Sobi™ Satellite Symposium

ICML Congress 2025

Treatment sequencing in R/R DLBCL: Dissecting the emerging challenge from bench to bedside

Tuesday, 17 June 2025, 16:30 – 18:00

NP-42405

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Date of preparation: June 2025

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Faculty disclosures

	Andrew Davies	Romano Danesi	Gloria Iacoboni	Marek Trněný
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Introductions

Prof Andrew Davies (Chair)

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Southampton, UK

Professor Gloria Iacoboni

Vall d'Hebron Institute of Oncology,
Barcelona, Spain

Professor Romano Danesi

University of Milan,
Milan, Italy

Professor Marek Trněný

Charles University,
Prague, Czech Republic

Today’s agenda

Evolving strategies and challenges in R/R DLBCL
Andrew Davies (UK)

Can preclinical data help? Insights from pharmacology
Romano Danesi (Italy)

Learnings from clinical trials and RWE
Gloria Iacoboni (Spain)

Clinical decision-making in practice
Marek Trněný (Czech Republic)

Treatment sequencing on the horizon: What is next?
Andrew Davies (UK)

Q&A Session and Closing Remarks
All, Andrew Davies (Chair)

Evolving strategies, evolving challenges in relapsed/refractory diffuse large B-cell lymphoma

Professor Andrew Davies

University of Southampton,
Southampton, United Kingdom

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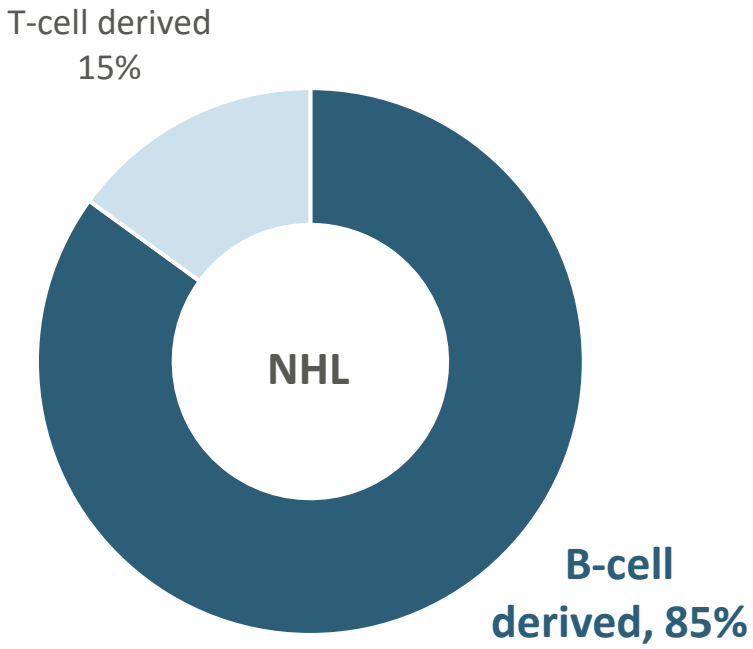
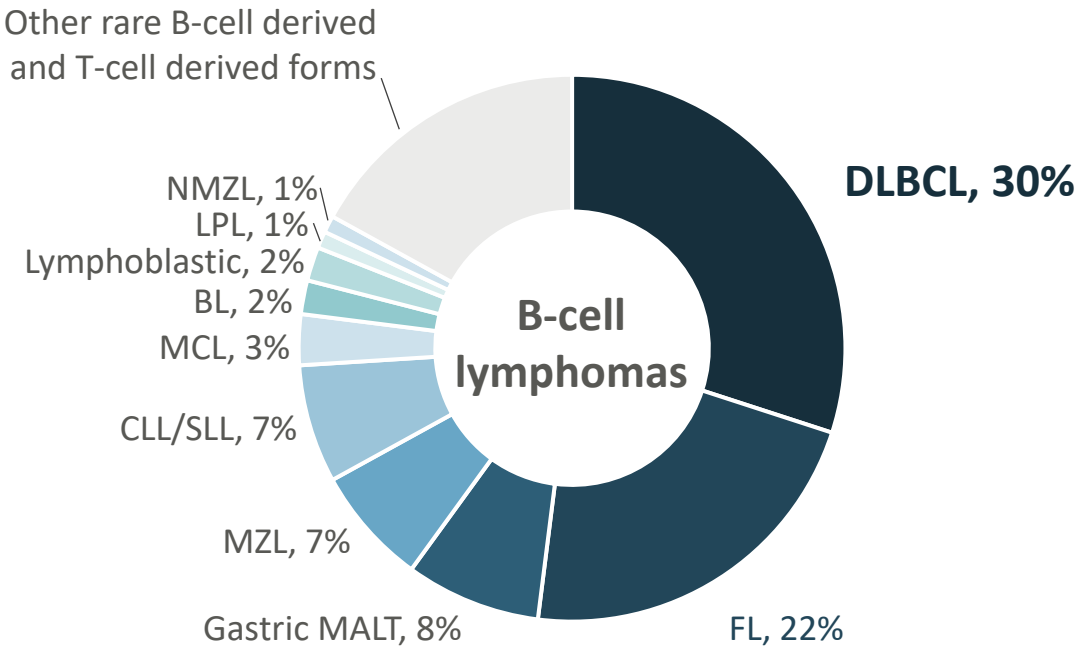
DLBCL is the most common type of mature B-cell neoplasm[1–3]





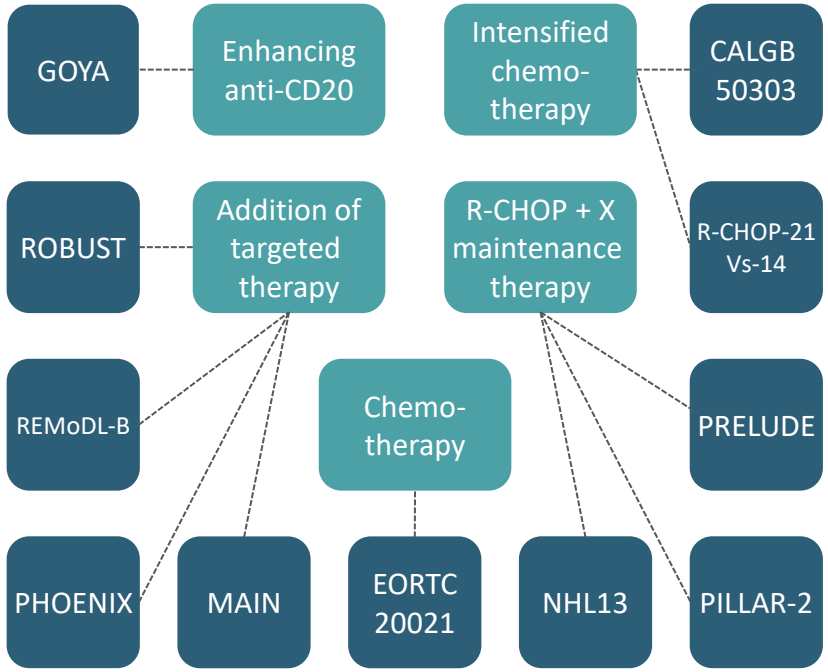
The WHO has classified >100 **NHL types**. There are **2 major NHL groups** arising from **transformed B-cells and T-cells**[1]

Although mature B-cell neoplasms encompass **many unique diagnostic subtypes, DLBCL is the most common**[2,3,*]

*Pie chart represents the percentages for B- and T-cell derived NHL; T-cell derived types are not distinguished (shown in light grey).
BL, Burkitt lymphoma; CLL, chronic lymphocytic leukaemia; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; LPL, lymphoplasmacytic lymphoma; MALT, mucosa-associated lymphoid tissue lymphomas; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; NMZL, nodal marginal zone lymphoma; NHL, non-Hodgkin lymphoma; SLL, small-cell lymphocytic lymphoma; WHO, World Health Organization.

1. Tognon et al. *Cancer* 2015 **2.** Ma et al. *Haematologica* 2022 **3.** Leukemia and Lymphoma Society 2022.

Treatment options for 1L DLBCL had not advanced for 20 years, and many trials failed to show an efficacy benefit[1-11]



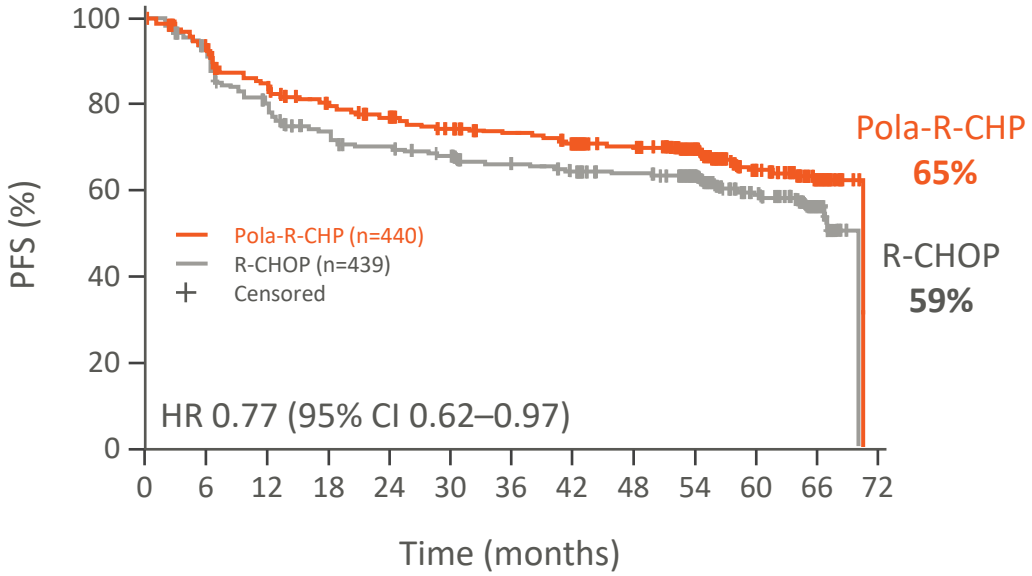
NP-42406

CHOP, cyclophosphamide, doxorubicin, vincristine and prednisolone; DLBCL, diffuse large B-cell lymphoma; R, rituximab.

1. Vitolo et al. *J Clin Oncol* 2017 **2.** Vitolo et al. *Hematol Oncol* 2019 **3.** Davies et al. *Lancet Oncol* 2019 **4.** Younes et al. *J Clin Oncol* 2019 **5.** Seymour et al. *Haematologica* 2014 **6.** Aurer et al. *Eur J Haematol* 2011 **7.** Bartlett et al. *J Clin Oncol* 2019 **8.** Cunningham et al. *Lancet* 2013 **9.** Crump et al. *J Clin Oncol* 2016 **10.** Witzig et al. *Ann Oncol* 2018 **11.** Jaeger et al. *Haematologica* 2015.

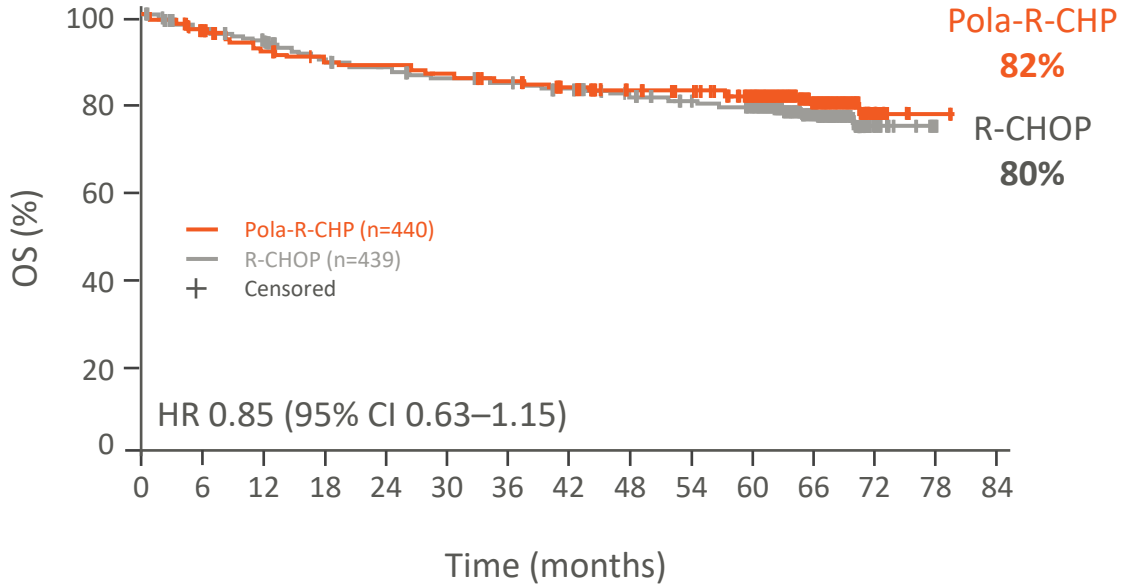
Pola-R-CHP, the only new treatment option approved in 1L DLBCL in recent years[1]

5-year PFS



No. at risk													
Pola-R-CHP	440	407	357	335	318	303	292	280	258	213	100	56	NE
R-CHOP	439	391	332	302	287	274	258	251	240	192	95	54	NE

5-year OS



No. at risk															
Pola-R-CHP	440	424	399	389	381	373	366	355	343	338	319	124	12	1	NE
R-CHOP	439	415	403	382	372	361	357	347	338	329	311	128	13	1	NE

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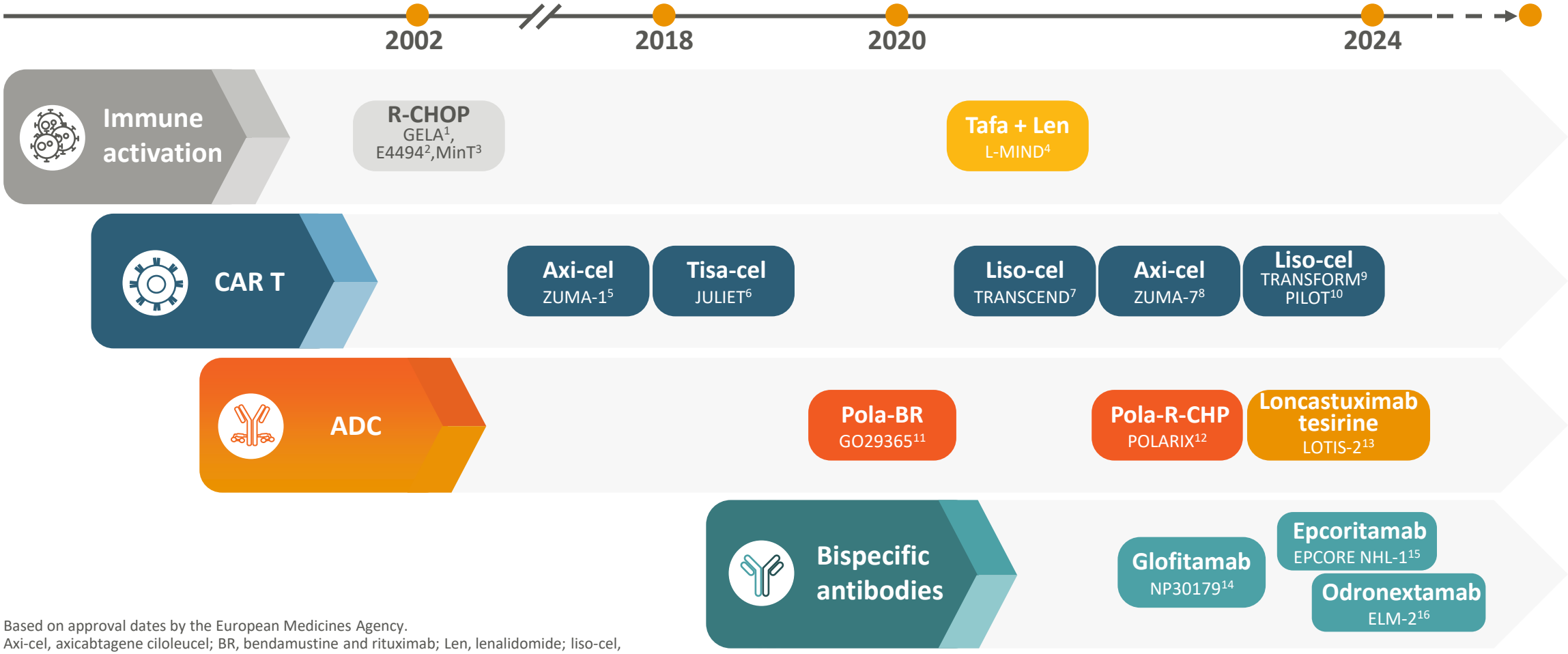
1L, first-line; CI, confidence interval; DLBCL, diffuse large B-cell lymphoma; HR, hazard ratio; NE, no event; OS, overall survival; PFS, progression-free survival; Pola, polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin, prednisone; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone.

1. Salles et al. ASH 2024; Oral presentation #469.

Since 2017, nine therapies with varying mechanisms of action and targets have been approved in DLBCL[1–16]



Based on approval dates by the European Medicines Agency.
Axi-cel, axicabtagene ciloleucel; BR, bendamustine and rituximab; Len, lenalidomide; liso-cel, lisocabtagene maraleucel; pola, polatuzumab vedotin; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; tafa, tafasitamab; tisa-cel, tisagenlecleucel.

1. Coiffier et al. *N Engl J Med* 2002 **2.** Habermann et al. *J Clin Oncol* 2006 **3.** Clinicaltrials.gov NCT00400907 **4.** Clinicaltrials.gov NCT02399085 **5.** Clinicaltrials.gov NCT02348216 **6.** Clinicaltrials.gov NCT02445248 **7.** Clinicaltrials.gov NCT02631044 **8.** Clinicaltrials.gov NCT03391466 **9.** Clinicaltrials.gov NCT03575351 **10.** Clinicaltrials.gov NCT03483103 **11.** Clinicaltrials.gov NCT02257567 **12.** Clinicaltrials.gov NCT03274492 **13.** Clinicaltrials.gov NCT03589469 **14.** Clinicaltrials.gov NCT03075696 **15.** Clinicaltrials.gov NCT03625037 **16.** Clinicaltrials.gov NCT03888105.

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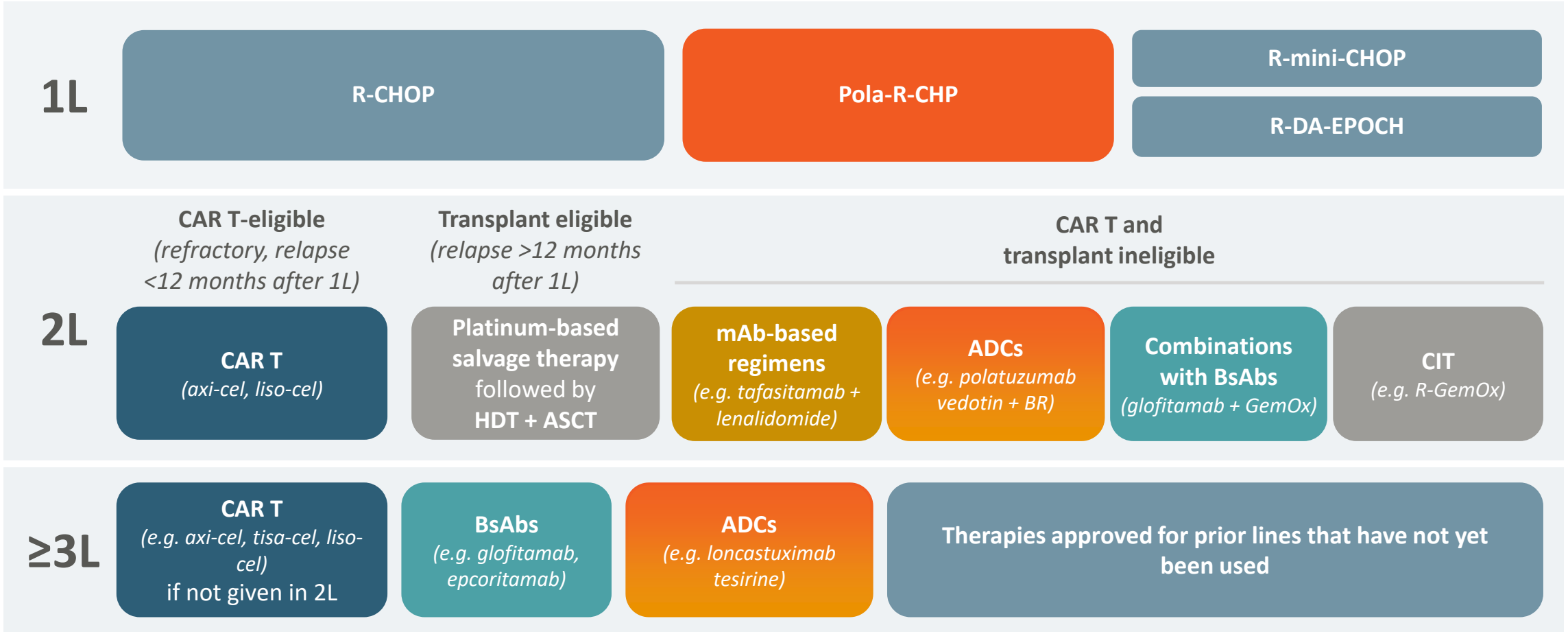
Numerous treatment options are now available for DLBCL in each line[1–9]



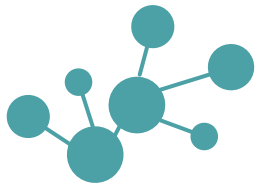
ADC, antibody-drug conjugate; ASCT, autologous stem cell transplantation; axi-cel, axicabtagene ciloleucel; BR, bendamustine and rituximab; BsAb, bispecific antibody; CAR T, chimeric antigen receptor T-cell therapy; CIT, chemo-immunotherapy; DLBCL, diffuse large B-cell lymphoma; HDT, high-dose therapy; L, line; liso-cel, lisocabtagene maraleucel; mAb, monoclonal antibody; pola, polatuzumab vedotin; R-CH(O)P, rituximab, cyclophosphamide, doxorubicin, (vincristine), and prednisone; R-DA-EPOCH, rituximab, dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin; R-GemOx, rituximab, gemcitabine, and oxaliplatin; tisa-cel, tisagenlecleucel. **1.** Sehn & Salles *N Engl J Med* 2021 **2.** Frontzek et al. *Ther Adv Hematol* 2022 **3.** Peyrade et al. *Blood* 2010 **4.** Polivy SmPC 2023 **5.** Columvi SmPC 2023 **6.** Tepkinly SmPC 2023 **7.** Zynlonta SmPC 2023 **8.** Bartlett et al. *J Clin Oncol* 2019 **9.** Roche Press release 2025.

NP-42406

The changing landscape leads to a paradox of choice[1]

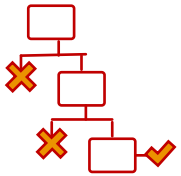
- **Treatment options** for R/R DLBCL are **increasing, but not all therapies are available in all countries**
- Many factors, including **patient and disease characteristics and prior therapies**, should be considered during the treatment journey

Optimal sequencing and combination strategies are yet to be established
There is no evidence-based consensus on how to best order these agents



More choice

More treatment options



More challenging to manage R/R DLBCL

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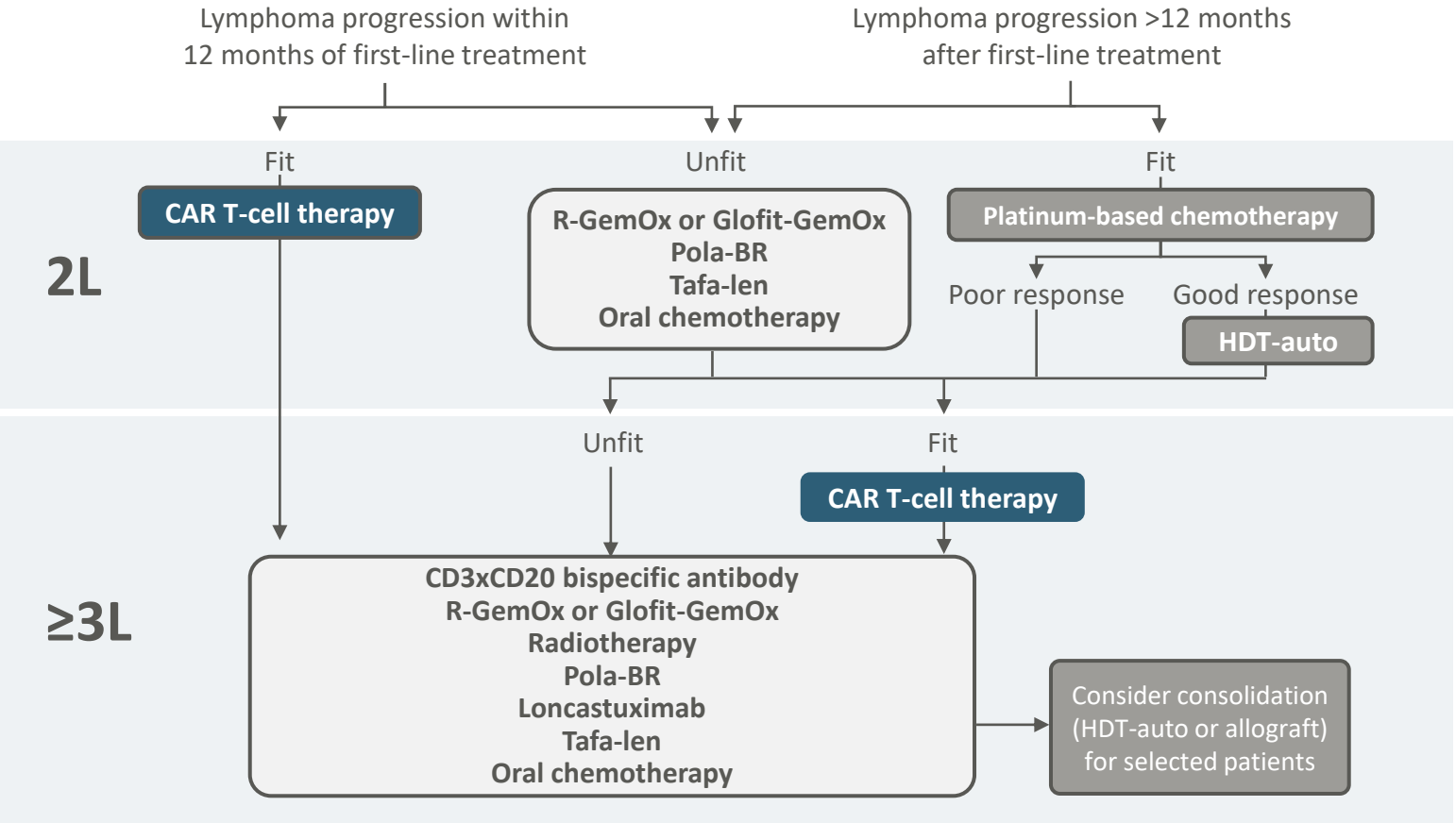
DLBCL, diffuse large B-cell lymphoma; R/R, relapsed or refractory.

1. Brooks & Caimi. *Blood Rev* 2023.

Several treatment algorithms have been proposed, but there is no consensus[1]

R/R DLBCL treatment algorithm, Chaganti et al[1]



While CAR-T is now established as a key treatment strategy in 2L, the choice of a sequencing algorithm is highly dependant on **availability** and **location** among **other factors**

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2L, second line; 3L, third line; BR, bendamustine and rituximab; CAR-T, chimeric antigen receptor T-cell therapy; DLBCL, diffuse large B-cell lymphoma; GemOx, gemcitabine and oxaliplatin; glofit, glofitamab; HDT-auto, haematopoietic stem cell transplantation with autologous stem cell transplantation; len, lenalidomide; Pola, polatuzumab vedotin; R, rituximab; R/R, relapsed or refractory; Tafa, tafasitamab.

1. Chaganti et al. *Br J Haematol* 2025.

Many factors impact how we sequence treatments in R/R DLBCL[1]

Disease factors
Biomarkers Clinical presentation
Refractoriness Antigen expression

Healthcare facility factors
Processing Logistics

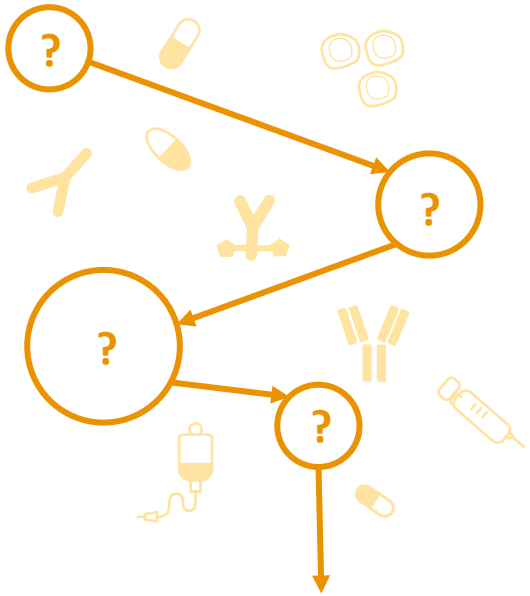
Treatment factors
Efficacy Tolerability
Sequencing Cumulative toxicity
Schedule of administration

Patient factors
Age Fitness
Comorbidities Patient preference

Geographic factors
Access to care Drug availability

Socioeconomic factors
Family/social support

Optimal sequence of agents for an individual patient with **R/R DLBCL**



Potential curability

NP-42406

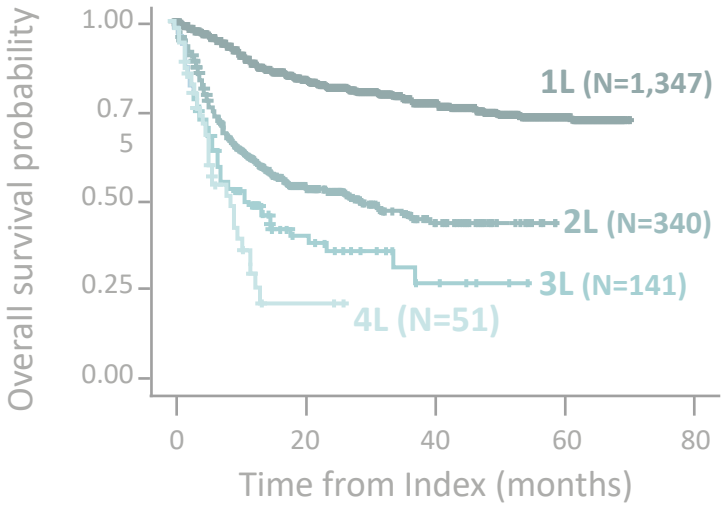
DLBCL, diffuse large B-cell lymphoma; R/R, relapsed or refractory.
1. Brooks & Caimi. *Blood Rev* 2023.

Treatment challenges in DLBCL: Factors of poor prognosis[1–8]

High-risk features[1–5]

- Primary refractory[1]
- DH/TH disease[2,3]
- Transformed[4]
- HGBL[5]

Increasing lines of therapy reduce OS[6]



Patients in later lines of therapy have lower 1- and 3-year OS vs 1L[6]

Early relapse after 1L CIT[7,8]

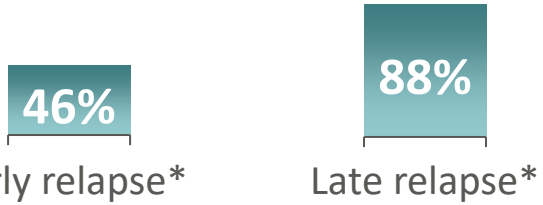
<1 year **Relapse[7]** >1 year

24.2 mos Median OS

42.65 mos Median OS

13% Patients with early relapse alive after 8 years of FU[7]

ORR to salvage CIT[8]



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*Early defined as <1 year after diagnosis, late as >1-year post-diagnosis. CIT, chemo-immunotherapy; DH/TH, double-hit/triple-hit; DLBCL, diffuse large B-cell lymphoma; FU, follow-up; HGBL, high-grade B-cell lymphoma; L, line of therapy; mos, months; ORR, overall response rate; OS, overall survival.

1. Crump et al. *Blood* 2017 **2.** Herrera et al. *J Clin Oncol* 2017 **3.** McPhail et al. *Haematologica* 2018 **4.** Wagner-Johnston et al. *Blood* 2015 **5.** Olszewski et al. *Blood* 2022 **6.** Sineshaw et al. *Cancer Med* 2024 **7.** Chen et al. *Clin Exp Med* 2024 **8.** Gisselbrecht et al. *J Clin Oncol* 2010.

CAR-T may not be the ultimate solution in R/R DLBCL[1–5]

2L CAR-T cell therapies[1–3]

	Axi-cel[1]	Liso-cel[2]
ORR	83%	87%
PFS	14.7 mo	NR

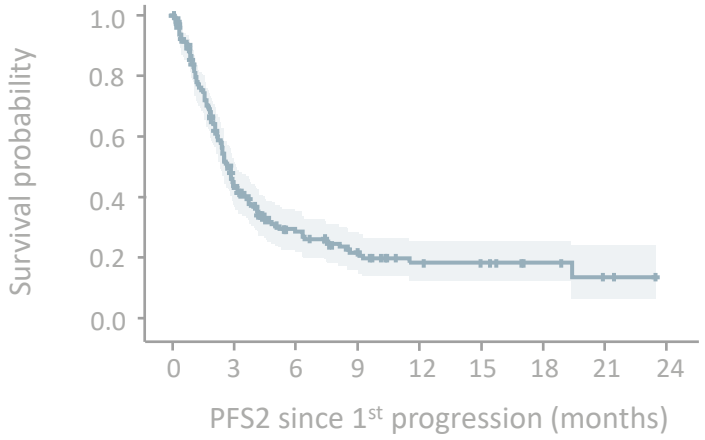
CAR-T therapies significantly improve survival in 2L[1,2]

Limitations[3]

Availability and manufacturing time

Adverse events (e.g. CRS, ICANS)

PFS post-CAR-T failure in the DESCAR-T registry[4]



After failing CAR T-cell therapy, **mPFS was 2.8 months and mOS was 5.2 months**[4]

Prognostic factors for OS after axi-cel or tisa-cel[5]

IPI at apheresis*
≥2 vs 0–1 (HR: 2.18)

Response to CAR-T*
SD/PD vs CR/PR (HR 3.08)

Histotype*
Other vs PMBCL/tFL (HR: 4.54)

ctDNA
6-mos OS with bispecific antibodies post-CAR-T:
Low ctDNA†: **68%**
High ctDNA†: **20%**

A 5-variable tool (ECOG PS, Hb, LDH, EN sites, time from CAR-T to PD) may predict OS post–3L CAR-T[6]

*Using a multivariable Cox model. †Prior to bispecific therapy. Axi-cel, axicabtagene ciloleucel; CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; CRS, cytokine release syndrome; ctDNA, circulating tumour DNA; ECOG PS, Eastern Cooperative Oncology Group performance status; EN, extranodal; Hb, haemoglobin; HR, hazard ratio; ICANS, immune effector cell-associated neurotoxicity syndrome; IPI, International Prognostic Index; L, line of therapy; LDH, lactate dehydrogenase; liso-cel, lisocabtagene maraleucel; ORR, overall response rate; (m)OS, (median) overall survival; (m)PFS, median progression-free survival; PD, progressive disease; PMBCL, primary mediastinal B-cell lymphoma; PR, partial response; SD, stable disease; tFL, transformed follicular lymphoma; tisa-cel, tisagenlecleucel.

1. Locke et al. *N Engl J Med* 2022 **2.** Abramson et al. *Blood* 2023 **3.** Duarte C & Kamdar M. *Am Soc Clin Oncol Educ Book* 2023 **4.** Di Blasi et al. *Blood* 2022 **5.** Dodero et la. *Br J Haematol* 2024 **6.** Iacoboni et al. *J Hematol Oncol* 2024.

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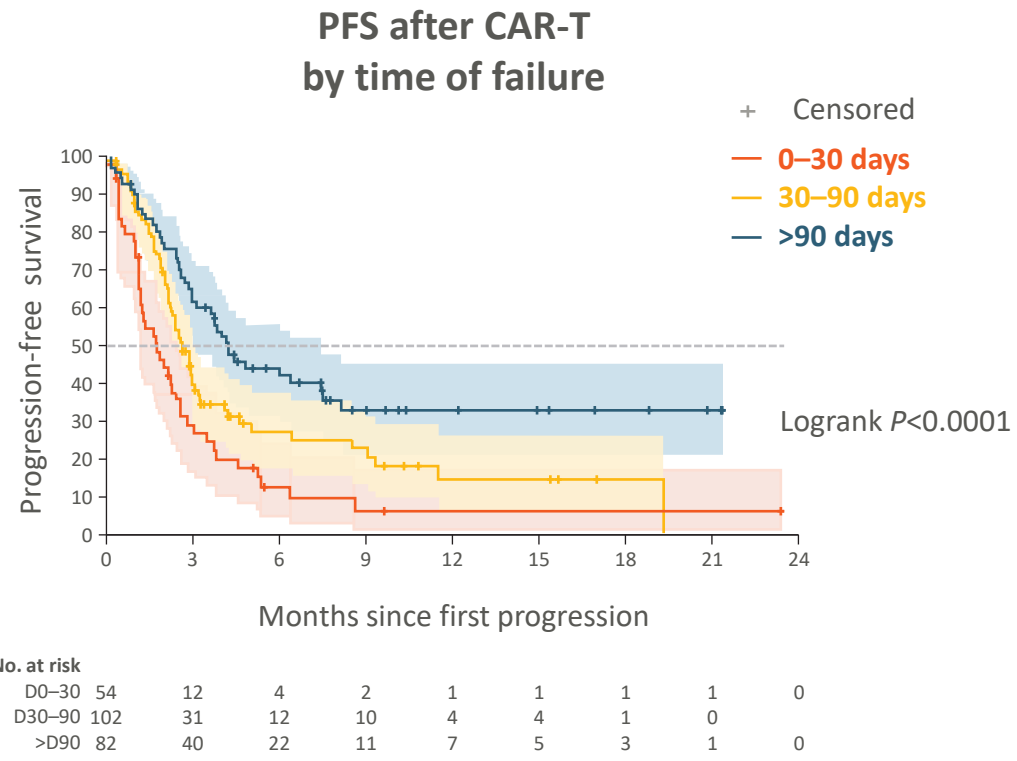
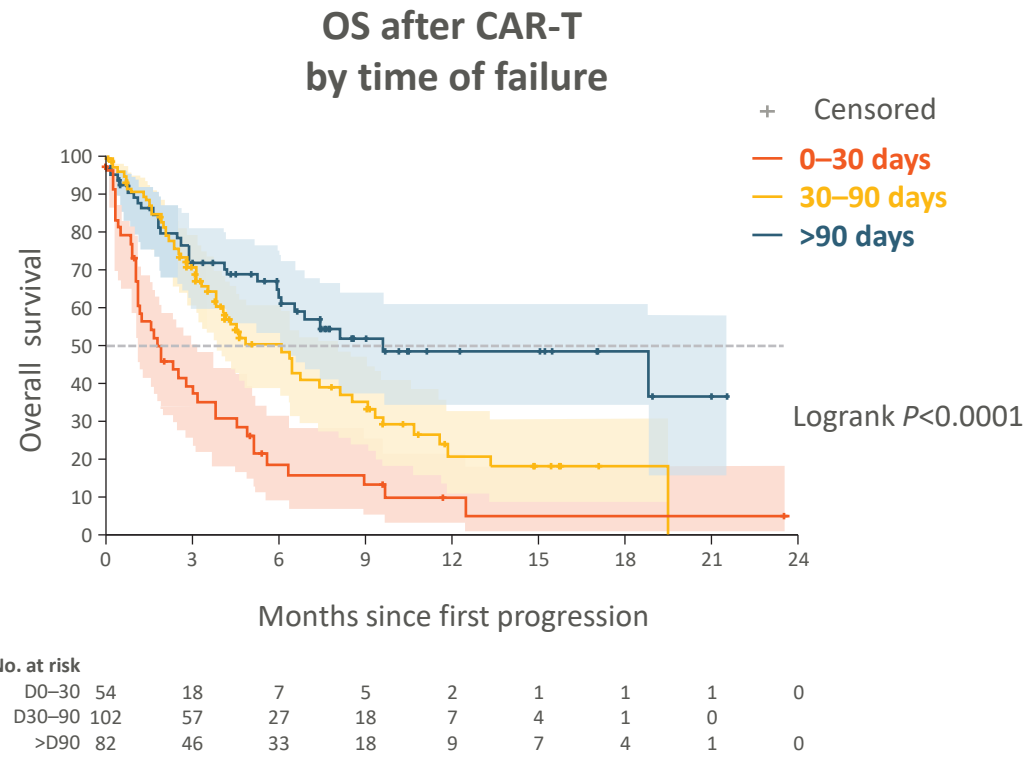
Outcomes are particularly poor for patients who progress very early after CAR-T infusion[1]





PFS2 **0–30 days, 1.7 months** | **30–90 days, 2.6 months** | **>90 days, 4.2 months**

OS2 **0–30 days, 1.9 months** | **30–90 days, 6.1 months** | **>90 days, 9.6 months**

CAR-T, chimeric antigen receptor T-cell therapy; D, day; No., number; OS, overall survival; OS2, overall survival from second-line treatment; PFS, progression-free survival; PFS2, progression-free survival from second-line treatment.

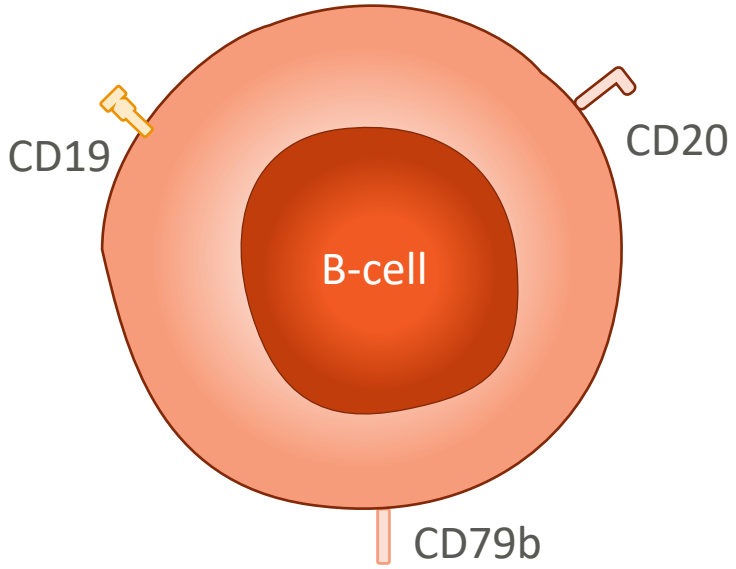
1. Di Blasi et al. *Blood* 2022.

NP-42406

Antigen expression as a guide to treatment sequencing in DLBCL[1–9]

CD19-targeted therapies

- **CAR T-cell therapies[1-3]**
- **Tafasitamab[4]**
- **Loncastuximab tesirine[5]**



CD20-targeted therapies

- **Bispecific antibodies[6,7]**
- **Rituximab[8]**

CD79b-targeted therapies

- **Polatuzumab vedotin[9]**

NP-42406

CAR, chimeric antigen receptor; DLBCL, diffuse large B-cell lymphoma.
1. Yescarta SmPC 2024 **2.** Kymriah SmPC 2024 **3.** Breyanzi SmPC 2024 **4.** Minjuvi SmPC 2024 **5.** Zynlonta SmPC 2024 **6.** Columvi SmPC 2024 **7.** Tepkinly SmPC 2024 **8.** MabThera SmPC 2024 **9.** Polivy SmPC 2023.

Can we use CD19-targeted agents before CAR-T?[1,2]

Impact of CD19 expression post-tafasitamab on response to CAR-T cell therapy[1]

12 biopsies of lymph node tumours from the L-MIND study[1]
(4 pre- and 8 post-tafasitamab biopsies from six patients)

CD19 expressed in all biopsies

No somatic mutations in the CD19 gene and CD19 exon skipping

No impact of duration of tafasitamab therapy

The dynamics of epitope occupancy are not well characterised

CD19 expression appears **maintained after Tafa + Len** treatment, potentially allowing a subsequent CD19-directed therapy

Initial data support retained CD19 expression after treatment with Loncastuximab[2]

14 patients received CAR-T after Loncastuximab in LOTIS-2 trial

10 paired biopsies were available

10/10 of patients with repeat biopsies* between Loncastuximab tesirine treatment and CAR-T infusion† had **positive CD19 expression** after **Loncastuximab tesirine**

Median time between Loncastuximab tesirine and CAR-T infusion: **120 days**

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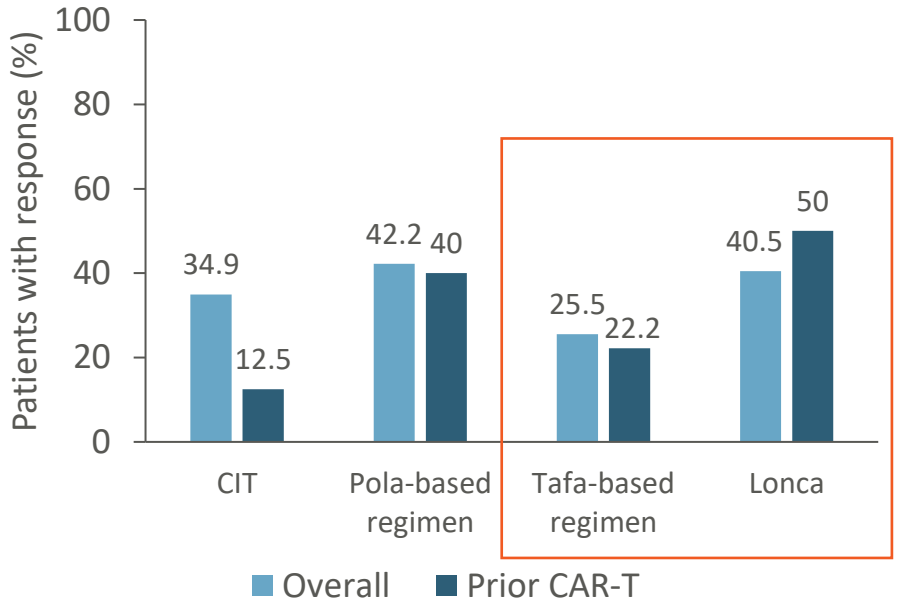
*10/14 patients had repeat biopsies between Loncastuximab tesirine treatment and CAR-T administration for IHC staining. †Axi-cel: 36%, liso-cel: 21%, tisa-cel: 14%, investigational anti-CD19: CAR-T 29%.
Axi-cel, axicabtagene ciloleucel; CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; IHC, immunohistochemistry; Len, lenalidomide; liso-cel, lisocabtagene maraleucel; Loncastuximab, loncastuximab tesirine; ORR, overall response rate; PR, partial response; Tafa, tafasitamab; tisa-cel, tisagenlecleucel.

1. Duell et al. *Blood* 2024 **2.** Thapa et al. *Blood Adv* 2020.

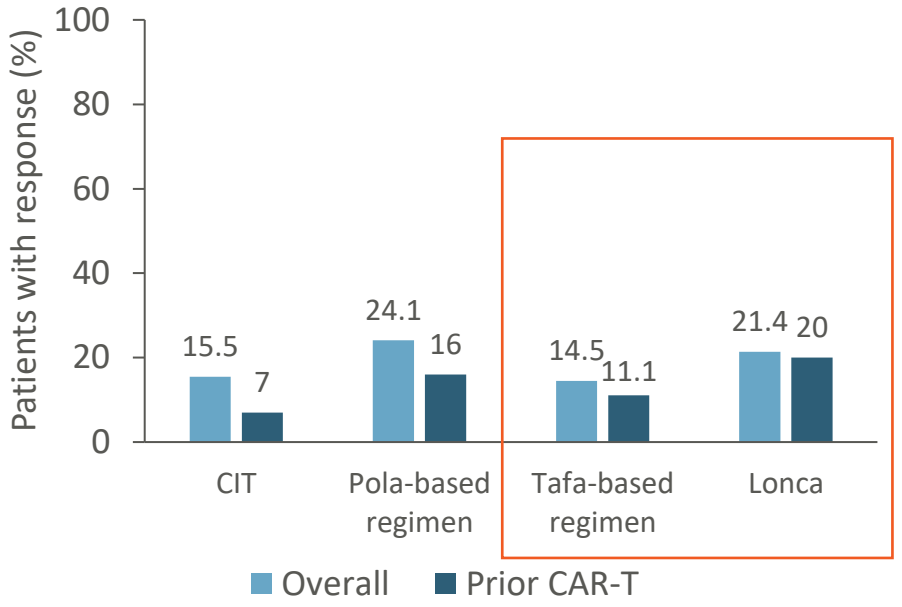
Can we use CD19-targeted agents after CAR-T?[1]

CD19-targeted agents appear to have efficacy when used after CAR-T
However, outcomes between therapies cannot be compared as baseline characteristics differed

ORR* to 2L+ treatment overall and in R/R LBCL patients with prior CAR-T



CR* to 2L+ treatment overall and in R/R LBCL patients with prior CAR-T



*Treatment response and progression were abstracted from medical records (e.g., PET/PET-CT/CT scans) and reviewed and validated by an assigned study clinician.
2L, second line; CAR-T, chimeric antigen receptor T-cell therapy; CIT, chemoimmunotherapy; CR, complete response; CT, computed tomography; LBCL, large B-cell lymphoma; Lonca, loncastuximab tesirine; ORR, overall response rate; OS, overall survival; PET, positron emission tomography; Pola, polatuzumab vedotin; R/R, relapsed or refractory; Tafa, tafasitamab.

1. Nastoupil et al. *Clin Lymphoma Myeloma Leuk* 2025.

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What is the importance of CD20 expression in decision making?[1–3]

New data are emerging on the changes in expression of CD20 with novel therapies and on its impact on outcomes, to be further explored[1-3]

- Poor outcomes after epcoritamab and glofitamab treatment have been observed in patients without detectable CD20, potentially representing an emerging unmet need[1]

- CD20 loss was common in patients who relapsed or progressed after glofitamab[2,3]

- Additional data are needed to understand how this could impact treatment sequencing in DLBCL in the future[3]

NP-42406

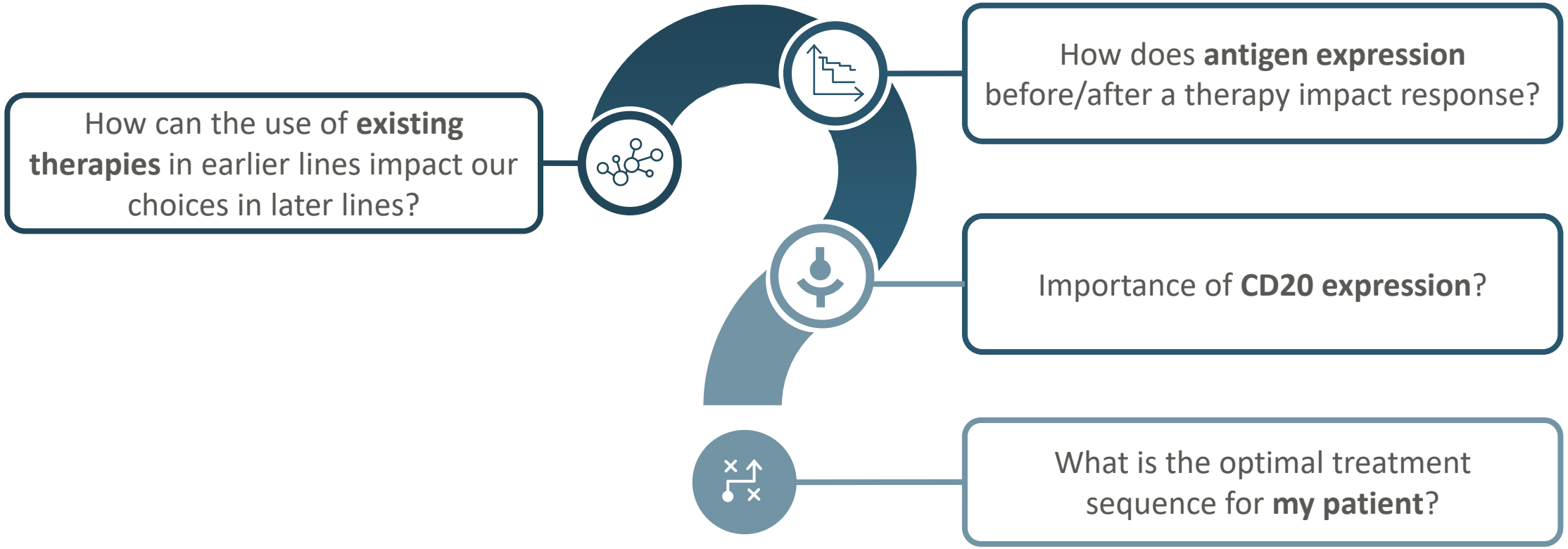
*Among 22 patients with available biopsies, n=10 converted from $CD20^+$ to $CD20^-$; n=2 remained persistently $CD20^-$; n=10 had unknown pretreatment status.
CR, complete response; DLBCL, diffuse large B-cell lymphoma; mos, months; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response.
1. Brooks et al. ASH 2024; Oral presentation #111 **2.** Grigg et al. *Br J Haematol* 2024 **3.** Carlo-Stella *Br J Haematol* 2024.

Summary

- The treatment landscape of R/R DLBCL has changed extensively in the past few years and new challenges are emerging
- Our clinical choices depend on multiple parameters, including patient and disease related factors, guidelines, efficacy and safety and local drug availability
- Antigen expression is rising as a new key element for treatment sequencing decisions
- Increasing data are available to support clinical decisions, but key evidence is still missing to confidently navigate treatment sequencing in an increasingly complex environment

NP-42406

There are many challenges and open questions in DLBCL



NP-42406

ADC, antibody-drug conjugate; CAR, chimeric antigen receptor; DLBCL, diffuse large B-cell lymphoma.

Can preclinical data shed a light on treatment sequencing?

Professor Romano Danesi

University of Milan, Milan, Italy

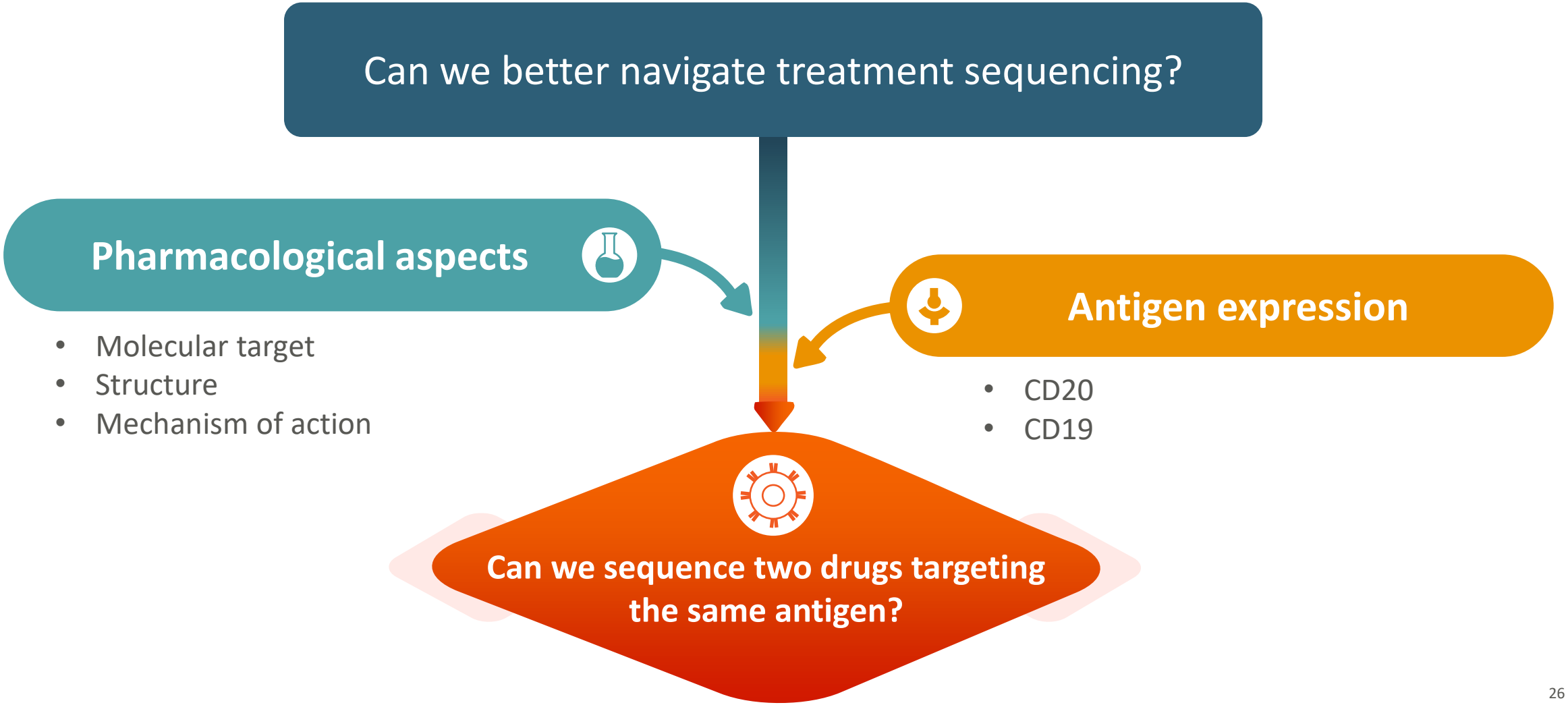
NP-42407

When considering treatment sequencing, how often do you rely on pharmacological properties (drug structure, mechanism of action and pharmacology) to guide your decisions? (Select one)

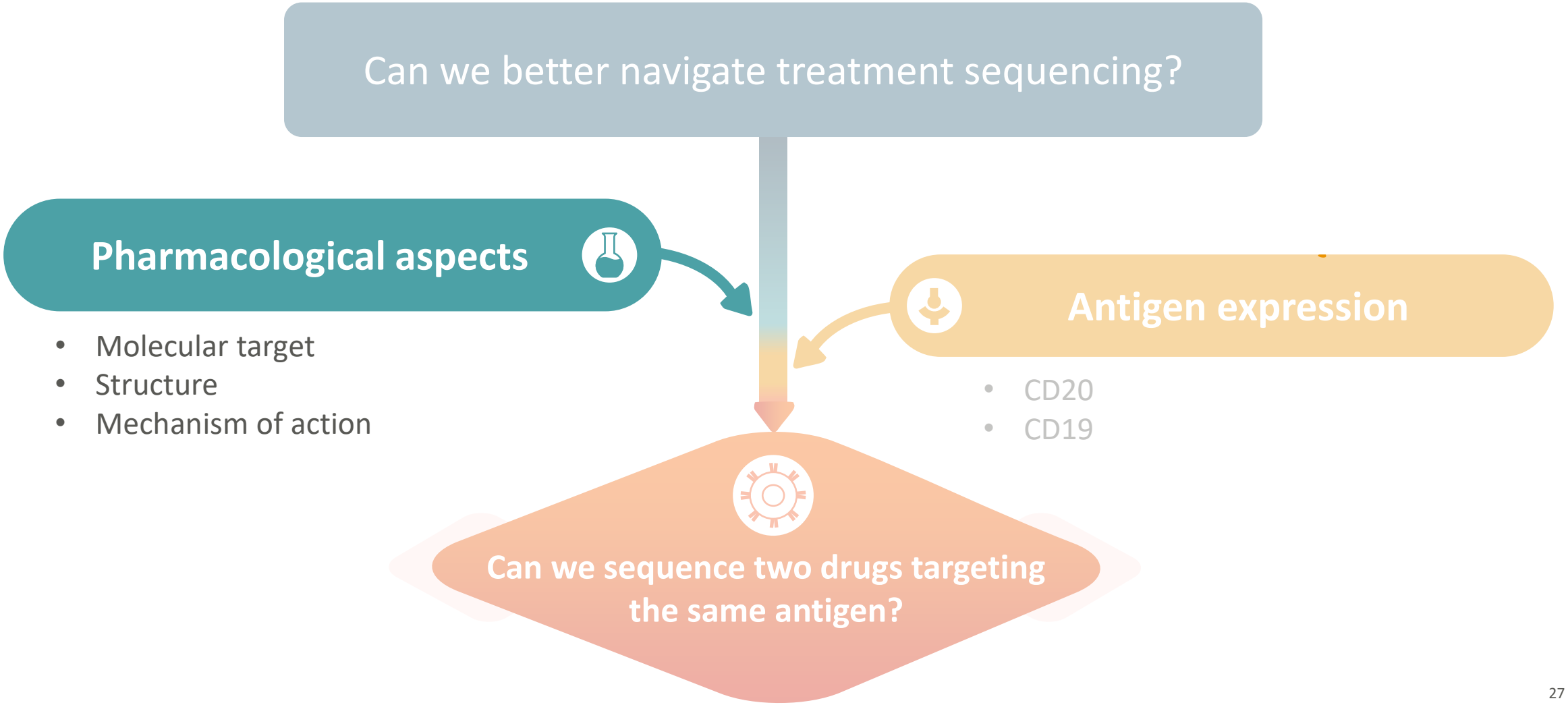
A. Always
B. Often
C. Occasionally
D. Rarely
E. Never

NP-42407

How can preclinical evidence help us in decision-making?



How can preclinical evidence help us in decision-making?



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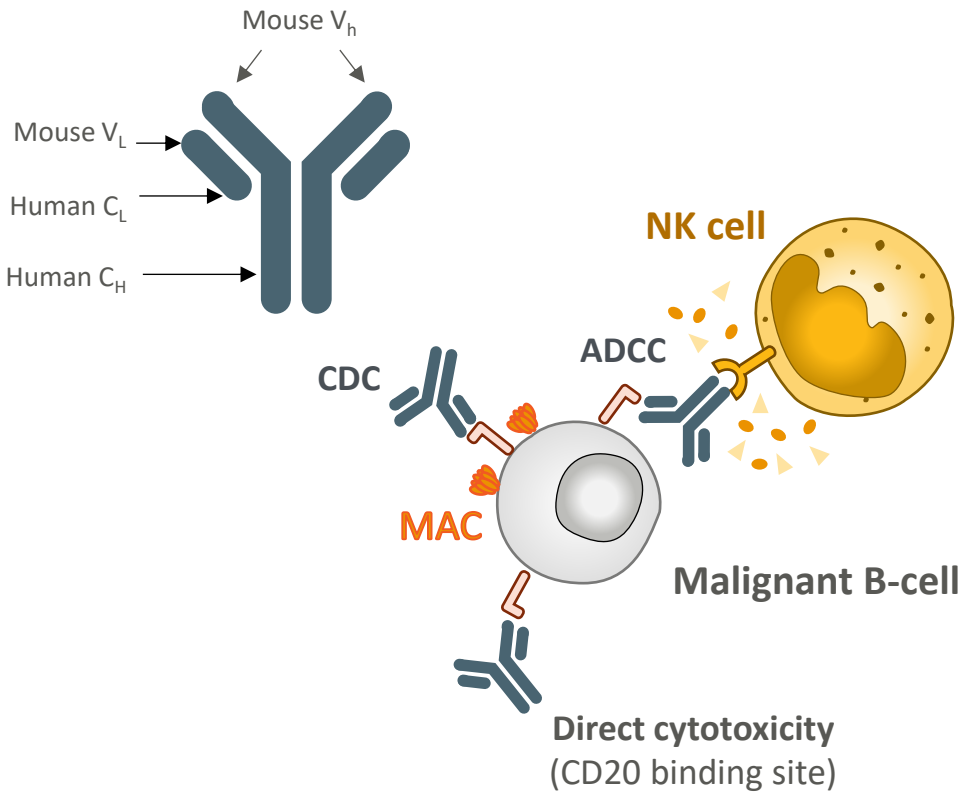
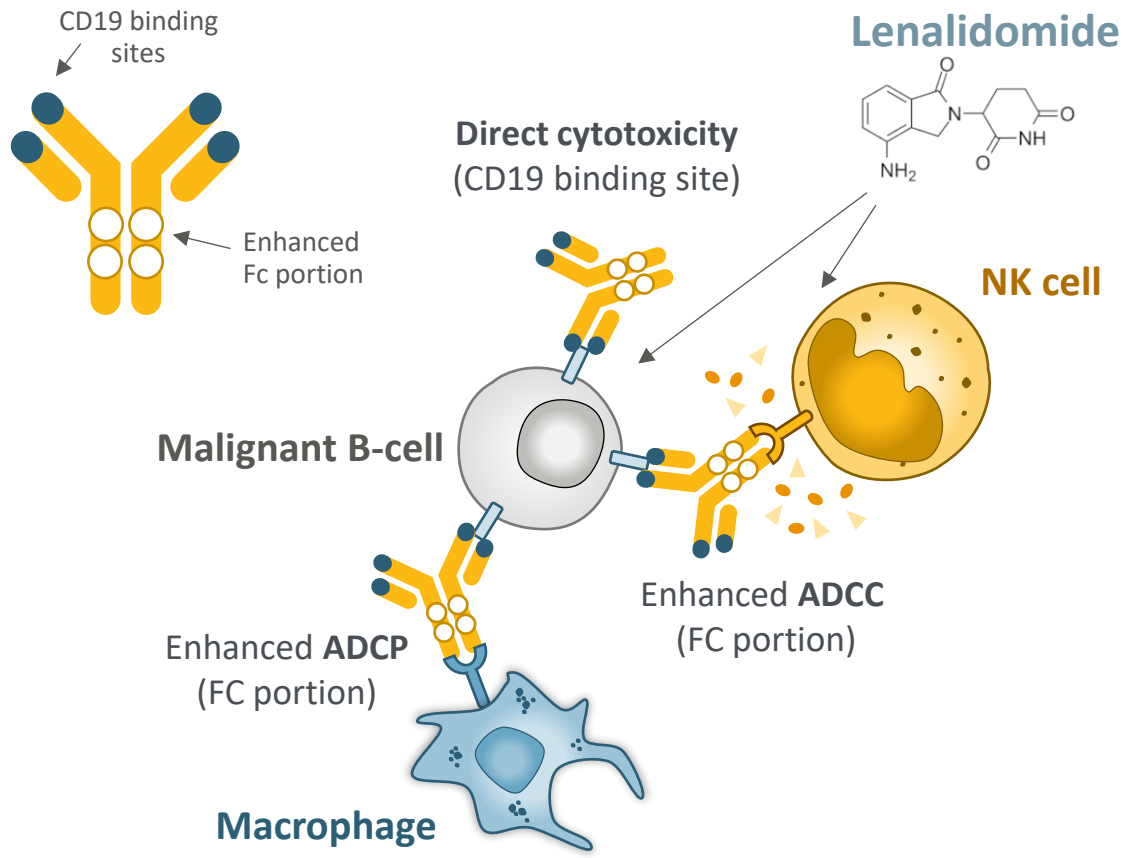
Structures and mechanisms of action of unconjugated ("naked") antibodies[1–5]

Rituximab (anti-CD20 mAb)[1,2]



Tafasitamab (anti-CD19 mAb)[3–5]



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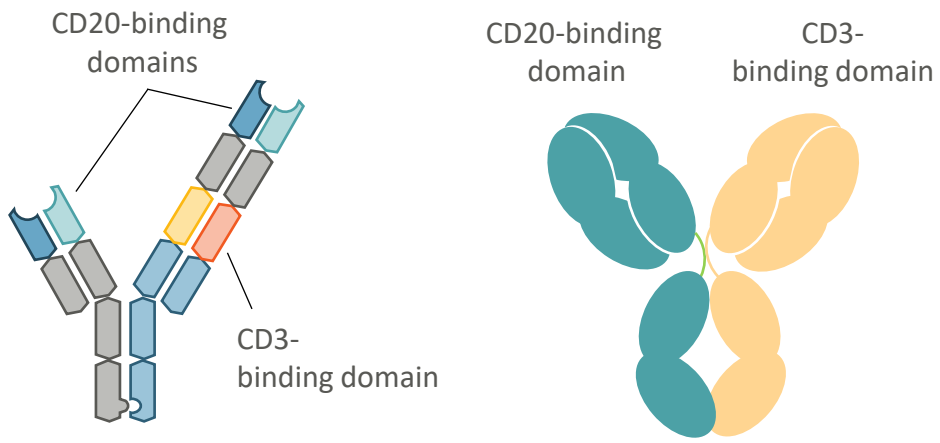
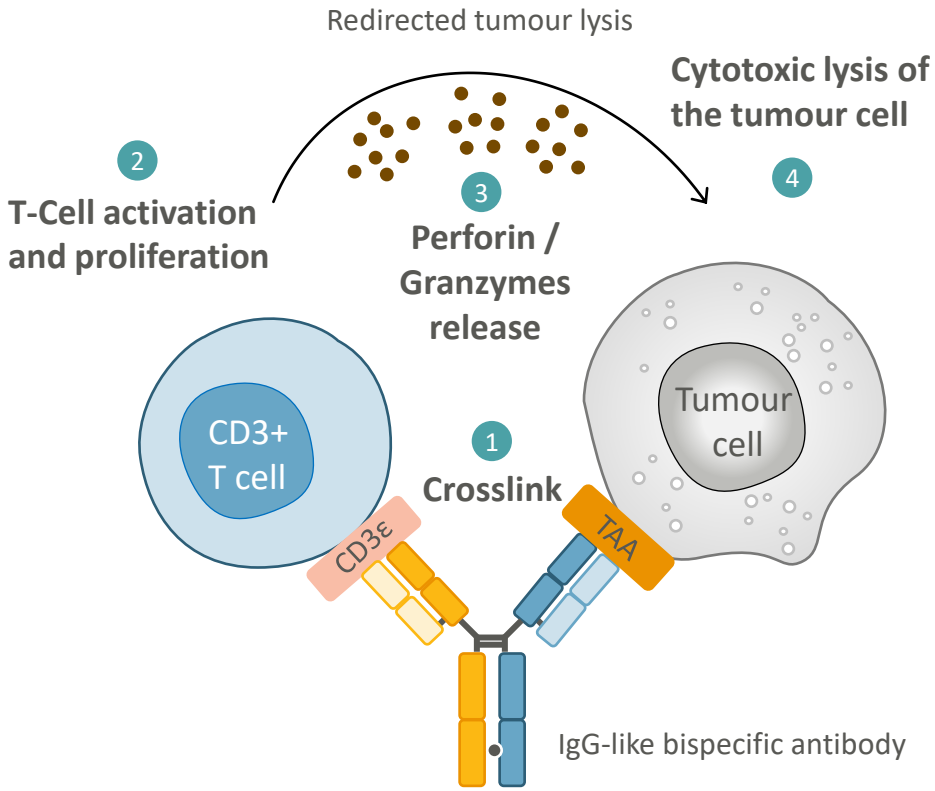
ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; CDC, complement-dependent cytotoxicity; Fc, fraction crystallisable; mAb, monoclonal antibody; MAC, membrane attack complex; NK, natural killer; R/R, relapsed or refractory.

1. MabThera SmPC 2024 **2.** Mohammed et al. *J Med Blood* 2019 **3.** Minjuvi SmPC 2021 **4.** Cheson et al. *Blood Cancer J* 2021 **5.** Salles et al. *Lancet Oncol* 2020.

Structures and mechanisms of action of bispecific antibodies[1–5]



Fully humanised mouse IgG1-based bispecific antibodies which target CD20 and CD3[1–3]



CD3 bispecific T-cell redirection mechanism of action in cancer immunotherapy[4,5]

NP-42407

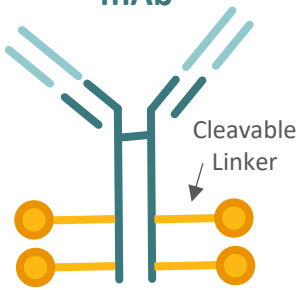
IgG, immunoglobulin G; TAA, tumour-associated antigen.

1. Lussanna et al. *J Clin Oncol* 2021 **2.** Columvi SmPC December 2024 **3.** Engelberts et al. *EBioMedicine* 2020 **4.** Zhou et al. *Biomarker Res* 2021 **5.** Singh et al. *Br J Cancer* 2021.

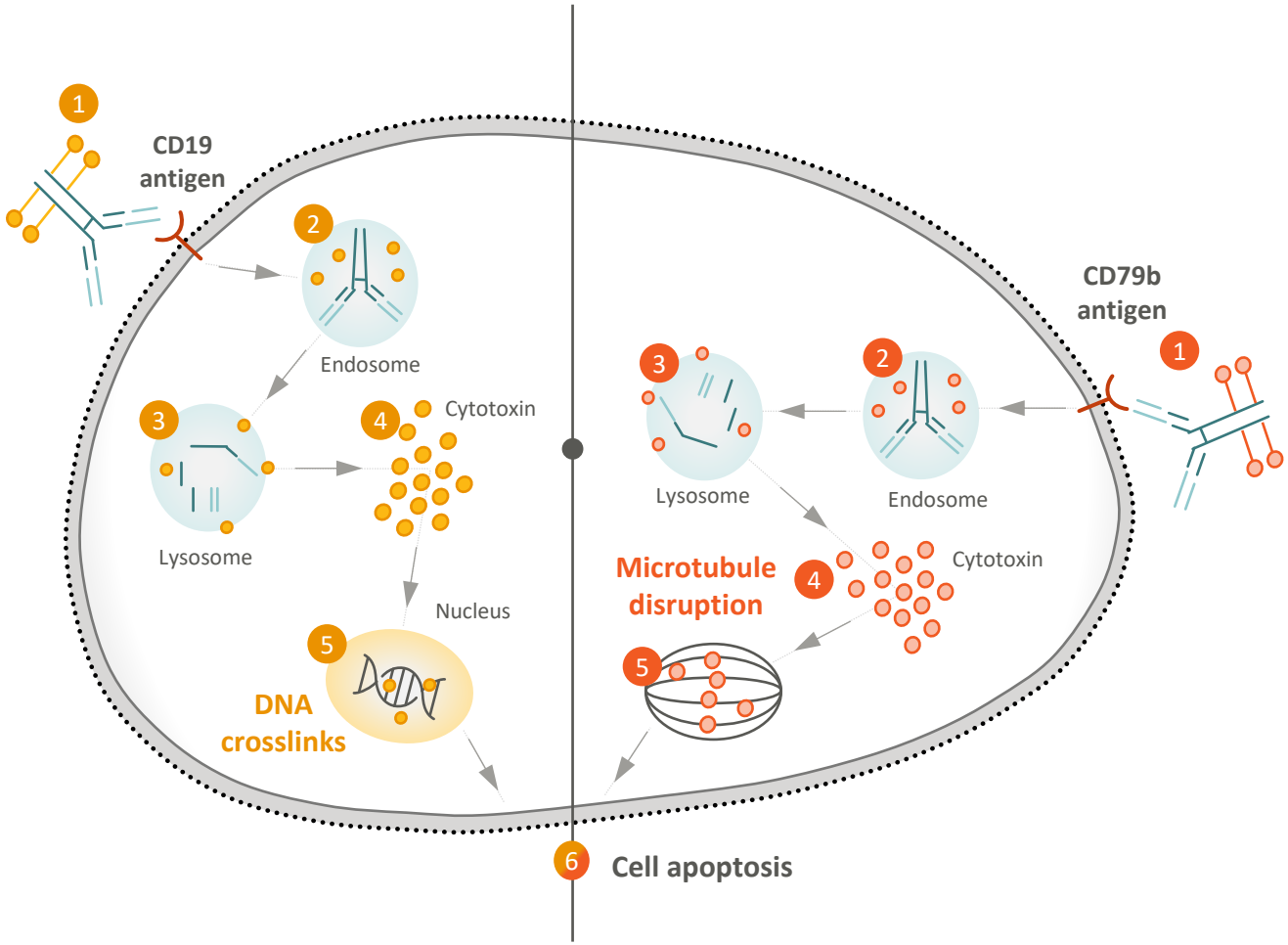
Structures and mechanisms of action of antibody-drug conjugates[1–2]

Loncastuximab tesirine

Anti-CD19 mAb

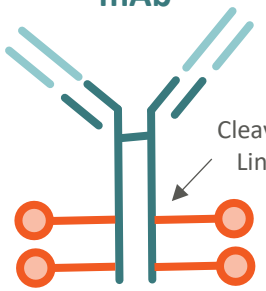


SG3199 payload
(PBD dimer)



Polatuzumab vedotin

Anti-CD79b mAb



MMAE payload

NP-42407

ADC, antibody-drug conjugate; DLBCL, diffuse large B-cell lymphoma; mAb, monoclonal antibody; MMAE, monomethyl auristatin E; PBD, pyrrolobenzodiazepine.
1. Alderuccio et al. *Blood Rev* 2022 **2.** Joubert et al. *Pharmaceuticals (Basel)* 2020.

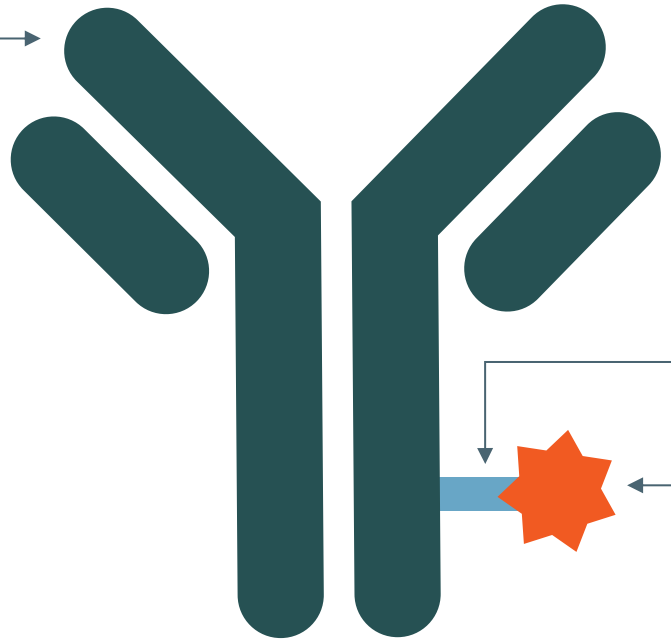
Antibody-drug conjugates have multiple properties that can be varied for clinical efficacy[1–3]

Antibody

- Strong antigen recognition, low immunogenicity, long half-life, and high molecular weight

Target antigen

- High tumour expression, low healthy tissue expression, strong antibody recognition



Linker

- Stable in circulation, efficient payload release at target site, prevents premature release at non-target tissue, efficient linker technology, and site of conjugation

Cytotoxic payload

- Highly potent
- Optimal DAR, which affects drug distribution and PK

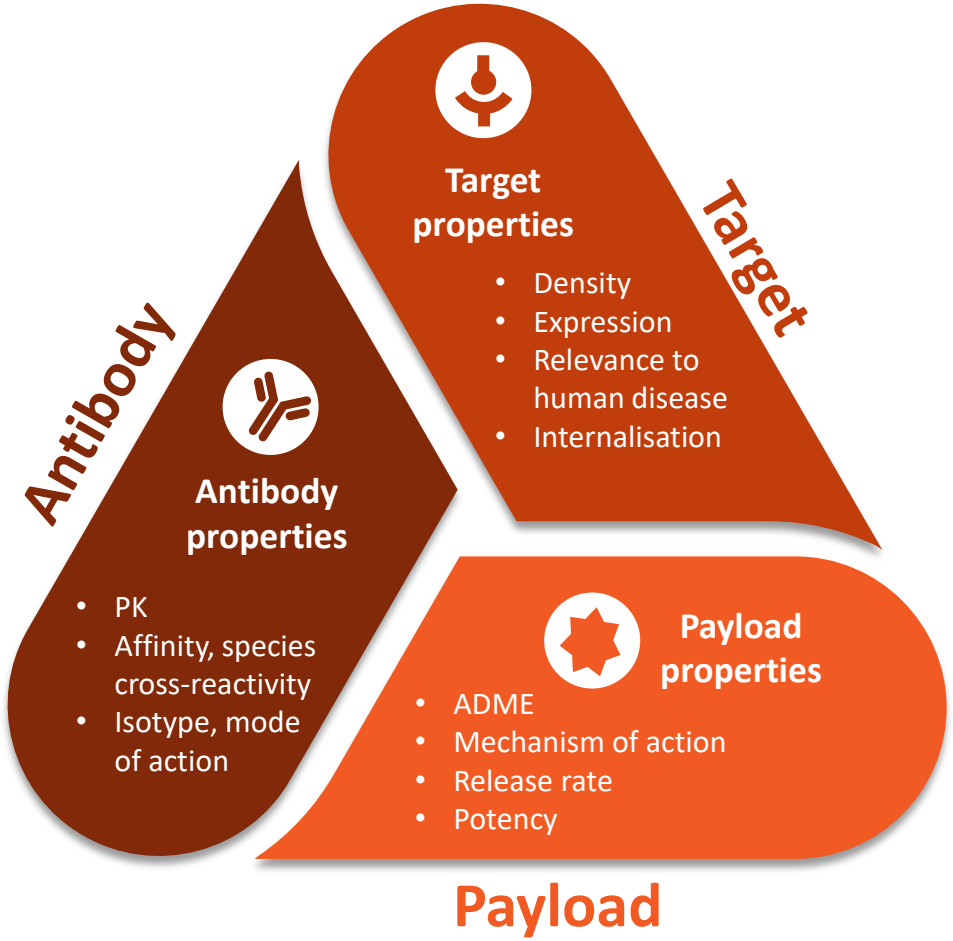
NP-42407

DAR, drug-antibody ratio; PK, pharmacokinetics.

1. Nathwani and Chen. *Clin Investig* 2014 **2.** Chau et al. *Lancet* 2019 **3.** Barreca et al. *Explor Target Antitumor Ther* 2022.

Efficacy of ADCs is determined by multiple properties[1,2]

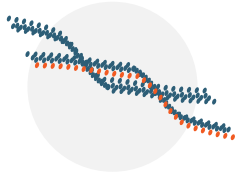
Payload delivery is impacted by ADC properties[1]



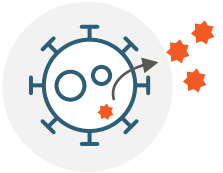
Efficacy may also be limited by drug resistance[2]

Downregulation of the target antigen

Defects in binding/internalisation



Alterations in microtubule dynamics

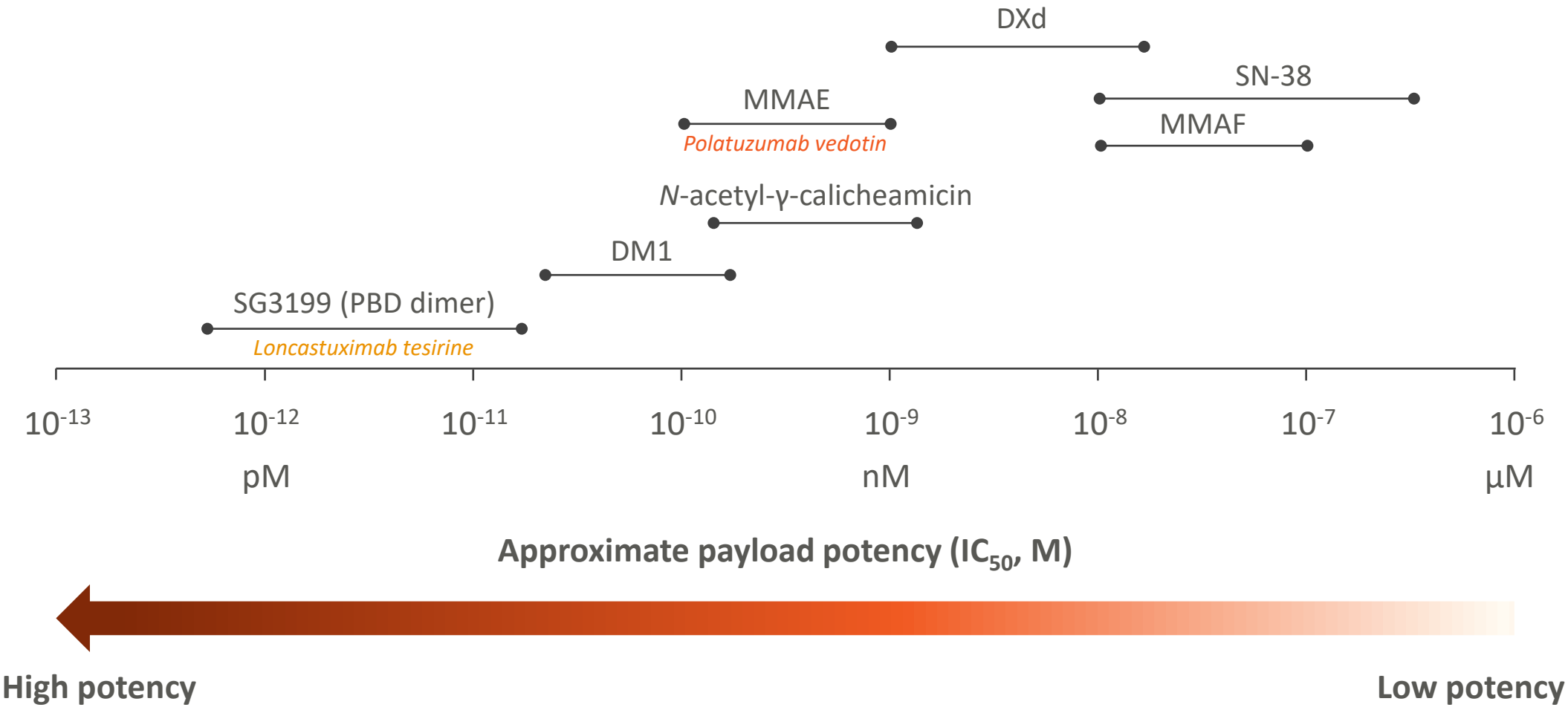


Reduced drug retention

NP-42407

ADC, antibody drug-conjugate; ADME, absorption, distribution, metabolism, excretion; PK, pharmacokinetics.
1. Sadekar et al. *AAPS J* 2015 **2.** Joubert et al. *Pharmaceuticals (Basel)* 2020.

Target antigen density and payload potency impact clinical efficacy of ADCs[1]



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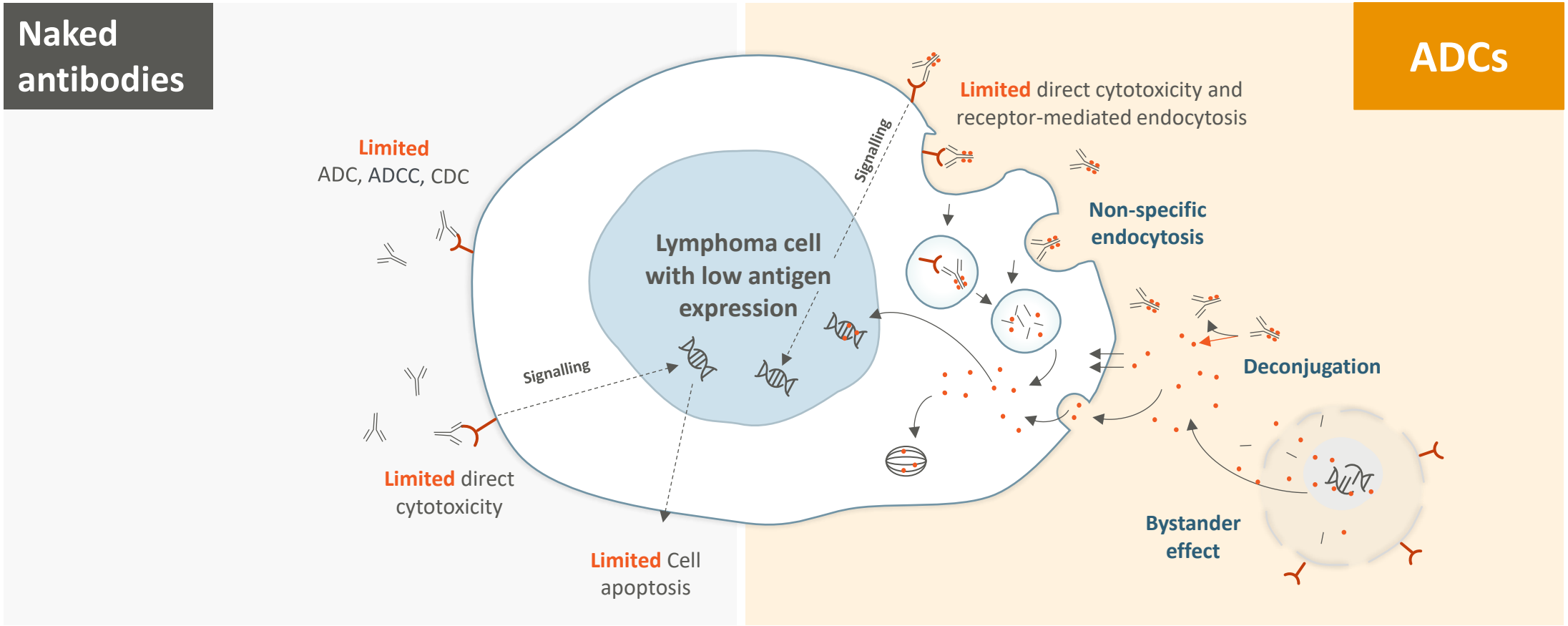
ADC, antibody-drug conjugate; MMAE, monomethyl auristatin E; MMAF, monomethyl auristatin F; PBD, pyrrolobenzodiazepine.

1. Tong et al. *Molecules* 2021.

Imaged adapted from Tong et al. *Molecules* 2021.

ADCs have additional mechanisms to overcome low antigen expression and deliver their potent payload[1,2]

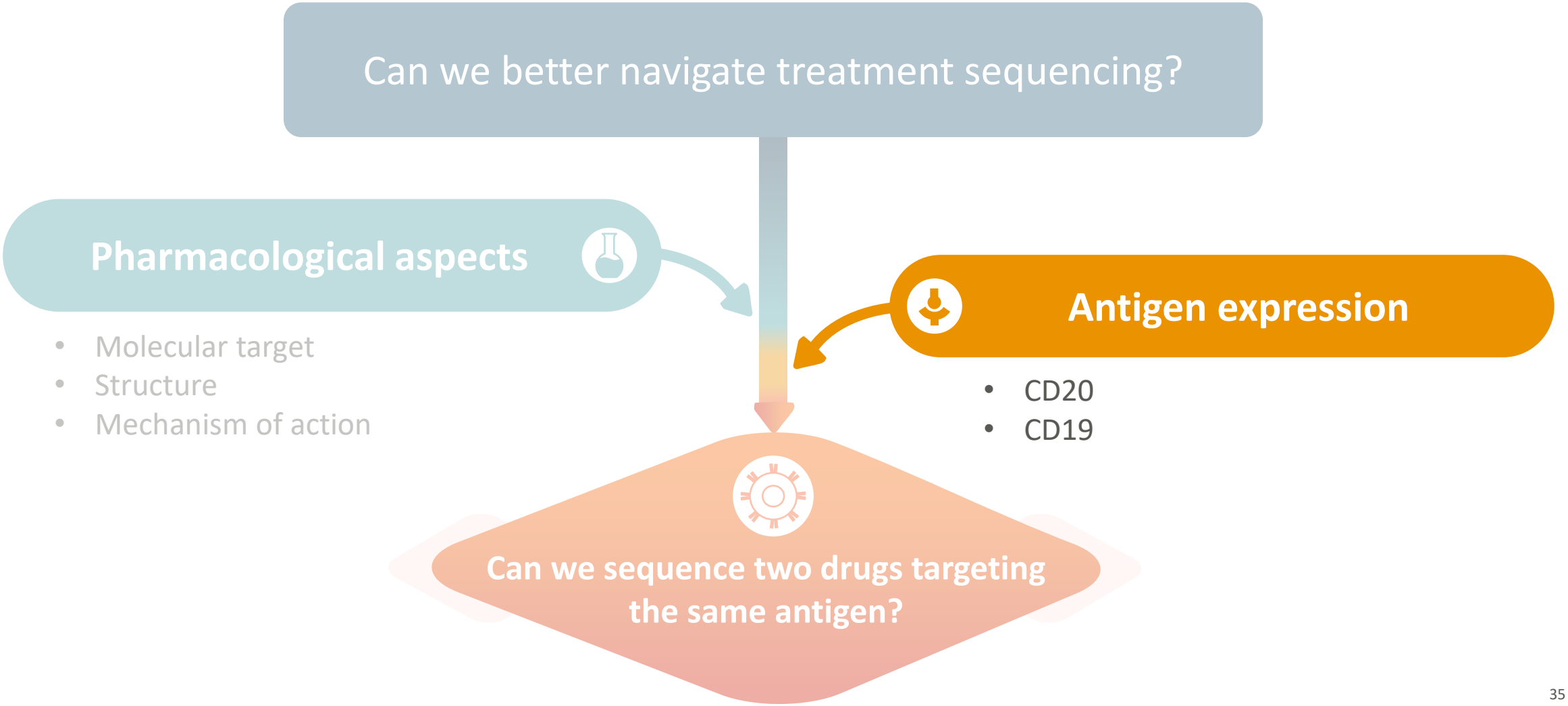


ADCs must balance the **potency** of the payload with the **density** of target antigen expression to achieve **optimal clinical activity**[1]

ADC, antibody-drug conjugate; ADCC, antibody-dependent cellular cytotoxicity; CDC, complement-dependent cytotoxicity.

1. Mahalingaiah et al. *Pharmacol Ther* 2019 **2.** Maecker et al. *MAbs* 2023.

How can preclinical evidence help us in decision-making?



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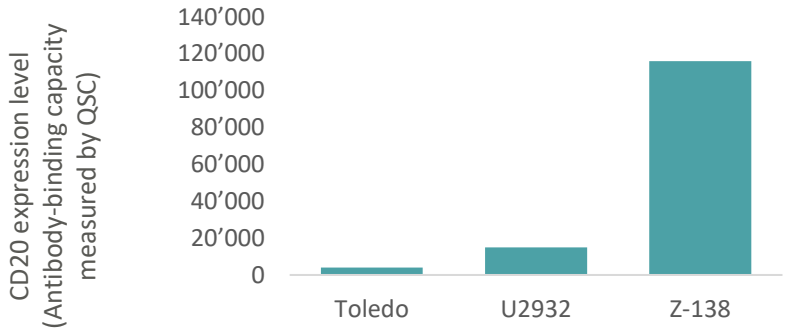
In vitro CD20 expression appears not to be correlated with bispecific antibody activity[1–3]

Glofitamab demonstrated anti-tumour activity in cells expressing low levels of CD20[1,2]

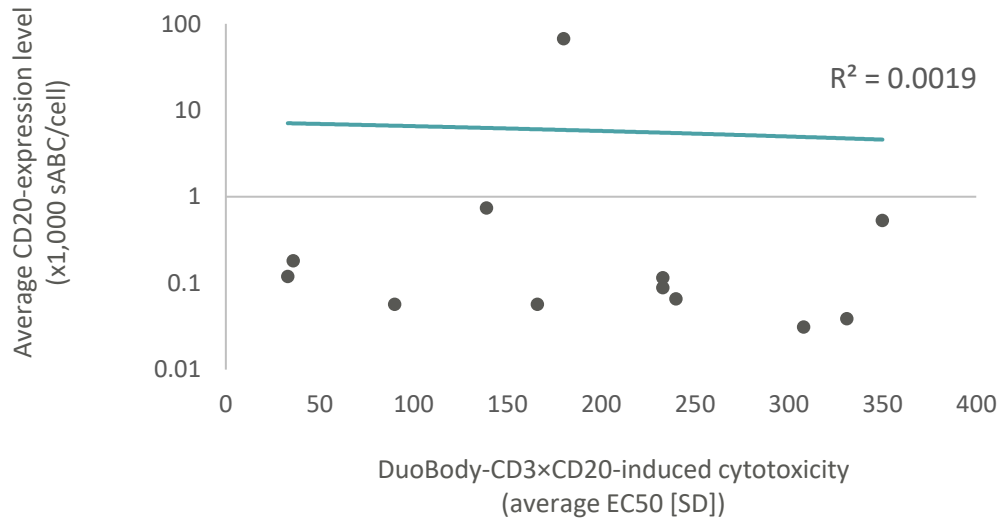
There was no relationship observed between CD20 expression and cytotoxicity of epcoritamab in cells[3]

Tumour cell lines CD20 expression and EC_{50} values of tumour cell lysis



EC_{50} tumour lysis (pM), glofitamab	Toledo	U2932	Z-138
	0.4	7.2	4.0

Correlation between CD20 expression and CD3×CD20-induced cytotoxicity



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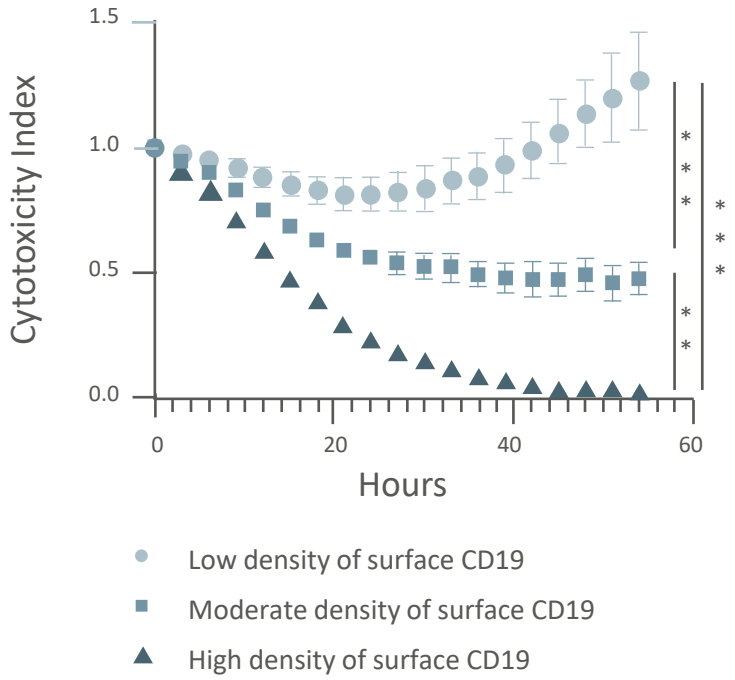
EC_{50}, half maximal effective concentration; QSC, Quantum™ Simply Cellular®; sABC, specific antigen binding capacity; SD, standard deviation.

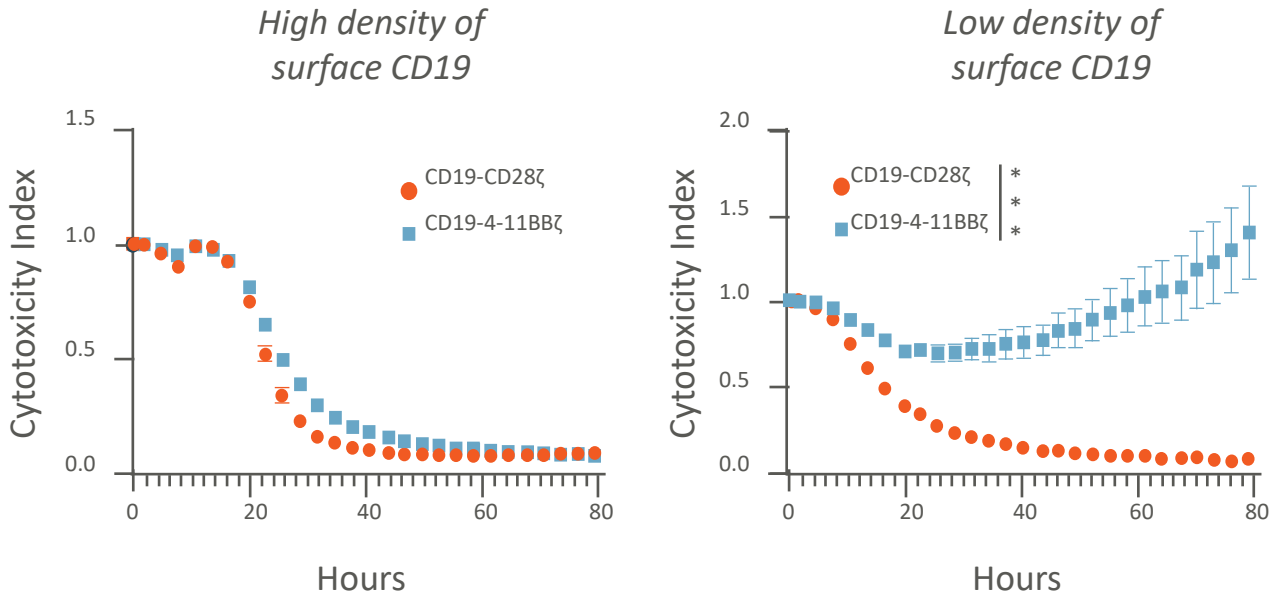
1. Bacac et al. *Clin Cancer Res* 2018 **2.** Bacac et al. *Clin Cancer Res* 2018 (supplement) **3.** Engelberts et al. *EBioMedicine* 2020.

CD19 CAR-T activity in preclinical models is dependent on antigen density[1]

Tumour cell killing of **CD19–4-1BBζ** depends on the density of surface CD19



CD19–CD28ζ was more efficient at targeting **CD19-low** tumour cells than **CD19-4-1BBζ***



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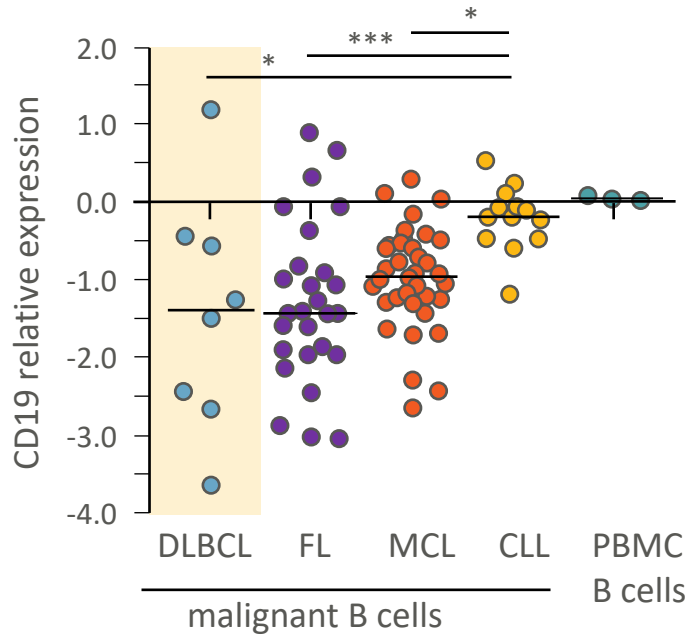
*Neither of the constructs employed in the study completely match the manufacturing processes for the FDA approved clinical products. **p<0.01. ***p<0.0001.
Axi-cel, axicabtagene ciloleucel; CAR-T, chimeric antigen receptor T-cell therapy; FDA, food and drug administration; tisa-cel, tisagenlecleucel.

1. Majzner et al. *Cancer Discov* 2020.

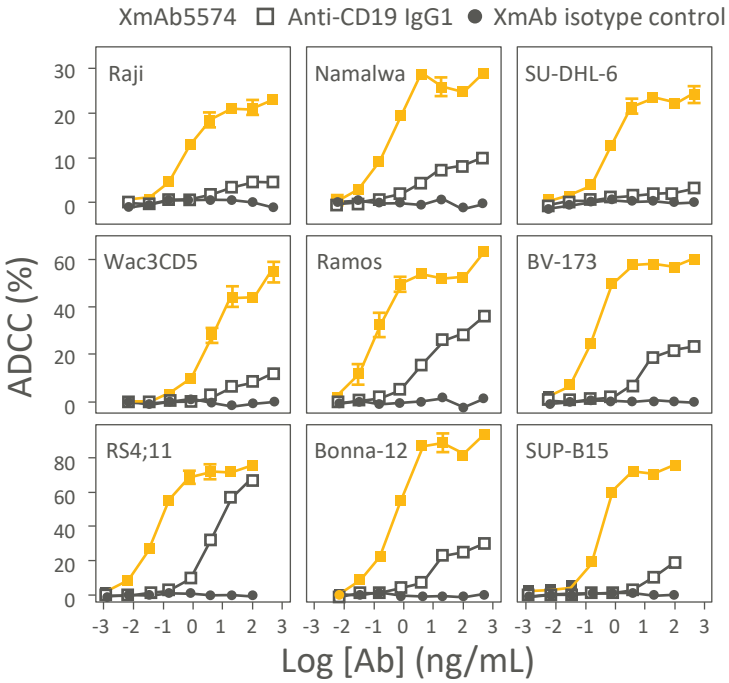
In vitro activity of tafasitamab shows no correlation with CD19 levels[1–2]

CD19 expression in lymphoma cells can be heterogeneous in DLBCL[1]



CD19 protein expression, relative to healthy donor PBMC B-cells (Log2 scale)

Tafasitamab showed no correlation with CD19 expression[2]



Tafasitamab enhanced ADCC in tumour cell lines with different CD19 expression levels

* p<0.05. *** p<0.001.

ADCC, antibody-dependent cell-mediated cytotoxicity; DLBCL, diffuse large B-cell lymphoma; EC_{50}, half maximal effective concentration; FL, follicular lymphoma; MCL, mantle cell lymphoma; PBMC, peripheral blood mononuclear cell; tafa, tafasitamab.

1. Majzner et al. *Cancer Discov* 2020 **2.** Horton et al. *Cancer Res* 2008.

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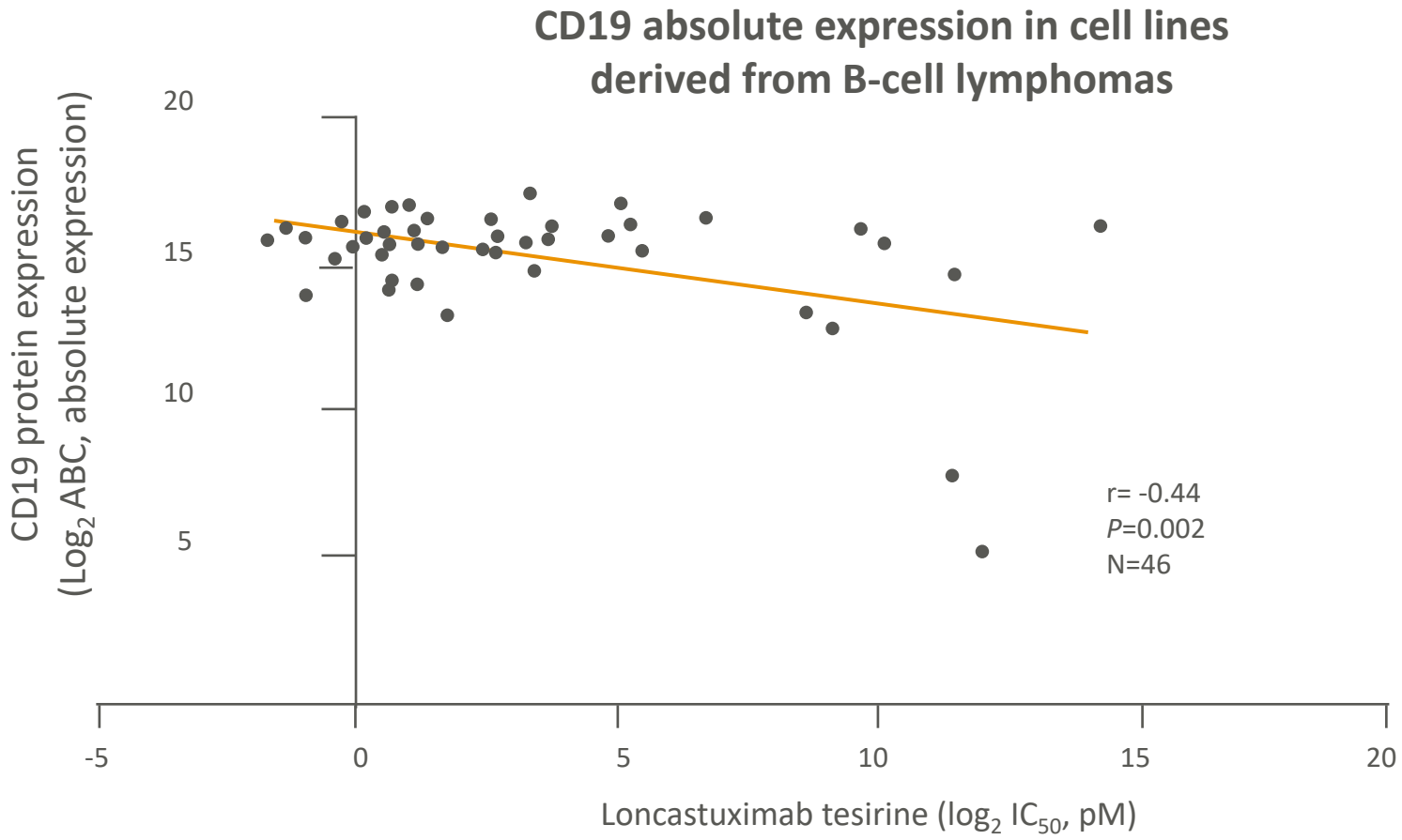
In vitro antitumour activity of Loncastuximab shows a low correlation with CD19 levels[1]



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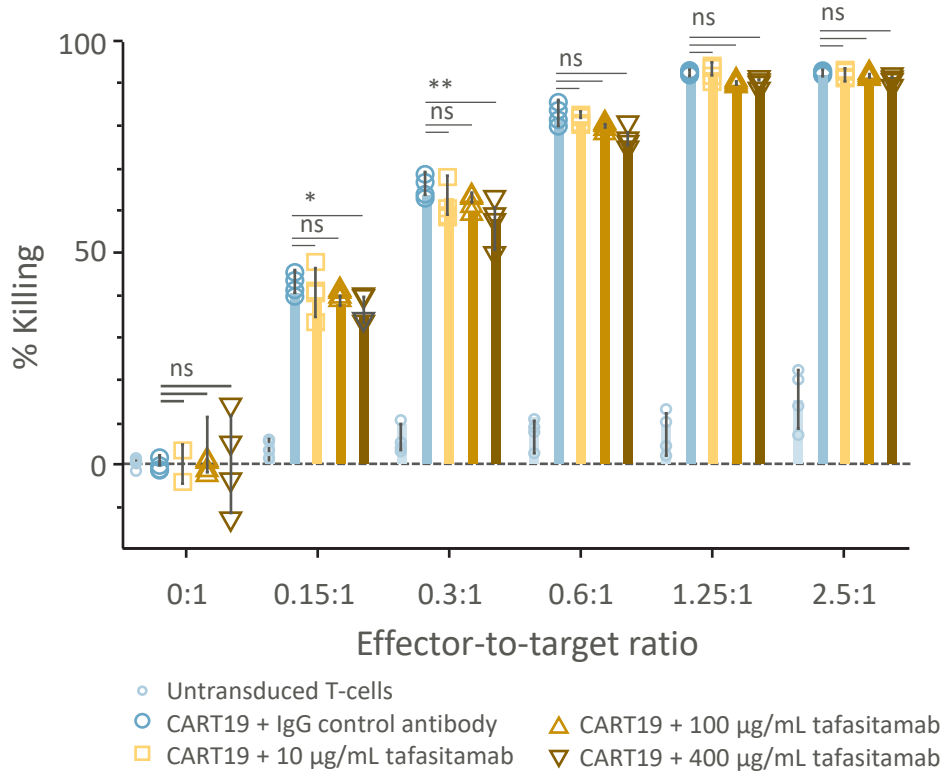
IC_{50}, half maximal inhibitory concentration.

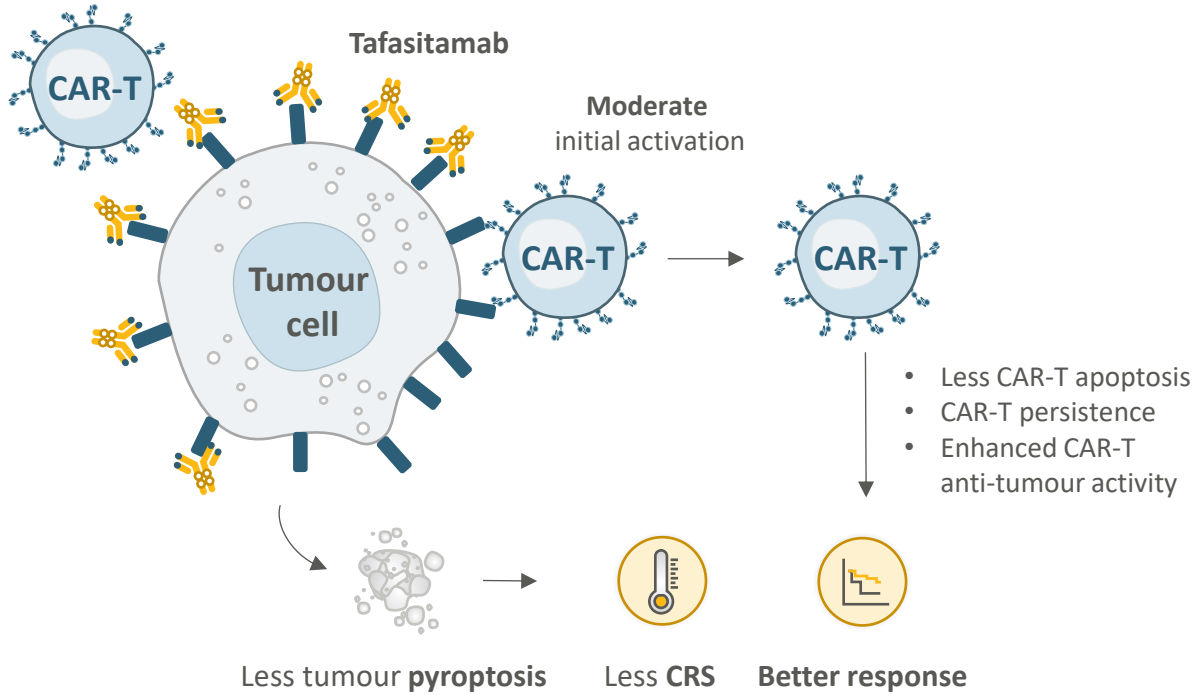
1. Tarantelli et al. *Haematologica* 2024.

CD19-directed therapies may not decrease the efficacy of subsequent CAR-T cell therapy[1]

Prior treatment with tafasitamab does not impact CAR T-cell therapy functions in cells†



Sequential therapy of tafasitamab followed by CAR T-cell therapy **increased the therapeutic index** of CAR T-cell therapy in mice



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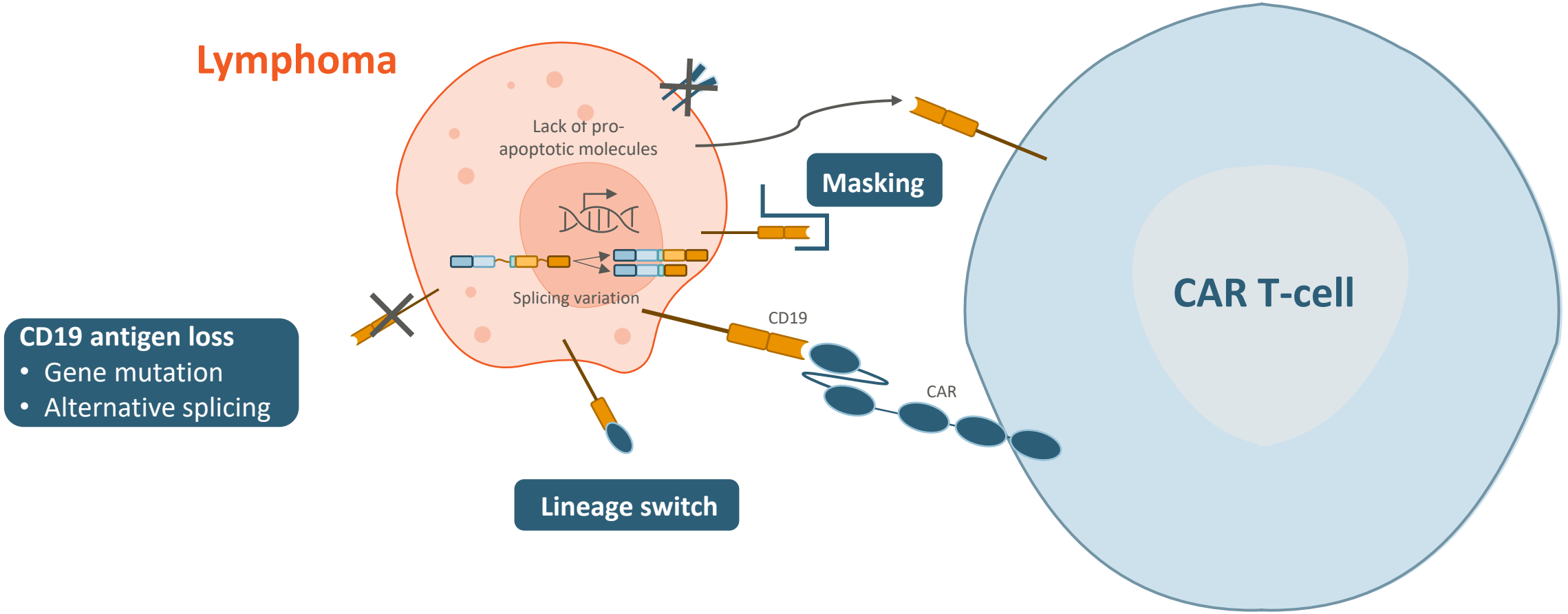
*p<0.05. **p=0.01. †Antigen specific killing, degranulation, cytokine production or proliferation of CART19.
CAR-T, chimeric antigen receptor T-cell therapy; CRS, cytokine release syndrome; tafa, tafasitamab.

1. Sakemura et al. *Blood* 2023.

Multiple mechanisms can lead to loss of CD19 expression after CAR-T cell therapy[1]



Additional mechanisms may contribute to CD19 downregulation after CAR-T.
CAR-T, chimeric antigen receptor T-cell therapy.
1. Ong at et. *Eur J Haematol* 2024.

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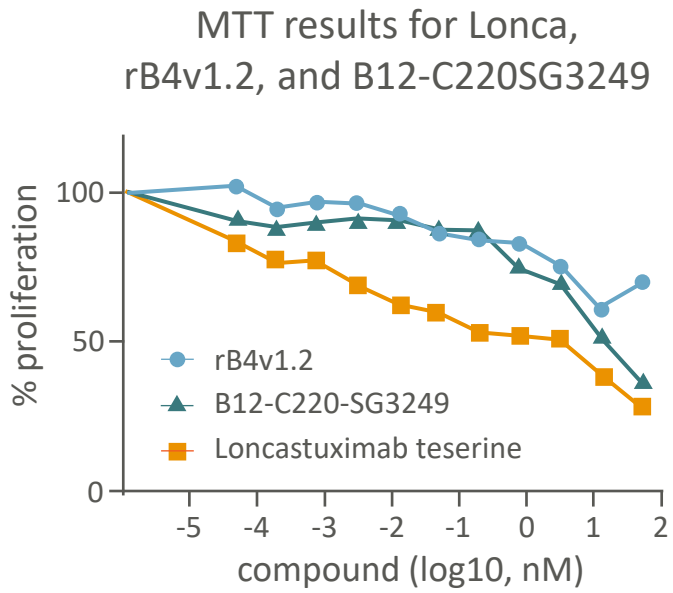
CD19-directed therapies may be effective after progression post-CAR-T[1,2]

Lonca was investigated in xenograft cells from a patient who progressed following CD19-targeting CAR-T



- Surface CD19: **26.72-fold** vs isotype
- Antiproliferative activity of lonca: **Maintained** (IC50=0.7 nm)
- Cell sensitivity to SG3199: **Maintained** (IC50=0.37 pm)

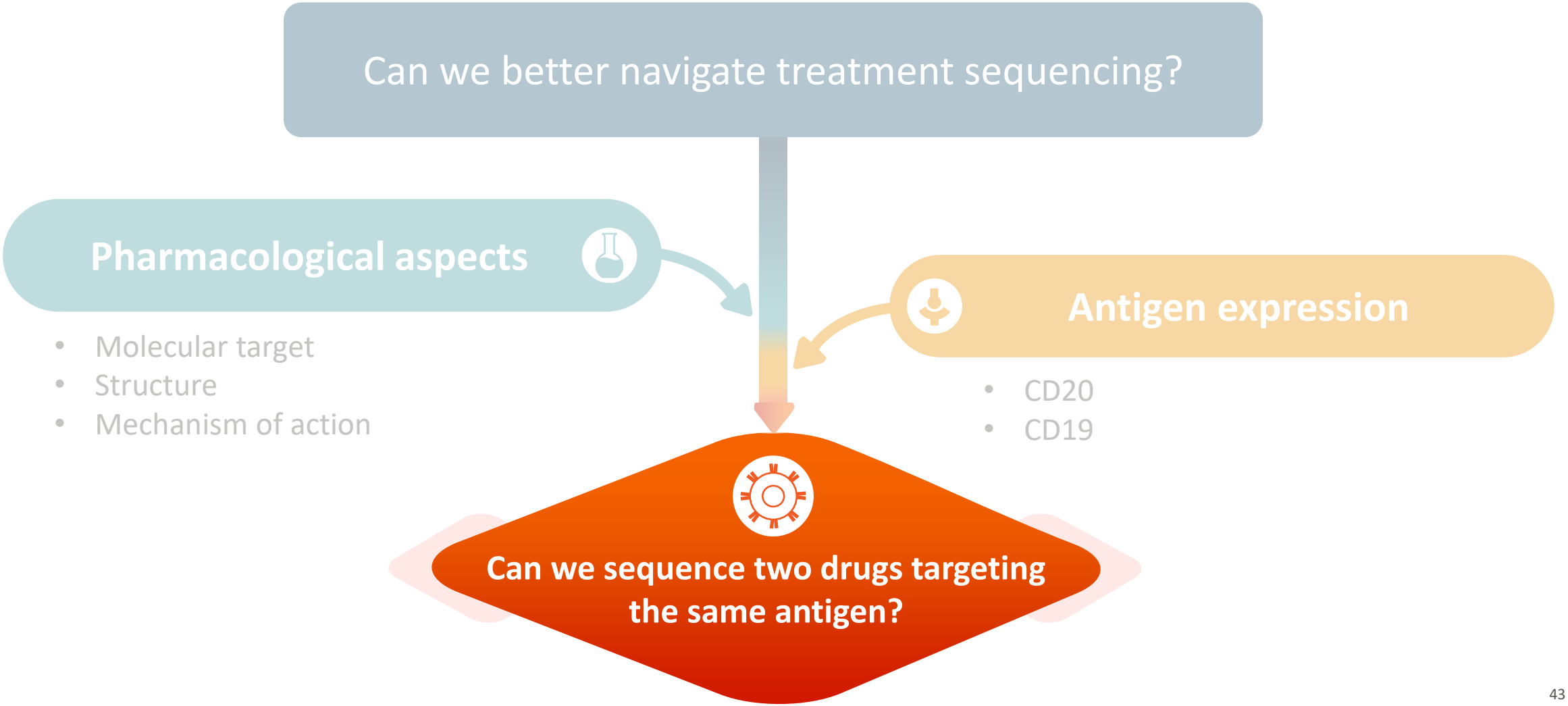
Loncastuximab tesirine is **active** in lymphoma cells **following chimeric antigen receptor T-cell therapy**

NP-42407

CAR-T, chimeric antigen receptor T-cell therapy; Lonca, loncastuximab tesirine; MTT, methylthiazol tetrazolium.

1. Tarantelli et al. *Haematologica* 2024 **2.** Tarantelli et al. *Haematologica* 2024 (supplement).

How can preclinical evidence help us in decision-making?



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Summary

- Preclinical insights may help fill gaps in the clinical data and understand how antigen expression change after treatment
- ADCs' unique pharmacological features may limit their impact on antigen expression and make them less sensitive to antigen loss
- As new therapies emerge and others move to earlier lines, careful considerations for antigen re-expression, drug target engagement and potency may help in sequencing

ADC, antibody-drug conjugate.

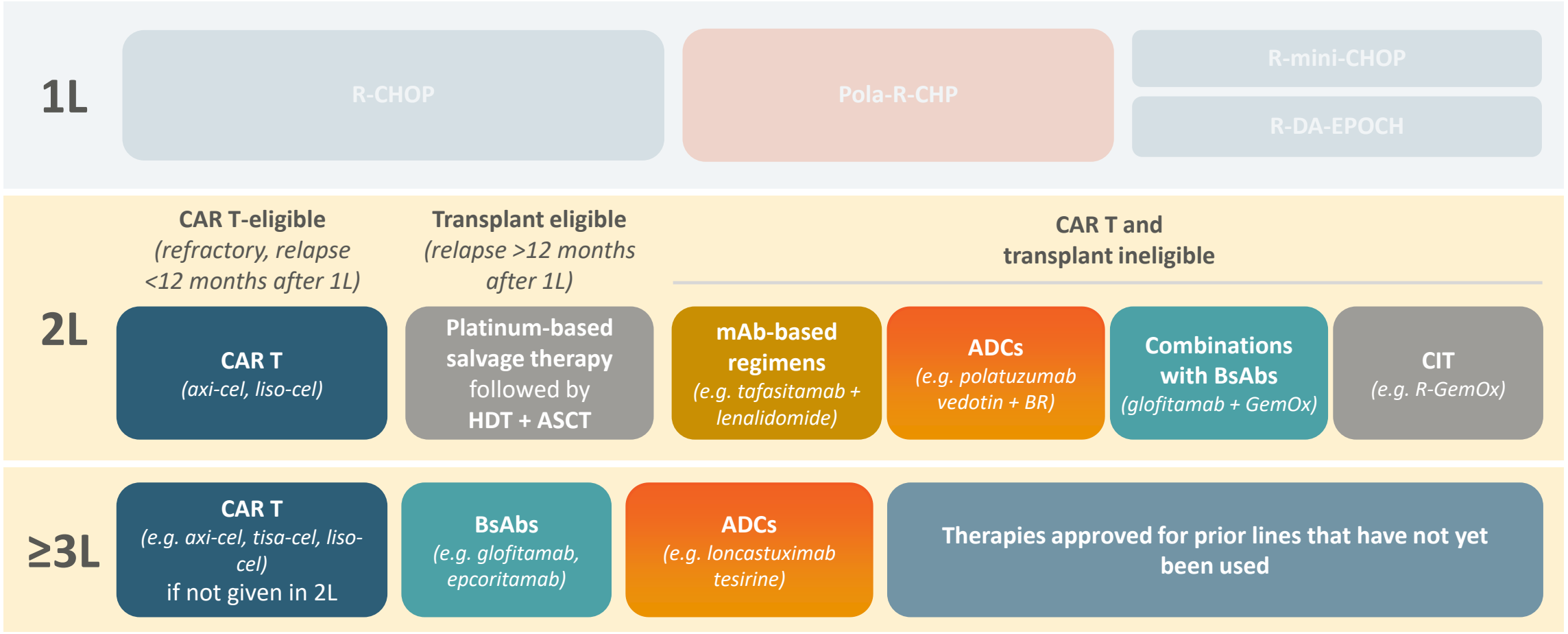
Learnings from clinical trials and real life

Professor Gloria Iacoboni

Vall d'Hebron Institute of Oncology,
Barcelona, Spain

NP-42408

Numerous treatment options are now available for DLBCL in each line[1–9]



ADC, antibody-drug conjugate; ASCT, autologous stem cell transplantation; axi-cel, axicabtagene ciloleucel; BR, bendamustine and rituximab; BsAb, bispecific antibody; CAR T, chimeric antigen receptor T-cell therapy; CIT, chemo-immunotherapy; DLBCL, diffuse large B-cell lymphoma; HDT, high-dose therapy; L, line; liso-cel, lisocabtagene maraleucel; mAb, monoclonal antibody; pola, polatuzumab vedotin; R-CH(O)P, rituximab, cyclophosphamide, doxorubicin, (vincristine), and prednisone; R-DA-EPOCH, rituximab, dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin; R-GemOx, rituximab, gemcitabine, and oxaliplatin; tisa-cel, tisagenlecleucel. **1.** Sehn & Salles *N Engl J Med* 2021 **2.** Frontzek et al. *Ther Adv Hematol* 2022 **3.** Peyrade et al. *Blood* 2010 **4.** Polivy SmPC 2023 **5.** Columvi SmPC 2023 **6.** Tepkinly SmPC 2023 **7.** Zynlonta SmPC 2023 **8.** Bartlett et al. *J Clin Oncol* 2019 **9.** Roche Press release 2025.

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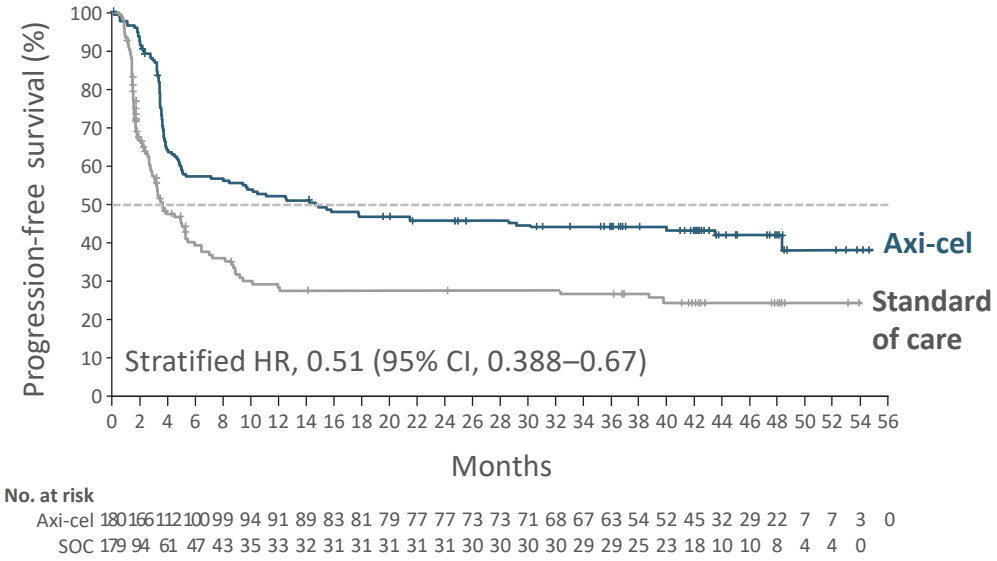
CAR-T is the new 2L standard of care for patients who relapse within 12 months after first-line therapy[1–3]

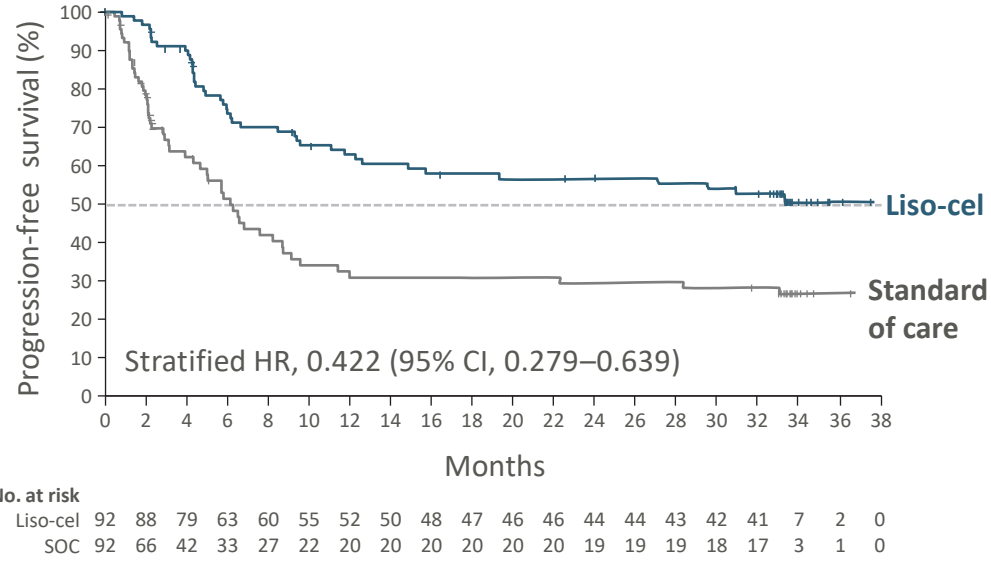
Axi-cel vs standard of care in 2L[1]



4-year PFS: 42%

4-year OS: 55%

Liso-cel vs standard of care in 2L[2,3]



3-year PFS: 50.9%

3-year OS: 62.8%

Median follow-up of 47.2 months (range, 39.8–60.0) for axi-cel[1], and 33.9 months (range, 0.9–53.0) for liso-cel[2]. CAR T-cell therapies were first approved in R/R DLBCL as a 3L of therapy.

2L, second line; 3L, third line; axi-cel, axicabtagene ciloleucel; CAR T, chimeric antigen receptor T-cell therapy; DLBCL, diffuse large B-cell lymphoma; liso-cel, lisocabtagene maraleucel; OS, overall survival; PFS, progression-free survival; R/R, relapsed or refractory.

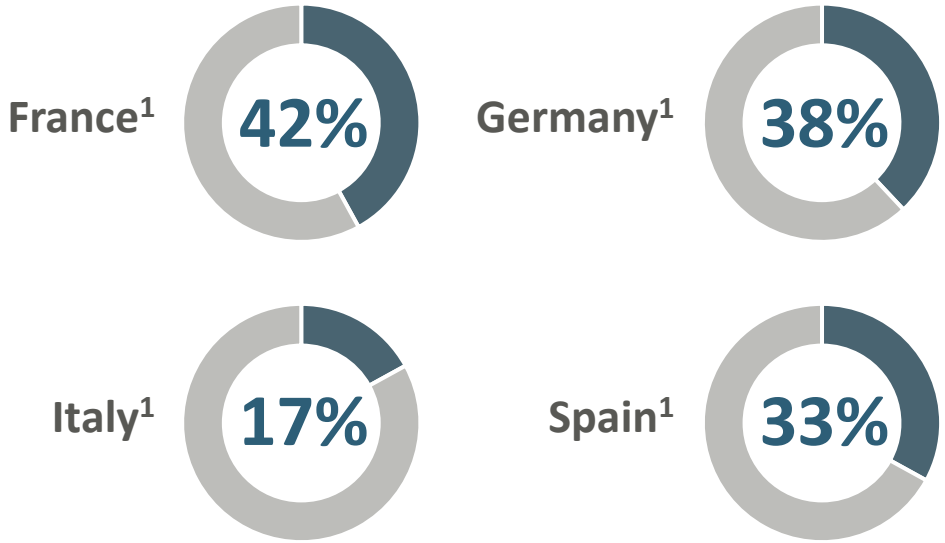
1. Westin et al. *Blood* 2023 **2.** Abramson et al. EHA 2024; Oral presentation #S272 **3.** Kamdar et al. *J Clin Oncol* 2024.

NP-42408

However, many patients who are eligible to receive CAR T-cell therapies do not receive an infusion[1–9]

Among patients meeting the EMA label indication for CAR T-cell therapy, less than half received a CAR T-cell therapy infusion

CAR T-cell therapy use in DLBCL in four European countries[1]



Common challenges resulting in limited access or delays in CAR T-cell therapy

- **Patient selection criteria**[2]
- **Manufacturing issues**[6]
- **Cost and reimbursement issues**[3,4]
- **Time to infusion**[7]
- **Requirements for centres**[5]
- **Risk of relapse and toxicities**[8,9]

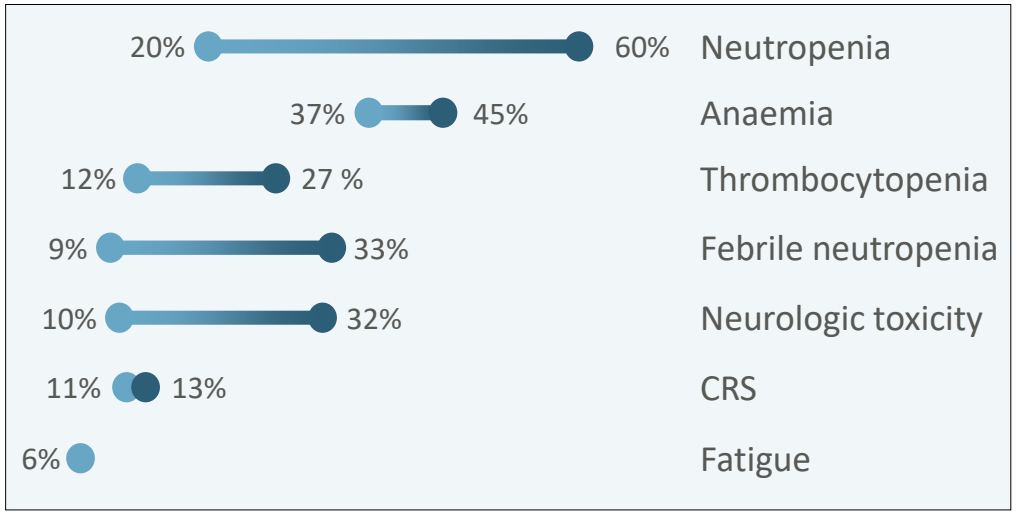
NP-42408

CAR, chimeric antigen receptor; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; EMA, European Medicines Agency; R/R, relapsed or refractory.

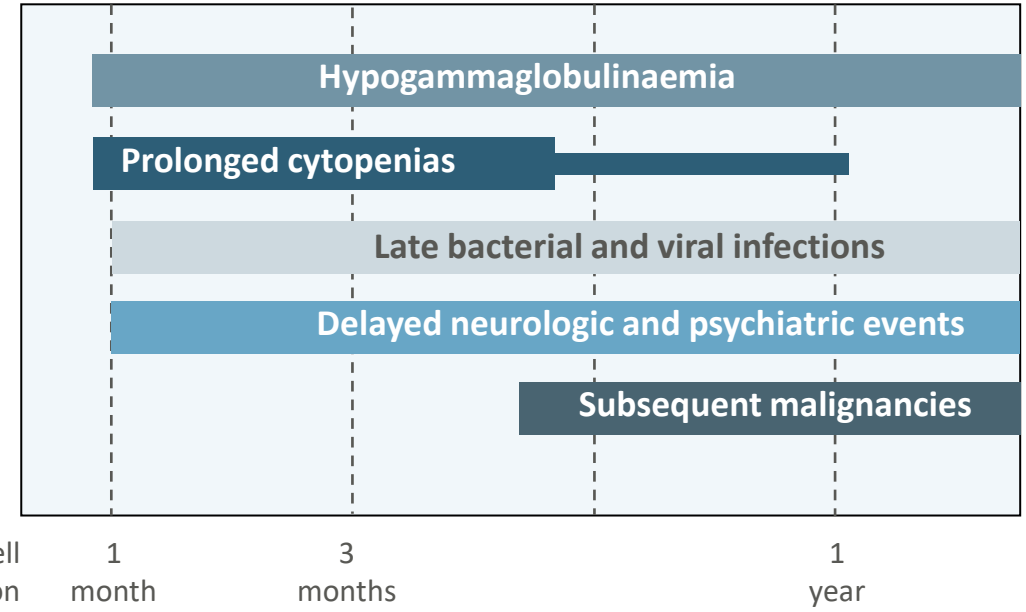
1. Albendea MAC et al. *Front Med* 2023 **2.** Glass & Kersten. *Springer Open* 2022 **3.** Haag *Springer Open* 2022 **4.** Dana-Farber Cancer Institute website **5.** Chomienne et al. *HemaSphere* 2019 **6.** Frontzek et al. *Ther Adv Hematol* 2022 **7.** Bücklein et al. *HemaSphere* 2023 **8.** Di Blasi et al. *Blood* 2020 **9.** Sermer et al. *Hematol Oncol* 2019.

CAR-T cell therapy safety is well understood, but may result in long-term toxicities, potentially impacting sequencing[1–10]

Most common (≥5%) **Grade ≥3 adverse events of special interest** in pivotal trials with CAR T-cell therapies[1–3]



Long-term toxicity[4]



Real-world safety for CAR T-cell therapy is broadly similar to findings from pivotal studies[5–10]

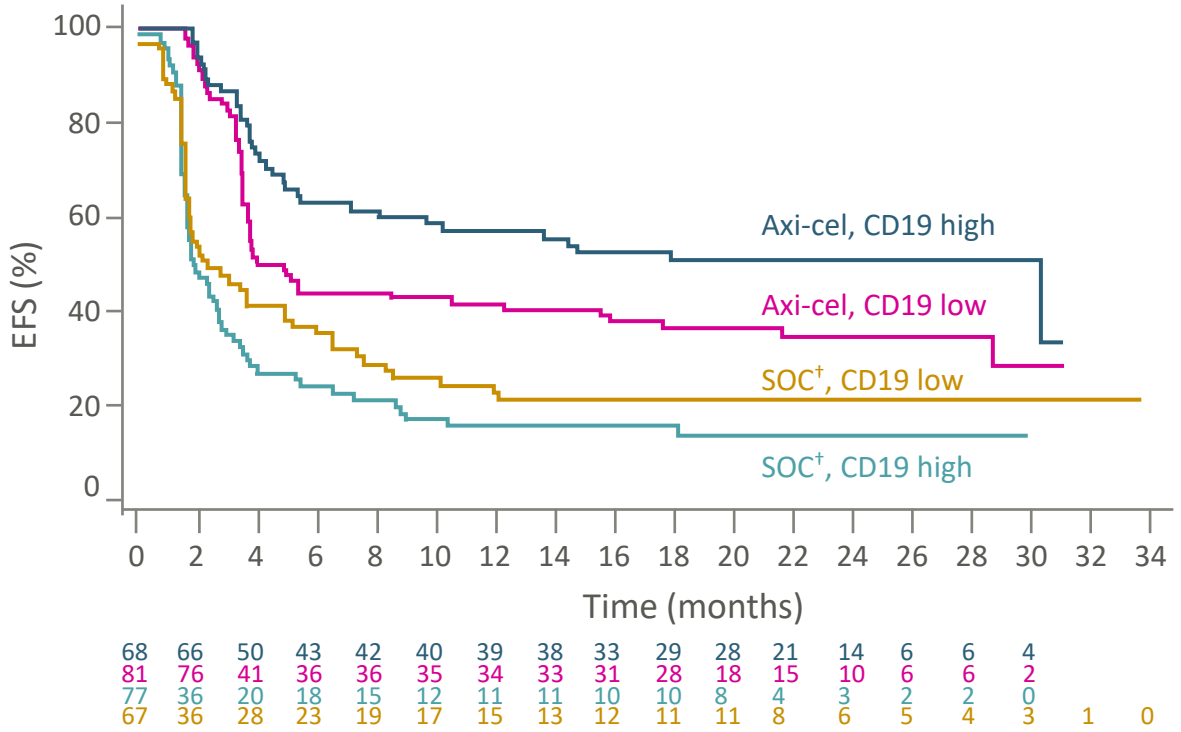
CAR-T, chimeric antigen receptor T-cell therapy; CRS, cytokine release syndrome.

1. Locke et al. *Lancet Oncol* 2019 **2.** Abramson et al. *Lancet* 2020 **3.** Schuster et al. *Lancet Oncol* 2021 **4.** Chakraborty et al. *Transplant Cell Ther* 2021 **5.** Kuhnl et al. *Blood* 2024 **6.** Yan et al. Blood 2024 **7.** Lee et al. *Blood* 2024 **8.** Bobillo et al. *Blood* 2024 **9.** Ahmed et al. ASH 2024; Oral presentation #472 **10.** Montoto et al. *Blood* 2024.

NP-42408

CD19 expression and CAR-T therapy: What do we know?[1–6]

Currently available data support a correlation between CD19 expression levels and CAR T-cell therapy outcomes[1]



Loss or downregulation of CD19 can be seen after CAR-T

- Loss of CD19 expression may be a mechanism for relapse in patients with DLBCL after CAR-T[2]
- **6–30%** patients show CD19 loss or downregulation[3–5]
- However:
  - **Limitations** exist with current techniques and different approaches (e.g. qPCR) may improve CD19 evaluation[6]
  - **CD19 expression** at CAR-T failure is **not predictive** of refractoriness or relapse[4]
  - **Tumours may still be susceptible to further CD19-targeted agents**

NP-42408

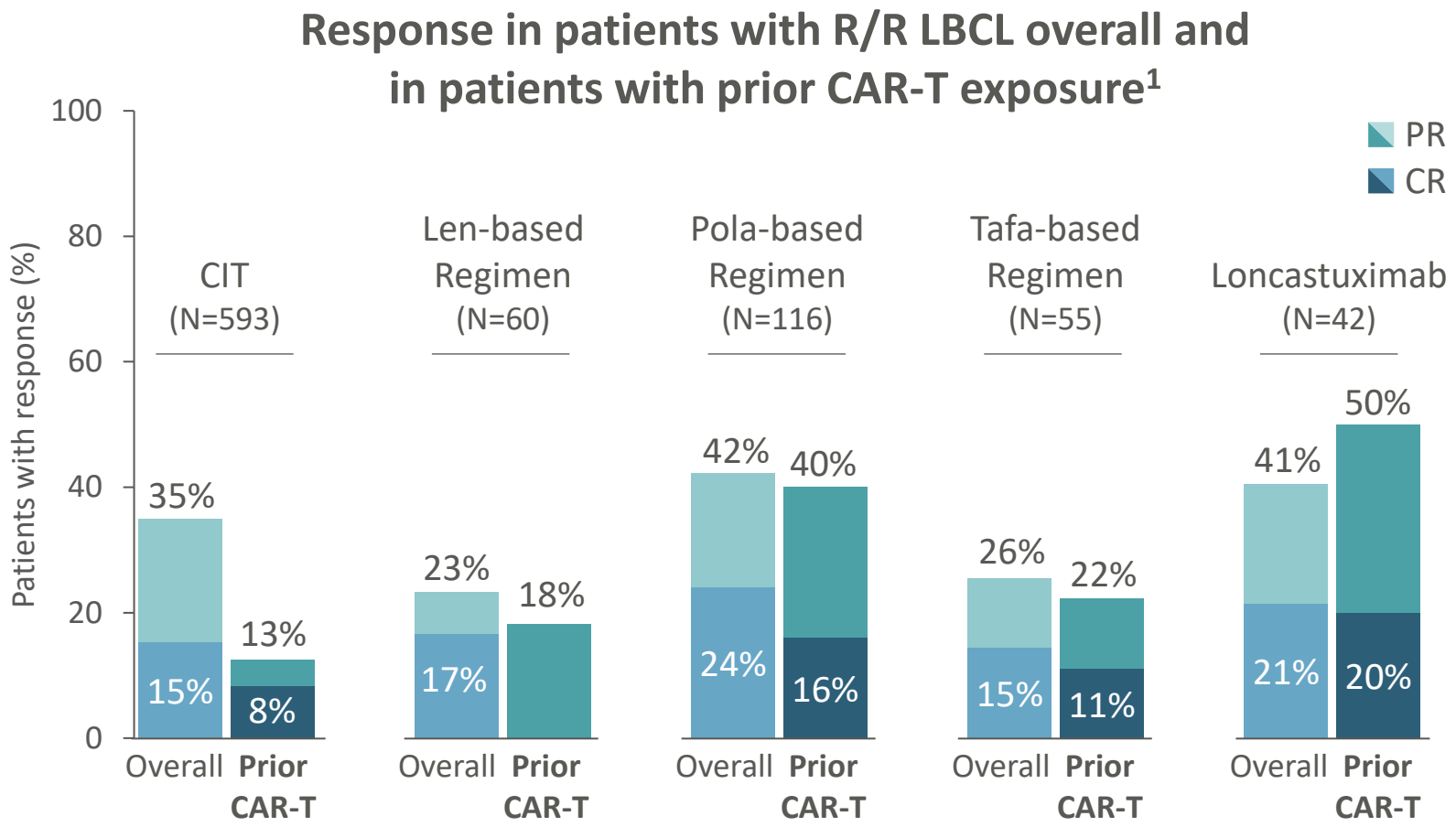
*SOC defined as 2–3 cycles of protocol-defined, investigator-selected, platinum-based chemotherapy with intention to subsequently undergo high-dose chemotherapy with autologous stem cell transplantation for chemosensitive patients. Axi-cel, axicabtagene ciloleucel; CAR-T, chimeric antigen receptor T-cell; EFS, event-free survival; qPCR, quantitative polymerase chain reaction; R/R, relapsed or refractory; SOC, standard of care.

1. Locke et al. *Nat Med* 2024 **2.** Shalabi et al. *Haematologica* 2018 **3.** Spiegel et al. *Blood* 2021 **4.** Tomas et al. *Leukemia* 2023 **5.** Plaks et al. *Blood* 2021 **6.** Hernani et al. *EJHaem* 2025.

Which of the following therapies have you used most frequently after CAR-T failure in R/R DLBCL? (Select one)

A. Lenalidomide +/- tafasitamab
B. ADC: Loncastuximab tesirine
C. ADC: Polatuzumab vedotin + BR
D. Bispecific antibody: Glofitamab
E. Bispecific antibody: Epcoritamab
F. Chemoimmunotherapy
G. Other

A growing body of evidence may help us understand how to sequence therapies, particularly after CAR-T[1]



Multisite retrospective observational study of adults with R/R LBCL treated with CIT* or novel therapy[1]

Baseline characteristics varied considerably between treatments[1]

NP-42408

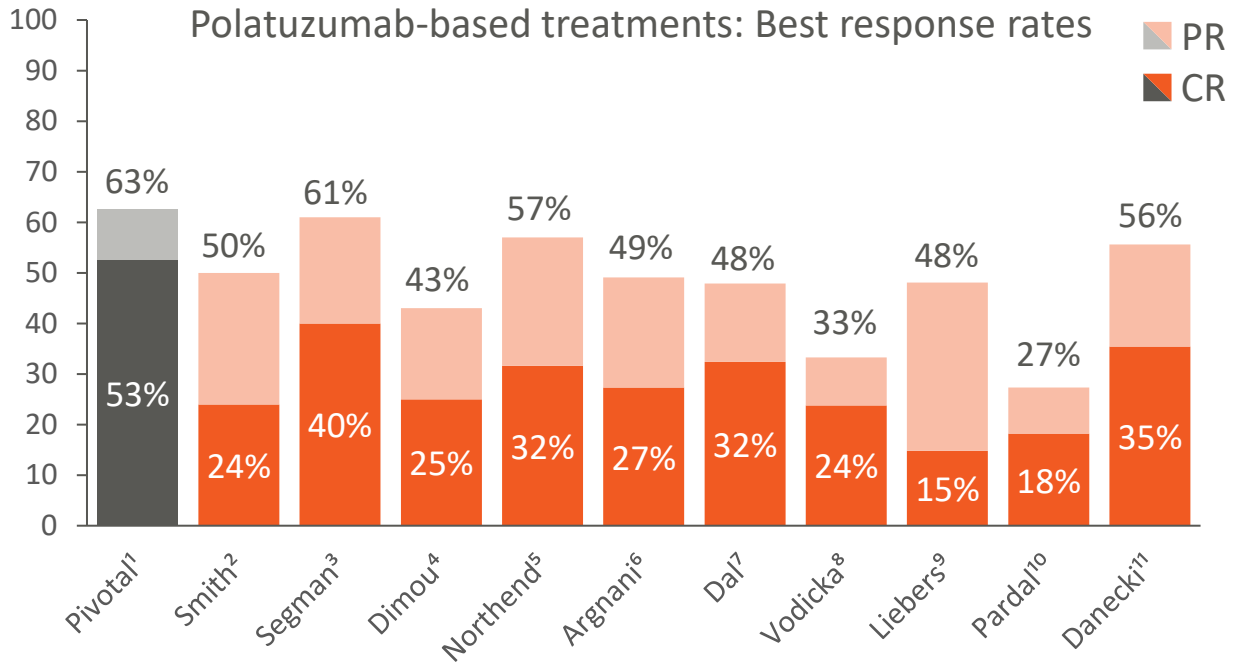
*Treatment response and progression were abstracted from medical records (e.g., PET/PET-CT/CT scans) and reviewed and validated by an assigned study clinician.
CAR-T, chimeric antigen receptor T-cell therapy; CIT, chemoimmunotherapy; CR, complete response; CT, computed tomography; LBCL, large B-cell lymphoma; Len, lenalidomide; Loncastuximab, loncastuximab tesirine; ORR, overall response rate; PET, positron emission tomography; Pola, polatuzumab vedotin; R/R, relapsed or refractory; Tafa, tafasitamab.

1. Nastoupil et al. *Clin Lymphoma Myeloma Leuk* 2024.

Polatuzumab vedotin + BR in R/R DLBCL: Pivotal data and RWE[1–11]

Compared to the pivotal study[1], patients treated with polatuzumab vedotin in the real world are more likely to be treated in later lines and to have received prior CAR-T therapies[1–11]

	Pivotal study[1]	RWE[2–11]
Median age (range), years	67 (33–86)	(17–88)
ECOG PS ≥2, %	15	9–51
Median (range) of prior LoT, n	2 (1–7)	(1–9)
Refractory to last therapy, %	75	23–87
Prior CAR-T, %	NA	9–26
mPFS, months	9.2	2.0–11.6
mOS, months	12.4	5.0–9.0



Old and new challenges: Bendamustine impact on T-cell fitness; Polatuzumab re-challenge after use in 1L

BR, bendamustine and rituximab; CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; LoT, line of therapy; mOS, median overall survival; mPFS, median progression-free survival; ORR, overall response rate; PR, partial response; RWE, real-world evidence.

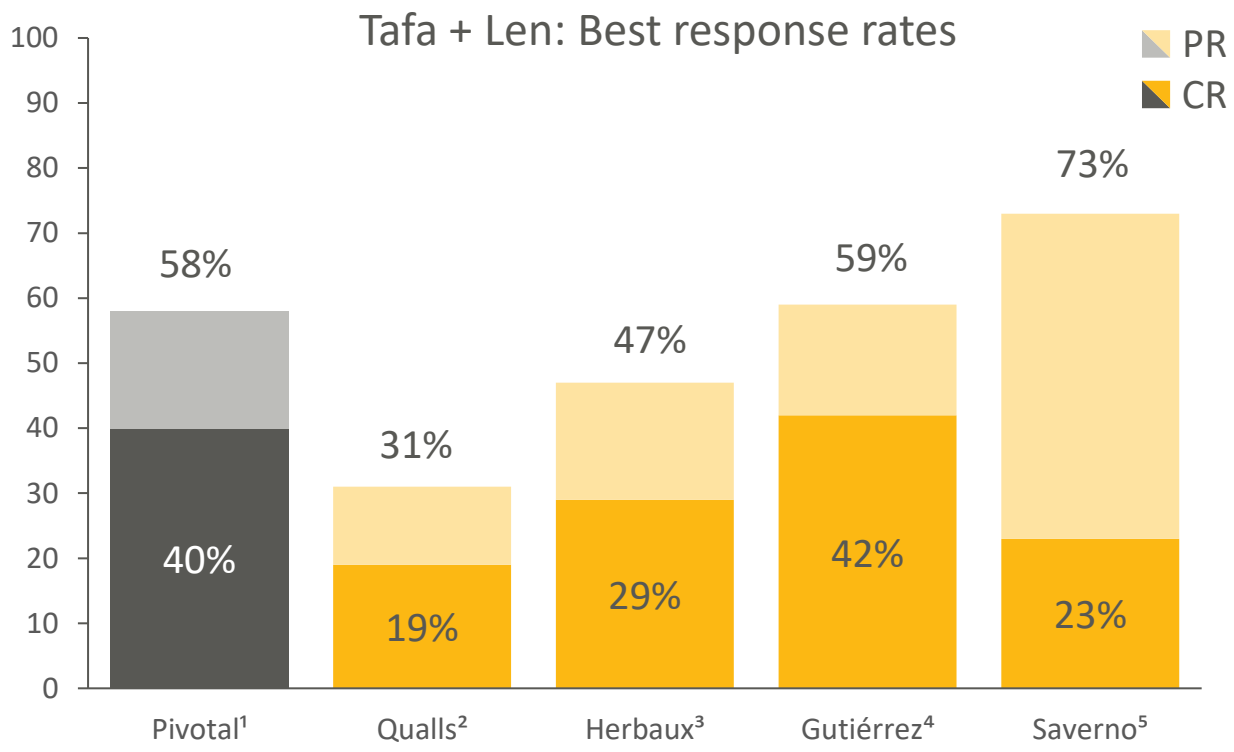
1. Sehn et al. *J Clin Oncol* 2020 **2.** Smith et al. *Clin Lymphoma Myeloma Leuk* 2021 **3.** Segman et al. *Leuk Lymphoma* 2021 **4.** Dimou et al. *Hematol Oncol* 2021 **5.** Northend et al. *Blood Adv* 2022 **6.** Argnani et al. *Hemasphere* 2022 **7.** Dal et al. *Ann Hematol* 2023 **8.** Vodicka et al. *Eur J Haematol* 2022 **9.** Liebers et al. *Blood Adv* 2021 **10.** Pardal et al. EHA 2024; Abstract #PB3006 **11.** Danecki et al. EHA 2024; Abstract #P1182.

NP-42408

Tafasitamab + lenalidomide in R/R DLBCL: Pivotal data and RWE[1–5]

Clinical trial[1] and real-world data[2–5] show a better efficacy of tafasitamab + lenalidomide in earlier lines and in lower risk disease

	L-MIND[1]	RWE[2–5]
Median age (range), years	72 (41–86)	(32–93)[3]
IPI 3–5, %	51	71–81
Median (range) of prior LoT, n	2 (1–4)	(1–13)
Refractory to last therapy, %	43	72[2]
mPFS, months	11.6	4.7–11.3
mOS, months	33.5	10.0–Not reached

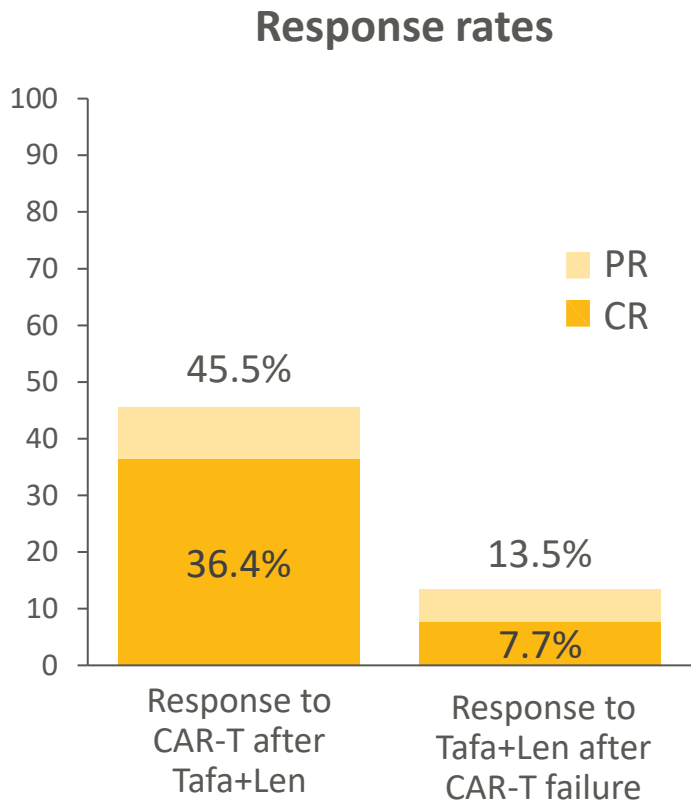


NP-42408

CR, complete response; IPI, International Prognostic Index; LoT, line of therapy; mOS, median overall survival; mPFS, median progression-free survival; PR, partial response; RWE, real-world evidence.
1. Duell et al. *Haematologica* 2021 **2.** Qualls et al. *Blood* 2023 **3.** Herbaux et al. EHA 2024; Abstract #P1214 **4.** Gutiérrez et al. EHA 2024; Abstract #P1203 **5.** Saverno et al. *Blood* 2024.

CD19 expression after tafasitamab seems to be maintained, however, efficacy after CAR-T remains poor[1,2]

	Tafa+Len before CAR-T[1,*]	Tafa+Len after CAR-T[1]
Number of patients	15	52
Median age (range), years	71 (47–80)	65.5 (20–81)
Median (range) of prior LoT, n	3 (2–7)	2 (1–6)
mPFS, months	3.0	3.0
mOS, months	8.0	4.7



Only 2/15 patients received Tafa+Len as the last line of therapy before CAR-T

Better outcomes for patients starting Tafa+Len more than 6 months after CAR-T

CD19 epitope masking by tafasitamab may lead to delays in subsequent use of CAR T-cell therapy[2]

Tafasitamab + lenalidomide efficacy immediately before CAR-T remains to be elucidated; outcomes after CAR-T failure seem poor[1]

*Use of tafa+len at any time before CAR-T. CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; Len, lenalidomide; mOS, median overall survival; mPFS, median progression-free survival; PR, partial response; R/R, relapsed or refractory; Tafa, tafasitamab.

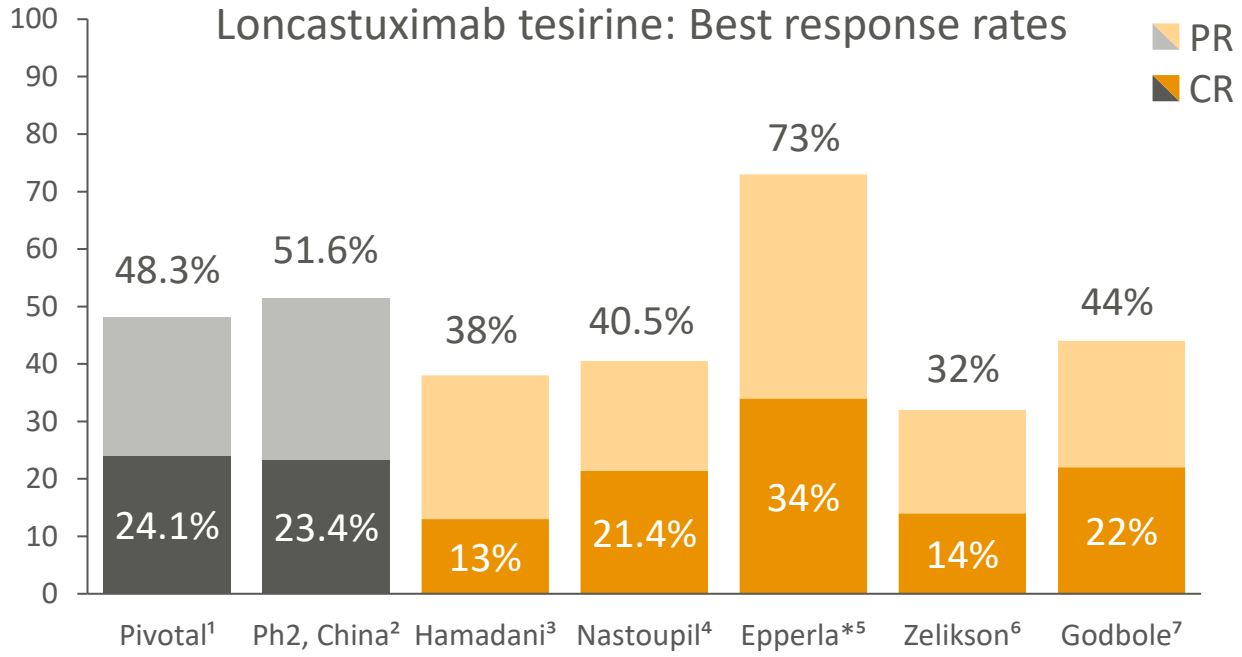
1. Camus et al. *Blood Adv* 2024 **2.** Fitzgerald et al. L*euk Lymphoma* 2022.

NP-42408

Loncastuximab tesirine as a single agent in R/R DLBCL: Pivotal data and RWE[1–7]

Compared to the LOTIS-2 study[1], real-world cohorts were enriched with higher risk (DH/TH, HGBL), more heavily pretreated patients and later lines of therapy[3–7]

	LOTIS-2 study[1]	Ph2 study, China[2]	RWE[3–7]
Median age (range), years	66 (22–94)	60 (26–81)	(24–86)
ECOG PS ≥2, %	6	7.8	26–33[2,5]
Median (range) of prior LoT, n	3 (2–7)	3 (2–12)	(2–7)
Prior CAR-T, %	10	6.3	47.6–100
mPFS, months	4.9	5.0	2.1–NR
mOS, months	9.5	9.3	4.6–NR



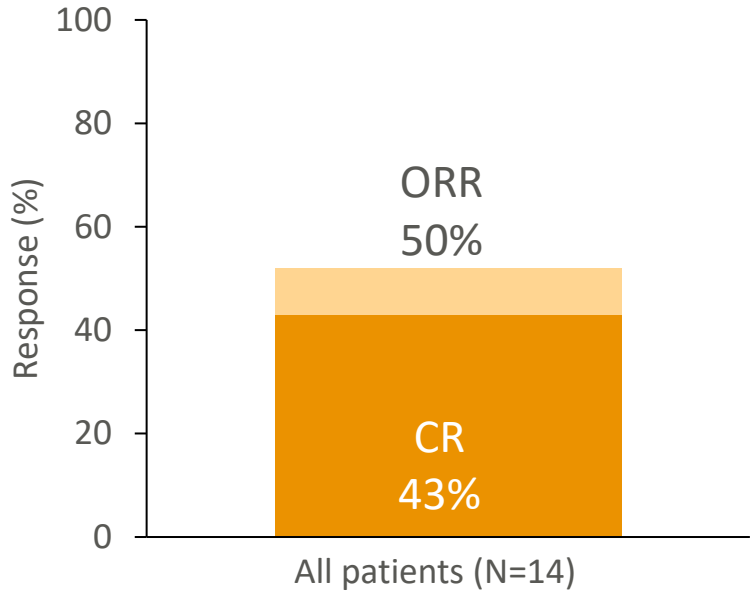
NP-42408

*Outcomes shown for patients with R/R DLBCL who initiated loncastuximab monotherapy as their 3L treatment after progressing on 2L CAR-T. CAR-T, chimeric antigen receptor T-cell therapy; DH, double-hit; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; HGBL, high-grade B-cell lymphoma; LoT, lines of therapy; mOS, median overall survival; mPFS, median progression-free survival; NR, not reached; ORR, overall response rate; Ph2, Phase 2 study; PR, partial response; R/R, relapsed/refractory; RWE, real-world evidence; TH, triple-hit.

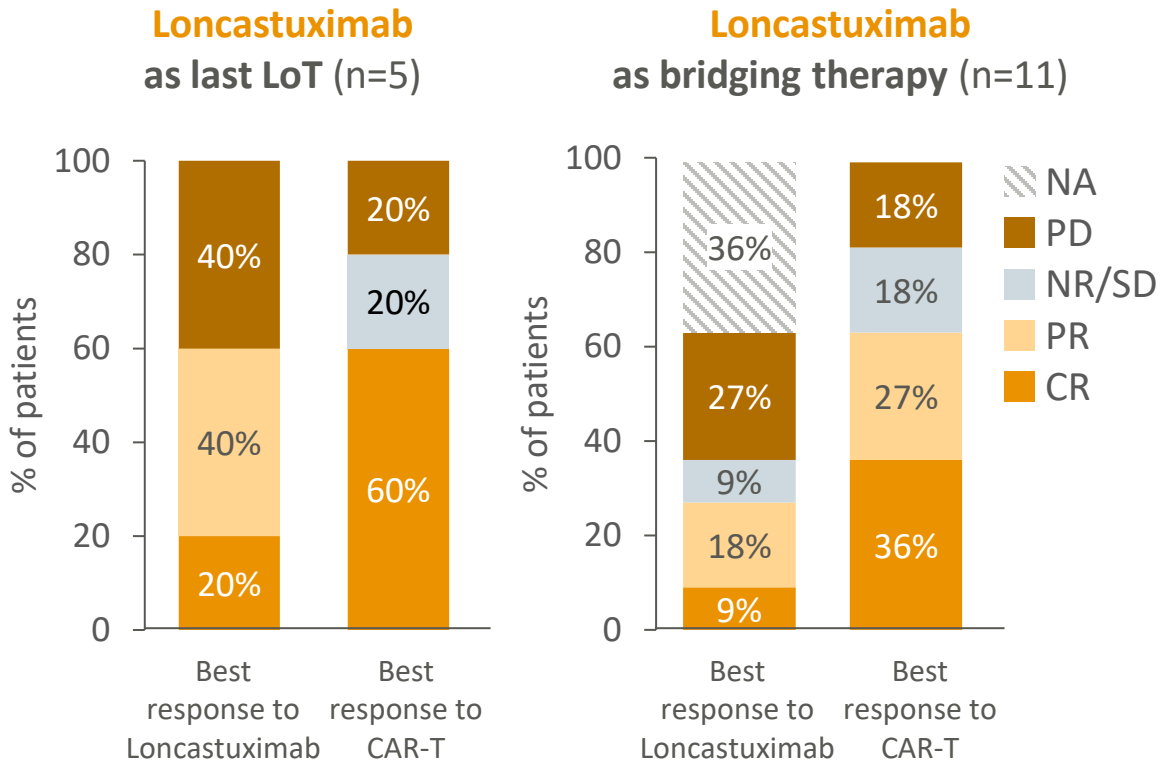
1. Caimi et al. *Lancet Oncol* 2021 **2.** Lin et al. *Haematologica* 2025 **3.** Hamadani et al. *eJHaem* 2024 **4.** Nastoupil et al. *Clin Lymphoma Myeloma Leuk* 2024 **5.** Epperla et al. *Blood Cancer J* 2024 **6.** Zelikson et al. *Haematologica* 2025 **7.** Godbole et al. *Blood* 2024.

Loncastuximab before CAR-T does not seem to impact outcomes[1,2]

In clinical studies, CAR-T cell therapy efficacy is maintained after Loncastuximab[1,*]



Similarly in RWE, CAR-T responses seem not impacted by previous Loncastuximab[2]



*14 patients from LOTIS-1 and LOTIS-2 received CAR-T after relapsing or progressing with Loncastuximab. CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; Loncastuximab, loncastuximab tesirine; LoT, line of therapy; NA, not assessed; NR, no response; PD, progressive disease; ORR, overall response rate; PR, partial response; R/R, relapsed or refractory; SD, stable disease.

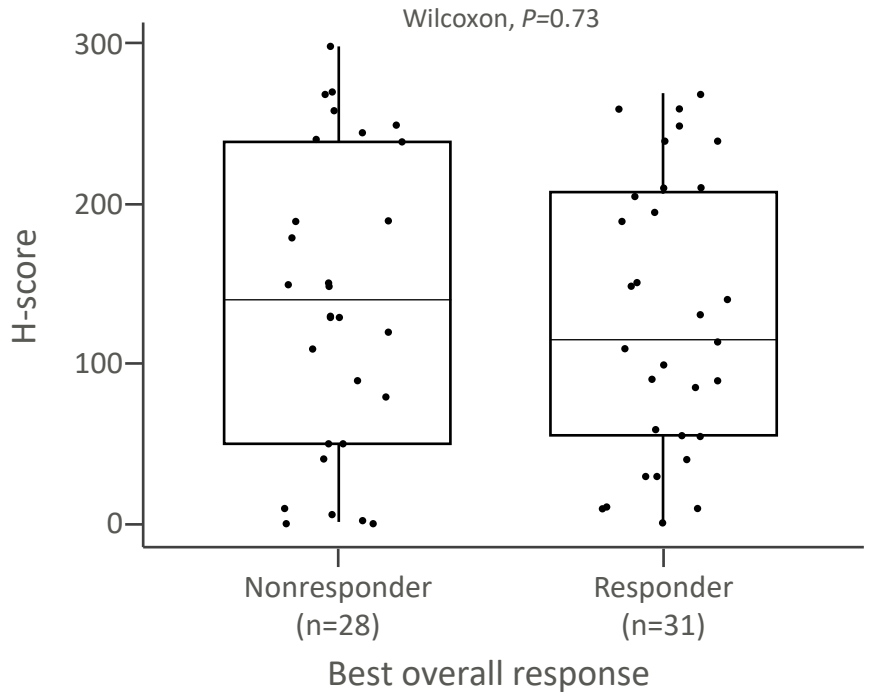
1. Thapa et al. *Blood Adv* 2020 **2.** Hamadani et al. *EJHaem* 2024.

NP-42408

Loncastuximab use after CAR-T: Data from clinical trials[1,2]

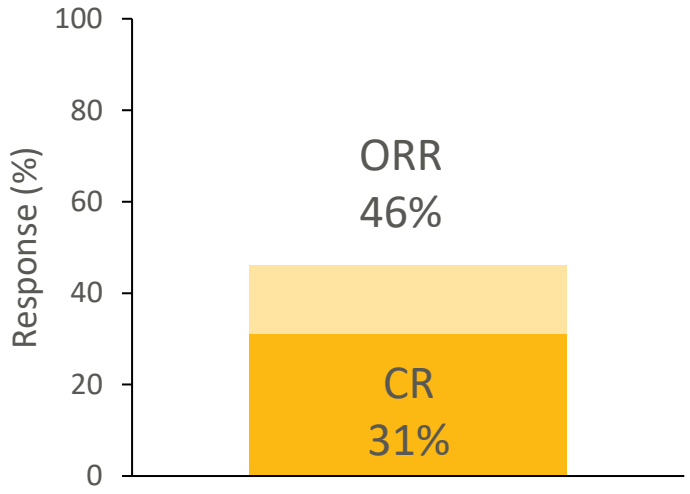
Responses to Loncastuximab were also seen in patients with low CD19 expression[1]

Baseline tumour CD19 H-score by response to Loncastuximab* (N=59)†



Patients responded to Loncastuximab treatment after CAR-T[2]

13 patients from LOTIS-2 had received prior CAR-T‡; 5 responded and 1 had stable disease after CAR-T



Response to Lonca† was seen in **6/13 (46.2%)** patients already treated with CAR T-cell therapy

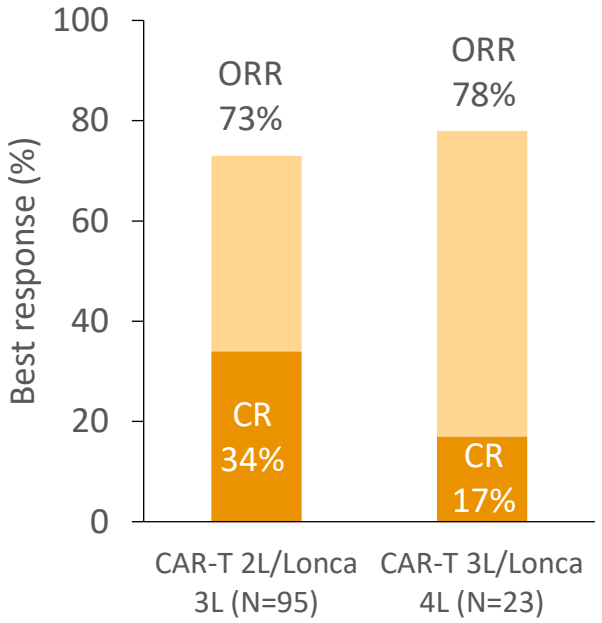
NP-42408

*In 59 patients with any prior systemic therapies, 10 patients received CD19-directed CAR-T as their last therapy. Patients who had received previous CD19-directed therapy must have had a biopsy confirming CD19 protein expression after completion of the CD19-directed therapy. †Independent assessment. ‡CD19 expression was required per protocol, but no prior CAR-T patients failed screening due to a lack of CD19. CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; H-score, HistoScore; Loncastuximab, loncastuximab tesirine; ORR, overall response rate; PR, partial response.

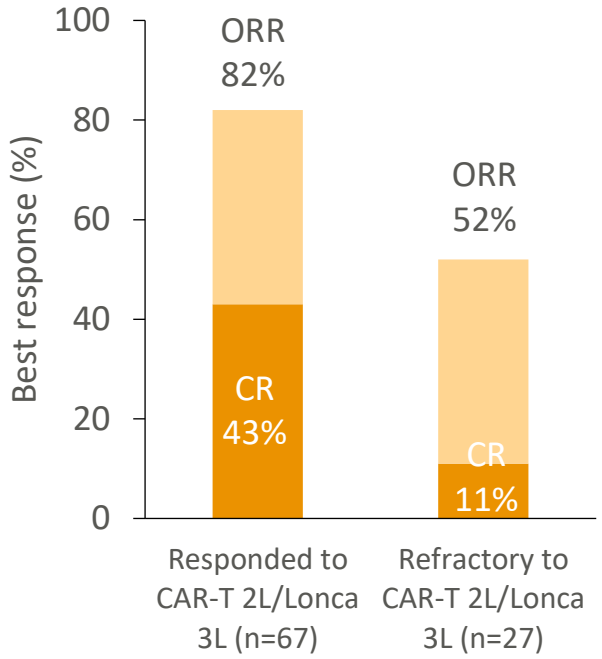
1. Caimi et al. *eJHaem* 2023 **2.** Caimi et al. *Clin Lymphoma Myeloma Leuk* 2022.

Loncastuximab use after CAR-T: Retrospective chart review[1]

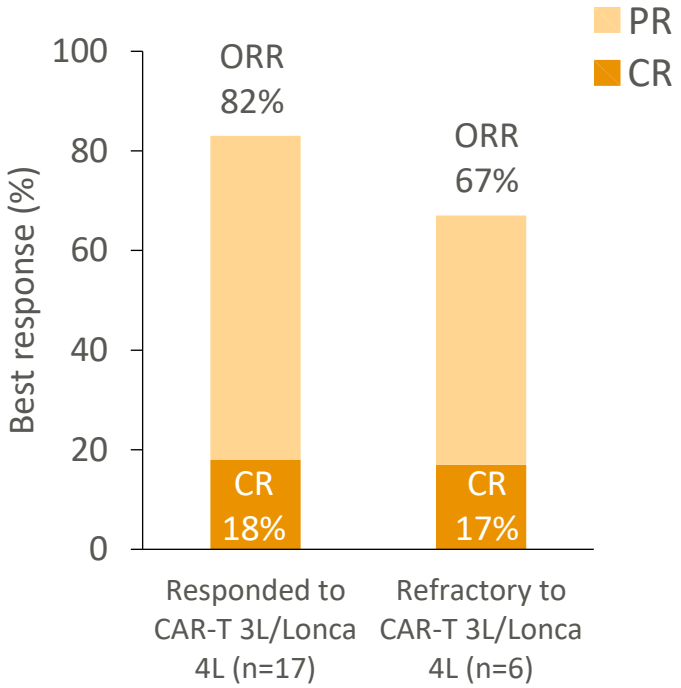
Best response to Loncastuximab as a single agent in 3L and 4L post CAR-T



In 3L Loncastuximab showed effectiveness after CAR-T failure



Loncastuximab showed effectiveness in 4L after CAR-T failure (small cohort)



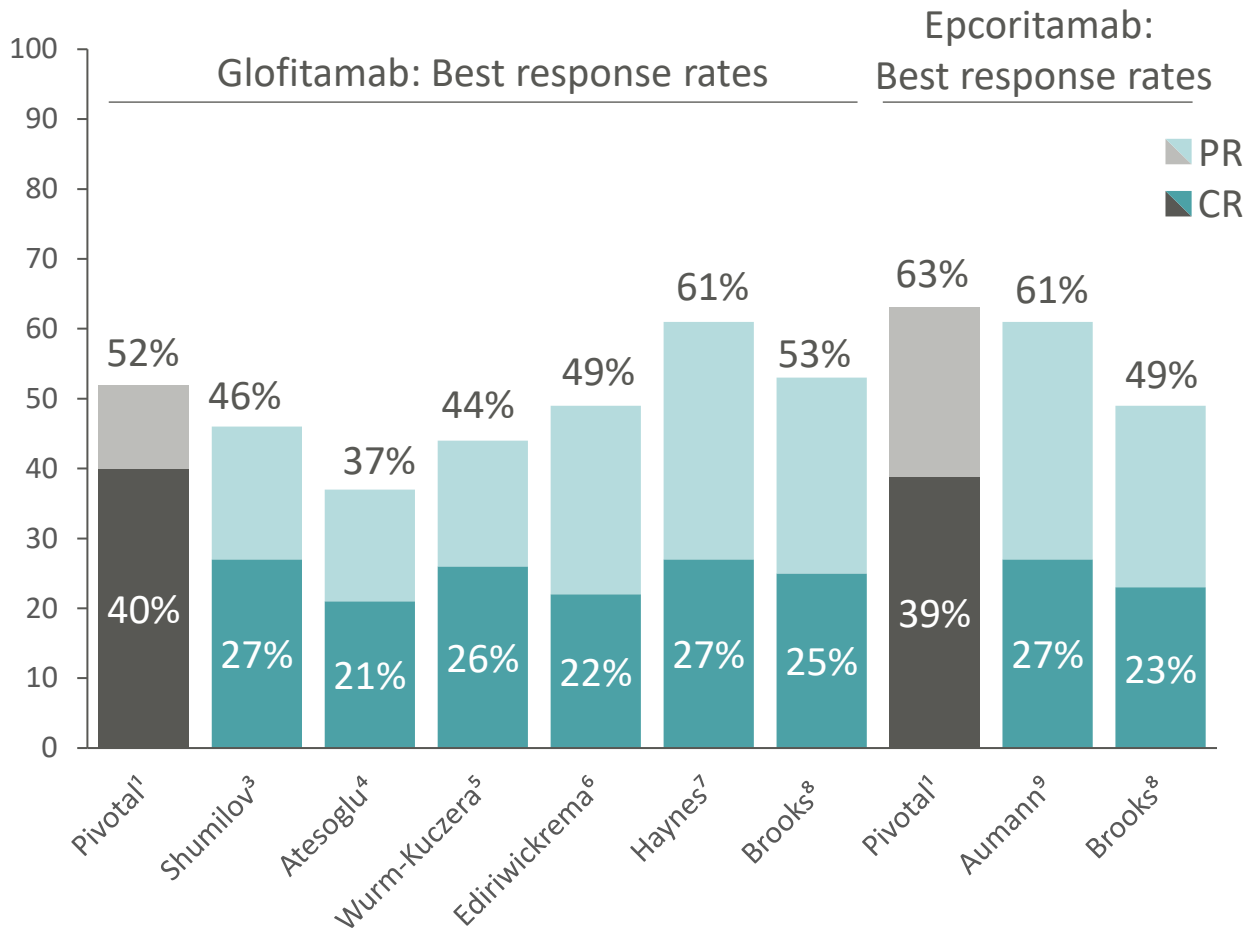
NP-42408

CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; L, line; Longa/loncastuximab, loncastuximab tesirine; ORR, overall response rate; PR, partial response; R/R, relapsed or refractory.

1. Epperla et al. *Blood Cancer J* 2024.

Bispecific antibodies: Pivotal data and RWE[1–9]

	Pivotal studies[1,2]	RWE[3–9]
Age range, years	20–90	19–94
ECOG PS ≥2, %	0–3	9–40
Range of prior LoT, n	2–≥4	1–14
Refractory to last therapy, %	83–86	54–84
Prior CAR-T, %	33–39	60–71
mPFS, months	4.4–4.9	3.0–10.8
mOS, months	11.5–Not reached	5.7–Not reached



Epcoritamab and glofitamab are increasingly explored in the real world, where responses seem lower than in pivotal trials[8]

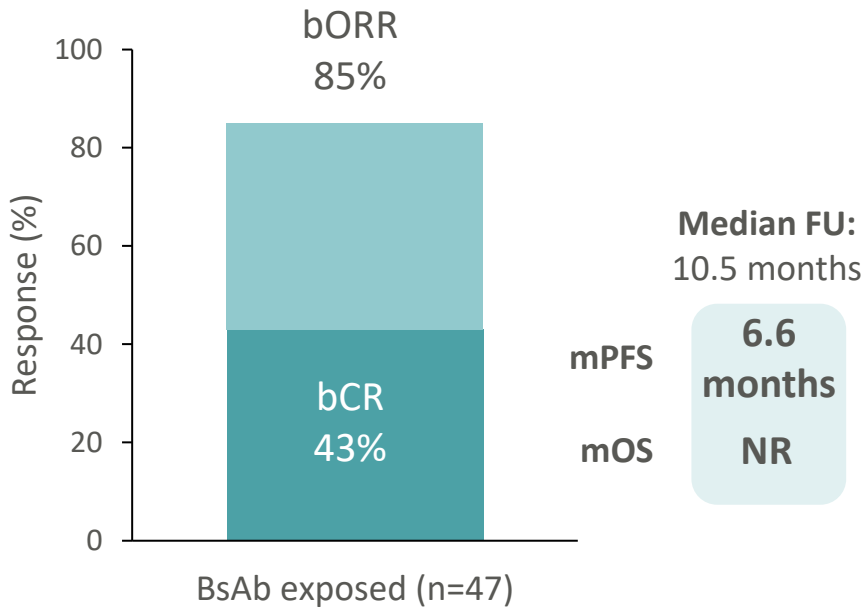
CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; LoT, line of therapy; mOS, median overall survival; mPFS, median progression-free survival; PR, partial response; RWE, real-world evidence.

1. Dickinson et al. *N Engl J Med* 2022 **2.** Thieblemont et al. *J Clin Oncol* 2022 **3.** Shumilov et al. *Blood Adv* 2024 **4.** Atesoglu et al. *Hematol Oncol* 2023 **5.** Wurm-Kuczera et al. EHA 2024; Abstract #P1166 **6.** Ediriwickrema et al. EHA 2024; Abstract #P2094 **7.** Haynes et al. *Blood* 2024 **8.** Brooks et al. *Blood* 2024 **9.** Aumann et al. *Blood* 2024.

Use of bispecific antibodies before CAR-T[1]

CD19-directed CAR T-cell therapy remains effective in R/R LBCL patients after prior exposure to bispecific antibodies

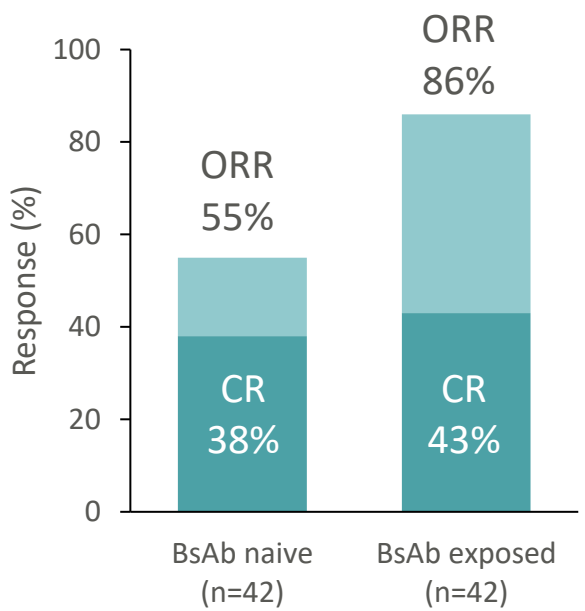
Best overall response to CD19-targeted CAR-T*† with prior BsAb‡ treatment



Median FU: 10.5 months

mPFS	6.6 months
mOS	NR

Best overall response to CD19-targeted CAR-T† in patients with prior BsAb‡ treatment vs PSM-matched BsAb-naïve control patients§



	BsAB naïve	BsAB exposed
1-year PFS	29%	43%
1-year OS	37%	55%

*Between 2018 and January 2023; patients exposed to CD19/CD3 BsAbs were excluded. †2 (47%) patients received axicabtagene ciloleucel (axi-cel), 20 (42%) tisagenlecleucel (tisa-cel) and 5 (11%) lisocabtagene maraleucel (liso-cel). ‡In 26 (55%) patients, BsAb therapy was the last regimen before CAR T-cells. §The 5 patients who received liso-cel were not included in this analysis due to the lack of an available control partner.
Axi-cel, axicabtagene ciloleucel; bCR, best complete response; BsAb, bispecific antibody; CAR T, chimeric antigen receptor T-cell; CR, complete response; FU, follow-up; LBCL, large B-cell lymphoma; liso-cel, lisocabtagene maraleucel; mOS, median overall survival; mPFS, median progression-free survival; ORR, overall response rate; PSM, propensity score matching; R/R, relapsed/refractory; tisa-cel, tisagenlecleucel.

1. Crochet et al. *Blood* 2024.

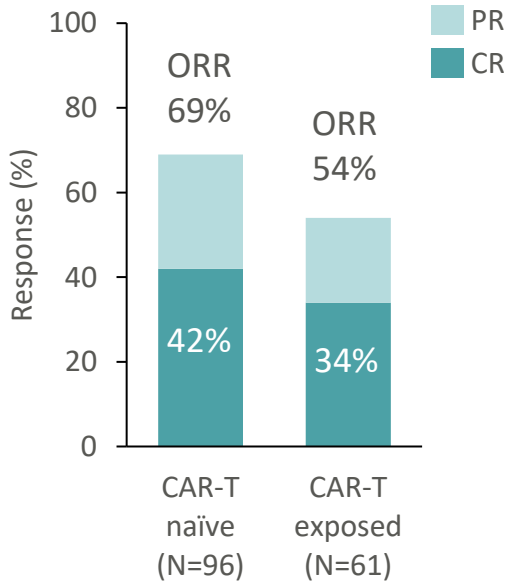
NP-42408

Use of bispecific antibodies after CAR-T

Bispecifics demonstrated clinical activity in patients who had received prior CAR-T[1–4]

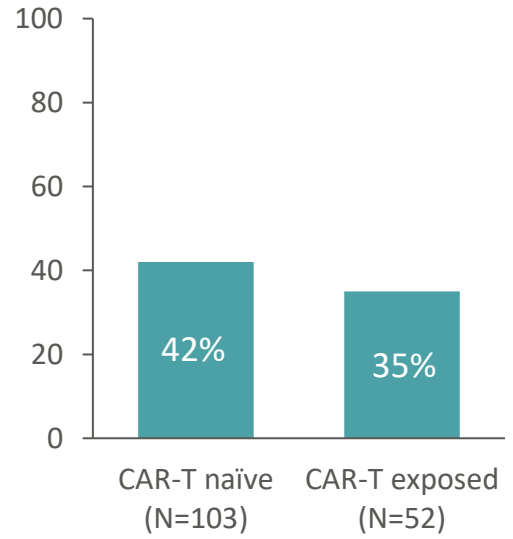
61 (38.9%) patients from EPCORE NHL-1 received prior CAR-T[1,*]

Best response to epcoritamab



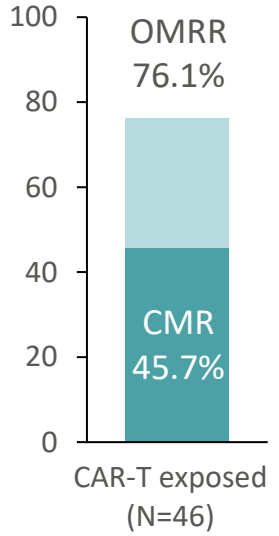
52 (33%) patients from NCT03075696 received prior CAR-T[2,†]

Complete response to glofitamab



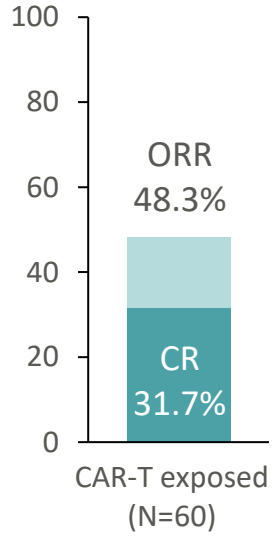
46 patients from NCT04703686 received prior CAR-T[3]

Metabolic response to glofitamab



60 patients from ELM-1 received prior CAR-T[4,‡]

Best response to odronextamab



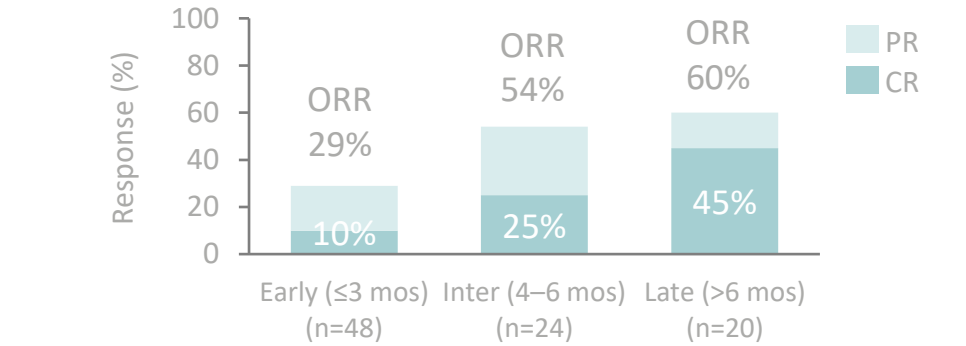
*46 of these patients (75.4%) had progressive disease within 6 months of CAR-T. †46 of these patients (89%) had disease that was refractory to CAR-T. ‡50 of these patients (71.7%) had disease that was refractory to CAR-T in any line. CAR-T, chimeric antigen receptor T-cell therapy; CMR, complete metabolic response; CR, complete response; OMRR, overall metabolic response rate; ORR, overall response rate; PR, partial response.

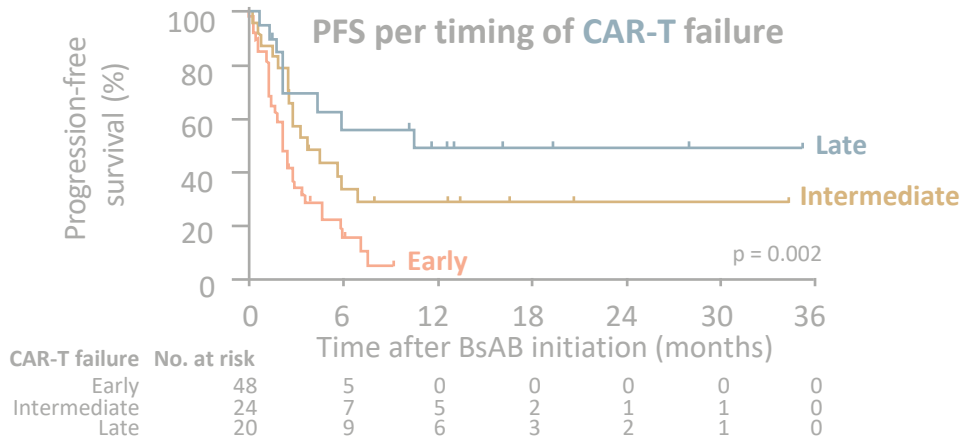
1. Thieblemont et al. *J Clin Oncol* 2023 **2.** Dickinson et al. *N Engl J Med* 2022 **3.** Cartron et al. *Nat Cancer* 2025 **4.** Topp et al. *Blood* 2025.

NP-42408

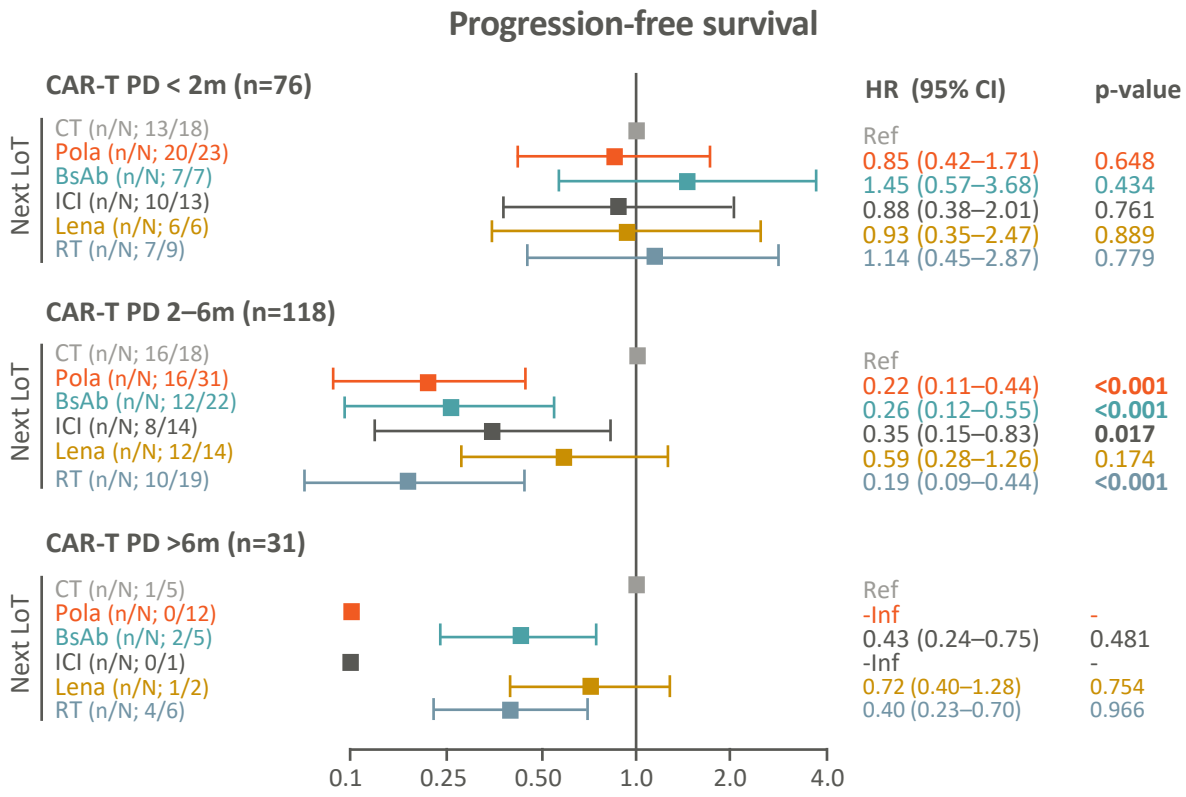
Initial data on T-cell engaging immunotherapies suggest inferior outcomes in early CAR-T failure[1,2]

Response to glofitamab and epcoritamab* may be impaired in early post-CAR-T failure[1,2]





BsAbs can achieve prolonged survival after CAR-T failure[2]



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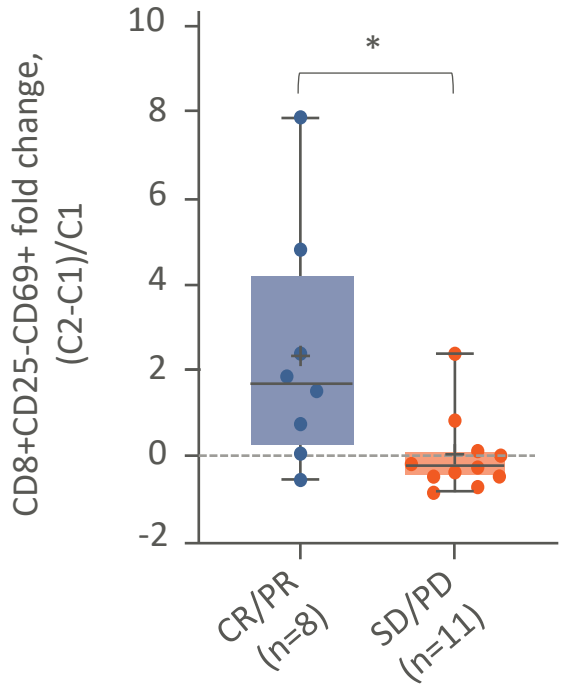
*92% received glofitamab, 6% received epcoritamab, 1% received mosunetuzumab. †Significant difference. BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; CT, chemotherapy; DLBCL, diffuse large B-cell lymphoma; EFS, event-free survival; ICI, immune checkpoint inhibitor; Lena, lenalidomide; LoT, line of therapy; mos, months; mOS, median overall survival; mPFS, median progression-free survival; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; Pola, polatuzumab vedotin; PR, partial response; RT, radiotherapy; SD, stable disease.

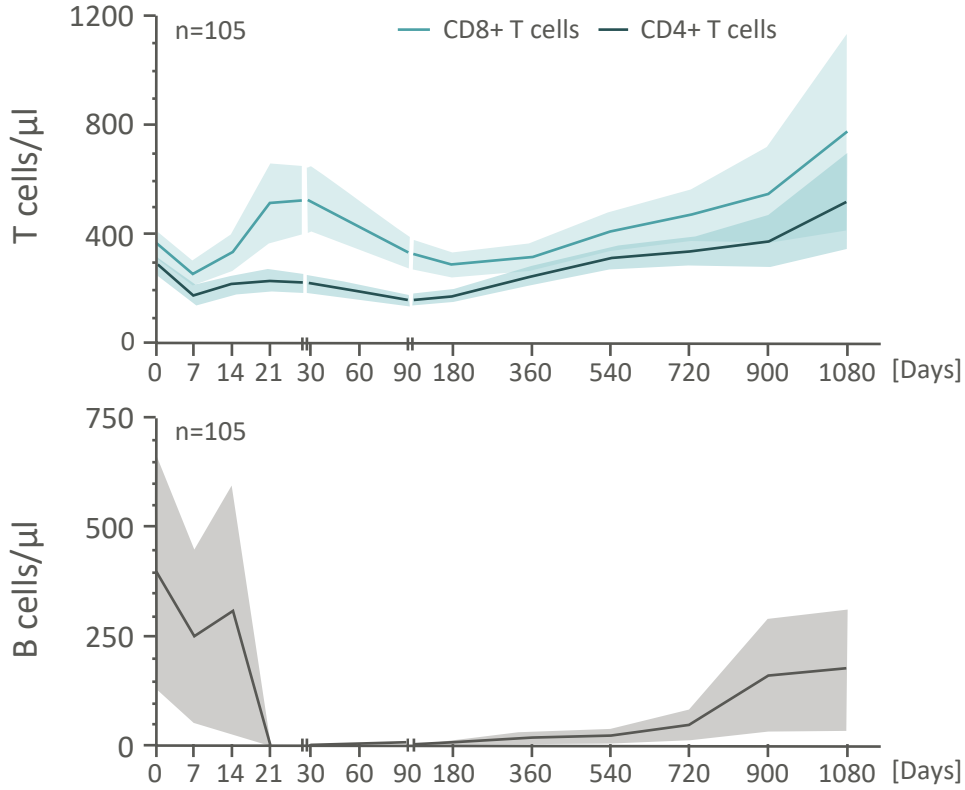
1. Shumilov et al. *Blood Adv* 2025 **2.** Iacoboni et al. *Hemasphere* 2024 (suppl.).

T-cell exhaustion and low immune recovery may explain lower outcomes with bispecific antibodies after CAR-T failure

T-cell exhaustion may play a role[1,*]



Lack of immune recovery after CAR T-cell therapy may predict worse survival outcomes[2]



*Larger fold increase observed in activated CD8+ T cells for responding vs nonresponding patients p=0.02.
CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.
1. Chong et al. *Blood Adv* 2025 **2.** Stock et al. *Hemasphere* 2025.

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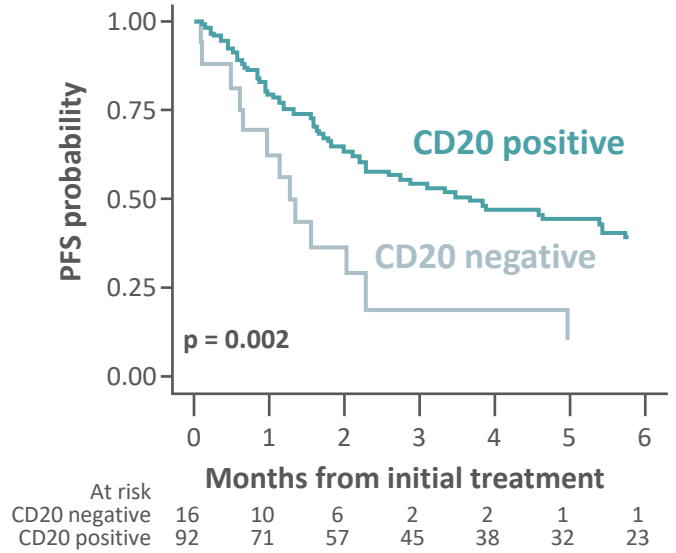
CD20 loss and impact on outcomes: Emerging data[1–4]

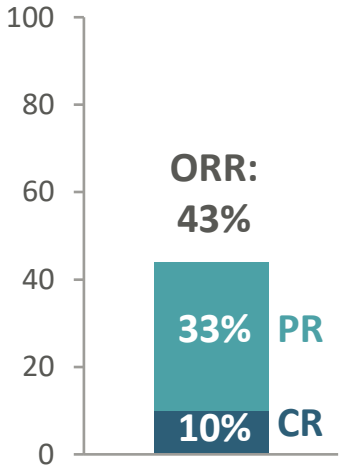
CD20 loss may impact on outcomes after bispecific antibodies[1]

17/19 (**89%**) pts with paired samples lost CD20



CD20 loss seems common in patients failing glofitamab[2,3]

High rates of CD20 loss (**59%**) at relapse post-glofitamab*



Response rates[3]
(n=18/42*)

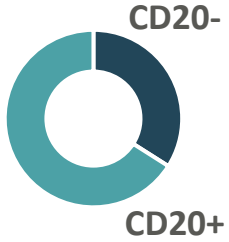
Median PFS:
2 months

CD20 loss observed in patients failing mosunetuzumab[4]

On-treatment† biopsies (n=30)

97% maintained CD20 levels while on treatment

Paired biopsies at progression (n=32)



34% showed CD20 loss
PFS reduction was observed

Poor outcomes and loss of CD20 expression after bispecifics failure represents an unmet medical need in DLBCL[3]

*Among 22 patients with available biopsies, n=10 converted from CD20^{+} to CD20^{-}; n=2 remained persistently CD20^{-}; n=10 had unknown pretreatment status. †Cycle 1, Day 15 to Cycle 3, Day 1.
CR, complete response; DLBCL, diffuse large B-cell lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; TTP, time to progression; pts, patients.
1. Brooks et al. ASH 2024; Oral presentation #111 **2.** Grigg et al. *Br J Haematol* 2024 **3.** Carlo-Stella *Br J Haematol* 2024 **4.** Schuster et al. *Blood* 2024.

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Summary

We have an increasing amount of data and experience on novel therapies, however, a clear algorithm remains elusive

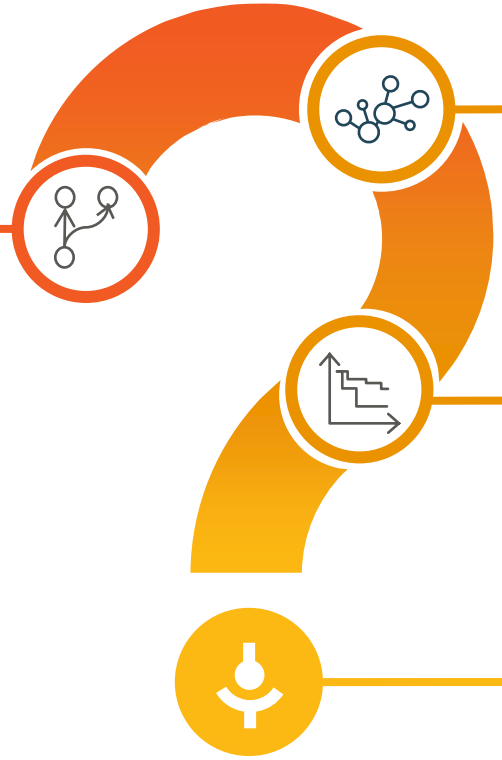
The factors impacting treatment sequencing are starting to be better understood, but the picture is still to be completed:

- The sequential use of CD19-targeted therapies seems not to impact efficacy
- The incidence and impact of CD20 loss is of emerging importance
- CAR-T failures are particularly challenging with all therapies, factors to guide clinical choices are under exploration

As research moves forward, we need to refine our ability to tailor our decisions for our patients and determine the optimal next choice

Open questions remain

How can we choose the best sequence of therapies for our patients with DLBCL?



- How do we handle CAR-T failure?
- How are therapies impacting our next choices?
- How will CD19 expression levels impact efficacy in the post CAR-T space?

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CAR-T, chimeric antigen receptor T-cell therapy; DLBCL, diffuse large B-cell lymphoma.

Clinical decision-making in practice

Professor Marek Trněný

Charles University,
Prague, Czech Republic

NP-42409

Male, born 1951

Diagnosis

- April 2023
  - Summary: DLBCL (WHO 2022)[1], HGBCL (ICC 2022)[2]
  - Ann Arbor stage IVB, LDH>ULN, ECOG PS 1, age 72 years, paravertebral masses
  - Rearrangements: MYC and BCL6
  - IPI 4 – High risk

Relevant medical history

- Comorbidities: Hypertension, DM on treatment

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DLBCL, diffuse large B-cell lymphoma; DM, diabetes mellitus; ECOG PS, Eastern Cooperative Oncology Group performance status; HGBCL, high-grade B-cell lymphoma; ICC, International Consensus Classification; IPI, International Prognostic Index; LDH, lactate dehydrogenase; ULN, upper limit of normal; WHO, World Health Organization.

1. Alaggio et al. *Leukemia* 2022 **2.** Campo et al. *Blood* 2022.

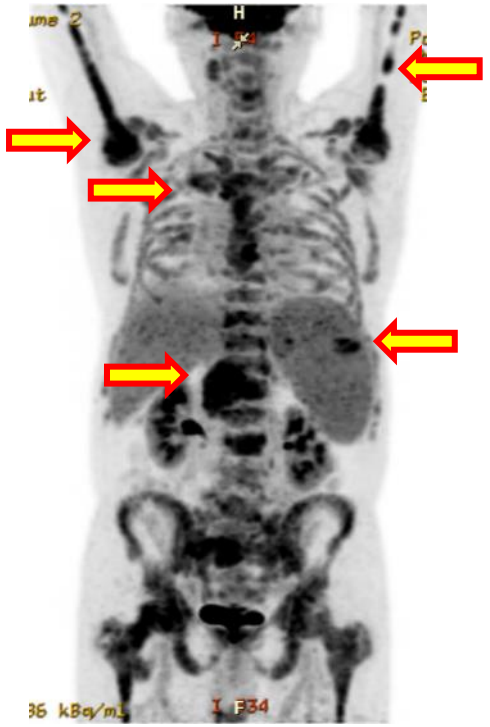
First-line therapy

R-CHOP

- 6 cycles
- April–August 2023

- Interim PET-CT → **PR**
- EOT PET-CT (September 2023) → **CMR**

03.05.2023



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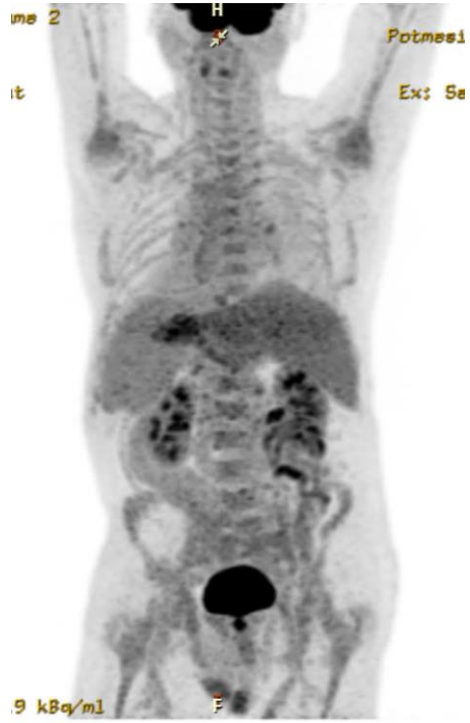

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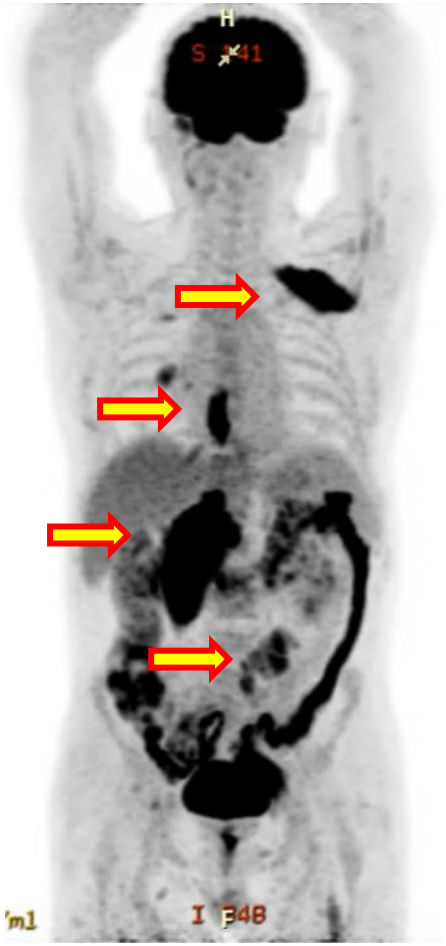
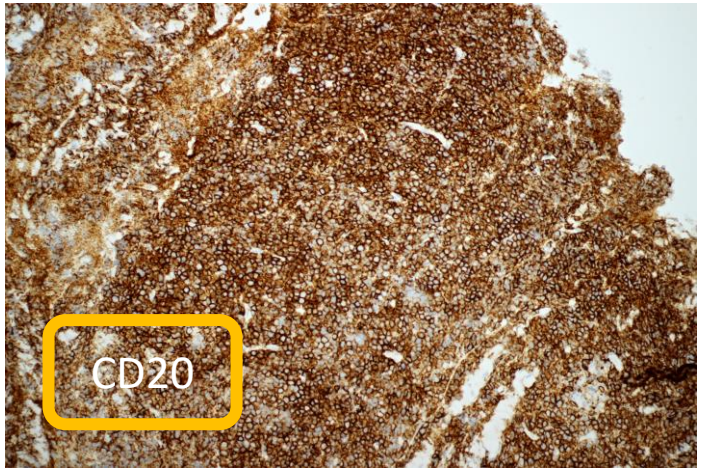
CMR, complete metabolic remission; EOT, end of treatment; PET-CT, positron emission tomography–computed tomography; PR, partial response; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone.

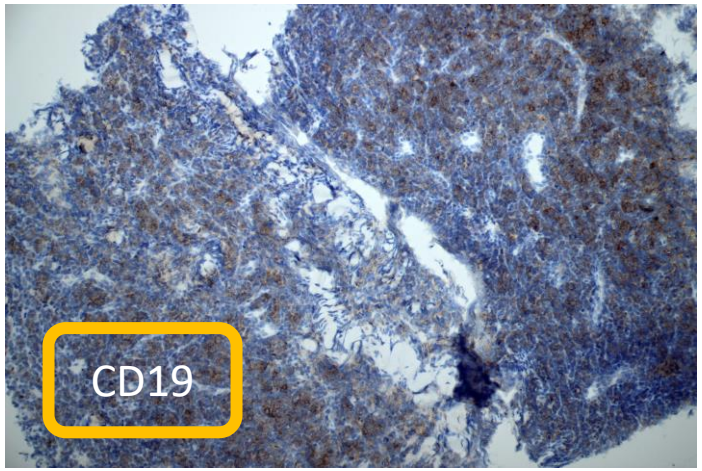
First relapse

March 2024

- B symptoms (weight loss)
- Ann Arbor stage IVB
- ECOG PS 1
- 73 years old
- **Re-biopsy:**
  - HGBCL NOS or HGBCL “double hit” (ICC 2022[1])
  - Ki-67: 100%







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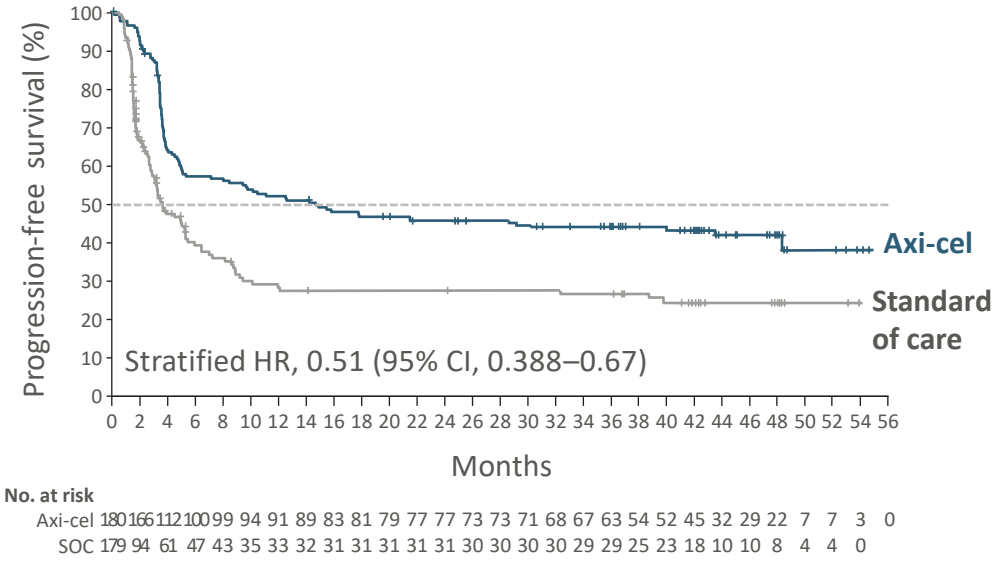
ECOG PS, Eastern Cooperative Oncology Group performance status; HGBCL, high-grade B-cell lymphoma; NOS, not otherwise specified.

1. Campo et al. *Blood* 2022.

CAR-T is the new 2L standard of care for patients who relapse within 12 months after first-line therapy[1–3]

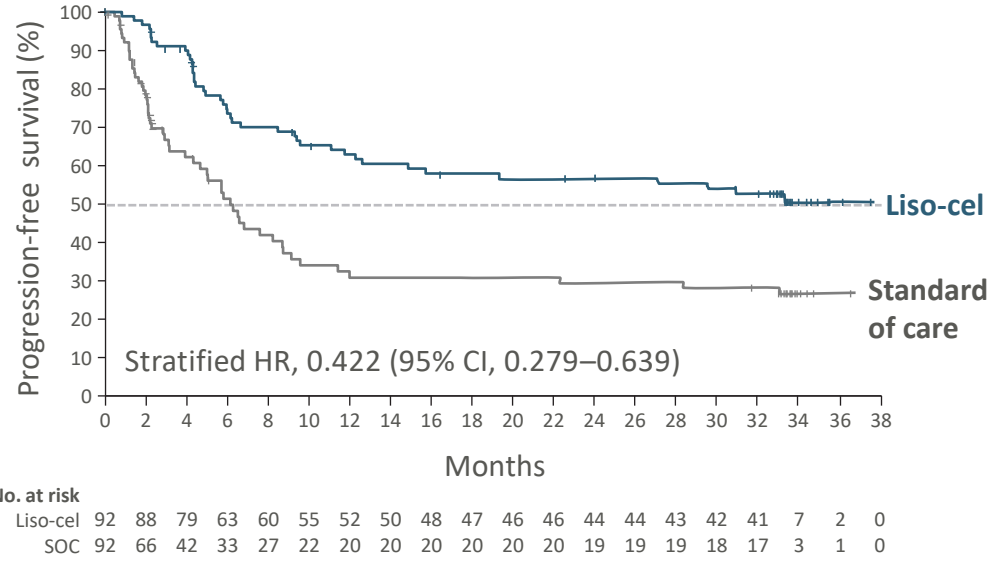
Axi-cel vs standard of care in 2L[1]



4-year PFS: 42%

4-year OS: 55%

Liso-cel vs standard of care in 2L[2,3]



3-year PFS: 50.9%

3-year OS: 62.8%

Median follow-up of 47.2 months (range, 39.8–60.0) for axi-cel[1], and 33.9 months (range, 0.9–53.0) for liso-cel[2]. CAR T-cell therapies were first approved in R/R DLBCL as a 3L of therapy.

2L, second line; 3L, third line; axi-cel, axicabtagene ciloleucel; CAR T, chimeric antigen receptor T-cell therapy; DLBCL, diffuse large B-cell lymphoma; liso-cel, lisocabtagene maraleucel; OS, overall survival; PFS, progression-free survival; R/R, relapsed or refractory.

1. Westin et al. *Blood* 2023 **2.** Abramson et al. EHA 2024; Oral presentation #S272 **3.** Kamdar et al. *J Clin Oncol* 2024.

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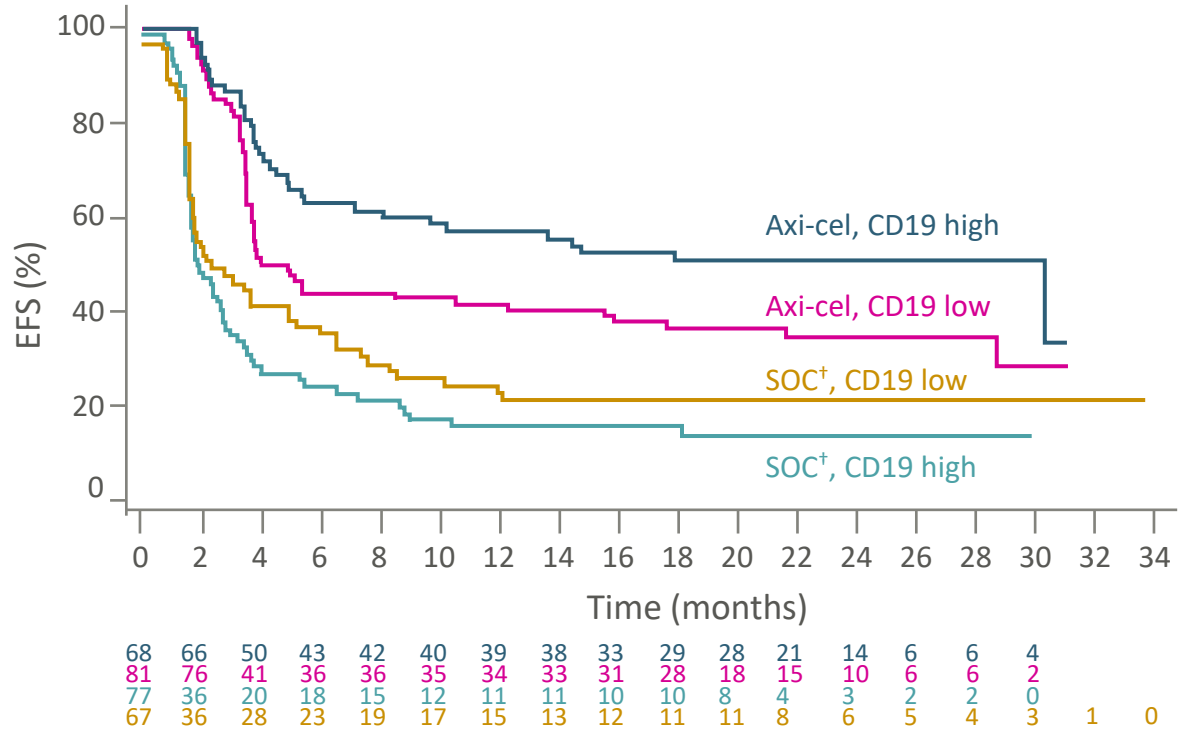
CD19 expression and CAR-T therapy: What do we know?

Currently available data support a correlation between CD19 expression levels and CAR T-cell therapy outcomes[1]



*SOC defined as 2–3 cycles of protocol-defined, investigator-selected, platinum-based chemotherapy with intention to subsequently undergo high-dose chemotherapy with autologous stem cell transplantation for chemosensitive patients. Axi-cel, axicabtagene ciloleucel; CAR-T, chimeric antigen receptor T-cell; EFS, event-free survival; SOC, standard of care.

1. Locke et al. *Nat Med* 2024.

Which treatment would you choose for second-line therapy? (Select one)

A. CAR T-cell therapy?
B. Salvage + ASCT?
C. Tafa-Len?
D. Pola-BR?
E. Clinical Trial?

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ASCT, autologous stem cell transplantation; BR, bendamustine and rituximab; CAR-T, chimeric antigen receptor T-cell; pola, polatuzumab vedotin; Tafa-Len, tafasitamab and lenalidomide.

Second-line therapy: CAR-T

R-ICE bridge

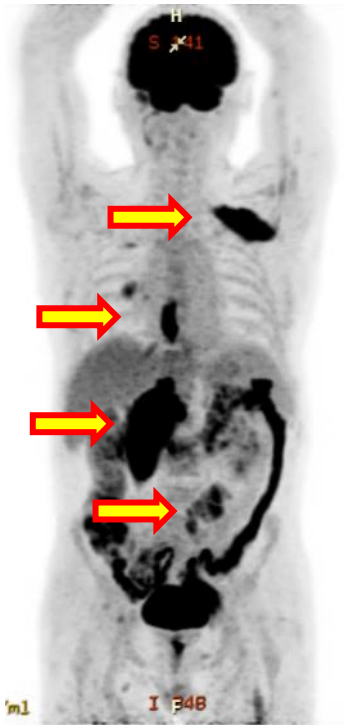
- Apheresis, April 2024
  - WBC 3.6×10^9/L
  - Absolute lymphocyte count 0.7×10^9/L

Axi-cel

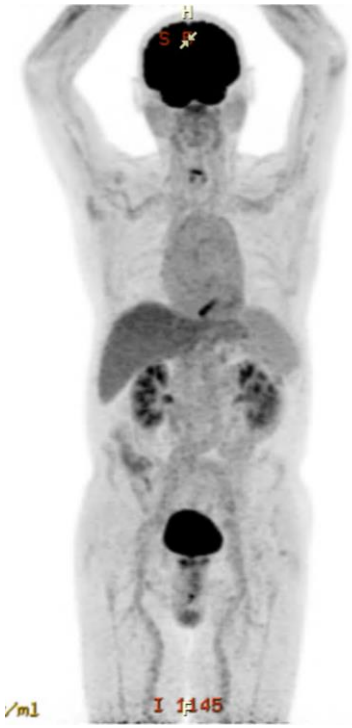
- May 2024
- CRS Gr1, ICANS Gr1, tocilizumab
  - CAR T-cell peak expansion: CD4+CAR T-cell: 23.4%, CD8+ CAR T-cell 25.1%

- PET-CT d+30 → **CMR**

15.03.2024



26.06.2024



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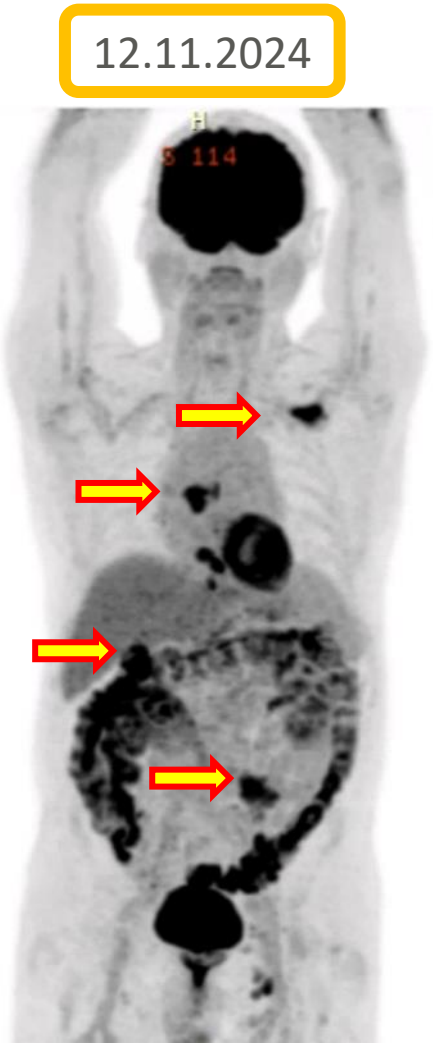
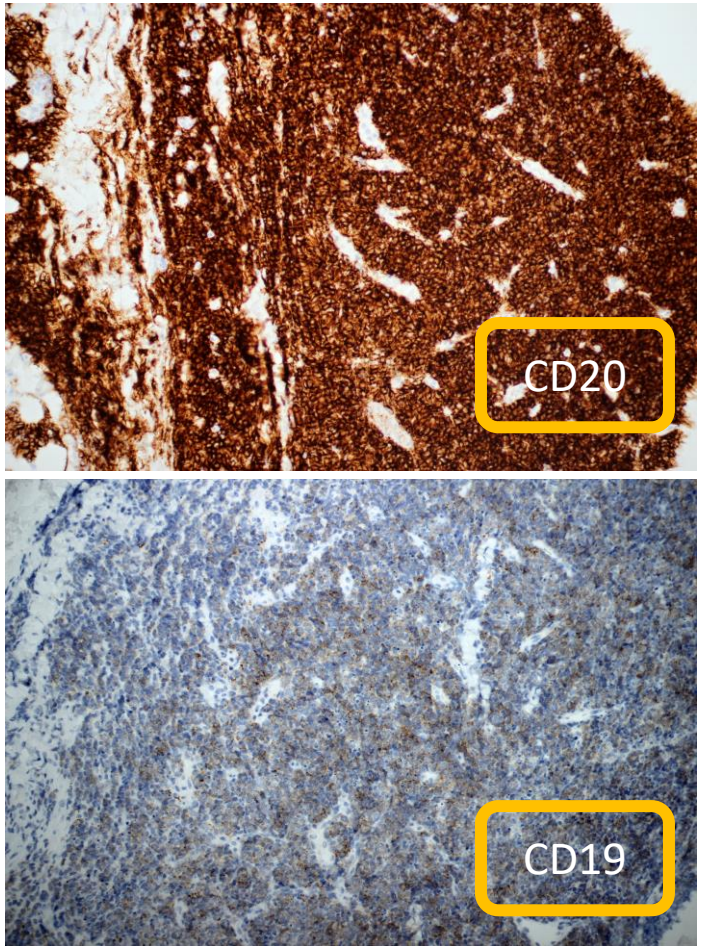
Axi-cel, axicabtagene ciloleucel; CAR-T, chimeric antigen receptor T-cell therapy; CMR, complete metabolic remission; CRS, cytokine release syndrome; Gr, grade; ICANS, immune effector cell-associated neurotoxicity syndrome; PET-CT, positron emission tomography–computed tomography; R-ICE, rituximab, ifosfamide, carboplatin, etoposide; WBC, white blood cell.

Second relapse

November 2024

- Ann Arbor stage IVA (subcutaneous, lymph nodes, paravertebral)
- ECOG PS 1
- 73.5 years old
- **Re-biopsy:**
  - CD20+
  - CD19+





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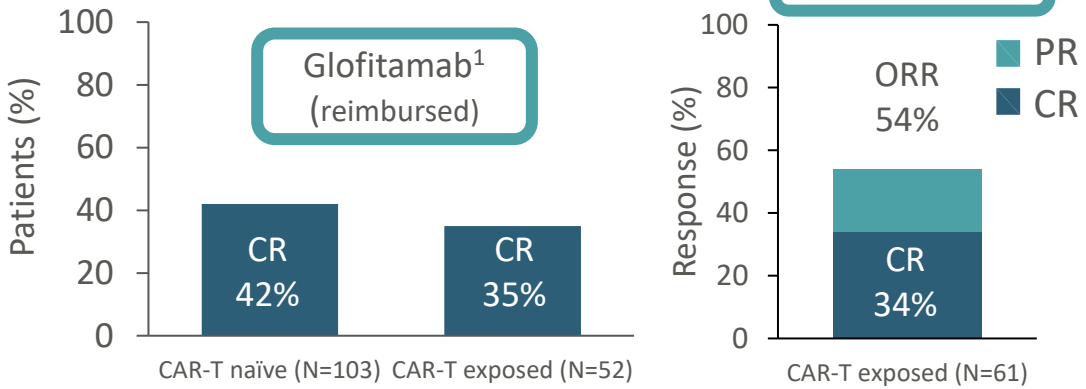
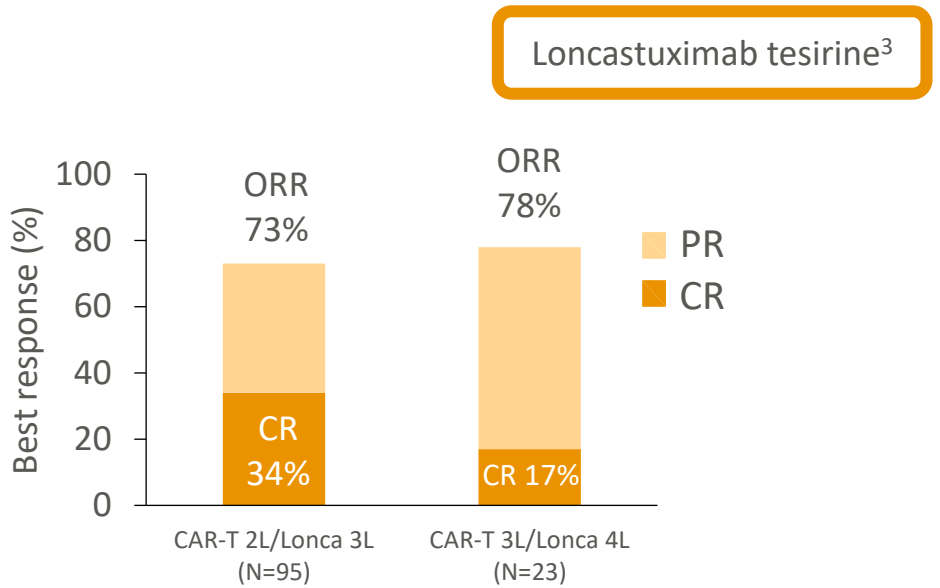
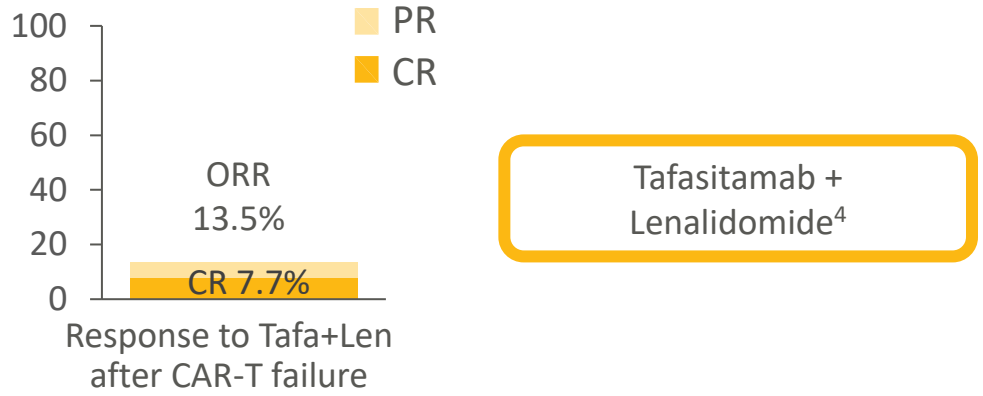
ECOG PS, Eastern Cooperative Oncology Group performance status.

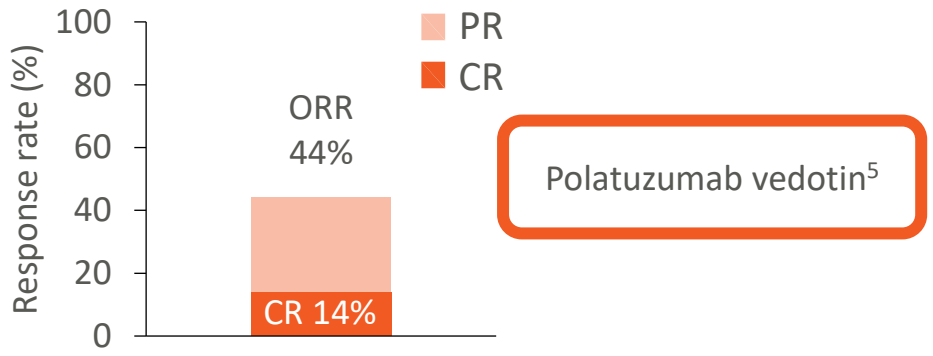
Third-line therapy?







Tafasitamab + Lenalidomide[4]



Polatuzumab vedotin[5]

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CAR-T, chimeric antigen receptor T-cell; CI, confidence interval; CR, complete remission; Longa, loncastuximab tesirine; NA, not achieved; ORR, overall response rate; 3L, third line.

1. Dickinson et al. *N Engl J Med* 2022 **2.** Thieblemont et al. *J Clin Oncol* 2023 **3.** Epperla et al. *Blood Cancer J* 2024 **4.** Camus et al. *Blood Adv* 2024 **5.** Gouni et al *Blood Adv* 2022.

Which treatment would you choose for third-line therapy? (Select one)

A. Salvage + ASCT?
B. Glofitamab? Epcoritamab?
C. Tafa-Len?
D. Pola-BR?
E. Loncastuximab tesirine?
F. Immunochemotherapy?

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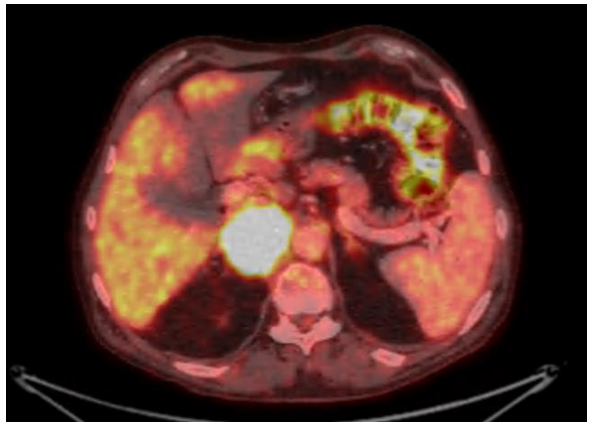
ASCT, autologous stem cell transplantation; BR, bendamustine and rituximab; pola, polatuzumab vedotin; Tafa-Len, tafasitamab and lenalidomide.

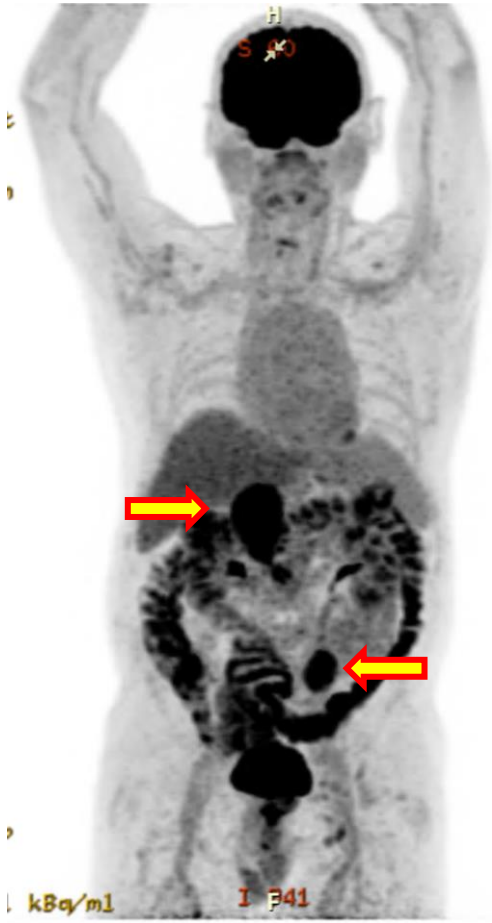
Third line therapy

Glofitamab

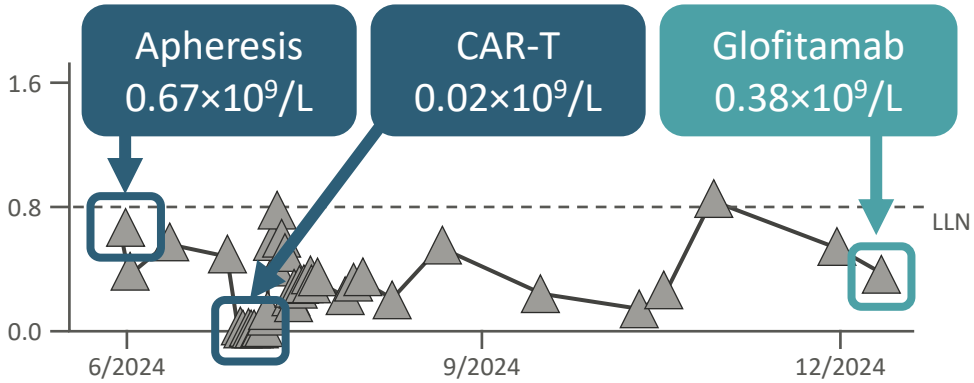
- 3 cycles
- November 2024–January 2025
- CRS Gr1, ICANS Gr0

- PET-CT January 2025 → **PD**





Absolute lymphocyte count



CAR-T, chimeric antigen receptor T-cell therapy; CRS, cytokine release syndrome; Gr, grade; ICANS, immune effector cell-associated neurotoxicity syndrome; LLN, lower limit of normal; PD, progressive disease; PET-CT, positron emission tomography–computed tomography.

Which treatment would you choose for fourth line therapy? (Select one)

A. Tafa-Len?
B. Pola-BR?
C. Loncastuximab tesirine?
D. Immunochemotherapy?

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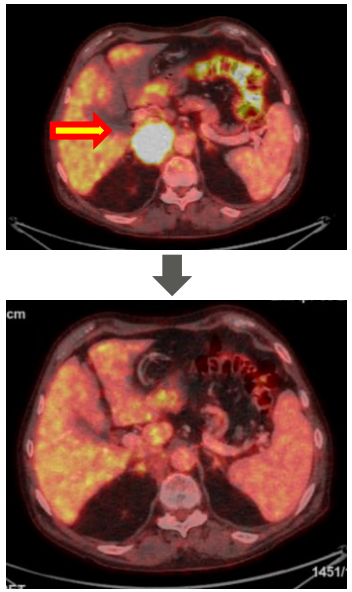
BR, bendamustine and rituximab; pola, polatuzumab vedotin; Tafa-Len, tafasitamab and lenalidomide.

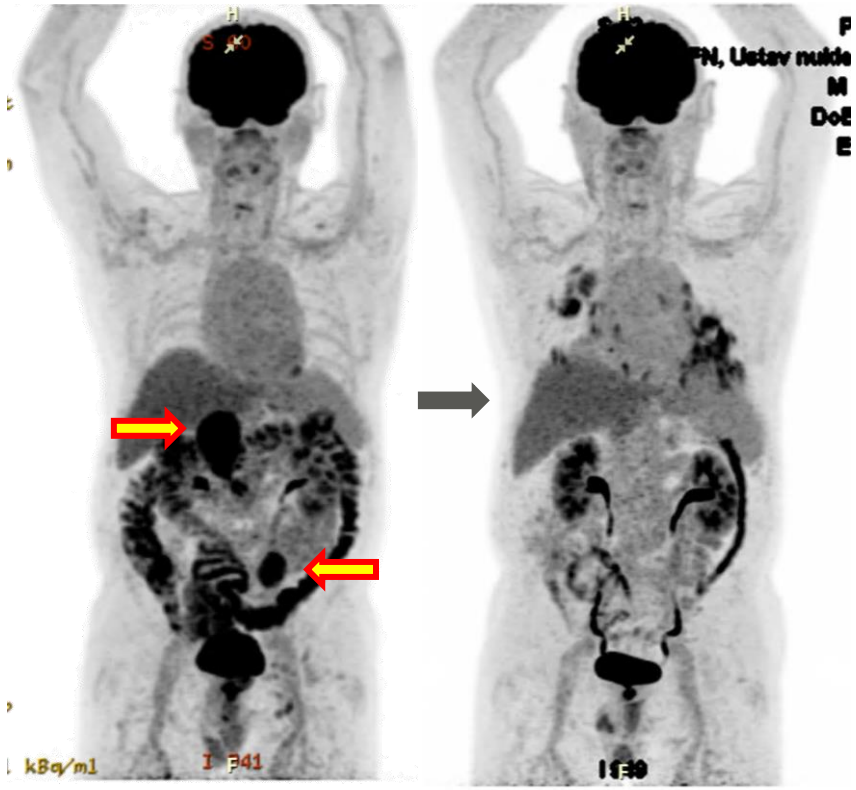
Fourth line therapy

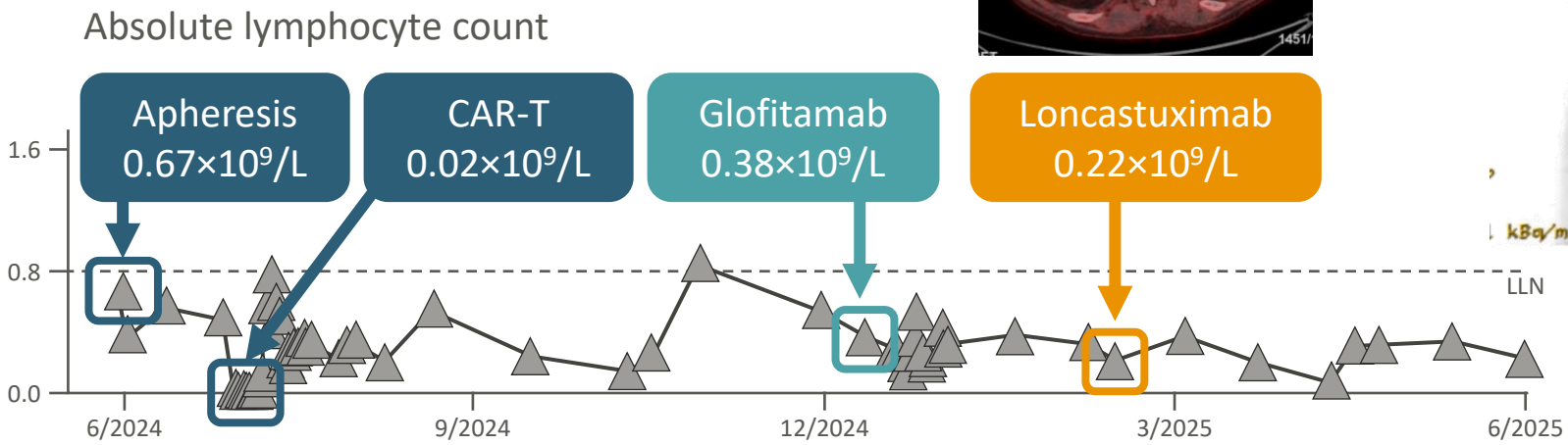
Loncastuximab tesirine

- 5 cycles (February–June 2025)
  - Skin toxicity Gr1, cytopenia, pneumonia Gr2 after 3rd cycle, febrile neutropenia after 5th cycle (hospitalised 4 days)
  - Treatment ongoing

- PET-CT April 2025 → **CMR**







CAR-T, chimeric antigen receptor T-cell therapy; CMR, complete metabolic response; Gr, grade; LLN, lower limit of normal; PET-CT, positron emission tomography–computed tomography.

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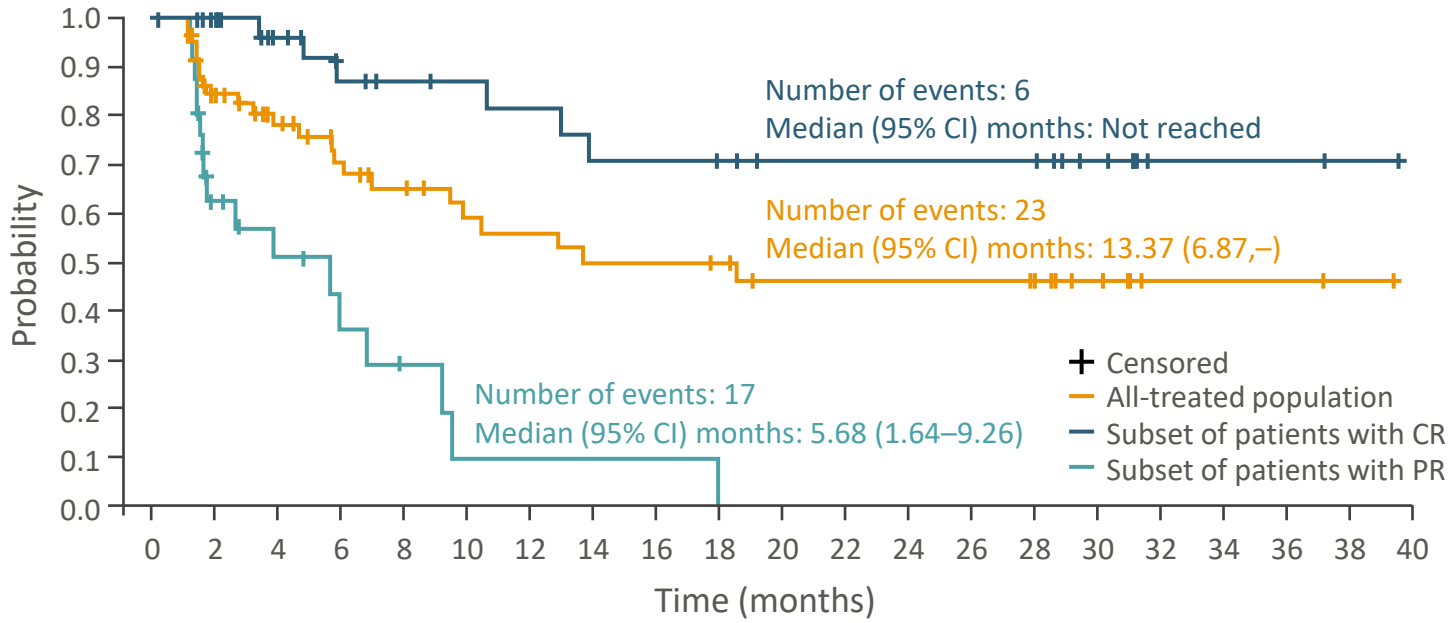
Among heavily pretreated patients with R/R DLBCL in the pivotal LOTIS-2 study, Lonca demonstrated durable responses[1]



Patients at risk

All-treated population	70	63	42	38	33	29	25	22	21	20	18	17	17	16	15	15	15	15	13	11	11	11	11	11	11	11	11	11	7	6	5	2	2	2	2	2	2	1	1	0
Subset of patients with CR	36	35	30	29	25	22	20	18	18	17	17	16	16	15	14	14	14	14	12	11	11	11	11	11	11	11	11	11	7	6	5	2	2	2	2	2	2	1	1	0
Subset of patients with PR	34	28	12	9	8	7	5	4	3	3	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Duration of response curve for the all-treated population (N=145) and the subsets of patients with a best response of complete response (CR) (N=36) and partial response (PR) (N=34). Reasons for censor included stem cell transplant. CI, confidence interval; CR, complete response; DLBCL, diffuse large B-cell lymphoma; Lonca, loncastuximab tesirine; NR, not reached; PR, partial response; R/R relapsed or refractory.

1. Caimi et al. *Haematologica* 2024.

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Summary

- **Despite novel therapies** being available in R/R DLBCL, there remains an **unmet medical need** for patients with high-risk disease or early CAR-T failure
- **RWE** is becoming increasingly relevant for guiding treatment decisions
- Not all therapeutic options are widely available across **geographies**
- In the absence of head-to-head studies, decisions need to be **tailored** to patient's and disease's characteristics
- Treatment sequencing is expected to evolve. **How we make the best use of our available options** is a continuous learning[1]

CAR-T, chimeric antigen receptor T-cell therapy; DLBCL, diffuse large B-cell lymphoma; R/R, relapsed or refractory; RWE, real-world evidence.

1. Brooks & Caimi. *Blood Rev* 2024.

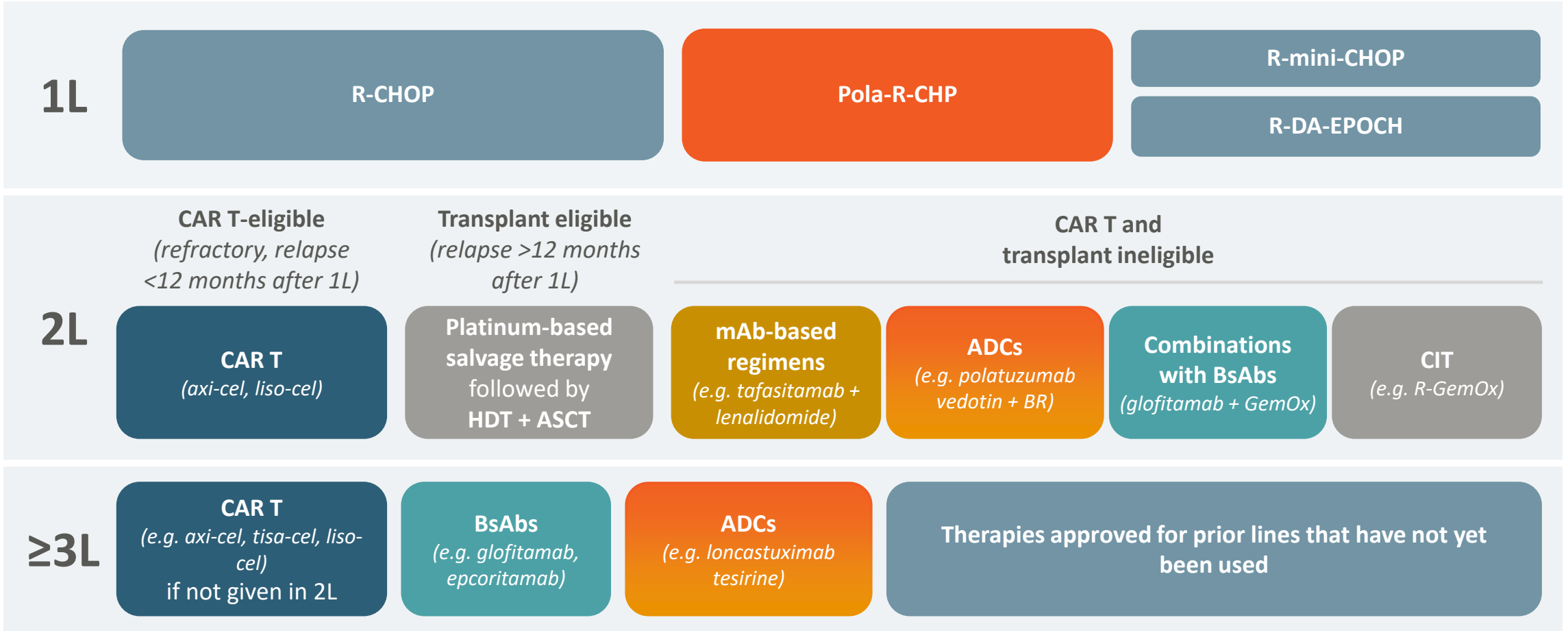
Treatment sequencing on the horizon: What is next?

Professor Andrew Davies

University of Southampton,
Southampton, United Kingdom

NP-42410

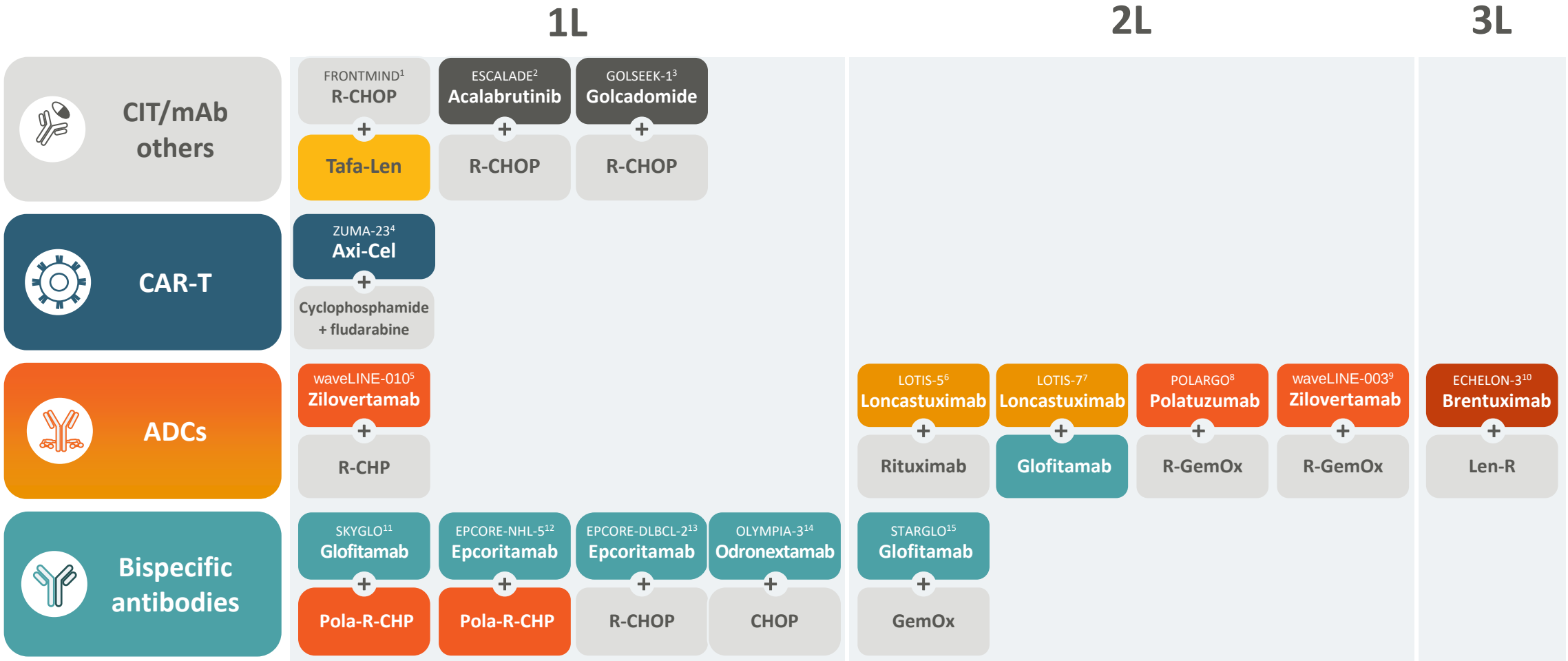
Numerous treatment options are now available for DLBCL in each line[1–9]



ADC, antibody-drug conjugate; ASCT, autologous stem cell transplantation; axi-cel, axicabtagene ciloleucel; BR, bendamustine and rituximab; BsAb, bispecific antibody; CAR T, chimeric antigen receptor T-cell therapy; CIT, chemo-immunotherapy; DLBCL, diffuse large B-cell lymphoma; HDT, high-dose therapy; L, line; liso-cel, lisocabtagene maraleucel; mAb, monoclonal antibody; pola, polatuzumab vedotin; R-CH(O)P, rituximab, cyclophosphamide, doxorubicin, (vincristine), and prednisone; R-DA-EPOCH, rituximab, dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin; R-GemOx, rituximab, gemcitabine, and oxaliplatin; tisa-cel, tisagenlecleucel. **1.** Sehn & Salles *N Engl J Med* 2021 **2.** Frontzek et al. *Ther Adv Hematol* 2022 **3.** Peyrade et al. *Blood* 2010 **4.** Polivy SmPC 2023 **5.** Columvi SmPC 2023 **6.** Tepkinly SmPC 2023 **7.** Zynlonta SmPC 2023 **8.** Bartlett et al. *J Clin Oncol* 2019 **9.** Roche Press release 2025.

NP-42410

And new combination therapies are under evaluation in DLBCL, potentially changing our future approach even more[1–15]

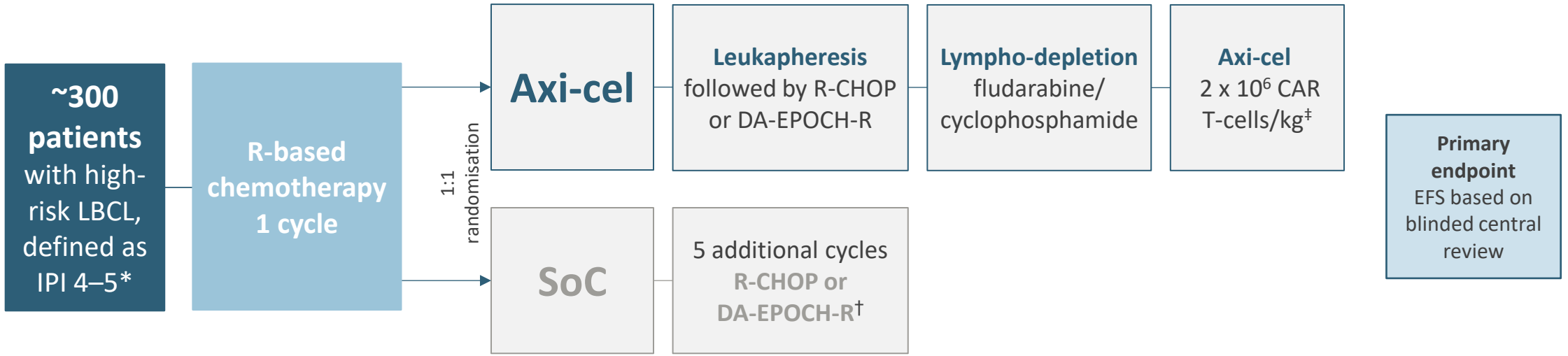


Ongoing company-sponsored, registration studies. ADCs, antibody-drug conjugates; axi-cel, axicabtagene ciloleucel; BR, bendamustine and rituximab; CAR-T, chimeric antigen receptor T-cell therapy; DLBCL, diffuse large B-cell lymphoma; Len, lenalidomide; liso-cel, lisocabtagenemaraleucel; pola, polatuxumab vedotin; R, rituximab; (R-)CH(O)P, (rituximab,) cyclophosphamide, doxorubicin, (vincristine,) and prednisone; (R-)GemOx, (rituximab,) gemcitabine, and oxaliplatin; tafa, tafasitamab; tisa-cel, tisagenlecleucel. **1.** ClinicalTrials.gov NCT04824092 **2.** ClinicalTrials.gov NCT04529772 **3.** ClinicalTrials.gov NCT06356129 **4.** ClinicalTrials.gov NCT05605899 **5.** ClinicalTrials.gov NCT06717347 **6.** ClinicalTrials.gov NCT04384484 **7.** ClinicalTrials.gov NCT04970901 **8.** ClinicalTrials.gov NCT04182204 **9.** ClinicalTrials.gov NCT05139017 **10.** ClinicalTrials.gov NCT04404283 **11.** ClinicalTrials.gov NCT06047080 **12.** ClinicalTrials.gov NCT05283720 **13.** ClinicalTrials.gov NCT05578976 **14.** ClinicalTrials.gov NCT06091865 **15.** ClinicalTrials.gov NCT04408638.

NP-42410

Will CAR-T be used in 1L?

ZUMA-23[1] (NCT05605899)



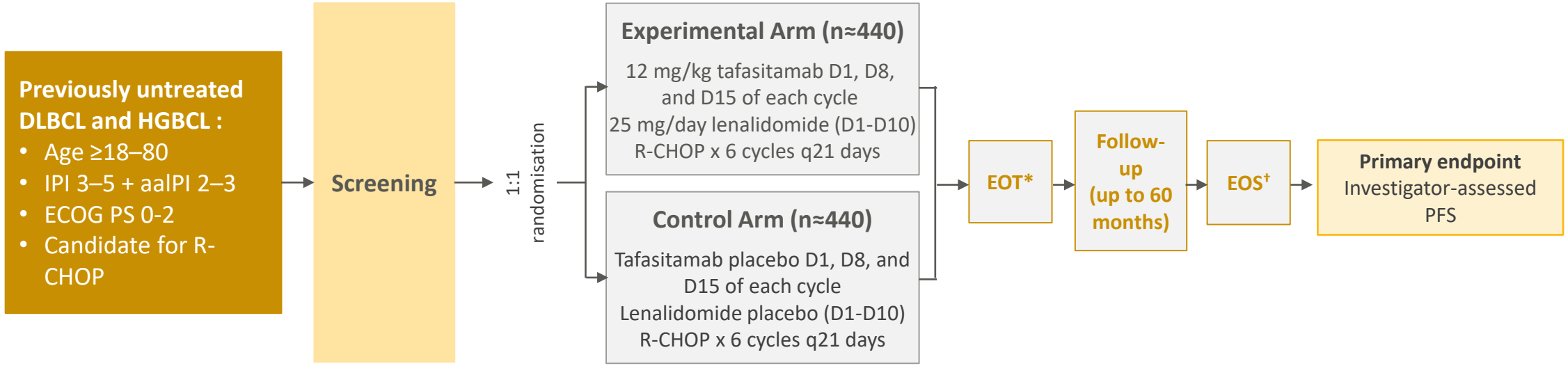
NP-42410

*Patients with a history of HIV and/or hepatitis B or C and undetectable viral loads may enrol. Key exclusion criteria include LBCL of the central nervous system. †R-CHOP or DA-EPOCH-R, based on the investigator's choice.
‡Prophylactic corticosteroids may be administered to reduce the incidence and severity of cytokine release syndrome at the investigator's discretion.
1L, first-line; axi-cel, axicabtagene ciloleucel; CAR-T, chimeric antigen receptor T-cell therapy; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; DA, dose-adjusted; EFS, event-free survival; EPOCH, etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin; HIV, human immunodeficiency virus; IPI, International Prognostic Index; LBCL, large B-cell lymphoma; R, rituximab; SOC, standard of care.

1. Westin et al. *HemaSphere* 2023.

Will tafasitamab be used in 1L?

frontMIND[2] (NCT04824092)



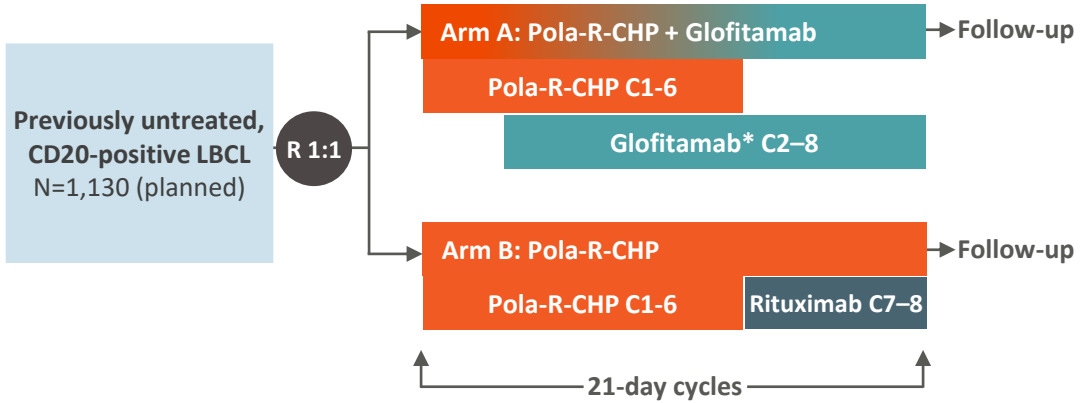
NP-42410

*EOT is defined as D21 of the last treatment cycle the patient started. †EOS is expected to occur approximately 5 years after the first patient is enrolled, to allow all patients a minimum of 3 years follow-up post-treatment.
C, cycle; D, day; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end of treatment; EOS, end of study; HGBL, high-grade B-cell lymphoma; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; q, every.

2. Vitolo et al. *Hemasphere* 2022.

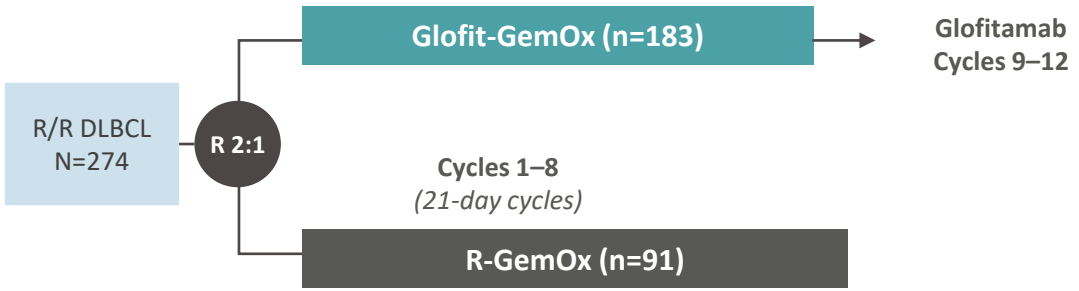
How will glofitamab play in earlier lines of treatment?

SKYGLO[1]



Primary endpoint
PFS by independent review

STARGLO[2,3]



Primary endpoint
OS

12.9 months	vs	25.5 months
for R-GemOx (95% CI 7.9–18.5)	HR 0.62 p=0.0064	for Glofit-GemOx (95% CI 18.3–NE)

NP-42410

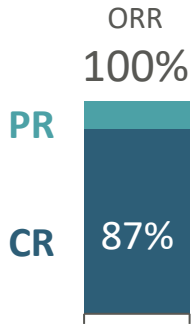
*Administered with step-up dosing. ASCT, autologous stem cell transplantation; C, cycle; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; HR, hazard ratio; LBCL, large B-cell lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; pola, polatuzumab vedotin; PR, partial response; R-CHP, rituximab, cyclophosphamide, doxorubicin, prednisone.

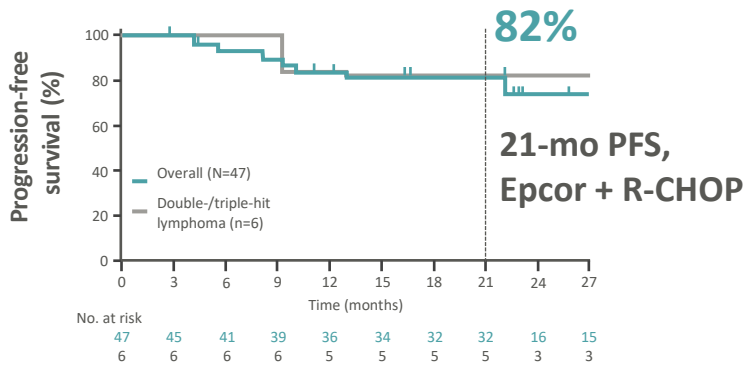
1. Advani et al. ASH 2024; Poster 1718.1 **2.** Abramson *Lancet* 2024 **3.** ClinicalTrials.gov NCT04408638.

Phase 1/2 studies are also investigating epcoritamab in earlier lines and in combination

EPCORE DLBCL-2[1,2,*]

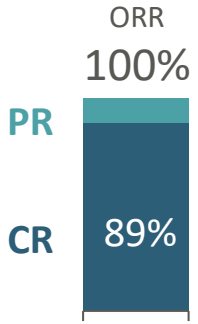
1L DLBCL | **Epcoritamab (up to 1 year) + R-CHOP (6 cycles)** | **Primary endpoint** ORR

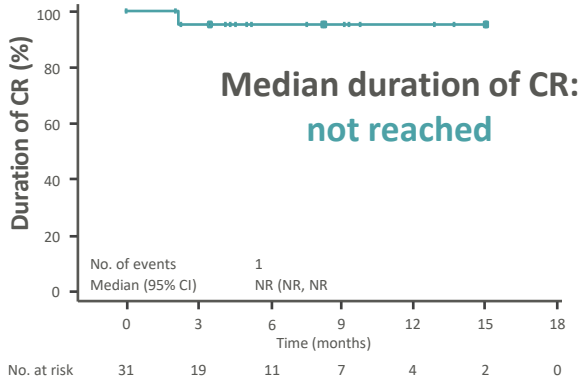




EPCORE NHL-5[3,†]

1L DLBCL | **Epcoritamab (8 cycles) + Pola-R-CHP (6 cycles)** | **Primary endpoint** DLTs





NP-42410

*NCT04663347. Data as of 15 May 2024. † Data cutoff: 29 February 2024.
C, cycle; CR, complete response; D, day; DLBCL, diffuse large B-cell lymphoma; DLT, dose-limiting toxicity; Epcor, epcoritamab; IV, intravenous; Mo, months; NHL, non-Hodgkin lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; Q(3/4)W, every (3/4) weeks; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; SC, subcutaneous; SUD, step up dose; Yr, year.
1. Falchi et al. ASH 2024; Oral presentation #581 **2.** Leslie et al. ASH 2024; Poster #3106 **3.** Kerr et al. SOHO 2024; Poster # ABCL-417.

Acalabrutinib and golcadomide in 1L DLBCL

ESCALADE[1]

Enrolment (N=600)

- Age ≤ 65y with previously untreated DLBCL
- Stage II–IV disease
- T-IPI score 2–5
- Biopsy sample for central cell of origin testing

R 1:1

- **Arm A: Acalabrutinib + R-CHOP (n≈300)**
- **Arm B: Placebo + R-CHOP (n≈300)**

Primary endpoint
Prolongation of PFS

GOLSEEK-1[2]

Target enrolment (n=850)
Key eligibility criteria

- Previously untreated LBCL
- HR 1–2 IPI or IPI 3–5
- Age 18–80
- ECOG PS 0–2
- Measurable disease per Lugano

R 1:1

- **Golcadomide + R-CHOP for 6 cycles**
- **Placebo + R-CHOP for 6 cycles**

Primary endpoint
PFS by investigator

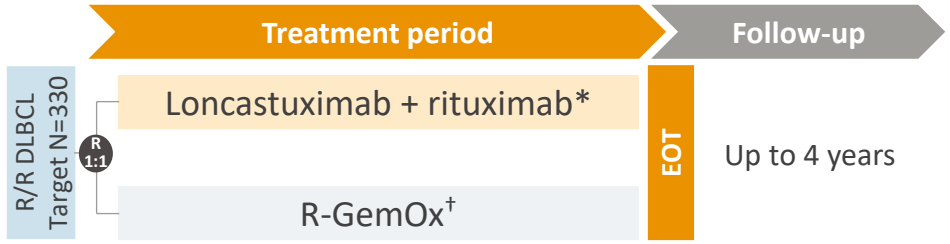
NP-42410

DLBCL, diffuse large B-cell lymphoma; EOT, end of treatment; G-CSF, granulocyte colony-stimulating factor; GEP, gene expression profiling; GCB, germinal center B-cell; PFS, progression-free survival; R-IPI, revised international prognostic index; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone.

1. Sehn et al. *J Clin Oncol* 2021 **2.** Hoffmann et al. *Blood* 2024.

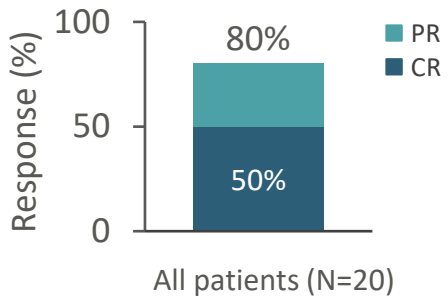
Loncastuximab in earlier lines and in combination

LOTIS-5[1,2]

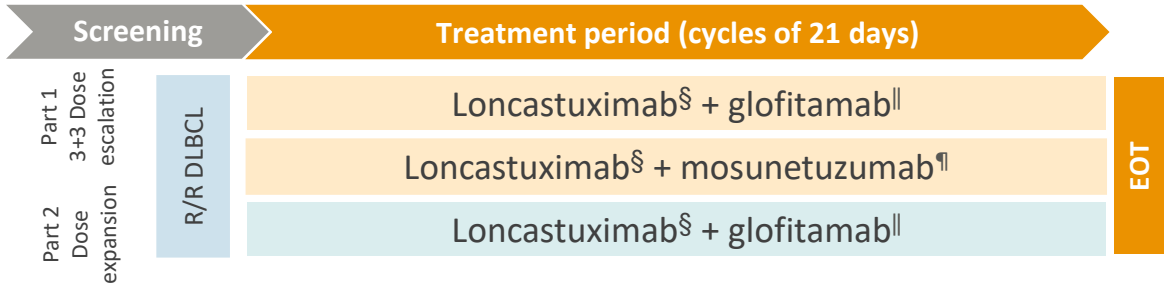


Primary endpoint
PFS by independent central review

Safety run-in analysis[2,‡]



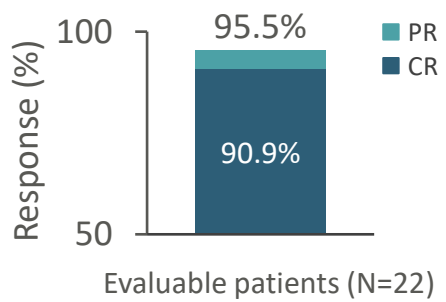
LOTIS-7[3,4]



Primary endpoint
Safety, tolerability

Oral presentation
Friday 20th June 15:00
Aggressive B-cell Lymphomas, Room A

Lonca + glofit[4]



Not reached
median DOR

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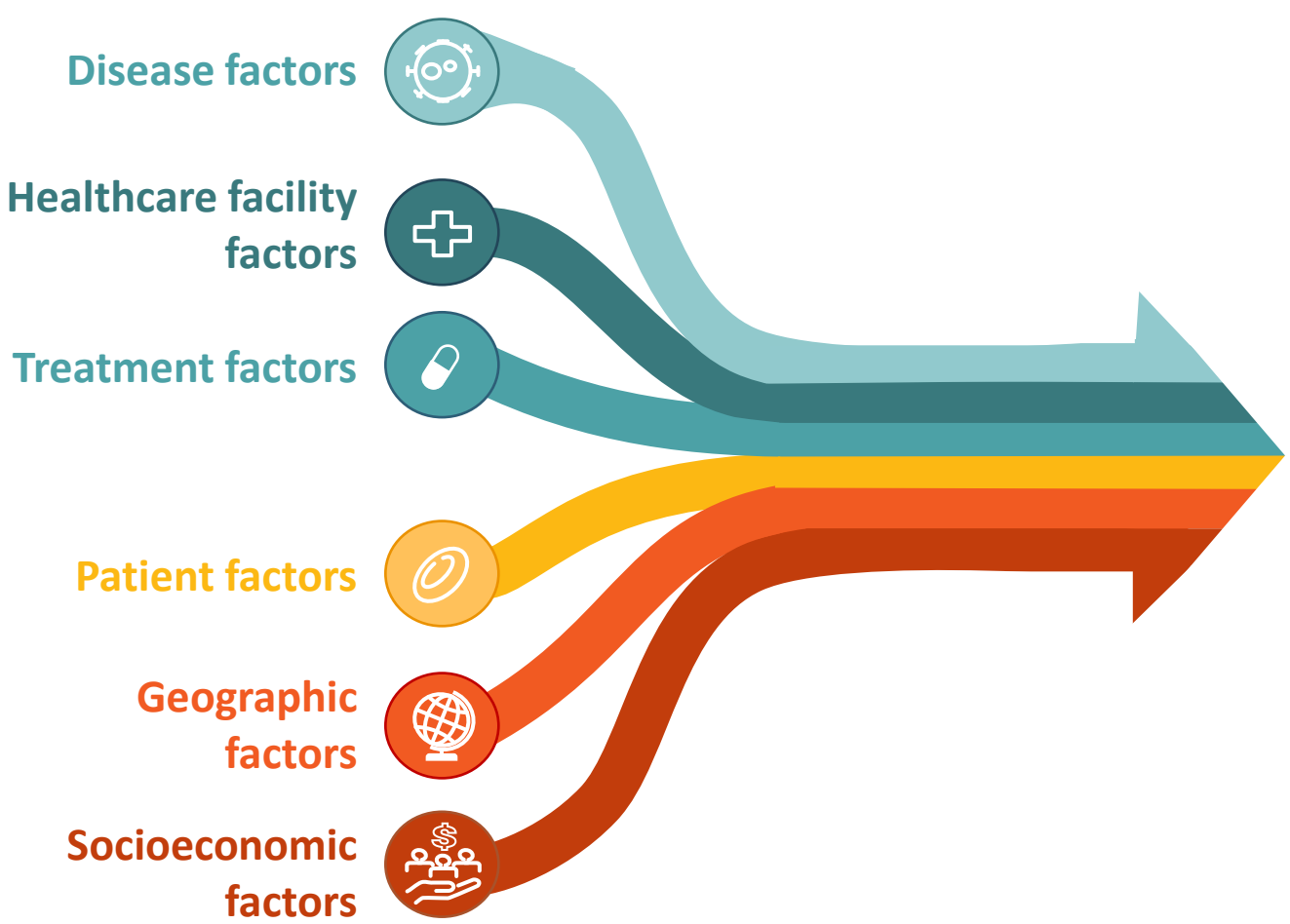
*Loncastuximab tesirine 150 µg/kg + rituximab 375 mg/m² Q3W for 2 cycles, followed by Loncastuximab tesirine 75 µg/kg + rituximab 375 mg/m² Q3W for up to 6 additional cycles. †Rituximab 375 mg/m² + gemcitabine 1,000 mg/m² + oxaliplatin 100 mg/m² Q2W for up to 8 cycles. ‡Data cut-off: 10 April 2023. §Loncastuximab tesirine 150 µg Q3W for Cycles 1 and 2, followed by 75 µg for subsequent cycles. ‖Glofitamab 2.5 mg on Cycle 1 Day 8, 10 mg on Cycle 1 Day 15, and 10 mg or 30 mg on Day 1 of Cycles 2–12. ¶ Mosunetuzumab 5 mg on Cycle 1 Day 1, 15 mg or 45 mg on Cycle 1 Day 8, and 45 mg for Cycle 1 Day 15 and Day 1 of Cycles 2–8. CR, complete response; DLBCL, diffuse large B-cell lymphoma; B-NHL, B-cell non-Hodgkin lymphoma; DOR, duration of response; EOT, end of treatment; GemOx, gemcitabine and oxaliplatin; glofit, glofitamab; Lonca, loncastuximab tesirine; PFS, progression-free survival; PR, partial response; R/R, relapsed/refractory.

1. Clinicaltrials.gov NCT04384484 **2.** Carlo-Stella et al. EHA 2025 **3.** Clinicaltrials.gov NCT04970901 **4.** Alderuccio et al. EHA 2025; Abstract #PS1911.

Multiple factors have a role in defining the next treatment[1]



With therapies moving to **earlier lines**, and **new classes** of drugs under investigation, how will we choose the **best next line of therapy** for our patients?

NP-42410

1. Brooks & Caimi. *Blood Rev* 2024.

Summary

- The DLBCL landscape is expected to extensively change in the next years
- Many clinical studies are ongoing, and some have shown very promising results
- The future approach is led by combinations
- How the earlier use of novel treatments will affect the subsequent strategies is to be understood
- More choice means more responsibility for deciding the best way to cure our patients

Panel discussion and Q&A

All faculty

Chair: Professor Andrew Davies

Get ready to interact: Q&A

In-person attendees:

1

Scan the QR code at the bottom right of the screen using your phone or tablet device

2

Select what you want to do

Q&A:
'Ask a question' button

…or use the **microphones** available in the room!

Virtual attendees:

Use the 'Q&A' button **to the right** of your live stream video

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We value your feedback on this symposium

Thank you!

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