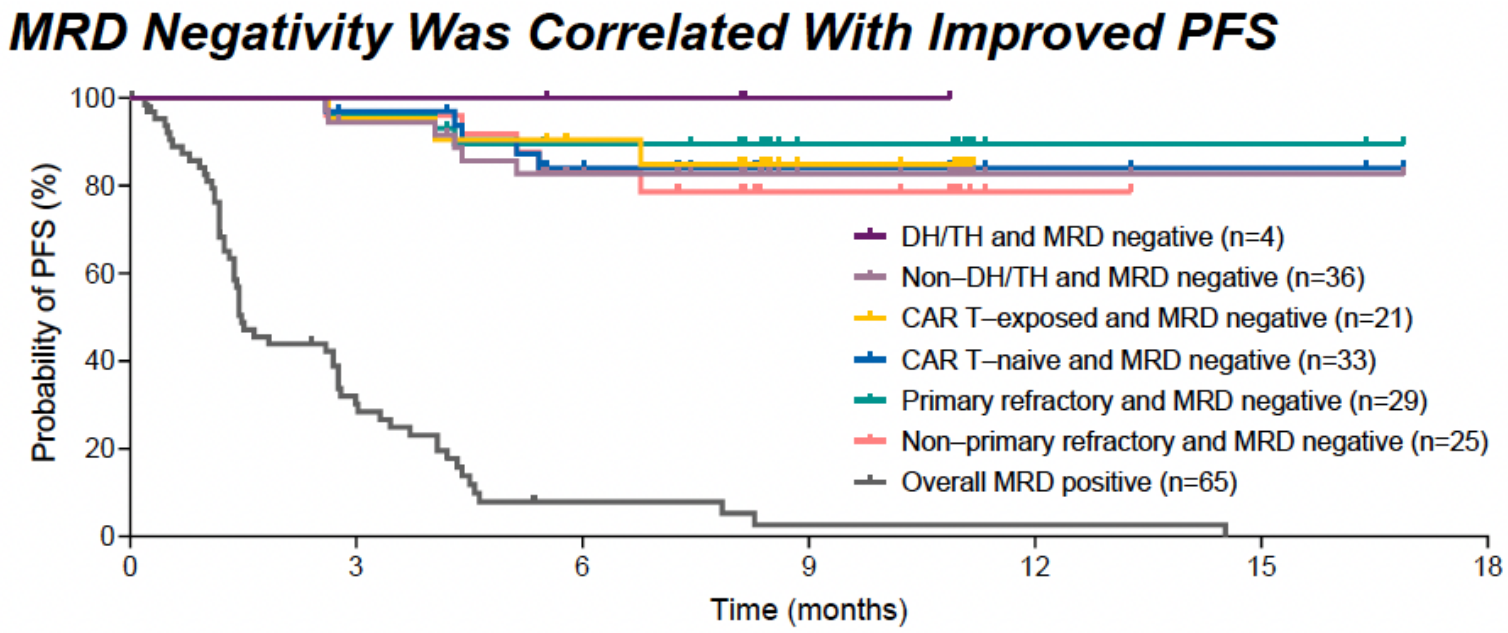
Kaplan-Meier estimate	LBCL (N=157)
Median PFS for complete responders (95% CI)	NR (14.5-NR)
Complete responders remaining in CR at 9 mo, %	88.7
Median PFS, mo (95% CI)	4.4 (3.0-7.9)
PFS at 6 mo, % (95% CI)	43.9 (35.7-51.7)
Median OS, months (95% CI)	18.5 (11.7-NR)
Median OS for patients who achieved a CR (95% CI)	NR (NR-NR)



tract LB2364. **3.**

Jurczak W, et al. EHA 2023. Abstract P1118.

Epcoritamab in R/R DLBCL



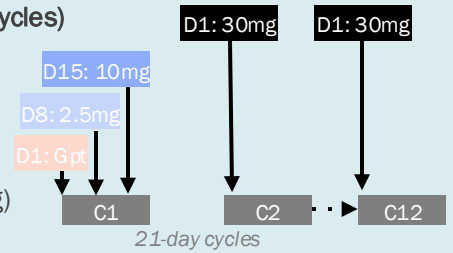
Phillips et al, ASH 2022

Phase 2 Study of Glofitamab in Patients with 3L+ R/R DLBCL: Study Design and Patients

Key Inclusion Criteria:
- DLBCL NOS, HGBCL, transformed FL or PMBCL
- ECOG PS 0–1
- ≥2 prior therapies, including anti-CD20 antibody and anthracycline

Glofitamab IV Administration:
Fixed-duration treatment (Max 12 Cycles)

CRS mitigation:
- obinutuzumab pretreatment (1 x 1000mg)
- C1 step-up dosing
- monitoring after first dose (2.5mg)



Primary endpoint: CR (best response) rate by IRC[a]
Key secondary endpoints: ORR rate[b], DoR, DoCR[b], PFS, and OS

Baseline Characteristic, n (%)		N=154
Median age, years (range)		66.0 (21–90)
ECOG PS	0	69 (44.8)
	1	84 (54.5)
Ann Arbor stage	I	10 (6.5)
	II	25 (16.2)
	III	31 (20.1)
	IV	85 (55.2)
NHL subtype	DLBCL	110 (71.4)
	trFL	27 (17.5)
	HGBCL	11 (7.1)
	PMBCL	6 (3.9)
Median no. of prior lines, n (range)		3 (2-7)
≥3 prior lines		92 (59.7)
Prior anti-CD20 Ab		154 (100.0)
Prior anthracycline		149 (96.8)
Prior CAR-T		51 (33.1)
Prior ASCT		28 (18.2)
Refractory to any prior therapy		139 (90.3)
Refractory to last prior therapy		132 (85.7)
Primary refractory		90 (58.4)
Refractory to prior CAR-T		46 (29.9)
Refractory to any prior anti-CD20		128 (83.1)

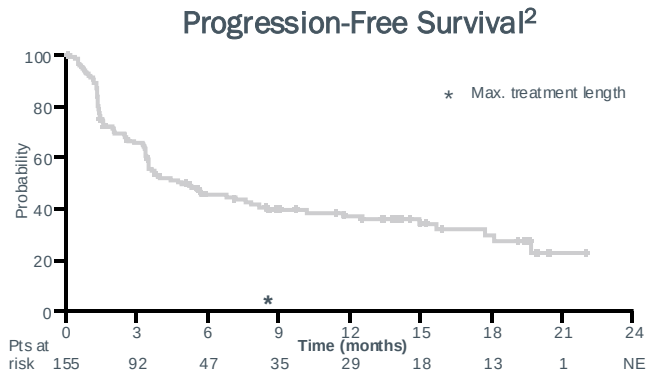
[a]By PET-CT (Lugano critera). [b]By IRC and investigator.

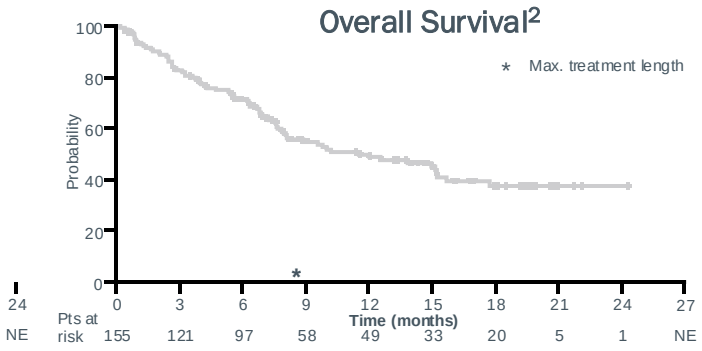
Dickinson M, et al. ASCO 2022. Abstract 7500.

Phase 2 Study of Glofitamab in Patients with 3L+ R/R DLBCL: Efficacy

Efficacy Endpoint[1,2]	Glofitamab 2.5/10/30mg (n=155)
CR rate[a]	61 (39.4%) [95% CI: 31.6%-47.5%]
ORR[a]	80 (51.6%) [95% CI: 43.5%-59.7%]
Median PFS follow-up, mo (range)	12.6 (0–22)
Median PFS, months (95% CI)	4.9 (3.4, 8.1)
Median OS, months (95% CI)	11.5 (7.9, 15.7)
12-month OS rate, % (95% CI)	49.8 (41.1, 58.5)

Duration of Overall Response[2]	n=80
Median DoR follow-up, mo (range)	10.6 (0–21)
12-months DoR, % (95% CI)	63.6 (51.1, 76.2)
ORs ongoing at CCOD, n (%)	53 (66.3)
Duration of CR[2]	**n=61**
Median DoCR follow-up, mo (range)	10.6 (0–21)
12-months DoCR, % (95% CI)	77.6 (64.3, 90.8)
CRs ongoing at CCOD, n (%)	49 (80.3)





1. Cheson, et al. J Clin Oncol 2014. **2.** Dickinson M, et al. ASCO 2022. Abstract 7500.

Emerging Data in R/R DLBCL

ASH 2023, Tandem 2024, EHA 2024, ASCO 2024

Despite recent advances, there remains an **unmet need** for safe and readily available regimens for R/R DLBCL[1,2]

Agents	Study Name Trial Design	Patients	ORR	CR	Median OS	Median PFS	Safety
Glofitamab + GemOx[3]	**STARGLO Phase 3, randomized, open-label, controlled**	**R/R DLBCL (n=183); 63% 1 pLOT; 37% ≥2 pLOT**	**68% (IRC)**	**58% (IRC)**	**25.5 mo (20.7 mo median f/u)**	**13.8 mo (IRC; 16.1 mo median f/u)**	**Consistent with known risks of individual study drugs**
Odronextamab[4]	**ELM-2 Phase 2, open-label**	**R/R DLBCL (n=127) Median (range) pLOT = 2 (2-8)**	**52% (ICR)**	**31.5% (ICR)**	**9.2 mo**	**4.4 mo**	**Consistent with previous reports**
Lonca-T[5]	**RWE**	**Post–CAR T-cell therapy in 2L or 3L**	**73% (3L Lonca-T) 78% (4L Lonca-T)**	**34% (3L Lonca-T) 17% (4L Lonca-T)**	**Not reported**	**Not reported**	**Low rate of discontinuation due to AEs (7%)**
Brentuximab vedotin + Len + R (BV + R^2)[6]	ECHELON-3 Phase 3, randomized, double blind, controlled	R/R DLBCL (n=112); Median (range) pLOT = 3 (2-8)	64%	40%	13.8 mo (15.5 mo median f/u)	4.2 mo (11.1 mo median f/u)	No new safety signals with addition of BV to R^2

No head-to-head studies have been conducted, and direct comparisons cannot be made between these studies.

1. Ip A, et al. *Adv Ther.* 2024;41(3):1226-1244. **2.** Sineshaw HM, et al. *Cancer Med.* 2024;13(7):e7173.
3. Abramson JS, et al. EHA 2024. Abstract LB3438. **4.** Ayyappan S, et al. ASH 2023. Abstract 436. **5.** Epperla N, et al. *Transplant Cell Ther.* 2024;30(Suppl 2):S353. **6.** Kim JA, et al. ASCO 2024. Abstract LBA7005.

Epcoritamab + R-DHAX/C in Transplant-Eligible Patients (Pts) With High-Risk Relapsed or Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL)

Yasmin H. Karimi, MD,[1*] Pau Abrisqueta, MD, PhD,[2] Sven de Vos, MD, PhD,[3] Marcel Nijland, MD, PhD,[4] Fritz Offner, MD, PhD,[5] Kojo Osei-Bonsu, MD,[6] Ali Rana, MD, PhD,[7] Kimberly G. Archer,[7] Yaou Song, MS,[7] Raul Cordoba, MD, PhD,[8] Lorenzo Falchi, MD[9]

[1]University of Michigan Comprehensive Cancer Center, Ann Arbor, MI, USA; [2]Hospital Universitario Vall d'Hebron, Barcelona, Spain; [3]Ronald Reagan University of California Los Angeles Medical Center, Los Angeles, CA, USA; [4]University Medical Center Groningen and University of Groningen, Groningen, Netherlands; [5]Universitair Ziekenhuis Gent, Ghent, Belgium; [6]AbbVie, North Chicago, IL, USA; [7]Genmab, Plainsboro, NJ, USA; [8]Fundacion Jimenez Diaz University Hospital, Health Research Institute IIS-FJD, Madrid, Spain; [9]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Presented at the American Society of Clinical Oncology Annual Meeting; May 31–June 4, 2024; Chicago, IL
(Poster number: 7032)

Study Design: EPCORE® NHL-2 Arm 4

A phase 1b/2, open-label trial evaluating the safety and antitumor activity of epcoritamab + R-DHAX/C in adults with R/R DLBCL who are eligible for transplant

Key inclusion criteria

- R/R CD20+ DLBCL
  - DLBCL, NOS
  - "Double-hit" or "triple-hit" DLBCL[a]
  - FL grade 3B
  - T-cell/ histiocyte-rich DLBCL
- Eligible for R-DHAX/C and HDT-ASCT
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Data cutoff: January 31, 2024
Median follow-up: 27.7 mo

Dose escalation, n=8

Step-up dosing[b]

Epcoritamab (SC)
24 mg (n=3) or 48 mg (n=5)
QW C1–4,
Q2W C5–9,
Q4W C10+*

+ R-DHAX/C
C1–3

Primary objectives: DLTs/Safety and tolerability
Key secondary objective: Antitumor activity

Expansion, n=21

Step-up dosing[b]

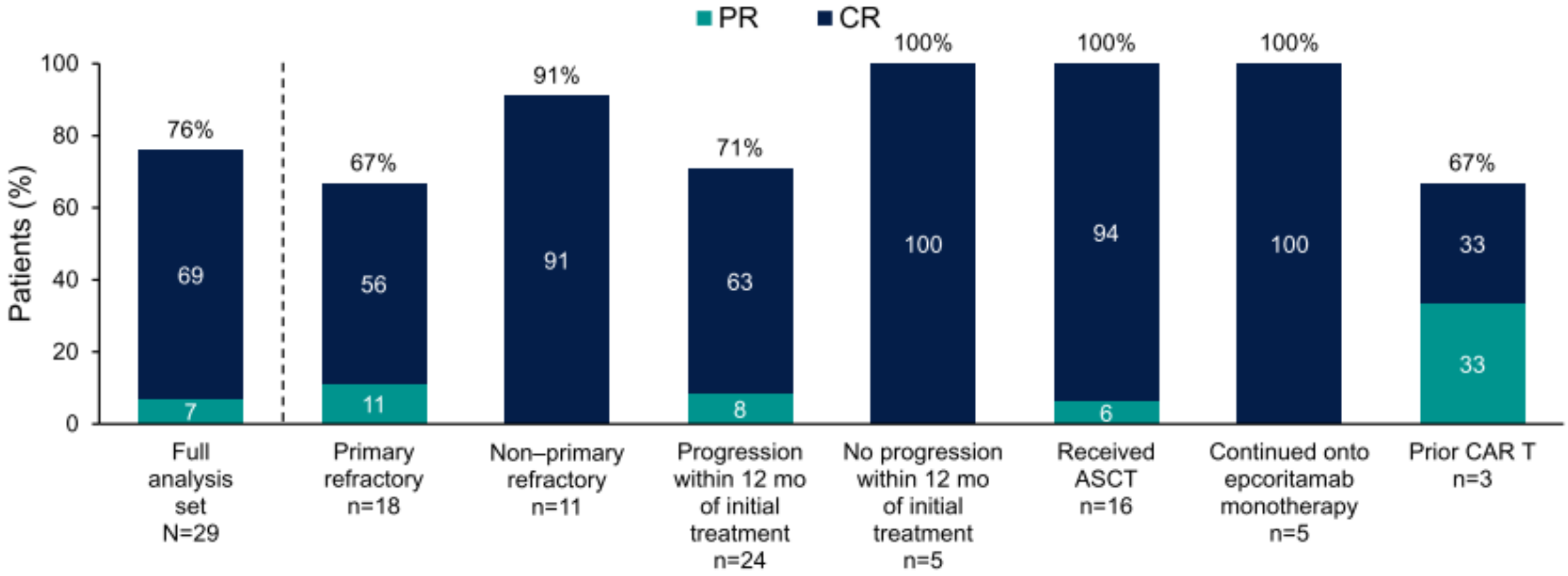
Epcoritamab (SC)
48 mg
QW C1–4,
Q2W C5–9,
Q4W C10+*

+ R-DHAX/C
C1–3

Primary endpoint: ORR per Lugano criteria[c]
***Epcoritamab treatment until HDT-ASCT or PD (whichever is earlier)**

R-DHAX/C regimen in C1–3, 21 d each: rituximab 375 mg/m^2 IV Q3W; dexamethasone 40 mg/d IV or orally on D1–4; cytarabine 2 g/m^2 IV repeated after 12 h Q3W; carboplatin AUC = 5 mg/mL x min (Calvert formula) or oxaliplatin 100 mg/m^2 IV Q3W. Cycle 4 was 21 d. Cycles 5+ were 28 d. C, cycle; CT, computed tomography; d, day(s); DLT, dose-limiting toxicity; ECOG, Eastern Cooperative Oncology Group; FL, follicular lymphoma; h, hour(s); HGBCL, high-grade B-cell lymphoma; IV, intravenous; min, minute(s); mo, month(s); MRI, magnetic resonance imaging; NOS, not otherwise specified; ORR, overall response rate; PD, progressive disease; PET, positron emission tomography; PS, performance status; QW, every week; Q2W, every 2 weeks; Q3W, every 3 weeks; Q4W, every 4 weeks; SC, subcutaneous; SUD, step-up dose; wk, week(s). [a]Classified as HGBCL, with *MYC* and *BCL2* and/or *BCL6* translocations. [b]SUD 1: 0.16 mg; SUD 2: 0.8 mg. Corticosteroid prophylaxis was used in C1 to mitigate CRS. [c]Tumor response was evaluated by PET-CT obtained at 6, 12, 18, 24, 36, and 48 wk, and every 24 wk thereafter, until PD. ClinicalTrials.gov: NCT04663347. EudraCT: 2020-000845-15.

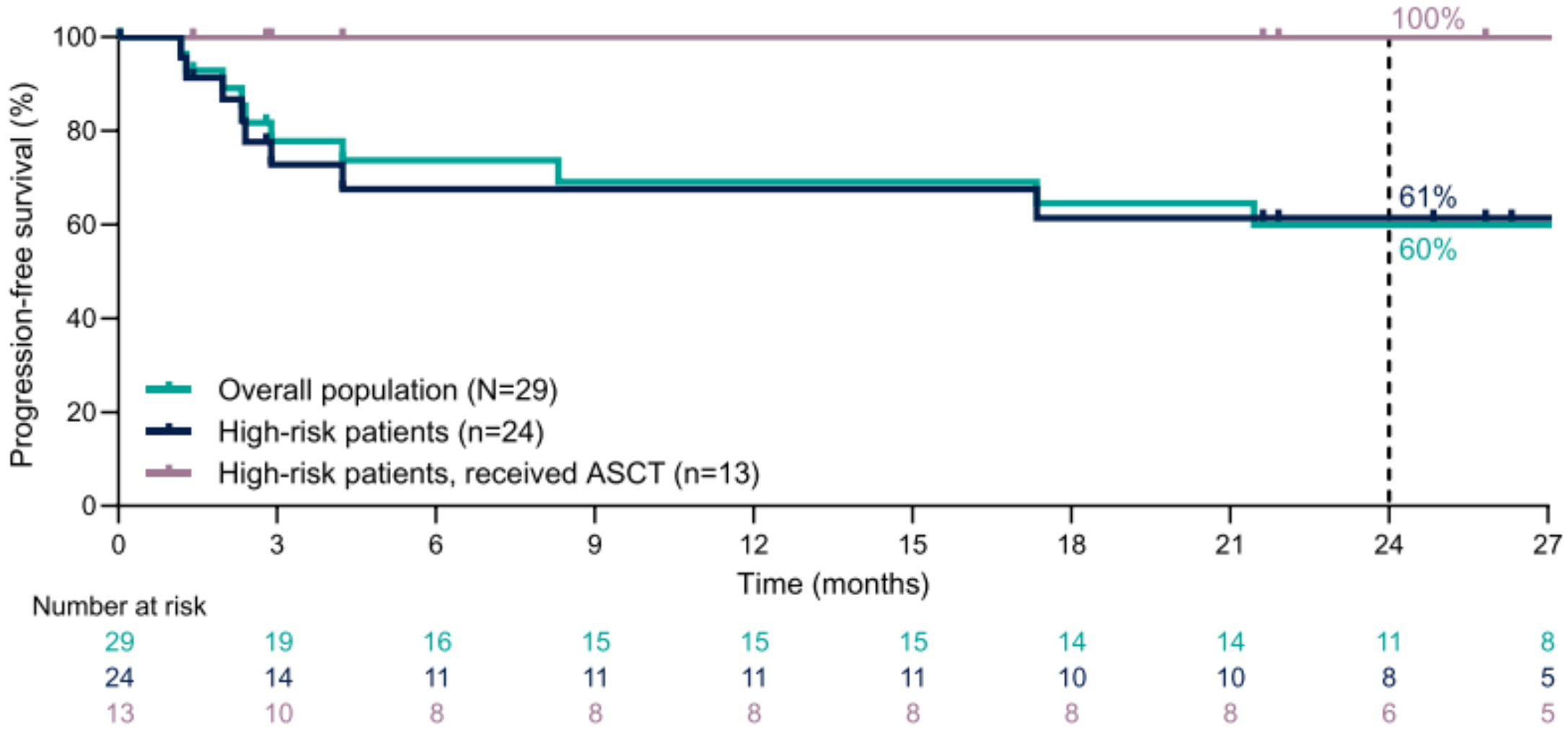
Response Rates Were High Regardless of High-Risk Status



- Overall, median time to response was 1.4 mo (range, 1.2–4.2) and median time to CR was 1.5 mo (range, 1.2–15.5)

PR, partial response.

High Rate of PFS in High-Risk Patients Who Received ASCT



High risk indicates patients with primary refractory disease or who relapsed within 12 months of initial therapy. Kaplan–Meier estimates of patients remaining progression free are shown.
PFS, progression-free survival.

CAR T-Cell Therapy Remain Effective in Patients with Relapse/Refractory B-Cell Non-Hodgkin Lymphoma after Bispecific Antibodies Exposure: Results of a Lysa Study Based on the Descar-T Registry

Figure 1. PFS in LBCL subgroup after CAR T-Cell therapy

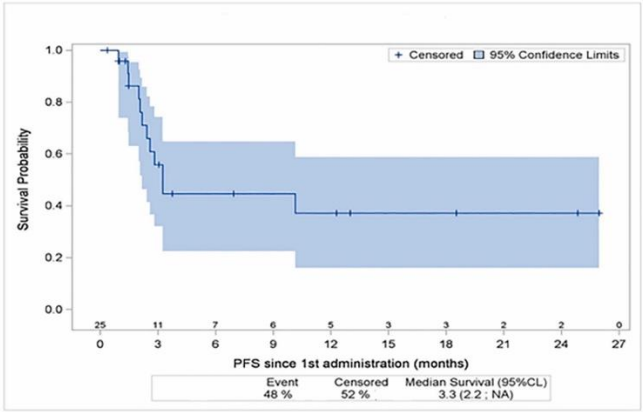


Table 1: Outcomes after CAR T-cells for DLBCL patients with R/R disease after prior bispecific antibodies

	BA therapy		CAR T-cells therapy	
Treatment description	(CD20xCD3)	91.4%	Axi-cel	72%
	(CD19xCD3)	4.3%		
			Tisa-cel	28%
	(CD22xCD3)	4.3%		
Response Rate				
ORR	43.5%		91.6%	
CR	21.7%		45.8%	
PR	21.7%		45.8%	
SD	13.0%		0%	
PD	43.5%		8.3%	
Median PFS [95% CI] (mo)	3.1 [2.9 ; 4.2]		3.3 [2.2 ; NR]	
6 mo PFS [95% CI]	17.4% [5.4% ; 35%]		44.6% [22.4% ; 64.7%]	
1 year PFS [95% CI]	4.3% [0.3% ; 18.2%]		37.2% [15.9% ; 58.7%]	
Median DOR [95% CI] (mo)	2.7 [1.6 ; 4]		2.4 [1.4 ; NR]	
1 year DOR [95% CI]	10% [0.6% ; 35.8%]		40.7% [17.4% ; 63.1%]	

DLBCL:Bottom Line

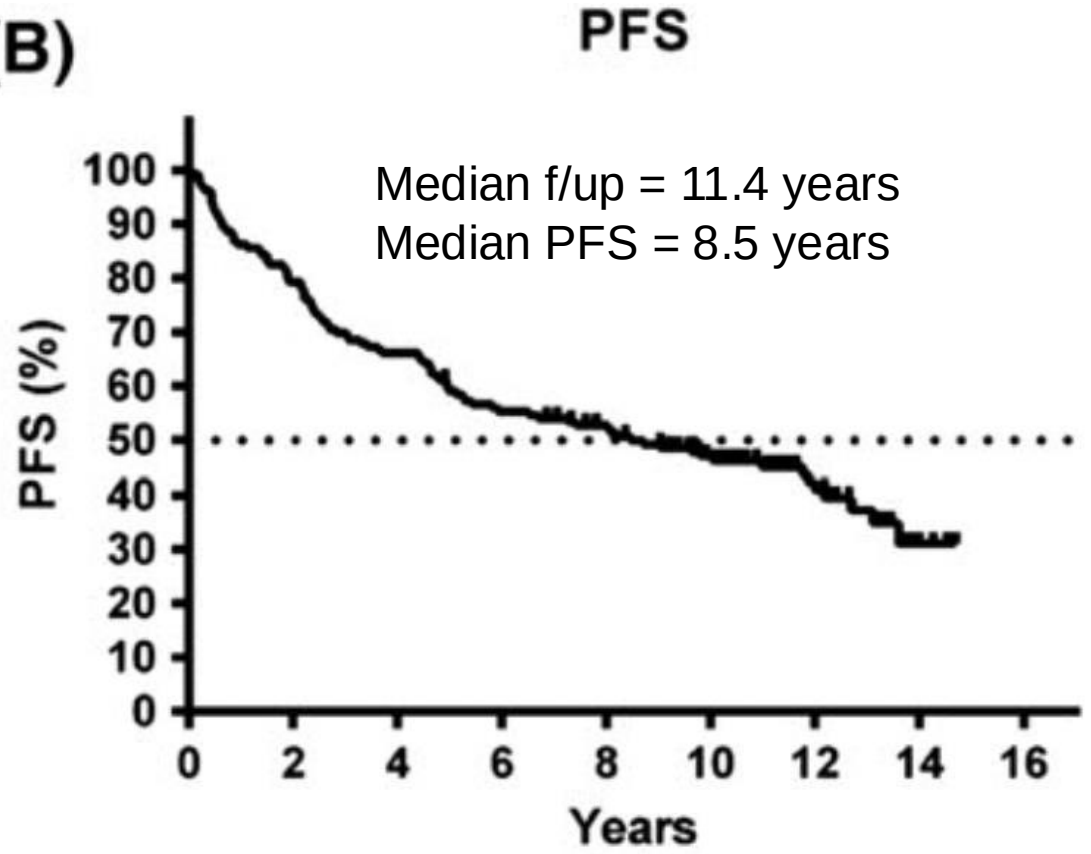
- **Stage I/II-R-CHOP x 3 + IF XRT**
  - **Vs R-CHOP x 4 w/o XRT (Flyer trial)-low IPI**
- **Stage III/IV-R-CHOP x 6 vs Pola-CHP**
  - **Many: Pola-CHP "all comers"-Me: Only in higher risk (high IPI/DEL/ABC)**
  - **DHL (?DEL)- DA-R-EPOCH + CNS ppx**
  - **Elderly R-CEOP, R-EPOCH**
- **Chemo-sensitive relapse (fit < 70)-RICE/R-DHAP/R-Gem-Ox + AutoPSCT**
  - **Many (R/R w/in 1 yr-CAR T), Me: chemosensitivity counts-ASCT**
- **Primary Refractory (?) relapse w/in 12 months consider CAR T**
- **Chemo-insensitive/post-Auto relapse/CAR T failure-consider mini-Allo**
- **NO SOC for other salvage, But:**
  - **Consider Tafa/Len 2nd line not ASCT/CAR T candidate**
  - **Lonca and bispecifics 3rd line**
  - Bispecific-chemo combinations are emerging as a VERY effective strategy-Should I change my line of research? 🤔
- **Always consider clinical trials at *every* step**

Brief Update on the Treatment of Previously Untreated Mantle Cell Lymphoma

- Transplant ineligible-BR (Rummel et al)
- Transplant eligible
  - Nordic Maxi-R-CHOPR/HDAC + ASCT + R maintenance
  - EMCLN- R-CHOP/DHAP +ASCT + R maintenance

Long-term follow-up of Second Nordic Mantle Cell Lymphoma trial

6 cycles of maxiCHOP-R/HiDAC-R followed by autoHCT

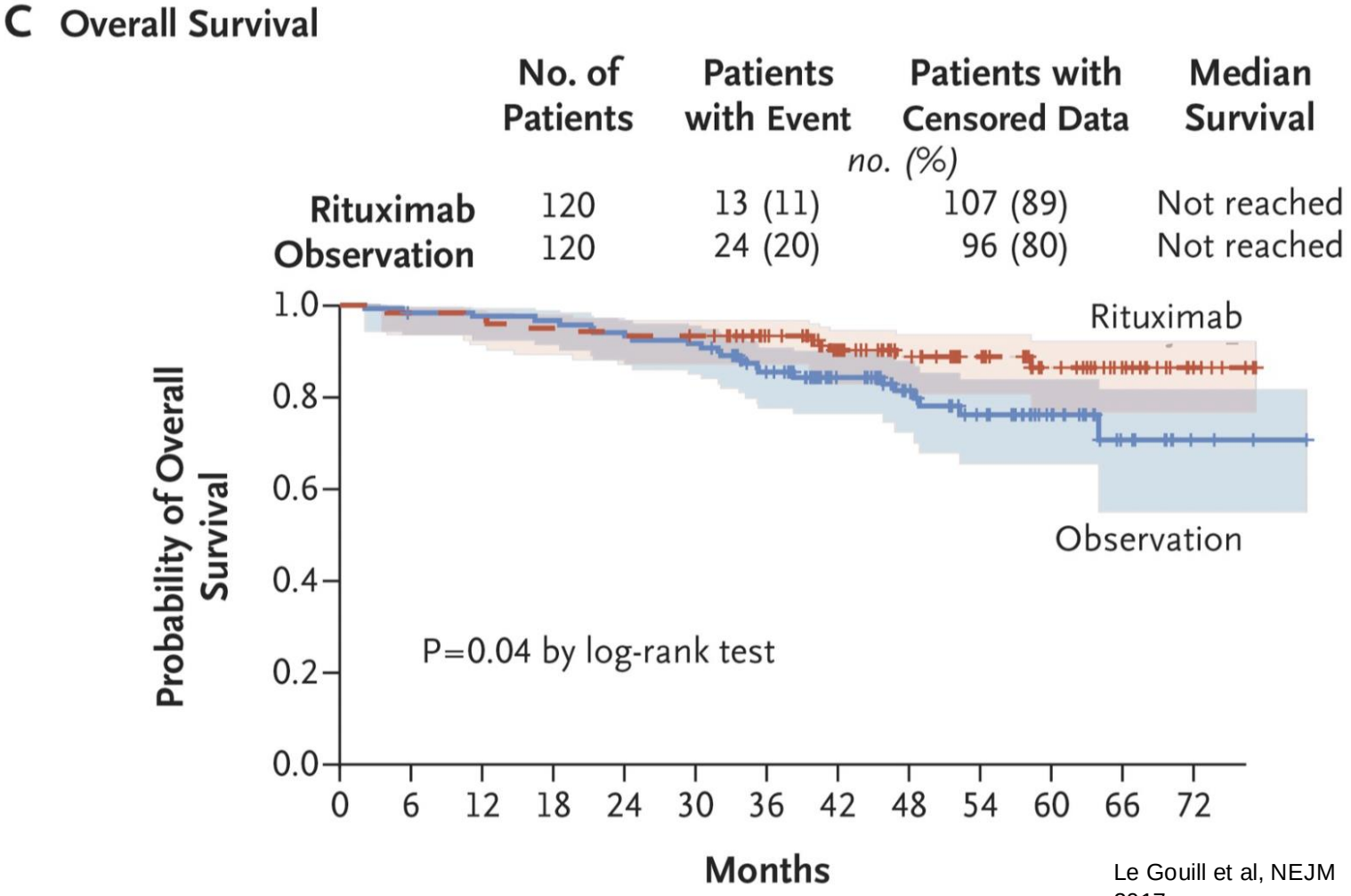


Median f/up = 11.4 years
Median PFS = 8.5 years

40% still in CR1 after >12 years, but no plateau in survival curve

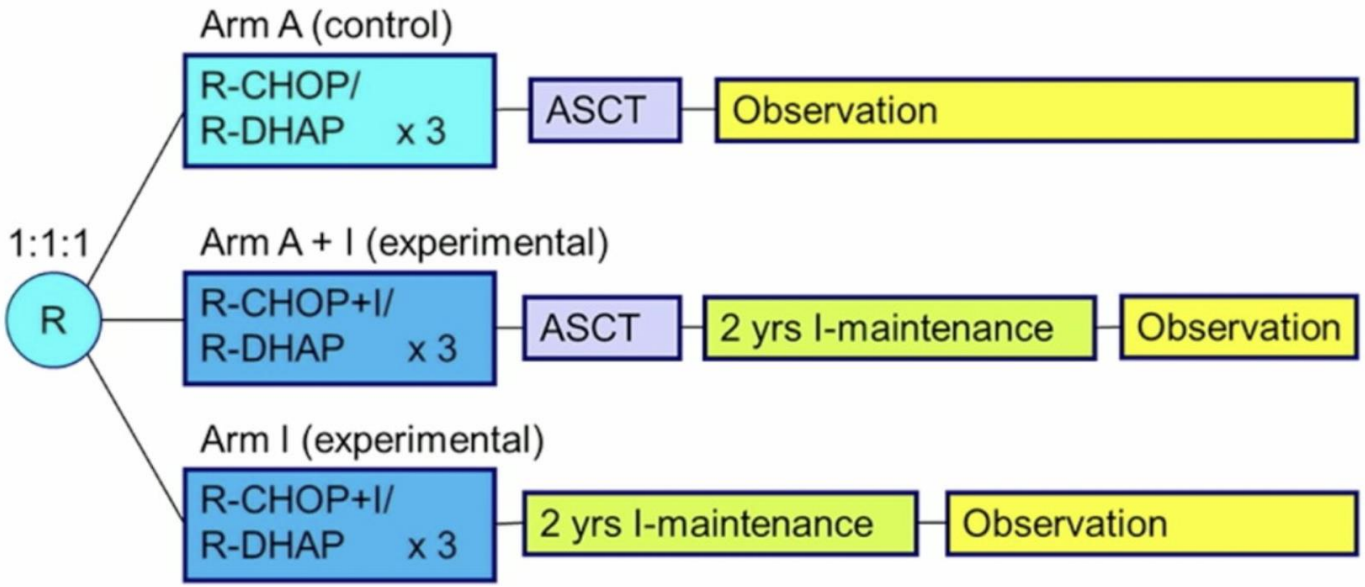
Eskelund et al, BJH 2016

Rituximab maintenance after autologous HCT

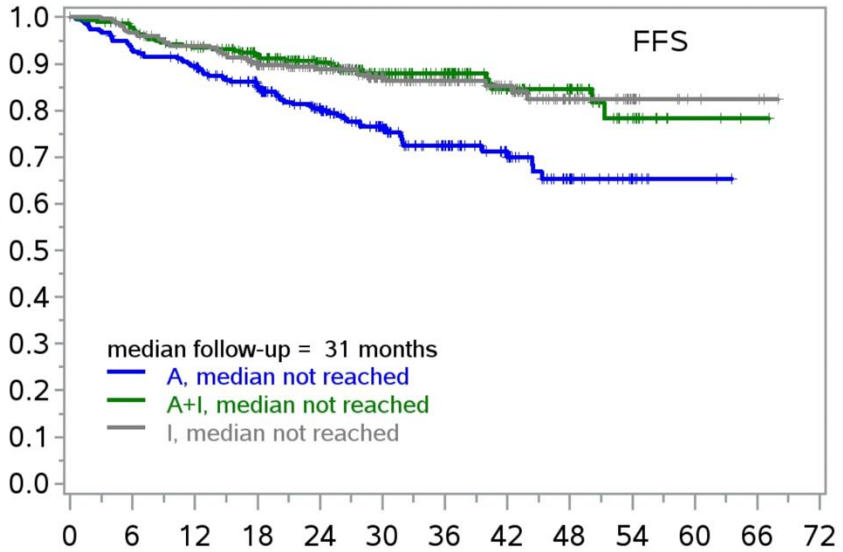


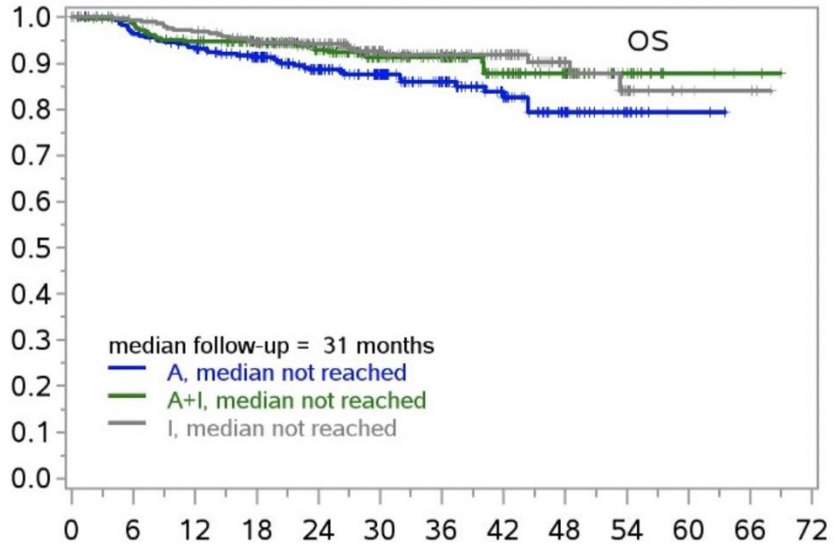
Le Gouill et al, NEJM 2017

TRIANGLE: Trial Design

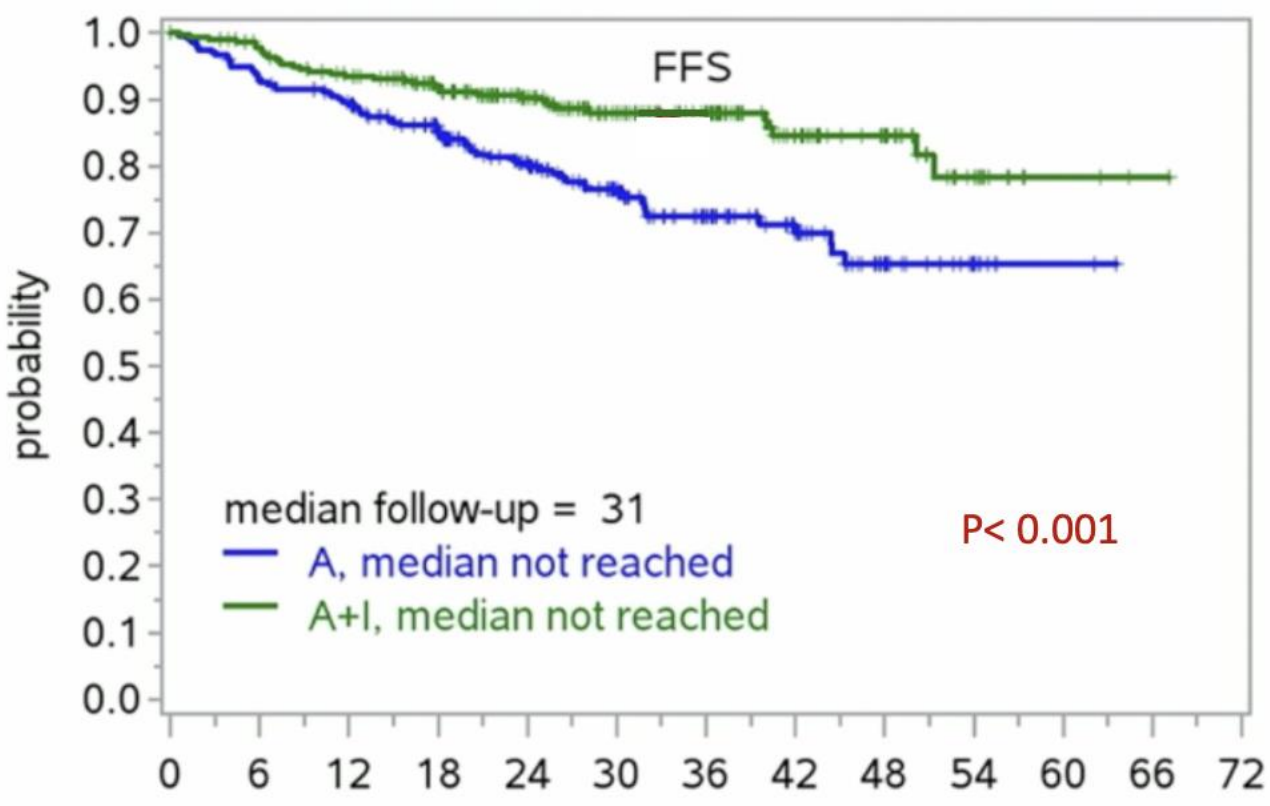


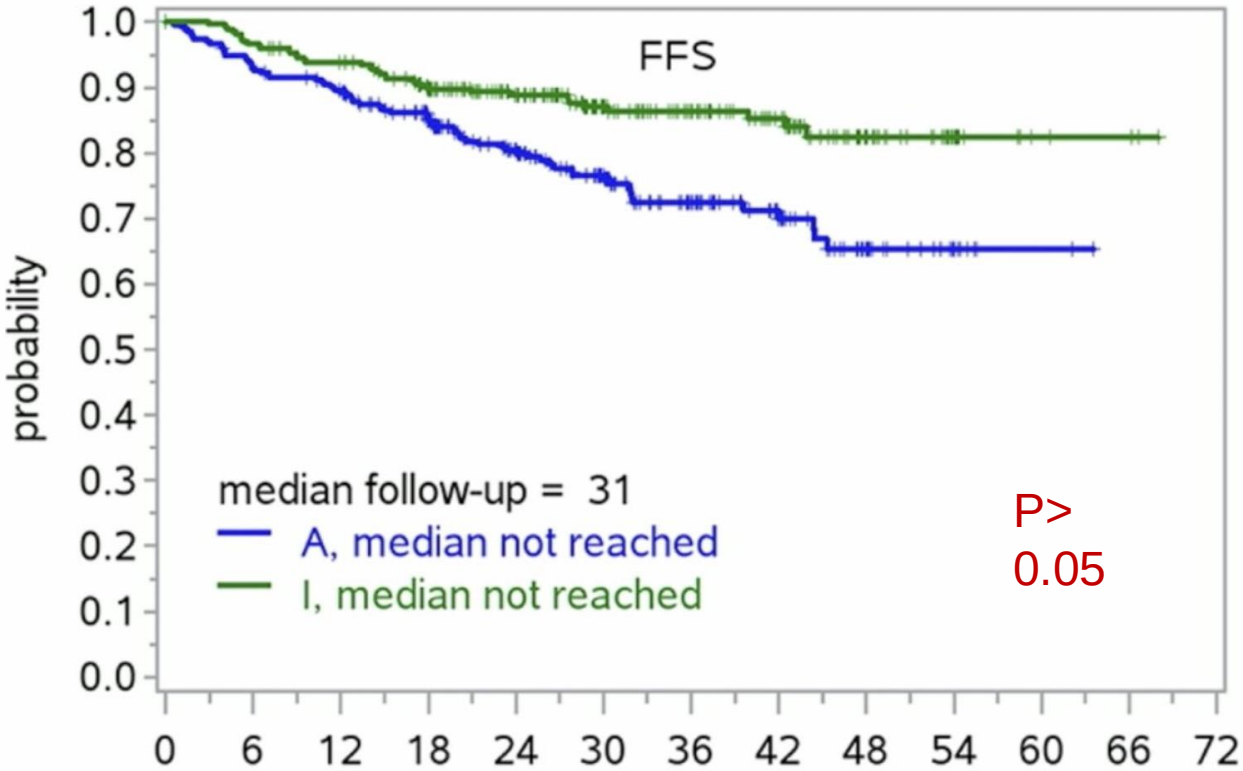
- R maintenance was added following national guidelines in all 3 trial arms
- Rituximab maintenance (without or with Ibrutinib) was started in 168 (58 %)/165 (57 %)/158 (54 %) of A/A+I/I randomized patients.





Dreyling et al, ASH 2022





Ibrutinib + Rituximab for untreated MCL-median 3 Yr PFS 87%-Jain et al JCO 2021

Dreyling et al, ASH 2022

Conclusions/Thoughts

- Should R-CHOP-I/R-DHAP + RI maintenance be considered the SOC?
- Is longer F/U needed?

- **Lymphoma/CAR T trials at UCDCC and UCHMC**
- LonaT+DA-R-EPOCH untreated high risk DLBCL
- Bendamustine/Brentuxumab R/R Follicular Lymphoma
- Obinu/Ibrutinib/Venetoclax untreated Follicular
- Mosentuzumab/Lenalidomide/Pola R/R DLBCL + post CAR
  - Risk adapted post CAR T
- R/R DLBCL Odronextamab +/- CAR T
  - w/in 12 d of CAR T
- R/R DLBCL Epcoritamab + R-DHAX/P + ASCT
  - CAR T failures allowed
- “Home grown” CAR T fresh infusion w/in 7-9 d of collection


Questions?