3rd Edition
Unmet challenges in high-risk hematological malignancies : from benchside to clinical practice
Turin, septembre 21-22, 2023

Emerging immunotherapy in B-cell lymphomas
The role of bispecific antibodies

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Conflict of interest

- Commercial
  - Consultancy/honoraria: Novartis, BMS/Celgene, Bayer, AbbVie, Gilead Sciences, Roche, Janssen, Kite, Incyte, Amgen, Takeda
- Educational activities
  - Janssen, Roche

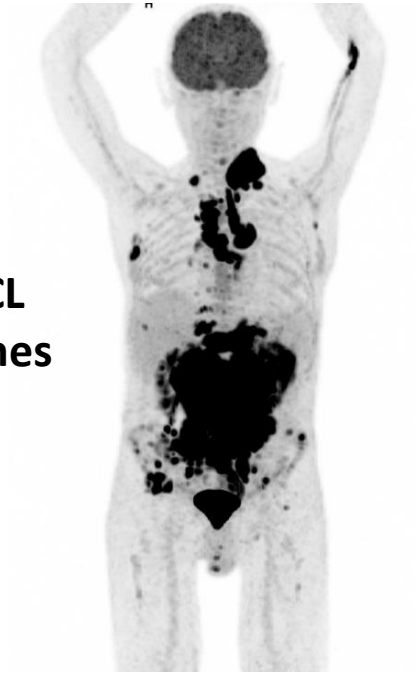
Emerging immunotherapy

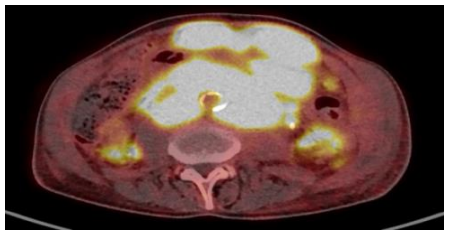
AIM : to enhance the immune response against tumor cells

To use our own immunity to cure cancer

Case report
THE, male, 63 years old

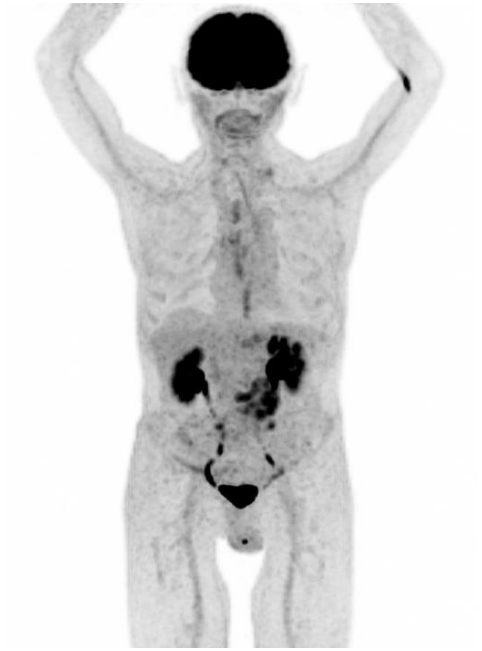
- R/R DLBCL
- 3 prior lines

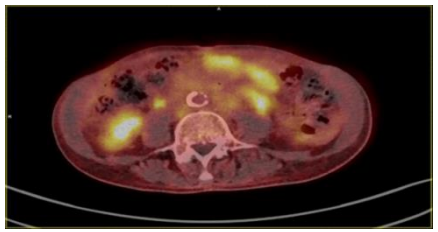




Metabolic tumoral volume 1200ml

Emerging immunotherapy





CURE

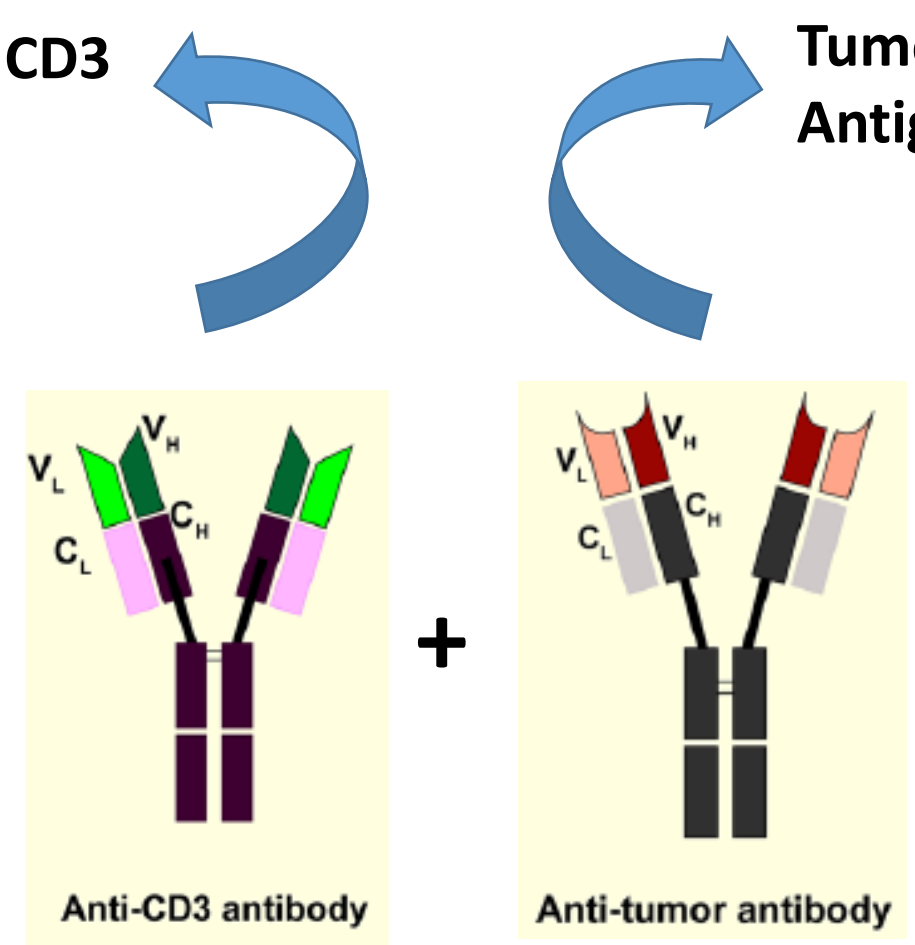
Immunotherapy in oncology

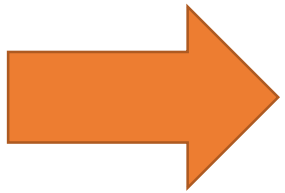
includes a broad range of agents, including

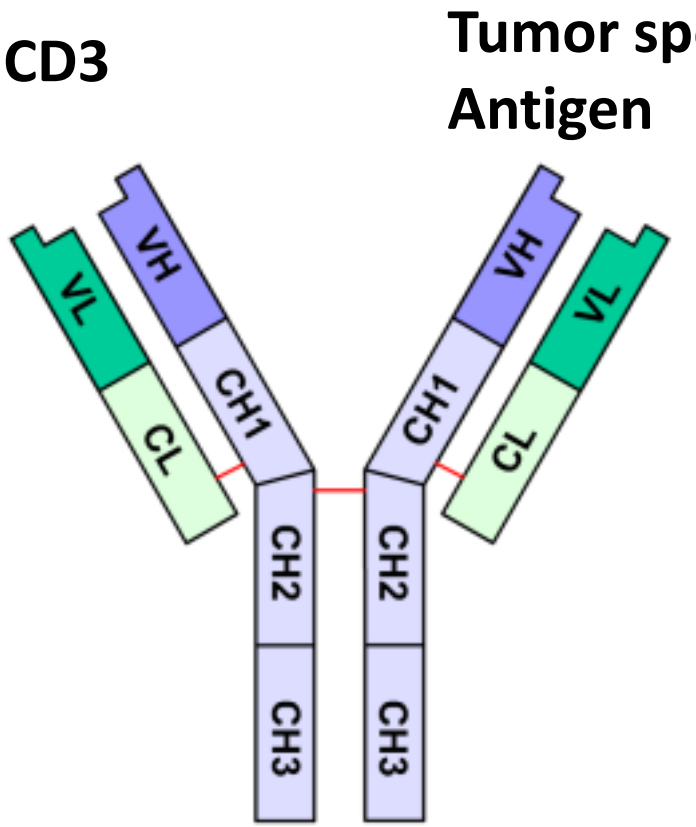
- **antibodies**
- **vaccines**
- **cytokines**
- **oncolytic viruses**
- **bispecific antibodies (BsAbs)**
- **cellular therapies : CAR T-cells**

June C & Sadelain M. N Engl J Med 2018;379:64-73.

Structure of Bs Abs (1)







designed to target simultaneously

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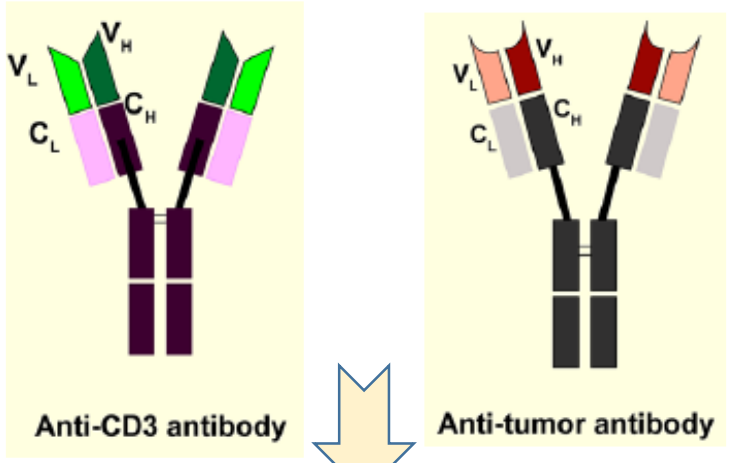
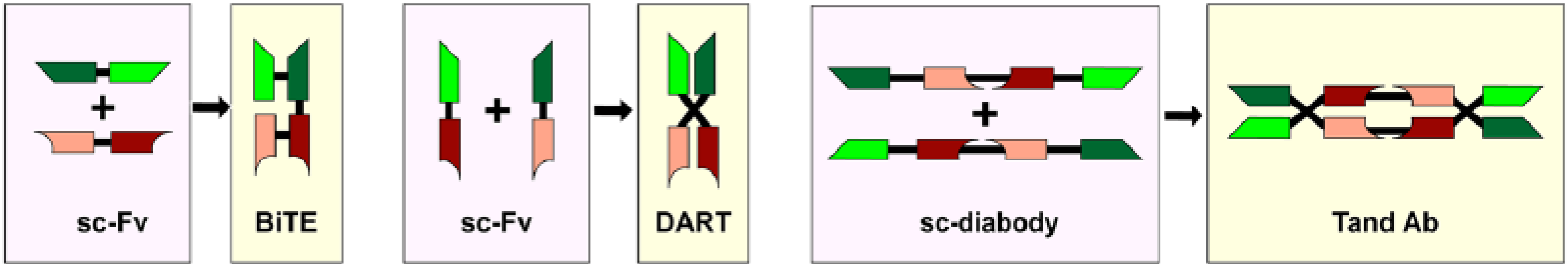
Structure and classification of Bs Abs (2)



No Fc fragment, ScFV

Fast activity +++
Tissues diffusion +++
Easy manufacture +++
Short half-life +++



scFV single chain variable fragment
BiTEs Bispecific T-cell Engager - DART = dual Affinity Retargeting antibody
Tand Ab Tandem = tandem diabody

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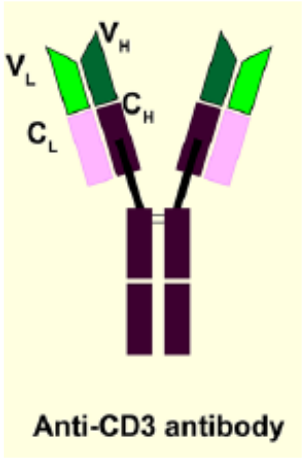
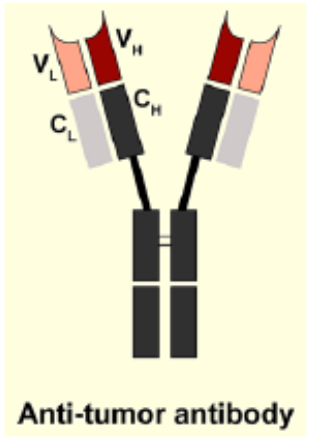
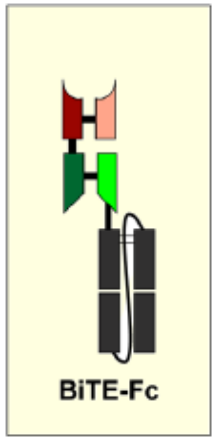
Structure and classification of Bs Abs (2)

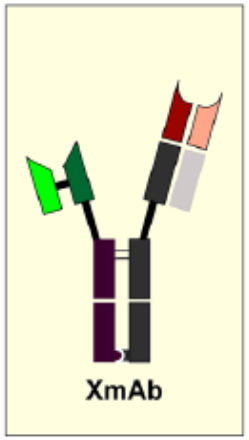


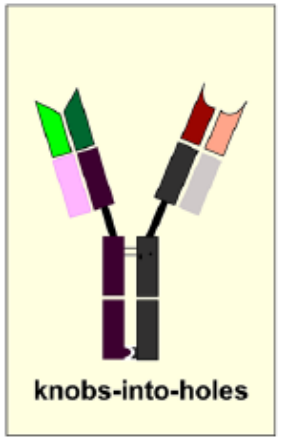


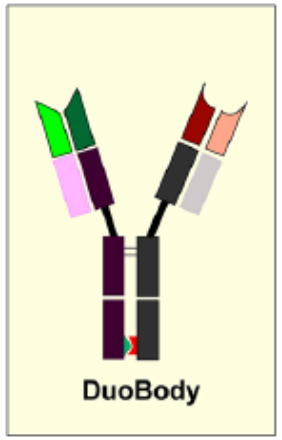
With Fc, "Full Ab"

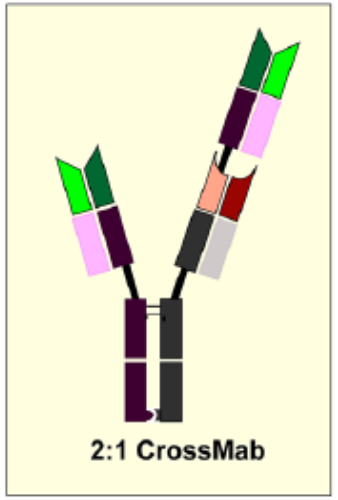
Fast activity +
Lower tissues diffusion ++
Complex manufacture ++
Longer half-life +++











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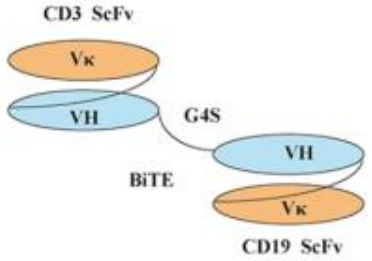
In hematology, Bispecifics T-cell Engagers (BiTEs) under clinical development

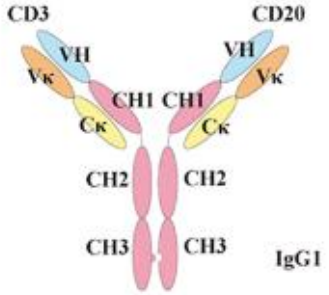
CD3 x CD19



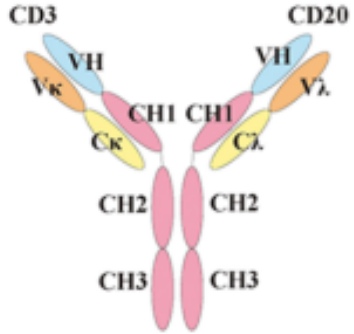
Blinatumomab

CD3 x CD20

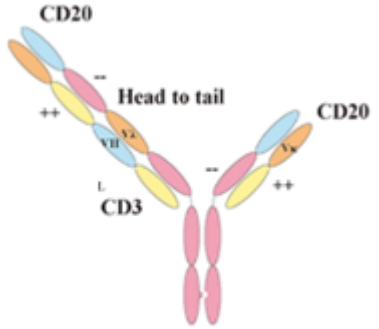
Ig G-based



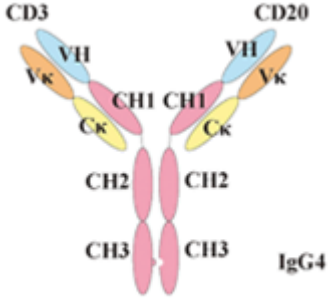
Mosunetuzumab



Epcoritamab

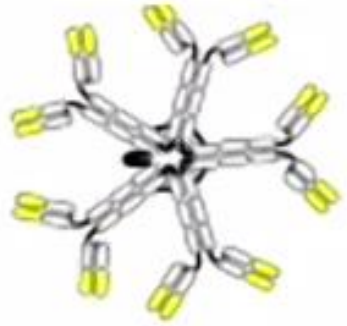


Glofitamab



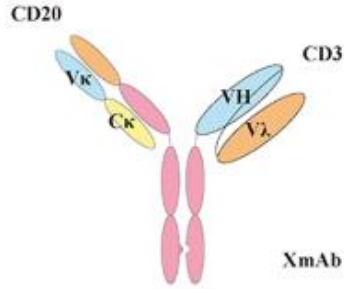
Odronextamab

Ig M-based



Imvotamab

Under development

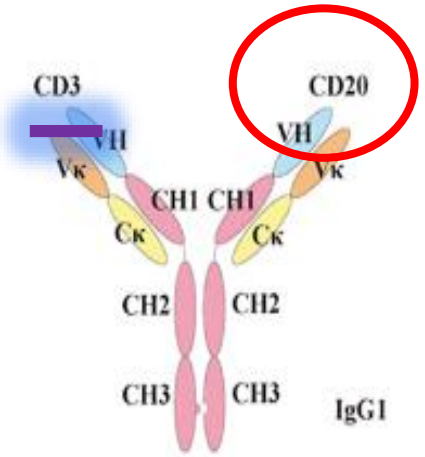


Plamotamab

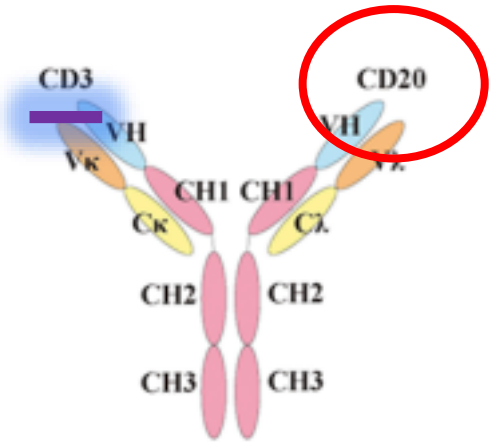
Adapted Ma et al. Frontiers in Immunology 2021

Avidity binding to CD20

1:1 format

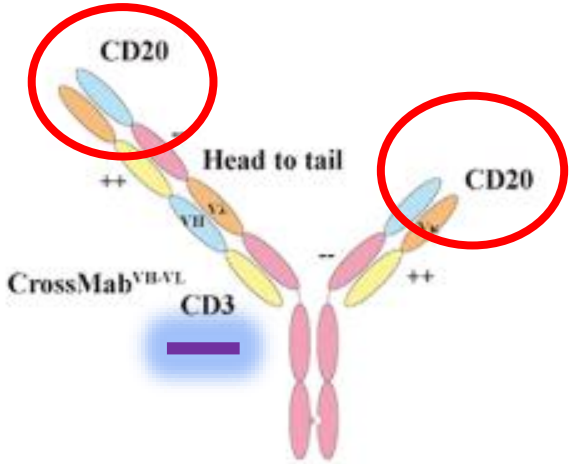


Mosunetuzumab



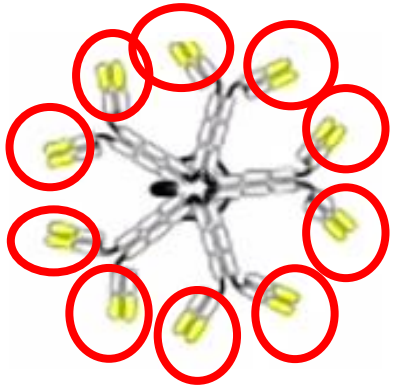
Epcoritamab

2:1 format



Glofitamab

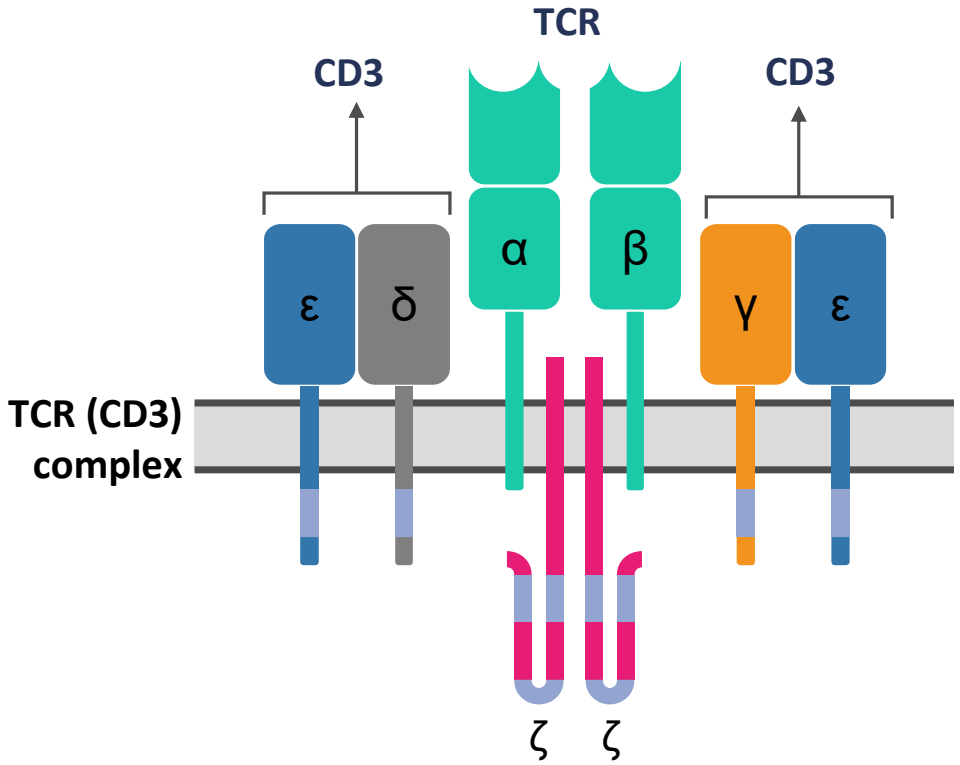
10:1 format



Imvotamab

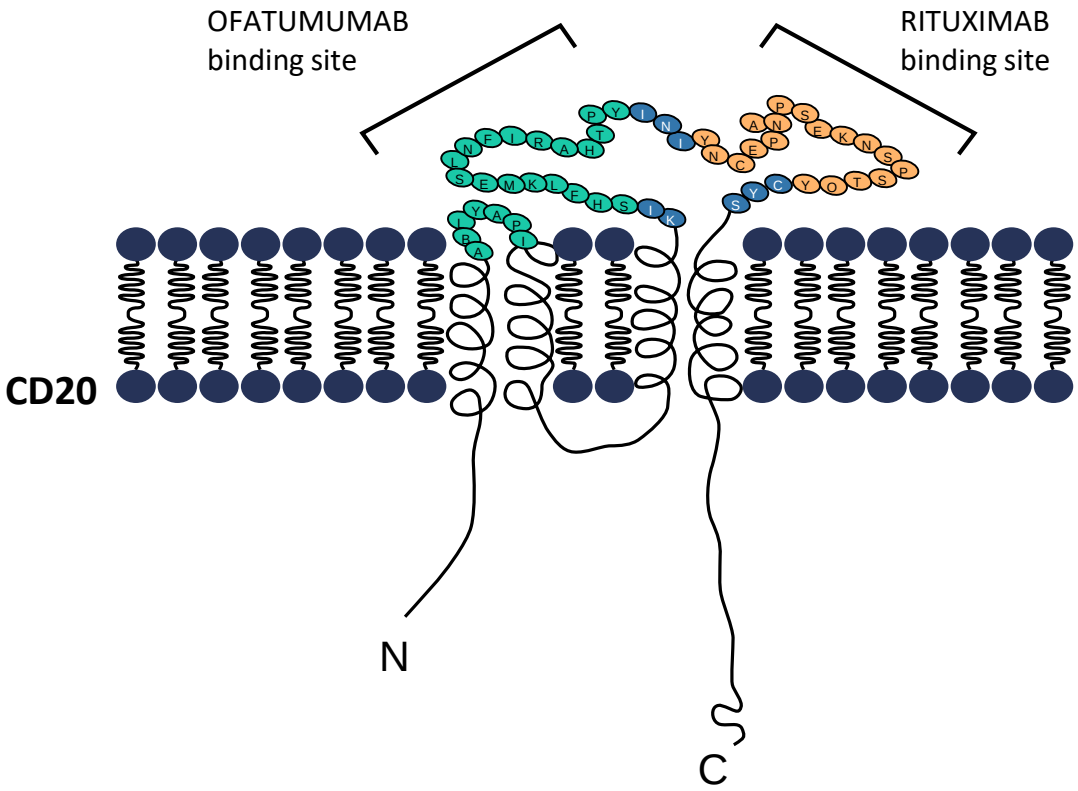
Bacac M, *et al. Clin Cancer Res* 2018; **24**;4785–97

Binding sites of CD3xCD20 antibodies



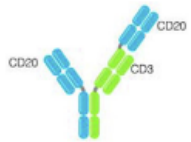
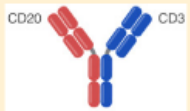
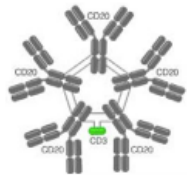
Franco R, *et al. Front Pharmacol* 2016

Analogy with



Klein C, *et al. Mabs* 2013

Comparative characteristics of CD20XCD3 BsAb currently in development in B NHL

	Product name	Schematic depiction	Format	Technology	CD20:CD3 ratio
Advanced development	Mosunetuzumab[18]		IgG1	Knobs-into-holes (different Fabs)	1:1
	Glofitamab[15]		IgG1	Head-to-tail fusion	2:1
	Epcoritamab[16]		IgG1	Controlled Fab-arm exchange	1:1
	Odronexamab[17]		IgG4	Heavy chains with different affinity	1:1
Under development	Plamotamab[90]		IgG1	Fab-Fc x scFv-Fc	1:1
	IgM 2323[19]		IgM	IgM + modified J chain	10:1

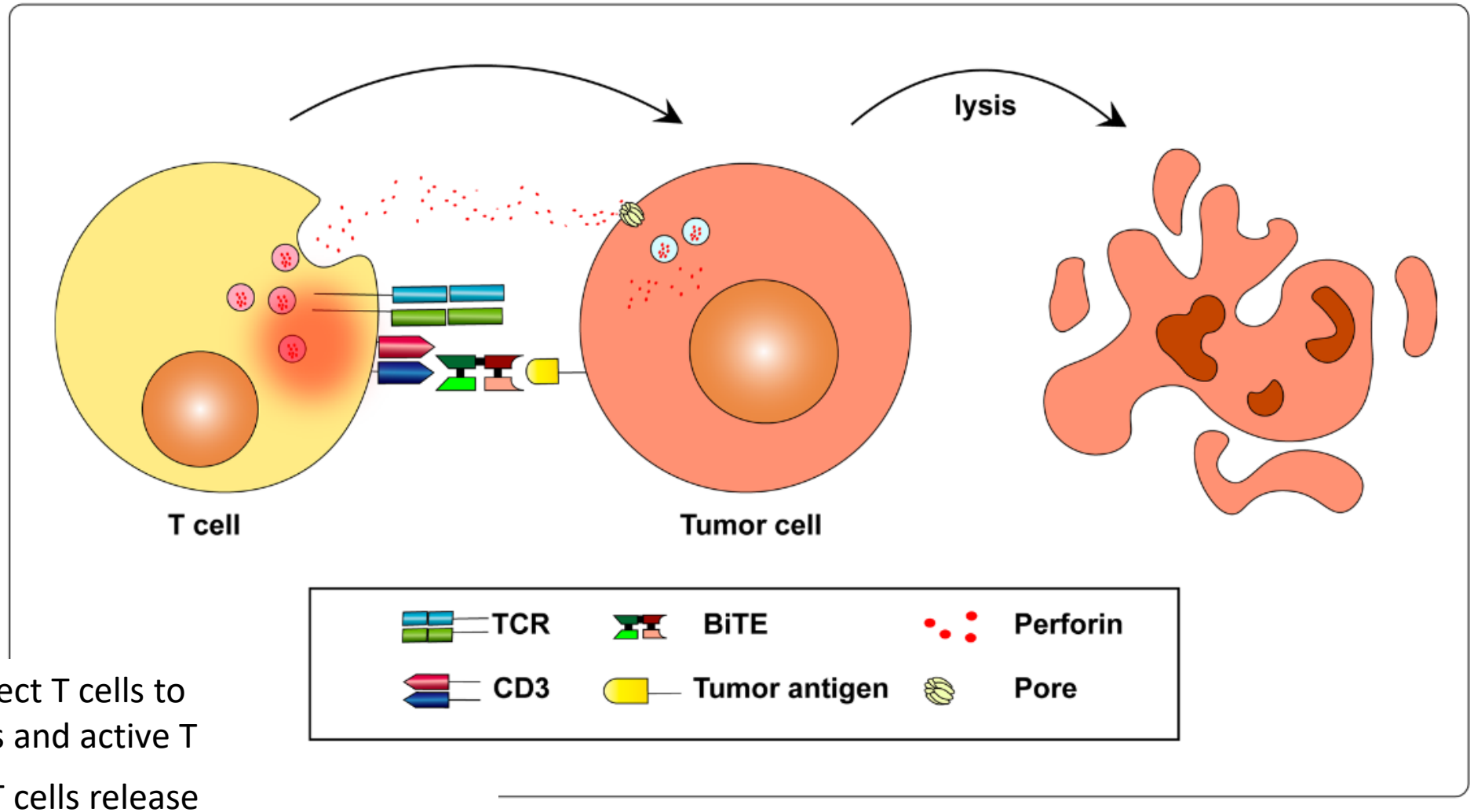
Falchi et al. Blood 2023

Comparative characteristics of CD20XCD3 BsAb in B NHL

	structure	Target ratio : CD3 ratio	Half-life	Administration	Fc binding	Complement binding	CD3 recognition
Blinatumomab	scFv	1:1	20 min	IV	No	No	CD3δε
Mosunetuzumab	IgG1	1:1	7-21 d	IV / sc	minimal	No	CD3δε
Epcoritamab	IgG4	1:1	7-21 d	sc	minimal	No	CD3ε
Glofitamab	IgG1	2:1	7-21 d	IV	minimal	No	CD3ε
TNB486	IgG4	1:1	7-21 d	IV	minimal	No	CD3δε
Imvotamab	IgM	10:1	3-7 d	IV	Yes	Yes	CD3δε

Mode of action

Tumor cell lysis mediated by the BiTEs

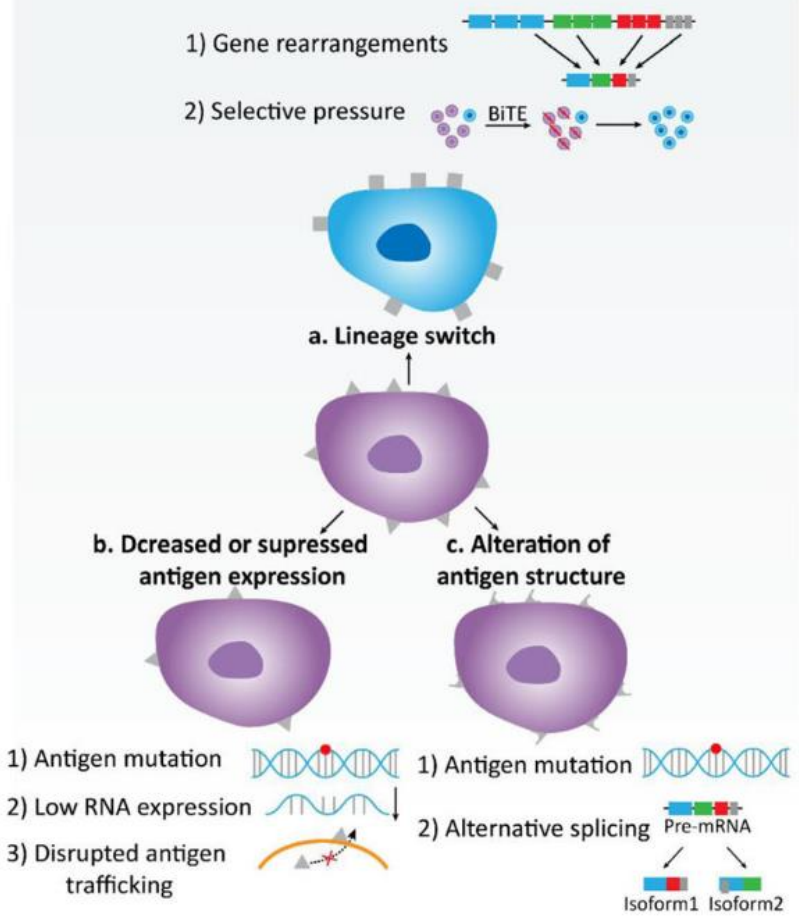


- BiTEs redirect T cells to tumor cells and active T
- Activated T cells release perforin and other granzymes through immunological synapses

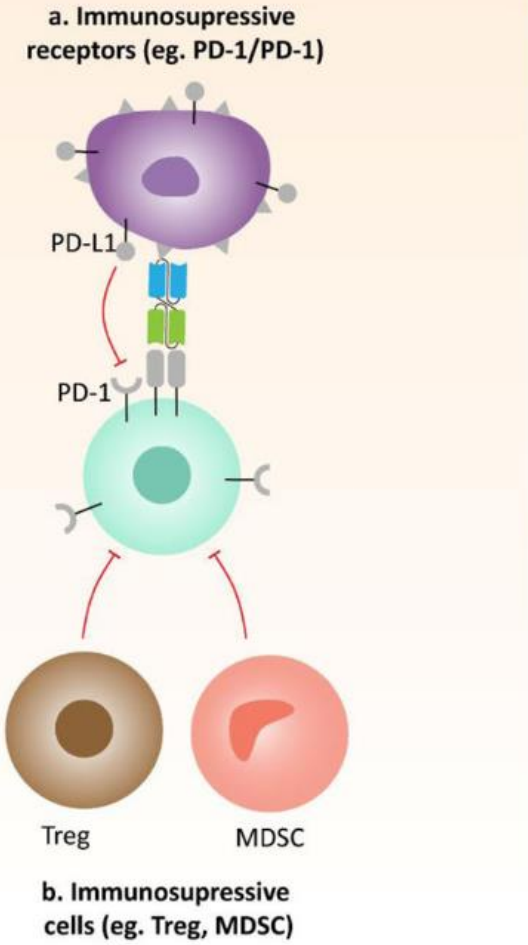
Tian et al J Hematol Oncol 2021

Mechanisms of resistance

Loss of antigen

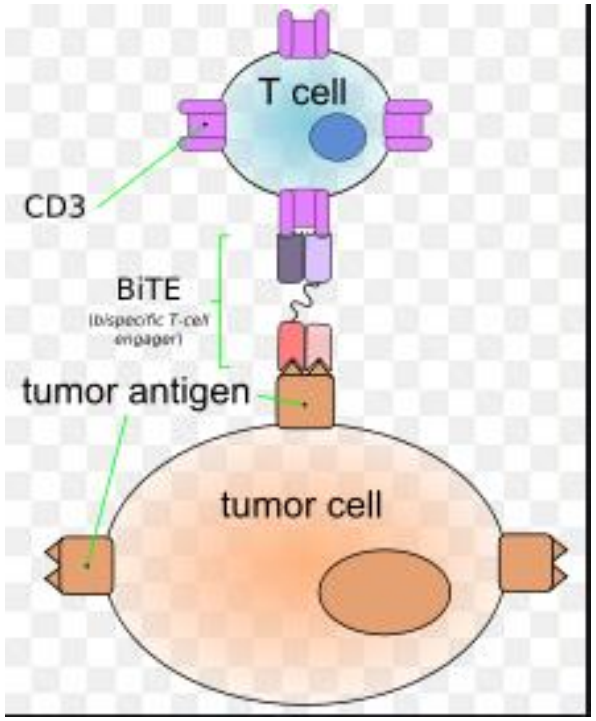


Immunosuppressive TME



Zhou et al. Biomarker Research2021

Bispecific T-cell engager (BiTE)



Wikipedia

- First approved by FDA in 2014 in R/R ALL
- Currently evaluated for R/R lymphoma, R/R myeloma
- Off the shelf, ready to be used
- Repeated infusions until progression or toxicity
- Ramp-up infusions during 3 weeks
- Side effects : neurotoxicity and cytokine release syndrome

Single-agent phase 1/2 studies of bispecific antibodies in B-NHL

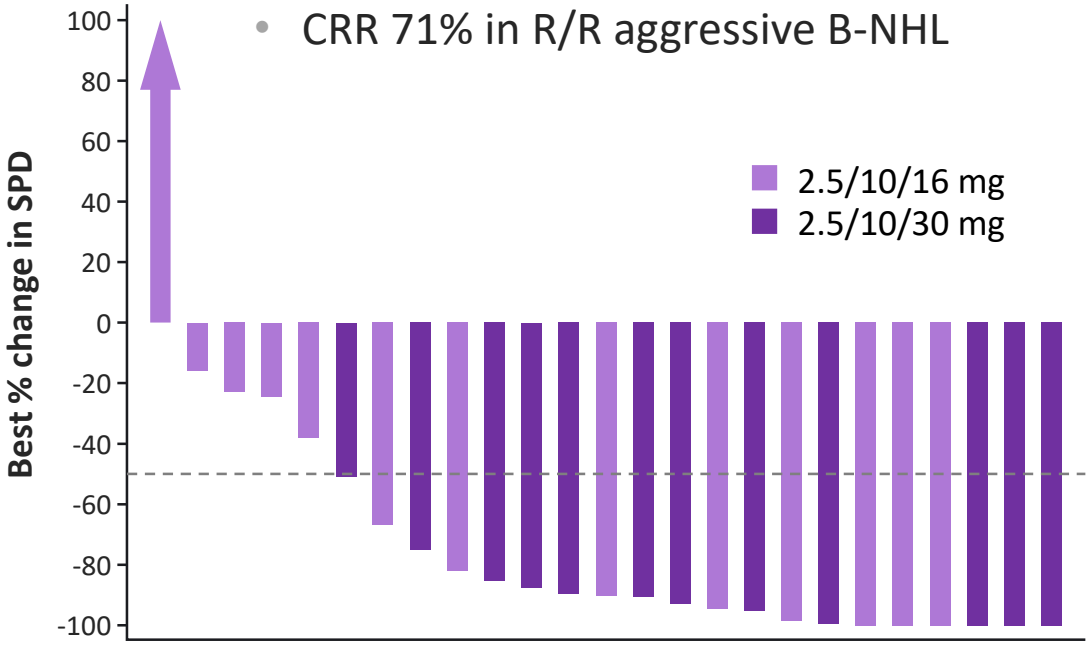
Activities in single agent phase 1-2 in aggressive B-cell lymphomas

Target	Drug	Phase	No*	Efficacy	Références
CD19/CD3	Blinatumomab	2	25	ORR 43% CR 19%	Viardot et al. Blood 2016
CD20/CD3	Glofitamab D-7obinutuzumab	1b	171	ORR 79% CR 71%	Hutchings M, *et al. J Clin Oncol* 2021
CD20/CD3	Mosunetuzumab	1/1b	171	ORR 37.1% CR 19.4%	Schuster SJ, et al. ASH 2019: Abstract 6
CD20/CD3	Odronextamab	1	53	ORR 55% CR 55%	Bannerji R ASH 2019 #762
CD20/CD3	Epcoritamab subcutaneous	1/2	73	ORR 91% CR 55%	Hutchings M, *et al. Lancet* 2021

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

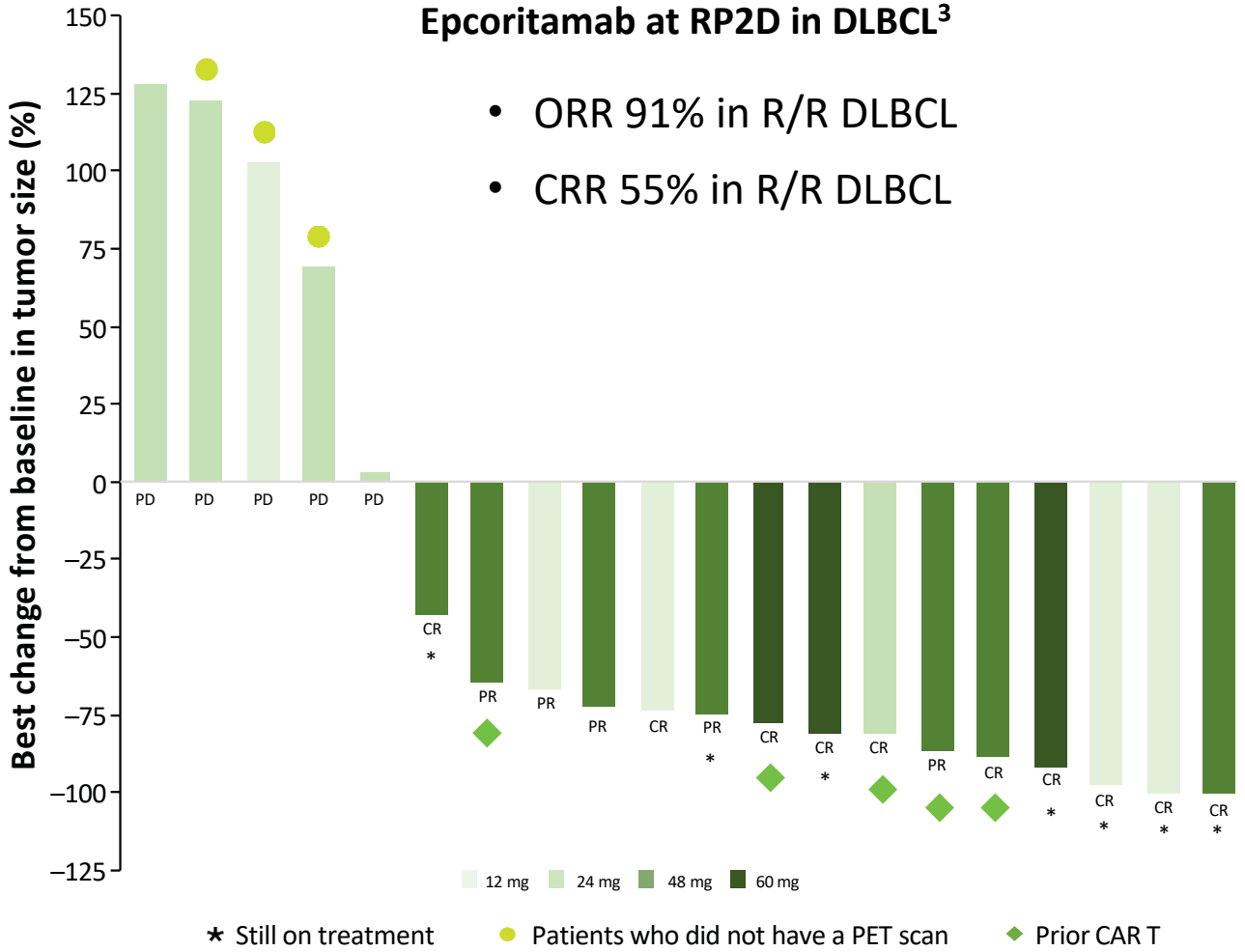
Glofitamab at RP2D in aggressive NHL[1,2]

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



Epcoritamab at RP2D in DLBCL[3]

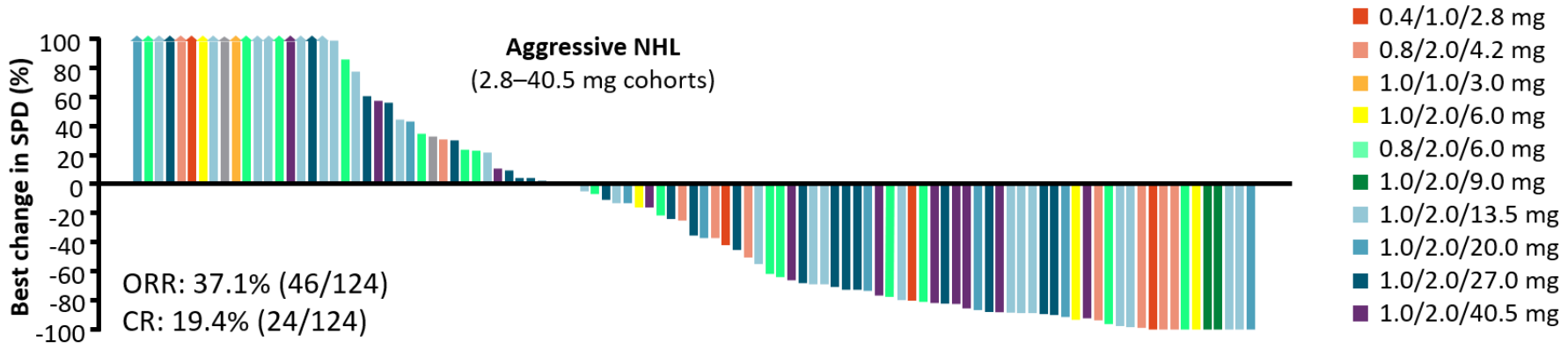
- ORR 91% in R/R DLBCL
- CRR 55% in R/R DLBCL



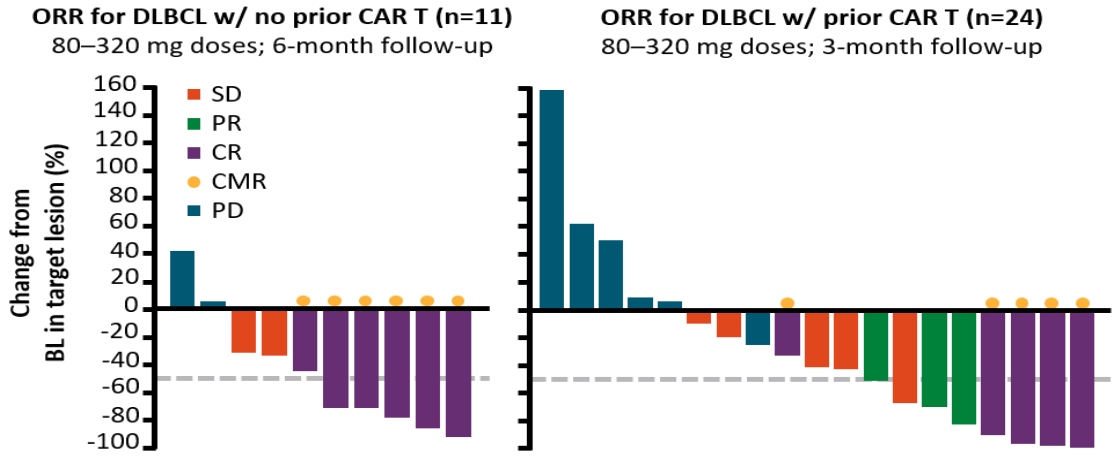
1. Hutchings M, *et al. J Clin Oncol* 2021; **39**:1959–1970; 2. Carlo-Stella C, *et al.* ICML 2021. Abstract 15 (oral); 3. Hutchings M, *et al. Lancet* 2021; 398(10306): 1157-1169.

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).

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

Glofitamab – expansion cohort

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

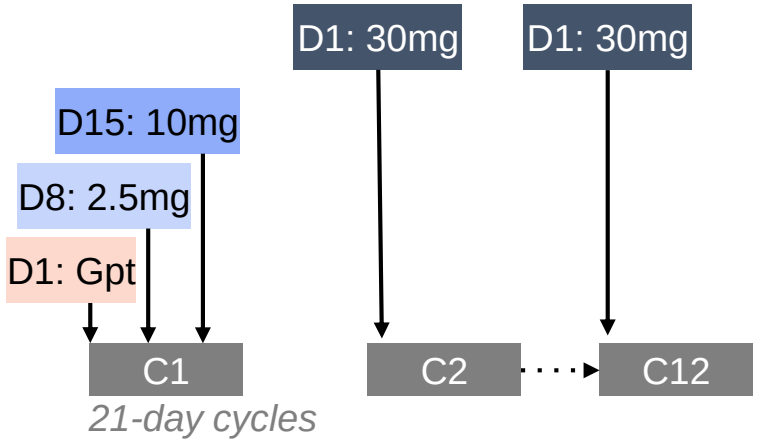
Glofitamab IV administration

Fixed-duration treatment

- max. 12 cycles

CRS mitigation:

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



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

Michael Dickinson,et al. NEJM 2022 & EHA 2022 oral presentation

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.

Michael Dickinson,et al. NEJM 2022 & EHA 2022 oral presentation

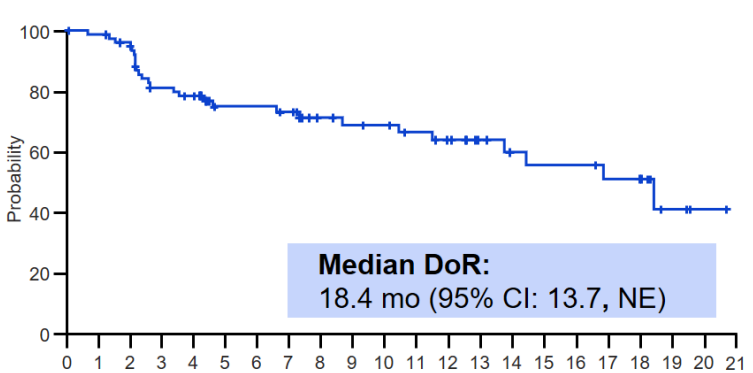
Glofitamab – expansion cohort
Response and duration of response

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)

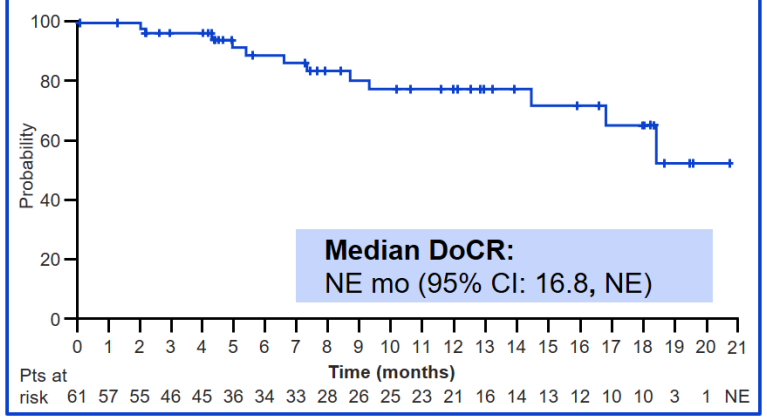
Prior CART : 33%

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)**
ORRs 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)

Michael Dickinson,et al. NEJM 2022 & EHA 2022 oral presentation

Epcoritamab – in aggressive BCL

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 Investigator Review Committee (IRC)
- **Key secondary endpoints:** DOR, TTR, PFS, OS, CR rate, and safety/tolerability

Catherine Thieblemont, et al. J Clin Oncol 2022 & 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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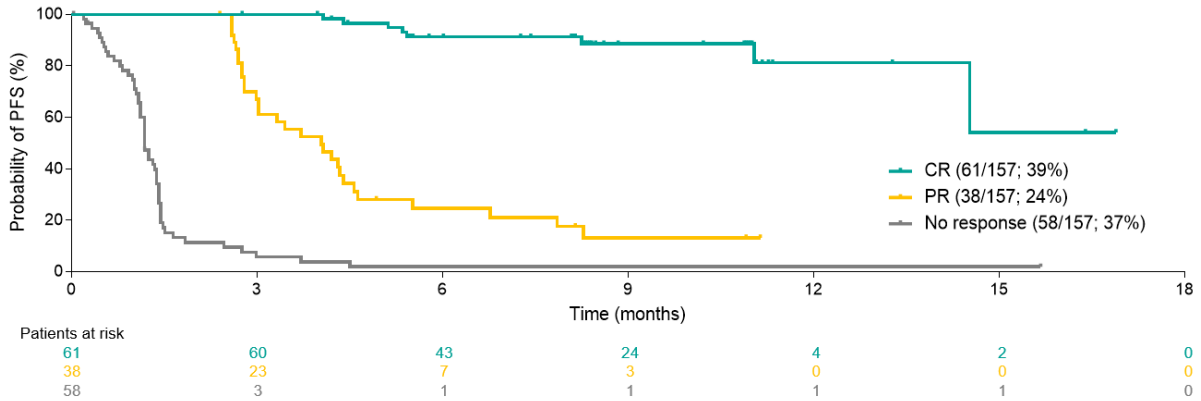
Epcoritamab – expansion cohort
Response rate

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)

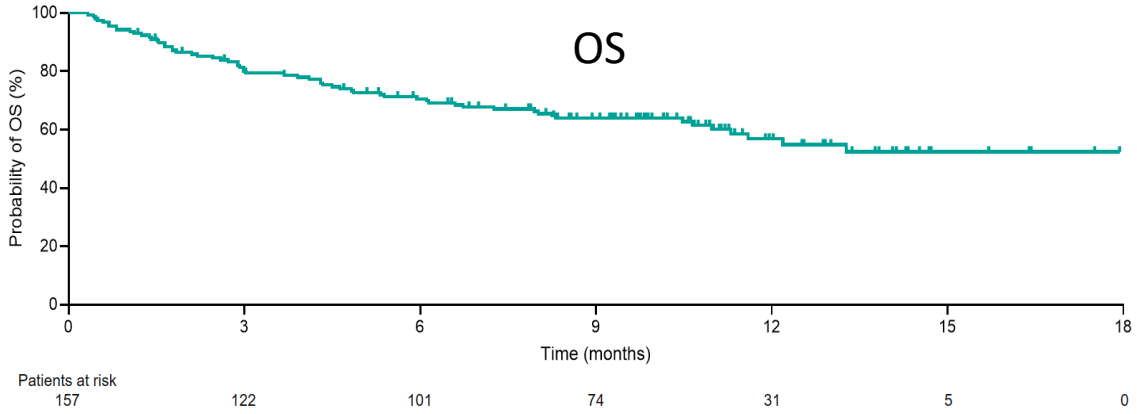
Prior CART : 39%

PFS



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)

OS



Kaplan–Meier Estimate	N=157
Median OS	**Not reached**
OS at 6 mo, % (95% CI)	70.6 (62.7–77.2)
OS at 12 mo, % (95% CI)	56.9 (47.3–65.4)

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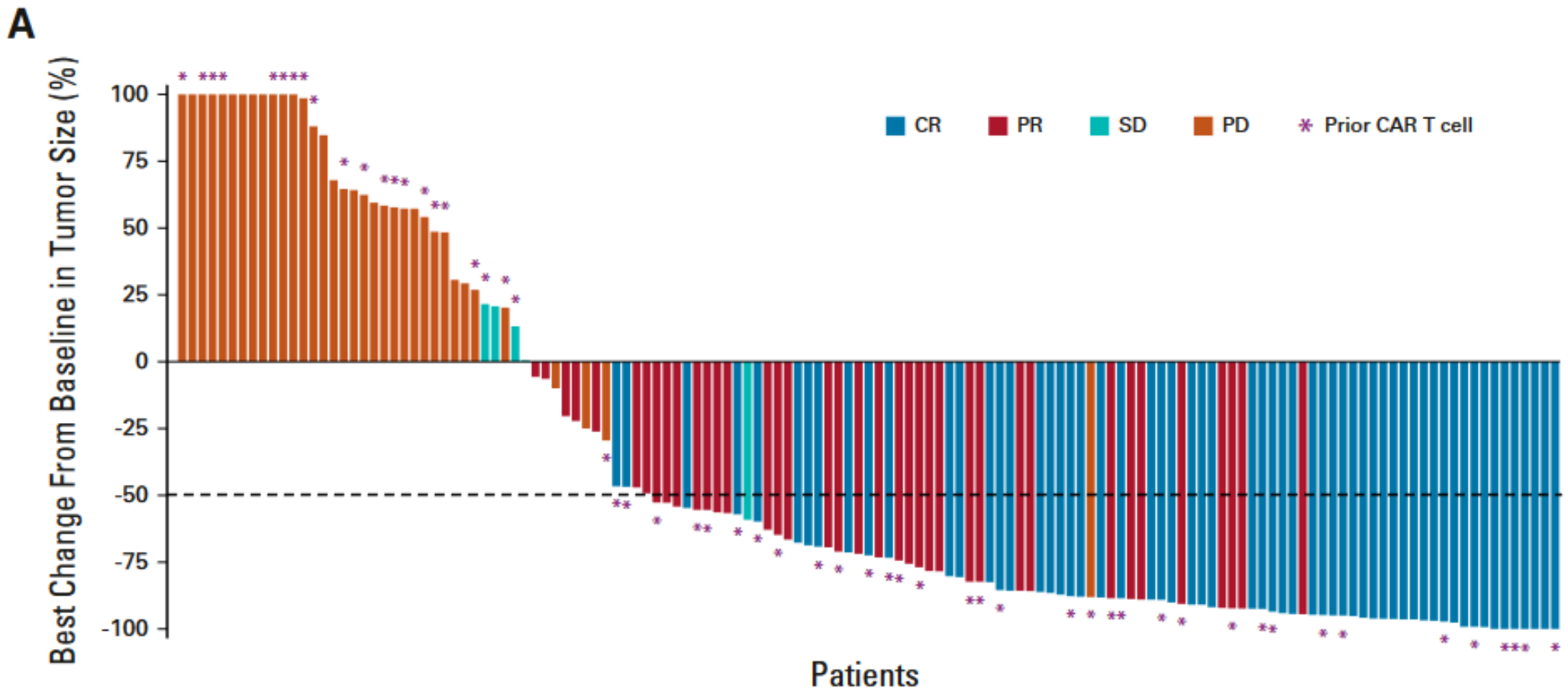
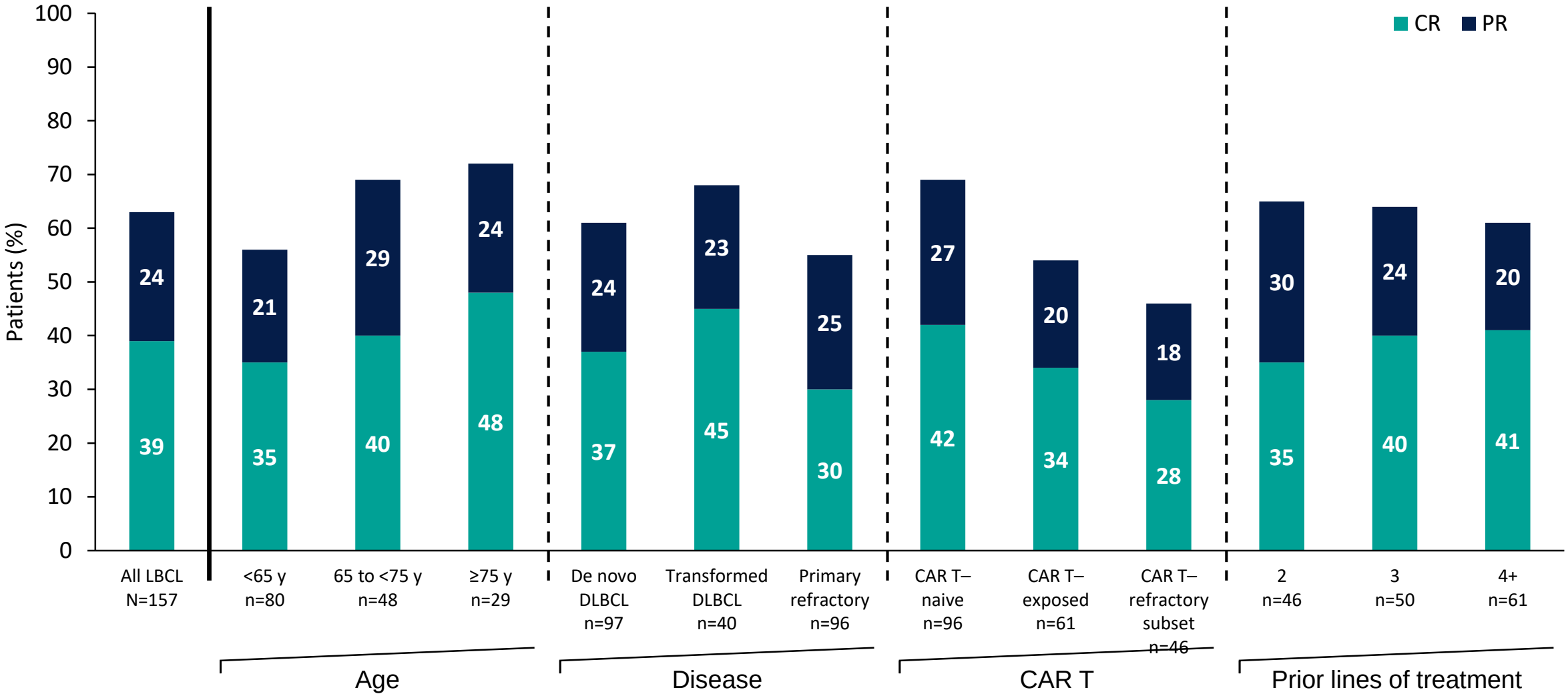
Epcoritamab in R/R DLBCL



Thieblemont et al., JCO 2022

Deep Responses Consistent Across Key Subgroups



Based on IRC assessment and Lugano criteria.

Thieblemont C, et al. J Clin Oncol 2022

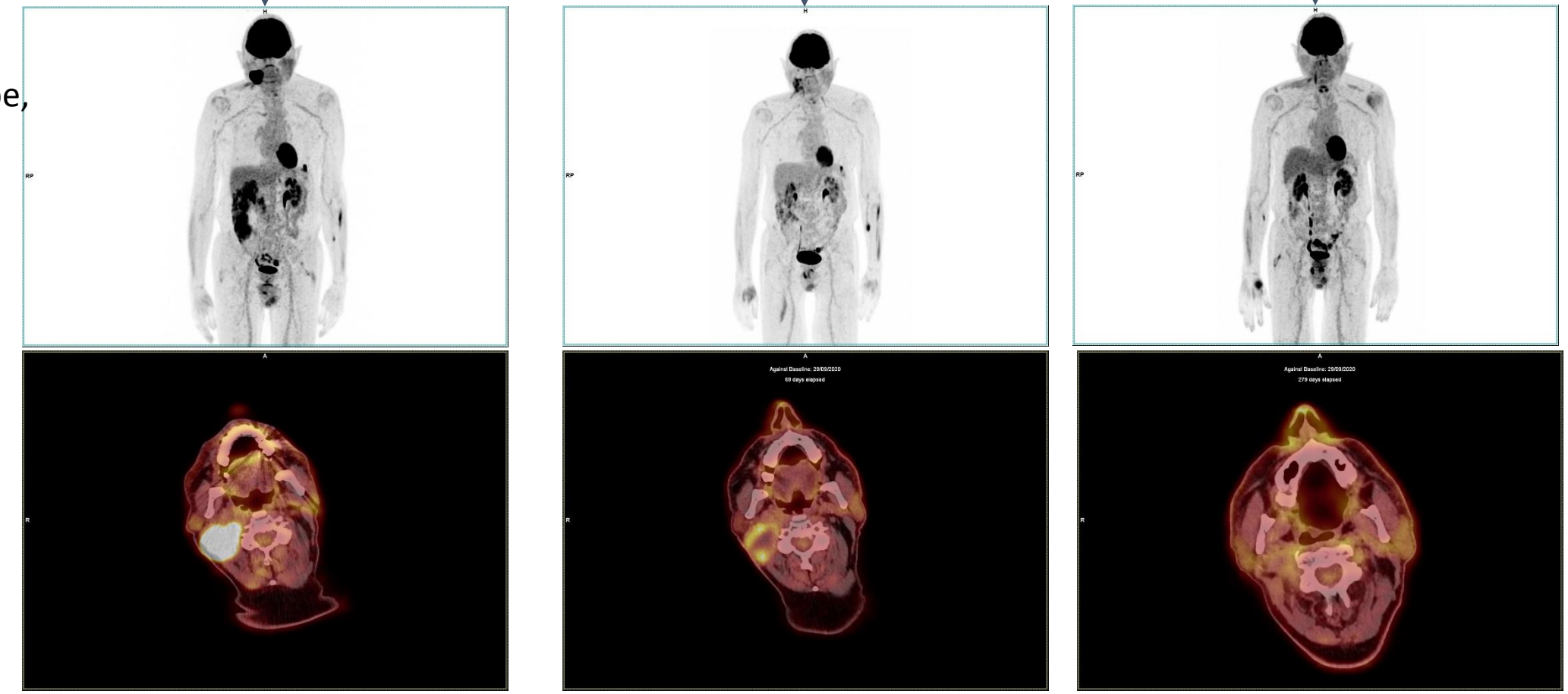
Patient 1. FET

Assessment CR
PR
SD
PD

D1 W6 W12 W18 W24 W36 W48 W60

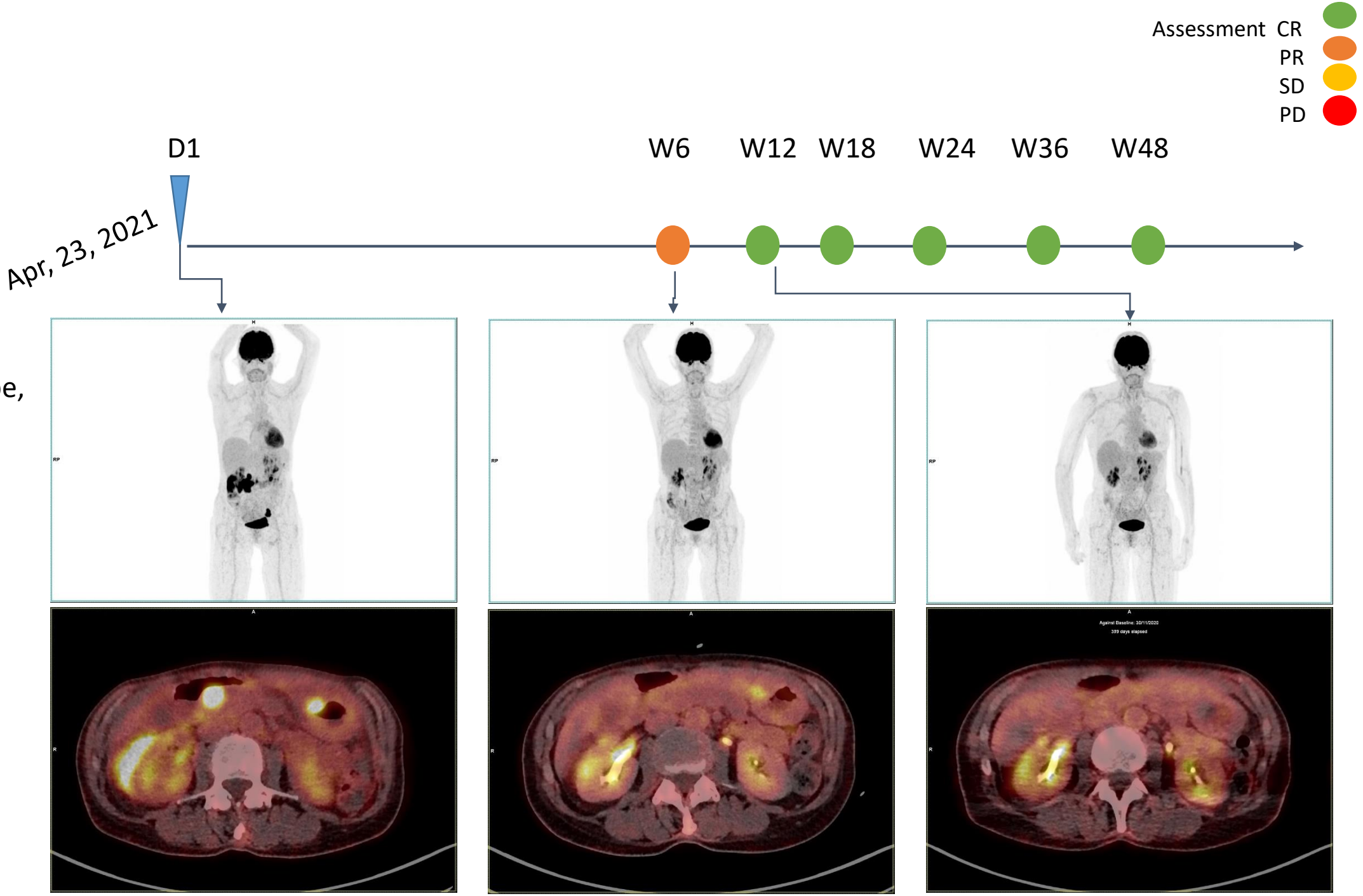
Oct, 29, 2020

79 y o
PS = 1, No B symptoms
DLBCL GC subtype, Ki67 90%
Prior lines, n=7
No prior CAR T
Stage III
LDH level :Nl



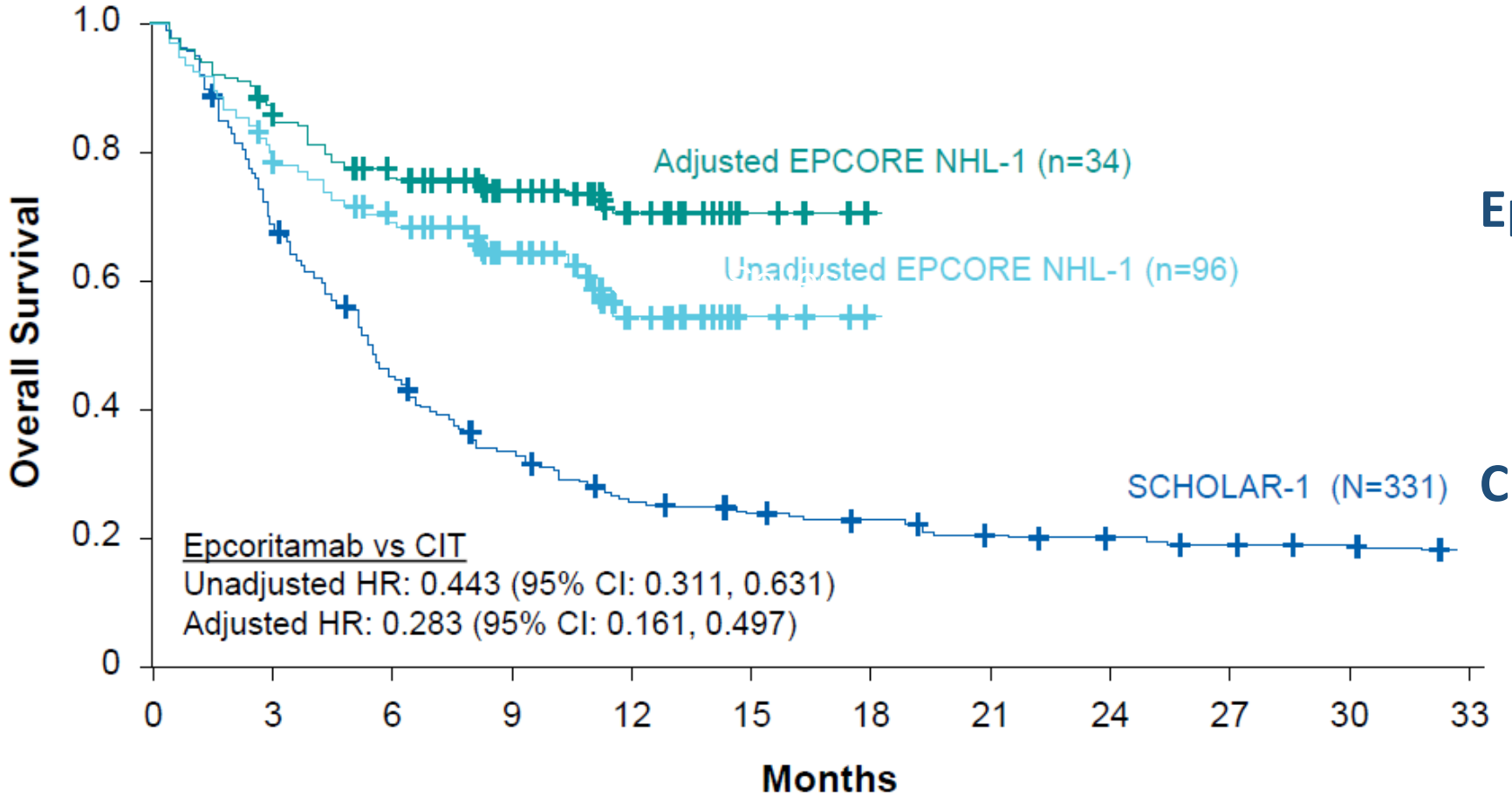
Patient 2. LEF

59 y o
PS = 1, No B symptoms
DLBCL GC subtype, Ki67 80%
Double HIT
Prior lines, n=5
Prior CAR T
Stage III
Elevated LDH



OS: Epcoritamab vs Chemotherapy (historical comparison)

Figure 3. Comparison of OS vs SCHOLAR-1



Epcoritamab

Chemotherapy

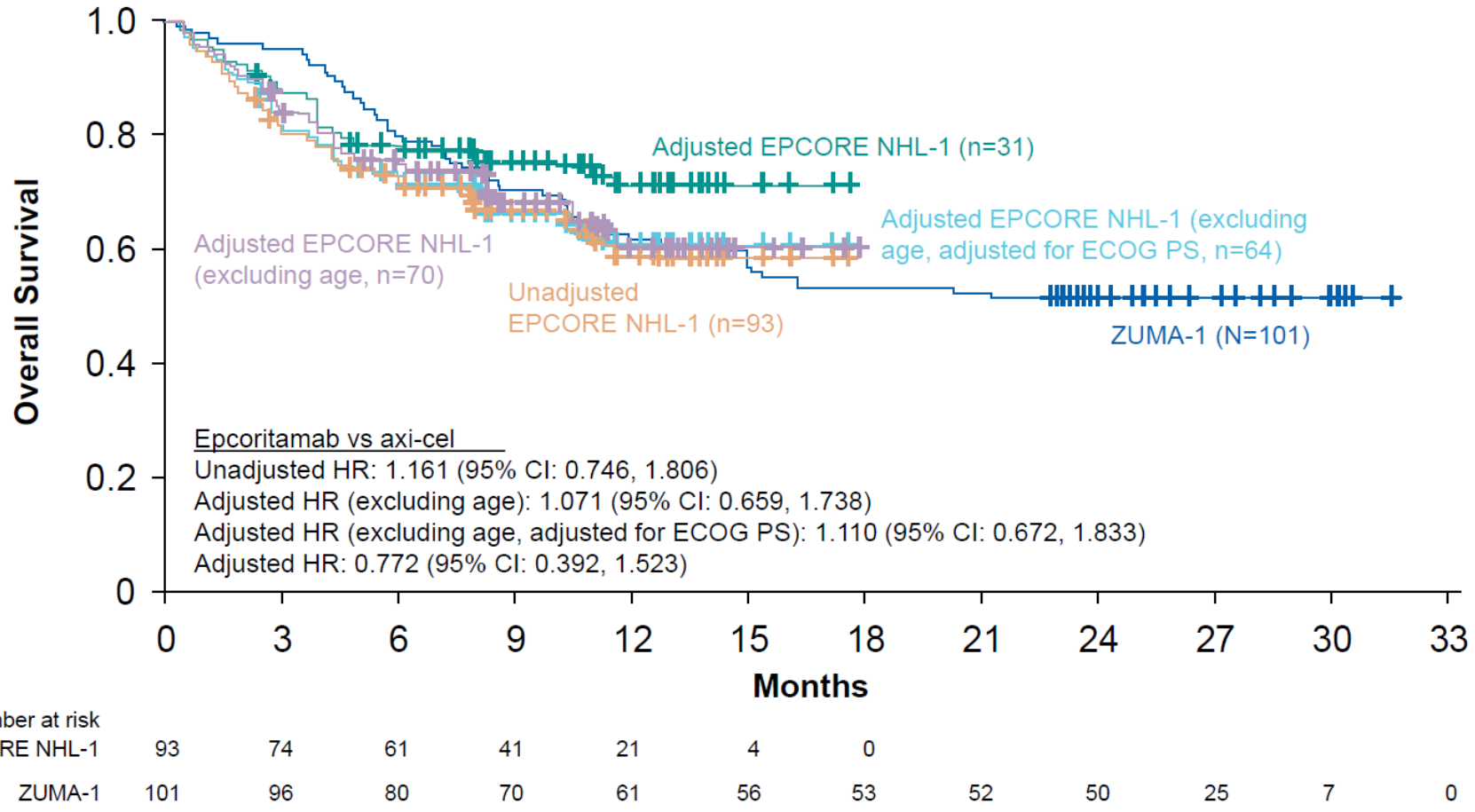
CIT, chemoimmunotherapy; HR, hazard ratio; OS, overall survival.

Salles G et al., *ASH, 2022, Abstr 4912*

OS : epco vs CAR-T (Historical comparison)

Université de Paris

Figure 4. Comparison of OS vs non-ITT ZUMA-1 Study Population



Salles G et al., *ASH, 2022, Abstr 4912*

CRS/neurologic AEs with CD3xCD20 Bs Abs

Administration

Ramp-up administration ++++

Cycling, 21 days		C1 D1	C1 D8	C1 D15	C2	C3
Epcoritamab	sc	0.16mg	0.8mg	48mg /24mg	48mg /24mg	48mg /24mg
Mosunetuzumab	IV / sc	1 mg	2 mg	30 mg	30 mg	30 mg
Glofitamab	IV	Obinutuzumab 1000	2.5 mg	10 mg	30 mg	30 mg
Odronextamab	IV	D1,D2 0.2 +0.5mg	D8,D9 4 +20mg	D15,D16 80mg	80mg	80mg

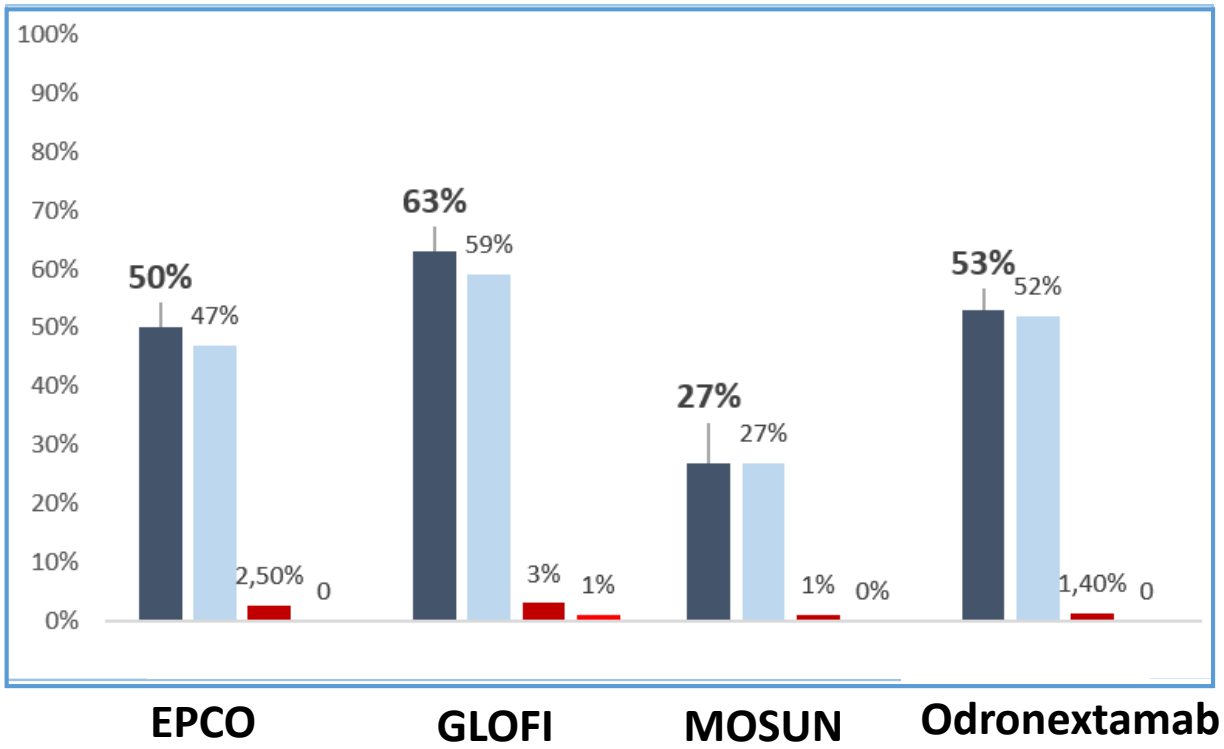
Timing of CRS

Study	Bispecific	Treatment Day	Median time to CRS	Median duration CRS
NCT03625037[1]	**Epcoritamab**	C1D1 (5.8%) C1D8 (11.8%) **C1D15 (42.8%)** C1D22 (4.9%) C2D1+ (3%)	**20 hrs**	**48 hrs**
NCT03075696[2]	**Glofitamab**	**C1D8 (42.8%)** **C1D15 (25.2%)** **C2 (26%)** C3+ (0.9%)	**13.5 hrs (range: 6-52 hrs)**	**30.5 hrs (range 0.5-317)**
NCT02500407[3]	**Mosunetuzumab**	**C1D1 (14.7%)** C1D8 (6.2%) **C1D15 (16.1%)** C2 (1.2%) C3+ (2.9%)	**24 hrs**	**48 hrs (1-20 days)**
NCT03888105[4]	**Odronextamab**	C1 step up	**NA**	**48 hrs (1-133 days)**

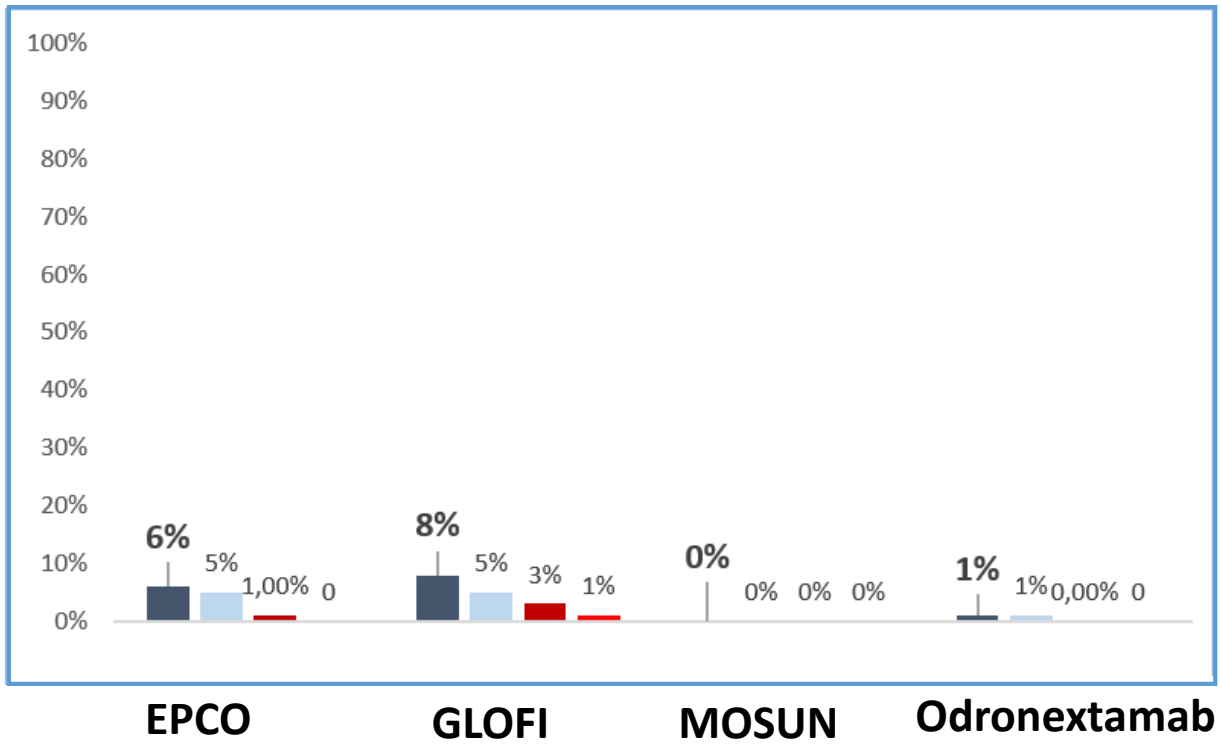
1. Thieblemont C, et al *J Clin Oncol.* 2022:JCO2201725. 2.Dickinson MJ, et al. *N Engl J Med.* 2022;387(24):2220-2231. 3.Budde LE, et al *J Clin Oncol.* 2022;40(5):481-491. 4Kim W-S, et al. *Blood.* 2022;140(Supplement 1):1070-1071.

Reported incidence

CRS



ICANS



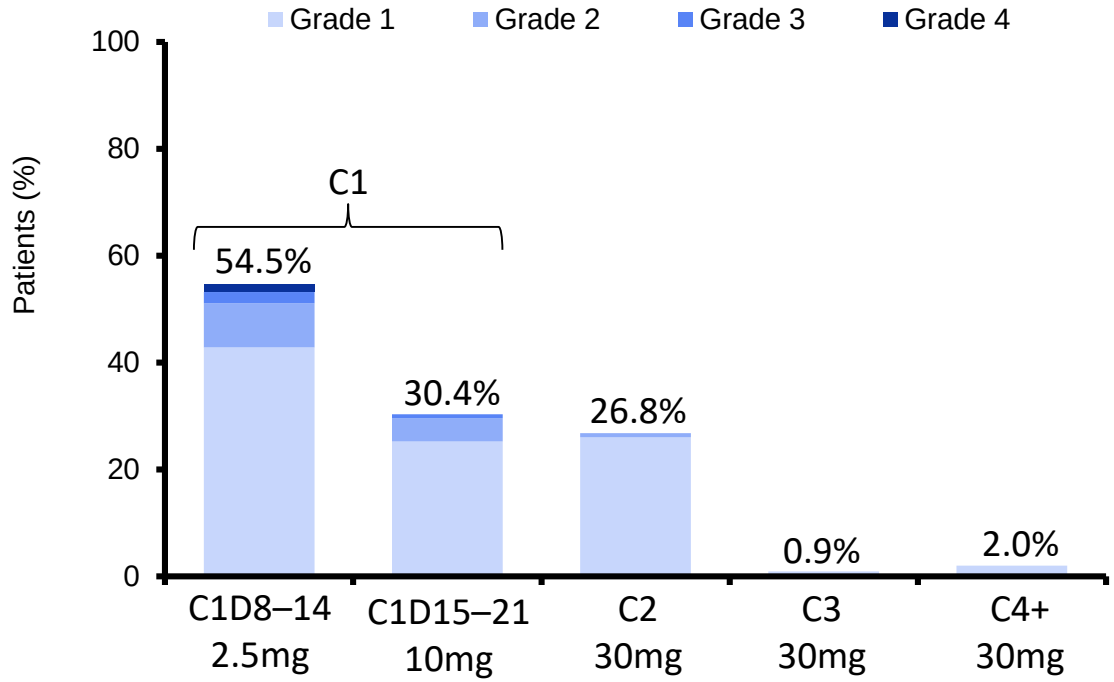
all Grade 1-2 Grade 3 Grade 4-5

Thieblemont C, et al *J Clin Oncol.* 2022:JCO2201725. Dickinson MJ, et al. *N Engl J Med.* 2022;387(24):2220-2231. Budde LE, et al *J Clin Oncol.* 2022;40(5):481-491.Kim W-S, et al. *Blood.* 2022;140(Supplement 1):1070-1071.

Cytokine release syndrome - Glofitamab

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

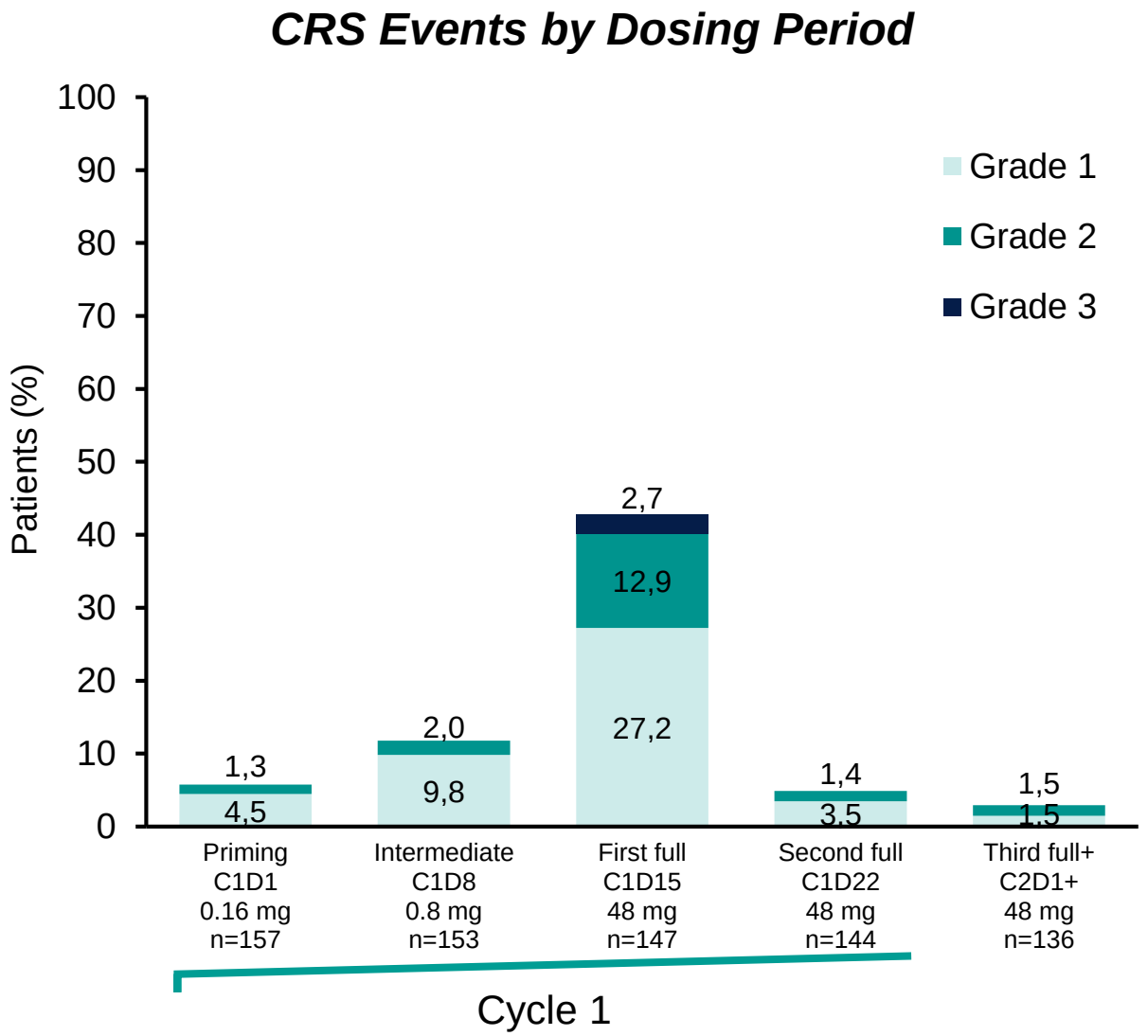
Dickinson M, et al. NEJM 2022 & EHA 2022 oral presentation

Cytokine release syndrome - Epcoritamab

	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



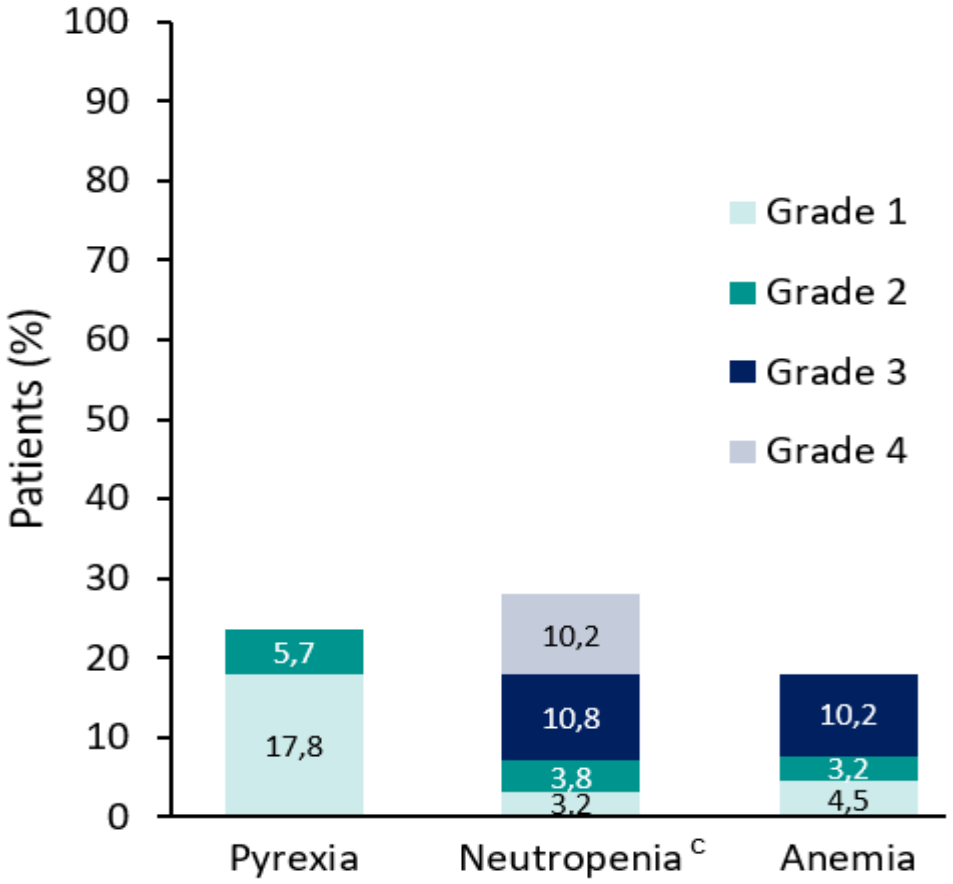
Thieblemont C, et al. J Clin Oncol 2022 and EHA oral presentation

Premedications

	Premed steroids + dephenydramine + paracetamol
Epcoritamab	Prednisone 100mg daily on days 1-4, days 8-11, days 15-18, days 22-25
Mosunetuzumab	20 mg dex C1D1, C1 D8, C1D15 , C2D1
Glofitamab	20 mg dex C1D1, C1 D8, C1D15 , C2D1, C3D1
Odronextamab	20 mg dex C1D1&D2, C1 D8&D9, C1D15&D16 , C2D1, C3D1 10mg dex 12-24h before C1D1, C1D8, C1D15

Neutropenia

		Grade ≥ 3 neutropenia
Schuster GO29781	Mosunetuzumab N=270	**42 (16%)**
Thieblemont GCT3013-01	Epcoritamab N=157	**33 (21%)**
Hutchings	Glofitamab N=171	**43 (25%)**
Bannerji	Odornextamab N=127	**NR**

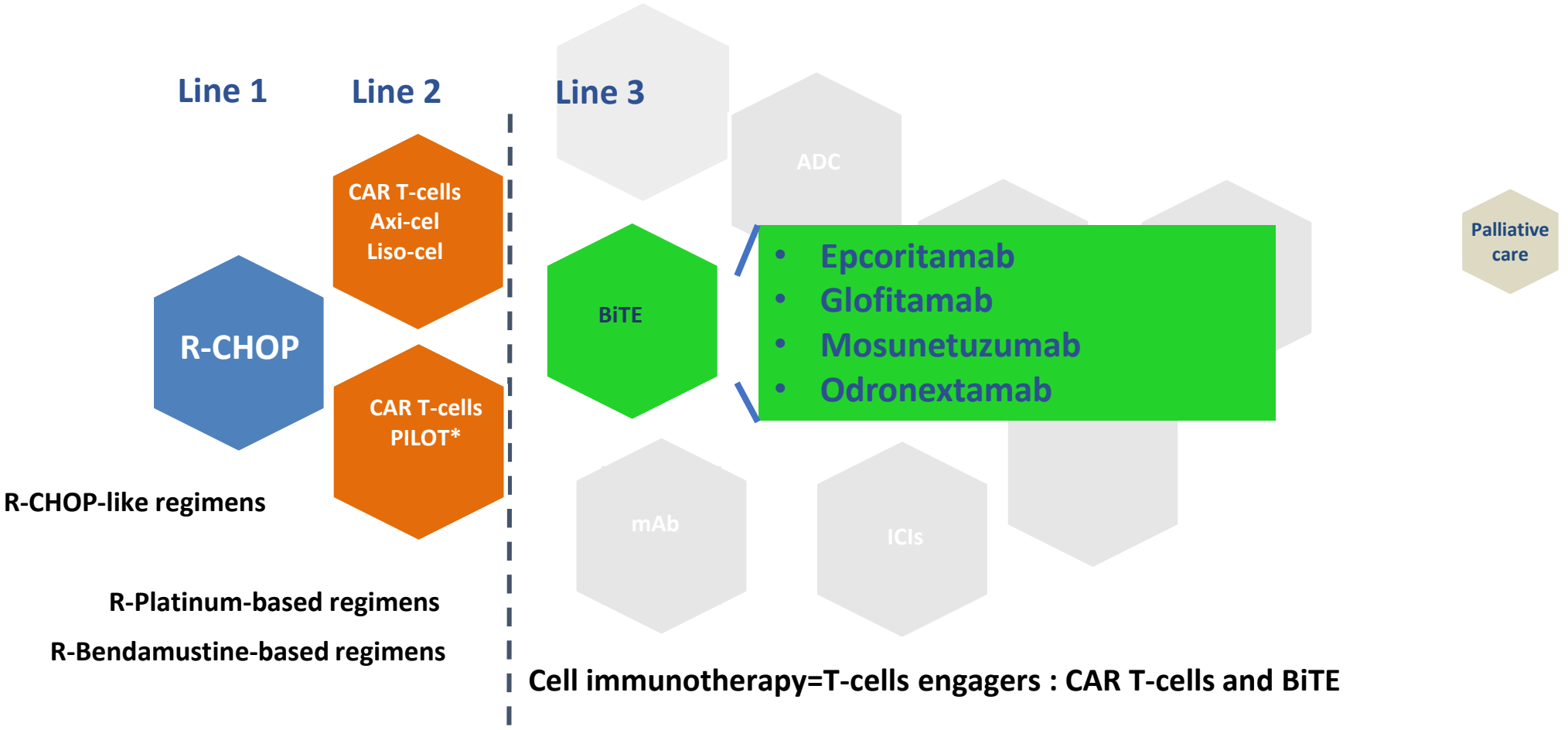


Thieblemont C, et al. J Clin Oncol 2022 and EHA oral presentation

Future and perspectives

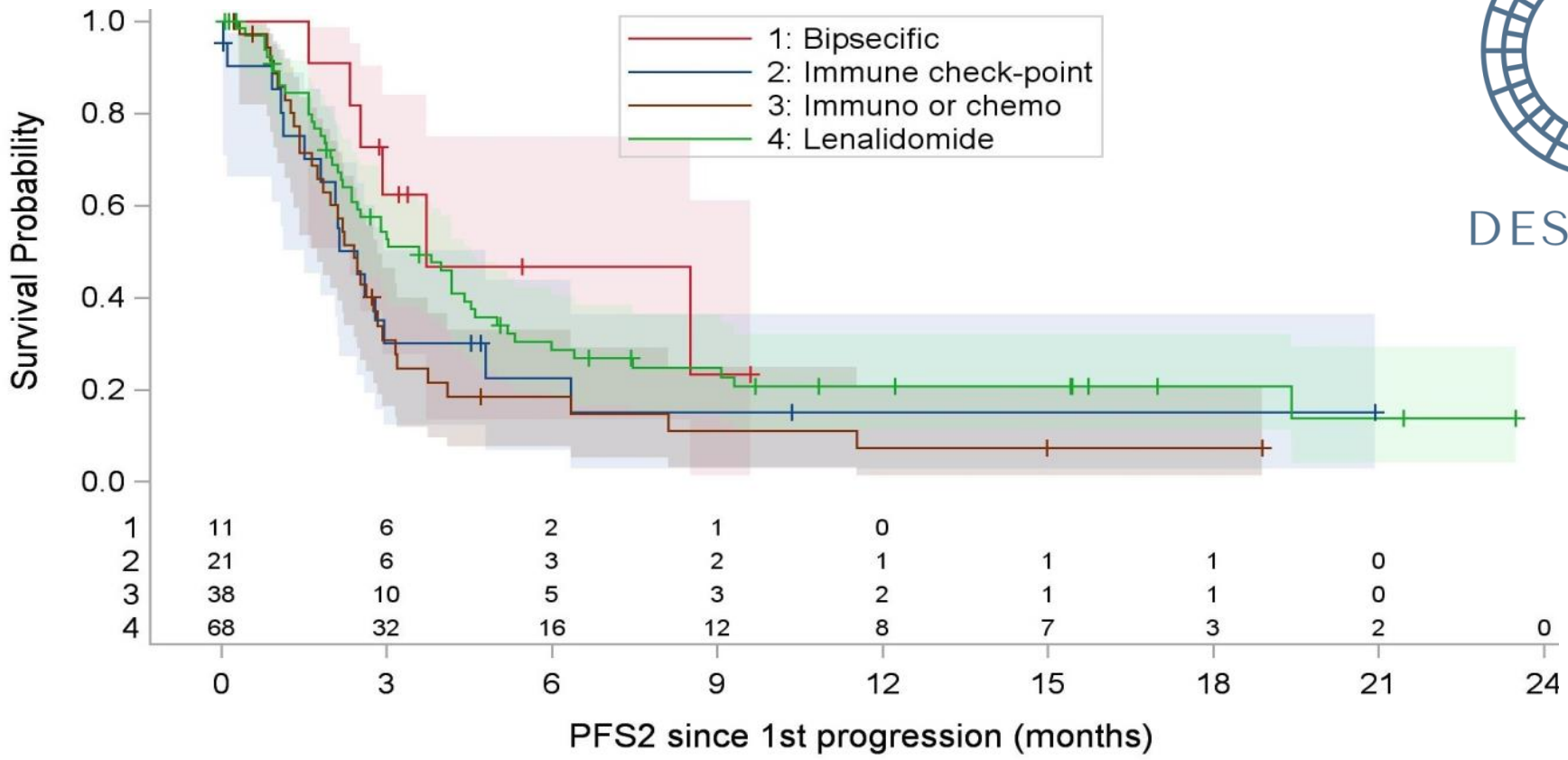
- Combining or sequencing?
- Can we move in first line ?

3rd line treatment



*Sehgal A et al. Lancet Oncol 2022

Relapse after CAR T cells



	No. of Subjects	Event	Censored	Median Survival (95%CL
Bipsecific	11	54.5 % (6)	45.5 % (5)	3.7 (2.3 ; NA)
Immune check-point	21	76.2 % (16)	23.8 % (5)	2.5 (1.5 ; 4.8)
Immuno or chemo	38	81.6 % (31)	18.4 % (7)	2.4 (1.7 ; 2.8)
Lenalidomide	68	72.1 % (49)	27.9 % (19)	3.6 (2.4 ; 4.5)

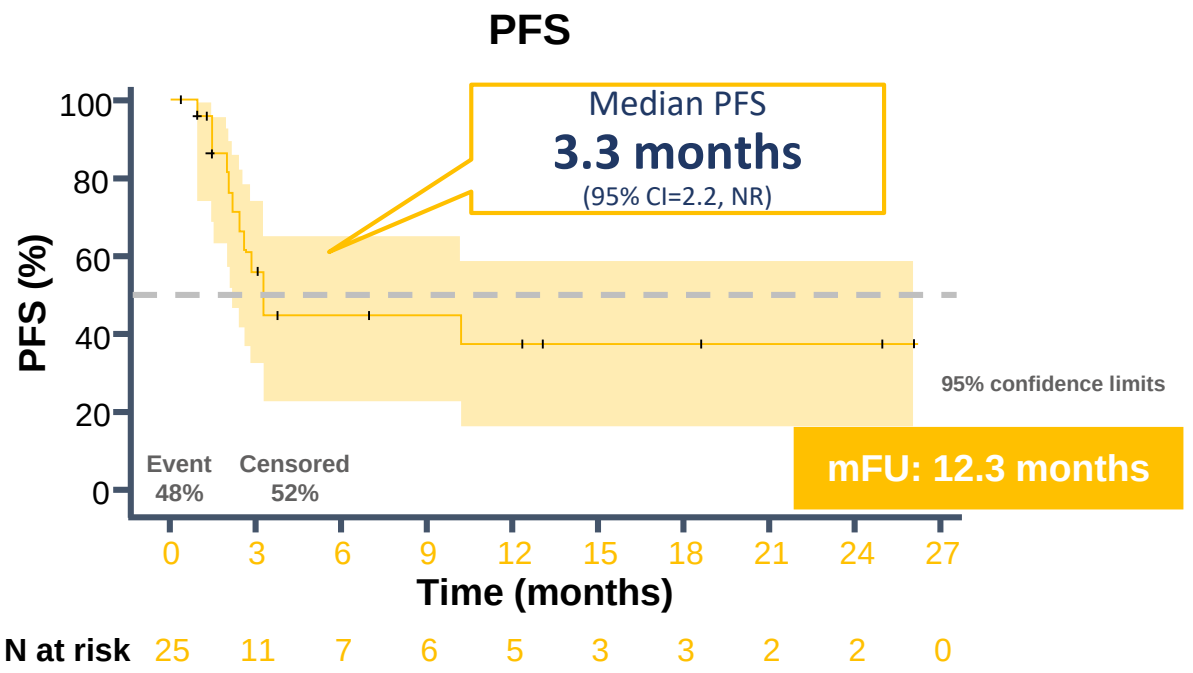
Di Blasi et al. ASH 2021, Blood 2022

CAR T-cells after BsAb treatment

DESCAR-T

Patients with aggressive LBCL
n=28

Outcomes post-CAR T	R/R LBCL subgroup (n=23)
CAR T received, % Axi-cel Tisa-cel	 72 28
ORR, % **CR** **PR**	**91.6** **45.8** **45.8**
Median PFS, mo (95% CI) 6-mo PFS, % (95% CI) 1-year PFS, % (95% CI)	3.3 (2.2, NR) 44.6 (22.4, 64.7) 37.2 (15.9, 58.7)
Median DOR, mo (95% CI) 1-year DOR, % (95% CI)	2.4 (1.4, NR) 40.7 (17.4, 63.1)



Initial results suggest CAR T may be effective as post-BsAb salvage therapy, however, longer follow-up in larger cohorts are needed

[a] n=20 DLBCL, n=2 FL, n=1 Grade 3b FL, n=3 MCL, n=2 other LBCL

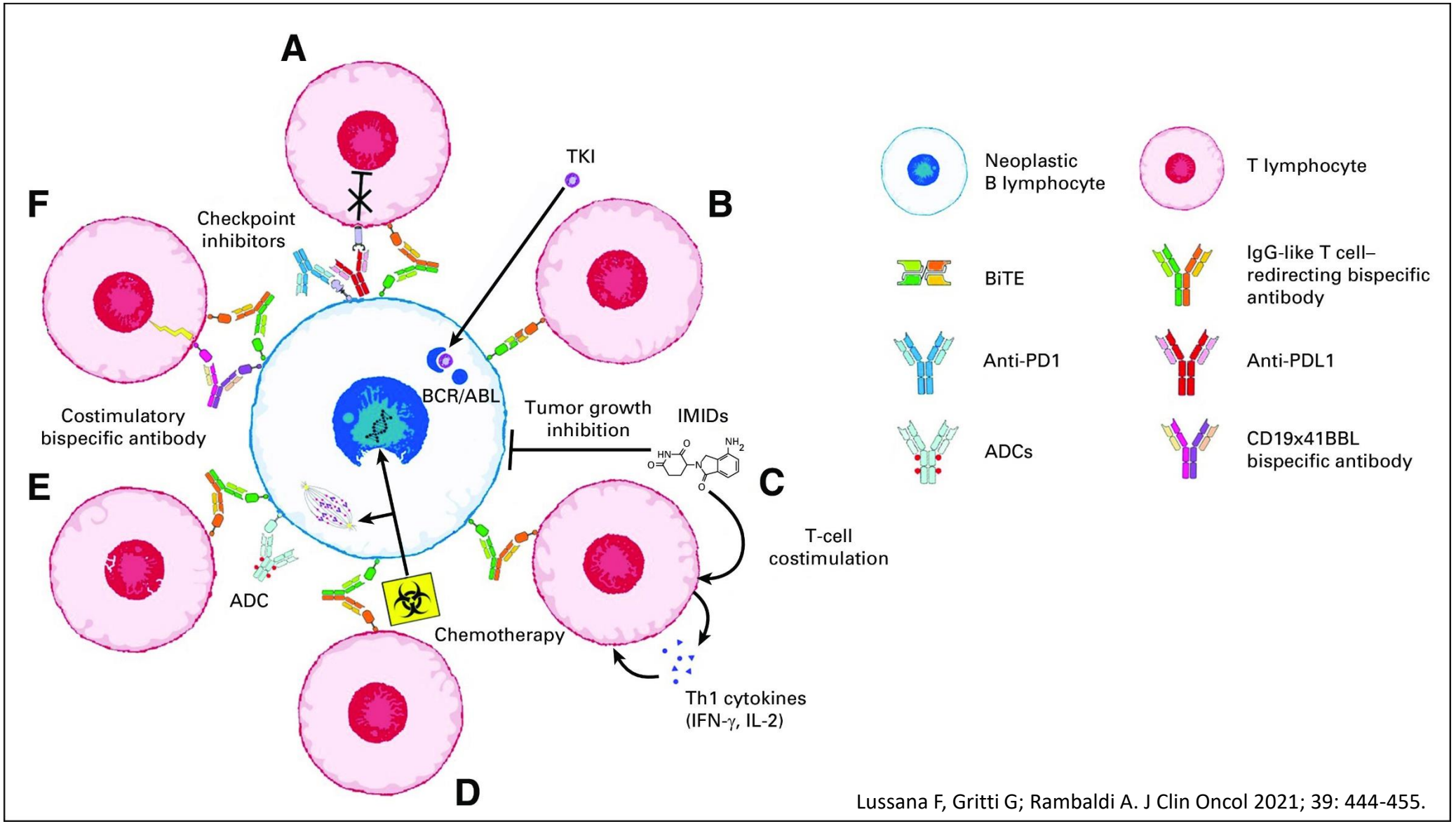
axi-cel: axicabtagene ciloleucel; BA: bispecific antibody; CAR: chimeric antigen receptor; CD: cluster of differentiation; CI: confidence interval; CL: confidence limit; CR: complete response; DOR: duration of response; NR: not reached; ORR: overall response rate; PD: progressive disease; PFS: progression-free survival; PR: partial response; SD: stable disease; tisa-cel: tisagenlecleucel

Crochet G, *et al.* ASH 2022 (Abstract 2026; poster).

MOSUN	**First line**	**Aggressive NHL**	Mosunetuzumab + CHOP or polatuzumab vedotin- CHP	Untreated NHL	Phase 1b/2	NCT03677141
		Indolent NHL	Mosunetuzumab (SC) + lenalidomide	FL and MZL	Phase 2	NCT04792502
GLOFI	**First line**	**Aggressive NHL**	Glofitamab + R-CHOP or Polatuzumab vedotin- R-CHP	Untreated DLBCL (young, high risk)	Phase 1/2	NCT04914741
	R/R in combination	**Indolent NHL**	Mosunetuzumab + lenalidomide vs glofitamab + **lenalidomide** ± obinutuzumab	R/R FL	Phase 1/2	NCT04246086
		Aggressive NHL	Mosunetuzumab **+ GemOx** or glofitamab + **GemOx**	R/R DLBCL or high grade DLBCL	Phase 1b	NCT04313608
			Glofitamab + **GemOx** vs R-GemOx	R/R DLBCL	Phase 3	NCT04408638
		NHL	Glofitamab + **atezolizumab** or **polatuzumab vedotin**	R/R NHL	Phase 1b	NCT03533283
			Glofitamab + **RO7227166**	R/R NHL	Phase 1	NCT04077723
			Mosunetuzumab or glofitamab in combination with **CC-220 and CC-99282**	R/R NHL	Phase 1b	NCT05169515
EPCO	**R/R or first line in combination**	**NHL**	Epcoritamab + R-DHAX/C Epcoritamab + GemOx Epcoritamab + R-Lenalidomide Epcoritamab + R-CHOP Epcoritamab + R-B	R/R DLBCL R/R DLBCL R/R FL Untreated DLBCL Untreated FL	Phase 1b/2	NCT04663347
	R/R in combination	**Aggressive NHL**	Epcoritamab vs R-GemOx or R-B	R/R DLBCL	Phase 3	NCT04628494
ODRO	**R/R in combination**	**NHL**	Odronextamab + cepilimab	R/R NHL	Phase 1	NCT02651662

For review. Barca et al. Frontiers in Immunology 2022

How to get deeper and more durable responses



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

Conclusions

- The CD3/CD20 bispecific antibodies show an antitumor activity which is unprecedented in heavily pretreated r/r B-NHL
- 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

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Cell ImmunoT program

Lymphoma Team

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