What Clinicians Want to Know: Addressing Current Questions and Controversies Regarding the Role of CAR T-Cell Therapy and Bispecific Antibodies in the Management of Lymphoma

A CME Friday Satellite Symposium Preceding the 66th ASH Annual Meeting

Friday, December 6, 2024
11:30 AM – 1:30 PM PT (2:30 PM – 4:30 PM ET)

Faculty

Jennifer Crombie, MD
Martin Hutchings, MD, PhD
Matthew Lunning, DO
Tycel Phillips, MD

Moderator

Jeremy S Abramson, MD, MMSc

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Faculty

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Moderator

Jeremy S Abramson, MD, MMSc
Director, Center for Lymphoma
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Associate Professor of Medicine
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Dr Crombie — Disclosures
Faculty

Advisory Committees	AbbVie Inc, ADC Therapeutics, Genentech, a member of the Roche Group, Genmab US Inc, Regeneron Pharmaceuticals Inc, Seagen Inc
Consulting Agreement	Genentech, a member of the Roche Group
Contracted Research	AbbVie Inc, Bayer HealthCare Pharmaceuticals, Genentech, a member of the Roche Group, Merck

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Prof Hutchings — Disclosures
Faculty

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Data and Safety Monitoring Boards/Committees	Genmab US Inc, Roche Laboratories Inc

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Dr Lunning — Disclosures
Faculty

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Research Funding	Bristol Myers Squibb, Fate Therapeutics, Sana Biotechnology

Dr Phillips — Disclosures
Faculty

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Steering Committee	Genentech, a member of the Roche Group

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Dr Abramson — Disclosures
Moderator

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Contracted Research	Bristol Myers Squibb, Celgene Corporation, Cellectis, Genentech, a member of the Roche Group, Merck, Mustang Bio, Regeneron Pharmaceuticals Inc, Seagen Inc, Takeda Pharmaceuticals USA Inc

Commercial Support

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What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of Acute Myeloid Leukemia

A CME Friday Satellite Symposium and Webcast Preceding the 66th ASH Annual Meeting

Friday, December 6, 2024

3:15 PM – 5:15 PM PT (6:15 PM – 8:15 PM ET)

Faculty

Alexander Perl, MD

Richard M Stone, MD

Eunice S Wang, MD

Andrew H Wei, MBBS, PhD

Moderator

Eytan M Stein, MD

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What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of Multiple Myeloma

A CME Friday Satellite Symposium and Webcast Preceding the 66th ASH Annual Meeting

Friday, December 6, 2024

3:15 PM – 5:15 PM PT (6:15 PM – 8:15 PM ET)

Faculty

Professor Philippe Moreau, MD

Robert Z Orlowski, MD, PhD

Noopur Raje, MD

Paul G Richardson, MD

Moderator

Sagar Lonial, MD

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Rounds with the Investigators: Compelling Teaching Cases Focused on the Management of Breast Cancer

A 3-Part CME Hybrid Satellite Symposium Series in Partnership with the 2024 San Antonio Breast Cancer Symposium®

HER2-Low and HER2-Ultralow Breast Cancer

Tuesday, December 10, 2024

7:15 PM – 8:45 PM CT

New Developments in Endocrine Treatment for Breast Cancer

Wednesday, December 11, 2024

7:15 PM – 9:15 PM CT

Management of Metastatic Breast Cancer

Thursday, December 12, 2024

7:00 PM – 9:00 PM CT

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Save The Date

Fourth Annual
National General Medical Oncology Summit

A Multitumor CME/MOC-, NCPD- and ACPE-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute

Friday to Sunday, February 28 to March 2, 2025

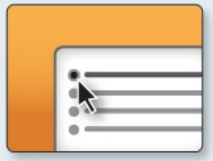
Fontainebleau Hotel, Miami Beach, Florida

Moderated by Neil Love, MD

Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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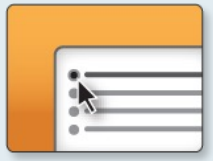
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get CME Credit: A CME credit link will be provided in the chat room at the conclusion of the program.

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
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What Clinicians Want to Know: Addressing Current Questions and Controversies Regarding the Role of CAR T-Cell Therapy and Bispecific Antibodies in the Management of Lymphoma

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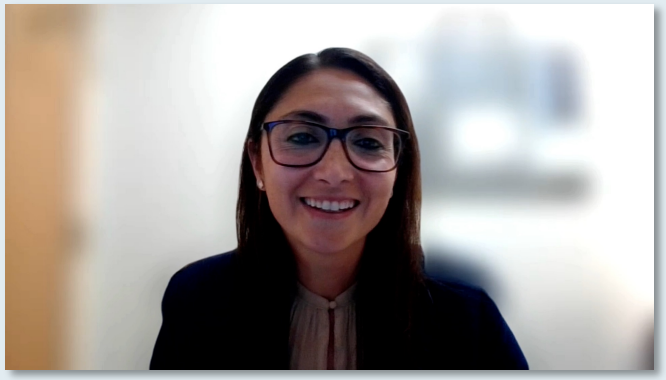
Contributing General Medical Oncologists

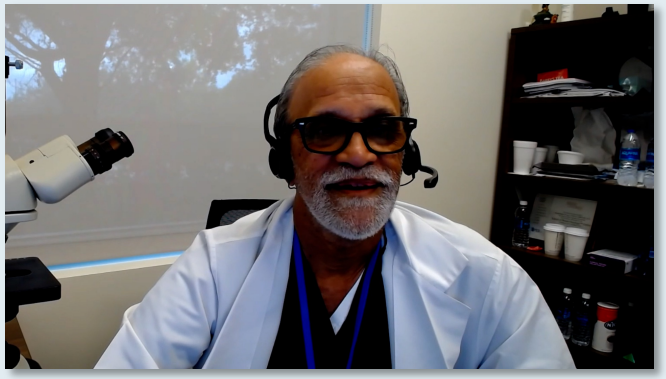
Susmitha Apuri, MD
Florida Cancer Specialists
& Research Institute
Inverness and Lecanto,
Florida

Eric H Lee, MD, PhD
Los Angeles Cancer
Network
Fountain Valley, California



Shams Bufalino, MD
Advocate Lutheran
General Hospital
Park Ridge, Illinois

Yanjun Ma, MD
Tennessee Oncology
Murfreesboro, Tennessee



Kapisthalam (KS) Kumar, MD
Florida Cancer Specialists
& Research Institute
Trinity, Florida

Henna Malik, MD
Texas Oncology
Houston, Texas

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Agenda

Module 1: Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Abramson

Module 2: Bispecific Antibody Therapy for DLBCL — Prof Hutchings

Module 3: CAR T-Cell Therapy for Other Lymphoma Subtypes — Dr Lunning

Module 4: Bispecific Antibody Therapy for Follicular Lymphoma and Other Lymphoma Subtypes — Dr Phillips

Module 5: Tolerability Considerations with CAR T-Cell and Bispecific Antibody Therapy — Dr Crombie

Agenda

Module 1: Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Abramson

Module 2: Bispecific Antibody Therapy for DLBCL — Prof Hutchings

Module 3: CAR T-Cell Therapy for Other Lymphoma Subtypes — Dr Lunning

Module 4: Bispecific Antibody Therapy for Follicular Lymphoma and Other Lymphoma Subtypes — Dr Phillips

Module 5: Tolerability Considerations with CAR T-Cell and Bispecific Antibody Therapy — Dr Crombie

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Case Presentation: 62-year-old woman with DLBCL in retroperitoneum and bowel, s/p 6 cycles of R-CHOP with refractory disease

Dr Eric Lee (Fountain Valley, California)

QUESTIONS FOR THE FACULTY

What local gastrointestinal complications of DLBCL have you observed?

What is your usual approach to primary refractory DLBCL in younger and older patients? How, if at all, does the presence of comorbidities affect your decision-making?

How would you compare the efficacy and tolerability of the 3 available CD19-directed CAR T-cell products for DLBCL?

QUESTIONS FOR THE FACULTY

Regulatory and reimbursement issues aside, which second-line therapy would you recommend for a younger (eg, 65-year-old), transplant-eligible patient with DLBCL who experienced disease relapse 10 months after R-CHOP?

Regulatory and reimbursement issues aside, which third-line therapy would you most likely recommend for a 70-year-old patient with Stage IV DLBCL and no significant comorbidities who received first-line R-CHOP and subsequently experienced disease progression on second-line R-DHAP followed by transplant?

Case Presentation: 79-year-old frail man with Klinefelter syndrome and recurrent DLCBL with disease relapse after R-mini-CHOP

Dr Susmitha Apuri (Inverness and Lecanto, Florida)

QUESTIONS FOR THE FACULTY

For a patient such as the one discussed, how do longstanding neurologic symptoms (abnormal balance, poor coordination, falls) related to Klinefelter syndrome affect eligibility for CAR T-cell therapy? How would you approach monitoring for neurotoxicity/ICANS with CAR T-cell therapy for this type of patient?

How do age and comorbidities affect eligibility for CAR T-cell therapy? How important is social support, and how does this factor into decision-making? When you are going to administer CAR T-cell therapy to an older patient with DLBCL, which platform do you generally prefer?

Mass General Brigham
Mass General Cancer Center

Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL)

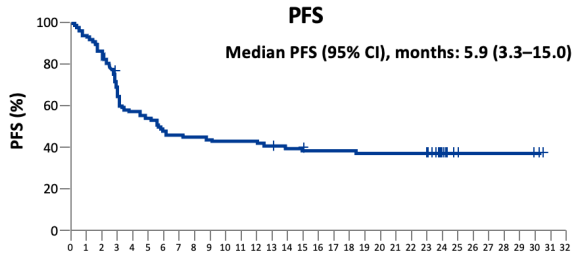
Jeremy S. Abramson, MD, MMSc
Massachusetts General Hospital
Harvard Medical School

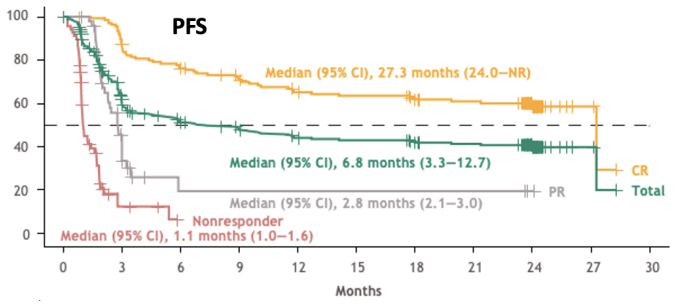
HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

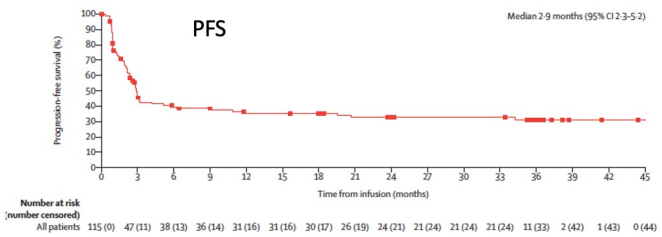
Long term efficacy and safety for 3rd line+ CAR in DLBCL

CAR T-cells can CURE chemotherapy-refractory LBCL in the 3rd line or later setting

	Axicabtagene Ciloleucel ZUMA-1	Lisocabtagene Maraleucel TRANSCEND	Tisagenlecleucel JULIET
Construct	antiCD19-CD28tm-**CD28**-CD3z	antiCD19-CD28tm-**41BB**-CD3z	antiCD19-CD8αtm-**41BB**-CD3z
Med Age, y (range)	58 (23–76)	63 (18–86)	56 (22–76)
ORR/CRR % (IRC)	74/54	73/53	52/40
Median PFS, mos	5.9	6.8	2.9
PFS (2y) %	42	41	30
Median OS, mos	25.8	27.3	11.1
CRS (Any/severe) %	93/13	42/2	58/22 *different grading scale
NT (Any/severe) %	64/28	30/10	21/12
References	Neelapu, et al. NEJM 2017 Locke, et al. Lancet Onc 2019	Abramson, et al. Lancet 2020 Abramson, et al. Blood 2024	Schuster, et al. NEJM 2019 Schuster, et al. Lancet Onc. 2021





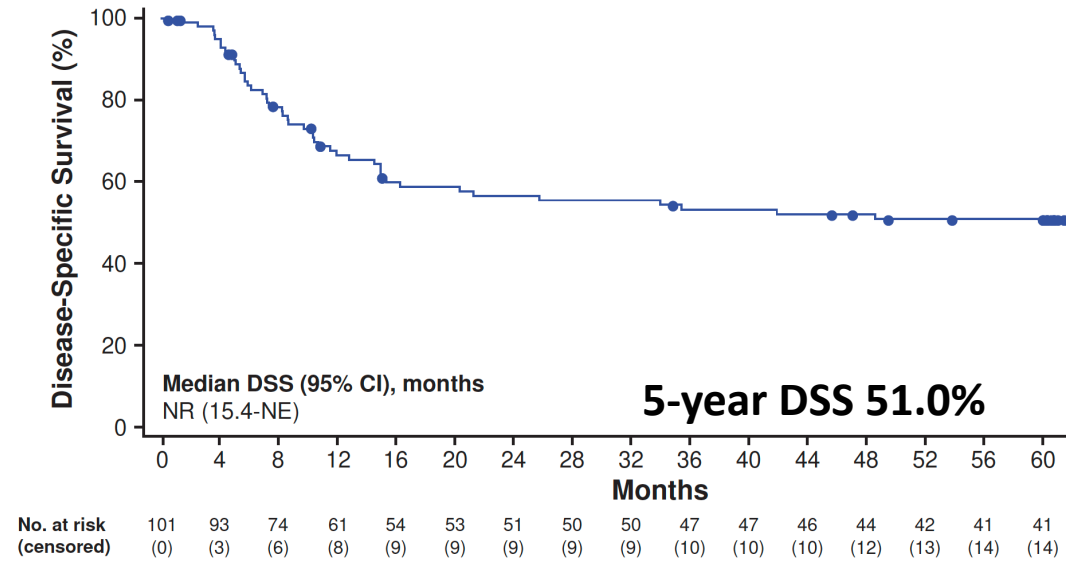


5-year Follow up From ZUMA-1 and TRANSCEND

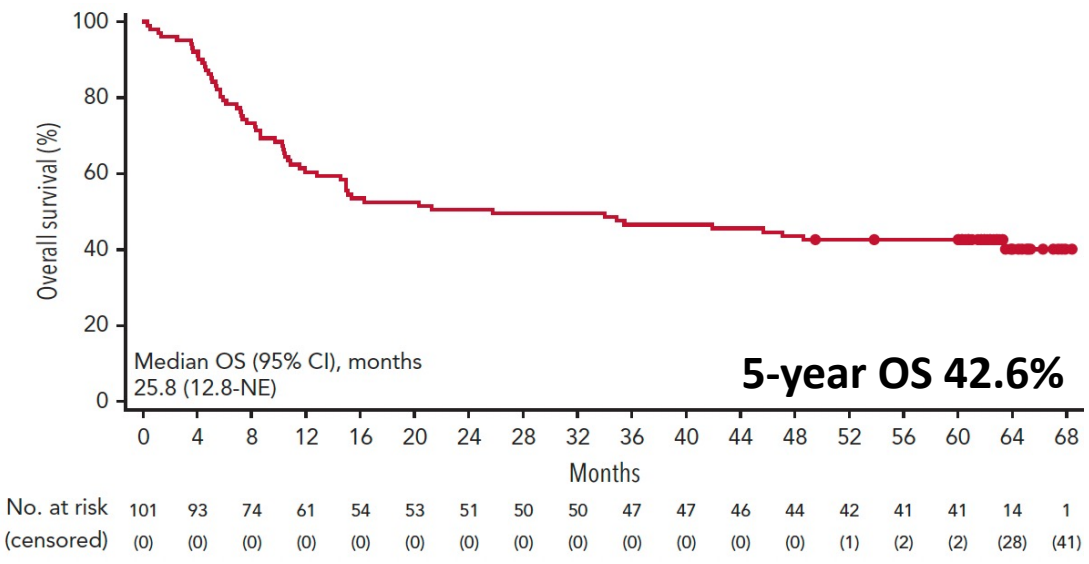
ZUMA-1

Neelapu, et al. Blood 2023

Disease Specific Survival



Overall Survival



TRANSCEND

Abramson, et al. Proc ASH 2024

5-y DSS: 52.0%

5-y OS: 38.1%

- After day 91, 14 (6%) pts had grade ≥ 3 infections (grade 5, n = 3, 2 of whom had additional anti-cancer therapies)
- Nineteen (8%) pts had second primary malignancies (non-melanoma skin cancers [n = 7], MDS [n = 9]).

Major findings from phase III trials for 2nd line CAR in DLBCL

Three randomized trials of Chimeric Antigen Receptor (CAR) T-cell therapy versus SOC in transplant-eligible DLBCL with early relapse or primary refractory disease

Clinical trials of CD19 CAR T-cell therapies in 2L ≤ 12 months LBCL

ZUMA-7
(N = 359)
Phase 3; axi-cel vs SOC

Primary Analysis of ZUMA-7: a Phase 3 Randomized Trial of Axicabtagene Ciloleucel versus Standard-of-Care Therapy in Patients with Relapsed/Refractory Large B-Cell Lymphoma

Frederick L. Locke, MD[1]; David B. Miklos, MD, PhD[2]; Caron A. Jacobson, MD, MMSc[3]; Miguel-Angel Perales, MD[4];

POSITIVE!

TRANSFORM
(N = 184)
Phase 3; liso-cel vs SOC

TRANSFORM Study: Lisocabtagene Maraleucel, a CD19-Directed Chimeric Antigen Receptor T Cell Therapy, Versus Standard of Care with Salvage Chemotherapy Followed by Autologous Stem Cell Transplantation as Second-Line Treatment in Patients with Relapsed or Refractory Large B-Cell Lymphoma: Results from the Randomized Phase 3 TRANSFORM Study

Manali Kamdar,[1] Scott R. Solomon,[2] Jon Arnason,[3] Patrick B. Johnston,[4] Bertram Glass,[5] Veronika Bachanova,[6] Sami

POSITIVE!

BELINDA
(N = 322)
Phase 3; tisa-cel vs SOC

Tisagenlecleucel vs Standard of Care as Second-Line Therapy of Primary Refractory or Relapsed Aggressive B-Cell Non-Hodgkin Lymphoma: Analysis of the Phase III BELINDA Study

Michael R. Bishop,[1] Michael Dickinson,[2] Duncan Purtill,[3] Pere Barba,[4] Armando Santoro,[5] Nada Hamad,[6] Koji Kato,[7] Anna Sureda,[8] Richard Greil,[9]

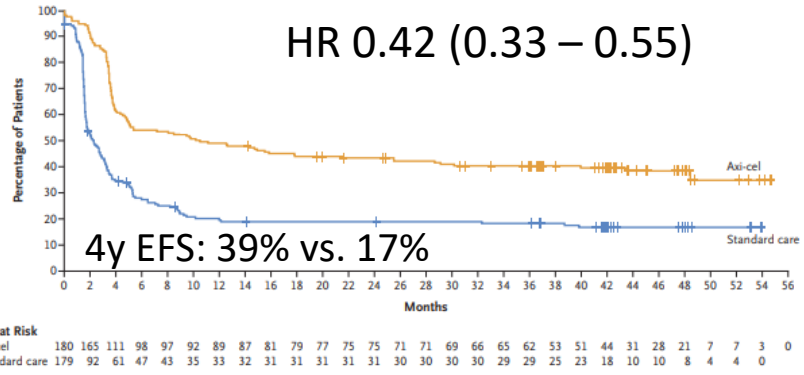
NEGATIVE!

Axi-cel vs. SOC as 2nd line therapy in primary refractory or early relapsed large B-cell lymphomas

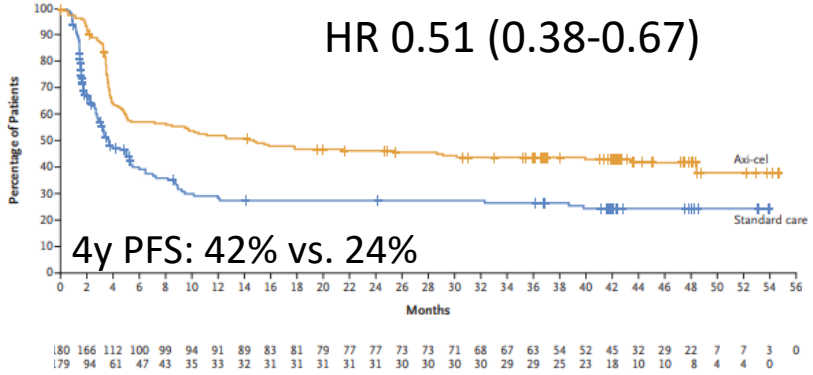
N=359
Refractory 75%
DHL 16%

ORR: 83% vs. 50%
CRR: 65% vs. 32%

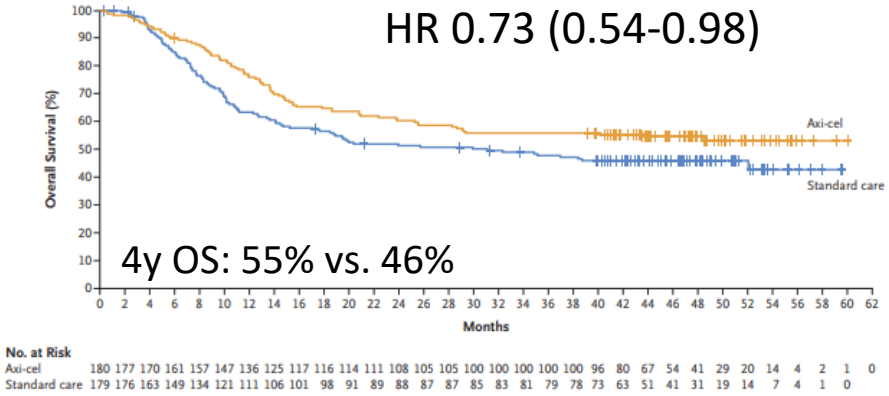
EFS
Median 10.8 vs. 2.3 mos
HR 0.42 (0.33 – 0.55)



PFS
Median 14.7 vs. 3.7 mos
HR 0.51 (0.38-0.67)



OS
Median NR vs. 31.1 mos
HR 0.73 (0.54-0.98)



Median Follow-up: 47.2 mo

Toxicity	Grade	%
CRS	Any grade	92
	Grade ≥3	6
Neurotox	Any grade	60
	Grade ≥3	21

Axi-cel associated with improved QOL by PRO

Locke, et al. NEJM 2021; Westin, et al. NEJM 2023

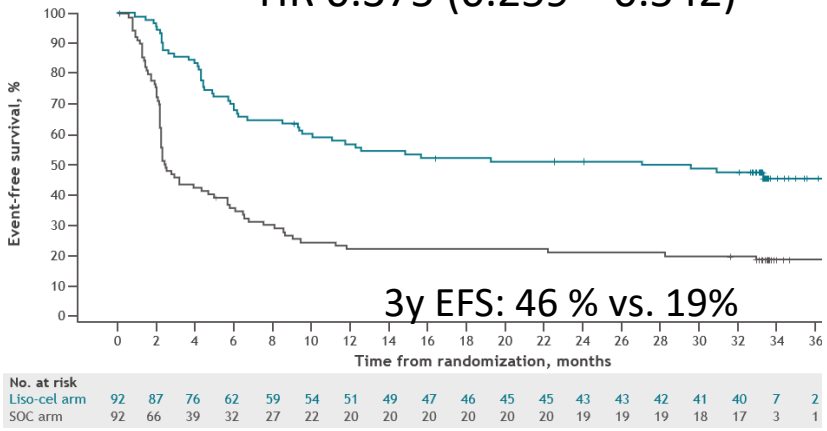
Liso-cel vs. SOC as 2nd line therapy in primary refractory or early relapsed large B-cell lymphomas

N=184
Refractory 73%
DHL 24%

ORR: 87% vs. 49%
CRR: 74% vs. 43%

EFS

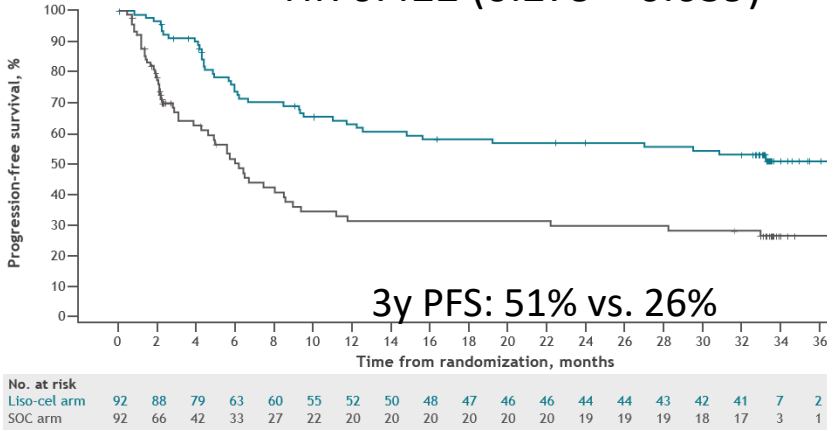
Median 29.5 vs. 2.4 mos
HR 0.375 (0.259—0.542)



3y EFS: 46 % vs. 19%

PFS

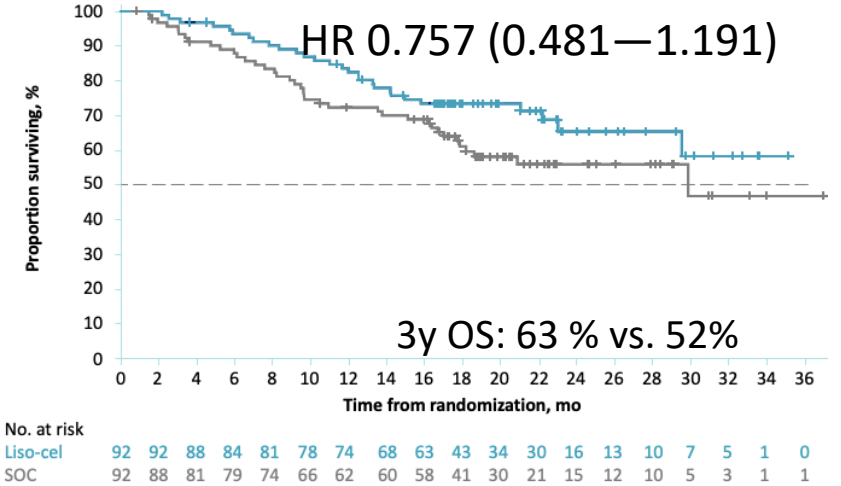
Median NR vs. 6.2 mos
HR 0.422 (0.279—0.639)



3y PFS: 51% vs. 26%

OS

Median NR vs. NR
HR 0.757 (0.481—1.191)



3y OS: 63 % vs. 52%

Median Follow-up: 34 mo

Toxicity	Grade	%
CRS	Any grade Grade 3	49 1
Neurotox	Any grade Grade 3	11 4

Liso-cel associated with improved QOL by PRO

Abramson, et al. Proc. EHA 2024; Abstract S272

SOC patients who received CAR as 3rd line treatment

ZUMA-7 (axi-cel)

	2nd line axi-cel	3rd line CAR on SOC arm (n = 68)
CR rate	65%	34%
Median PFS	14.7 mo	6.3 mo
Median OS	NR at 47 mo	16.3 mo

TRANSFORM (liso-cel)

	2nd line liso-cel	SOC Crossover subgroup (n = 57)
ORR / CRR	74%	53%
Median PFS	NR at 34 mo	5.9 mo
Median OS	NR at 34 mo	15.8 mo

CAR is more effective when used earlier in LBCL

Ghobadi A, et al. Blood Adv. 2024 ; Abramson, et al. Proc. EHA 2024; Abstract S272

Tisa-cel vs. SOC as 2nd line therapy in primary refractory or early relapsed large B-cell lymphomas

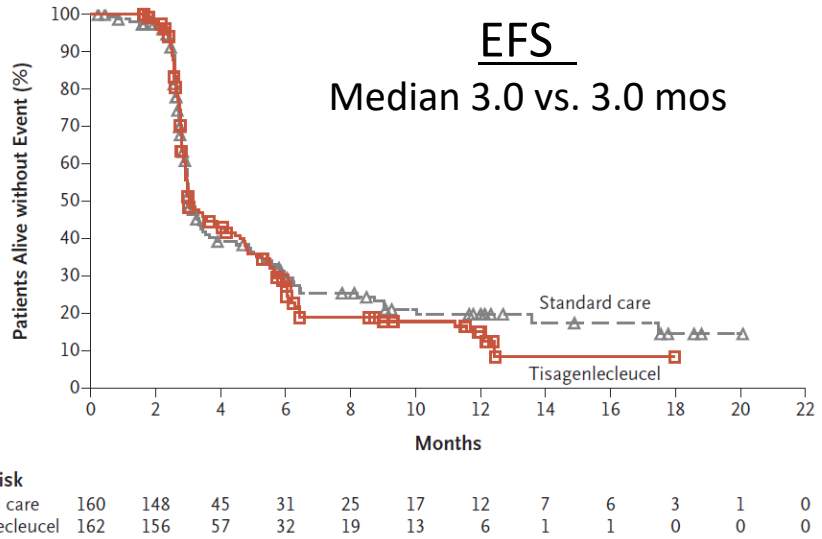
N=322
Refractory 75%
DHL 15%

ORR: 46% vs. 43%
CRR: 28% vs. 28%

51% of SOC crossed over to receive tisa-cel

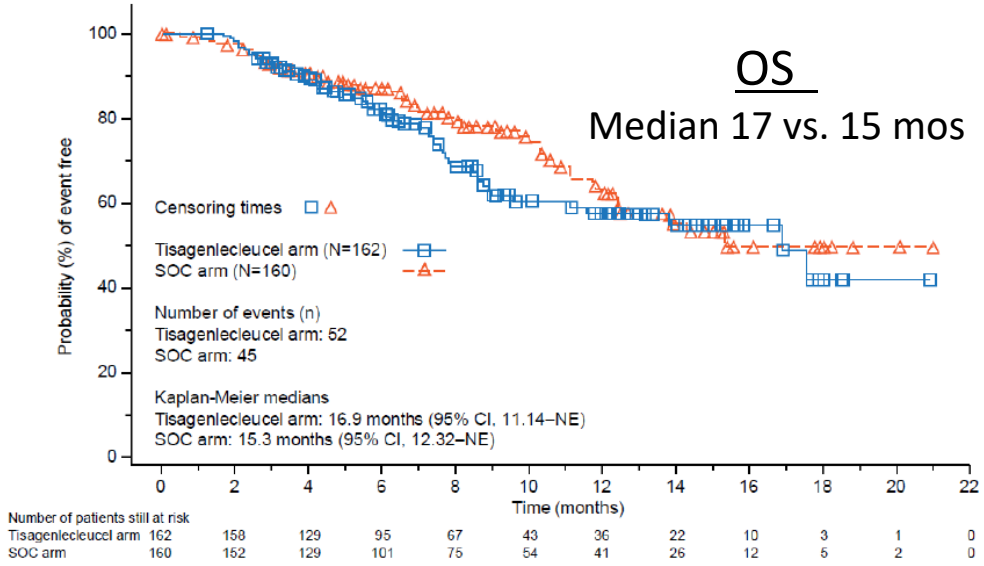
EFS

Median 3.0 vs. 3.0 mos



OS

Median 17 vs. 15 mos



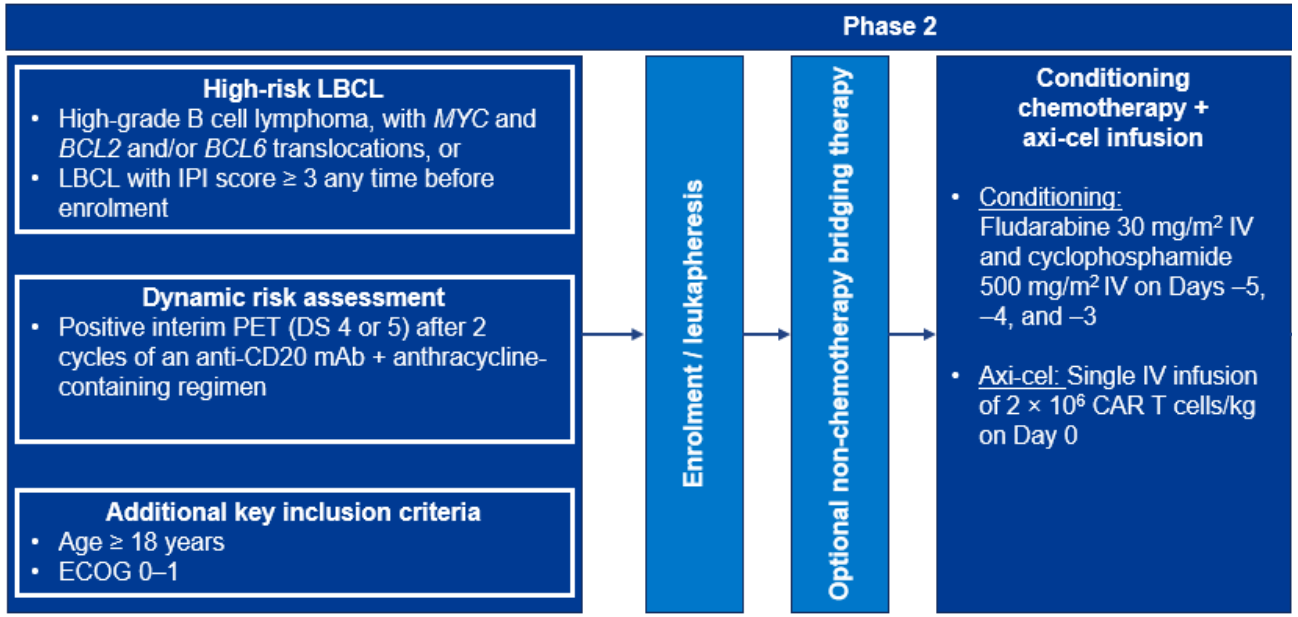
Toxicity	%
CRS	
Any grade	61
Grade ≥3	5
Neurotoxicity	
Any grade	10
Grade ≥3	2

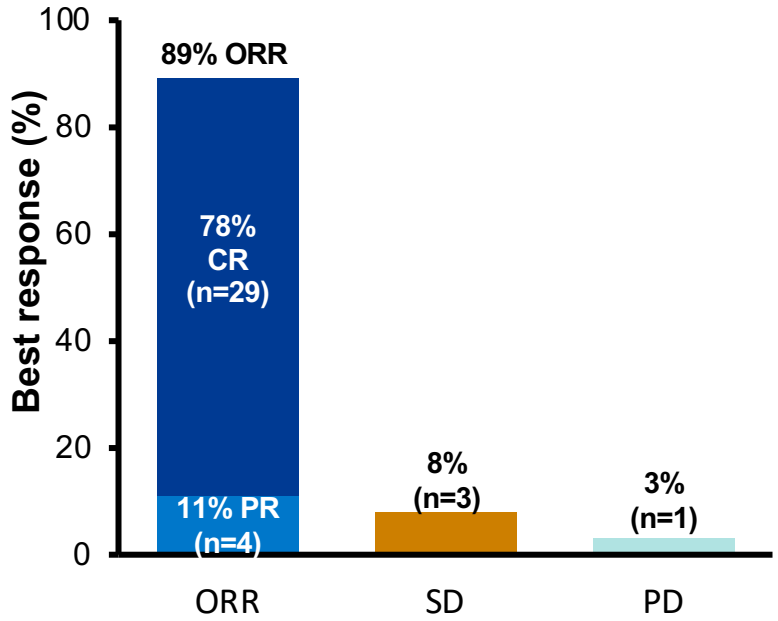
Median Follow-up: 10 mo

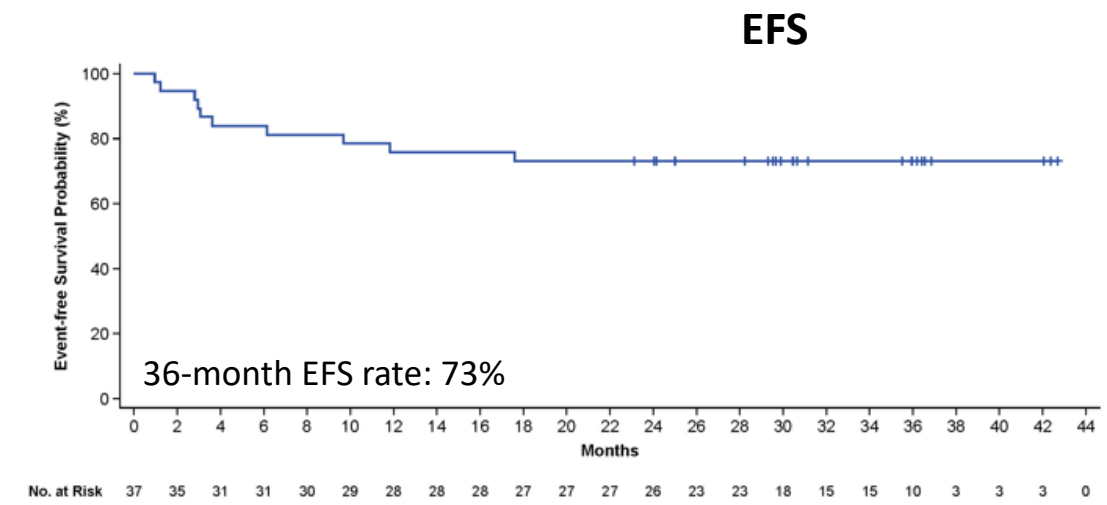
Bishop, et al. NEJM 2021

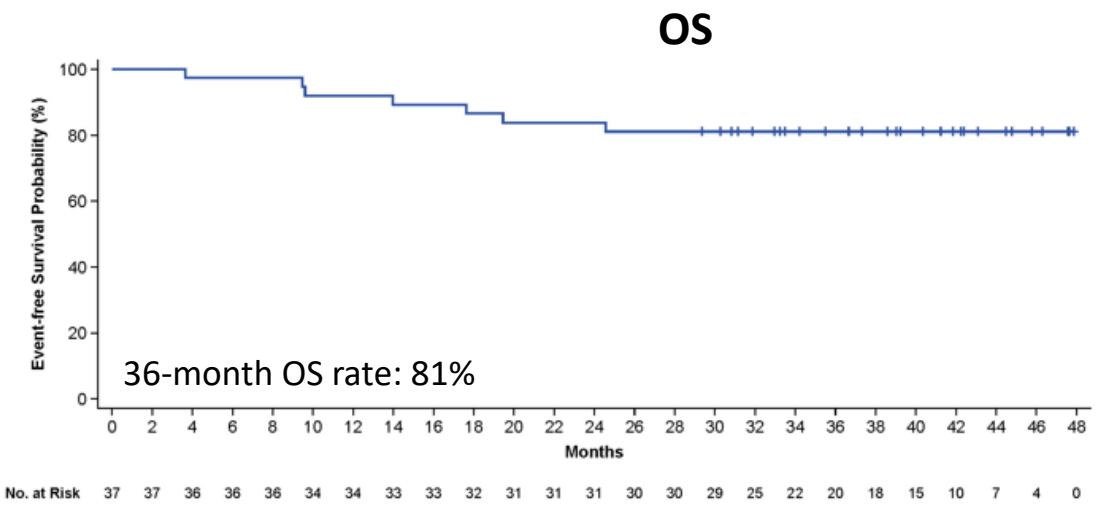
Can CAR move even earlier?

ZUMA-12 trial of Axi-cel in high-risk patients with suboptimal interim response to R-CHOP (n=37): 3-year update





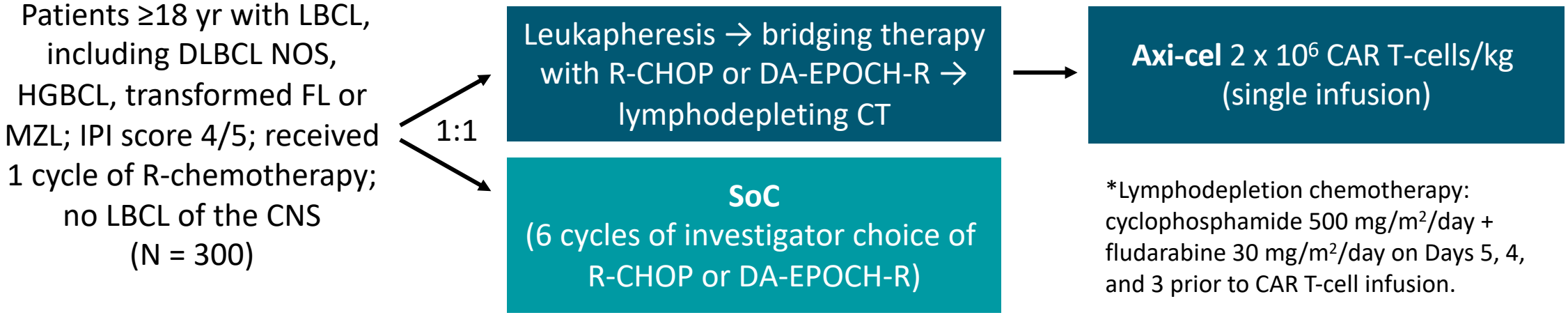




Chavez, et al. Proc ASH 2023; Neelapu SS, et al. Nature Med. 2022

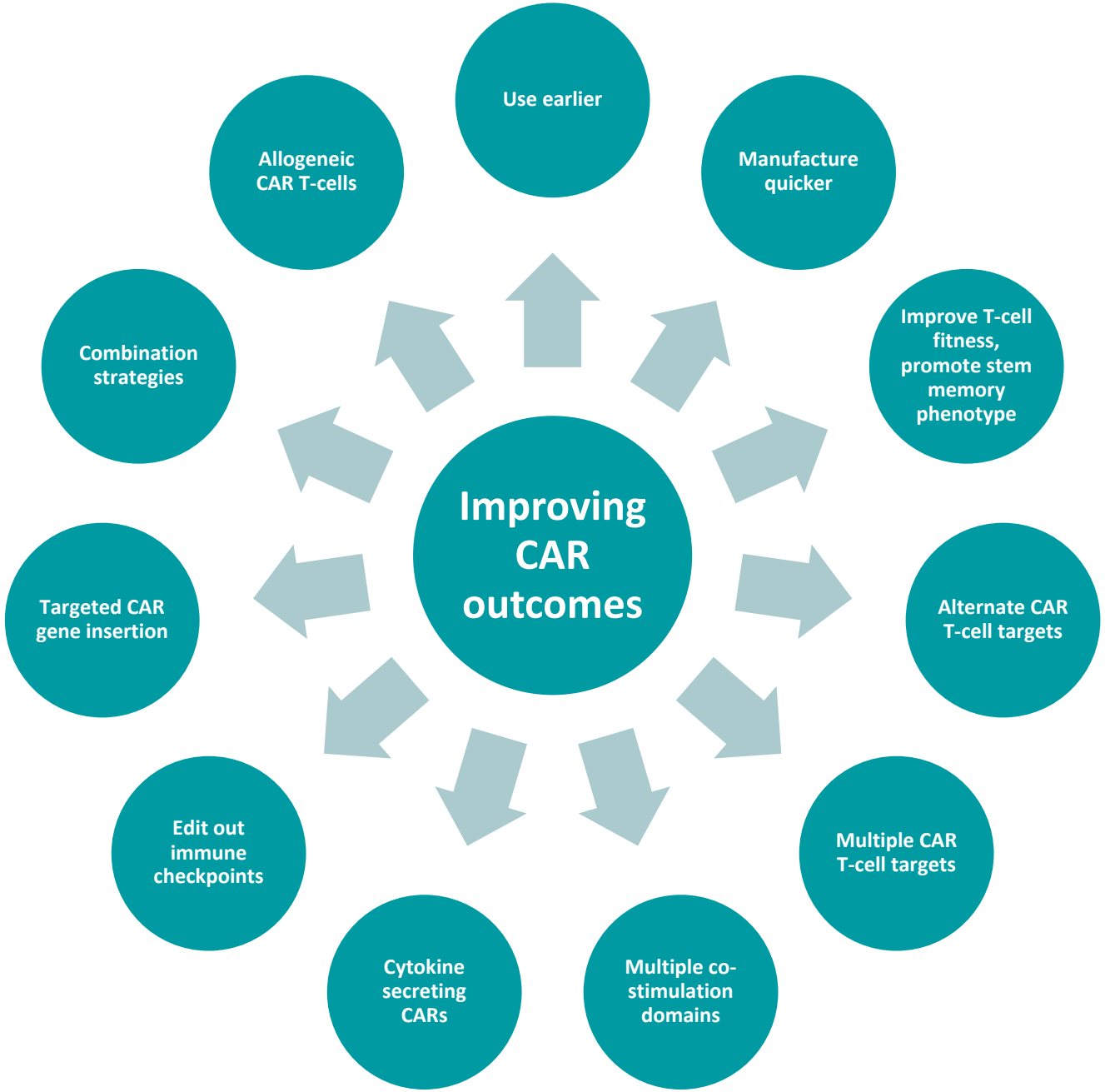
ZUMA-23: Axicabtagene Ciloleucel vs SoC as 1L Therapy in High-Risk LBCL

- Multicenter, randomized, adaptive, open-label phase III trial



- Primary endpoint: EFS
- Key secondary endpoints: OS and PFS
- Other secondary endpoints: safety, QoL, and pharmacokinetics

Early results with other CAR T-cell platforms for DLBCL


Improving CAR outcomes
Use earlier
Manufacture quicker
Improve T-cell fitness, promote stem memory phenotype
Alternate CAR T-cell targets
Multiple CAR T-cell targets
Multiple co-stimulation domains
Cytokine secreting CARs
Edit out immune checkpoints
Targeted CAR gene insertion
Combination strategies
Allogeneic CAR T-cells

Phase 2 study of rapcabtagene autoleucel in 3rd line+ LBCL

autologous anti-CD19 with rapid manufacturing

Baseline characteristics	N=63
Median age (range)	64 (26-81)
Median prior therapies	2 (2-6)
Refractory to prior tx	59%
Double hit	25%
IPI score ≥3	38%
Elevated LDH	43%

Response	N=60
Objective response	88%
Complete response	65%
Median DOR	15.2 mo
Medan PFS	11.9 mo

Safety	N=63
CRS	43%
Grade ≥3	6%
ICANS	6%
Grade ≥3	3%

Manufacturing time <2 days

Vein to vein time not reported

Riedell et al. Proc ASH 2024 #67

Phase 1 single center study of anti-CD22 CAR T-cell in patients relapsed after anti-CD19 CAR

Baseline characteristics	N=38
Median age (range)	65 (25-84)
Median prior therapies	4 (3-8)
Refractory to all prior tx	11 (29%)
Prior anti-CD19 CAR Median DOR to CAR19	37 (97%) 3 mo
Elevated LDH	32 (84%)

Successful manufacturing in 95%

Median time from apheresis to CAR22 infusion was 18 days

Safety	N=38
CRS Grade ≥3	36 (95%) 1 (3%)
ICANS Grade ≥3	4 (11%) 0
IEC-HS (HLH) Grade ≥3	5 (13%) 1 (3%)

Response	N=38
Objective response	68%
Complete response	53%

Time to event in pts treated at RP2D *(median f/u 36.7 mo)*	**N=29**
Median DOR	23.2 mo
Median PFS	3.0 mo
3-year PFS	30%
3-year OS	47%

Frank et al. Lancet 2024; Kramer Proc ASH 2024 #68

Phase 2 study of zamtocabtagene autoleucel in 3rd line+ LBCL

An anti-CD19/CD20 CAR with 14-day vein to vein time

Baseline characteristics	N=69
Median age (range)	63 (25-85)
≥3 prior lines of tx	27%
Elevated LDH	53%
≥2 extranodal sites	49%

Efficacy	Evaluable (n=59)
Objective response	73%
Complete response	49%
Median DOR	11.4 mo
12 month PFS	42%

Safety	N=69
CRS	46%
Grade 1-2	46%
Grade ≥3	0%
ICANS	17%
Grade 1-2	13%
Grade ≥3	4%
IEC-HS (HLH)	1%

Successful manufacturing of a fresh in specification product in 91.3%.

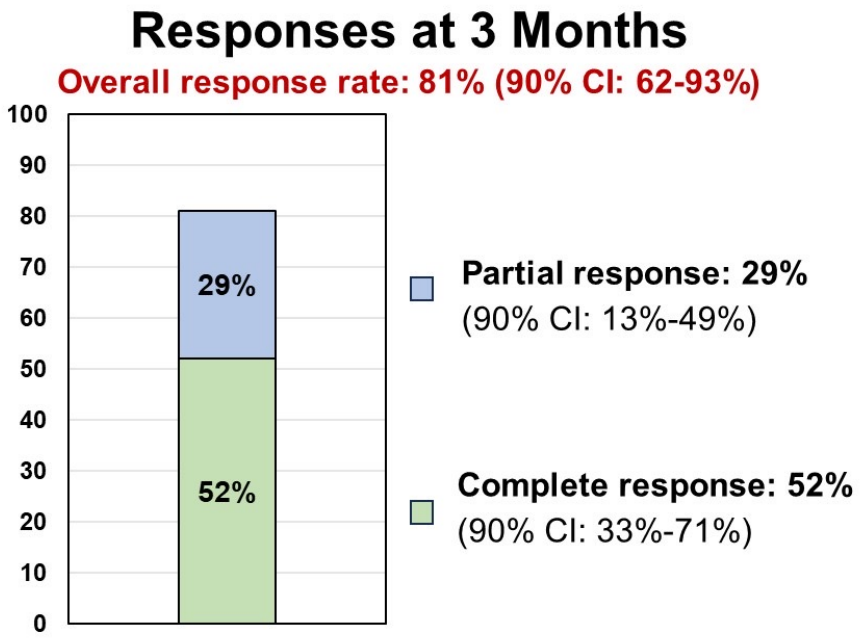
Antigen negativity at progression	N=24
CD19	N=2
CD20	N=3
Both CD19 & CD20	N=1

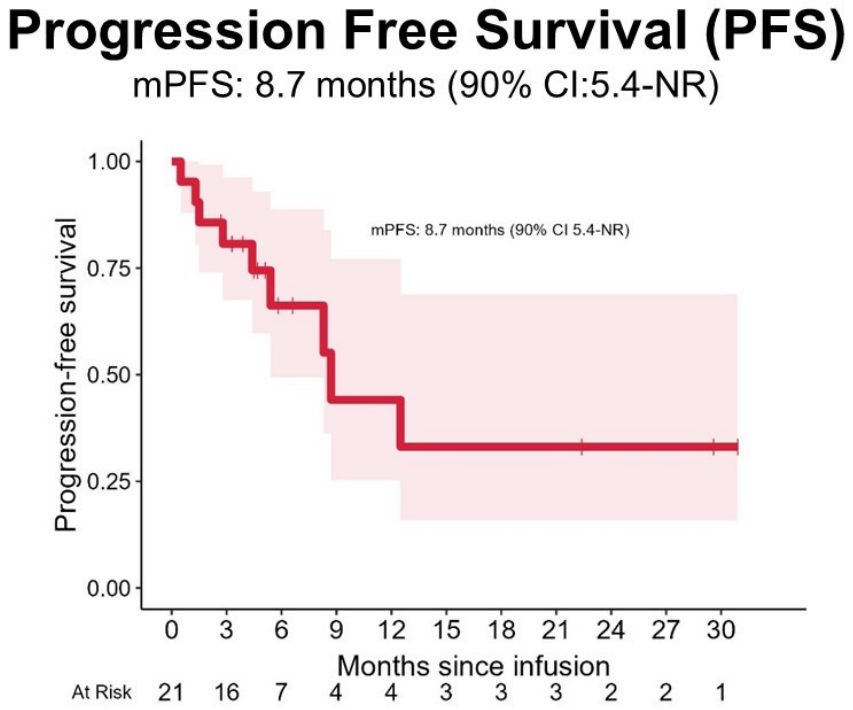
Shah et al. Proc ASH 2024 #68

huCART19-41BB-IL18 after failure of CD19 CAR

Baseline characteristics	N=21
Median age (range)	64 (59-68)
Median prior lines	7 (6-9)
Histology LBCL FL MCL	 12 6 3

AESI	Any grade	Grade 3
CRS	62%	14%
Neurotoxicity	17%	0



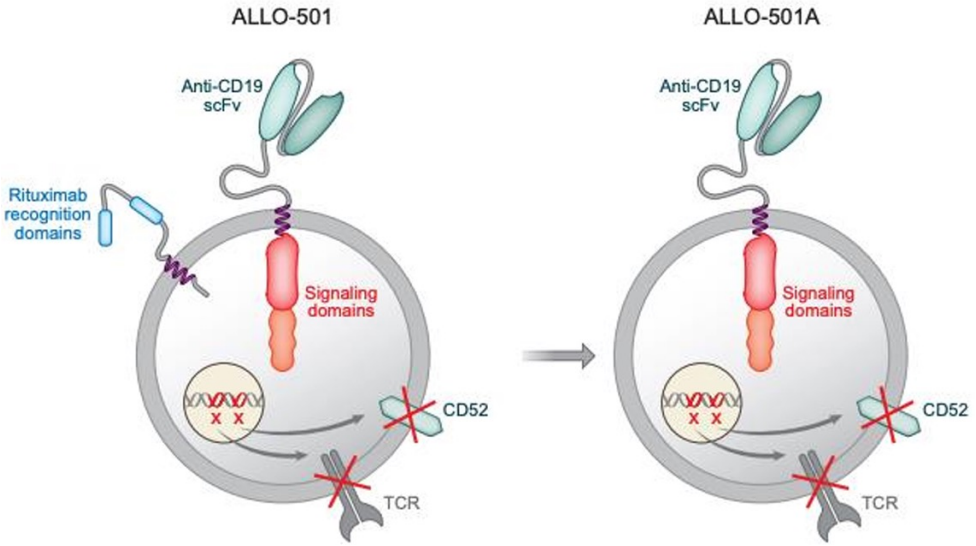


3 day manufacturing time!

Svoboda et al. Proc ASCO 2024

Phase 1 study of allo-501/501A in 3rd line+ LBCL

Analysis of patients treated at the RP2D

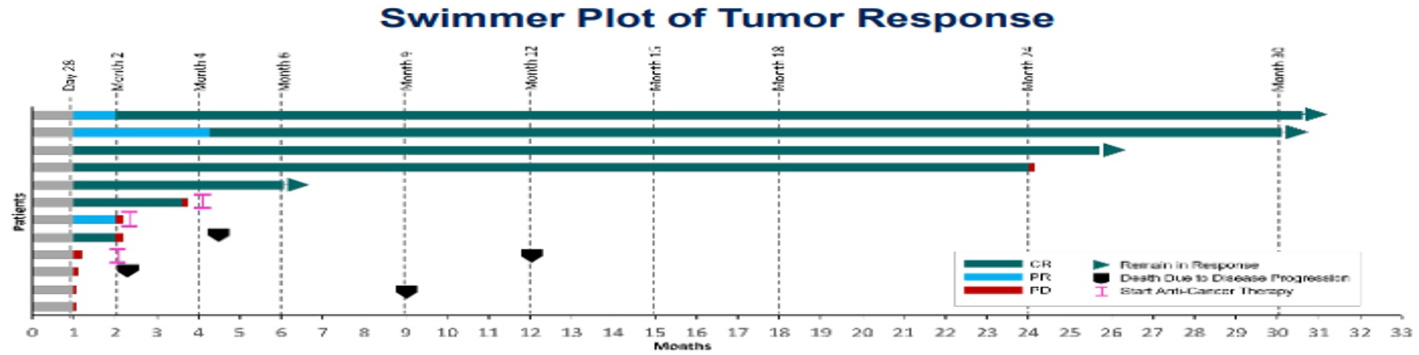


3-day lymphodepletion with FCA90	Single-dose of ALLO-501A or ALLO-501
F: fludarabine 30 mg/m²/day **C:** cyclophosphamide 300 mg/m²/day **A:** ALLO-647 30 mg/day (total dose: 90 mg)	120-360 x 10^6 viable CAR+ cells

Safety	N=12
CRS	33%
Grade ≥3	0%
ICANS	0%
GVHD	0%
Infection	67%
Grade ≥3	8%

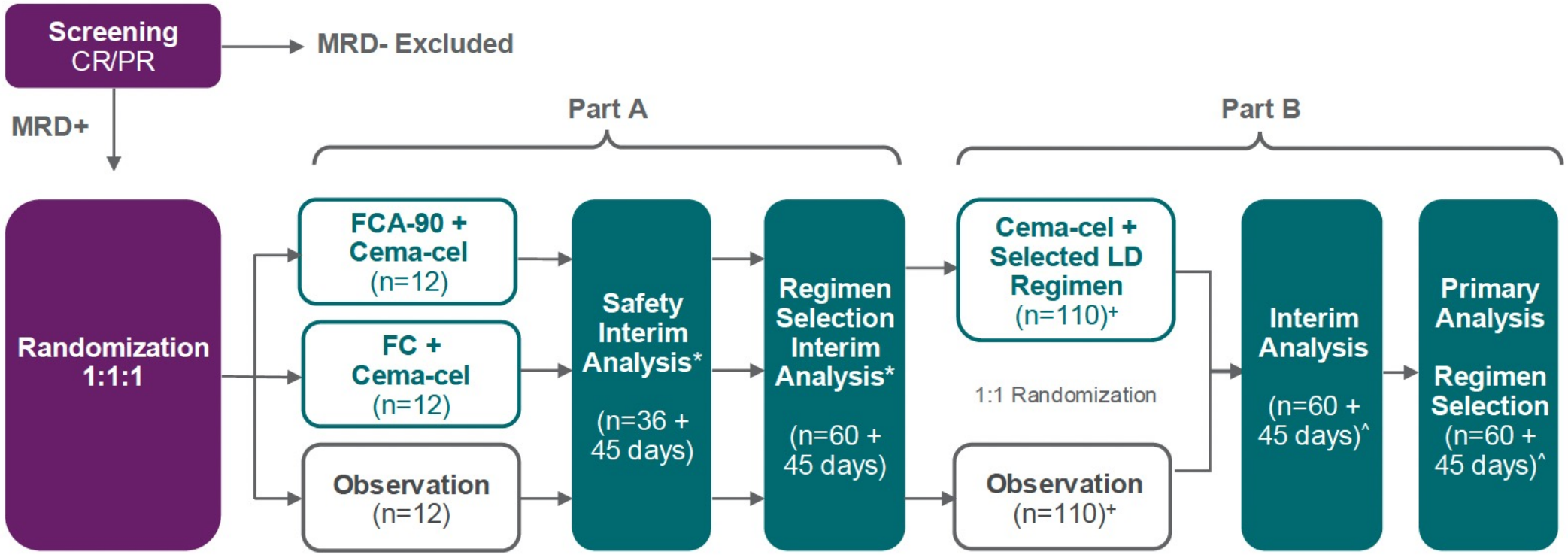
Efficacy	Evaluable (n=59)
Objective response	67%
Complete response	58%
Median DOR	12.3 mo

Baseline characteristics	N=12
Median age (range)	60
Median prior lines of tx	3
Double hit	33%
Elevated LDH	67%



Locke et al. Proc ASCO 2023

Randomized trial of cemacabtagene ansegedleucel (allo-501A) as consolidative therapy in LBCL pts with MRD+ CR/PR at EOT



*Continuous enrollment through the interim analyses in Part A and Part B
+Total enrollment into selected regimen and observation arms across Part A and Part B
^Events for hypothesis testing accrue from participants treated with the selected regimen and observed in both Parts A and B of the study
The primary analysis for the study will occur after 100 EFS events have occurred in any study arm

Agenda

Module 1: Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Abramson

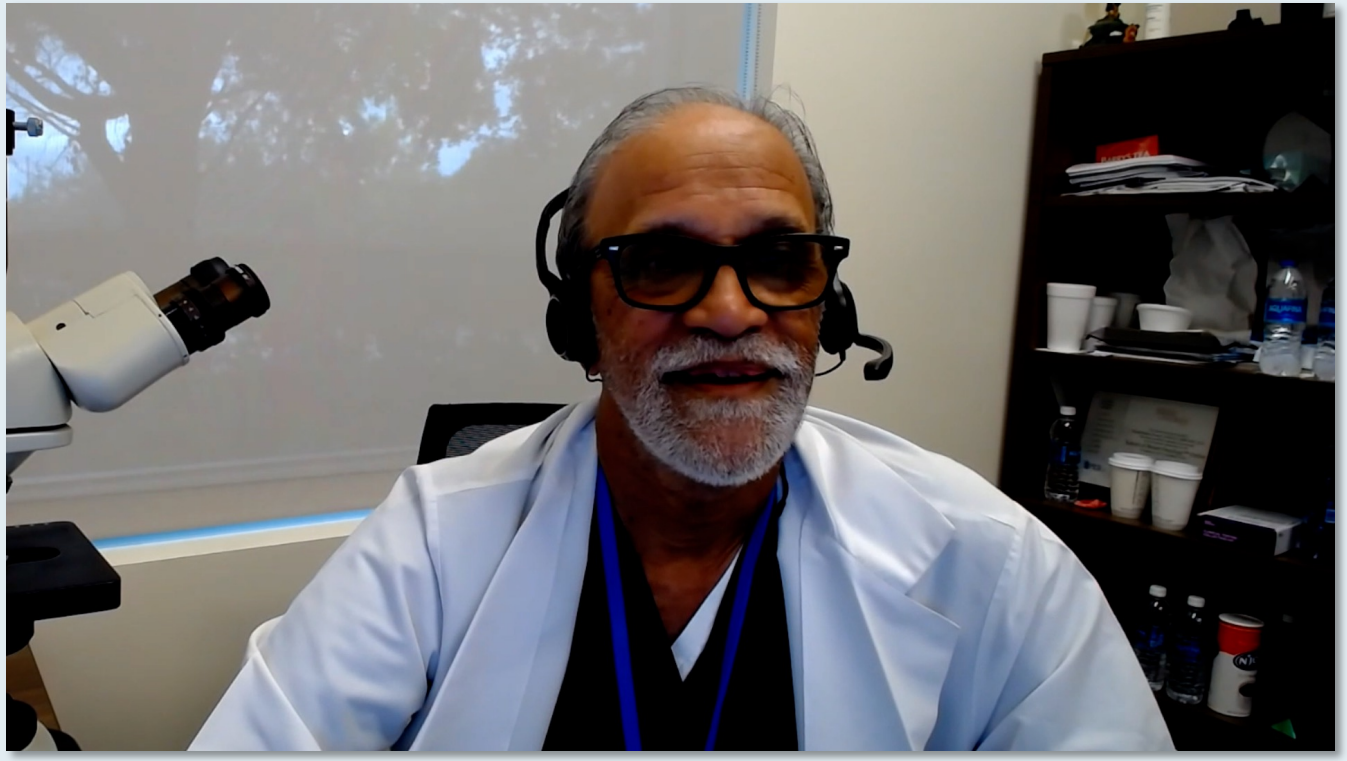
Module 2: Bispecific Antibody Therapy for DLBCL — Prof Hutchings

Module 3: CAR T-Cell Therapy for Other Lymphoma Subtypes — Dr Lunning

Module 4: Bispecific Antibody Therapy for Follicular Lymphoma and Other Lymphoma Subtypes — Dr Phillips

Module 5: Tolerability Considerations with CAR T-Cell and Bispecific Antibody Therapy — Dr Crombie

Case Presentation: 90-year-old woman with recurrent non-GCB DLBCL who received R-CHOP in 2014 now with disease recurrence after tafasitamab/lenalidomide



Dr KS Kumar (Trinity, Florida)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

How do age and comorbidities factor into decisions regarding the use of CD20 x CD3 bispecific antibodies for DLBCL?

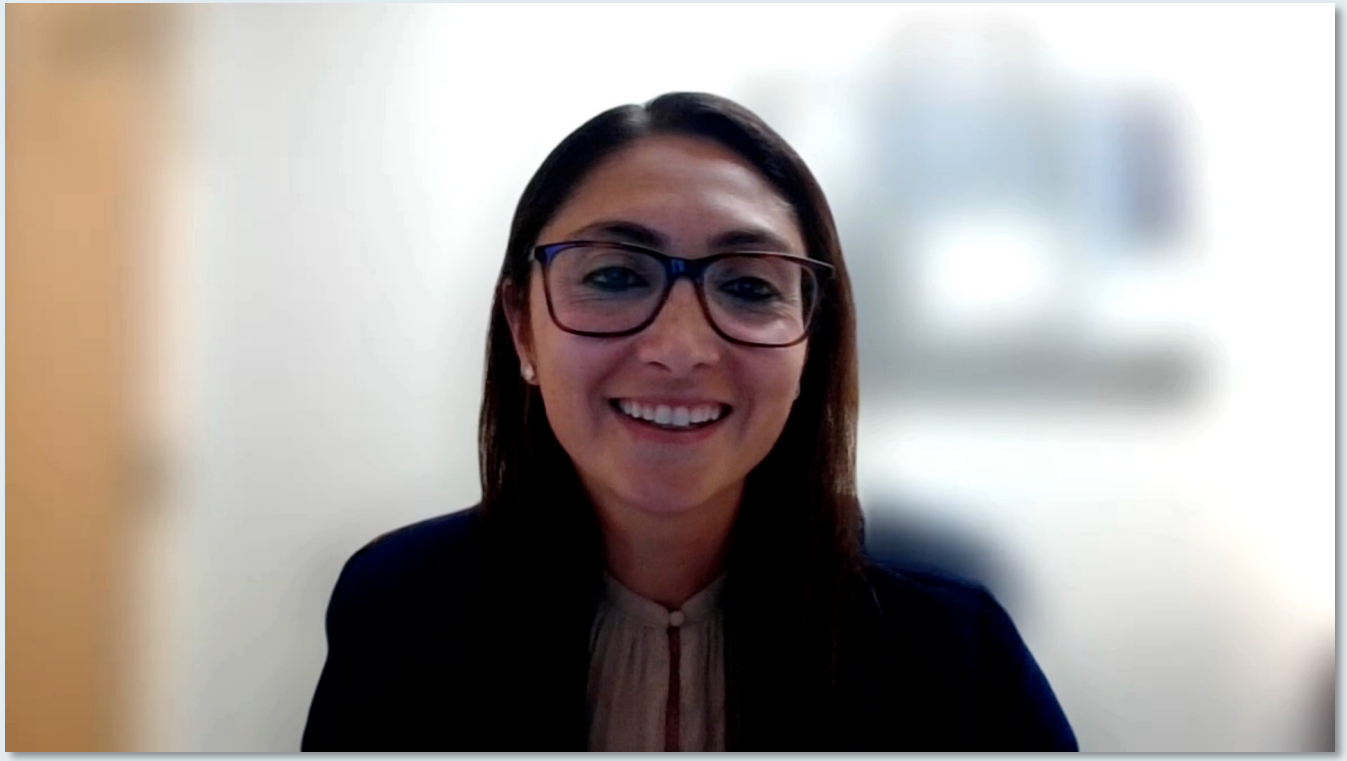
Which comorbidities are of greatest concern with these agents?

Which bispecific antibody, if any, is preferable for younger patients? What about older patients or those with comorbidities?

Do you believe there are fundamental differences in the activity or tolerability of mosunetuzumab, epcoritamab, glofitamab and odronextamab? Do any of these agents have specific advantages over the others?

RTP
RESEARCH
TO PRACTICE

Case Presentation: 81-year-old man diagnosed with DLBCL in 2018 who received R-CHOP and autologous transplant on disease progression in 2020 and CAR T-cell therapy followed by disease progression



Dr Shams Bufalino (Park Ridge, Illinois)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

How effective are bispecific antibodies after CAR T-cell therapy in DLBCL?

How do you generally sequence CAR T-cell therapy and bispecific antibodies in DLBCL?

Is there a role for repeat CAR T-cell therapy in DLBCL using different products?

Bispecific Antibody Therapy for DLBCL

UNIVERSITY OF COPENHAGEN

Research To Practice Symposium

San Diego – 6th December 2024

Martin Hutchings
Department of Haematology and Phase 1 Unit, Rigshospitalet
Department of Clinical Medicine, University of Copenhagen
Copenhagen, Denmark

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

Bispecific antibody	Aggressive B-NHL			Indolent B-NHL			CRS / > gr 2
	No	ORR	CRR	No	ORR	CRR	
Mosunetuzumab	124	**35%**	**19%**	68	66%	49%	27% / 1%
Odronextamab	45	**40%**	**36%**	32	91%	72%	91% / 7%
Glofitamab	69	**61%**	**49%**	29	69%	59%	50% / 3.5%
Epcoritamab	22	**68%**	**45%**	10	90%	50%	59% / 0%

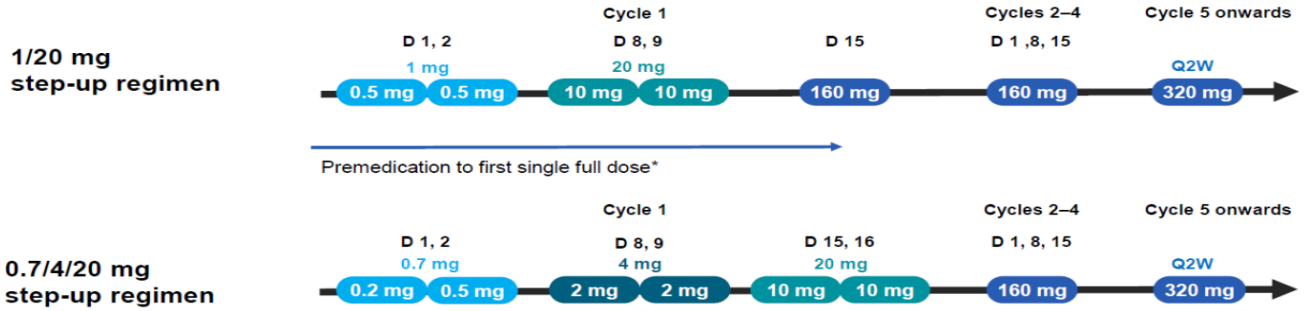
1. Budde E, et al. J Clin Oncol 2022;40(5):481-491.
2. Bannerji R, et al. Lancet Haematol 2022;9(5):e327-e339.
3. Hutchings M, et al. Clin Oncol. 2021;39(18):1959-1970.
4. Hutchings M, et al. Lancet 2021;398(10306):1157-1169.

Studies of CD20xCD3 bispecific antibodies for R/R DLBCL after ≥2 lines of treatment: prior therapies at enrollment

	Trial	Number of patients	Median (range) prior therapies	Primary refractory, n (%)	Refractory to most recent line, n (%)	Prior CAR T-cell therapy, n (%)	Prior ASCT, n (%)
Mosunetuzumab[1]	GO29781	88	3 (2–13)	–	70 (80)	26 (30)	15 (17)
Odronextamab[2]	ELM-2	140	2 (2–8)	80 (57)	–	–	–
Glofitamab[3]	NP30179	154	3 (2–7)	90 (58)	132 (86)	51 (33)	28 (18)
Epcoritamab[4]	EPCORE NHL-1	157[†]	3 (2–11)	96 (61)	130 (83)	61 (39)	31 (20)

1. Bartlett NL, et al. Blood Adv 2023;7(17):4926-4935.
2. Walewski J, et al. EHA 2023. Abstract P1115.
3. Dickinson M, et al. N Engl J Med 2022;387:2220–31.
. 4. Thieblemont C, et al. J Clin Oncol 2023; 41(12):2238-2247.

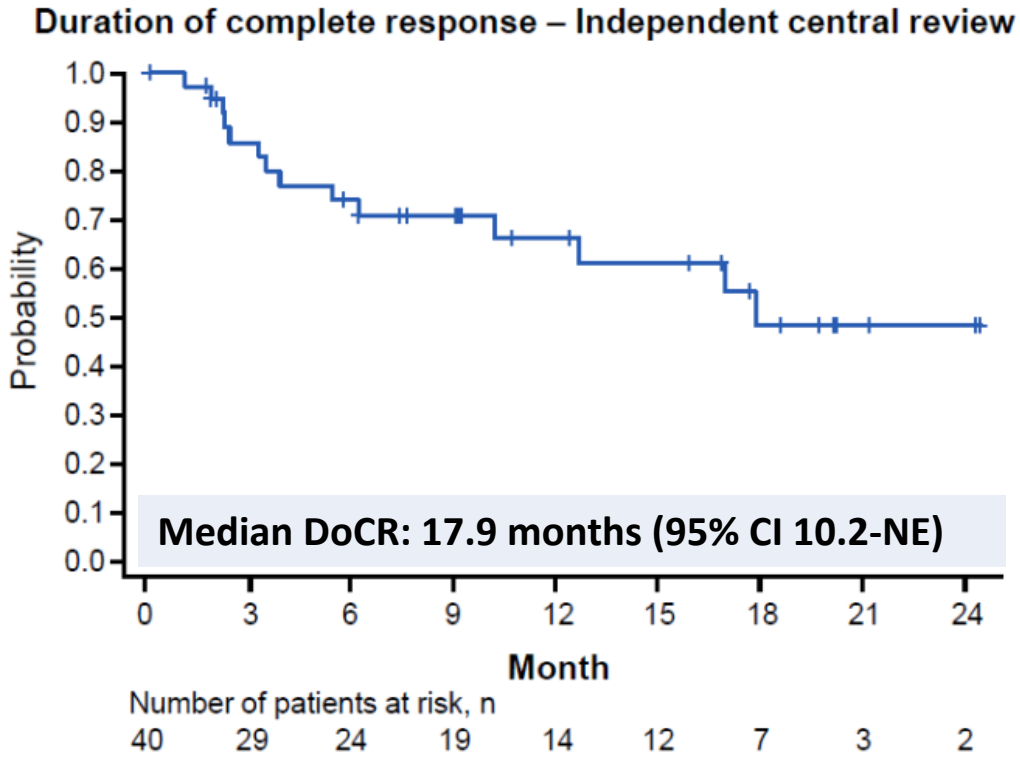
Phase II study of odronextamab in patients with R/R DLBCL



n, (%)	1/20 regimen N=67	0.7/4/20 regimen N=73
CRS any Grade	38 (56.7%)	39 (53.4%)
Grade 1	21 (31.3%)	28 (38.4%)
Grade 2	12 (17.9%)	10 (13.7%)
Grade 3	5 (7.5%)	1 (1.4%)
Grade 4	0	0

Best overall response	Independent central review N=130*
Objective response rate (ORR)†	**49.2%** [95% CI 40.4%–58.1%]
Complete response	**30.8%**

Median follow-up: 21.3 months (range 2.6–29.8)



Median DoCR: 17.9 months (95% CI 10.2-NE)

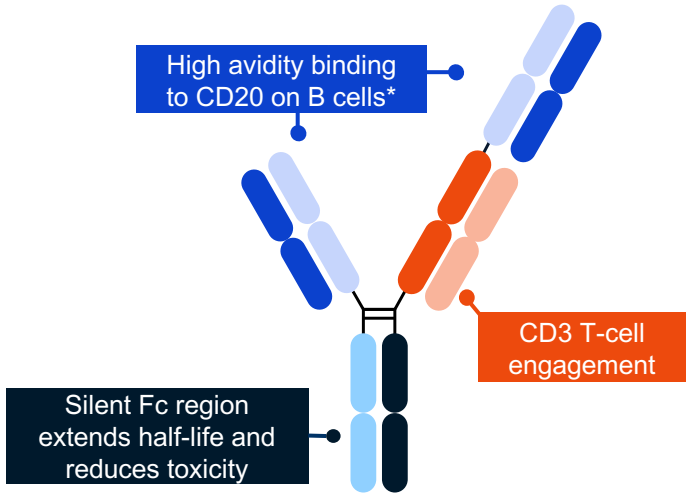
- 12-month DOCR: 66.4% (95% CI: 47.1–80.1)
- 18-month DOCR: 48.3% (95% CI: 26.1–67.4)

Poon M, et al. ICML 2023, abstract #93.

NP30179: Phase II dose expansion study of glofitamab in R/R DLBCL after ≥2 therapies – study design and patients

Key inclusion criteria

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



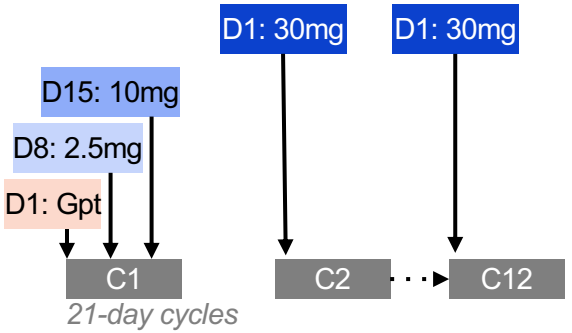
Glofitamab IV administration

Fixed-duration treatment

- max. 12 cycles

CRS mitigation:

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



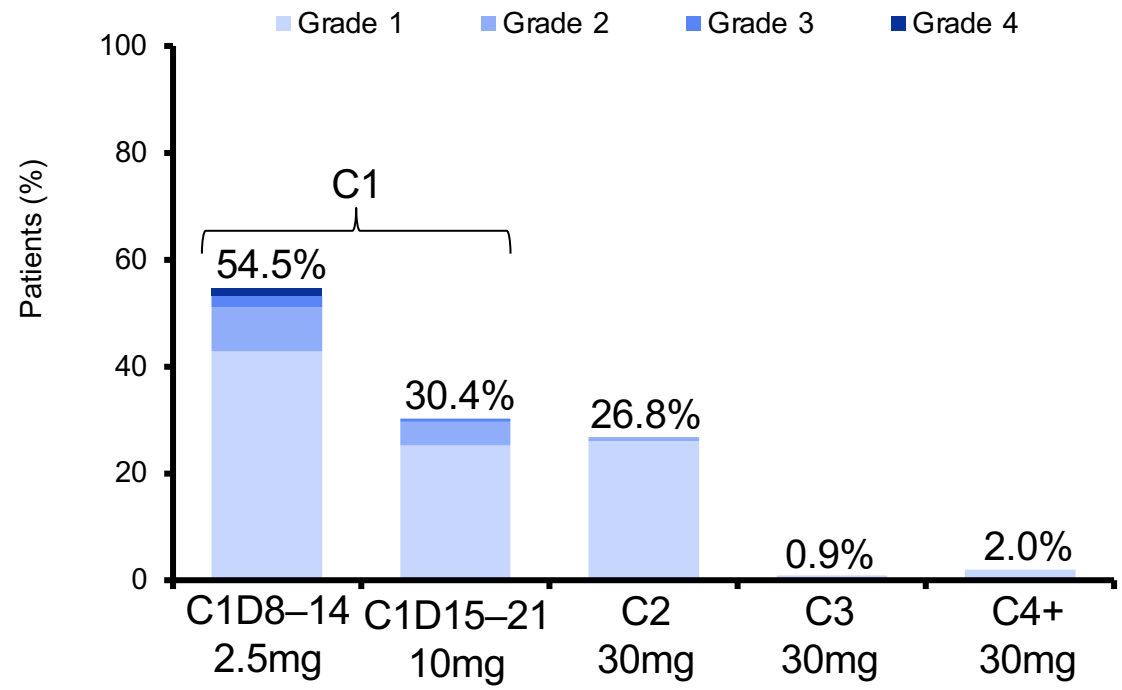
n (%)	N=155
Median no. of prior lines of therapy, n (range)	3 (2–7)
2 prior lines	61 (39)
≥3 prior lines	94 (61)
Prior anti-CD20 therapy	155 (100)
Prior anthracycline therapy	152 (98)
Prior CAR-T	52 (34)
Prior ASCT	29 (19)
Refractory to any prior therapy	139 (90)
Refractory to first prior therapy	91 (59)
Refractory to last prior therapy	131 (85)
Refractory to prior CAR-T	46/52 (88)
Refractory to any prior anti-CD20	129 (83)

Dickinson M, et al. N Engl J Med. 2022 Dec 15;387(24):2220-2231.
Hutchings M, et al. ASH 2023 (Abstract #179)

Phase II dose expansion study of glofitamab in R/R DLBCL after ≥2 therapies – cytokine release syndrome

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

CRS by cycle and grade†

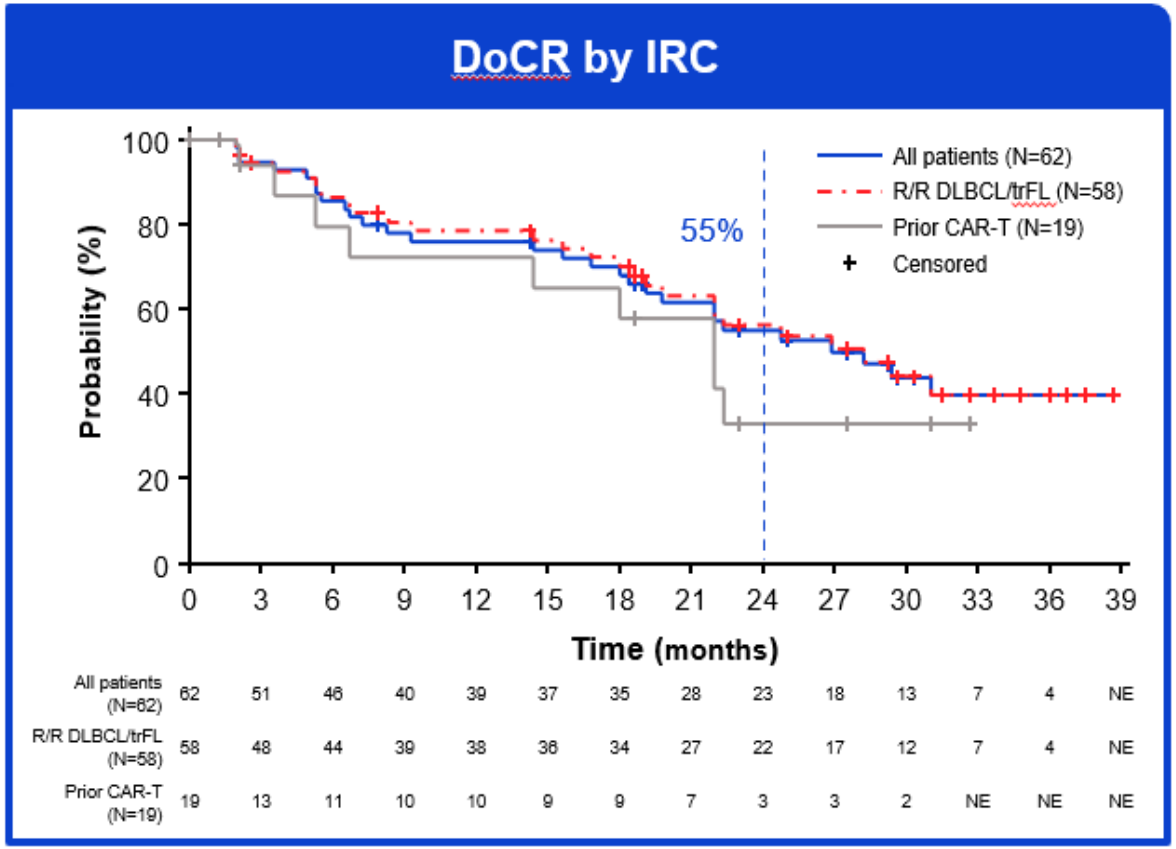


CRS was mostly low grade, time of onset was predictable, and most events occurred during C1

Dickinson M, et al. EHA 2022 oral presentation

Phase II dose expansion study of glofitamab
Response rates and duration of CR

	All patients (N=155)*	R/R DLBCL/ trFL (N=132)[1†‡]	Prior CAR-T (N=52)†
ORR, n (%) [95% CI]	80 (52) [43.5–59.7]	74 (56) [47.2–64.7]	26 (50) [35.8–64.2]
CR rate, n (%) [95% CI]	62 (40) [32.2–48.2]	58 (44) [35.3–52.8]	19 (37) [23.6–51.0]
Median DoCR, months (95% CI)	26.9 (19.8–NR)	28.3 (19.8–NR)	22.0 (6.7–NR)
24-month DoCR, % (95% CI)	55.0 (41.1–68.8)	56.2 (41.9–70.4)	33.1 (7.2–59.0)
Median CR follow-up, months (range)	29.6 (0–39)	29.6 (0–39)	23.0 (0–33)
Ongoing CRs, n/N (%)	34/62 (55)	32/58 (55)	10/19 (53)



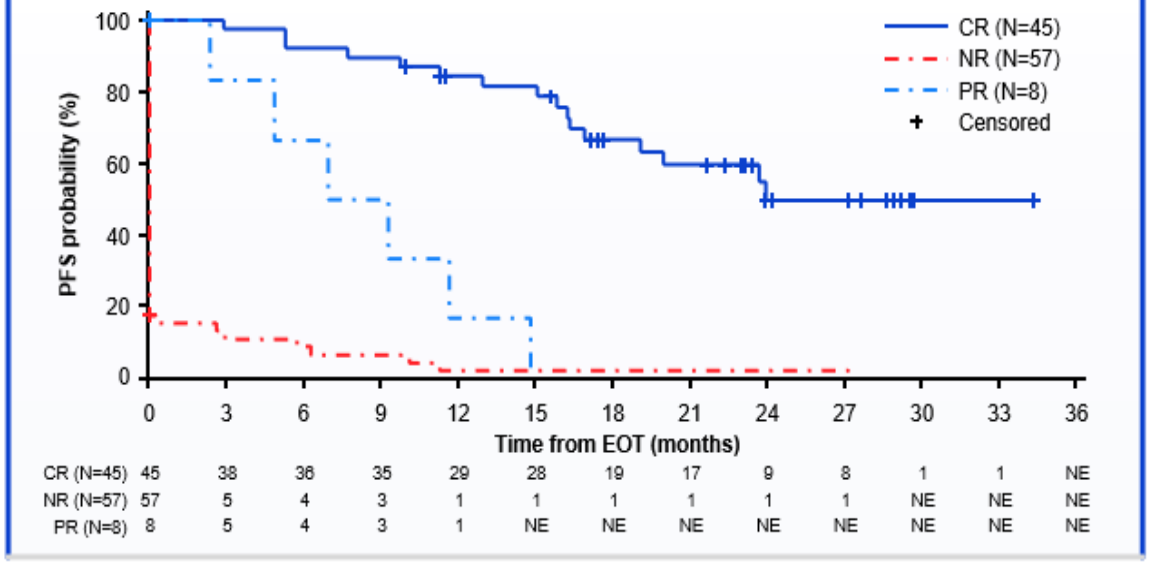
- Median time on study: 32.1 months (range: 0–43)

With 32 months median follow-up, glofitamab showed high response rates and durable remissions across subgroups

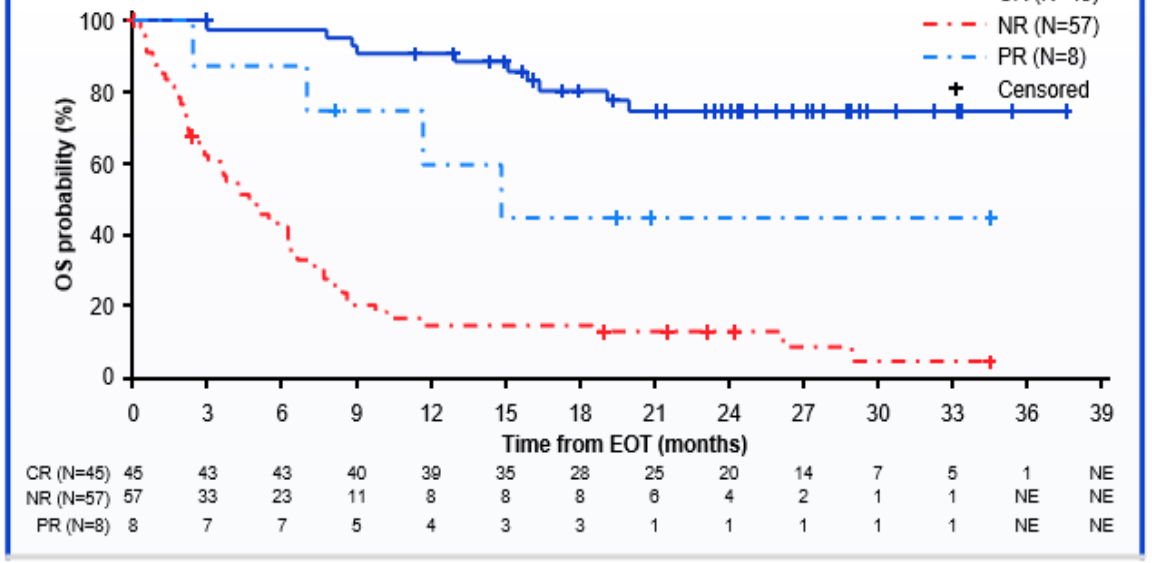
Hutchings M, et al. ASH 2023 (Abstract #179)

Phase II dose expansion study of glofitamab in R/R DLBCL after ≥2 therapies – ASH 2023 update

PFS



OS



Landmark PFS from EOT in patients with CR at EOT*	N=45
Median PFS, months (95% CI)	24.0 (19.1–NE)
18-month PFS rate, % (95% CI)	66.6 (51.0–82.2)

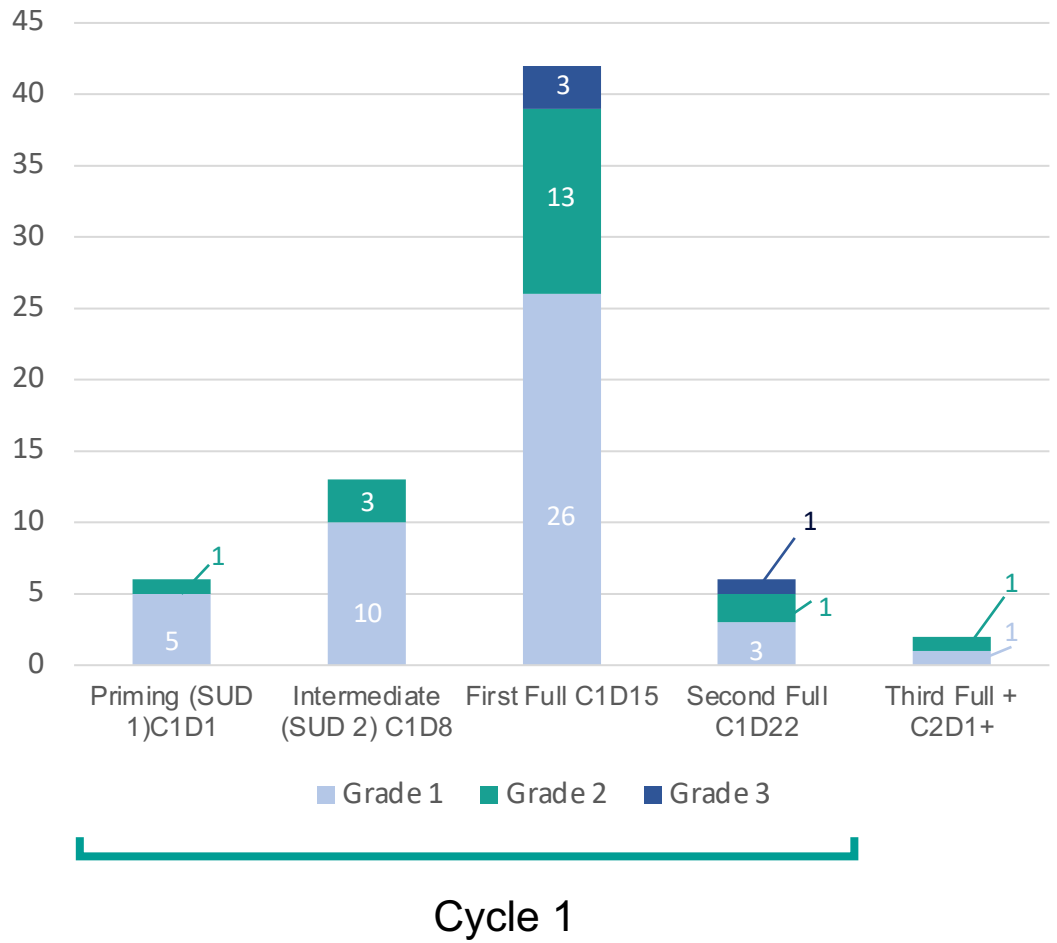
Landmark OS from EOT in patients with CR at EOT*	N=45
Median OS, months (95% CI)	NE (NE)
18-month OS rate, % (95% CI)	80.7 (68.6–92.8)

Majority of patients with a CR at EOT remained progression-free and alive at 18 months after EOT

Hutchings M, et al. ASH 2023 (Abstract #179)

Phase II dose expansion study of epcoritamab in patients with R/R LBCL – patients and safety

Prior Treatments	DLBCL, n=139	LBCL, N=157
Median time from initial diagnosis to first dose, mo	19	19
Median time from end of last therapy to first dose, mo	2.4	2.4
Median prior lines of therapy (range)	3 (2–11)	3 (2–11)
≥3 Lines of therapy, n (%)	97 (70)	110 (70)
Primary refractory[b] disease, n (%)	81 (58)	95 (61)
Refractory[b] to last systemic therapy, n (%)	114 (82)	130 (83)
Refractory[b] to ≥2 consecutive lines of therapy, n (%)	103 (74)	118 (75)
Prior ASCT, n (%)	26 (19)	31 (20)
Prior CAR T therapy, n (%)	53 (38)	61 (39)
Refractory[b] to CAR T therapy	39/53 (74)	46/61 (75)

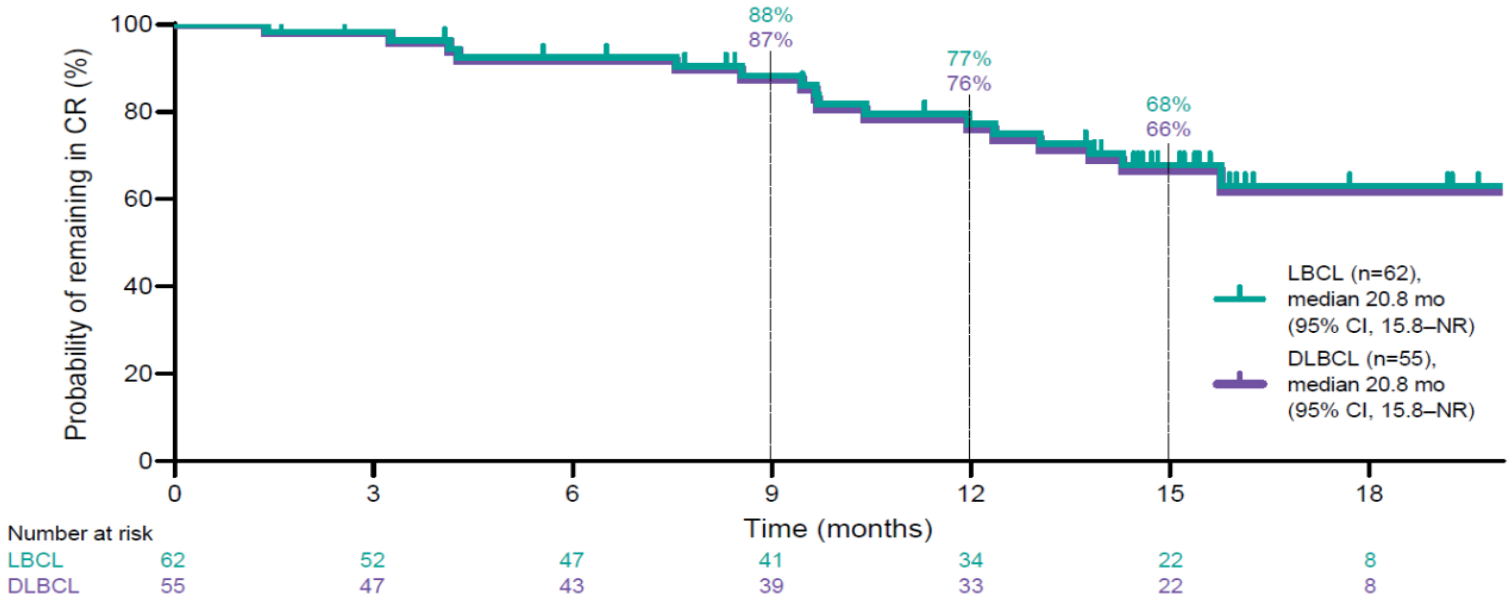


Thieblemont C, et al. J Clin Oncol 2022; 41(12): 2238-2247.

Phase II dose expansion study of epcoritamab in patients with R/R LBCL - response data

Best Overall Response, n (%)	LBCL N=157[a]	DLBCL n=139[a]	HGBCL n=9	PMBCL n=4	FL G3B n=5
Overall response	99 (63)	86 (62)	4 (44)	4 (100)	5 (100)
Complete response	62 (39)	55 (40)	2 (22)	2 (50)	3 (60)

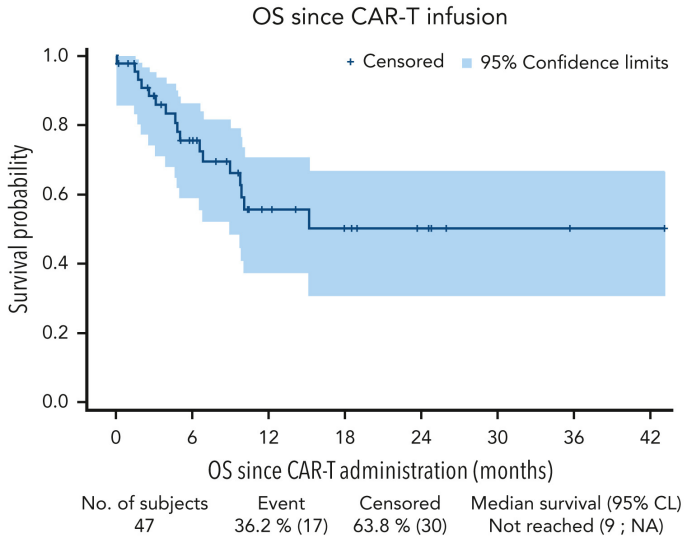
Durable Complete Responses

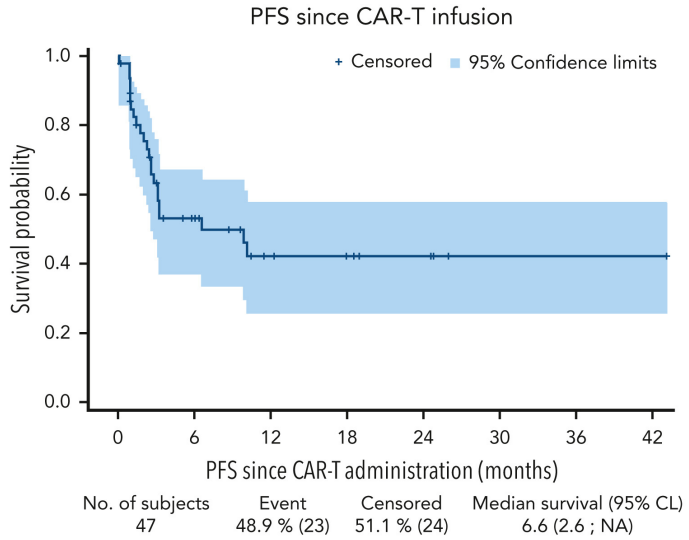


Karimu Y, et al. ASCO 2023 #7525 (poster).
Jurczak W, et al. EHA 2023 #P1118 (poster).
Thieblemont C, et al. ICML 2023 #94 (oral).

What is the optimal sequencing in DLBCL with all the new options (CAR-T and Bispecifics)?

- The phase 2 studies of glofitamab and epcoritamab show more or less the same response rates, the same complete response rates, and the same durability of responses in patients with and without prior CART exposure
- Retrospective analysis from the French DESCARTES database show that the opposite is also true:

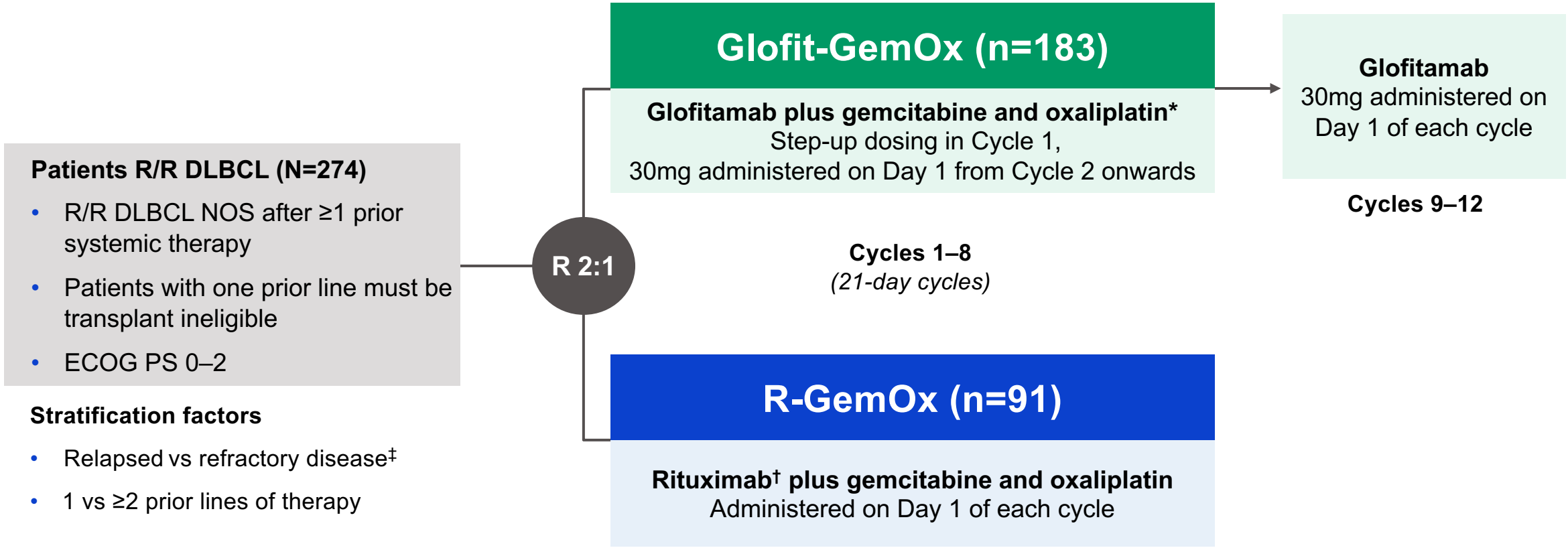




- The chronology of the development (CART with longer FU and a demonstrated curative potential) speaks in favour of CART before BsAbs
- This may change when we have randomised data on BsAbs in 1st and perhaps 2nd line

Crochet G, et al. Blood 2024; 144(3): 334-338.

STARGLO: Randomized Phase III trial in ASCT-ineligible patients with R/R DLBCL

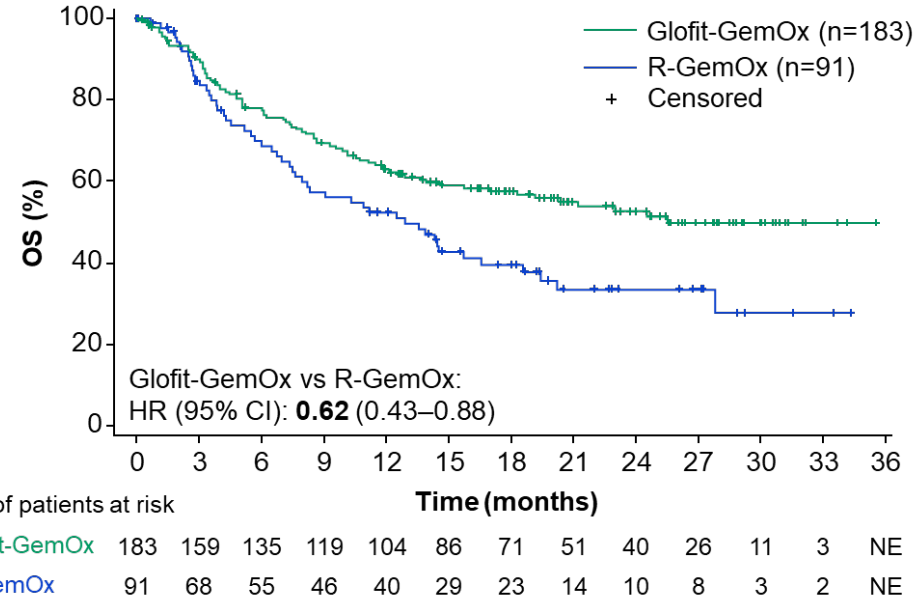


Glofit + GemOx is not indicated for use in DLBCL. Safety and efficacy have not been established

Abramson J, et al. EHA 2024. Abstract LB3438.

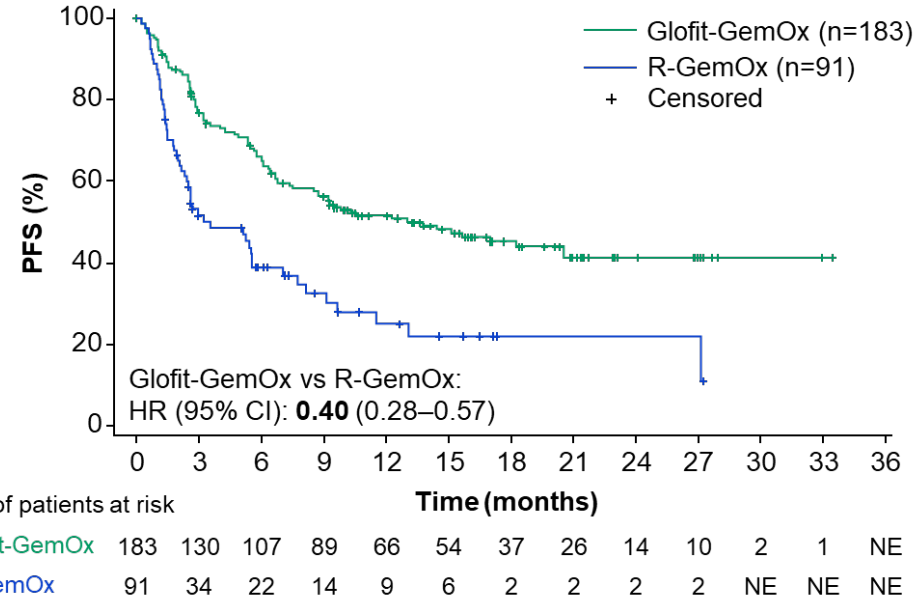
STARGLO: Overall survival (primary endpoint) and PFS

Updated analysis



	R-GemOx (n=91)	Glofit-GemOx (n=183)
Updated analysis (median follow-up: 20.7 months)		
OS, median (95% CI); months	12.9 (7.9–18.5)	25.5 (18.3–NE)
HR (95% CI)	**0.62** (0.43–0.88)	
p-value*	0.006	
24-month OS (95% CI)	33.5% (22.2–44.9)	52.8% (44.8–60.7)

Updated analysis



	R-GemOx (n=91)	Glofit-GemOx (n=183)
Updated analysis (median follow-up: 16.1 months)		
PFS, median (95% CI); months	3.6 (2.5–7.1)	13.8 (8.7–20.5)
HR (95% CI)	**0.40** (0.28–0.57)	
p-value*	<0.000001*	
12-month PFS (95% CI)	25.2% (13.6–36.9)	51.7% (44.0–59.4)

Glofit + GemOx is not indicated for use in DLBCL. Safety and efficacy have not been established

Abramson J, et al. EHA 2024. Abstract LB3438.

Summary

- The T-cell engaging bispecific antibodies show an antitumor activity which is unprecedented in heavily pretreated r/r DLBCL
- Data from DLBCL phase 2 expansion cohorts (25-40% with prior CAR-T):
  - Glofitamab: ORR 52%, CRR 40% *(FDA and EMA approved in 2023 for LBCL 3+ line)*
  - Epcoritamab: ORR 63%, CRR 39% *(FDA and EMA approved in 2023 for LBCL 3+ line)*
  - Odronextamab: ORR 49%, CRR 31% *(EMA approved in 2024 for LBCL 3+ line)*
- Complete responses are highly durable (for glofitamab also beyond EOT)
  - Suggests a curative potential even when given as single agents
- The toxicity profile is favourable:
  - Very little CRS > grade 2
  - Very little treatment-related CNS toxicity
- The toxicity profile and mechanism of action make the bispecifics ideal for combination strategies (chemotherapy, ADCs, costimulatory antibodies, etc.)
- Recent data show OS superiority of Glofitamab-GemOx over R-GemOx in r/r LBCL

Agenda

Module 1: Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Abramson

Module 2: Bispecific Antibody Therapy for DLBCL — Prof Hutchings

Module 3: CAR T-Cell Therapy for Other Lymphoma Subtypes — Dr Lunning

Module 4: Bispecific Antibody Therapy for Follicular Lymphoma and Other Lymphoma Subtypes — Dr Phillips

Module 5: Tolerability Considerations with CAR T-Cell and Bispecific Antibody Therapy — Dr Crombie

RTP
RESEARCH
TO PRACTICE

Case Presentation: 54-year-old woman with extensive follicular lymphoma that responds to BR but is followed by rapidly growing large cell lymphoma in neck and shoulder

Dr Yanjun Ma (Murfreesboro, Tennessee)

RTP
RESEARCH
TO PRACTICE

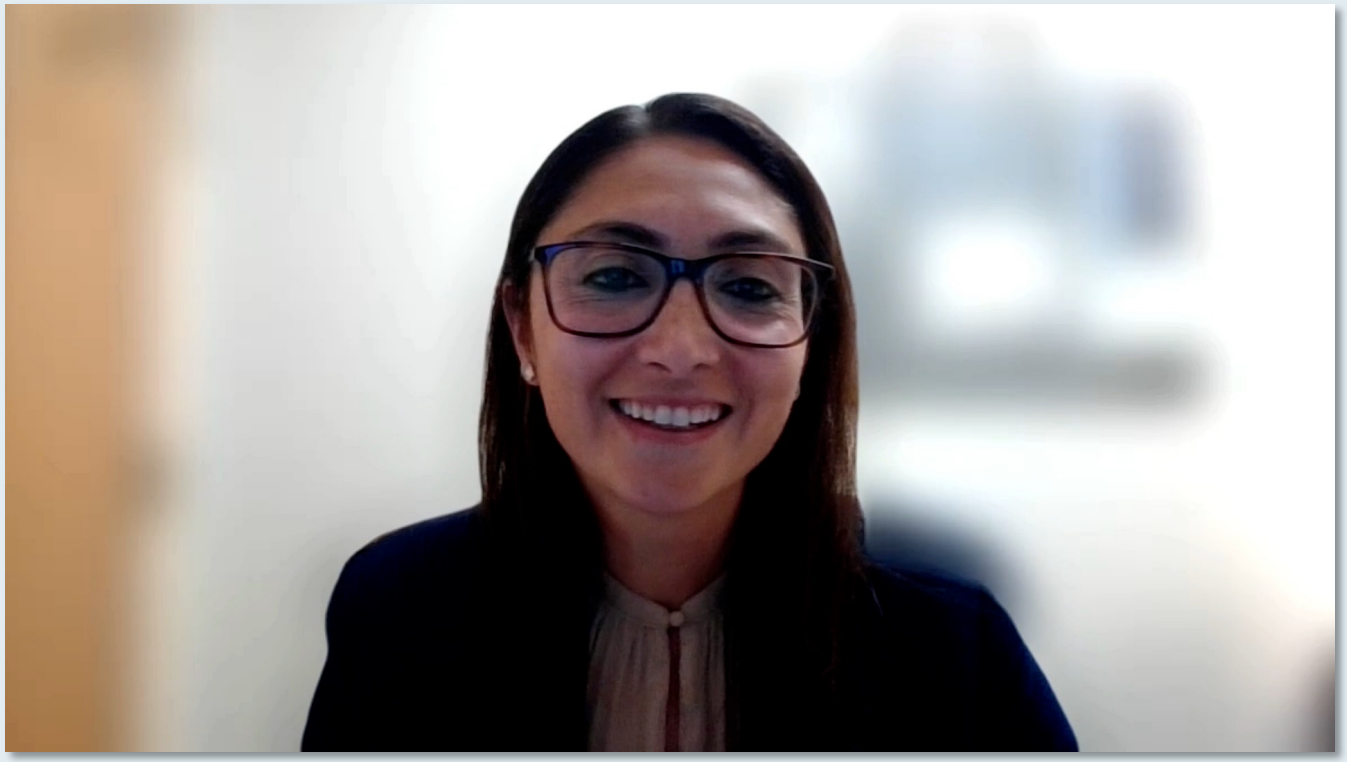
QUESTIONS FOR THE FACULTY

Is this case likely an example of transformed FL or 2 separate disease entities?

What is your experience with vascular compromise from DLBCL, and how effective is radiation therapy in this situation?

What systemic management strategy would you most likely recommend for this type of patient?

Case Presentation: 77-year-old man with primary CNS lymphoma in 2017, now with progressive systemic ABC-type DLBCL



Dr Shams Bufalino (Park Ridge, Illinois)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

What is your experience with systemic recurrence of primary CNS lymphoma?

Do you routinely include CNS prophylaxis when treating recurrence in situations like this one?

How effective is CAR T-cell therapy versus bispecific antibodies versus chemotherapy in controlling CNS disease?

Case Presentation: 88-year-old man with mild dementia and mantle cell lymphoma who received R-CHOP, lenalidomide/rituximab; ibrutinib resulted in response but was discontinued due to cytopenias

Dr Susmitha Apuri (Inverness and Lecanto, Florida)

QUESTIONS FOR THE FACULTY

Which patients with MCL represent ideal candidates for CAR T-cell therapy? For patients with MCL who are eligible for CAR T-cell therapy, do you use bridging therapy and, if so, what type?

What is the future role of bispecific antibody therapy in MCL? What has been documented regarding the efficacy and tolerability of this strategy?

For a patient with MCL who has run out of options, would you attempt to access a CD20 x CD3 bispecific antibody? If so, would you have a preference for any of the available agents?

A Happy Meal?: CAR T-Cell Therapy for FL & MCL

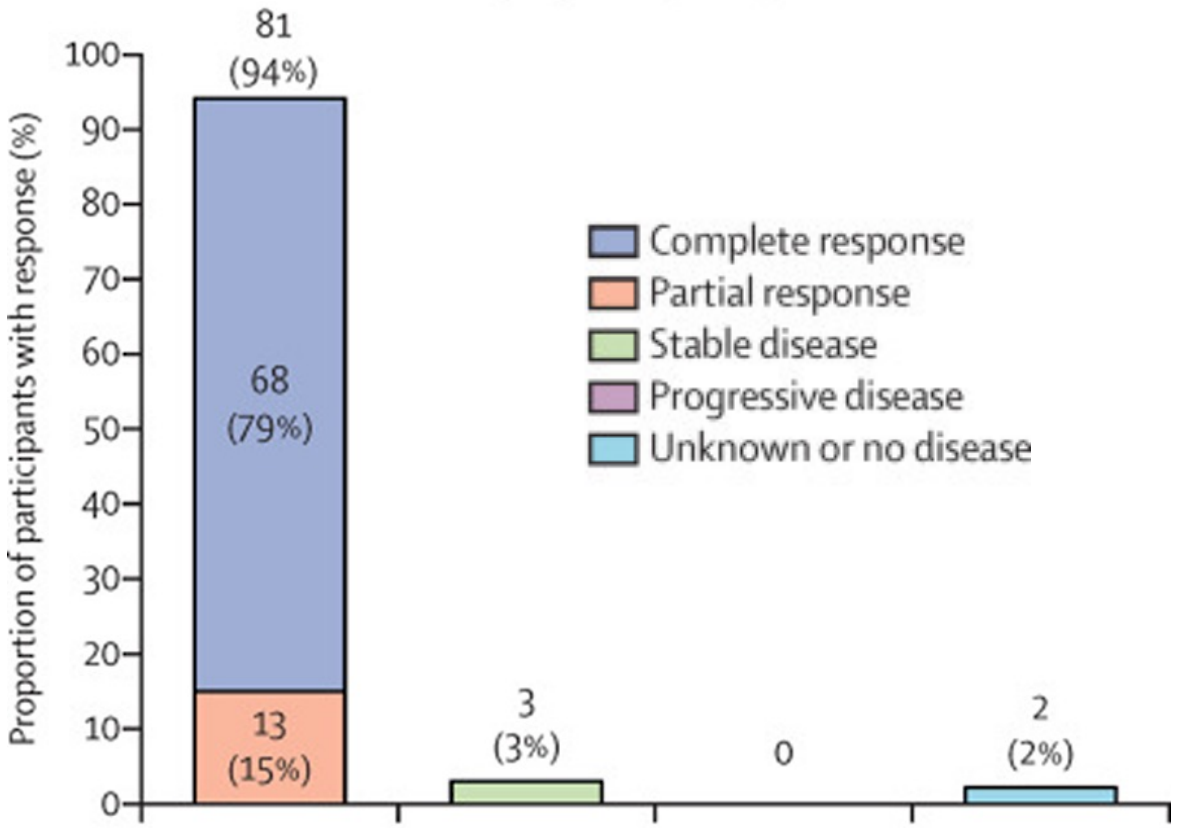
Matthew Lunning, DO, FACP
Associate Professor, Division of Oncology & Hematology
Medical Director, Gene & Cellular Therapy
Associate Vice Chair of Research, Department of Internal Medicine
Assistant Vice Chancellor for Clinical Research

University of Nebraska Medical Center
Nebraska Medicine

Items for Consideration

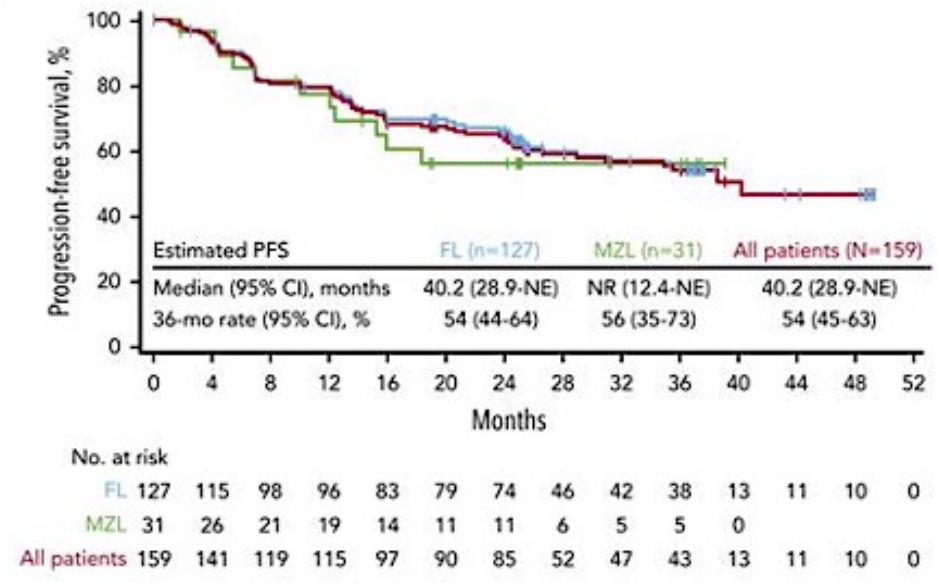
- When to order axi-cel, tisa-cel or liso-cel for relapsed/refractory (R/R) follicular lymphoma
- When to order brexu-cel or liso-cel for R/R mantle cell lymphoma

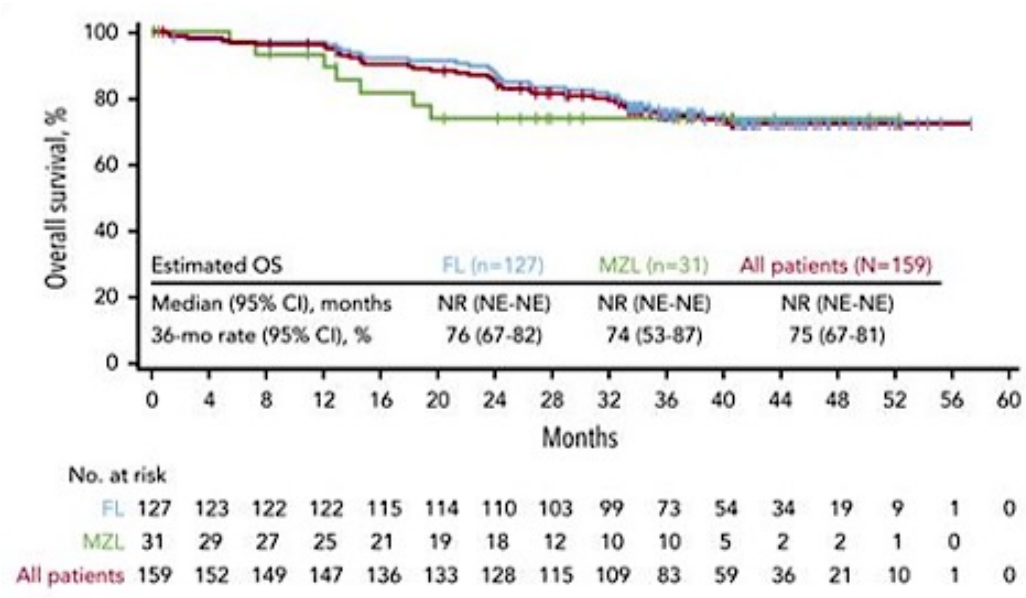
Welcome to the Cancer Candy Shop
Axi-cel in Rel/Ref FL: ZUMA-5



Jacobsen et al. 2022

Getting Your Money's Worth
Axi-cel in Rel/Ref FL: ZUMA-5

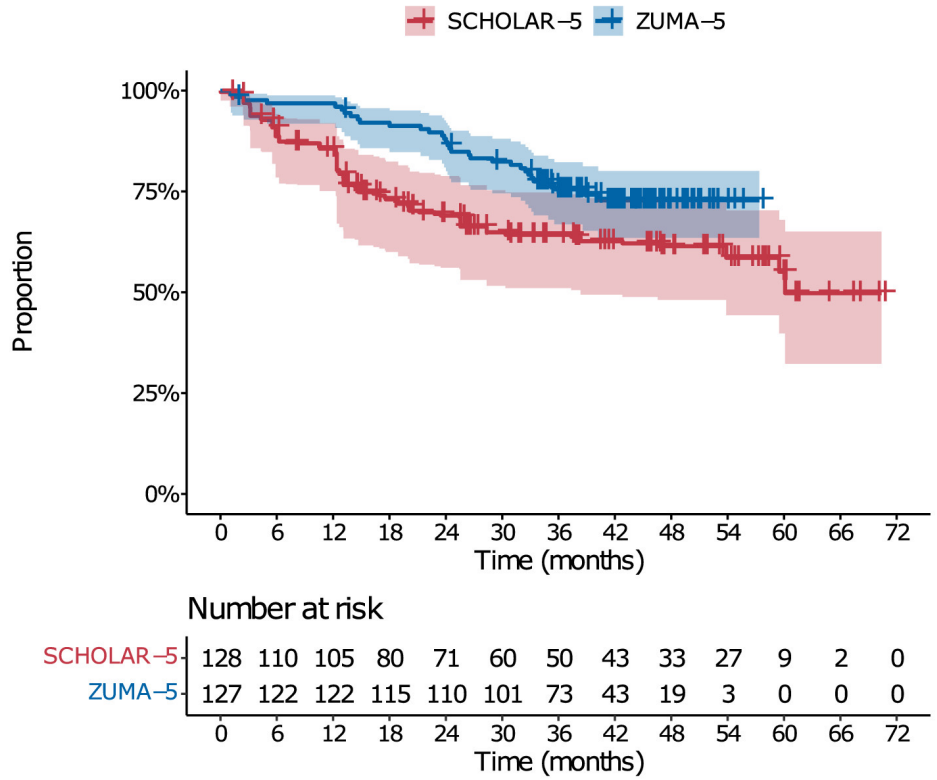


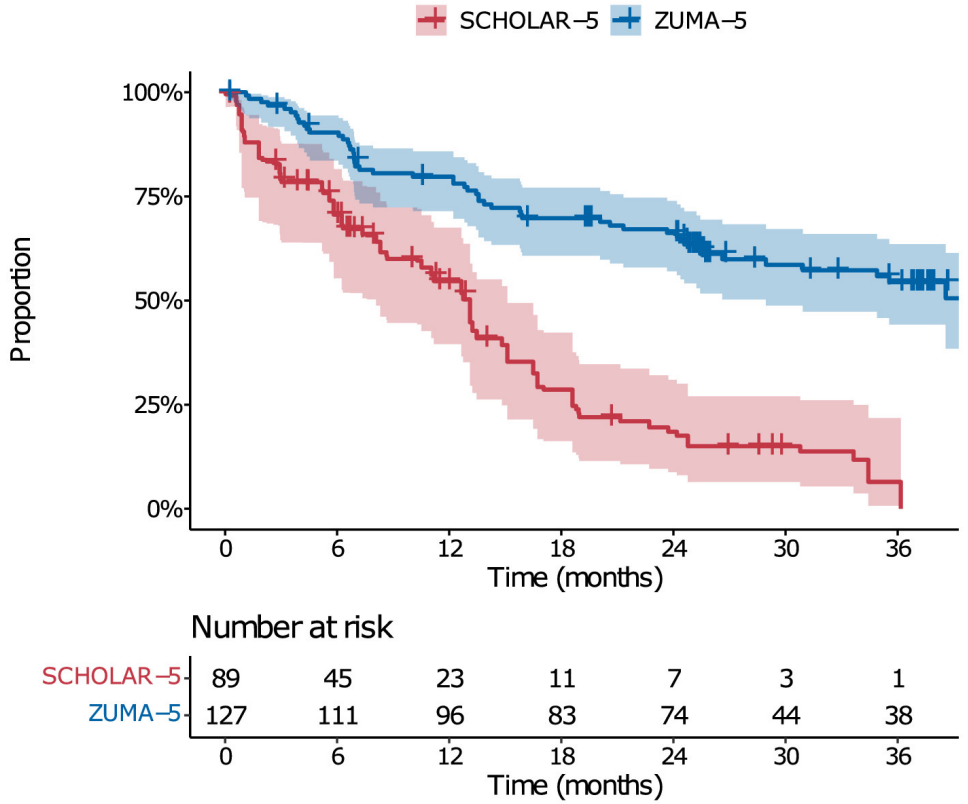


ASH 2024 Abs 864 12/9/24 @ 4PM PST:
5 year f/u
DOR: 60%

Jacobsen Lancet 2022; Neelapu et al. Blood 2024; Neelapu et al ASH 2024 Abs 864

Is the New Menu Better?
ZUMA-5 vs SCHOLAR-5





Ghone et al. Blood 2022

Something Less Filling?
Tisa-cel in Rel/Ref FL: ELARA

BACKGROUND. The primary analysis of the Phase II ELARA trial (NCT03568461, median follow-up of 17 months) showed:

86%	69%	67%
Overall response rate (ORR)	Complete response rate (CRR)	12-mo progression-free survival rate

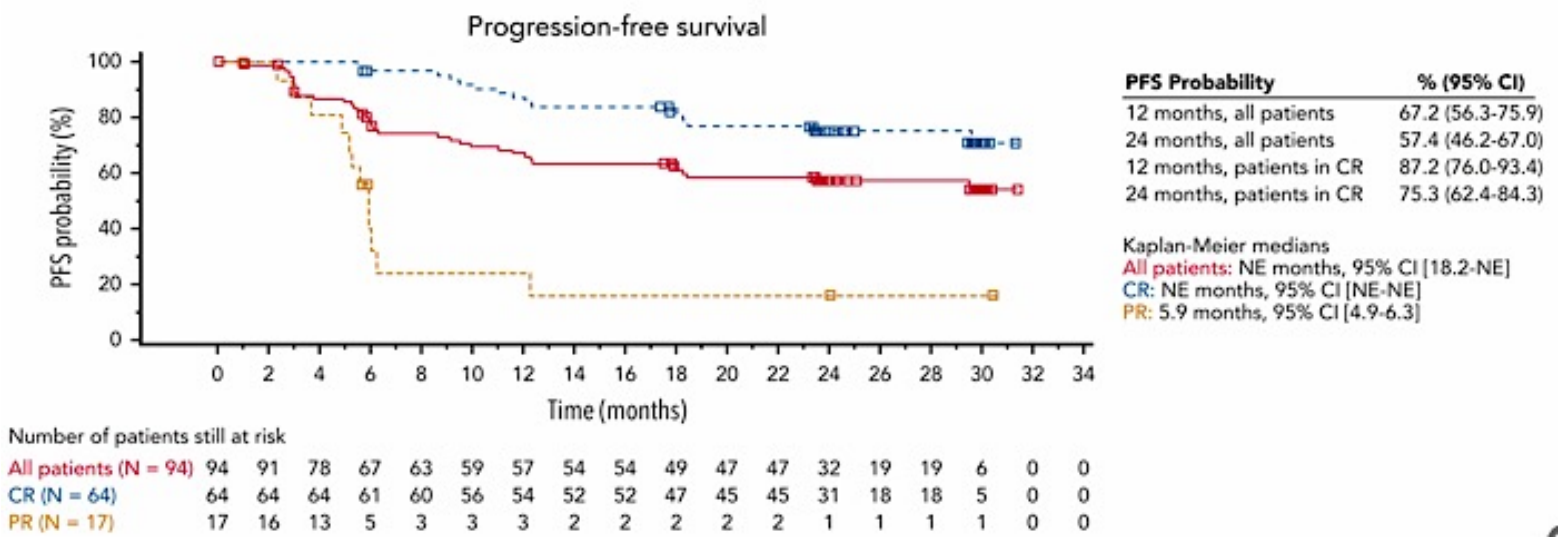
With a median follow-up of 29 months, high response rates were confirmed in patients with high-risk disease:

	ORR	CRR
POD24	82%	59%
High TMTV	75%	40%
Bulky Disease	86%	65%
High FLIPI	81%	61%
Double Refractory	85%	66%

POD24, progression of disease within 24 months from 1st immunochemotherapy TMTV, total metabolic tumor volume

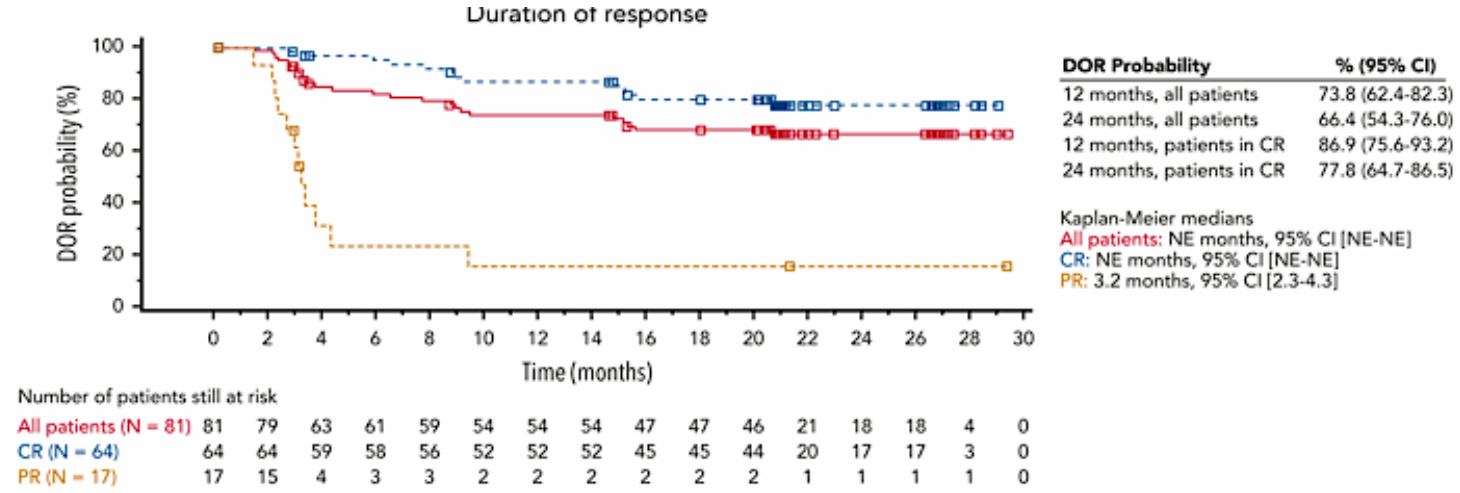
Dreyling et al. Blood 2024

Getting Your Money's Worth
Tisa-cel in Rel/Ref FL: ELARA



PFS Probability	% (95% CI)
12 months, all patients	67.2 (56.3-75.9)
24 months, all patients	57.4 (46.2-67.0)
12 months, patients in CR	87.2 (76.0-93.4)
24 months, patients in CR	75.3 (62.4-84.3)

Kaplan-Meier medians
All patients: NE months, 95% CI [18.2-NE]
CR: NE months, 95% CI [NE-NE]
PR: 5.9 months, 95% CI [4.9-6.3]

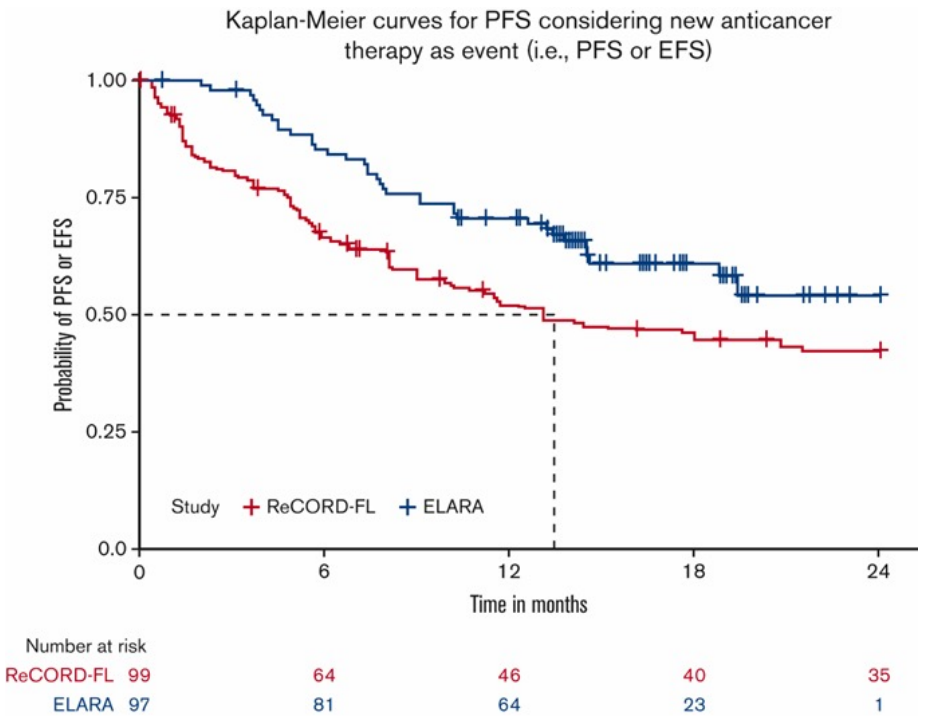


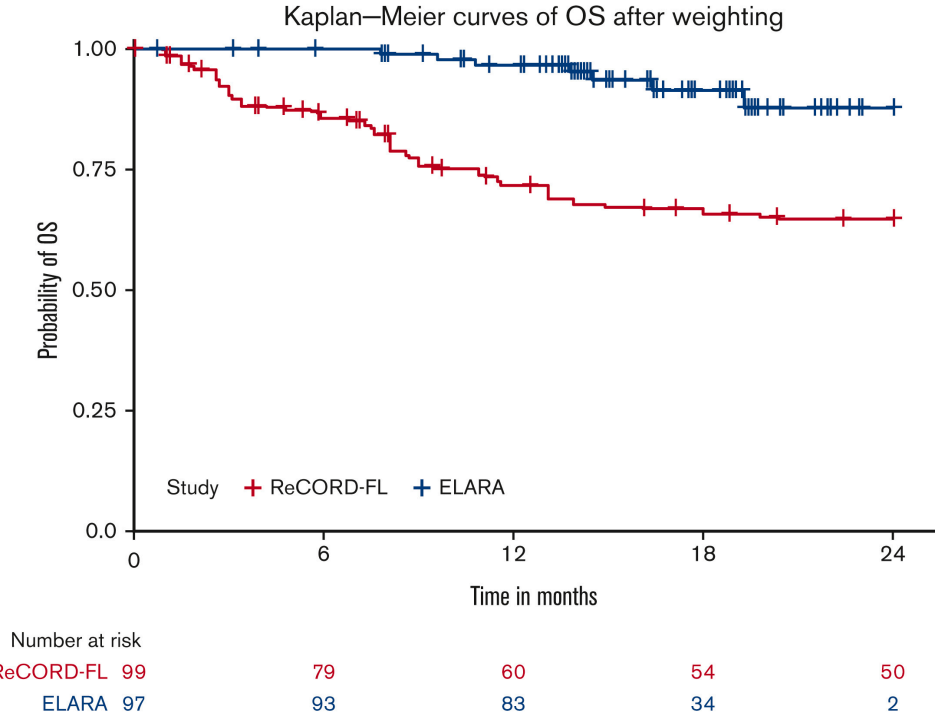
DOR Probability	% (95% CI)
12 months, all patients	73.8 (62.4-82.3)
24 months, all patients	66.4 (54.3-76.0)
12 months, patients in CR	86.9 (75.6-93.2)
24 months, patients in CR	77.8 (64.7-86.5)

Kaplan-Meier medians
All patients: NE months, 95% CI [NE-NE]
CR: NE months, 95% CI [NE-NE]
PR: 3.2 months, 95% CI [2.3-4.3]

Dreyling et al. Blood 2024

Less Filling but Fading Away?
Tisa-cel in Rel/Ref FL: ELARA





ASH 2024 Abs 4398 12/8/24 @ 6-8PM PST:
CIBMTR N=92 with 6.7 mo f/u
6 mo PFS: 79%

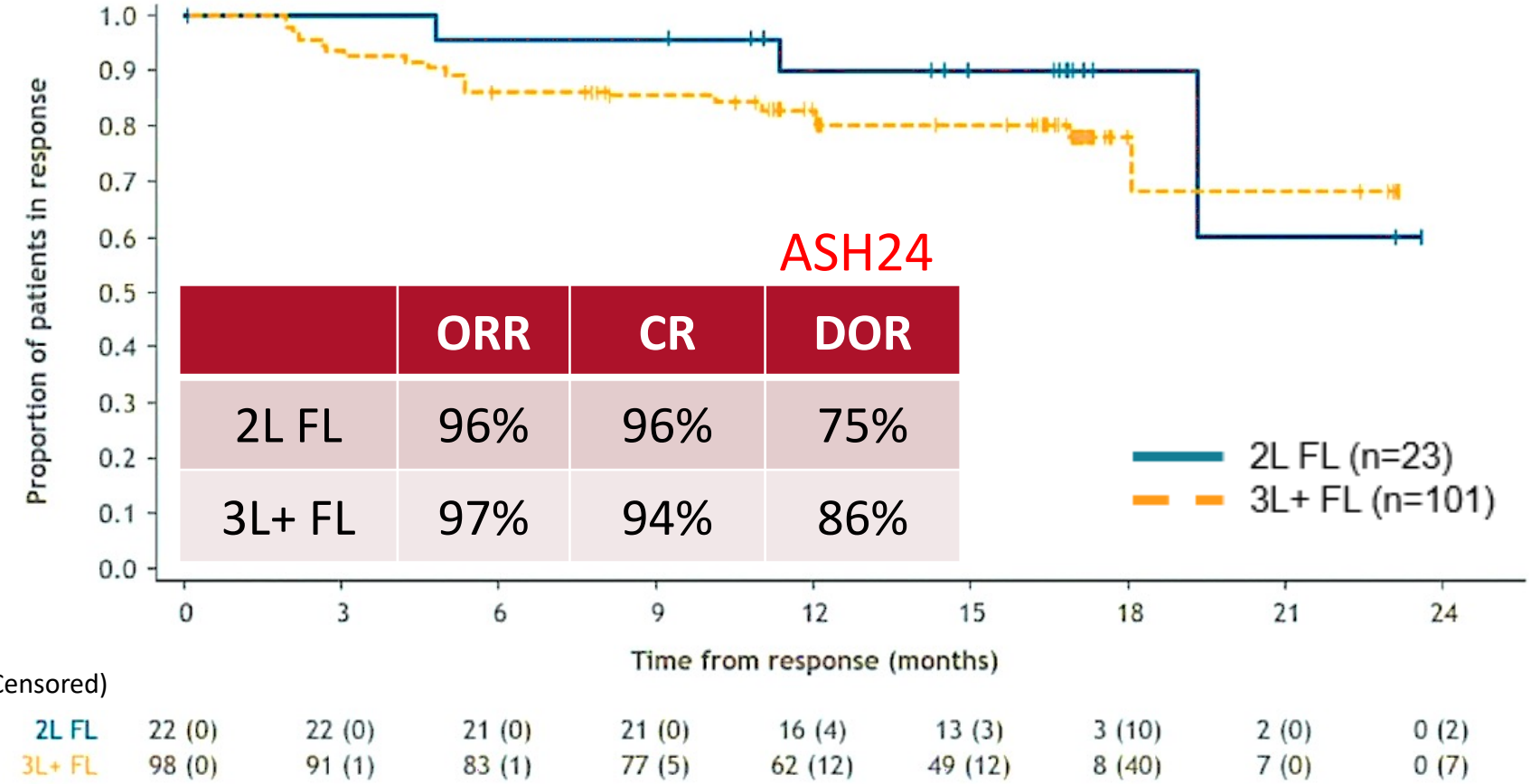
Salles et al. Blood Advances 2022; Landsburg et al. ASH 2024 Abs 4398

Can I Have it My Way?
Liso-cel in Rel/Ref FL: TRANSCEND-FL

Patient Characteristics		2L FL (n=23)	3L+ FL (n=107)
Median age (range), y		53 (34–69)	62 (23–80)
FL grade 1 or 2/3a at screening, n (%)		17 (74)/6 (26)	81 (76)/25 (23)
Ann Arbor stage at screening, n (%)	I/II	6 (26)	12 (11)
	III/IV	17 (74)	95 (89)
FLIPI at screening, n (%)	0–1/2	11 (48)/4 (17)	12 (11)/34 (32)
	3–5	8 (35)	61 (57)
LDH>ULN before LDC, n (%)		6 (26)	47 (44)
Met mGELF criteria at most recent relapse, n (%)		16 (70)	57 (53)
Median (range) prior lines of therapy		1 (1–1)	3 (2–10)
Prior HSCT, n (%)		0	33 (31)
Received prior rituximab and lenalidomide, n (%)		0	23 (21)
Refractory to last systemic therapy, n (%)		15 (65)	72 (67)
Double refractory (anti-CD20 & alkylator),[d] n (%)		11 (48)	69 (64)
POD24 from initial immunochemotherapy, n (%)		15 (65)	58 (54)
POD24 from diagnosis, n (%)		12 (52)	46 (43)
Received bridging therapy, n (%)		5 (22)	44 (41)

Morschhauser et al. Nat Med 2024

Less Filling & Memorable
Liso-cel in Rel/Ref FL: TRANSCEND-FL



ASH24

	ORR	CR	DOR
2L FL	96%	96%	75%
3L+ FL	97%	94%	86%

Morschhauser et al. Nat Med 2024; Nastoupil et al. ASH 2024 Abs 4387 12/9/24 @ 6-8 PM

The CAR-T Candy Shop in FL

	Axi-cel	Tisa-cel	Liso-cel
Patients	124	97	101
ORR	94%	86%	97%
CR	79%	68%	94%
mF/U	66m	29m	30m
Median PFS	57m (50%@60m)	37m (75%@12m)	NR @30m (3L+:73% @30m) (2L: 83% @ 30m)

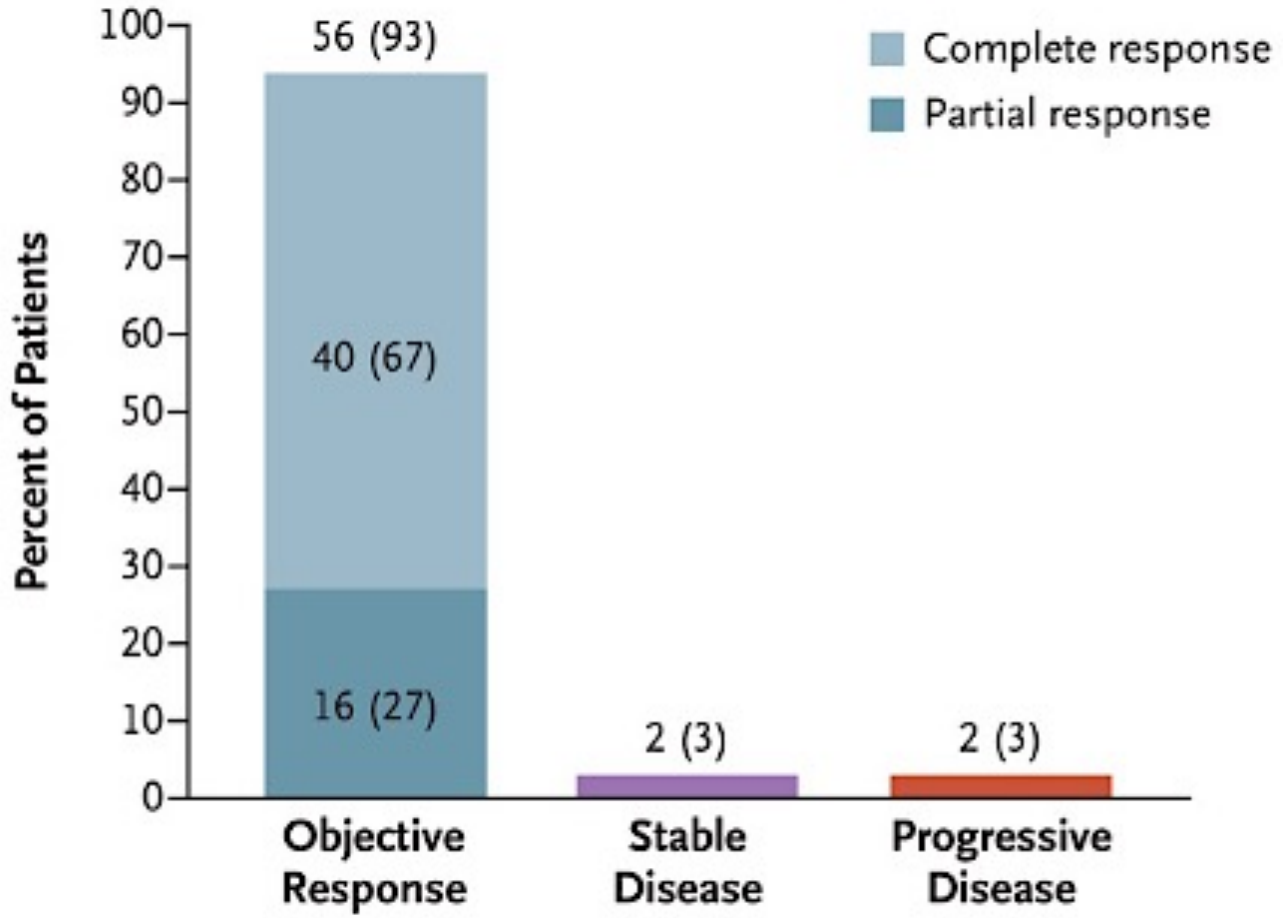
Neelapua et al. Blood 2024; Dreyling et al. Blood 2024; Morschhauser et al. Nat Med 2024; Neelapu et al ASH 2024 Abs 864 Nastoupil et al. ASH 2024 Abs 4387

Do They Taste Different?

	Axi-cel	Tisa-cel	Liso-cel
CRS (All Grade)	78%	49%	58%
CRS (Grade ≥3)	6%	0%	1%
ICANS (All Grade)	56%	23%	15%
ICANS (Grade ≥3)	18%	1%	2%

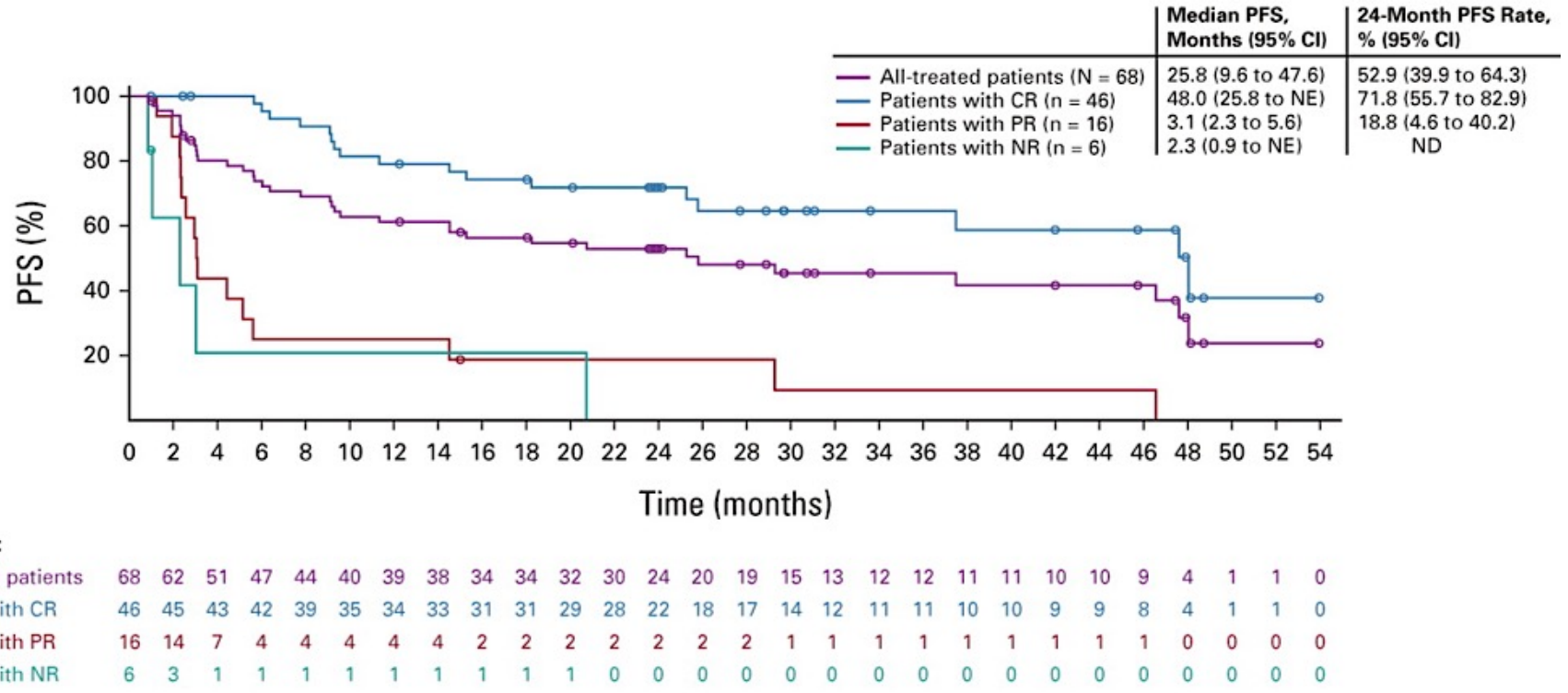
Neelapua et al. Blood 2024; Dreyling et al. Blood 2024; Morschhauser et al. Nat Med 2024

Welcome Back to the Cancer Candy Shop
Brexu-cel in Rel/Ref MCL: ZUMA-2



Wang et al. NEJM 2020

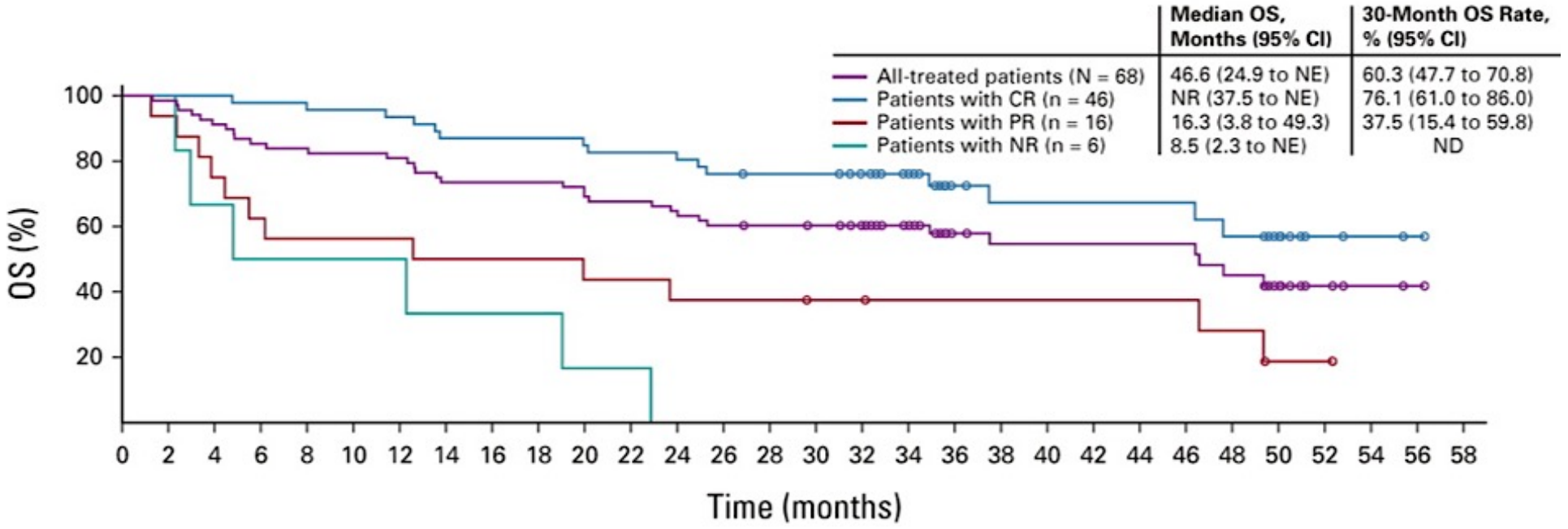
Getting Your Money's Worth
Brexu-cel in Rel/Ref MCL: ZUMA-2 (Cohort 1)



ASH 2024 Abs 4388 12/9/24 @ 6-8M PST:
68 mo f/u
mDOR: 37 mo (all CRs)

Wang et al. NEJM 2020; Wang et al. ASH 2024 Abs 4388

A New Condiment
Brexu-cel in Rel/Ref MCL: ZUMA-2 (Cohort 3)



ASH 2024 Abs 4388 12/9/24 @ 11:15 AM PST:

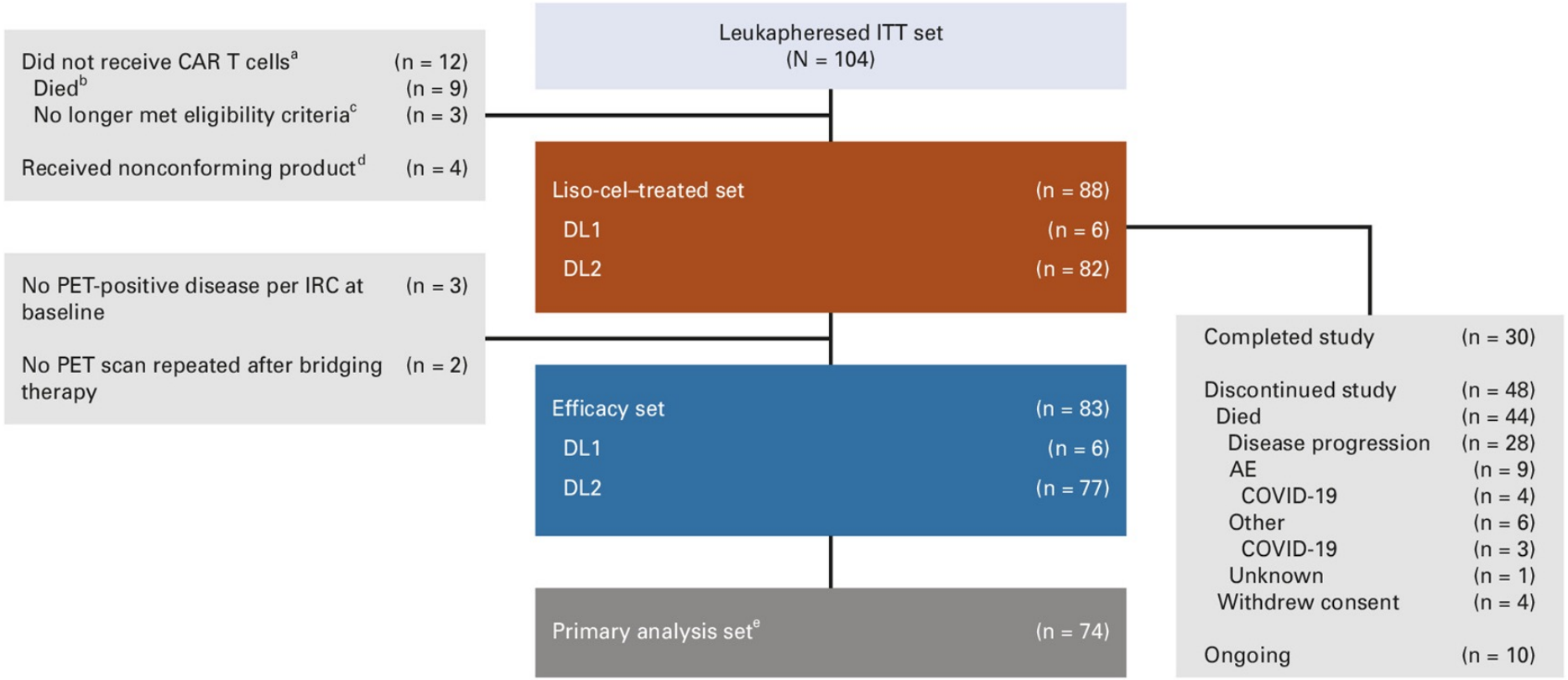
N=95 (BTKi naïve)

73% CR

mPFS: 27 mo

Wang et al. NEJM 2020 ; van Meerten et al. ASH 2024 Abs 748

How'd You Make That?
Liso-cel in Rel/Ref MCL: TRANSCEND-MCL



Wang et al. JCO 2024

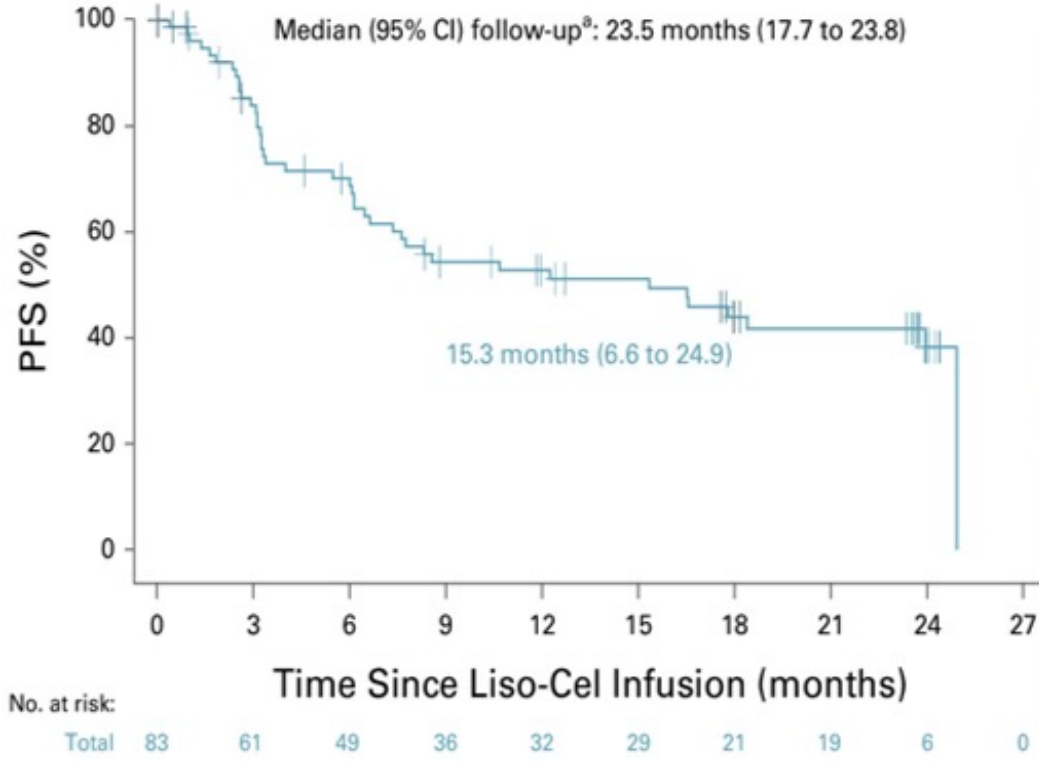
Hidden Ingredient
Liso-cel in Rel/Ref MCL: TRANSCEND-MCL

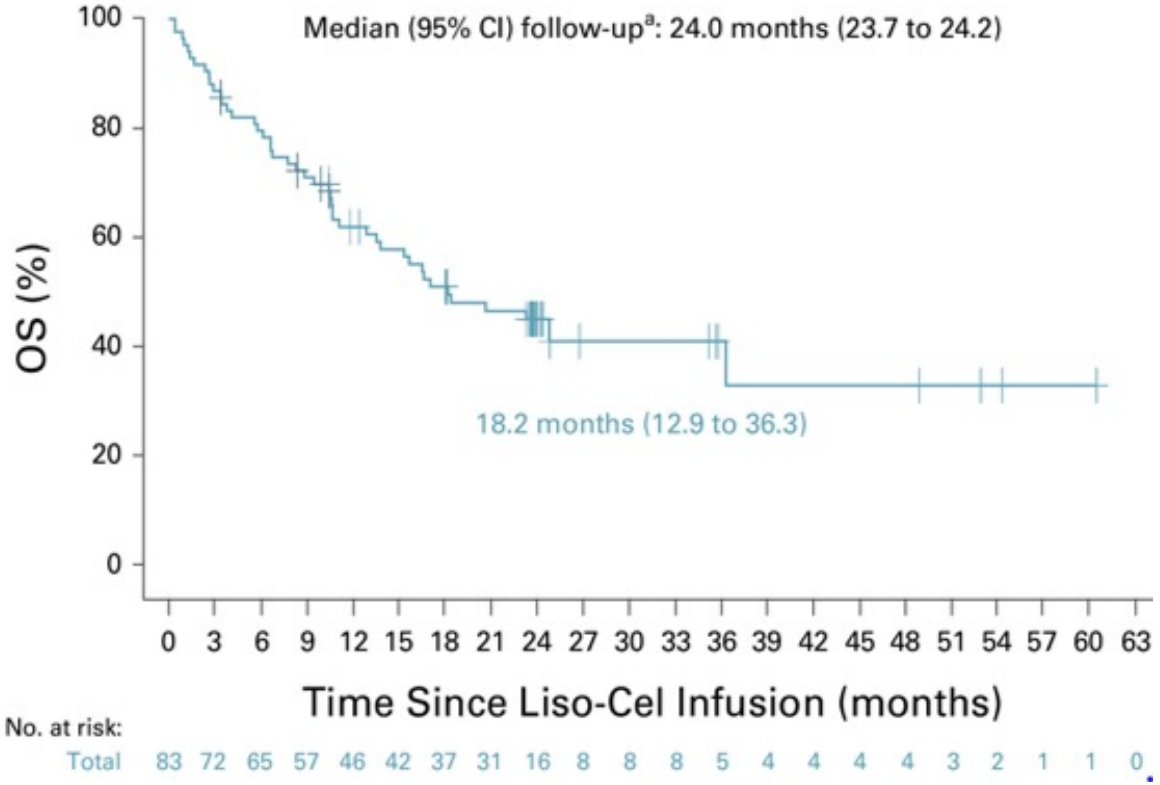
		Ki-67 proliferation index		*TP53* mutation		Blastoid morphology	
	Overall population (N = 88)	≥ 30% (n = 66)	< 30% (n = 15)	Yes (n = 20)	No (n = 34)	Yes (n = 27)	No (n = 48)
Median (range) age, y	68.5 (36–86)	68 (36–86)	71 (57–79)	71 (54–84)	69 (36–80)	68 (36–84)	70.5 (48–86)
≥ 65 y, n (%)	64 (73)	46 (70)	12 (80)	16 (80)	27 (79)	20 (74)	37 (77)
Median (range) prior lines of systemic therapy	3 (1–11)	3 (1–11)	3 (1–9)	3 (2–11)	3 (1–9)	3 (1–9)	3 (2–11)
≥ 5 prior lines of systemic therapy, n (%)	26 (30)	21 (32)	2 (13)	7 (35)	9 (26)	10 (37)	12 (25)
Prior HSCT, n (%)	29 (33)	22 (33)	3 (20)	4 (20)	11 (32)	13 (48)	11 (23)
Prior BTKi, n (%)	83 (94)	62 (94)	14 (93)	20 (100)	32 (94)	25 (93)	47 (98)
Refractory disease,[d] n (%)	61 (69)	48 (73)	9 (60)	11 (55)	21 (62)	24 (89)	26 (54)
Refractory to BTKi,[e] n (%)	47 (53)	37 (56)	6 (40)	7 (35)	21 (62)	18 (67)	24 (50)
Ki-67 proliferation index ≥ 30%, n (%)	66 (75)	66 (100)	0	14 (70)	25 (74)	24 (89)	33 (69)
TP53 mutation, n (%)	20 (23)	14 (21)	4 (27)	20 (100)	0	3 (11)	14 (29)
Blastoid morphology, n (%)	27 (31)	24 (36)	2 (13)	3 (15)	12 (35)	27 (100)	0
Secondary CNS lymphoma, n (%)	7 (8)	5 (8)	2 (13)	1 (5)	3 (9)	1 (4)	4 (8)
Complex karyotype, n (%)	26 (30)	21 (32)	3 (20)	7 (35)	16 (47)	10 (37)	13 (27)
Received bridging therapy, n (%)	58 (66)	49 (74)	5 (33)	13 (65)	21 (62)	19 (70)	30 (62.5)

TP53 checked
54/88=61%

Palomba et al. ASTCT 2024

Less Filling but Less Value?
Liso-cel in Rel/Ref MCL: TRANSCEND-MCL





Wang et al. JCO 2024

Is There a Special?

	Brexu-cel N=74	Liso-cel N=83
ORR	93%	83%
CR	67% (73%)	72%
Median PFS	25m (27 m)	15m
Median OS	47m (27 m)	18m

Wang NEJM 2020; Wang et al. JCO 2024; van Meerten et al. ASH 2024 Abs 748

I Don’t Remember Having That vs Can I Have That Again?

	Brexu-cel	Liso-cel
CRS (All Grade)	91%	61%
CRS (Grade ≥3)	15%	1%
ICANS (All Grade)	63%	31%
ICANS (Grade ≥3)	31%	9%

ZUMA-1 (Cohort 6)→ZUMA-24 (LBCL)--?→ZUMA-XY (MCL)--?

Wang NEJM 2020; Wang et al. JCO 2024

Select ASH 2024 Presentations

- **Primary Analysis of ZUMA-2 Cohort 3: Brexucabtagene Autoleucel (Brexu-Cel) in Patients (Pts) with Relapsed/Refractory Mantle Cell Lymphoma (R/R MCL) Who Were Naive to Bruton Tyrosine Kinase Inhibitors (BTKi)**
  - Abstract 748; Monday, December 9th – 11:15AM
- **5-Year Follow-Up Analysis from ZUMA-5: A Phase 2 Trial of Axicabtagene Ciloleucel (Axi-Cel) in Patients with Relapsed/Refractory Indolent Non-Hodgkin Lymphoma**
  - Abstract 864; Monday, December 9th – 4:00 PM
- **Lisocabtagene Maraleucel (liso-cel) in Patients (pts) with Relapsed or Refractory (R/R) Follicular Lymphoma (FL): Transcend FL 2-Year Follow-Up**
  - Abstract 4387; Monday, December 9th – 6:00 PM-8:00 PM
- **Five-Year Outcomes of Patients (Pts) with Relapsed/Refractory Mantle Cell Lymphoma (R/R MCL) Treated with Brexucabtagene Autoleucel (Brexu-cel) in ZUMA-2 Cohorts 1 and 2**
  - Abstract 4388; Monday, December 9th – 6:00 PM-8:00 PM
- **Efficacy and Safety of Tisagenlecleucel in Patients with Relapsed/Refractory Follicular Lymphoma: A Real-World Analysis from the Center for Blood and Marrow Transplant Research (CIBMTR) Registry**
  - Abstract 4398; Monday, December 9th – 6:00 PM-8:00 PM


What's My Money Shot?
@ Real NCT.gov
The Cancer Candy Shop
CAR-T
TCE
EZH2i
cBTKi
ncBTKi
BCL-2i
CBD
Psilocybin
ncBTKi/CAR-T/ncBTKi/TCE
EZH2/CAR-T/ TCE/EZH2
@ Real POD24
@ Real TP53 MCL

Agenda

Module 1: Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Abramson

Module 2: Bispecific Antibody Therapy for DLBCL — Prof Hutchings

Module 3: CAR T-Cell Therapy for Other Lymphoma Subtypes — Dr Lunning

Module 4: Bispecific Antibody Therapy for Follicular Lymphoma and Other Lymphoma Subtypes — Dr Phillips

Module 5: Tolerability Considerations with CAR T-Cell and Bispecific Antibody Therapy — Dr Crombie

Case Presentation: 78-year-old man with FL and complete response to bendamustine/rituximab followed by persistent cytopenia and now with bulky recurrent disease

Dr Henna Malik (Houston, Texas)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

What would you most likely recommend for this patient, and how would your approach differ if he were younger? How does this patient's history of cytopenias affect your strategy?

Do you have a preferred bispecific antibody for younger patients with FL? What about for older patients or those with comorbidities?

QUESTIONS FOR THE FACULTY

Do you believe odronextamab will be approved by the FDA in the near future? If this agent were to become available, how would you integrate it into your treatment armamentarium?

Based on your knowledge of available data, how would you compare the global efficacy of odronextamab to that of approved bispecific antibodies for patients with FL?

Case Presentation: 57-year-old woman with asymptomatic recurrence of FL who is s/p BR x 6 cycles and R maintenance x 18 months

Dr Eric Lee (Fountain Valley, California)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

What would you most likely recommend for this asymptomatic patient? Would your approach be any different given the early recurrence (POD24)? How, if at all, would your approach differ for an older patient with comorbidities?

In general, how do you typically sequence CAR T-cell therapy and bispecific antibodies for patients with FL?

Tycel Phillips, MD

Associate Professor

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Bispecific Antibodies in FL and MCL

Agenda

- Follicular Lymphoma
  - Mosunetuzumab
  - Epcoritamab
  - Odronextamab
- MCL
  - Glofitamab
  - Mosun/Pola
  - Everyone Else →

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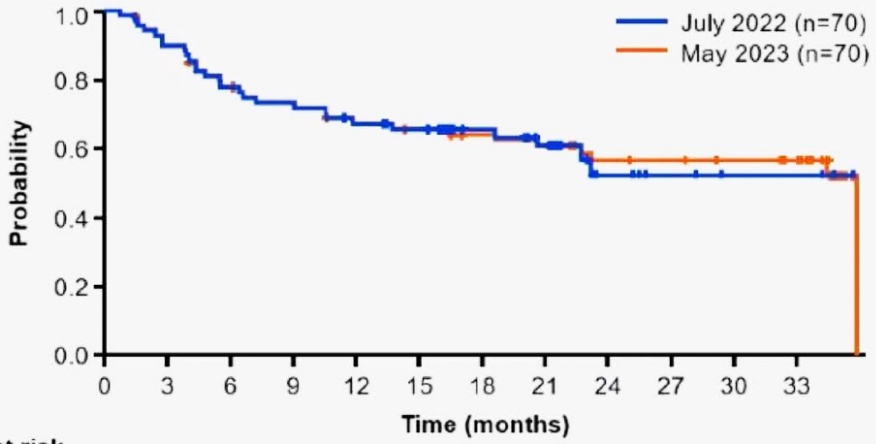
Mosunetuzumab Response/Safety in R/R FL

DOR (July 2022 vs May 2023 data cut-off)

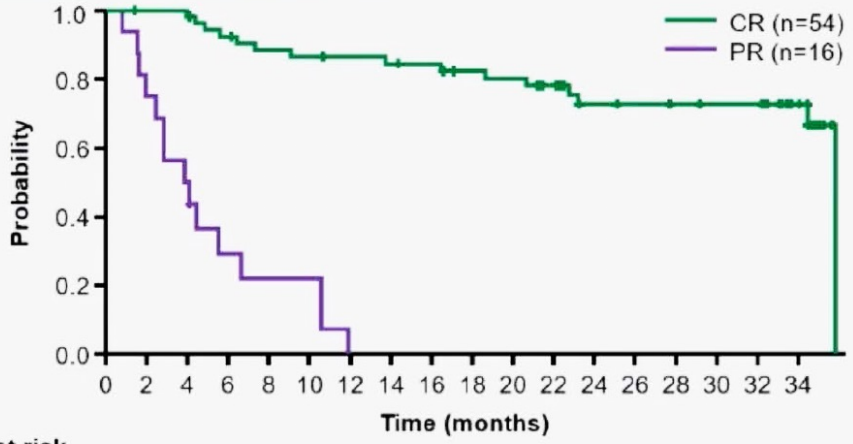


Patients at risk

July 2022	70	62	52	48	42	38	30	25	9	5	3	3
May 2023	70	62	52	48	43	41	38	36	26	25	23	21

	n=70
Median DOR, months (95% CI)*	35.9 (20.7–NE)
30-month DOR rate, % (95% CI)†	56.6% (44.2–68.9)

DOR for CR vs PR (May 2023 data cut-off)



Patients at risk

CR	54	53	52	48	45	44	43	42	41	38	37	34	26	25	24	23	23	15
PR	16	12	8	4	3	3	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE

Median DOR in patients with CR, months (95% CI); n=54*	35.9 (NE–NE)
Median DOR in patients with PR, months (95% CI); n=16*	4.0 (2.5–6.7)

72.7% (95% CI: 60.8–86.8) of patients with a CR are estimated to remain alive and progression-free 30 months after their first response

	N=90
Median PFS, months (95% CI)	**24.0** (12.0–NE)
36-month PFS (95% CI)	**43.2%** (31.3–55.2)

	N=90
Median OS, months (95% CI)	**NR** (NE–NE)
36-month OS (95% CI)	**82.4%** (73.8–91.0)

Schuster et al. ASH 2023; Abstract 603.

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Mosunetuzumab Response/Safety in R/R FL

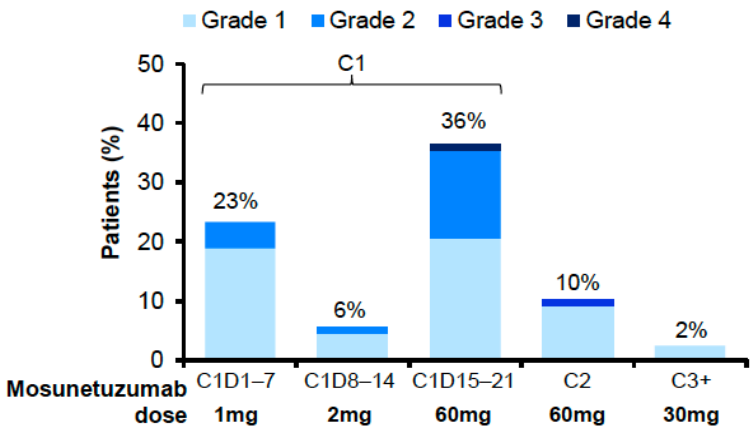
Safety profile

Adverse events (AEs)	N=90
AE	100%
Mosunetuzumab related	92%
Grade 3/4 AE	70%
Mosunetuzumab related	51%
Serious AE	47%
Mosunetuzumab related	33%
Grade 5 (fatal) AE	2%*
Mosunetuzumab related	0
AE leading to treatment discontinuation	4%†
Mosunetuzumab related	2%

CRS summary

CRS by ASTCT criteria[1]	N=90
CRS (any grade)	44%
Grade 1	26%
Grade 2	17%
Grade 3	1%
Grade 4	1%
Median time to CRS onset, hours (range)	
C1D1	5.2 (1.2–24)
C1D15	27 (0.1–391)
Median CRS duration, days (range)	3 (1–29)
Corticosteroids for CRS management	11%
Tocilizumab for CRS management	8%
Events resolved	100%

CRS by cycle and grade



CRS was predominantly low grade and during Cycle 1
All CRS events resolved; no new events were reported with 10 months of additional follow-up

Schuster et al. ASH 2023; Abstract 603.

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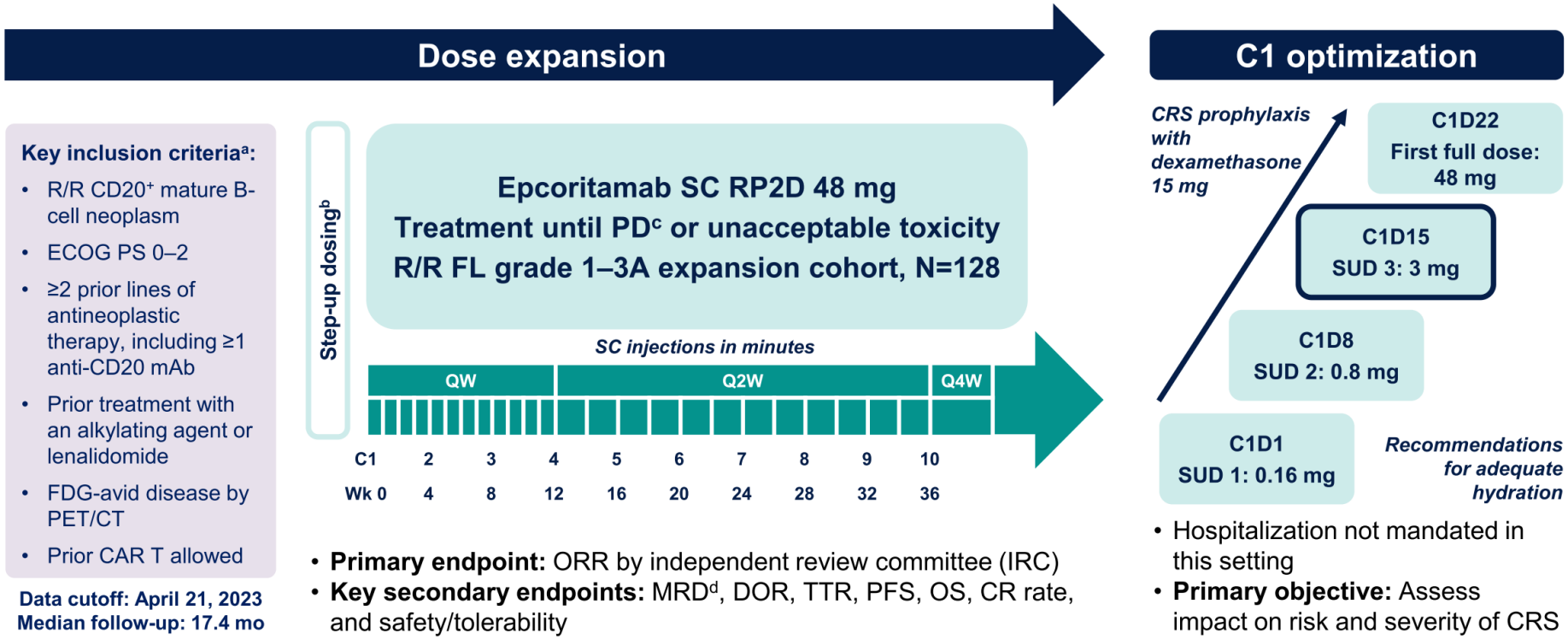
Epcoritamab

webviewer

Trial Design: Pivotal EPCORE™ NHL-1 Study



Phase 1/2 trial. [a]Patients enrolled in this trial (and excluded from trials of other T-cell–engaging therapies) included those with worse anemia, lymphopenia, and/or renal function. [b]Step-up dosing (SUD; priming [SUD 1] 0.16 mg and intermediate [SUD 2] 0.8 mg dosing before first full dose) and corticosteroid prophylaxis were used to mitigate CRS. [c]≥2 measurable (by CT/MRI) and FDG PET–positive lesions; radiographic disease evaluation was performed every 6 wk for the first 24 wk (6, 12, 18, and 24 wk), then every 12 wk (36 and 48 wk), and every 6 mo thereafter. [d]MRD was assessed in peripheral blood using the clonoSEQ® (Adaptive Biotechnologies, Seattle, WA) next-generation sequencing assay. ClinicalTrials.gov: NCT03625037; EudraCT: 2017-001748-36.

Vose et al. ASCO 2024; Abstract 7015.

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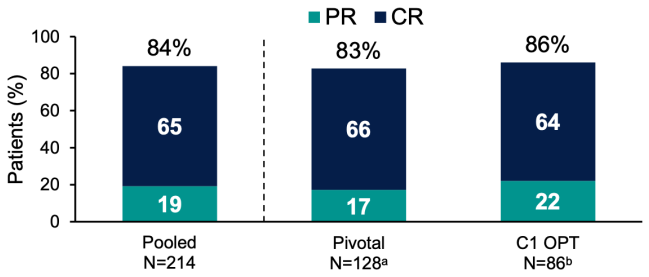
Safety/Response w/ Epcoritamab

Epcoritamab in R/R FL

High Rates of Complete Response and MRD Negativity



MRD-Negativity Rate	n (%)
Pooled (n=135)	89 (66)
Pivotal (n=91)	61 (67)
C1 OPT (n=44)	28 (64)

Based on MRD-evaluable population per clonoSEQ® PBMC assay with 10^{-6} cutoff.

- At 6 mo in C1 OPT, an estimated 86% of patients with CR remained in CR
- No impact on time to response in C1 OPT
  - Median time to response was 1.4 mo in both cohorts[c]
  - Median time to complete response was 1.5 mo in both cohorts[d]

CR was complete metabolic response (ie, PET negativity). CR, complete response; PBMC, peripheral blood mononuclear cell; PR, partial response. [a]Three patients (2%) were not evaluable. [b]Five patients (6%) were not evaluable. [c]Range: 1.2–4.4 in C1 OPT, 1.0–3.0 in pivotal. [d]Range: 1.2–4.7 in C1 OPT, 1.2–11.1 in pivotal.

C1 Optimization Reduced Risk and Severity of CRS

	Pivotal Cohort N=128	C1 Optimization Cohort[a] N=50
CRS, n (%)[b]	85 (66)	24 (48)
Grade 1	51 (40)	20 (40)
Grade 2	32 (25)	4 (8)
Grade 3	2 (2)	0
Treated with tocilizumab, n/n (%)	31/85 (36)	6/24 (25)
Leading to epcoritamab discontinuation, n (%)	**0**	**0**
CRS resolution, n/n (%)	**85/85 (100)**	**24/24 (100)**
Median time to resolution, d (range)	2 (1–54)	3 (1–14)

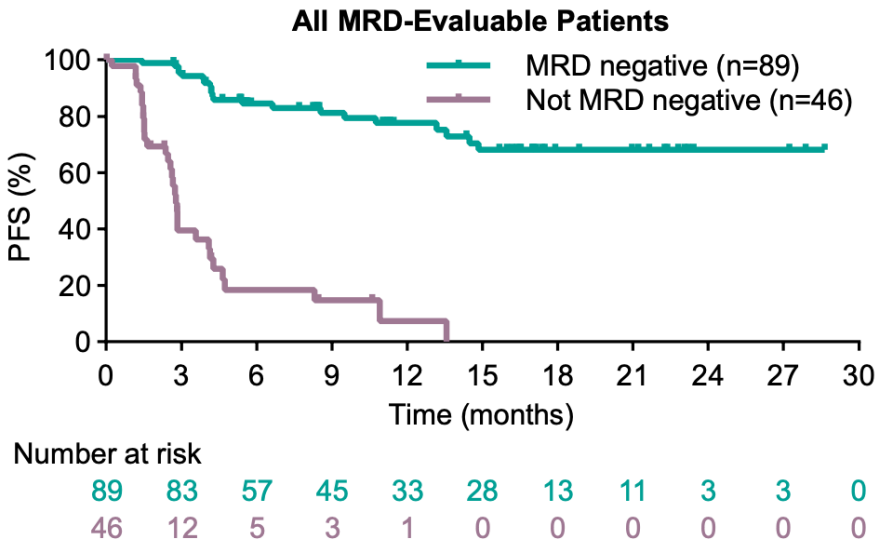
- Patient baseline characteristics were consistent between cohorts
- C1 optimization substantially reduced rate and severity of CRS
- In both cohorts, CRS was mostly confined to C1
- Similar response rates were observed in the C1 optimization cohort
- There were no cases of ICANS in the C1 optimization cohort; 8 cases were observed in the pivotal cohort (all grade 1–2 and resolved; none led to discontinuation)

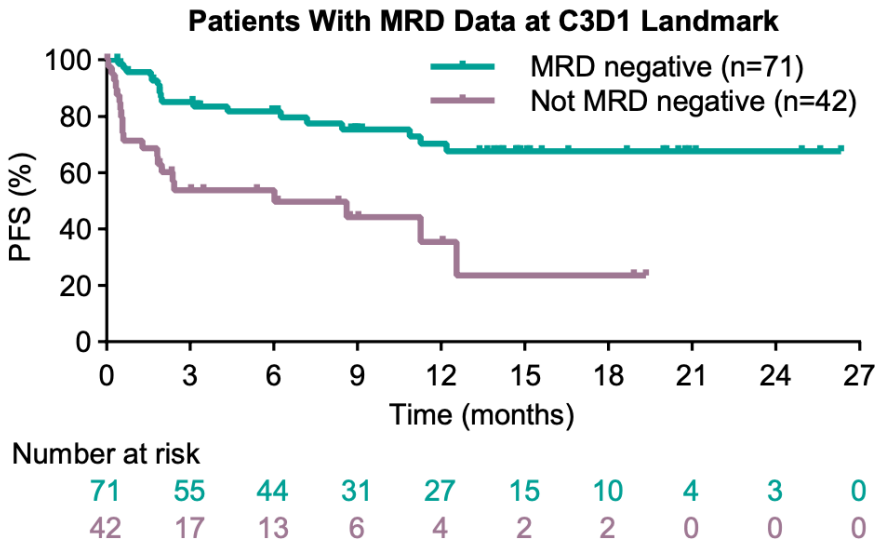
[a]Data cutoff: September 21, 2023. Median follow-up: 3.8 mo (range, 1.9–8.7). [b]Graded by Lee et al 2019 criteria.[1] **1.** Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-38.

Vose et al. ASCO 2024; Abstract 7015.

Response Continued

MRD Negativity (Overall and at C3D1) Associated With Favorable PFS





PFS assessed by investigator. MRD based on PBMC assay with 10^{-6} cutoff. MRD negative was defined as having MRD negativity at any time point.

Vose et al. ASCO 2024; Abstract 7015.

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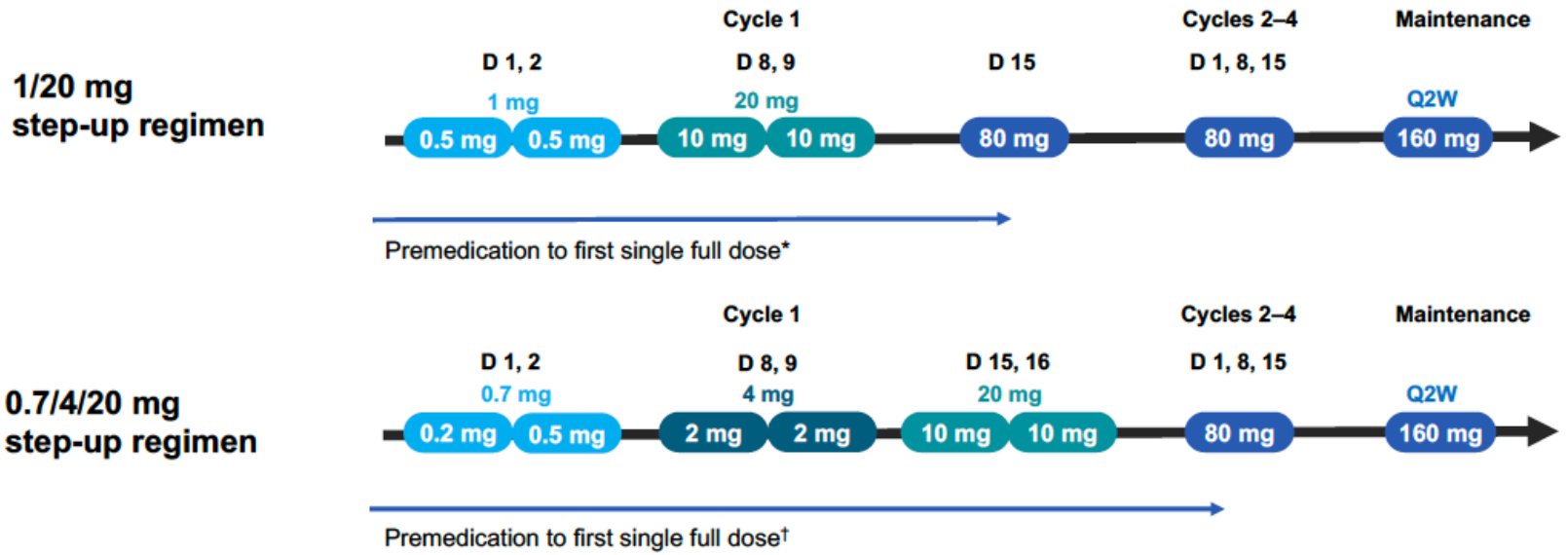
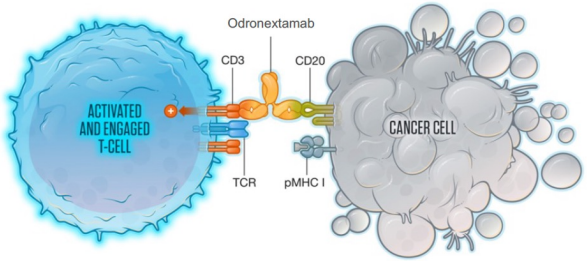
Odronextamab Dosing

Cycle 1 step-up regimen optimized during the course of the study to further mitigate the risk for cytokine release syndrome

- The study initiated with a Cycle 1 step-up regimen of 1/20/80 mg
- This was modified to 0.7/4/20 mg during Cycle 1 to further mitigate the risk of CRS



Odronextamab
Hinge-stabilized CD20×CD3 bispecific antibody



Binds CD20 on malignant B-cells and CD3 on T cells, to elicit T-cell-mediated cytotoxicity

Updated guidelines for tocilizumab and steroids introduced with 0.7/4/20 mg regimen.
*20 mg IV dexamethasone 1 to 3 hours prior to each split or initial single infusion; †10 mg dexamethasone orally 12 to 24 hours prior to the first split infusion. On each day of split or single infusion: dexamethasone 20 mg IV 1 to 3 hours before infusion; diphenhydramine 25 mg IV or orally and acetaminophen 650 mg orally 30 to 60 minutes before infusion.
CRS, cytokine release syndrome; D, day; IV, intravenous; Q2W, every 2 weeks.

Kim et al. ASH 2022; Abstract 949.

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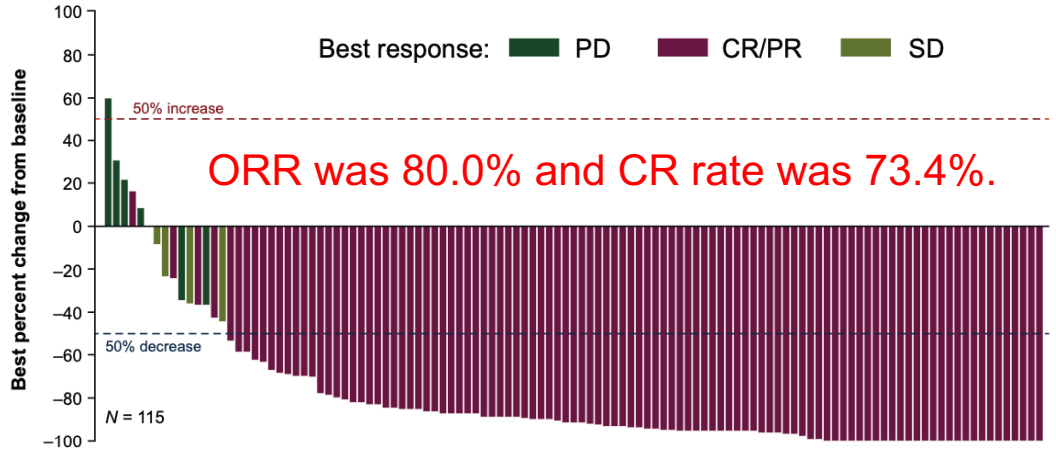
Safety/Efficacy w/ Odronextamab



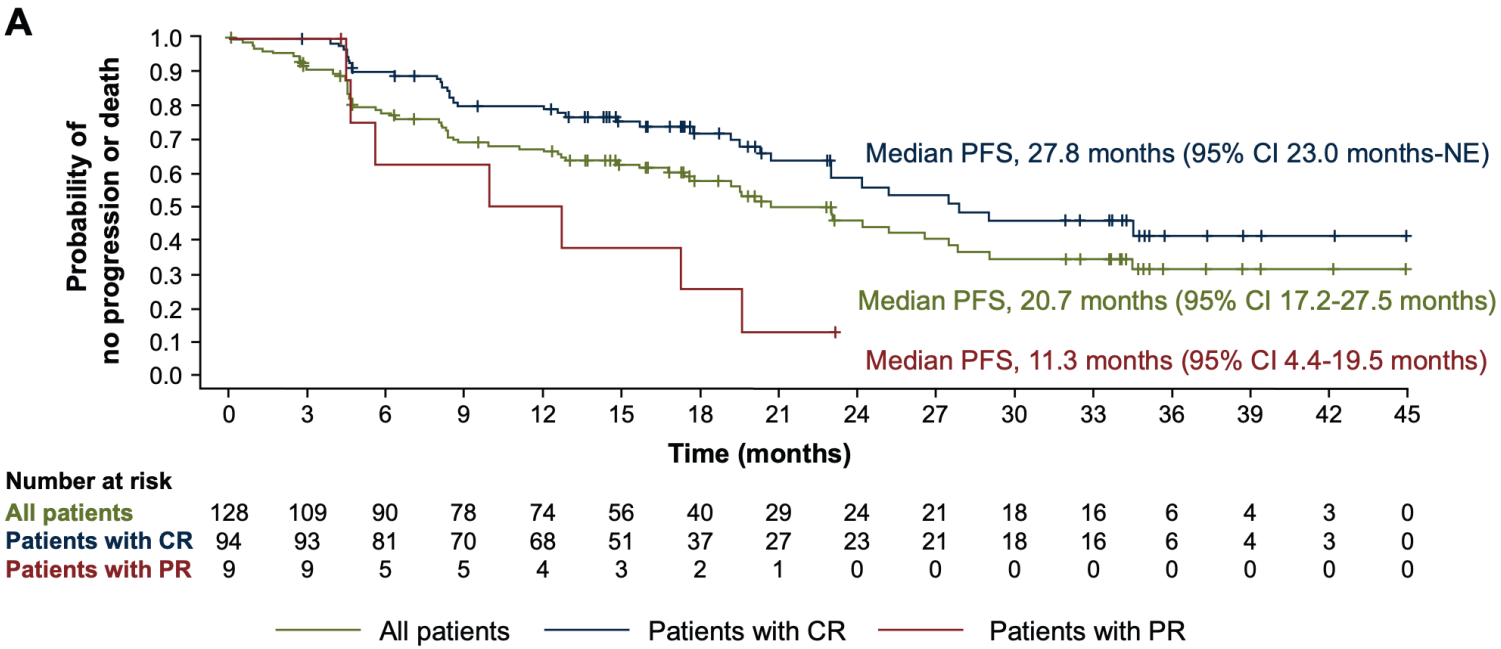


Table 2. Summary of TEAEs with odronextamab treatment

Event, preferred term[a], *n* (%)	*N* = 128	
	Any event	Treatment-related
Any TEAE	128 (100)	118 (92.2)
TEAEs occurring in >15% of patients		
CRS	72 (56.3)	72 (56.3)
Neutropenia	50 (39.1)	39 (30.5)
Pyrexia	48 (37.5)	31 (24.2)
Anemia	43 (33.6)	26 (20.3)
COVID-19	41 (32.0)	5 (3.9)
Infusion-related reaction	39 (30.5)	37 (28.9)
Diarrhea	36 (28.1)	12 (9.4)
Arthralgia	28 (21.9)	13 (10.2)
Hypokalemia	28 (21.9)	9 (7.0)
Nausea	25 (19.5)	13 (10.2)
Headache	24 (18.8)	13 (10.2)
Fatigue	24 (18.8)	17 (13.3)
Rash	23 (18.0)	15 (11.7)
Constipation	23 (18.0)	4 (3.1)
Alanine aminotransferase increased	23 (18.0)	18 (14.1)
Cough	20 (15.6)	4 (3.1)
Any grade 3 or higher TEAE	110 (85.9)	82 (64.1)
Serious TEAEs	87 (68.0)	57 (44.5)
TEAE leading to treatment discontinuation	20 (15.6)	10 (7.8)
TEAE leading to death	18 (14.1)	4 (3.1)

Kim TM et al. Ann Oncol. 2024;35(11):1039-1047.

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CRS

Adverse events: Cytokine release syndrome

n, (%)	1/20 regimen (N=68)	0.7/4/20 regimen (N=63)
CRS any Grade	38 (55.9%)	36 (57.1%)
Grade 1	22 (32.4%)	28 (44.4%)
Grade 2	12 (17.6%)	7 (11.1%)
Grade 3	4 (5.9%)	1 (1.6%)
Grade 4	0	0
Grade 5	0	0
Received corticosteroids	11 (16.2%)	17 (27.0%)
Received tocilizumab	9 (13.2%)	12 (19.0%)
Received vasopressors	4 (5.9%)	1 (1.6%)

Data cut-off date: Sep 15, 2022.
CRS per Lee 2019.
CRS, cytokine release syndrome; R/R FL, relapsed/refractory follicular lymphoma; ICU, intensive care unit.

- 0.7/4/20 mg step-up regimen reduced the incidence of grade 2 and grade 3 CRS
- Approximately half of patients with R/R FL had CRS, mostly grade 1
- Only 1 case of grade 3 CRS with 0.7/4/20 mg step-up regimen and no grade 4 or higher CRS events
- All CRS events resolved with a median time to resolution of 2 days (range 1–51)
- No patients required mechanical ventilation or ICU admission for the management of CRS

n (%)	1/20 regimen (N=68)	0.7/4/20 regimen (N=63)	All patients (N=131)
ICANS, any grade	1 (1.5%)	0	1 (0.8%)
Grade ≥3	0		0
Infusion related reaction, any grade	21 (30.9%)	16 (25.4%)	37 (28.2%)
Grade ≥3	4 (5.9%)	2 (3.2%)	6 (4.6%)
Infection, any grade	51 (75.0%)	35 (55.6%)	86 (65.6%)
Grades 1–2	23 (33.8%)	21 (33.3%)	44 (33.6%)
Grades 3–4	19 (27.9%)	11 (17.5%)	30 (22.9%)
Grade 5	9 (13.2%)	3 (4.8%)	12 (9.2%)
Tumor lysis syndrome, any grade	1 (1.5%)	0	1 (0.8%)
Grade ≥3	1 (1.5%)		1 (0.8%)

Kim et al. ASH 2022; Abstract 949.

Summary of Response FL

Drug	N	ORR	CR	PFS 24 m	OS 24 m	mDOR
Mosunetuzumab	90	78%	60%	48%	87%	NR
Odronextamab	121	81.8%	75.2%	55.3%*	N/A	20.5 m
Epcoritamab	128	82%	63%	49.4%*	N/A	NR

*18 months

Drug	DOR 12 m	DOCR 12 m	DOR 24 m	DOCR 24 m	mPFS	PFS 36 m	OS 36 m
Mosunetuzumab	67%	82%	53%*	63%	24m	43.2%	82.4%
Odronextamab	68.8%	72.2%	55%*	59.1%*	N/A	N/A	N/A
Epcoritamab	68.4%	N/A	58.4%*	72.7%*	N/A	N/A	N/A

*18 months

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Mosun/Len (untreated FL)

Study design

Key inclusion criteria

- CD20+ FL Grade 1–3a
- Previously untreated and require systemic therapy*
- ECOG PS 0–2

Objectives

- Primary: Safety and tolerability of Mosun-Len
- Other: Efficacy (response assessed every 3 cycles,† durability of response), biomarkers, and PK

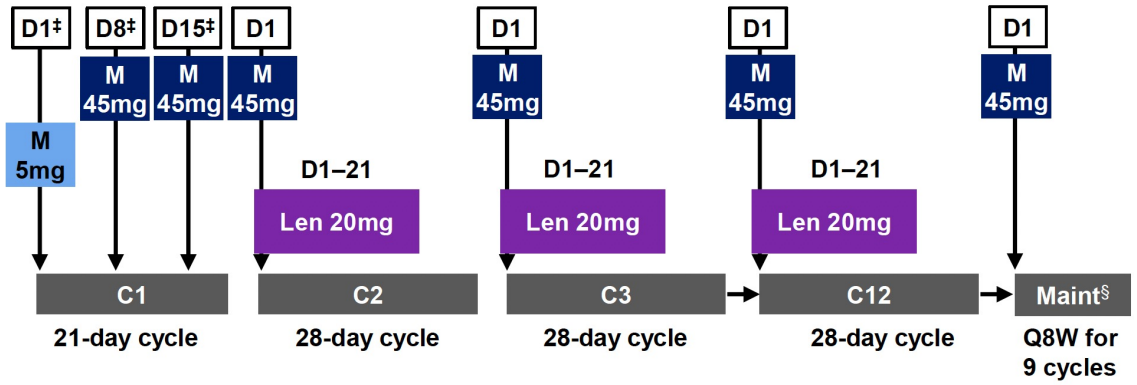
Mosun-Len administration

Mosun

- SC administration for 12 cycles (C1: Q3W; C2–12: Q4W)
- C1 step-up dosing (CRS mitigation)
- No mandatory hospitalization

Len

- Oral administration for 11 cycles (C2–12)



CCOD: July 20, 2023.*Investigator-assessed based on Groupe d'Etude des Lymphomes Folliculaires criteria. †During induction C1–C12. ‡A single dose of oral or IV dexamethasone or methylprednisolone as pre-medication to mitigate risk of CRS was required during C1 and optional after C1. §Mosun monotherapy maintenance option for patients who achieved complete or partial metabolic response after 12 cycles of induction therapy with Mosun-Len.
C, cycle; CCOD, clinical cut-off date; CRS, cytokine release syndrome; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; M, mosunetuzumab; Q3W, once every 3 weeks; Q4W, once every 4 weeks; Q8W, once every 8 weeks; maint, maintenance; PK, pharmacokinetics.

Morschhauser et al. ASH 2023; Abstract 605.

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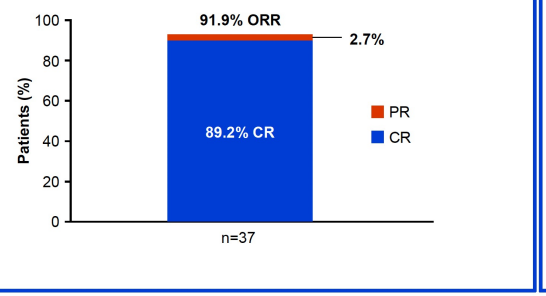
Efficacy/Safety

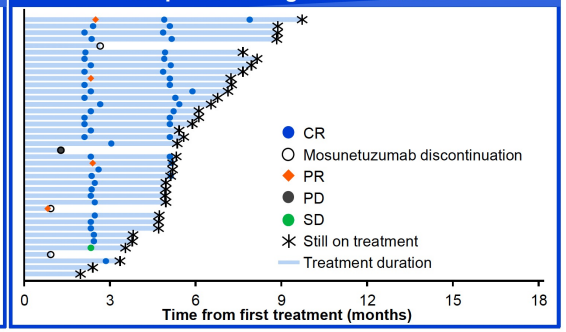
Response

- Median duration of follow-up: 5.2 months (range: 1–10); most patients (95%) had 3–9 months of follow-up at CCOD

Best overall response*



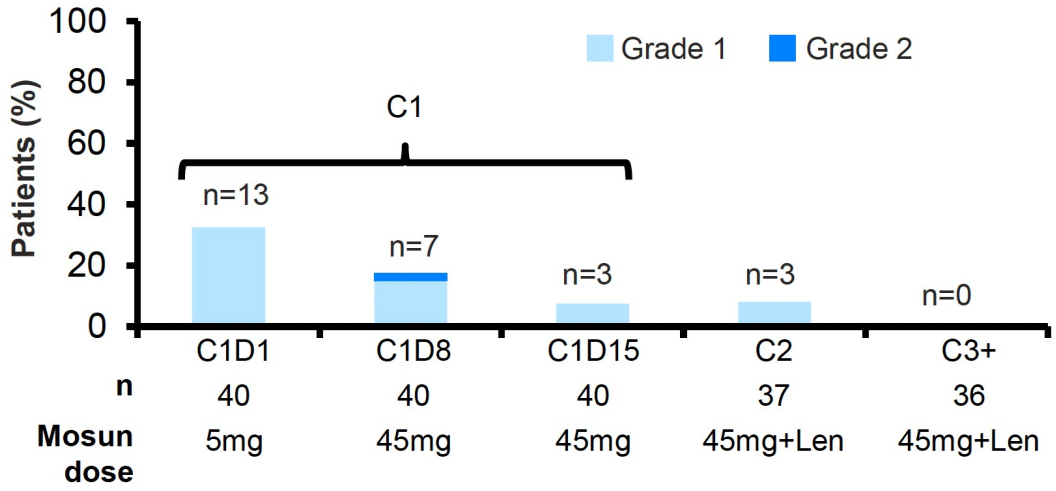
Response timing and duration†



ORR and CR rates were high. All patients who responded were still in response at the CCOD

CCOD: July 20, 2023.
*Thirty-seven patients reached the first treatment assessment (by PET-CT using Lugano 2014 criteria) and were efficacy evaluable. In the efficacy evaluable population one patient (2.7%) each had SD and PD; one patient (2.7%) did not have a response assessment due to early treatment discontinuation for uveitis. Transformed disease was observed in one patient with PR and another with PD during Cycles 1 and 2, respectively.
†Responses were with or without PET.
ORR, overall response rate; PD, progressive disease; PET, positron emission tomography; PR, partial response; SD, stable disease.

Patients with CRS† by cycle and grade



Morschhauser et al. ASH 2023; Abstract 605.

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Epcoritamab Combinations

Study Design: EPCORE NHL-2, Arm 6

A phase 1b/2, open-label trial evaluating the safety and antitumor activity of epcoritamab + R² in adults with previously untreated FL

Key inclusion criteria
- Previously untreated CD20⁺ FL
  - Grade 1, 2, or 3A
- Need for treatment based on symptoms or disease burden, as determined by GELF criteria[1]
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Data cutoff: September 16, 2022
Median follow-up, mo (range)[a]: 8.1 (1.4+ to 10.7)

Expansion, N=41

Step-up dosing

Epcoritamab (SC) 48 mg	Rituximab (IV)	Lenalidomide (oral)
QW C1–2, Q4W C3+ Treatment up to 2 years	375 mg/m² QW C1, Q4W C2–6	20 mg QD for 21 d in C1–12

- **Primary objective:** Antitumor activity (ORR)[b] and safety/tolerability
- **Key secondary endpoints:** DOR

Epcoritamab was administered in 28-d cycles as shown. Dose escalation (part of arm 2a, previously reported[2]) evaluated 24 and 48 mg epcoritamab + R². In arm 2a, epcoritamab schedule was QW in C1–3, Q2W in C4–9, and Q4W in C10+. [a]Median is Kaplan–Meier estimate. [b]Tumor response was evaluated by PET-CT obtained Q12W until CMR, and then Q24W, relative to the first study day, until disease progression. **1.** Brice P, et al. *J Clin Oncol.* 1997;15:1110-7. **2.** Falchi L, et al. ASCO 2022. Abstract 7524.

Study Design: EPCORE NHL-2 Arm 2

Arm 2 of EPCORE NHL-2, a phase 1b/2, open-label, multicenter trial, is evaluating the safety and antitumor activity of SC epcoritamab + standard R² for 12 cycles of 28 days, followed by epcoritamab monotherapy for a total of 2 years, in adults with R/R FL[a]

Key inclusion criteria
- R/R CD20⁺ FL
  - Grade 1, 2, or 3A
  - Stage II–IV
- Need for treatment based on symptoms or disease burden, as determined by GELF criteria[1]
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Data cutoff: March 25, 2022
Median follow-up for arm 2a: 8.6 mo

Dose escalation, n=6

Step-up dosing

Cohort 2a
Epcoritamab (SC) 24 mg (n=3) or 48 mg (n=3)
QW C1–3, Q2W C4–9, Q4W C10+
+ R²
C1–12

Primary objectives: DLT/Safety and tolerability
Key secondary objective: Antitumor activity[b]

Expansion, n=68

Step-up dosing

Cohort 2a
Epcoritamab (SC) 48 mg
QW C1–3, Q2W C4–9, Q4W C10+
+ R²
C1–12

Cohort 2b
Epcoritamab (SC) 48 mg
QW C1–2, Q4W C3+
+ R²
C1–12

Primary objective: Antitumor activity[b]
Treatment up to 2 years

[a]Patients received SC epcoritamab with step-up dosing (ie, priming and intermediate doses before first full dose) and corticosteroid prophylaxis as previously described[2] to mitigate CRS. Epcoritamab was administered in 28-d cycles as shown. Rituximab regimen: 375 mg/m² IV QW in C1 and Q4W in C2–5; lenalidomide regimen: 20 mg QD (oral administration) for 21 d in C1–12. [b]Tumor response was evaluated by PET-CT obtained at 6, 12, 18, 24, 36, and 48 wk, and every 24 wk thereafter, until disease progression. Lugano criteria and LYRIC were used to assess response. AEs were graded by CTCAE v5.0; CRS was evaluated by Lee et al[3] criteria. ClinicalTrials.gov Identifier: NCT04663347.

AE, adverse event; C, cycle; CT, computed tomography; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; GELF, Groupe d'Etude des Lymphomes Folliculaires; MRI, magnetic resonance imaging; NHL, non-Hodgkin lymphoma; PET-CT, positron emission tomography–computed tomography; QW, weekly; Q3W, every 3 weeks; Q4W, every 4 weeks; R/R, relapsed or refractory; R², rituximab and lenalidomide; SC, subcutaneous.

Falchi et al. ASCO 2022; Abstract 7524. Lori et al. ASCO 2024; Abstract 7014.

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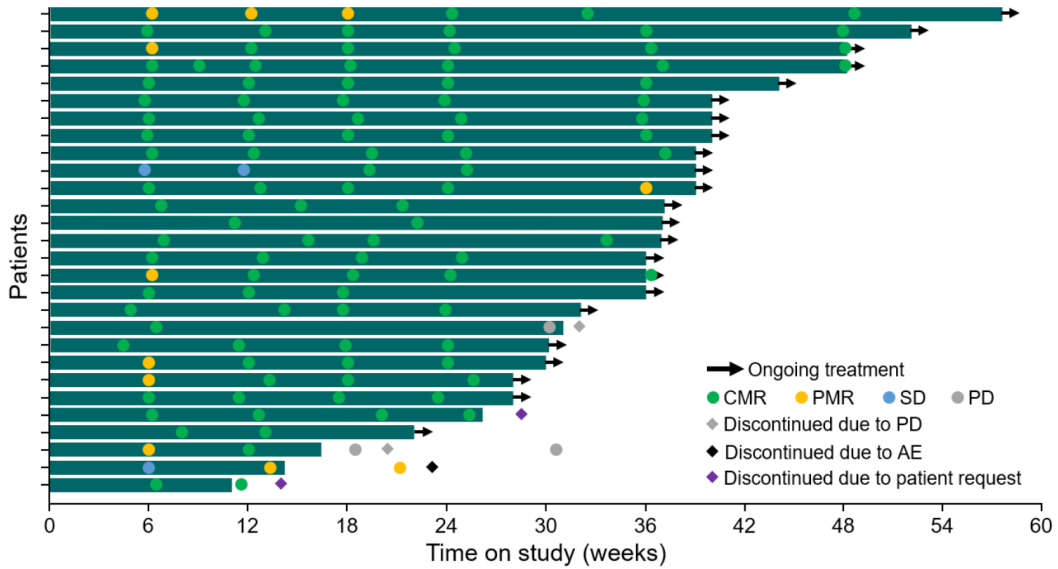
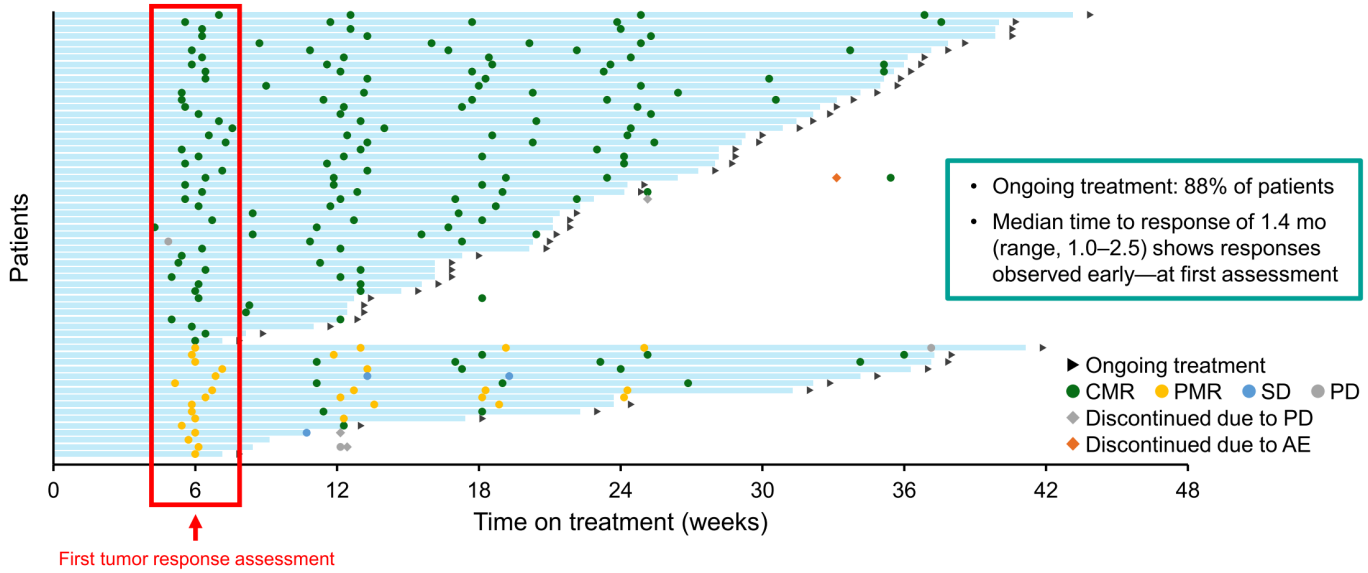
Response R/R

Response Profile for Arm 2a



Data cutoff: March 25, 2022. Per protocol, patients continued to receive scans if they discontinued treatment for reasons other than PD.

Depth and Duration of Response



Falchi et al. ASCO 2022; Abstract 7524.

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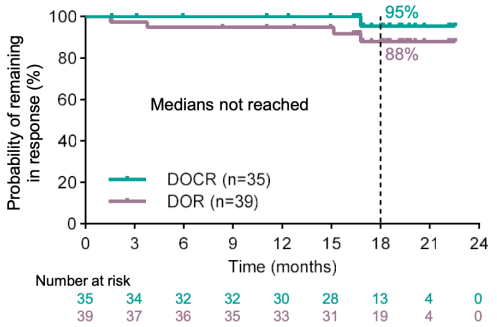
Response 1L

Epcoritamab + R² in 1L FL (arm 6) and epcoritamab maintenance after SOC in FL (arm 7)

Arm 6 (1L FL): Epcoritamab + R² Continued to Show Deep, Durable Responses

	N=41[a]
Overall response, n (%)	39 (95)
Complete response, n (%)	35 (85)
Partial response, n (%)	4 (10)
Progressive disease, n	0
Median time to response, mo (range)	2.7 (1.2–5.5)
Median time to complete response, mo (range)	2.8 (1.4–11.4)

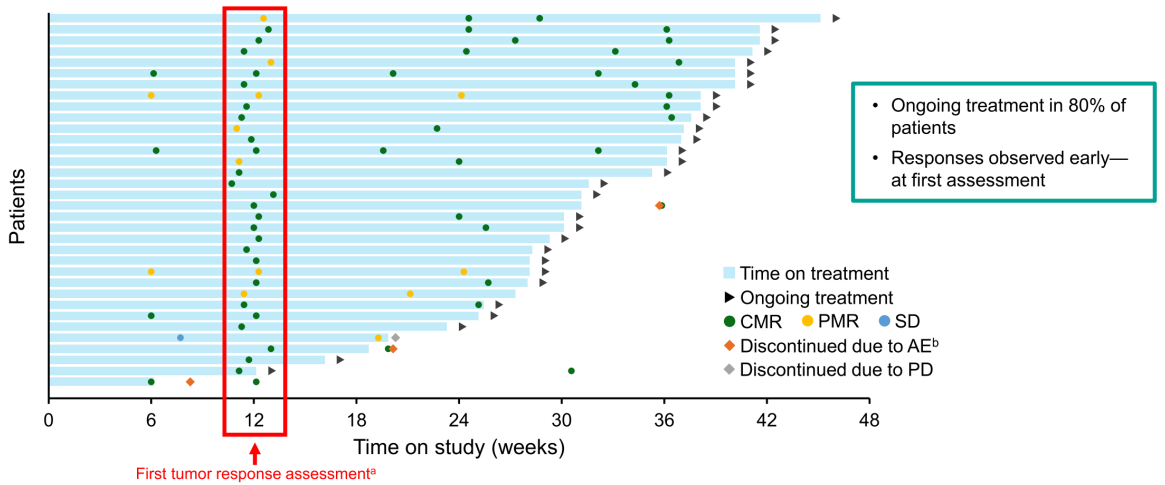


High rates of patients remaining in response and complete response were observed at 18 months

1L, previously untreated; DOCR, duration of complete response; DOR, duration of response; FL, follicular lymphoma; mo, month(s); R², rituximab + lenalidomide. Kaplan–Meier estimates of DOR and DOCR assessed by investigator. [a]A total of 2 patients were not evaluable.

5

Depth and Duration of Response



- Ongoing treatment in 80% of patients
- Responses observed early—at first assessment

Median follow-up, mo (range): 8.1 (1.4+ to 10.7). Per protocol, patients continued to receive scans if they discontinued treatment for reasons other than PD. [a]Most patients had first assessment at week 12, per protocol; some were assessed at week 6 based on investigator's discretion. [b]Two patients discontinued treatment due to COVID-19; 1 discontinued treatment due to pneumonitis.

9

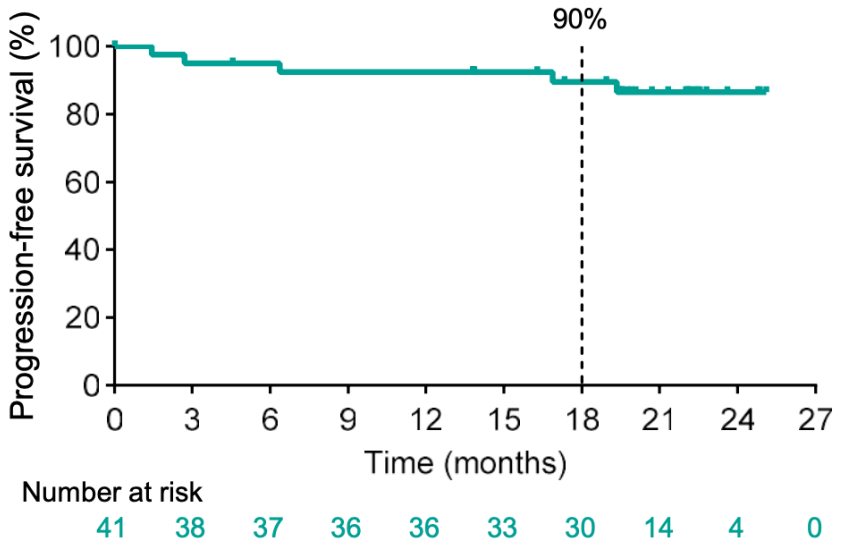
Median duration of response not reached (95% CI, NR–NR)

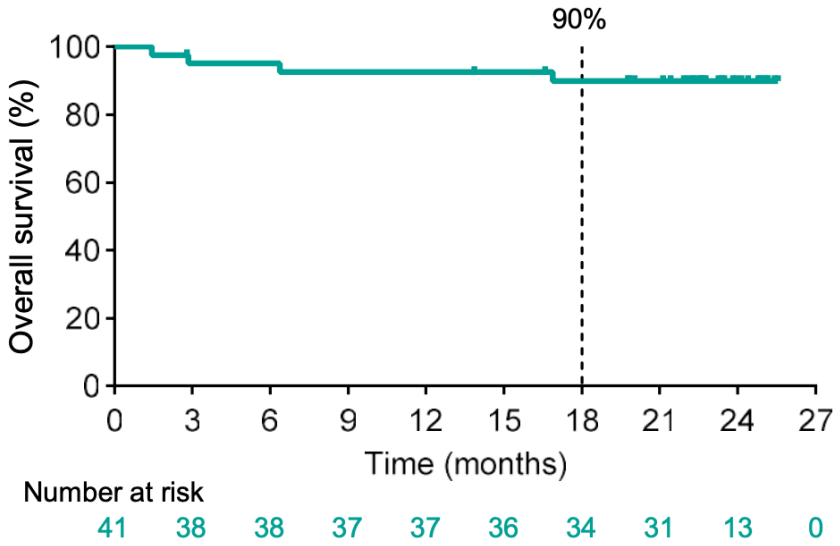
Lori et al. ASCO 2024; Abstract 7014.

Results Continued

Epcoritamab + R² in 1L FL (arm 6) and epcoritamab maintenance after SOC in FL (arm 7)

Arm 6 (1L FL): Progression-Free and Overall Survival





High rates of progression-free and overall survival were observed at 18 months

1L, previously untreated; FL, follicular lymphoma. Kaplan–Meier estimate of progression-free survival assessed by investigator.

Lori et al. ASCO 2024; Abstract 7014.

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CRS

CRS Graded by Lee et al[1] 2019 Criteria in Arm 2a

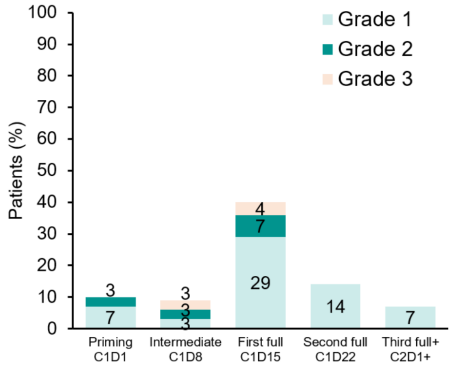
	Arm 2a N=30
CRS, n (%)	15 (50)
Grade 1	9 (30)
Grade 2	4 (13)
Grade 3	2 (7)
CRS resolution, n (%)	15 (100)
Median time to resolution, d (range)[a]	4 (1–15)
CRS leading to treatment discontinuation, n (%)	1 (3)
Tocilizumab use, n (%)	3 (10)

Data cutoff: March 25, 2022. [a]Median is Kaplan–Meier estimate based on longest CRS duration in patients with CRS; range is defined by shortest and longest CRS duration.

- CRS was mostly low grade; all cases resolved

CRS, cytokine release syndrome.
1. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-38.

CRS Events by Dosing Period in Arm 2a



- CRS o
occurre
mediar

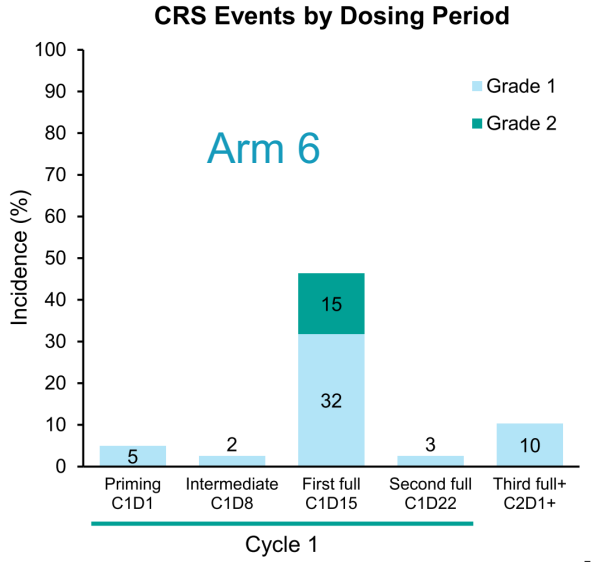
Data cutoff: March 25, 2022. Priming dose: n=30; intermediate dose: n=29; first full dose and later: n=28.

CRS Events

	Total, N=41
CRS, n (%)[a]	22 (54)
Grade 1	16 (39)
Grade 2	6 (15)
Median time to onset after first full dose, d (range)	3 (1–6)
CRS resolution, n (%)	22 (100)
Median time to resolution, d (range)[b]	4 (1–10)
Treated with tocilizumab, n (%)	4 (10)
Leading to treatment discontinuation, n (%)	**0**

[a]Graded by Lee et al 2019 criteria. [b]Median is Kaplan–Meier estimate based on longest CRS duration in patients with CRS.

- No grade ≥3 events
- All CRS events resolved
- Timing was predictable, with most cases occurring after the first full dose

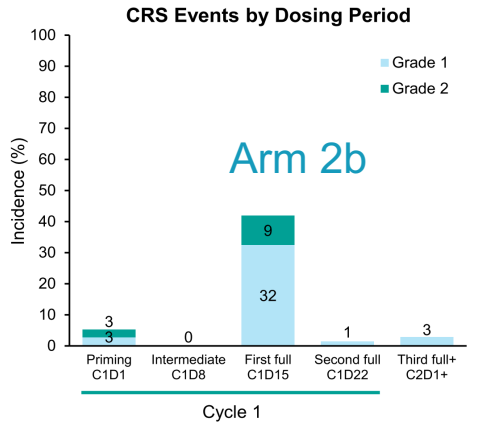


CRS Events

	Total, N=76
CRS, n (%)[a]	33 (43)
Grade 1	25 (33)
Grade 2	8 (11)
Median time to onset after first full dose, d (range)	2 (1–9)
CRS resolution, n (%)	33 (100)
Median time to resolution, d (range)[b]	2 (1–23)
Treated with tocilizumab, n (%)	8 (11)
Leading to treatment discontinuation, n (%)	**0**

[a]Graded by Lee et al 2019 criteria. [b]Median is Kaplan–Meier estimate based on longest CRS duration in patients with CRS.

- CRS occurrence was predictable, with most cases occurring following the first full dose
- No grade ≥3 CRS events
- These data support fully outpatient administration



Falchi et al. ASCO 2022; Abstract 7524.
Lori et al. ASCO 2024; Abstract 7014.

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Glofitamab

NP30179 Phase I/II study design

Study design[1]

- Multicenter, open-label, dose-escalation and dose-expansion study of glofitamab with Gpt

Glofitamab IV administration

- Fixed-duration treatment: maximum 12 cycles

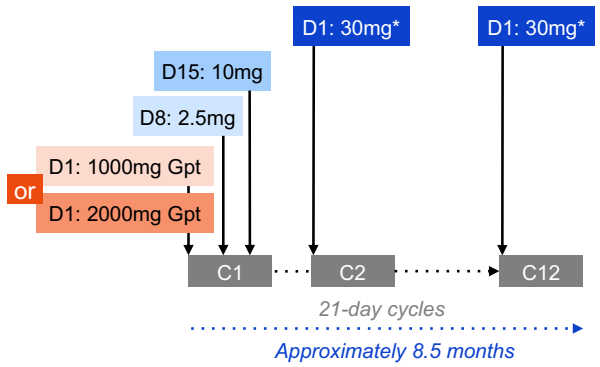
Population characteristics

- Age ≥18 years
- ≥1 prior systemic therapy
- ECOG PS 0 or 1

CRS mitigation

- Obinutuzumab pretreatment (1000mg or 2000mg)
- C1 step-up dosing
- Monitoring after first dose (2.5mg)

Dosing schedule

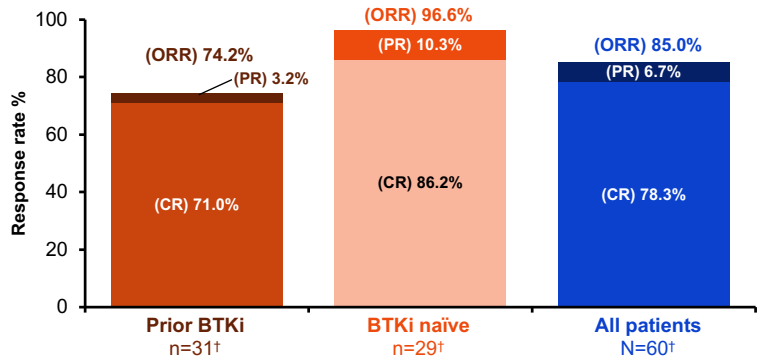


Clinical cut-off date: September 04, 2023.
*In the 1000mg Gpt cohort, two patients had 16mg glofitamab as their target dose in the dose escalation phase.
C, cycle; CRS, cytokine release syndrome; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; Gpt, obinutuzumab pretreatment; IV, intravenous.

1. NCT03075696. Available at: https:www.clinicaltrials.gov.

Response rates

Response rates* in patients with R/R MCL



- Median time to first response among responders (n=51): **42 days** (95% CI: 42.0–45.0)

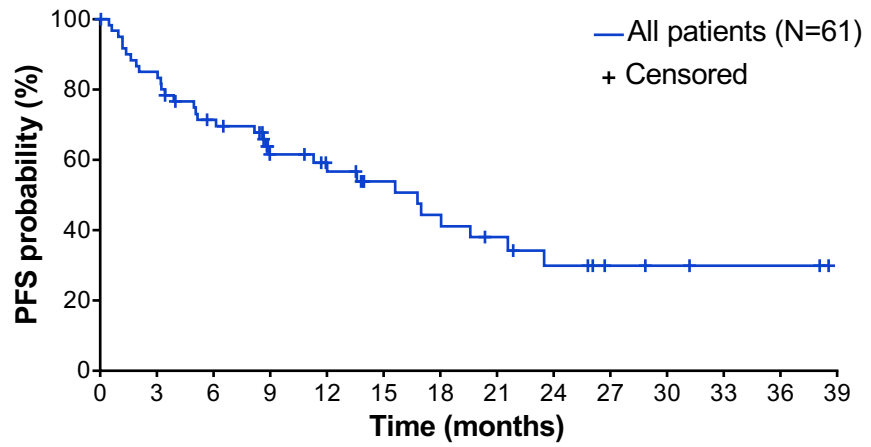
High CR and OR rates were observed in the overall population and in both BTKi-naïve patients and those with prior BKTi therapy

Clinical cut-off date: September 04, 2023.
*Investigator-assessed. †Efficacy evaluable population.
CI, confidence interval; ORR, overall response rate; PR, partial response.

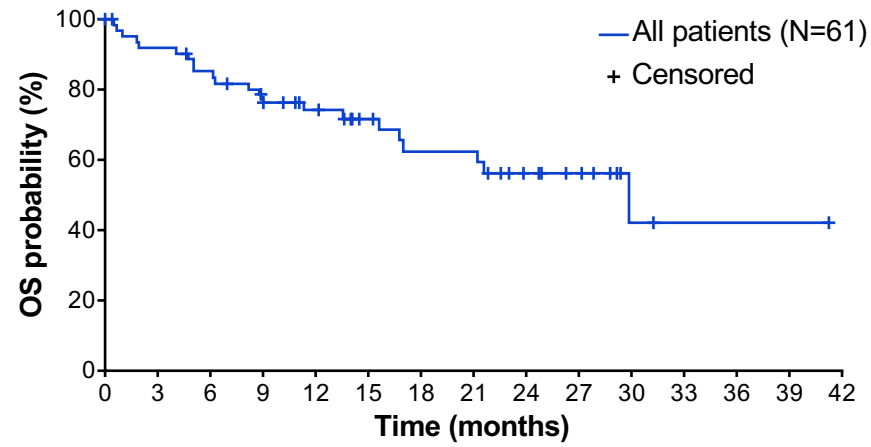
Phillips TJ et al. ASCO 2024; Abstract 7008.

Glofitamab in MCL Time-to-event endpoints

PFS



OS†



	Prior BTKi n=32*	All patients N=61*
Median PFS follow-up, months (95% CI)	26.1 (13.5–31.2)	19.6 (11.9–26.1)
Median PFS, months (95% CI)	8.6 (3.4–15.6)	16.8 (8.9–21.6)
15-month PFS rate, % (95% CI)	33.0 (14.8–51.1)	54.0 (40.1–67.8)

	Prior BTKi n=32*	All patients N=61*
Median OS follow-up, months (95% CI)	24.7 (13.6–28.8)	21.8 (14.0–24.9)
Median OS, months (95% CI)	21.2 (9.0–NE)	29.9 (17.0–NE)
15-month OS rate, % (95% CI)	55.0 (36.5–73.6)	71.4 (59.3–83.5)

Clinically significant PFS and OS at 15 months were achieved with fixed-duration glofitamab

Clinical cut-off date: September 04, 2023. *ITT population. †At the time of analysis, 22 patients had died, the majority due to PD (n=7) or COVID-19 (n=7); other causes of death were pneumonia (n=1), septic shock (n=1), cardiac arrest (n=1), and unknown/other (n=5). All patients who died due to COVID-19 had achieved a CR.
ITT, intention to treat; OS, overall survival; PD, progressive disease; PFS, progression-free survival.

Phillips TJ et al. ASCO 2024; Abstract 7008.

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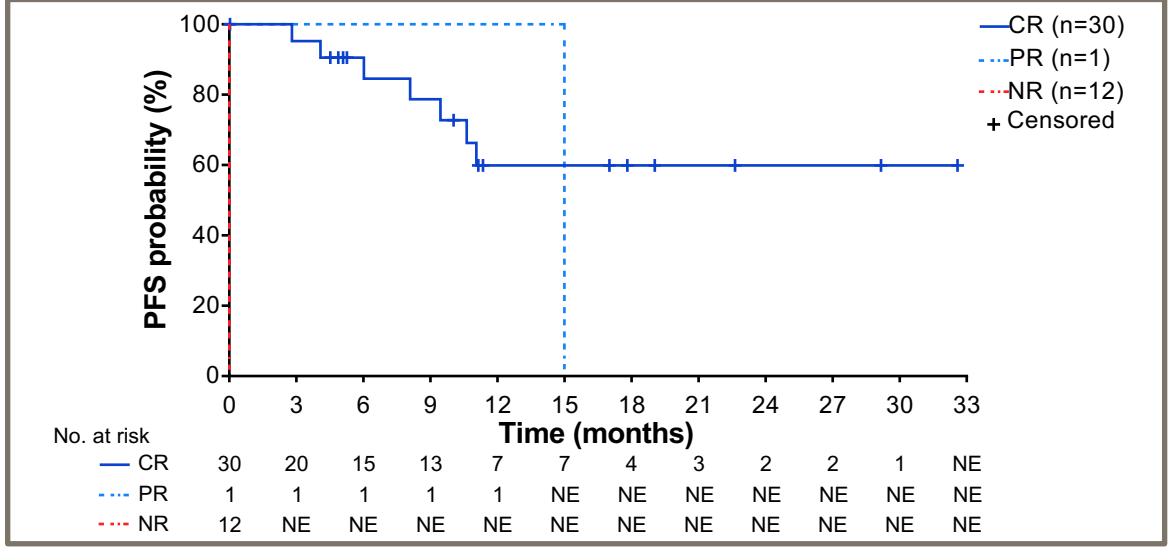
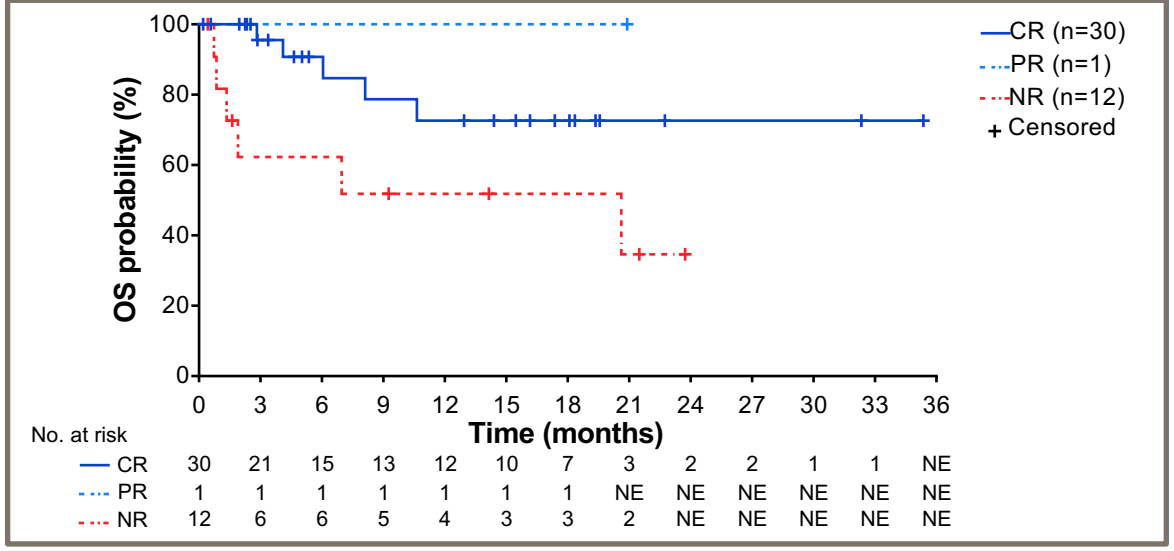
Landmark analyses by response at EOT

PFS



OS



Landmark PFS from EOT in patients with CR at EOT	n=30
Median PFS, months (95% CI)	NE (10.6–NE)
15-month PFS rate, % (95% CI)	59.2 (35.5–83.0)

Landmark OS from EOT in patients with CR at EOT	n=30
Median OS, months (95% CI)	NE (NE)
15-month OS rate, % (95% CI)	72.7 (51.9–93.5)

The majority of patients with a CR at EOT **remained progression-free and were alive** at 15 months post-EOT

Clinical cut-off date: September 04, 2023.

EOT, end of treatment; NR, no response.

Phillips TJ et al. ASCO 2024; Abstract 7008.

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Study design: Phase II dose expansion (Mosun/Pola-MCL)

Study design: Phase II dose expansion

Key inclusion criteria

- R/R MCL
- ECOG PS 0–2
- ≥2 prior therapies (including an anti-CD20 antibody, anthracycline or bendamustine therapy, and BTKi)

Objectives

- Primary: efficacy of mosun-pola (best ORR[1] by IRC)
- Secondary: efficacy by INV, durability of response, and safety

Mosun-pola fixed duration administration (NCT03671018)

Mosun

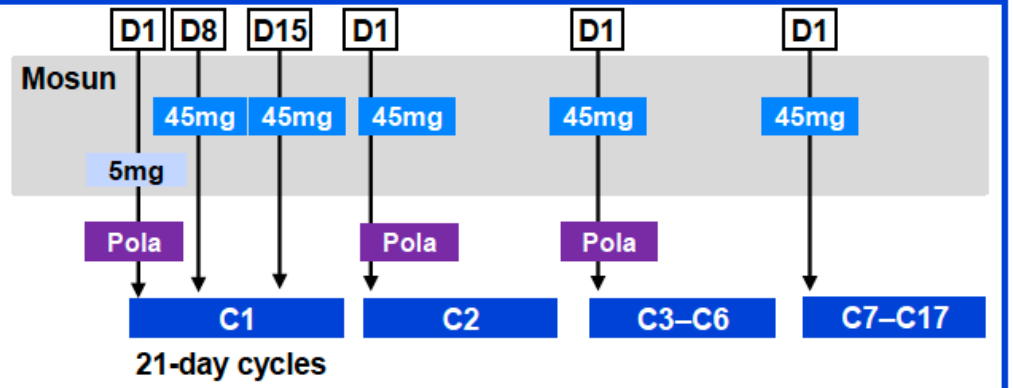
- SC administered in 21-day cycles with step-up dosing in Cycle (C) 1; total of 17 cycles

Pola

- 1.8mg/kg IV on Day [D],1 of C1–6

No mandatory hospitalization

All patients received corticosteroid premedication prior to each dose in C1*



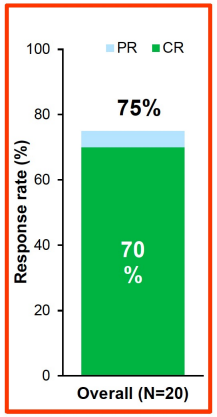
*From C2 and beyond, premedication was optional for patients who did not experience CRS in the previous cycle; corticosteroid premedication consisted of 20mg of dexamethasone or 80mg of methylprednisolone, either IV or orally.

1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68.

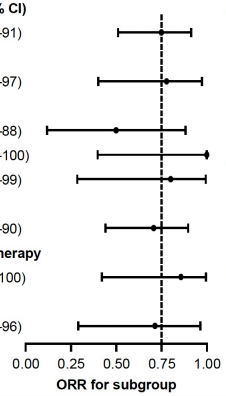
Response

INV-assessed best ORR

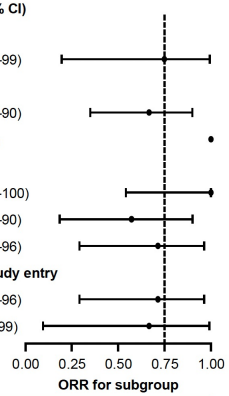
ORR and CR rates in the overall population were 75% and 70%, respectively



Subgroups	No. Patients	ORR (95% CI)
Overall	20 (100%)	75% (51–91)
Age group, in years		
≥70	9 (45%)	78% (40–97)
No. of prior lines of therapy		
3	6 (30%)	50% (12–88)
4	4 (20%)	100% (40–100)
≥5	5 (25%)	80% (28–99)
R/R to last prior therapy		
Refractory	17 (85%)	71% (44–90)
Relapse within 12 months of first prior therapy		
Yes	7 (35%)	86% (42–100)
Received prior CAR-T therapy		
Yes	7 (35%)	71% (29–96)



Subgroups	No. Patients	ORR (95% CI)
R/R to any prior CAR-T therapy		
Refractory	4 (57%)	75% (19–99)
Ki-67		
≥50%	12 (60%)	67% (35–90)
≥30% but <50%	1 (5%)	100%
TP53 aberration at study entry		
Mutation/deletion	6 (30%)	100% (54–100)
Wildtype	7 (35%)	57% (18–90)
Unknown/not done	7 (35%)	71% (29–96)
Morphologic characteristics of MCL at study entry		
Blastoid MCL	7 (35%)	71% (29–96)
Pleomorphic MCL	3 (15%)	67% (9–99)

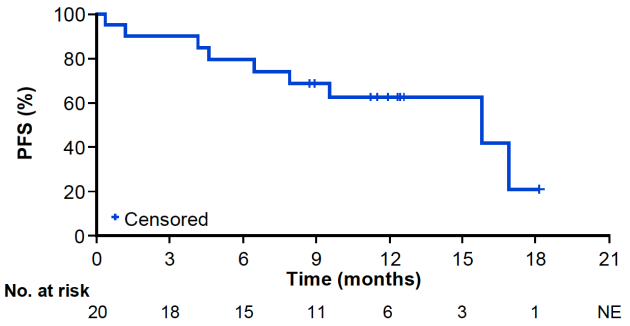


Best ORR rates were generally consistent across high-risk MCL subgroups

PFS and OS

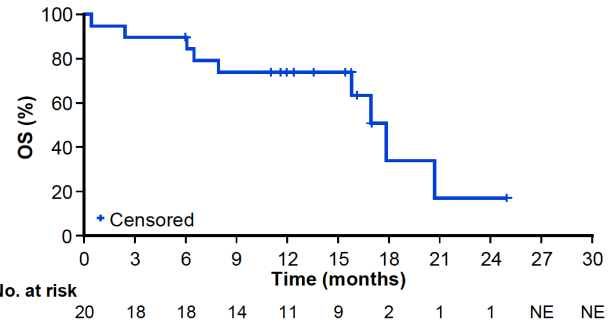
Median follow-up: 15.8 months (95% CI: 12.4–NE)

PFS



	N=20
Median PFS, months (95% CI)	15.8 (8.0–NE)
9-month event-free rate, % (95% CI)	68.8% (48.1–89.6)

OS



	N=20
Median OS, months (95% CI)	17.9 (15.8–20.7)
9-month event-free rate, % (95% CI)	74.1% (54.5–93.7)

Wang et al. ASH 2023; Abstract 734.

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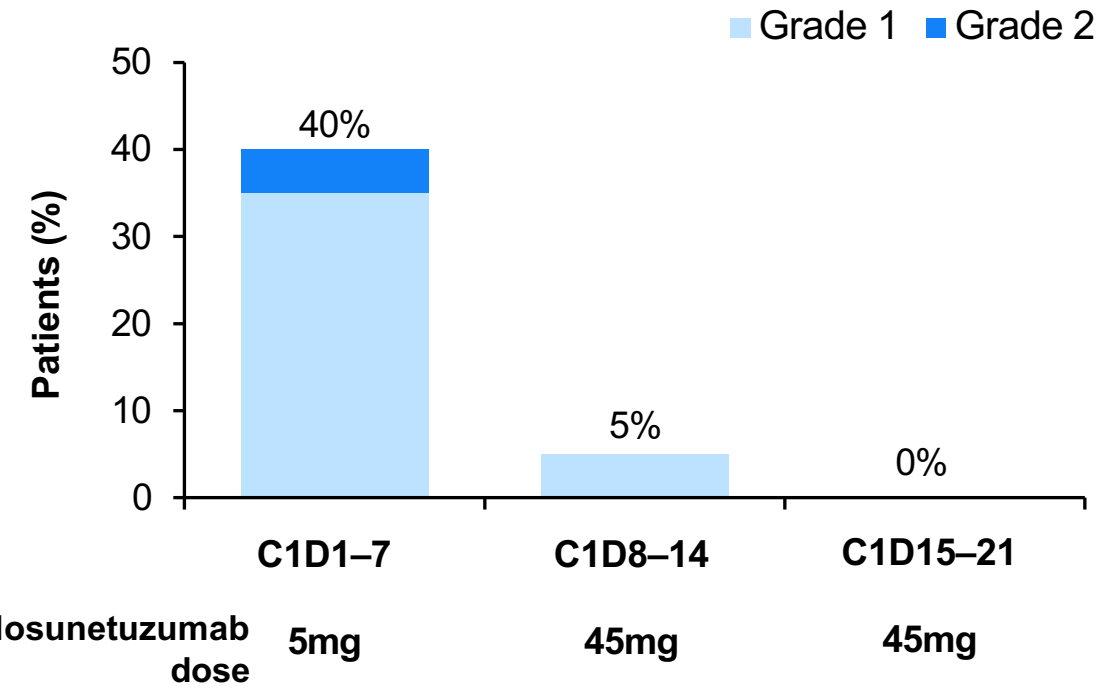
CRS summary

CRS by ASTCT criteria[1]	N=20
Any grade, n (%)	9 (45)
Grade 1	8 (40)
Grade 2*	1 (5)
Grade 3+	0
Median time to first CRS onset relative to last dose, days (range)	1 (0–2)
Median CRS duration, days (range)	3 (1–9)
CRS management, n (%)	
Corticosteroids	1 (5)
Tocilizumab	1 (5)
Low-flow oxygen	1 (5)

CRS by cycle and grade



All CRS events were low grade and resolved within C1

Clinical cut-off date: July 6, 2023. *This patient experienced Grade 2 fever, confusion, and hypoxia on D3; management included tocilizumab, low-flow oxygen, acetaminophen, and broad-spectrum antibiotics.
ASTCT, American Society for Transplantation and Cellular Therapy

1. Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625–38.

Wang et al. ASH 2023; Abstract 734.

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Conclusions

- Several bispecific antibodies with impressive clinical data in FL
  - Currently two with FDA approval (mosunetuzumab and epcoritamab)
    - Ongoing single agent and combo studies in 1L FL
  - Agents as well have demonstrated ability to be combined with lenalidomide in 1L and 2L+ setting (epco/mosun)
    - Phase 3 completed with mosun/len in R/R FL
- MCL more difficult space as evident by lack of data from other companies
  - Currently glofitamab w/ single data (data) and mosun/pola w/ combination data.
    - Ongoing phase 3 study with glofitamab vs. investigator's choice
    - Several IIT's ongoing

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Agenda

Module 1: Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Abramson

Module 2: Bispecific Antibody Therapy for DLBCL — Prof Hutchings

Module 3: CAR T-Cell Therapy for Other Lymphoma Subtypes — Dr Lunning

Module 4: Bispecific Antibody Therapy for Follicular Lymphoma and Other Lymphoma Subtypes — Dr Phillips

Module 5: Tolerability Considerations with CAR T-Cell and Bispecific Antibody Therapy — Dr Crombie

Dr KS Kumar
(Trinity, Florida)

Case Presentation: 75-year-old man with multiregimen-recurrent DLBCL with complete response 3 years ago to axicabtagene ciloleucel who develops acute myeloid leukemia while in remission

Dr Susmitha Apuri
(Inverness and Lecanto, Florida)

Case Presentation: 87-year-old woman with transformed GCB-type DLBCL and complete response to CAR-T therapy who then develops low-risk MDS

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

What is known about the risk of secondary solid tumors and hematologic cancers after CAR T-cell therapy and bispecific antibodies?

What are your thoughts about the reported increased incidence of T-cell malignancies after CAR T-cell treatment? What do you think is the pathophysiology?

What other long-term issues, including risk of infection, have been observed in patients receiving T cell-directed therapy? Do patients receiving T cell-directed therapy typically respond to/benefit from vaccines?

Dana-Farber Cancer Institute

Tolerability Considerations with CAR T-Cell and Bispecific Antibody Therapy

Jennifer Crombie, MD
Dana-Farber Cancer Institute
December 6, 2024

Outline

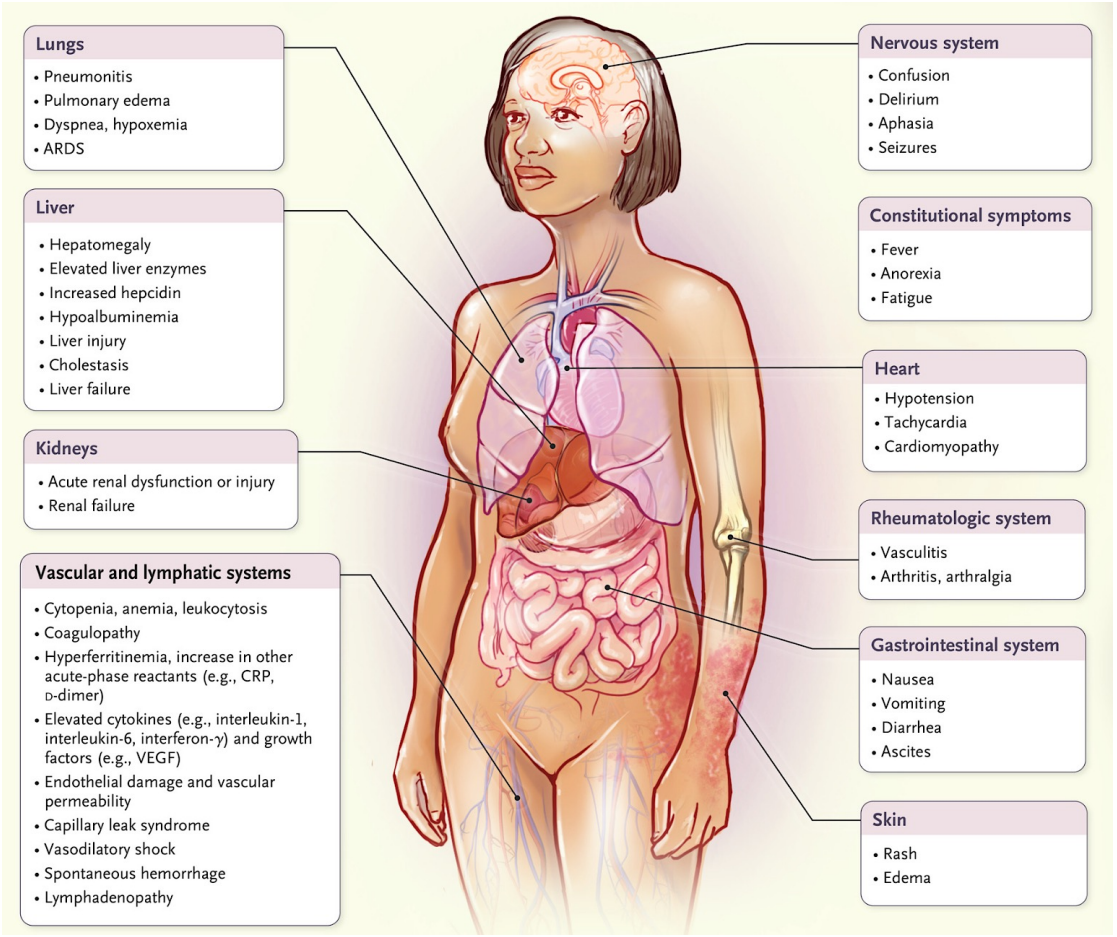
- Key toxicities with anti-CD19 CAR T-cell therapy
- Late toxicities with CAR T-cell therapy
- Risk of secondary malignancies with CAR T-cell therapy
- Key toxicities with CD20 x CD3 bispecific antibodies and management strategies
- Other safety concerns with bispecific antibodies

Outline

- Key toxicities with anti-CD19 CAR T-cell therapy
- Late toxicities with CAR T-cell therapy
- Risk of secondary malignancies with CAR T-cell therapy
- Key toxicities with CD20 x CD3 bispecific antibodies and management strategies
- Other safety concerns with bispecific antibodies

What is cytokine release syndrome (CRS)?

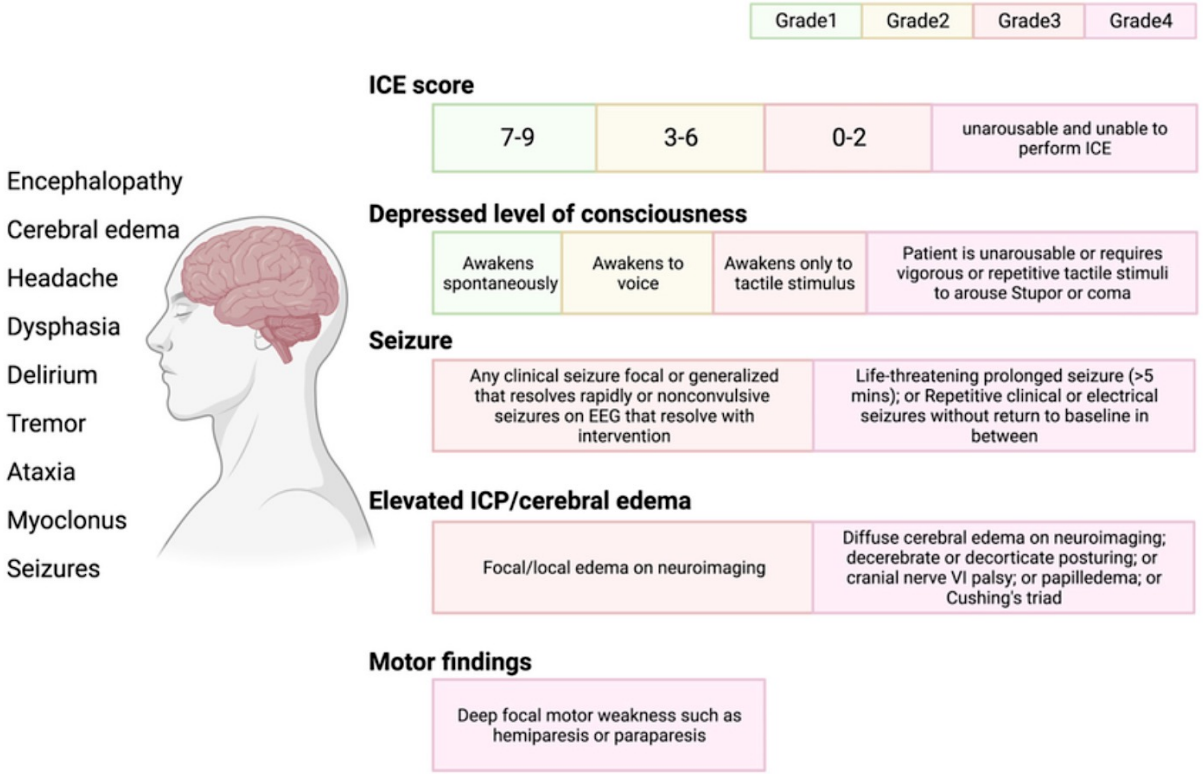
- Acute systemic inflammatory syndrome
- Increase in inflammatory cytokines
- Characterized by fever, hypotension, chills, headache, tachycardia, hypoxia



Fajgenbaum et al., NEJM, 2020

What is immune effector-cell associated neurotoxicity syndrome (ICANS)?

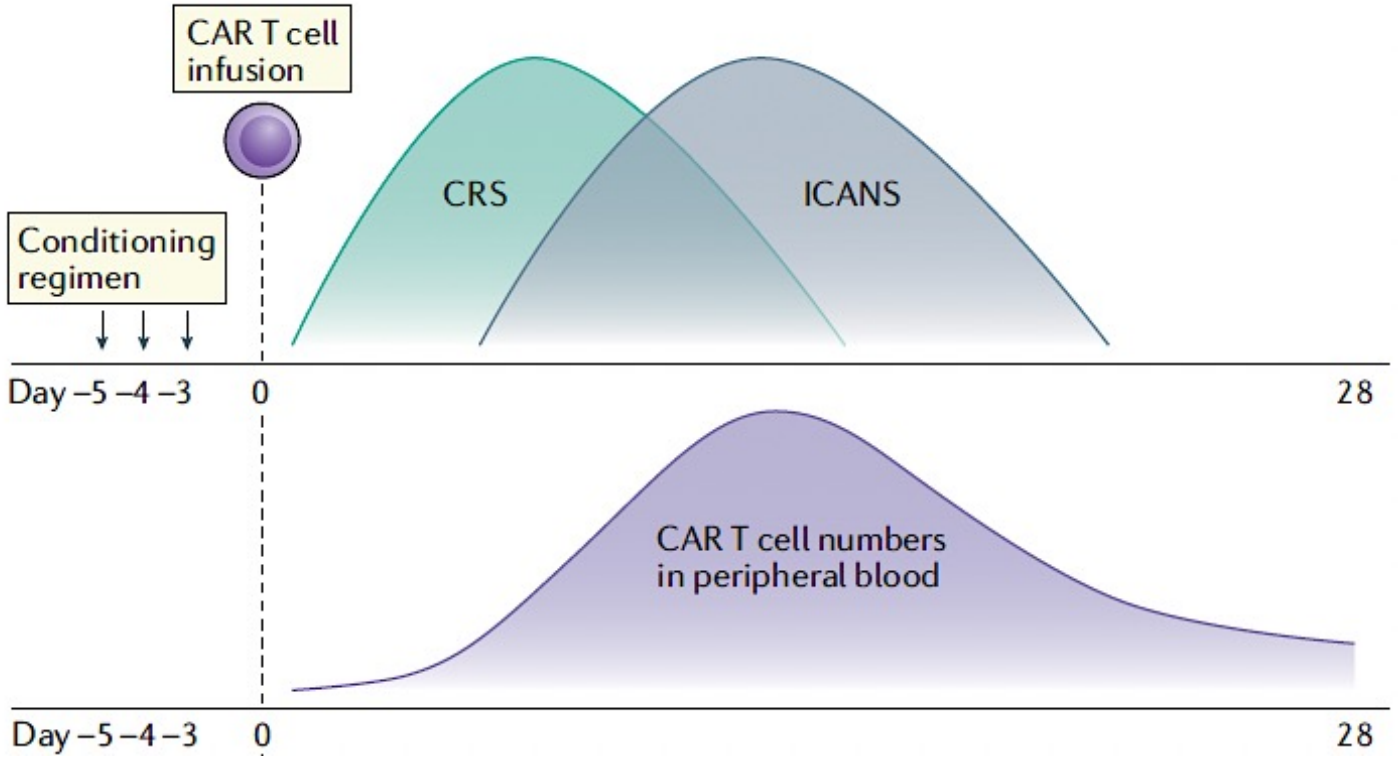
- Neurologic changes following effector-cell therapy
- May manifest as delirium, encephalopathy, aphasia, lethargy, difficulty concentrating, agitation, tremor, seizures, and, rarely, cerebral edema



Lee et al. BBMT, 2019, Zhang et al., Journal of Clinical Medicine, 2022

CRS and ICANS with CAR T-cell therapy

- Typically occur early after CART infusion



Morris et al. Nature Reviews Immunology, 2022

CRS and ICANS rates with CAR T-cell therapy in DLBCL

CAR T-Cell Product	Tisagenlecleucel, JULIET (N = 93); Lentivirus-41BB[4]	Axicabtagene Ciloleucel, ZUMA-1 (N = 108); Retrovirus-CD28[3]	Lisocabtagene Maraleucel, TRANSCEND (N = 102); Lentivirus-41BB[38]
Use of tocilizumab, %	15	45	17
Use of steroids, %	11	29	21
CRS all grades, %	58	93	37
CRS ≥ 3, %	23	12	1
Median time to CRS onset (range), days	3 (1–9)	2 (1–12)	5 (1–14)
Median duration CRS (range), days	7 (2–30)	8	NR
NT/ICANS all grades, %	NR	67	23
NT/ICANS ≥ 3, %	12	30	13
Median time to NT/ICANS onset (range), days			10 (3–23)
Nonrelapse fatal events, N	3 (4%) encephalitis; cerebral hemorrhage; mycosis (post-SCT)	3 (2.8%) cardiac arrests; HLH; pulmonary embolus	NR

Santomasso et al., ASCO Educational Book, 2019

CRS and ICANS rates in 2nd line DLBCL

CAR T-cell product	Axi-cel (ZUMA-7)	Liso-cel (TRANSFORM)
CRS all grades	92%	49%
CRS ≥ grade 3	6%	1%
Neurologic events all grades	60%	12%
Neurologic events ≥ grade 3	21%	4%

Locke et al., NEJM, 2021, Kamdar et al., Lancet, 2022

CRS and ICANS rates with CAR T-cell therapy in FL

CAR T-cell product	Axi-cel (ZUMA-5)	Liso-cel (TRANSCEND FL)	Tisa-cel (ELARA)
CRS all grades	78%	58%	48.5%
CRS ≥ grade 3	6%	1%	0%
Neurologic events all grades	56%	15%	37.1%
Neurologic events ≥ grade 3	15%	2%	3%

Jacobson et al., Lancet, 2021, Morschhauser et al., Lancet, 2024, Fowler et al., Nat. Med., 2022

CRS and ICANS rates with CAR T-cell therapy in MCL

CAR T-cell product	Brexu-cel (ZUMA-2)	Liso-cel (TRANSCEND NHL 001)
CRS all grades	91%	61%
CRS ≥ grade 3	15%	1%
Neurologic events all grades	63%	31%
Neurologic events ≥ grade 3	31%	9%

Wang et al., NEJM, 2020, Wang et al., JCO, 2024

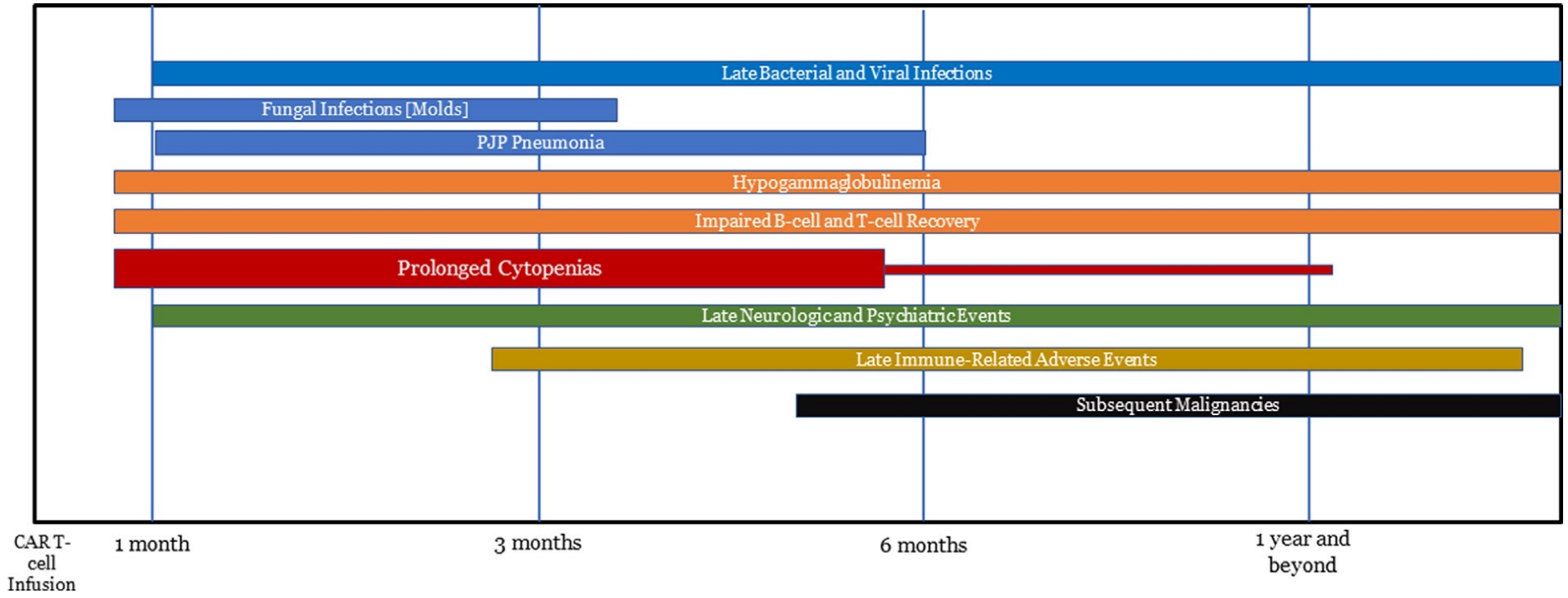
Optimal monitoring and management of CRS and ICANS

- **Toxicity prophylaxis:**
  - Infection: PCP and VZV prophylaxis
  - Neurologic toxicity: anti-seizure medication through day 30
- **Monitoring:**
  - Administered in CAR T-cell centers, remain local for at least 30 days
  - Often administered inpatient with daily monitoring
  - Outpatient administration for select patients increasing
- **Treatment:**
  - Steroids
  - Tocilizumab (anti-IL6R), Anakinra (IL-1R antagonist)
  - Guidelines available in package insert, NCCN guidelines, professional societies

Wang et al., NEJM, 2020, Wang et al., JCO, 2024

What are the late toxicities with CAR T-cell therapy?

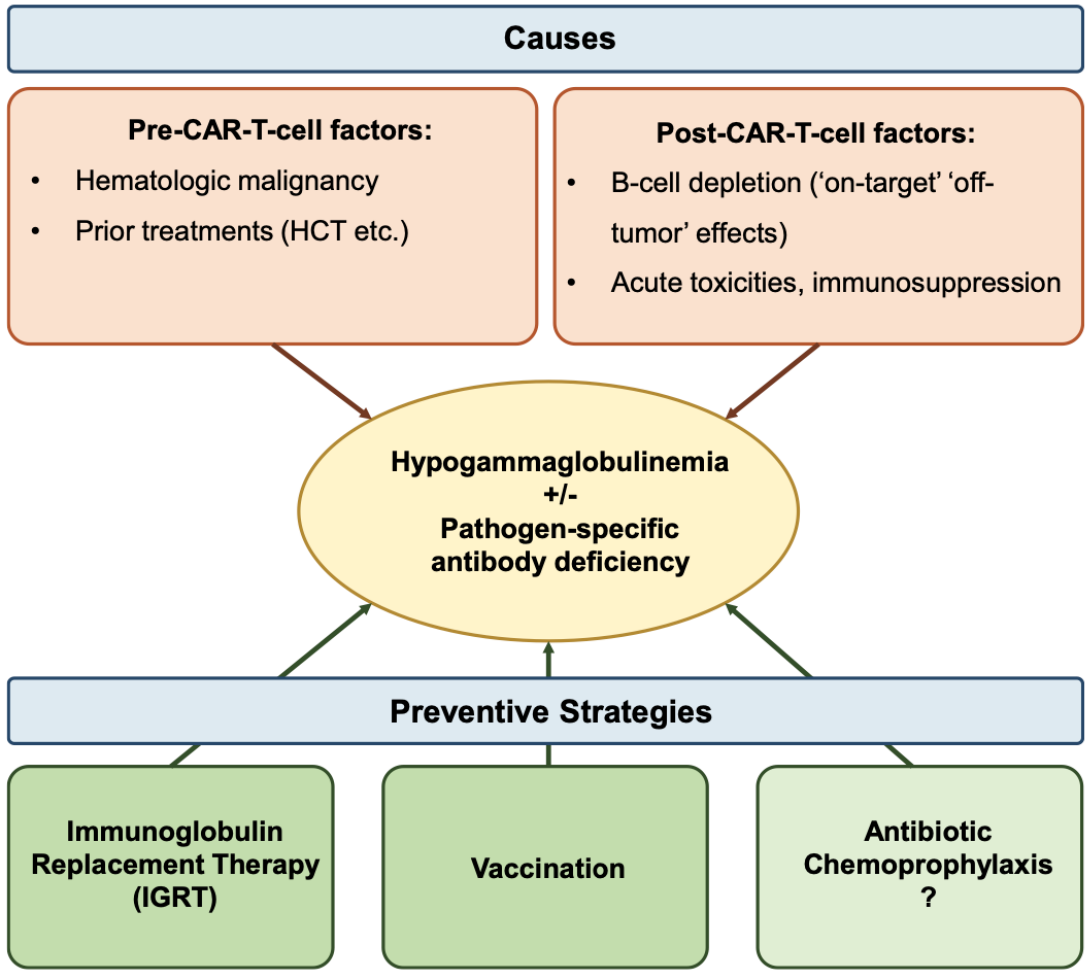
- Late toxicities:
  - Hypogammaglobulinemia, infections, prolonged cytopenias, delayed neurotoxicity



Chakrabordy et al., Transplant Cell Ther. 2021

What are the late toxicities with CAR T-cell therapy?

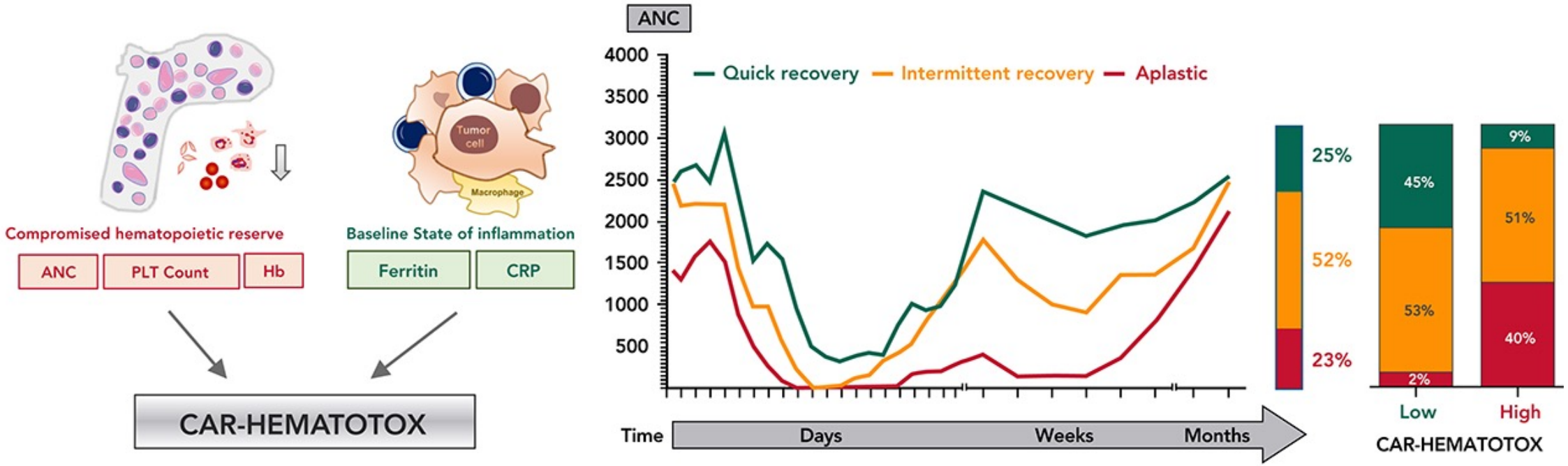
- Hypogammaglobulinemia: Persistent (≥6 months) in 10-62% of patients
- Infections: Grade 3 infections in 5-32% of patients
- Delayed neurologic toxicity: Rare



Brudno et al., Nature Reviews, 2024, Kampouri et al., Expert Review in Hematol., 2022

CAR-HEMATOTOX to predict prolonged cytopenias

- Prolonged cytopenias:
  - 21 days+ from approximately 30-60%, prolonged grade 3+ in 1-5%
- CAR-HEMATOTOX is a risk stratification tool



Rejeski et al., Blood, 2021

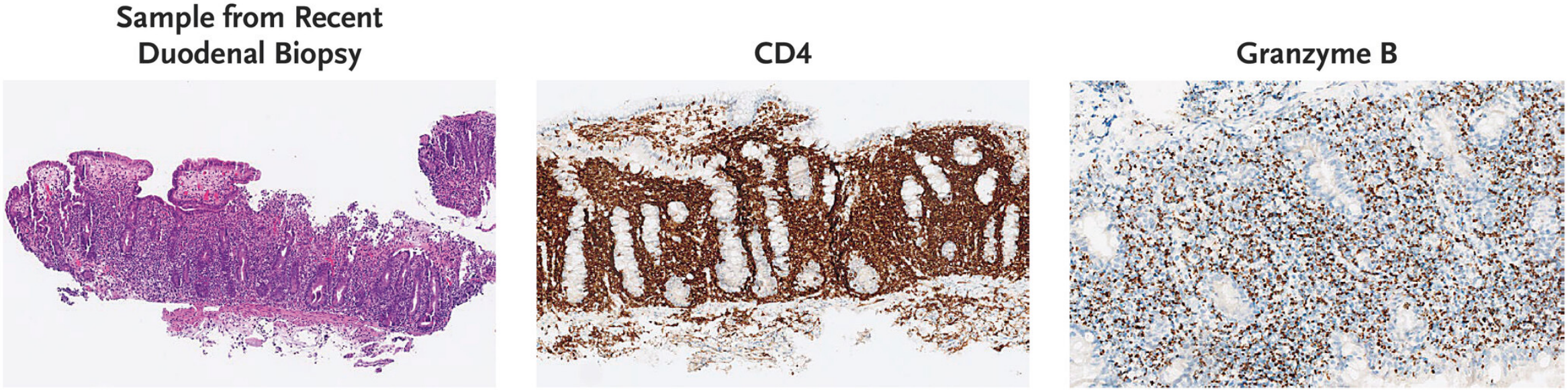
Is there a risk of T-cell lymphoma with CAR T-cell therapy?

- 2023: FDA posted safety communication regarding reports of T-cell malignancies in patients who had received CAR T-cell therapy
- 22 cases of T-cell lymphoma, with three of the lymphomas containing viral vectors
- A case of CD8+ T-cell lymphoma diagnosed approximately 3 months after commercial CD19-targeting CAR T-cell therapy

Food and Drug Administration, Nov 28, 2023
Ghilardi et al. Nat Med, 2023

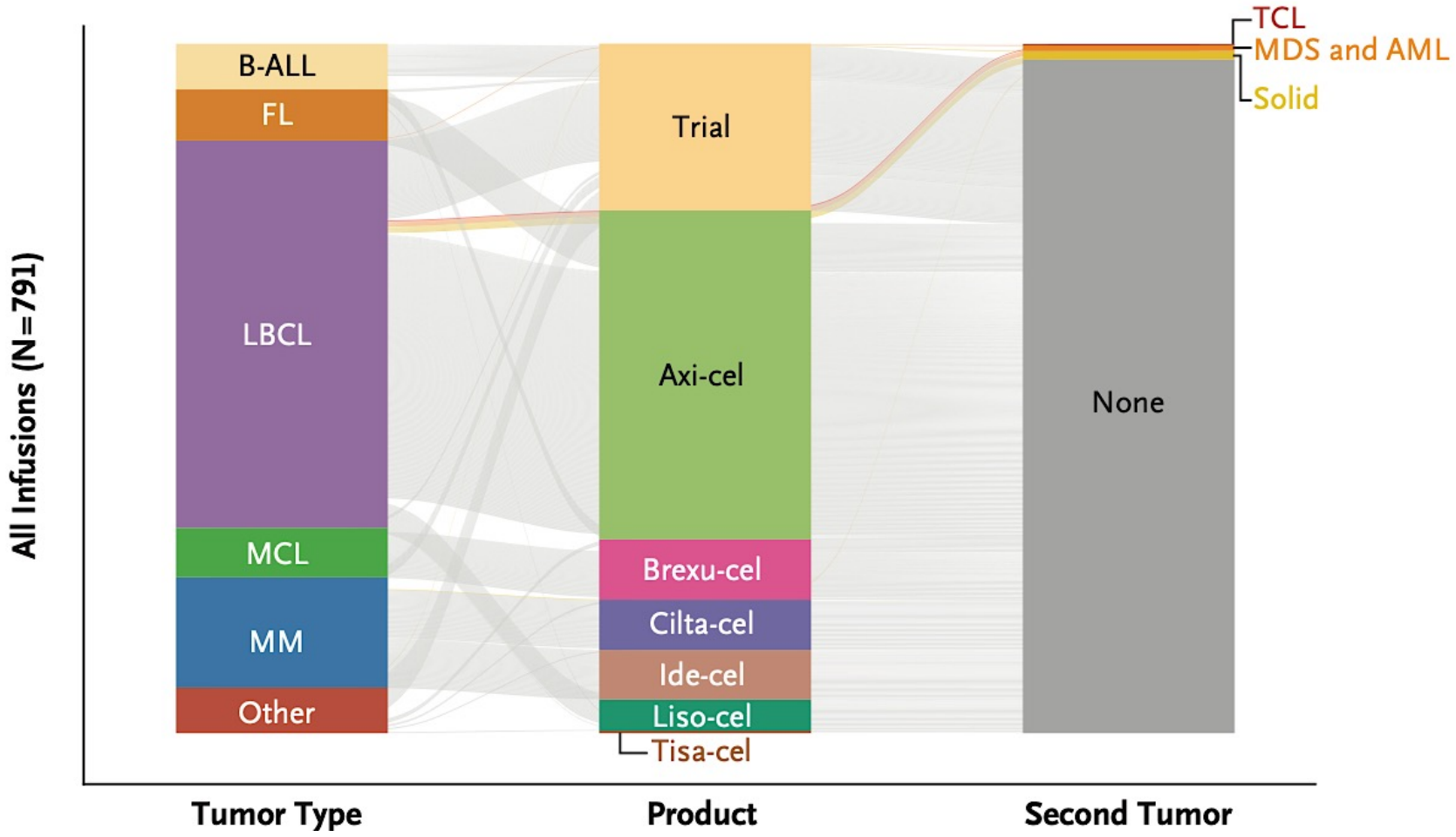
CD4+ T-cell lymphoma after BCMA CAR T-cell therapy

- Report of CD4+ indolent T-cell lymphoma of the GI tract 4 months after BCMA CAR T-cell therapy
- Targeted RNA sequencing revealed CAR T-cell gene products in the tumor cells



Ozdemirli et al. NEJM, 2024

Low risk of T-cell lymphoma in larger study



Hamilton et al., NEJM, 2024

Outline

- Key toxicities with anti-CD19 CAR T-cell therapy
- Late toxicities with CAR T-cell therapy
- Risk of secondary malignancies with CAR T-cell therapy
- Key toxicities with CD20 x CD3 bispecific antibodies and management strategies
- Other safety concerns with bispecific antibodies

CRS rates with available bispecific antibodies

Drug	Mosunetuzumab[3]					Epcoritamab[4]					Glofitamab[5]				
CRS occurrence	G1	G2	G3	G4	G5	G1	G2	G3	G4	G5	G1	G2	G3	G4	G5
	26%	17%	1%	1%	0%	34%	15%	3%	0%	0%	47%	12%	3%	1%	0%
	Time course for CRS onset C1D1: 23.3% C1D8: 5.6% C1D15: 36.4% C2D1: 10.3% C3+D1: 2.4%			Median time (h) to CRS onset C1D1: 5 C1D8: 20 C1D15: 27 C2D1: 38		Time course for CRS onset C1D1: 5.8% C1D8: 11.8% C1D15: 42.8% C1D22: 4.9% C3+ 3%			Median time (h) to CRS onset All doses: 24 C1D15: 20		Time course for CRS onset C1D8: 42.8% C1D15: 25.2% C2: 26% C3+: 0.9%			Median time (h) to CRS onset C1D8: 13.5 (range: 6-52)	

CRS: 44%

CRS 50% (DLBCL)
49% (FL)

CRS 63%

Crombie, Graff, Falchi, Karimi et al., Blood, 2024

Neurologic toxicity with BsAbs

Bispecific	Histology	N	ICANS (all)	ICANS (G3+)	Neuro AEs (all)	Neuro AEs (G2/3+)
Epcoritamab	LBCL	157	6%	1%	NA	NA
Glofitamab	NHL	171	5.7%	0	43.3%	NA
Glofitamab	LBCL	154	8%	3%	NA	NA
Mosunetuzumab	NHL	270	NA	NA	39%	4%
Mosunetuzumab	FL	90	5%	0%	NA	NA
Odronextamab	FL	128	1%	0%	NA	NA
Odronextamab	LBCL	141	0%	0%	NA	NA

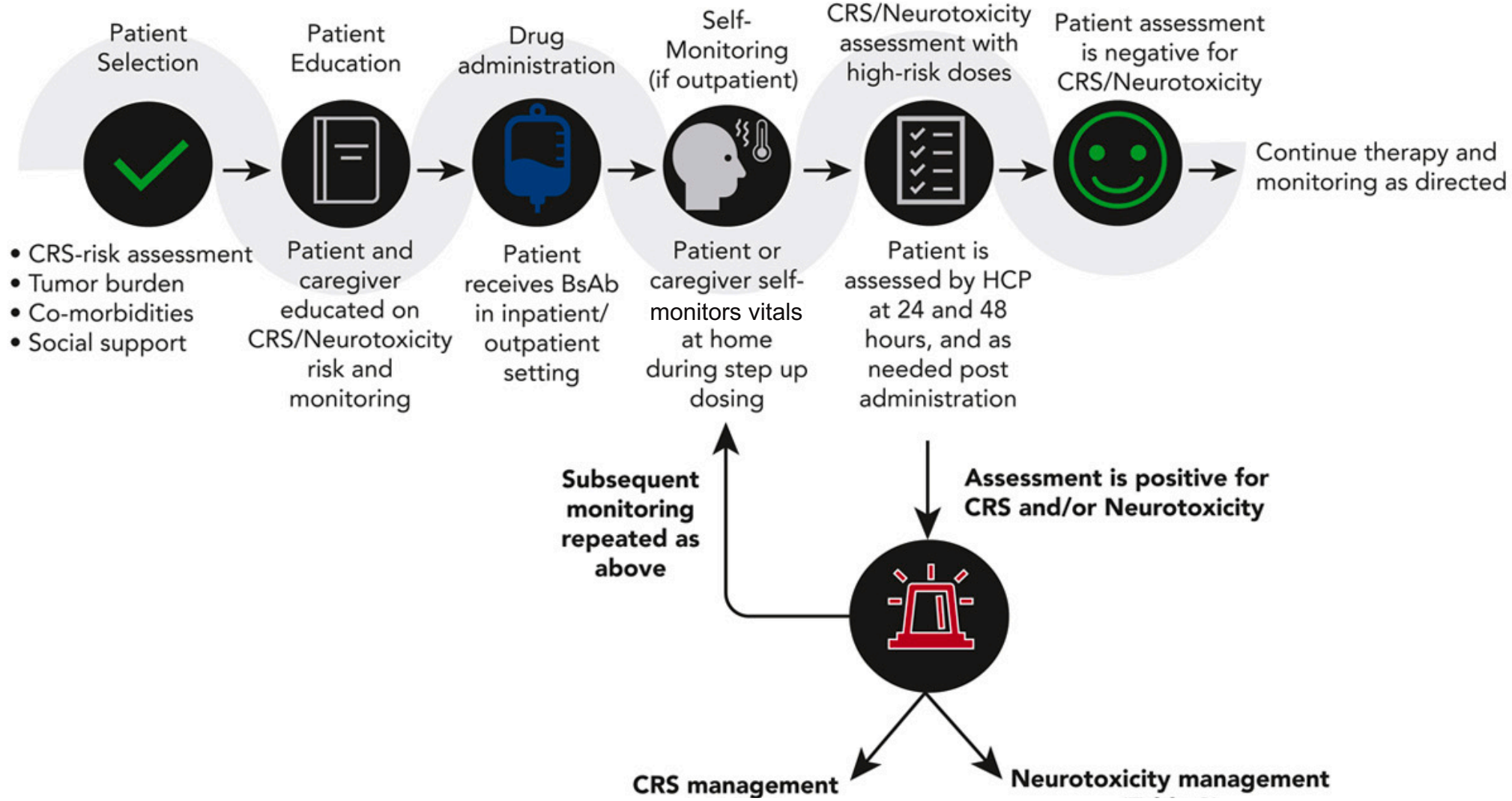
Thieblemont et al. JCO, 2022, Hutchings et al. JCO, 2021, Dickinson et al., NEJM, 2022, Budde et al., JCO, 2022, Budde et al., Lancet Oncol, 2022, Kim et al., Ann. Oncol., 2024, Ayyappan et al., ASH, 2023

Management of Toxicity

Consensus recommendations on the management of toxicity associated with CD3×CD20 bispecific antibody therapy

Jennifer L. Crombie,[1,*] Tara Graff,[2,*] Lorenzo Falchi,[3,*] Yasmin H. Karimi,[4,*] Rajat Bannerji,[5] Loretta Nastoupil,[6] Catherine Thieblemont,[7] Renata Ursu,[8] Nancy Bartlett,[9] Victoria Nachar,[4] Jonathan Weiss,[4] Jane Osterson,[2] Krish Patel,[10] Joshua Brody,[11] Jeremy S. Abramson,[12] Matthew Lunning,[13] Nirav N. Shah,[14] Ayed Ayed,[15] Manali Kamdar,[16] Benjamin Parsons,[17] Paolo Caimi,[18] Ian Flinn,[19] Alex Herrera,[20] Jeffrey Sharman,[21] Marshall McKenna,[5] Philippe Armand,[1] Brad Kahl,[9] Sonali Smith,[5,22] Andrew Zelenetz,[3] Lihua Elizabeth Budde,[20,†] Martin Hutchings,[23,†] Tycel Phillips,[4,†] and Michael Dickinson[24,†]

Toxicity Management Overview



Crombie, Graff, Falchi, Karimi et al., Blood, 2024

Management of Grade 1 CRS

Home:

- Acetaminophen
- Oral hydration
- Monitor temperature (and other vitals if able) every 1-2 hours

Home versus outpatient/ED evaluation:

- If recurrent fever, consider dexamethasone 10 mg once
- Consider earlier administration of steroids and immediate in-person evaluation for patients with multiple disease risk factors or comorbidities
- Consider daily dexamethasone with persistent symptoms

Additional management:

- Tocilizumab with protracted fever (e.g. >48 hours despite corticosteroids).
- Early tocilizumab after trial of dexamethasone should be considered in patients with multiple medical risk factors

Crombie, Graff, Falchi, Karimi et al., Blood, 2024

Management of Grade 2 CRS

- Evaluation in-person
- Recommend inpatient management for most cases of Grade 2 CRS unless qualified outpatient day hospital/infusion center and no hypoxia.
- Acetaminophen
- Dexamethasone 10 mg every 12 hours
- IVF/O2
- Administer tocilizumab if symptoms persist despite IV fluids and dexamethasone (approximately 4-6 hours after dosing) or if clinically unstable. Consider alternative agent (e.g. anakinra or siltuximab) if persistent symptoms despite maximal dosing

Crombie, Graff, Falchi, Karimi et al., Blood, 2024

Management of Grade 3/4 CRS

- Emergent inpatient admission (floor/ICU)
- Acetaminophen
- Dexamethasone until resolution to grade ≤ 1, followed by taper
- Evaluate for sepsis and consider empiric antibiotics
- Administer tocilizumab and consider alternative agent (e.g. anakinra or siltuximab) if persistent CRS despite maximal dosing

Crombie, Graff, Falchi, Karimi et al., Blood, 2024

Management of neurologic toxicity

- Monitoring:
  - Baseline evaluation helpful
  - No need for ongoing neurologic monitoring

- Recommendations:
  - No driving restrictions for patients who feel well

- Management:
  - Follow management for ICANS developed for CAR T-cell therapy if occurs
  - Consider alternative causes

Crombie, Graff, Falchi, Karimi et al., Blood, 2024

Other toxicities

- Tumor flare (0-7% across studies)
  - Consider inpatient treatment for high-risk patients
  - Early recognition
  - Steroids

- Cytopenias (neutropenia in 20-30% of patients across studies)
  - Growth factor as needed

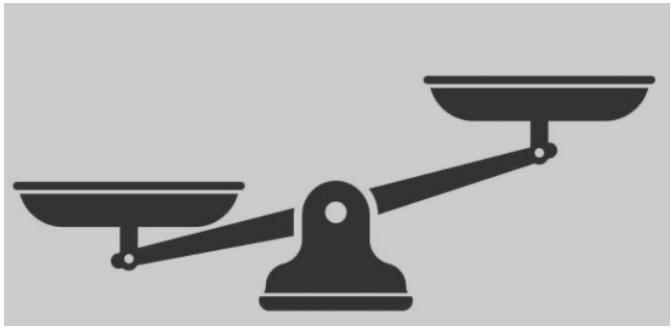
- Infections (20-30% across studies)
  - PCP and VZV prophylaxis recommended
  - Risk of viral infections (ie COVID-19)
  - Monitor for hypogammaglobulinemia, IVIG as needed

Thieblemont et al. JCO, 2022, Hutchings et al. JCO, 2021, Dickinson et al., NEJM, 2022, Budde et al., JCO, 2022, Budde et al., Lancet Oncol, 2022, Kim et al., Ann. Oncol., 2024, Ayyappan et al., ASH, 2023

CAR T-cell therapy versus bispecific antibody

Bispecific Antibodies

- Long-term follow-up required
- Need for longer treatment
- Ramp up for administration
- Off the Shelf
- Potential for community administration
- Lower CRS, ICANS



CAR T-Cell Therapy

- Manufacturing required
- Exclusive to specialized centers
- Logistics/caregiver requirement
- Higher CRS,ICANS
- One time dose with hospitalization
- Long-term efficacy

What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of Acute Myeloid Leukemia

A CME Friday Satellite Symposium and Webcast Preceding the 66th ASH Annual Meeting

Friday, December 6, 2024

3:15 PM – 5:15 PM PT (6:15 PM – 8:15 PM ET)

Faculty

Alexander Perl, MD

Richard M Stone, MD

Eunice S Wang, MD

Andrew H Wei, MBBS, PhD

Moderator

Eytan M Stein, MD

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Professor Philippe Moreau, MD

Robert Z Orlowski, MD, PhD

Noopur Raje, MD

Paul G Richardson, MD

Moderator

Sagar Lonial, MD

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