Bispecific antibodies in DLBCL

6th Postgraduate Lymphoma Conference

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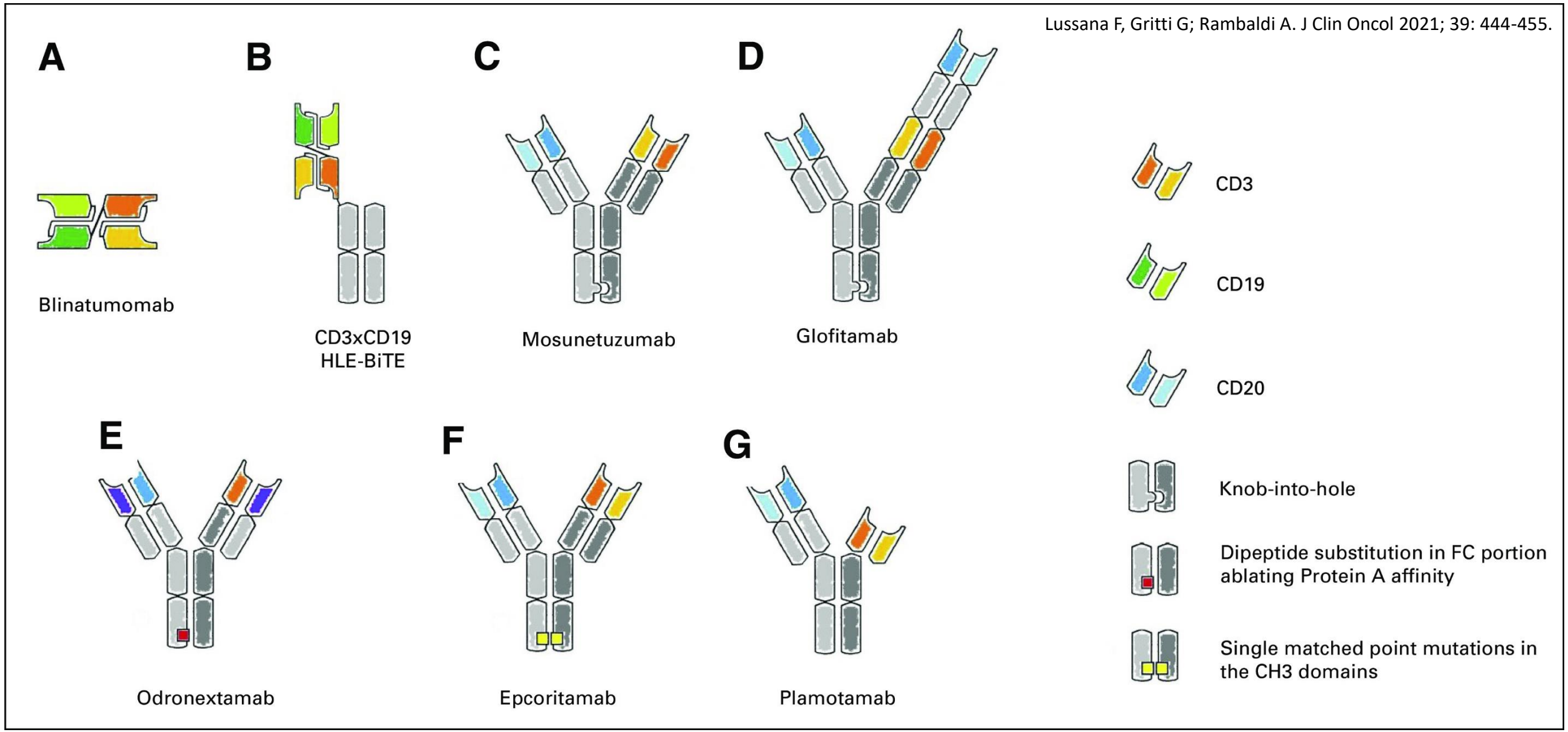
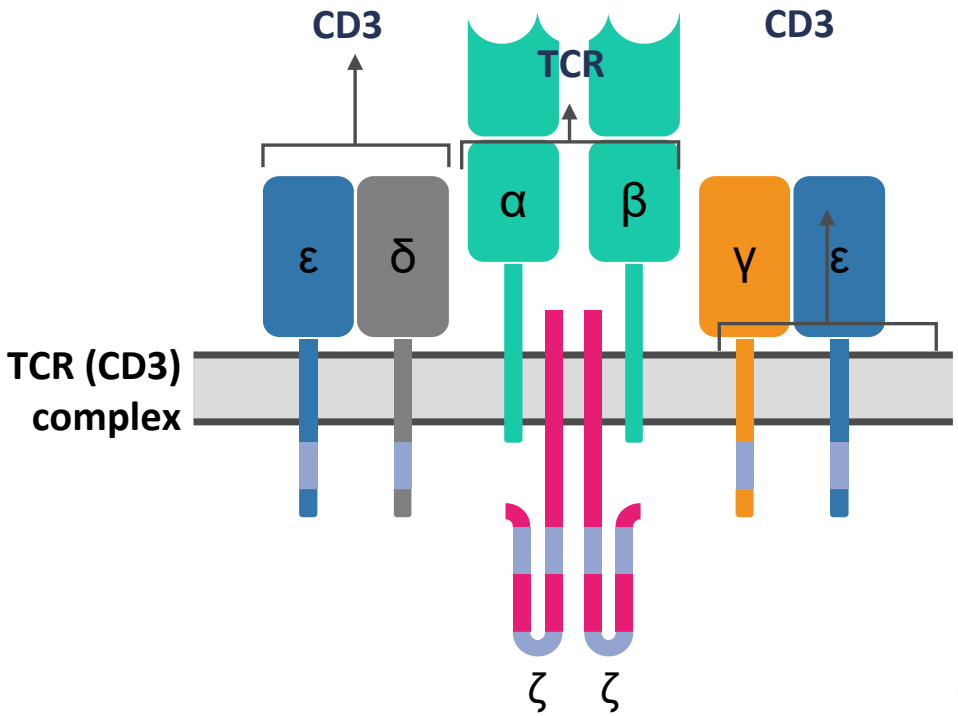
DISCLOSURES

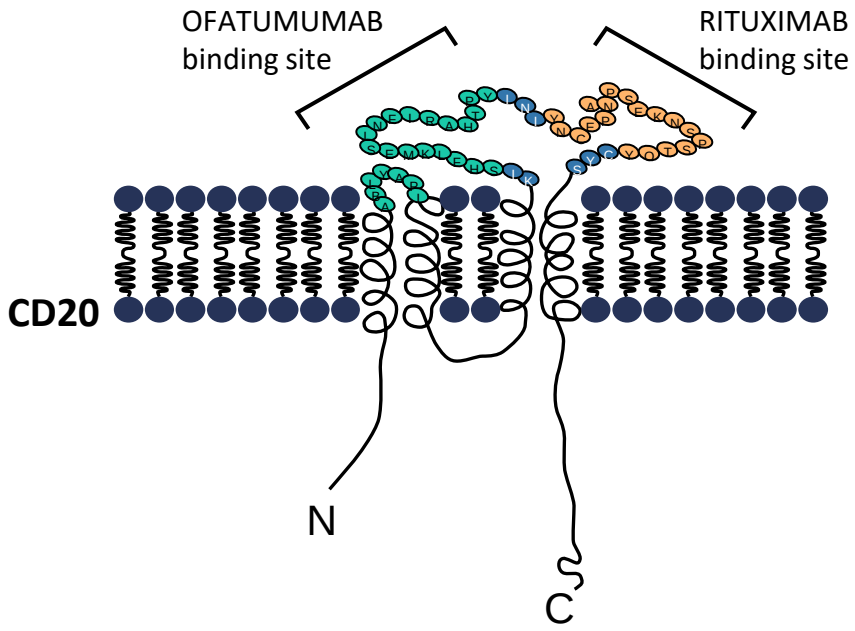
- **Scientific advisory boards:**
  - AbbVie, Celgene, Genmab, Janssen, Merck, Roche, Takeda
- **Research support (institution):**
  - Celgene, Genentech, Genmab, Incyte, Janssen, Novartis, Roche, Takeda

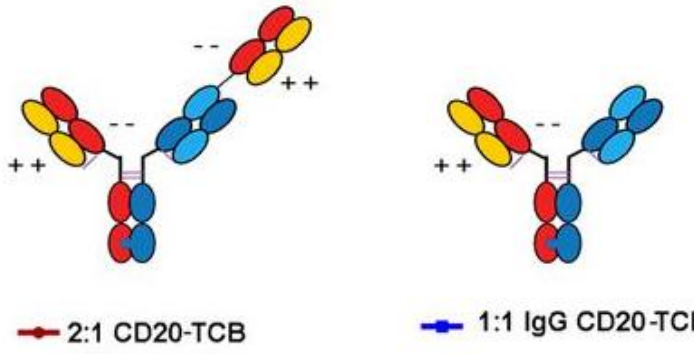
Bispecific CD3/CD20 antibodies in B-NHL



Binding sites and structure of CD3xCD20 antibodies

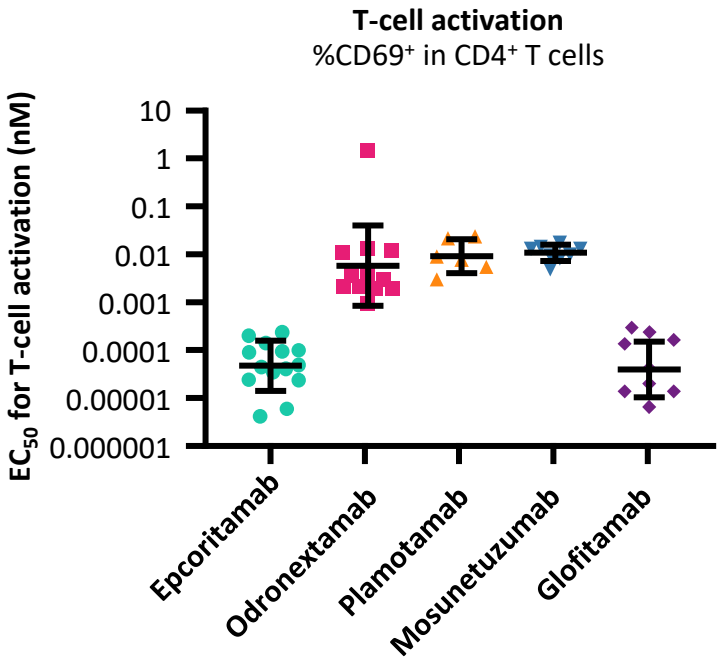


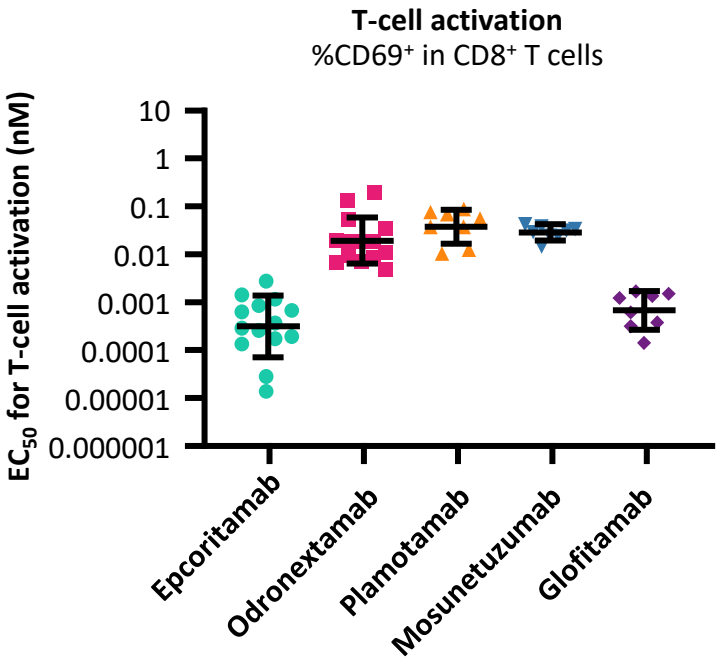


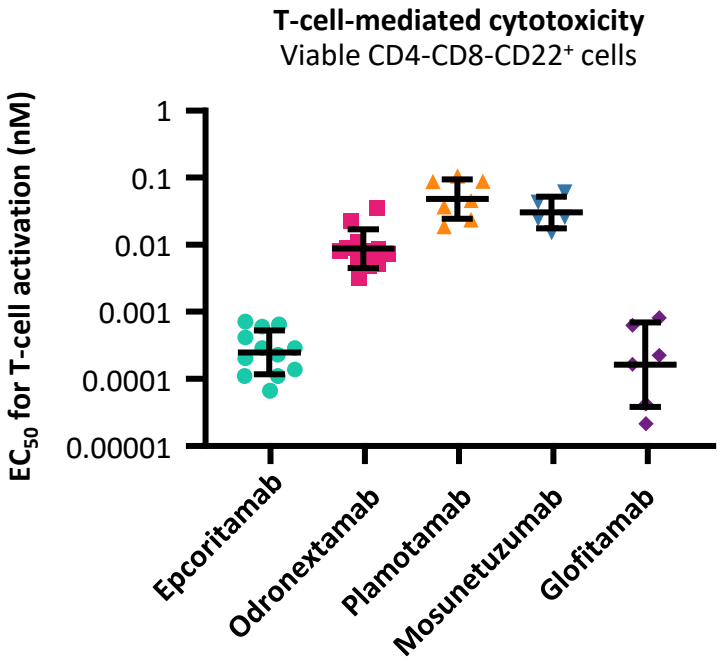


1. Franco R, *et al. Front Pharmacol* 2016; **7:** 1–10; 2. Klein C, *et al. Mabs* 2013; **5:** 22–33; 3. Bacac M, *et al. Clin Cancer Res* 2018; **24**;4785–97.

In vitro T-cell activation of CD3xCD20 antibodies





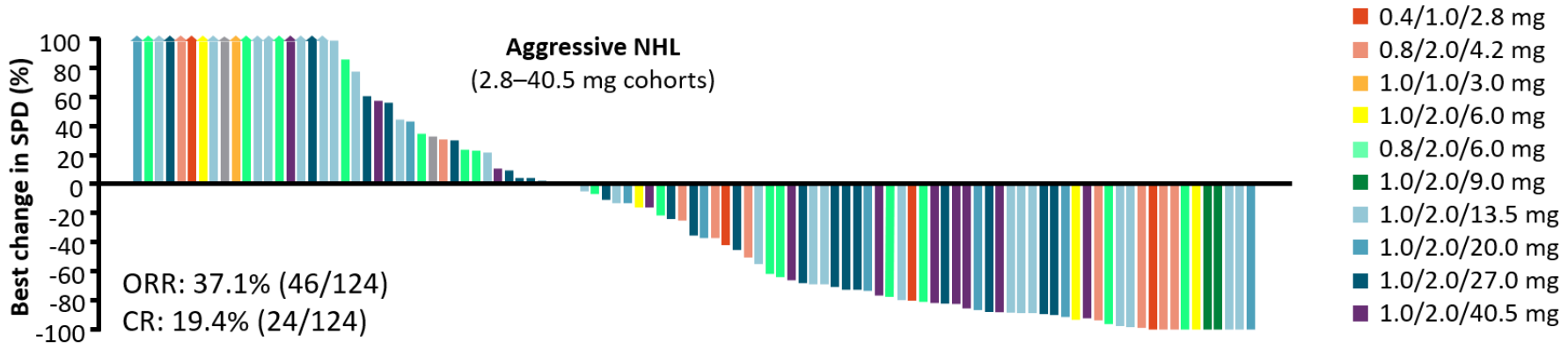


Hiemstra IH, *et al.* EHA 2019: poster presentation PS1301.

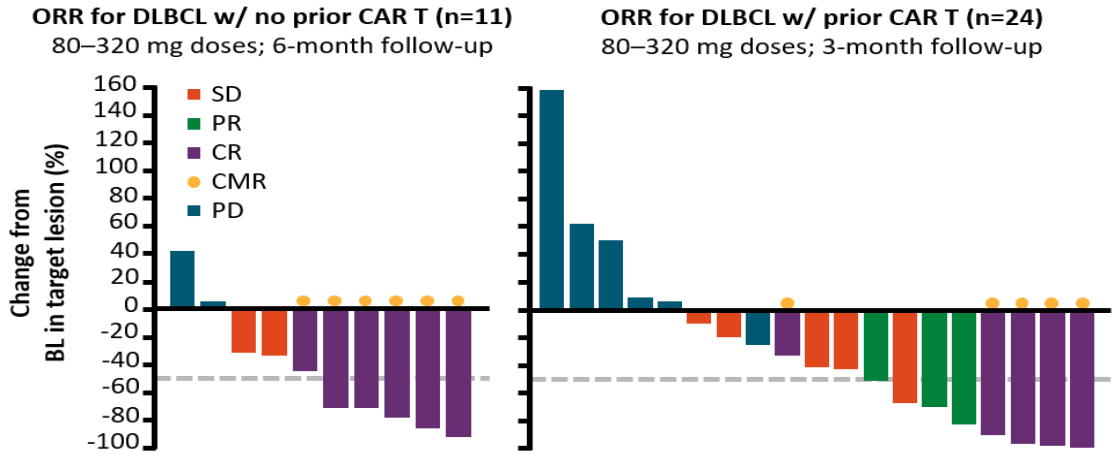
Single-agent phase 1 studies of bispecific CD3/CD20 antibodies in B-NHL

Activity of mosunetuzumab and odronextamab in r/r aggressive B-NHL

Mosunetuzumab in aggressive NHL[1]



Odronextamab in DLBCL[2]



R/R DLBCL w/no prior CAR T

- ORR: 55% (6/11); CR: 55% (6/11)
- Median duration of CR: NR
- 83% of CRs durable (≥3 months; ≤21 months)

R/R DLBCL w/ prior CAR T

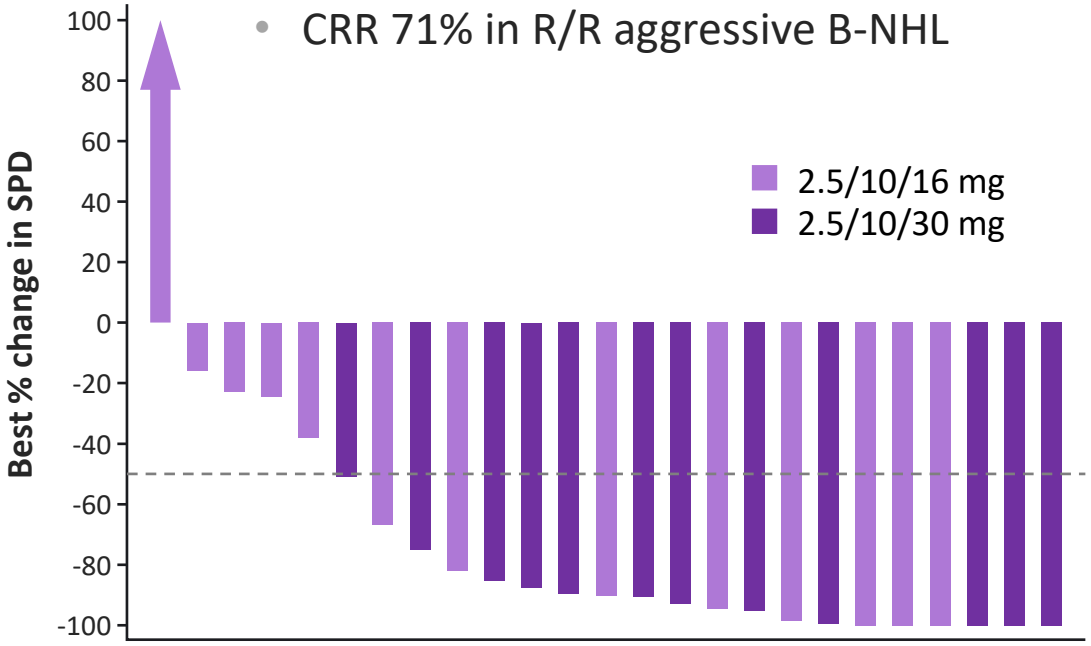
- ORR: 33% (8/24); CR: 21% (5/24)
- Median duration of CR: NR
- 100% of CRs ongoing at last assessment (≤20 months)

1. Schuster SJ, et al. ASH 2019: Abstract 6 (oral presentation) 2. Bannerji R, et al. ASH 2020: Abstract 400 (oral presentation).

Activity of glofitamab and epcoritamab in r/r aggressive B-NHL

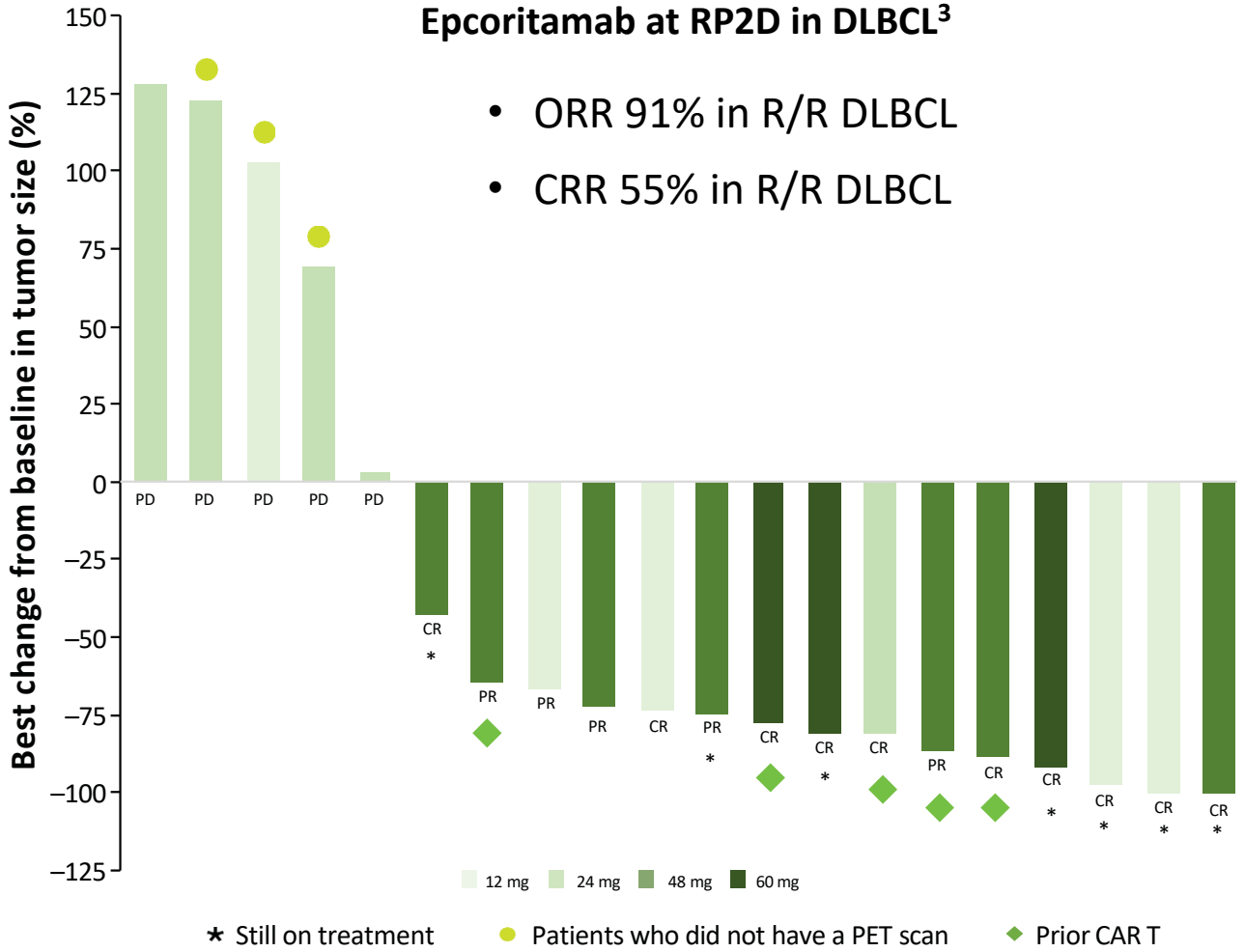
Glofitamab at RP2D in aggressive NHL[1,2]

- ORR 79% in R/R aggressive B-NHL
- CRR 71% in R/R aggressive B-NHL



Epcoritamab at RP2D in DLBCL[3]

- ORR 91% in R/R DLBCL
- CRR 55% in R/R DLBCL



1. Hutchings M, *et al. J Clin Oncol* 2021; **39**:1959–1970; 2. Carlo-Stella C, *et al.* ICML 2021. Abstract 15 (oral); 3. Hutchings M, *et al. Lancet* 2021; 398(10306): 1157-1169.

Recent data from the DLBCL phase 2 expansion cohorts of the glofitamab and epcoritamab studies

SUBCUTANEOUS EPCORITAMAB IN PATIENTS WITH RELAPSED OR REFRACTORY LARGE B-CELL LYMPHOMA (EPCORE NHL-1): PIVOTAL RESULTS FROM A PHASE 2 STUDY

Catherine Thieblemont,[1] Tycel Phillips,[2] Herve Ghesquieres,[3] Chan Y. Cheah,[4] Michael Roost Clausen,[5] David Cunningham,[6] Young Rok Do,[7] Tatyana Feldman,[8] Robin Gasiorowski,[9] Wojciech Jurczak,[10] Tae Min Kim,[11] David John Lewis,[12] Marjolein van der Poel,[13] Michelle Limei Poon,[14] Thomas Doerr,[15] Nurgul Kilavuz,[16] Menghui Chen,[16] Mariana Sacchi,[16] Brian Elliott,[16] Martin Hutchings,[17] Pieternella Lugtenburg[18]

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EPCORE NHL-1: LBCL Expansion Cohort

Dose escalation → **Dose expansion data cutoff: January 31, 2022**
Median follow-up: 10.7 mo

B-NHL:

- ✓ No DLTs
- ✓ MTD not reached
- ✓ RP2D identified
- ✓ Manageable safety profile
- ✓ Encouraging antitumor activity

Key inclusion criteria:

- R/R CD20+ mature B-cell neoplasm
- ECOG PS 0–2
- ≥2 prior lines of antineoplastic therapy, including ≥1 anti-CD20 mAb
- FDG PET–avid and measurable disease by CT/MRI
- Prior CAR T allowed

Step-up dosing[a]

Epcoritamab SC RP2D 48 mg
QW C1–3,
Q2W C4–9,
Q4W C10+

→ **Treatment until PD[b,c] or unacceptable toxicity**

→ **LBCL Cohort N=157**
DLBCL, HGBCL, PMBCL, and FL Gr3B

- To ensure patient safety and better characterize CRS, inpatient monitoring was required at first full dose for 24 h in this part of the study
- **Primary endpoint:** ORR by independent review committee (IRC)
- **Key secondary endpoints:** DOR, TTR, PFS, OS, CR rate, and safety/tolerability

[a]Step-up dosing (priming 0.16 mg and intermediate 0.8 mg dosing before first full dose) and corticosteroid prophylaxis were used to mitigate CRS. [b]Radiographic disease evaluation was performed every 6 wk for the first 24 wk (6, 12, 18, and 24 wk), then every 12 wk (36 and 48 wk), and every 6 mo thereafter. [c]Measurable disease with CT or MRI scan with involvement of ≥2 lesions/nodes with a long axis >1.5 cm and short axis >1.0 cm (or 1 lesion/node with a long axis >2.0 cm and short axis ≥1.0 cm) and FDG PET scan that demonstrates positive lesion(s) compatible with CT-defined (or MRI-defined) anatomical tumor sites for FDG-avid lymphomas. ClinicalTrials.gov: NCT03625037. EudraCT: 2017-001748-36.

Thieblemont C, et al. EHA 2022 oral presentation

Patients Were Challenging to Treat and Highly Refractory

Demographics	LBCL, N=157
Median age (range), y	64 (20–83)
<65 y, n (%)	80 (51)
65 to <75 y, n (%)	48 (31)
≥75 y, n (%)	29 (18)
ECOG PS, n (%)	
0	74 (47)
1	78 (50)
2	5 (3)
Disease Characteristics[a]	**LBCL, N=157**
Disease type, n (%)	
DLBCL	139 (89)
De novo	97/139 (70)
Transformed	40/139 (29)
Unknown	2/139 (1)
HGBCL	9 (6)
PMBCL	4 (3)
FL Gr3B	5 (3)

Prior Treatments	LBCL, N=157
Median time from initial diagnosis to first dose, y	1.6
Median time from end of last therapy to first dose, mo	2.4
Median prior lines of therapy (range)	3 (2–11)
≥3 Lines of therapy, n (%)	111 (71)
Primary refractory[b] disease, n (%)	96 (61)
Refractory[b] to last systemic therapy, n (%)	130 (83)
Refractory[b] to ≥2 consecutive lines of therapy, n (%)	119 (76)
Prior ASCT, n (%)	31 (20)
Prior CAR T therapy, n (%)	61 (39)
Progressed within 6 mo of CAR T therapy	46/61 (75)

[a]Double/triple-hit patients included, many with responses. [b]Refractory disease is defined as disease that either progressed during therapy or progressed within <6 months of completion of therapy.

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Few Discontinuations Due to AEs; 32% of Patients Remain on Treatment

Follow-up	LBCL N=157
Median follow-up (range), mo	10.7 (0.3–17.9)
Median number of treatment cycles (range)	5 (1–20)
Ongoing treatment, n (%)	51 (32)
Discontinued treatment, n (%)	106 (68)
PD	83 (53)
AE	11 (7)
Related[a]	3 (2)
Allogeneic transplant	7 (4)
Withdrawal by patient	4 (3)
Other	1 (1)

[a]Worsening CLIPPERS, CRS/fatigue, and ICANS.

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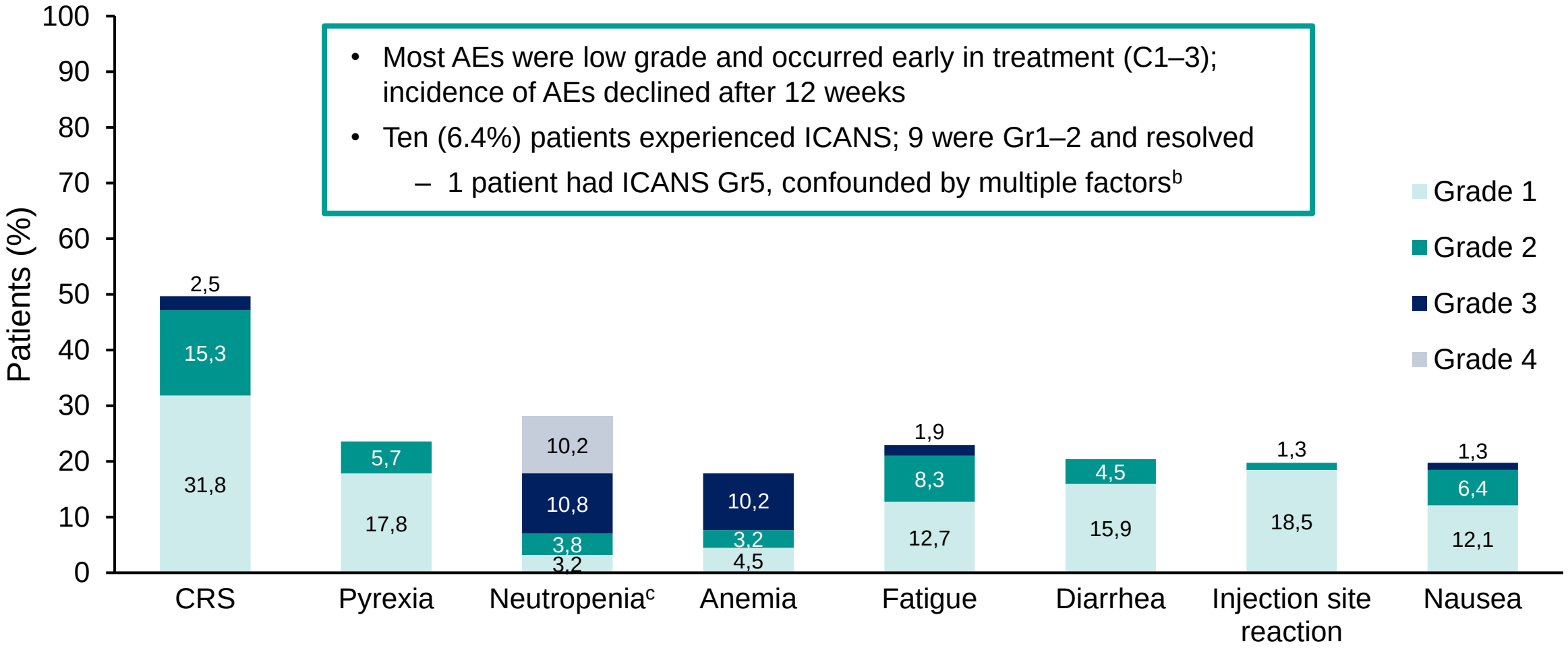
Adverse Events Were Primarily Low Grade

Treatment-Emergent Adverse Events[a] (≥15%) by Grade



[a]COVID incidence 4.5%. [b]Patient experienced ICANS after intermediate dose with multiple confounders, including extensive opioid use for Gr3 pancreatitis, hyperammonemia, multifocal cerebral infarcts in setting of possible microangiopathy, and tocilizumab administration. [c]Combined term includes neutropenia and decreased neutrophil count.

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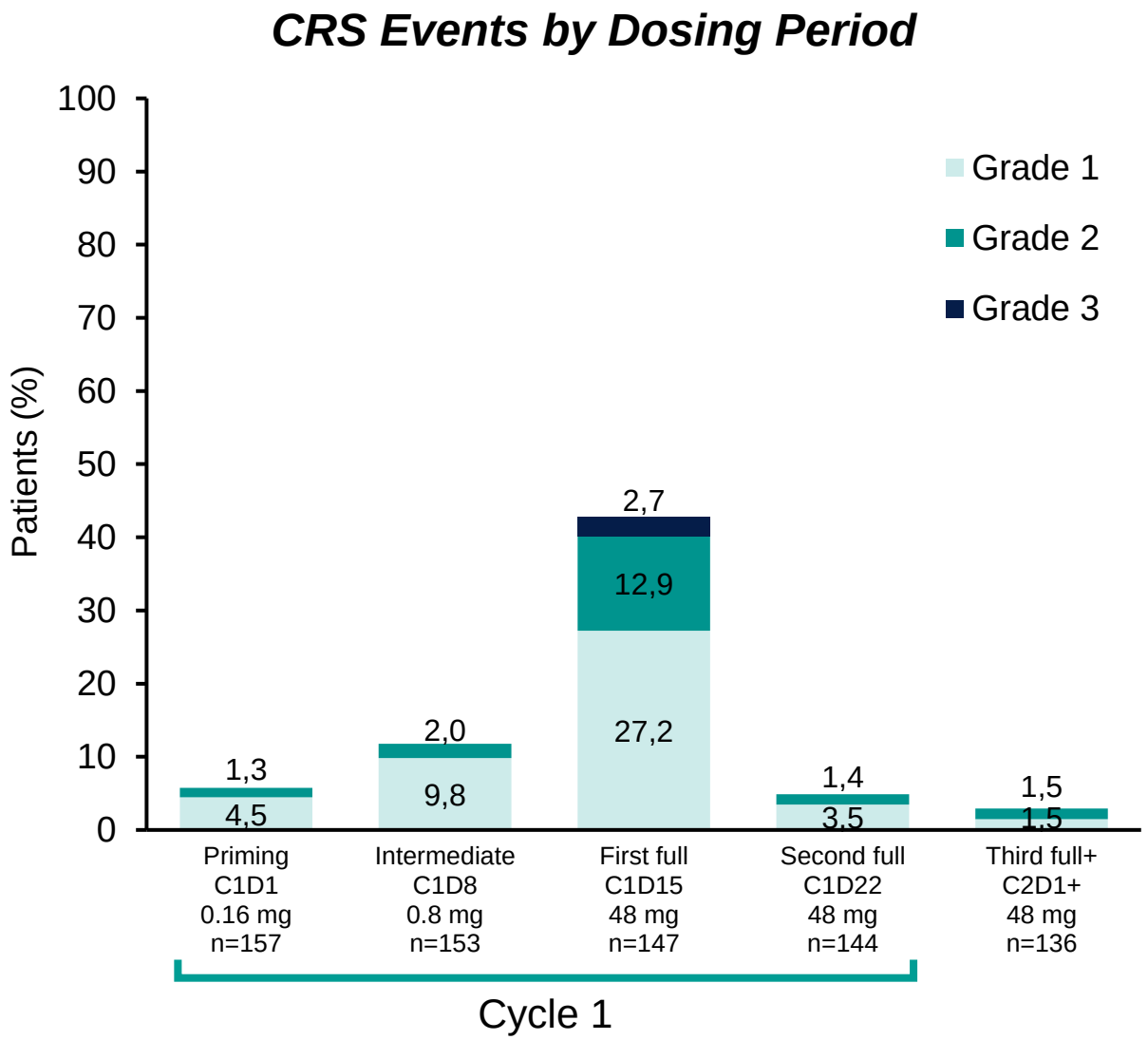
SC Administration and Step-up Dosing May Mitigate CRS

	LBCL N=157
CRS events, n (%)[a]	78 (49.7)
Grade 1	**50 (31.8)**
Grade 2	24 (15.3)
Grade 3	4 (2.5)
Median time to onset from first full dose, d	**0.8 (20 h)**
CRS resolution, n (%)	77 (98.7)
Median time to resolution from first full dose, d	**2 (48 h)**
Treated with tocilizumab, n (%)	22 (14.0)
Treated with corticosteroids, n (%)	16 (10.2)
Leading to treatment discontinuation, n (%)	**1 (0.6)**

[a]Graded by Lee et al. 2019 criteria.

CRS was primarily low grade and predictable: most events occurred following the first full dose



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High Response Rates Observed

Best Overall Response by IRC, n (%)[a]	LBCL N=157
Overall response	**99 (63)** [95% CI: 55–71]
Complete response	**61 (39)** [95% CI: 31–47]
Partial response	38 (24)
Stable disease	5 (3)
Progressive disease	37 (24)

[a]Based on Lugano criteria.

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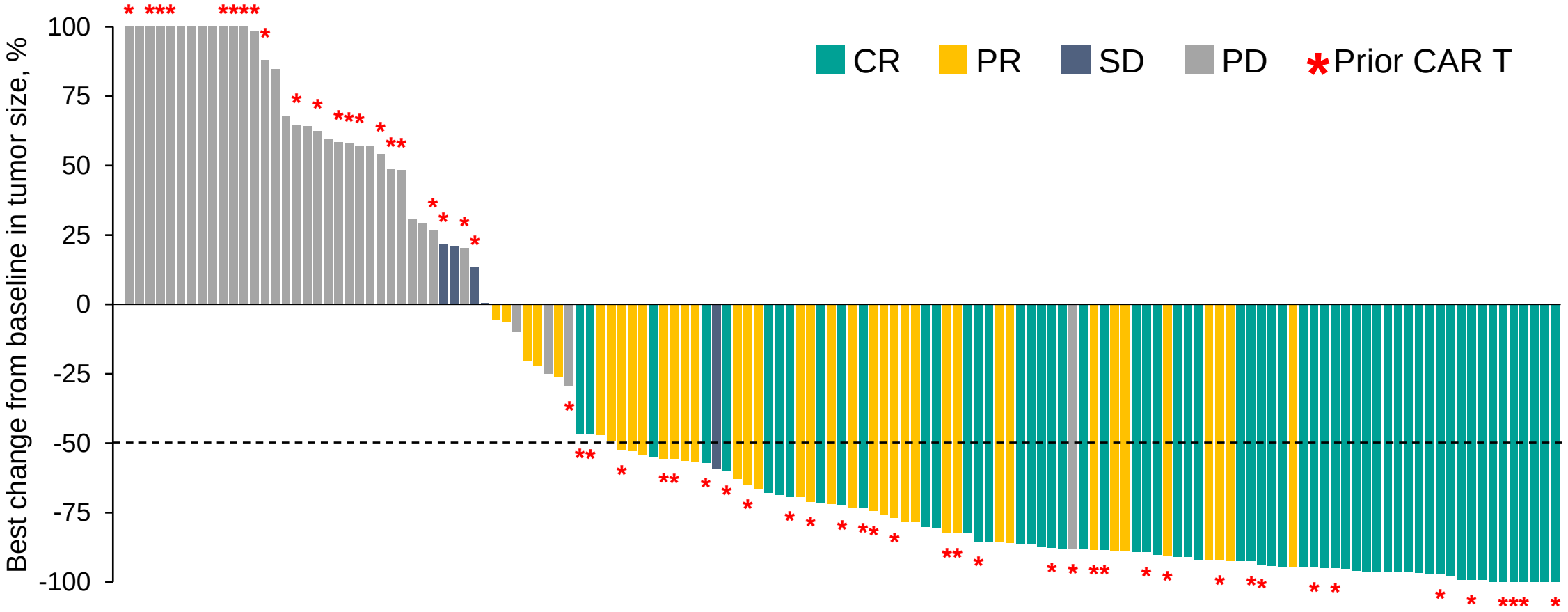
Epcoritamab Induced Deep Responses in R/R LBCL



Based on IRC assessment and Lugano criteria.

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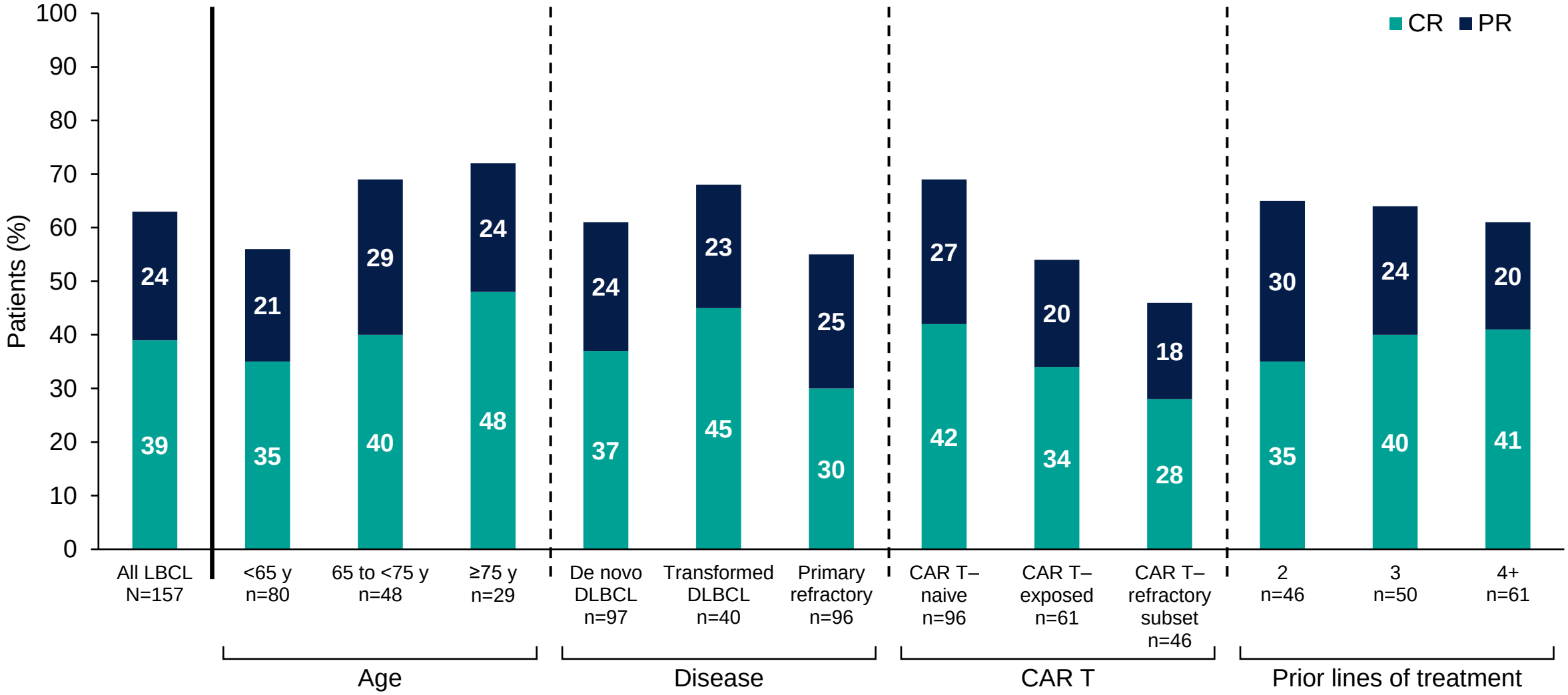
Deep Responses Consistent Across Key Subgroups



Based on IRC assessment and Lugano criteria.

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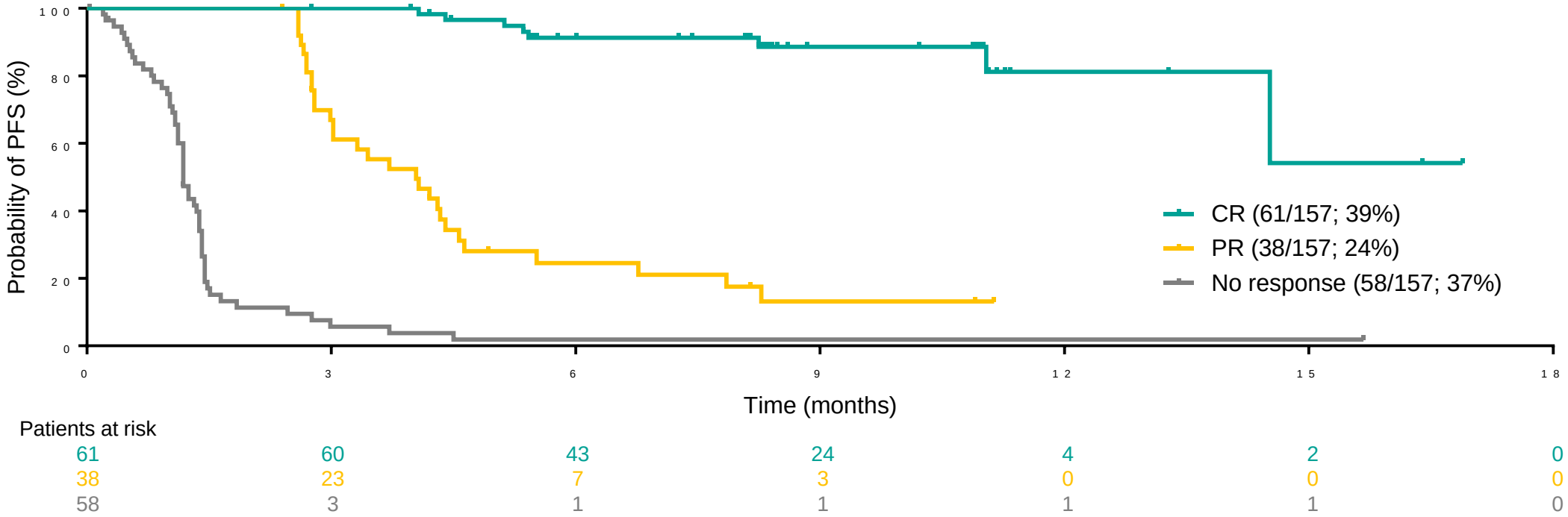
PFS by Best Response per IRC



Patients at risk

61	60	43	24	4	2	0
38	23	7	3	0	0	0
58	3	1	1	1	1	0

Kaplan–Meier Estimate	
Median PFS for complete responders	**Not reached**
Complete responders remaining in complete response at 9 mo	**89%**
Median PFS, mo (95% CI)	4.4 (3.0–7.9)
PFS at 6 mo, % (95% CI)	43.9 (35.7–51.7)

A correlation between depth of response and PFS was observed

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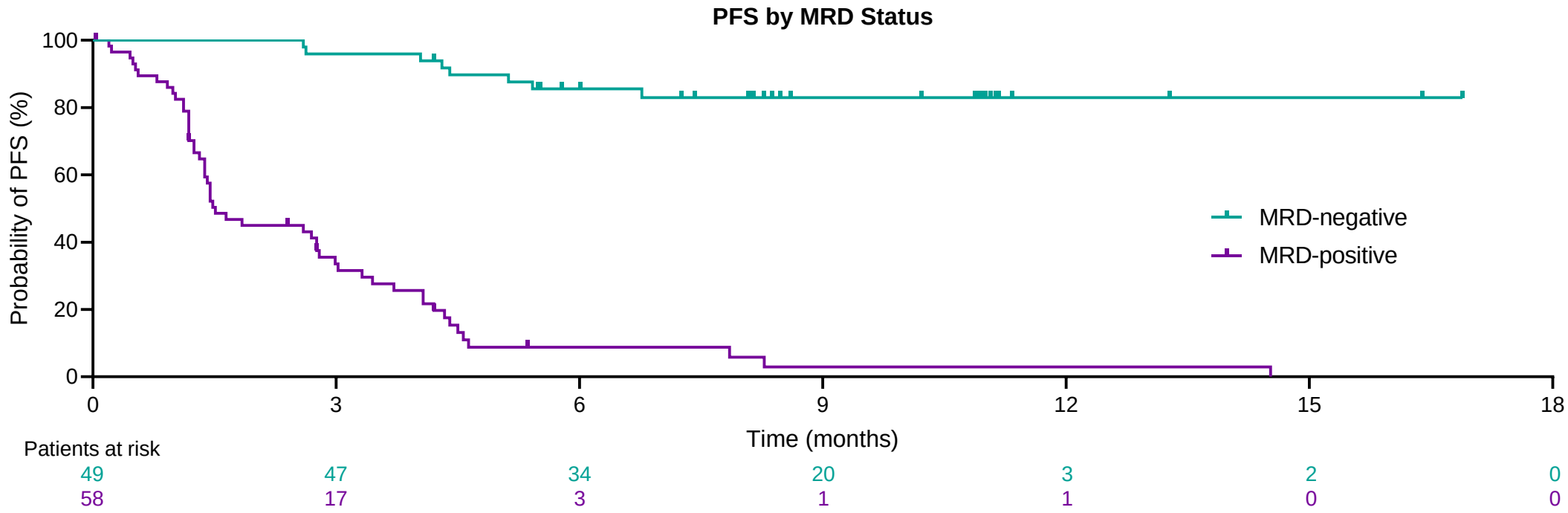
MRD Negativity Correlated With Improved PFS

- **Exploratory ctDNA analysis shows that MRD-negative responses were durable and correlated with PFS**



MRD Results per ctDNA Assay	All LBCL n=107
MRD-negative rate, n (%)	49 (45.8) [95% CI: 36.1–55.7]

Based on MRD-negative evaluable set, which included patients with ≥1 postbaseline MRD sample/evaluation who had detectable disease (n=104) or were not evaluated (n=3) at baseline. MRD negativity was defined as the absence of detectable clone sequences in plasma at any on-treatment time point (clonoSEQ).

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Glofitamab in patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) and ≥2 prior therapies: pivotal Phase II expansion results

Michael Dickinson,[1] *Carmelo Carlo-Stella,*[2] *Franck Morschhauser,*[3] *Emmanuel Bachy,*[4] *Paolo Corradini,*[5] *Gloria Iacoboni,*[6] *Cyrus Khan,*[7] *Tomasz Wróbel,*[8] *Fritz Offner,*[9] *Marek Trněný,*[10] *Shang-Ju Wu,*[11] *Guillaume Cartron,*[12] *Mark Hertzberg,*[13] *Anna Sureda,*[14] *David Perez-Callejo,*[15] *Linda Lundberg,*[15] *James Relf,*[16] *Emma Clark,*[16] *Kathryn Humphrey,*[16] *Martin Hutchings*[17]

[1]Peter MacCallum Cancer Centre, Royal Melbourne Hospital and The University of Melbourne, Melbourne, VIC, Australia; [2]Humanitas University and IRCCS Humanitas Research Hospital, Milan, Italy; [3]Hôpital Claude Huriez and CHU de Lille, Lille, France; [4]Centre Hospitalier Lyon-Sud, Lyon, France; [5]Università degli Studi di Milano and Fondazione Istituti di Ricovero e Cura a Carattere Scientifico (IRCSS) Istituto Nazionale dei Tumori, Milan, Italy; [6]Vall d'Hebron University Hospital, Barcelona, Spain; [7]Allegheny Health Network, Pittsburgh, PA, USA; [8]Uniwersytet Medyczny we Wrocławiu, Wroclaw, Poland; [9]Universitair Ziekenhuis Gent, Ghent, Belgium; [10]Charles University Hospital, Prague, Czech Republic; [11]National Taiwan University Hospital, Taipei, Taiwan; [12]CHU de Montpellier, Montpellier, France; [13]Prince of Wales Hospital and University of New South Wales, Sydney, NSW, Australia; [14]Institut Català d'Oncologia Hospitalet, Barcelona, Spain; [15]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [16]Roche Products Ltd, Welwyn Garden City, United Kingdom; [17]Rigshospitalet, Copenhagen, Denmark

Presented at the 2022 European Hematology Association (EHA) Annual Meeting | June 9–12, 2022

Study overview

Pivotal Phase II expansion in patients with R/R DLBCL and ≥2 prior therapies (NP30179)

Key inclusion criteria

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

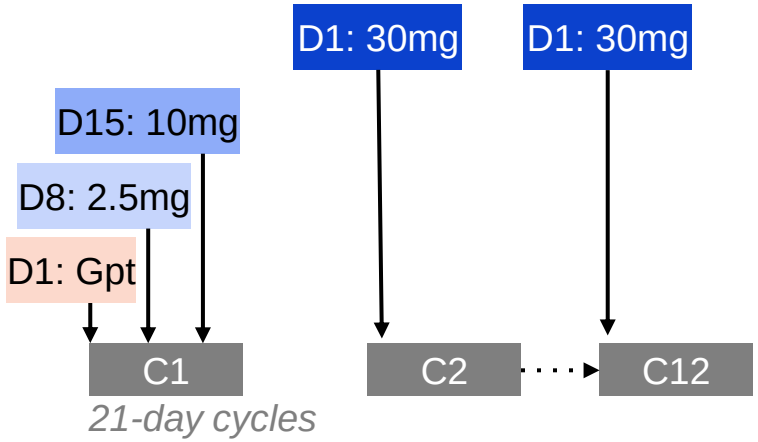
Glofitamab IV administration

Fixed-duration treatment

- max. 12 cycles

CRS mitigation:

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



Endpoints

- **Primary: CR (best response) rate by IRC***
- **Key secondary:** ORR rate,† DoR, DoCR,† PFS, and OS

*by PET-CT (Lugano criteria[1]); †by IRC and investigator. BCL, B-cell lymphoma; FL, follicular lymphoma; Gpt, obinutuzumab pretreatment; HGBCL, high-grade BCL; IRC, Independent Review Committee; NOS, not otherwise specified; PMBCL, primary mediastinal large BCL.

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Baseline characteristics

n (%)*		N=154†
Median age, years (range)		66.0 (21–90)
Male		100 (64.9)
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)
Bulky disease	>6cm	64 (41.6)
	>10cm	18 (11.7)

n (%)*	N=154
Median no. of prior lines, n (range)	3 (2–7)
2 prior lines	62 (40.3)
≥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)

Heavily pre-treated, highly refractory population

Clinical cut-off date: March 14, 2022; *unless otherwise specified; †safety-evaluable population (all treated patients); ‡ECOG PS 2, n=1 (0.6%); Ab, antibody; ASCT, autologous stem cell transplant; trFL, transformed follicular lymphoma.

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Response rates – primary endpoint met

Efficacy endpoint[1]	Glofitamab 2.5/10/30mg (n=155)
CR rate*	**61 (39.4%)** [95% CI: 31.6%, 47.5%]
ORR*	**80 (51.6%)** [95% CI: 43.5%, 59.7%]

- Median duration of follow-up: 12.6 months (range: 0–22)
- Responses were achieved early: median time to first CR was 42 days (95% CI: 42, 44)

– At time of primary analysis, primary endpoint met in the primary efficacy population (n=108)†: 35.2% CR rate by IRC significantly greater ($p<0.0001$) than 20% historical control CR rate‡

High CR/ORR rate at RP2D

*best response by intent-to-treat population; †the pivotal expansion cohort population; ‡the historical control CR rate was pre-specified based on a meta-analysis in patients with R/R DLBCL (where most [≥50%] had received ≥2 prior therapies) and compared with the CR rate in the primary efficacy-evaluable population using an exact binomial test (2-sided alpha level: 5%).

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Complete response rates by IRC in pre-specified subgroups

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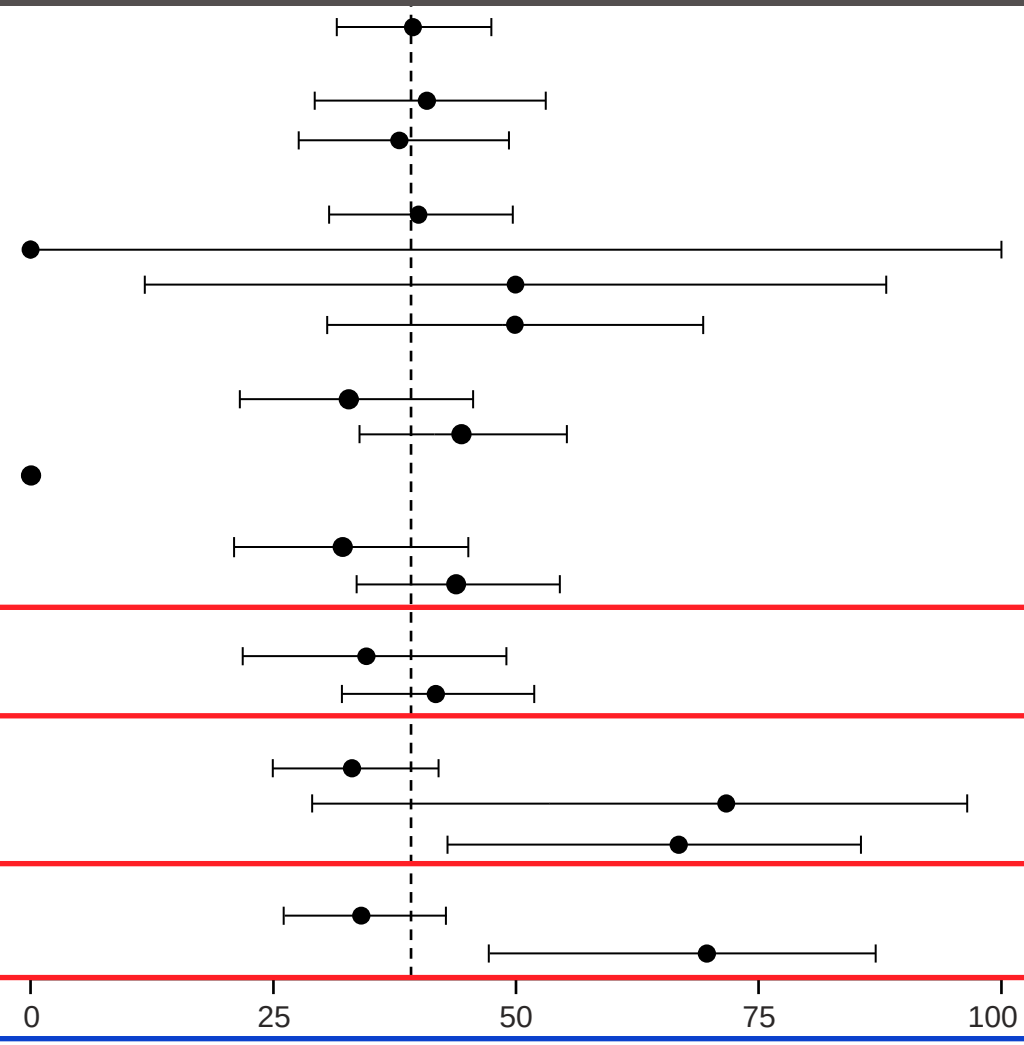
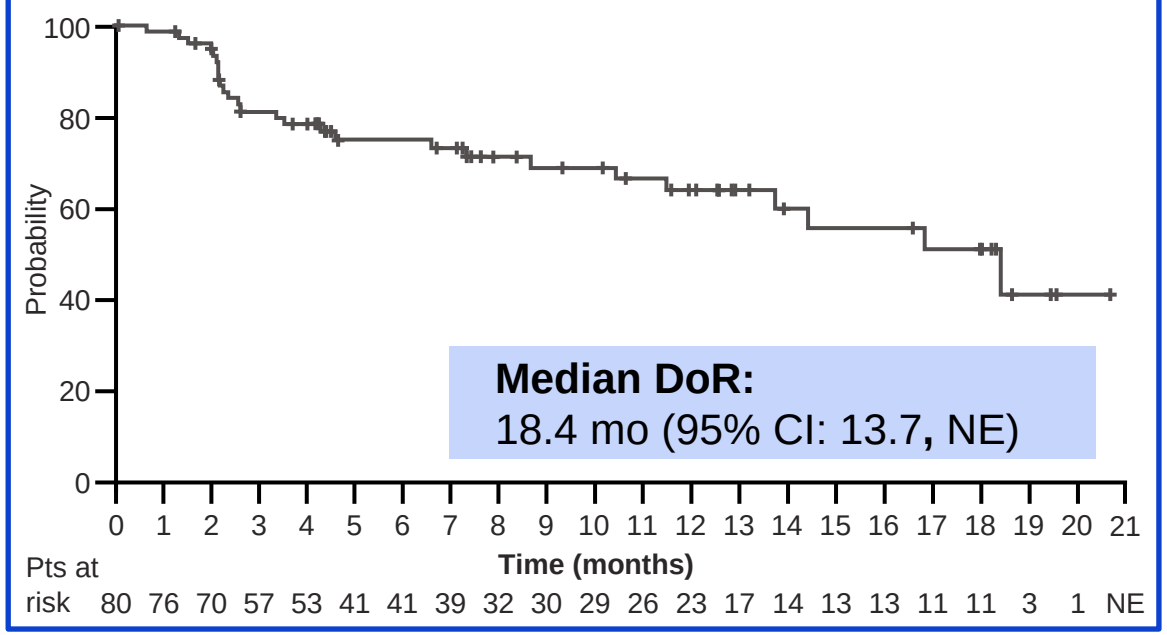
Subgroups	No. of patients	CR (95% CI) by IRC
Overall	155 (100%)	39% (32%, 48%)
Age group		
<65	71 (46%)	41% (29%, 53%)
≥65	84 (54%)	38% (28%, 49%)
NHL subtype at study entry		
DLBCL	110 (71%)	40% (31%, 50%)
HGBCL	11 (7%)	0%
PMBCL	6 (4%)	50% (12%, 88%)
trFL	28 (18%)	50% (31%, 69%)
Bulky disease >6cm		
Yes	64 (41%)	33% (22%, 46%)
No	90 (58%)	44% (34%, 55%)
Unknown/Missing	1 (1%)	0%
Number of prior line of therapies		
2	62 (40%)	32% (21%, 45%)
≥3	93 (60%)	44% (34%, 55%)
Prior CAR-T therapy		
Yes	52 (34%)	35% (22%, 49%)
No	103 (66%)	42% (32%, 52%)
Post ASCT		
No	127 (82%)	33% (25%, 42%)
Refractory	7 (5%)	71% (29%, 96%)
Relapsed	21 (14%)	67% (43%, 85%)
R/R to last prior therapy		
Refractory	132 (85%)	34% (26%, 43%)
Relapsed	23 (15%)	70% (47%, 87%)



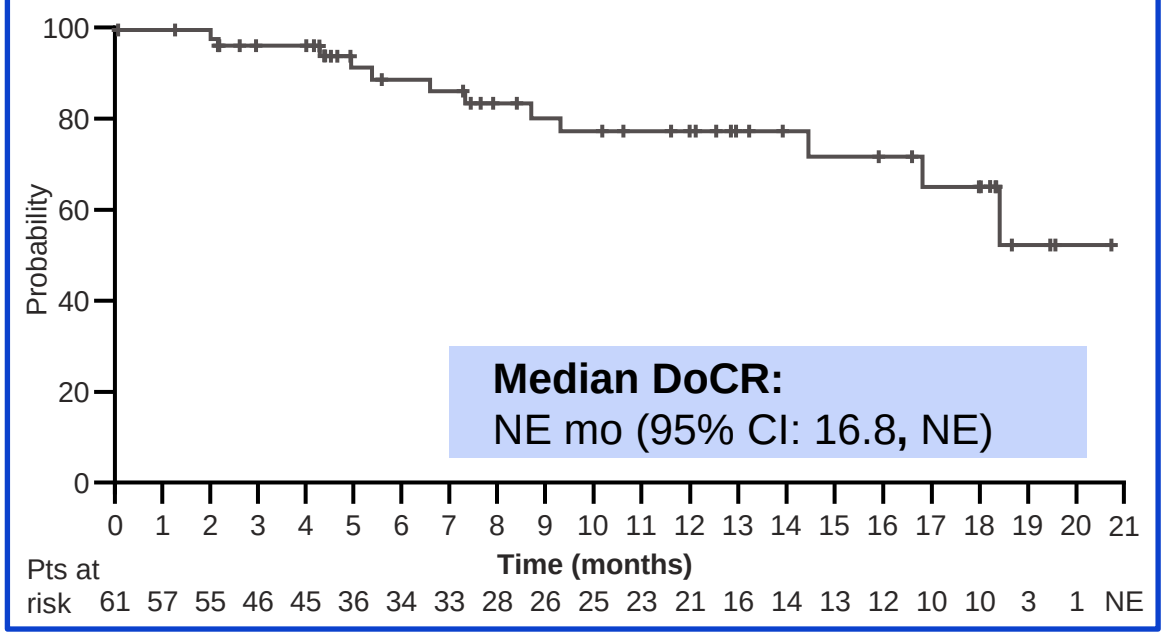
Durable responses maintained after cessation of therapy

Duration of overall response by IRC



	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 complete response by IRC



	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)

CCOD, clinical cut-off date; mo, months; NE, not estimable.

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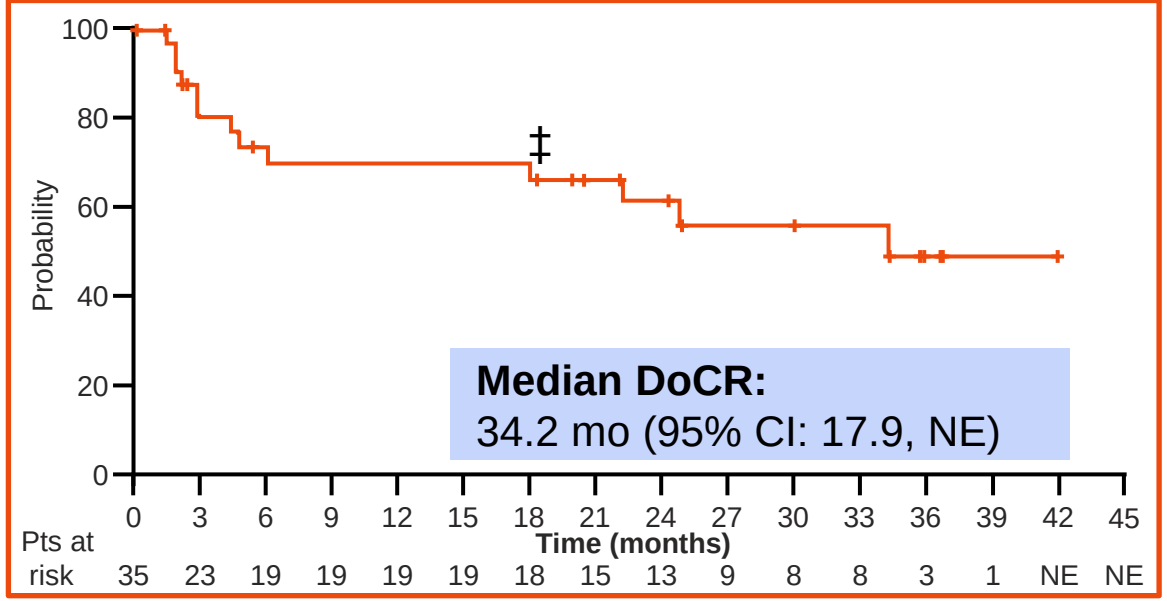
DoCR in earlier cohorts show durable responses beyond 24 months

Supporting cohort

- **Patients in earlier cohorts have extended follow up for duration of response**
  - R/R DLBCL, HGBCL, trFL and PMBCL ≥2 prior lines (n=101)
  - Doses ≥10mg* (RP2D not included) for a fixed treatment duration of 8–12 cycles (6–9 months)
  - CR rate: 35/101 (35%)†

Duration of complete response by IRC



	N=35
Median DoCR follow-up, mo (range)	**24.8 (0, 42)**
24-months DoCR, % (95% CI)	61.4 (43.1, 79.7)
CRs ongoing at CCOD, n (%)	22 (62.9)

Durable responses beyond 24 months achieved after fixed-duration treatment; median: 34.2 months

*10mg, 16mg, 25mg, 10/16mg, 2.5/10/16mg; †intent-to-treat population; RP2D, recommended Phase II dose;
‡DOCR: 17.9 months PD, 22.1 months PD re-treatment (remission), 24.7 months death (unknown reason), 34.2 months death (AML).

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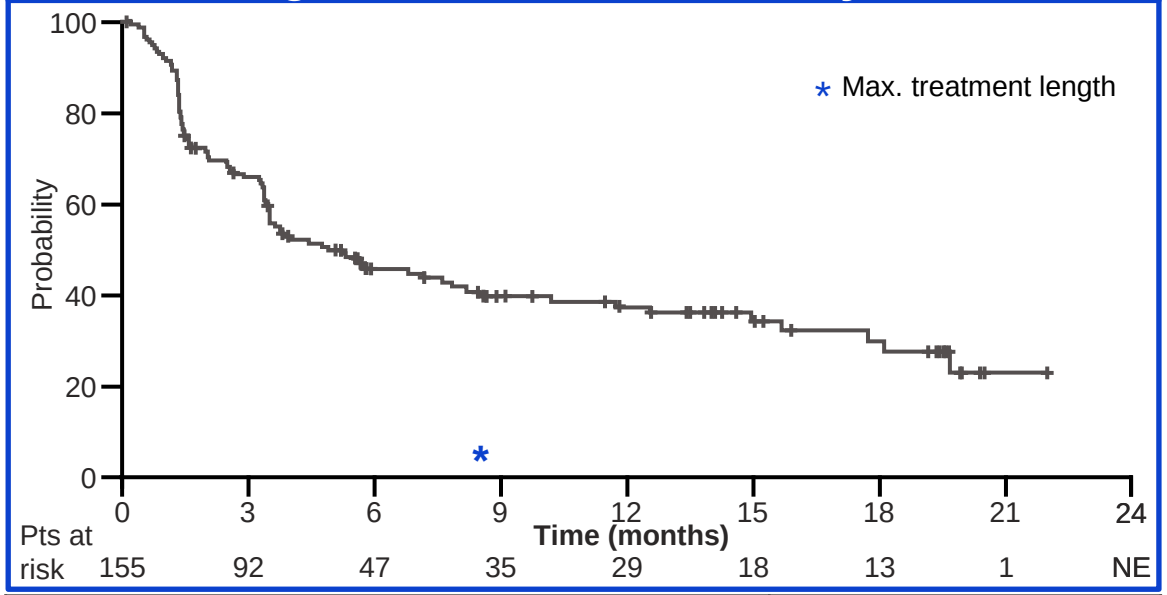
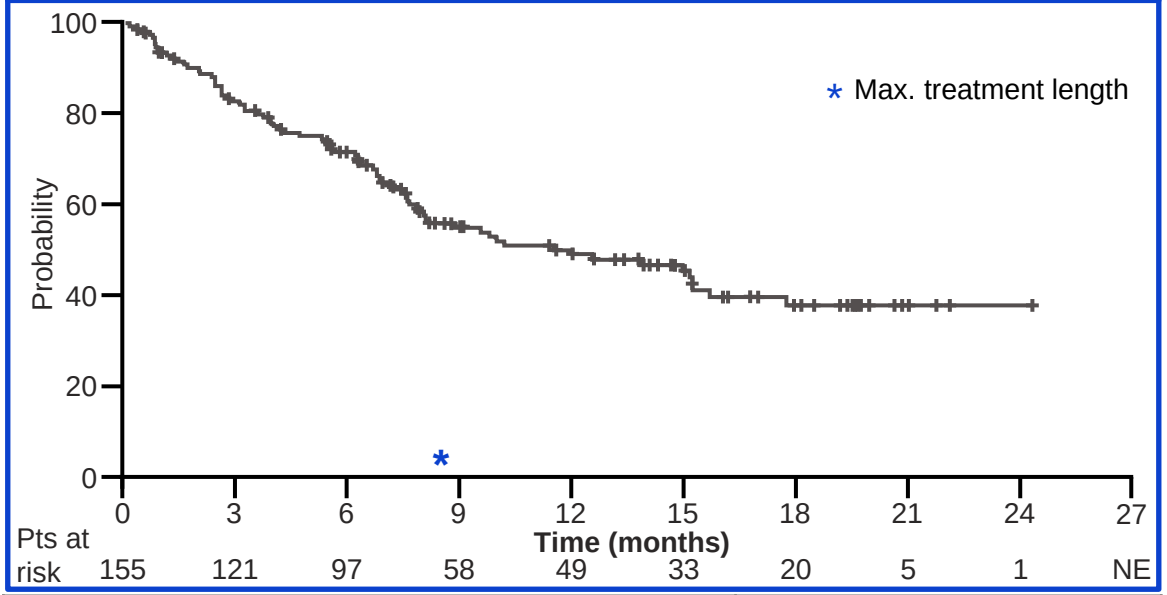
Time-to-event endpoints

Progression-free survival by IRC



	N=155
Median PFS follow-up, mo (range)	12.6 (0–22)
Median PFS, months (95% CI)‡	4.9 (3.4, 8.1)
6-month event-free rate, % (95% CI)	45.5 (37.2, 53.8)
12-month event-free rate, % (95% CI)	37.1 (28.5, 45.8)

Overall survival†



	N=155
Median OS, months (95% CI)‡	11.5 (7.9, 15.7)
12-month OS rate, % (95% CI)	49.8 (41.1, 58.5)

Clinically significant freedom from progression at 12 months and long-term overall survival

†including five deaths due to COVID-19; ‡KM estimates.

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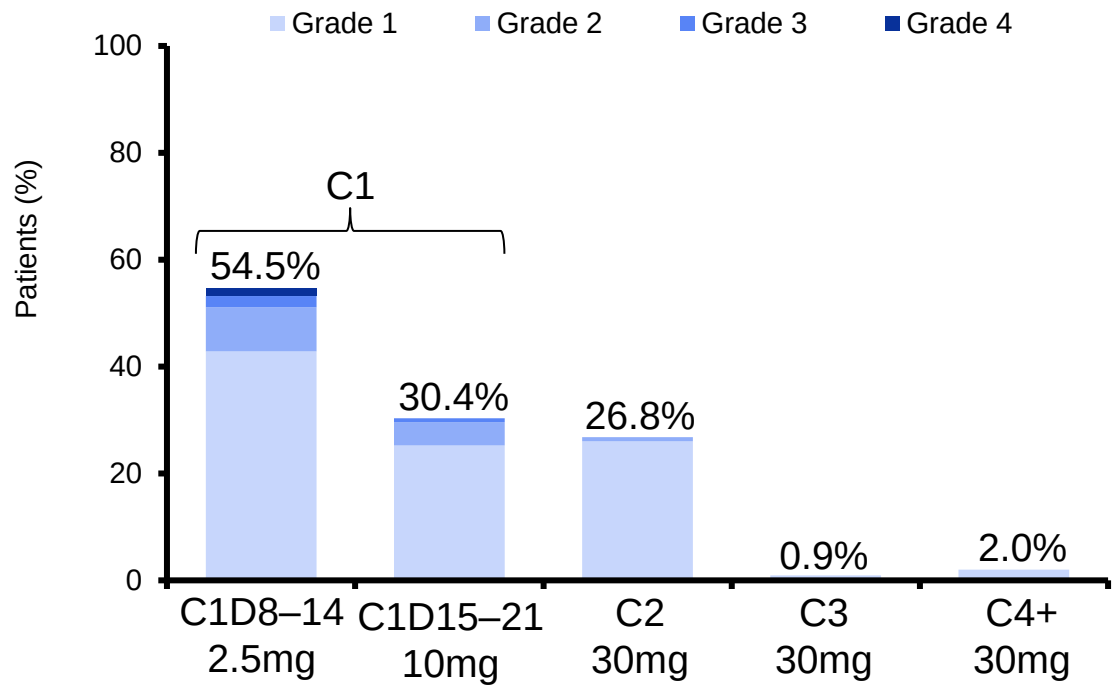
Cytokine release syndrome

n (%)	N=154
CRS (any grade)*	97 (63.0)
Grade 1 (fever)	73 (47.4)
Grade 2	18 (11.7)
Grade 3	4 (2.6)
Grade 4	2 (1.3)
Median time to CRS onset from C1D8 dose, hours (range)	13.6 (6.2–51.8)
Corticosteroids for CRS management	27/97 (27.8)
Tocilizumab for CRS management	31/97 (32.0)

CRS by cycle and grade†



CRS was mostly low grade, time of onset was predictable, and most events occurred during C1

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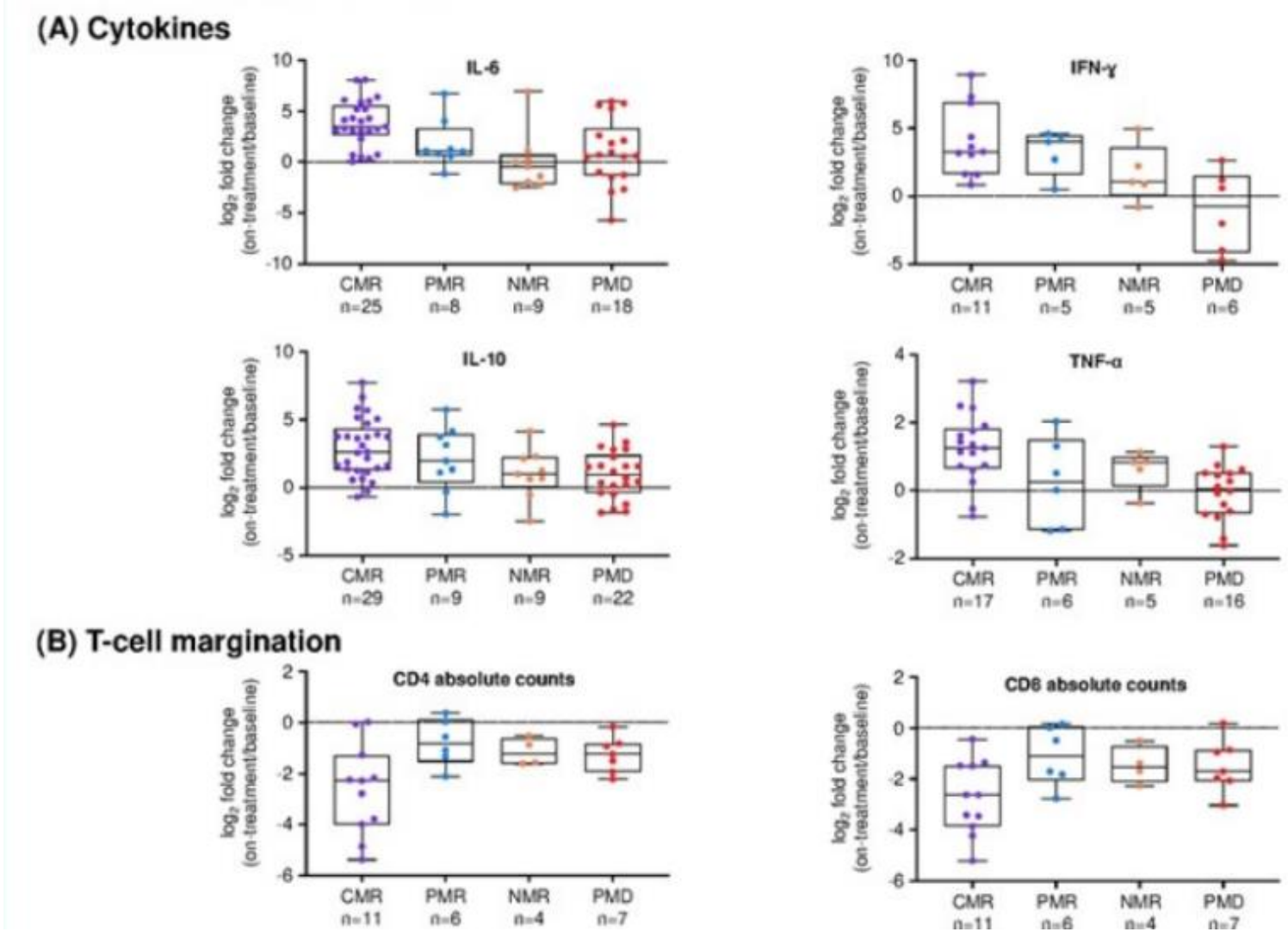
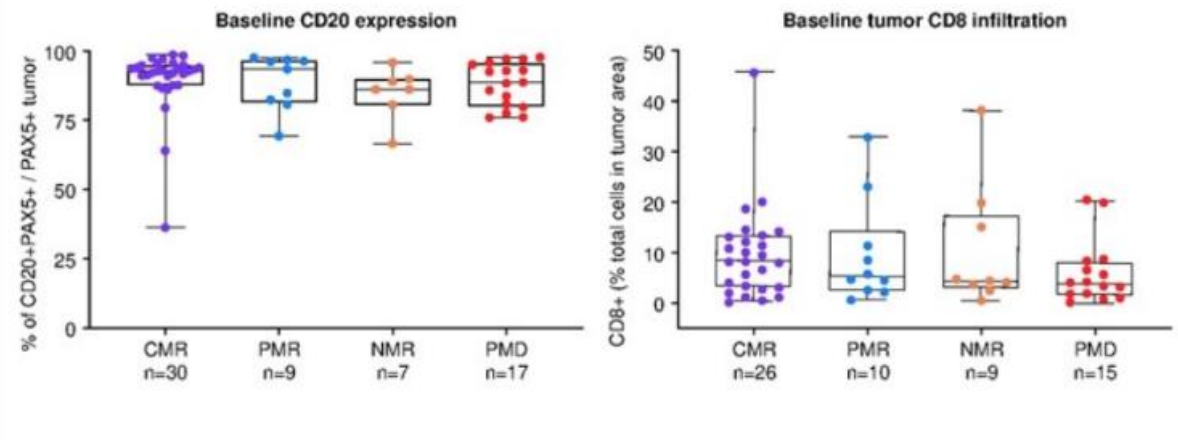
Immune correlates of response to glofitamab: Biomarker findings from the Ph 2 expansion study in patients with R/R DLBCL



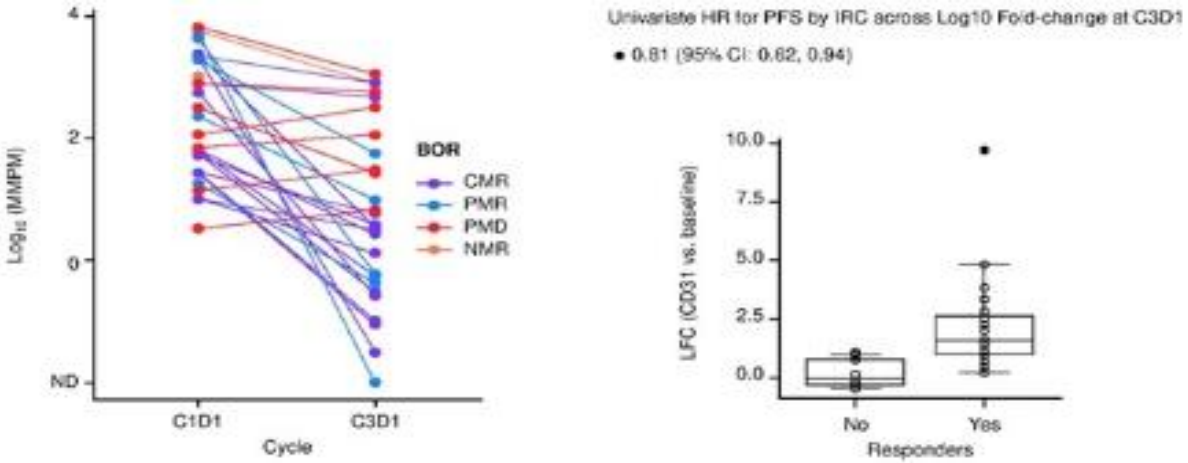
Emily Piccione, Martin Hutchings et al., Presented at EHA 2022; No. P1210

Immune correlates of response to glofitamab: Biomarker findings from the Ph 2 expansion study in patients with R/R DLBCL

Association of baseline tissue biomarkers with response to glofitamab



Association between ctDNA reduction and response to glofitamab



Key findings (N=107)

- Higher CD8+ T cells in CMR patients
- Responders have higher TME score
- Novel biomarkers identified in PB responders:
  - Higher baseline B cell
  - CD4 cell
  - CD4 EM cell
- Novel biomarkers identified in progressors:
  - PD1 expression on CD8 cells
- ctDNA in R/R DLBCL has prognostic value (consistent with Pola, CAR-T)

Emily Piccione, Martin Hutchings et al., Presented at EHA 2022; No. P1210

Combination studies

Epcoritamab + GemOx in transplant-ineligible R/R DLBCL patients: High response rate even in pts failing CAR-T therapy

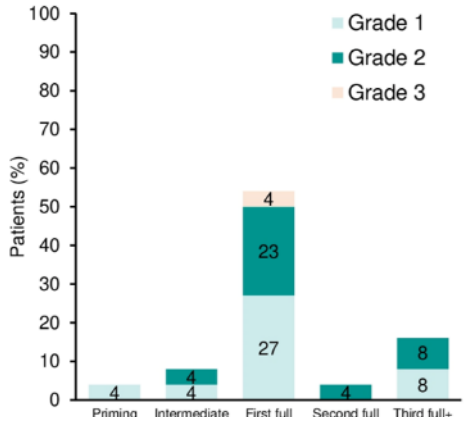
Follow-Up and Patient Disposition

	Total N=26
Median follow-up, mo (range)[a]	9.2 (1–15)
Ongoing treatment, n (%)	11 (42)
Discontinued treatment, n (%)	15 (58)
PD	6 (23)
AE[b]	5 (19)
Death[c]	3 (12)
Withdrawal by patient	1 (4)

CRS Graded by Lee et al[10] 2019 Criteria

	Total N=26
CRS, n (%)	18 (69)
Grade 1	7 (27)
Grade 2	10 (38)
Grade 3	1 (4)
CRS resolution, n (%)	18 (100)
Median time to resolution, d (range)[a]	2 (1–9)
CRS leading to treatment discontinuation, n (%)	0
Tocilizumab use, n (%)	5 (19)

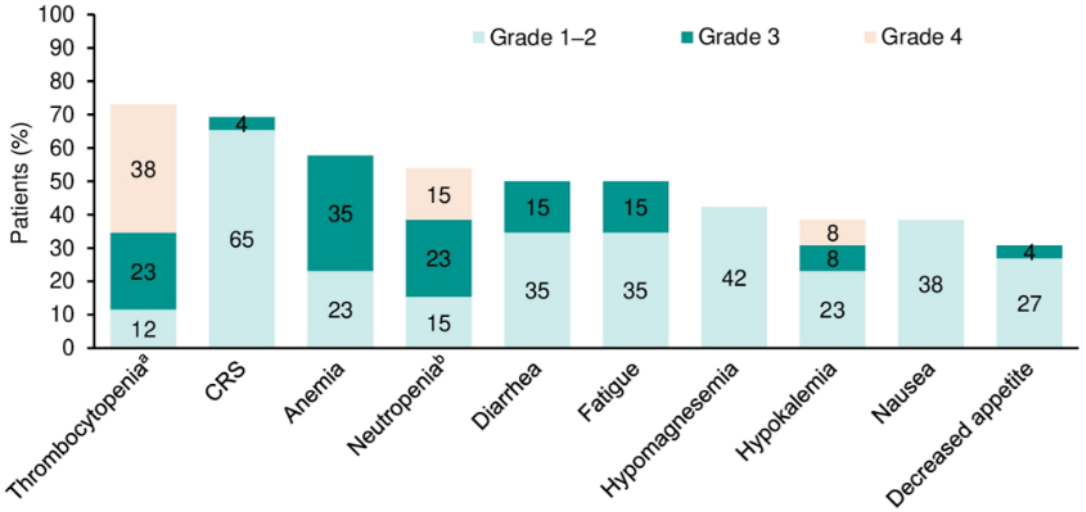
CRS Events by Dosing Period



Best Overall Responses

Response, n (%)[a]	Total n=25
Overall response	23 (92)
CMR	15 (60)
PMR	8 (32)
Stable disease	0
Progressive disease	0
No response assessment[b]	2 (8)

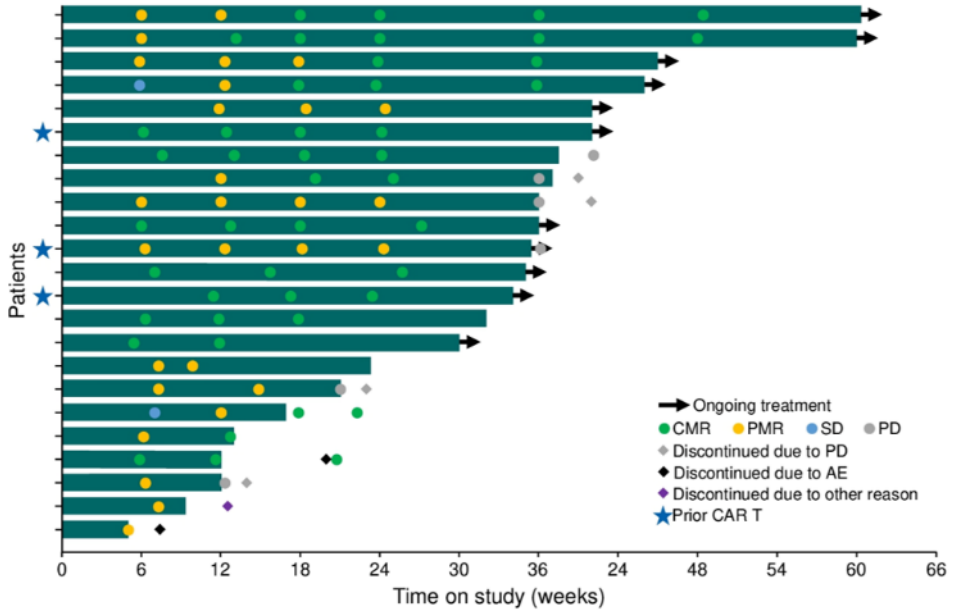
Treatment-Emergent Adverse Events (≥30%) by Grade



Key Results (N=26)

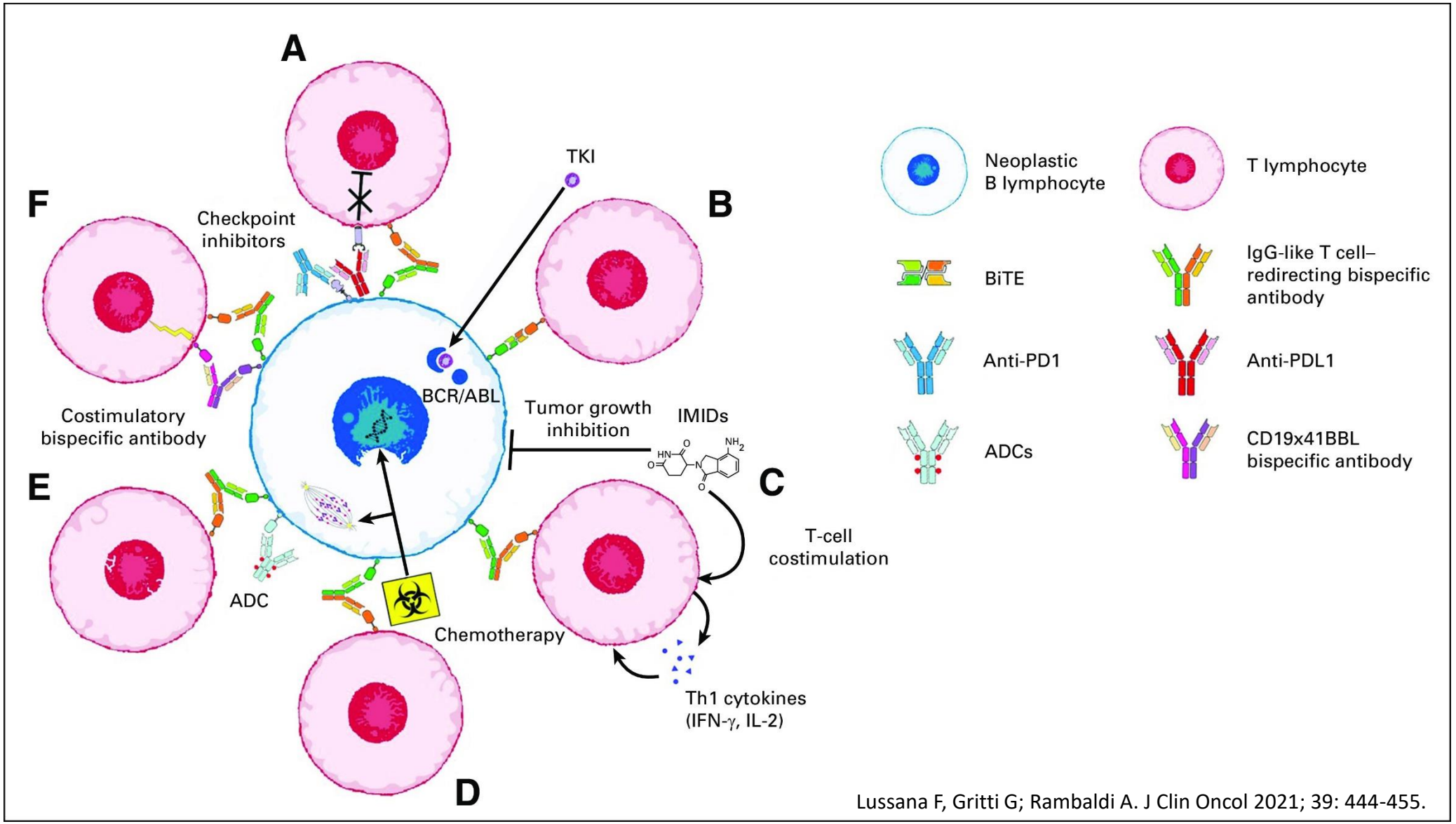
- One pt had ICANS (Gr3); one pts febrile neutropenia (Gr3)
- Infection rate: 62% any grade; 31% Gr3
- No TLS events
- Seven pts Gr 5 AEs; 2 related to Epco
- CRS mostly low grade, all events resolved; occurrence was predictable

Response Profile



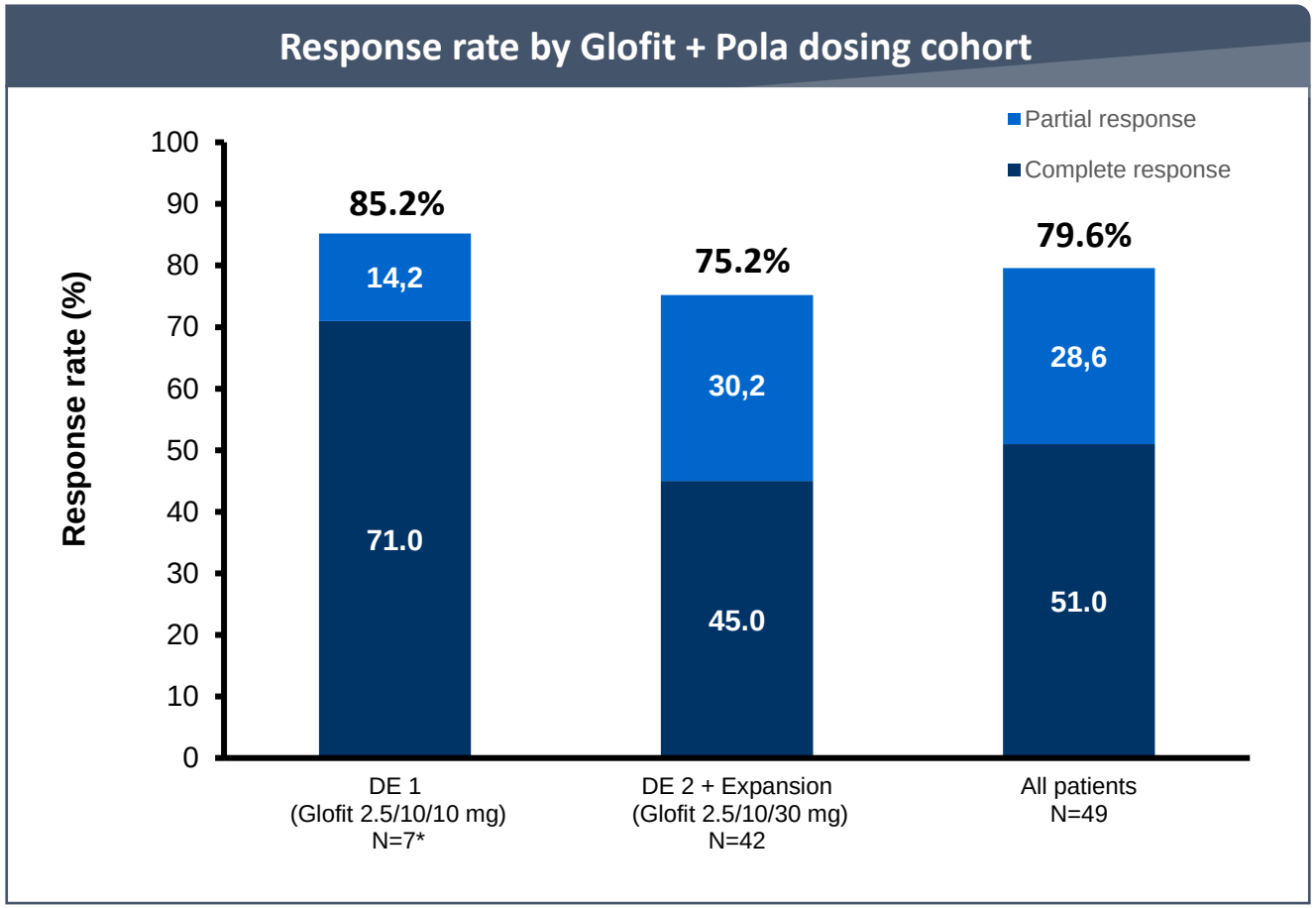
Joshua Brody, et al., Presented at ASCO/EHA 2022; No. 7527/181/P181

How to get deeper and more durable responses?



Lussana F, Gritti G; Rambaldi A. J Clin Oncol 2021; 39: 444-455.

NP39488: Glofitamab and Polatuzumab vedotin in DLBCL



- **49/59 patients were evaluable for interim response**
- **7/49 (14.3%) patients had PD as best response and discontinued study treatment**
- **Encouraging ORR and CR rates in patients with:**
  - trFL: ORR, 8/11 and CR, 7/11
  - HGBCL: ORR, 5/8 and CR, 4/8

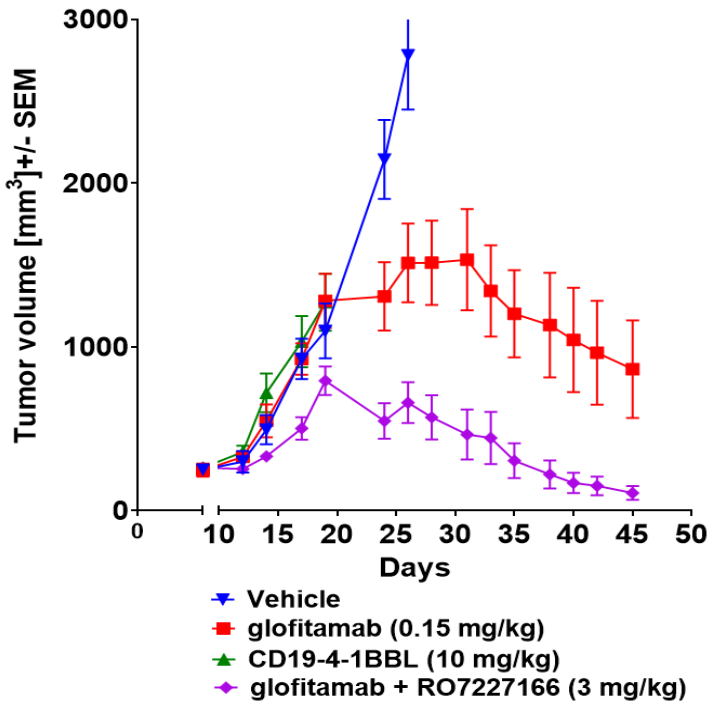
- **Glofit + Pola combination resulted in high response rates**

Hutchings M, et al. ASH 2021. Abstract 525.

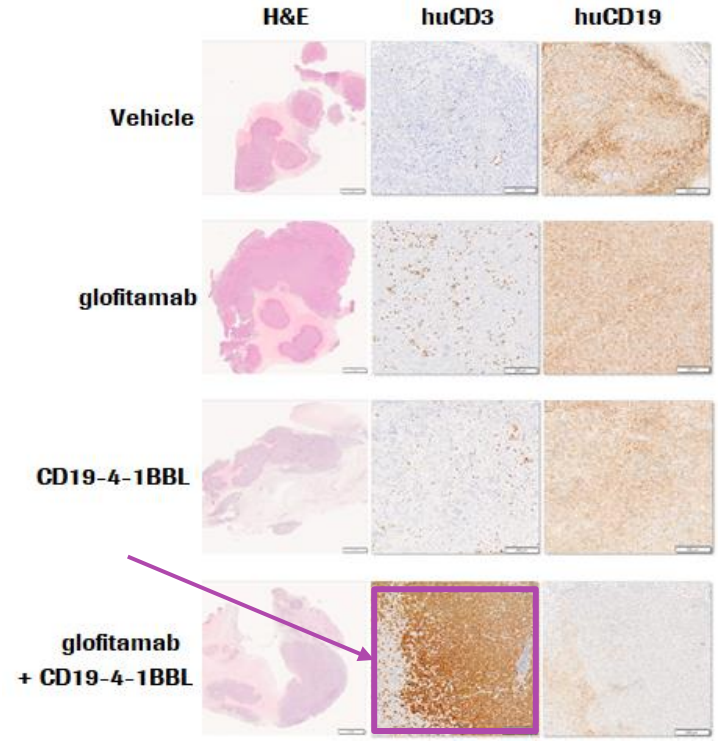
BP41072: Glofitamab + CD19-targeted 4-1BBL agonist

CD19 4-1BBL plus glofitamab is superior to glofitamab single-agent in vivo

Improved tumor growth inhibition

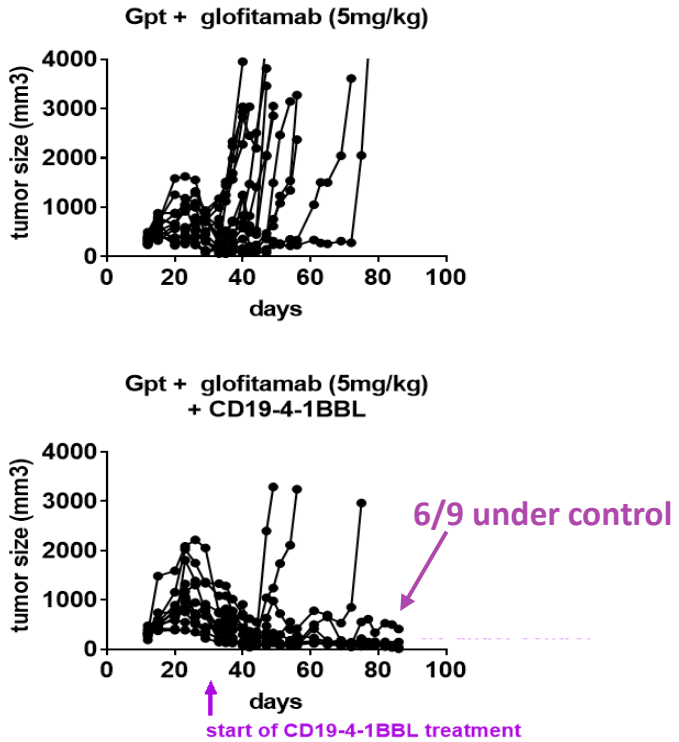


Significantly enhanced T cell infiltration



WSU DLCL2 s.c. in humanized mice

Prevention of tumor outgrowth during glofitamab monotherapy



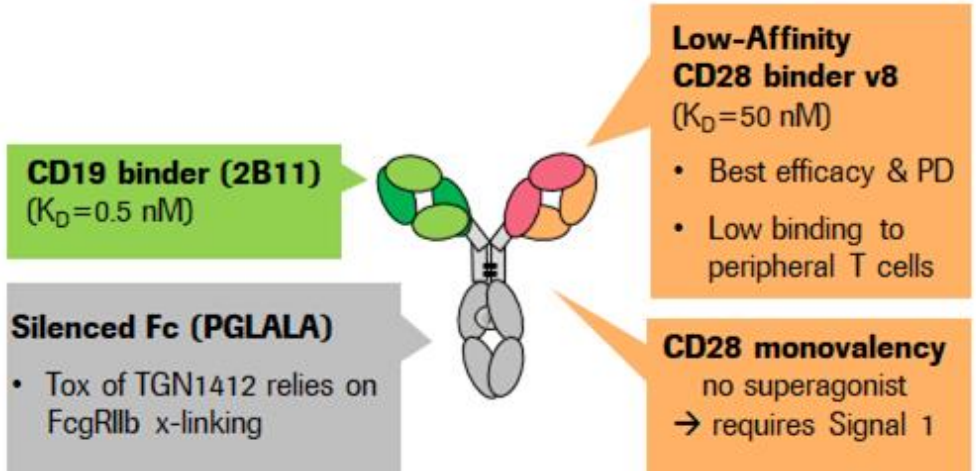
OCILY18 s.c. in humanized mice

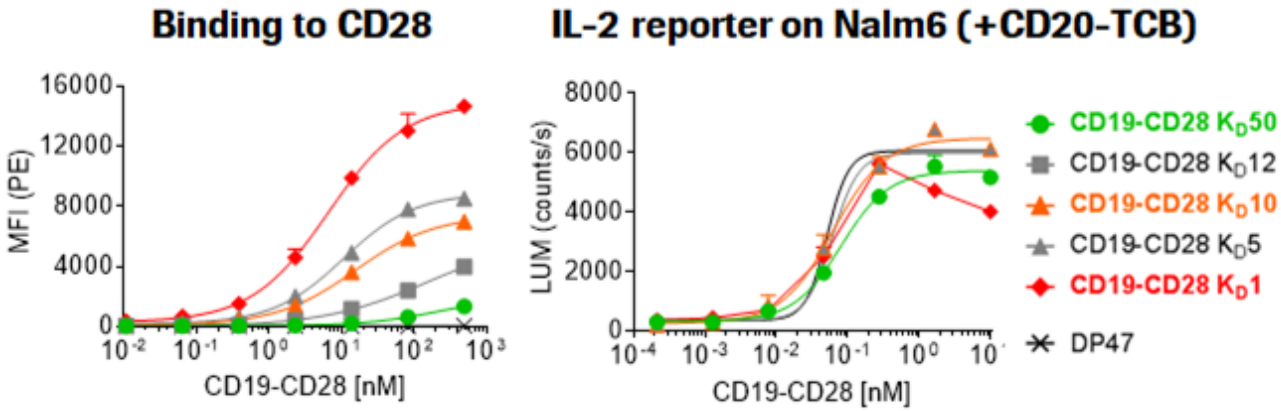
Hutchings M, et al. ASH 2020. Abstract 3269.

BP43131: Glofitamab + CD19-targeted CD28 agonist

Providing safe agonistic CD28 targeting w/o autonomous T cell activation

Reduce peripheral binding to CD28 w/o losing potency





Conclusions

- The CD3/CD20 bispecific antibodies show an antitumor activity which is unprecedented in heavily pretreated r/r B-NHL
- EHA 2022 data from DLBCL phase 2 expansion cohorts (35-40% with prior CAR-T):
  - Glofitamab: ORR 52%, CRR 39%
  - Epcoritamab: ORR 63%, CRR 39%
- The toxicity profile is favourable:
  - Very little CRS > grade 2
  - Very little treatment-related CNS toxicity
- CRS is highly predictable and almost always confined to the cycle 1
- The toxicity profile and mechanism of action make the bispecifics ideal for combination strategies

Acknowledgements

- Patients and their families
- Research nurses and study coordinators
- NP30179, GCT3013-01, NP39488, BP41072, BP43131 study teams and co-investigators
- Colleagues (Mike Dickinson, Catherine Thieblemont) who kindly provided figures for this presentation