Challenging Cases from the Community: Investigators Provide Perspectives on the Optimal Management of Diffuse Large B-Cell Lymphoma

A CME/MOC-Accredited Virtual Event

Tuesday, September 13, 2022

5:00 PM – 6:00 PM ET

Faculty

Jeremy Abramson, MD
Sonali M Smith, MD
Jason Westin, MD, MS

Moderator

Neil Love, MD

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Faculty

Jeremy Abramson, MD
Director, Center for Lymphoma
Massachusetts General Hospital
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Jason Westin, MD, MS
Director, Lymphoma Clinical Research
Section Chief, Aggressive Lymphoma
Department of Lymphoma and Myeloma
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Sonali M Smith, MD
Elwood V Jensen Professor of Medicine
Chief, Section of Hematology/Oncology
Co-Leader, Cancer Service Line
Co-Director, Lymphoma Program
The University of Chicago
Chicago, Illinois

MODERATOR
Neil Love, MD
Research To Practice

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This activity will also be featured as an "On Demand" session as part of the Society of Hematologic Oncology 2022 Annual Meeting.

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TO PRACTICE

Management of DLBCL
Where We Are, Where We're Headed

Accreditation Information

Target Audience

This activity is intended for hematologists, hematology-oncology fellows, medical oncologists, radiation oncologists and other healthcare providers involved in the treatment of diffuse large B-cell lymphoma.

Educational Objectives

Upon completion of this activity, participants should be able to

- Apply available clinical research findings in the formulation of evidence-based therapeutic approaches for the treatment of newly diagnosed and relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL).
- Appraise published Phase III clinical trial data documenting the benefit of CD79b-targeted therapy as a component of first-line treatment for patients with DLBCL, and consider the implications of these findings for current clinical management algorithms.
- Appreciate long-term efficacy and safety data with FDA-approved chimeric antigen receptor (CAR) T-cell therapies directed at CD19, and identify patients with R/R DLBCL for whom this approach may be warranted.
- Assess Phase III clinical trial data documenting the benefit of various CAR T-cell platforms as second-line therapy for patients with R/R DLBCL, and consider the potential application of these findings in routine clinical decision-making.
- Review pivotal clinical trial findings leading to the FDA approval of other novel compounds with unique mechanisms of action for R/R DLBCL, and identify patients for whom treatment with these approaches would be appropriate.
- Compare and contrast the side effects associated with available and emerging therapeutic strategies for DLBCL, and formulate supportive care plans to minimize and manage these toxicities.
- Recall ongoing clinical research evaluating novel agents and strategies for DLBCL, and counsel appropriate patients regarding the potential benefits of trial participation.

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Accreditation Information

In support of improving patient care, this activity has been planned and implemented by Medical Learning Institute, Inc. and Research To Practice. Medical Learning Institute, Inc. is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Physician Continuing Medical Education

Medical Learning Institute, Inc. (MLI) designates this live activity for a maximum of 1.0 *AMA PRA Category 1 Credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

MOC Statement

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.0 MOC point in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Participation information will be shared through the ACCME's Program and Activity Reporting System (PARS).

Support Statement

This CE activity is supported through educational grants from Genentech, a member of the Roche Group, and Kite, A Gilead Company.

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Dr Love — Disclosures

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Contracted Research	AbbVie Inc, Bristol-Myers Squibb Company, Genentech, a member of the Roche Group, Seagen Inc

Dr Smith — Disclosures

Consulting Agreements	Adaptive Biotechnologies Corporation, ADC Therapeutics, Bantam, Bristol-Myers Squibb Company, Gamida Cell, Gilead Sciences Inc, Janssen Biotech Inc, Karyopharm Therapeutics, MorphoSys
Contracted Research	Acerta Pharma — A member of the AstraZeneca Group, Bristol-Myers Squibb Company, Celgene Corporation, Epizyme Inc, Forty Seven Inc, Genentech, a member of the Roche Group, Karyopharm Therapeutics, Pharmacyclics LLC, an AbbVie Company, Portola Pharmaceuticals Inc, TG Therapeutics Inc
Speaking Engagement	ADC Therapeutics ICML

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Dr Westin — Disclosures

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Contracted Research	ADC Therapeutics, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Calithera Biosciences, Genentech, a member of the Roche Group, Incyte Corporation, Kite, A Gilead Company, MorphoSys, Novartis

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Disclaimer

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this CE activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed or suggested in this CE activity should not be used by clinicians without evaluation of their patient's conditions and possible contraindications and/or dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

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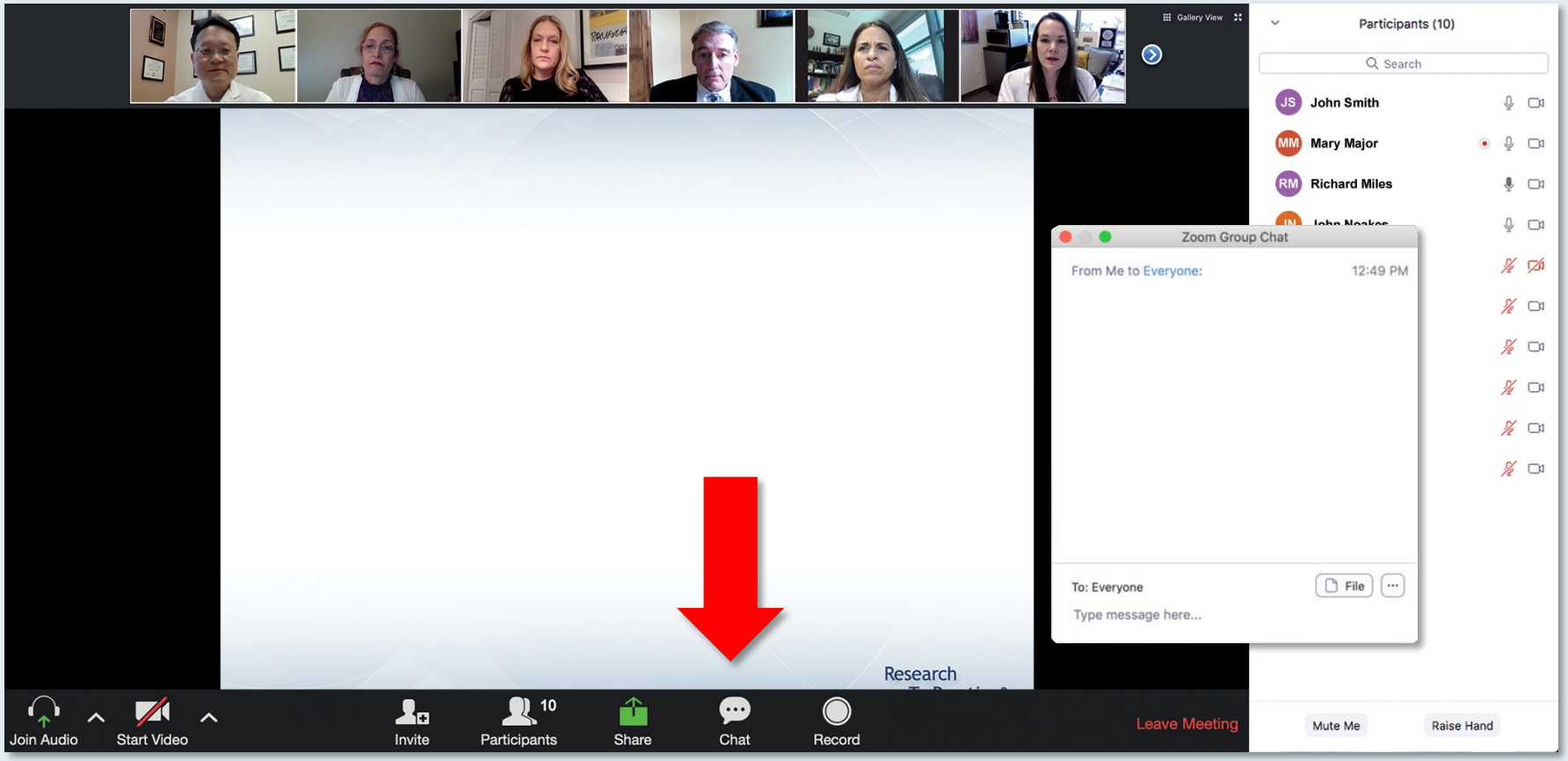
We Encourage Clinicians in Practice to Submit Questions



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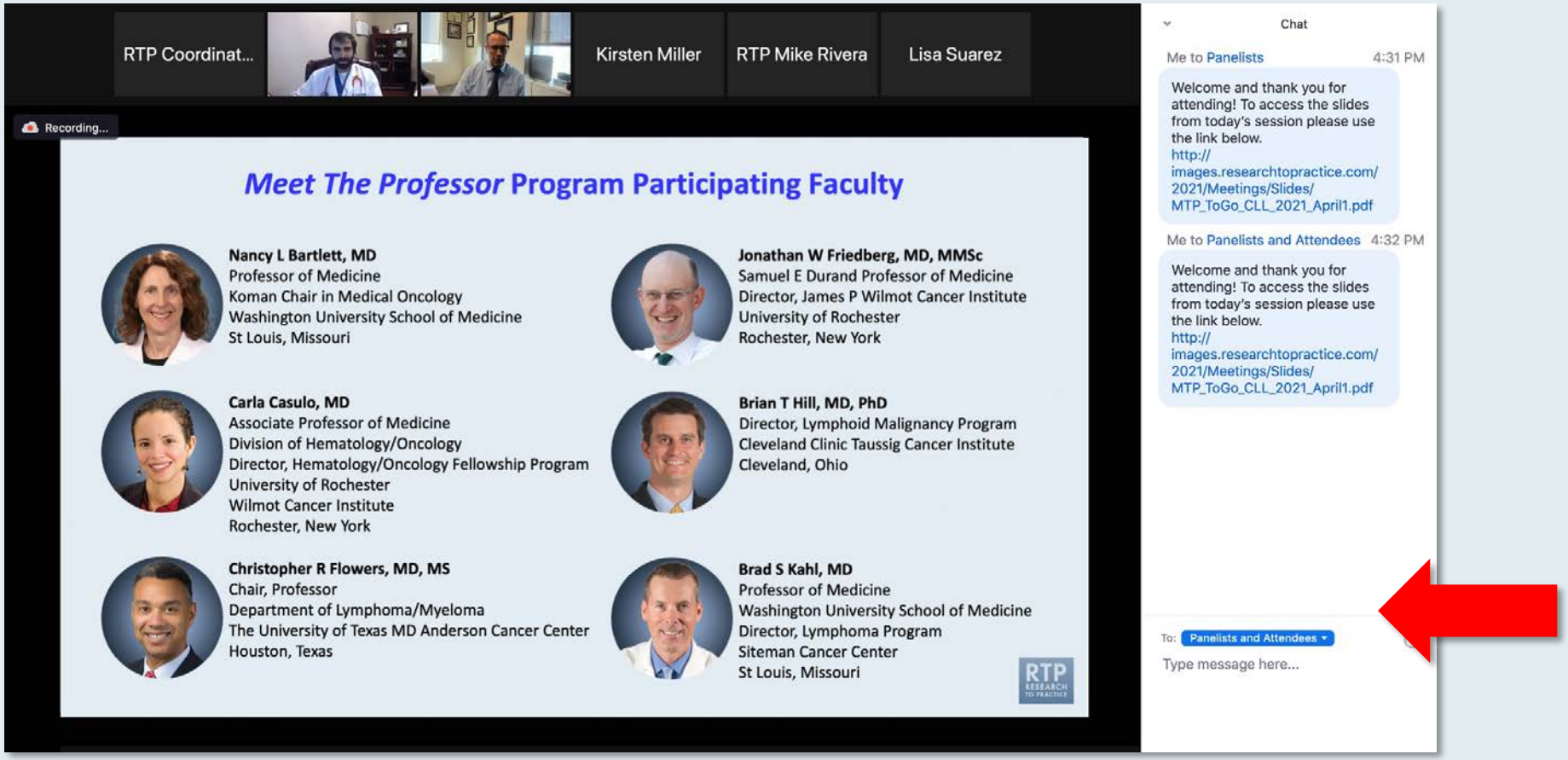
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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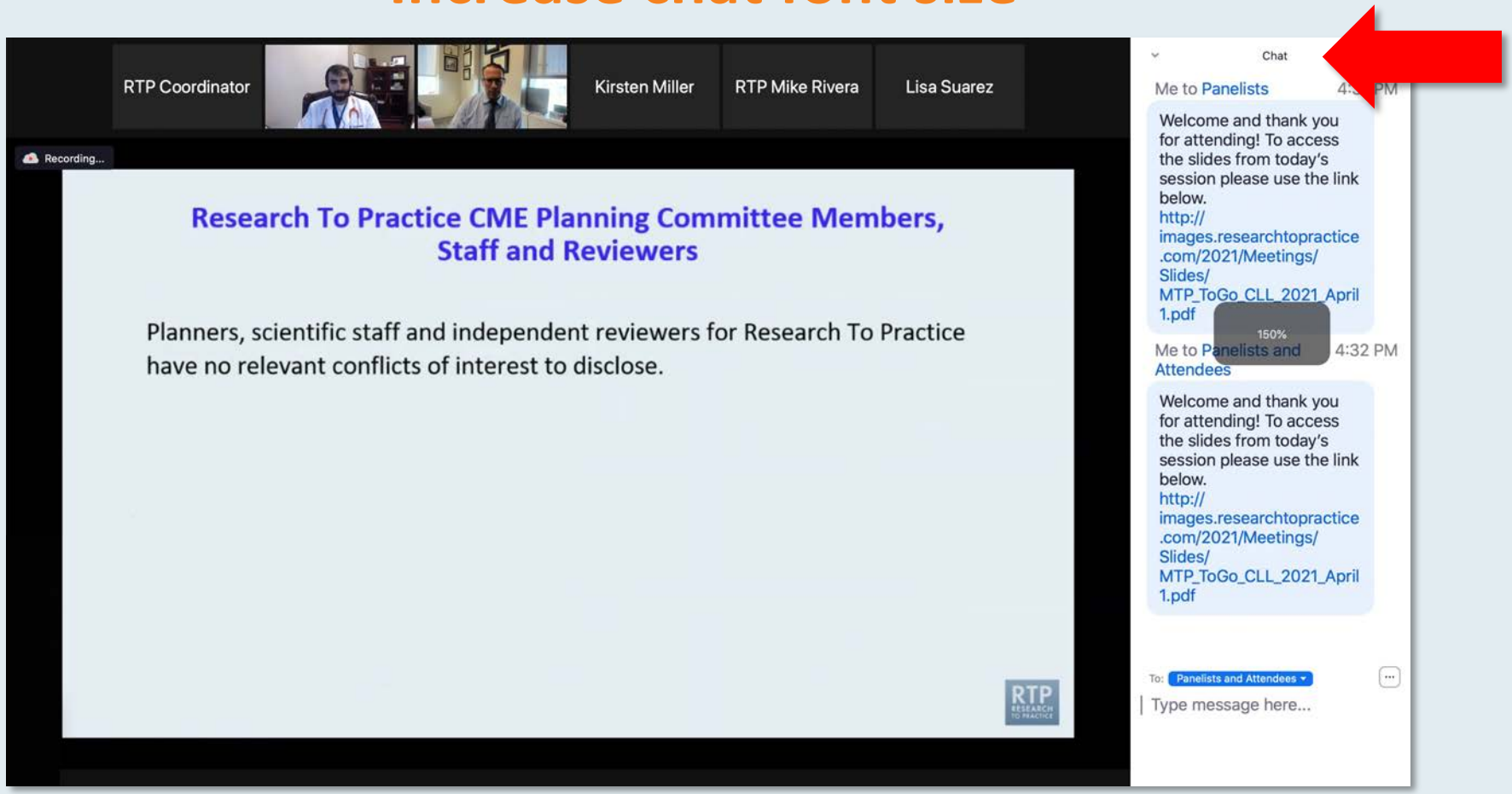

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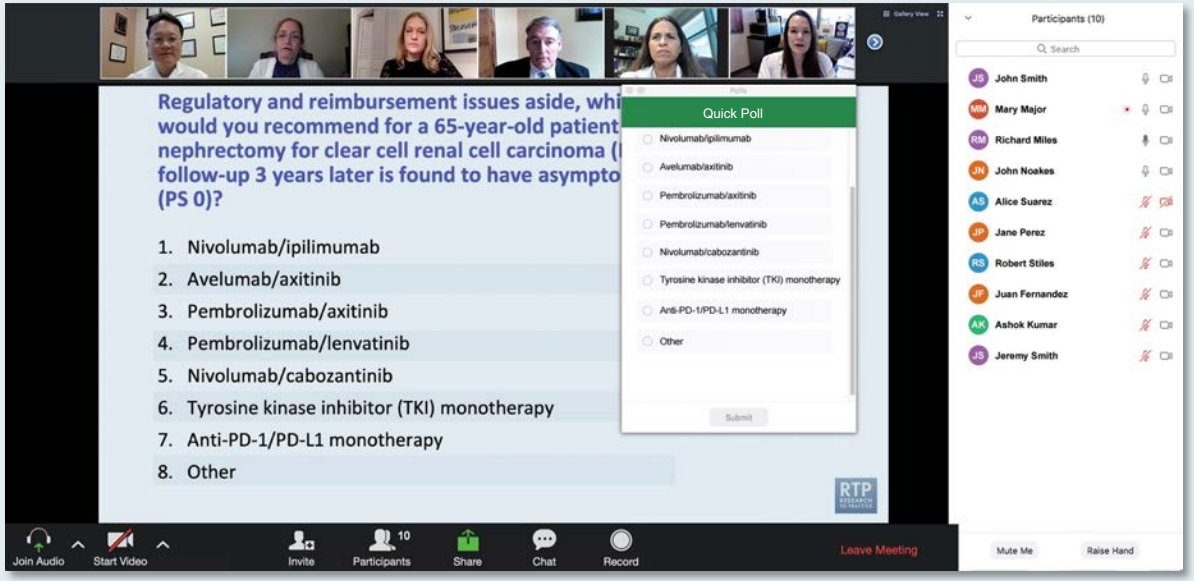

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ONCOLOGY TODAY™

WITH DR NEIL LOVE

Current and Future Management of Follicular Lymphoma

DR LORETTA NASTOUPIL

THE UNIVERSITY OF TEXAS
MD ANDERSON CANCER

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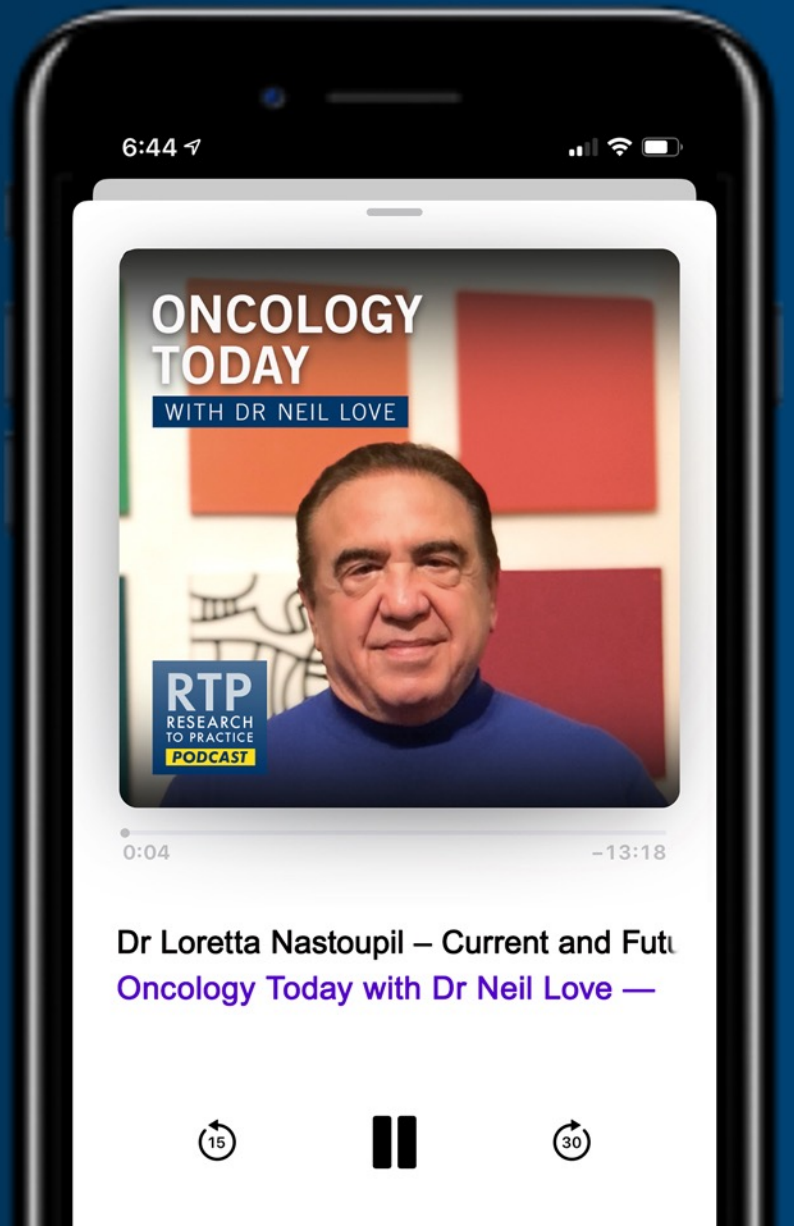

Oncology Today™ with Dr Neil Love — Management of Endometrial Cancer

A CME/MOC-Accredited Virtual Event

Wednesday, September 14, 2022
5:00 PM – 6:00 PM ET

Faculty

Michael J Birrer, MD, PhD

Moderator

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Meet The Professor

Optimizing the Management of Head and Neck and Thyroid Cancers

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5:00 PM – 6:00 PM ET

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The Clinical Implications of Key Recent Data Sets in Oncology: A Daylong Multitumor Educational Symposium in Partnership with Florida Cancer Specialists

Saturday, October 22, 2022

7:30 AM – 5:30 PM ET

JW Marriott Orlando| Orlando, Florida

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Matthew P Goetz, MD
Ian E Krop, MD, PhD
Ann S LaCasce, MD, MMSc
Corey J Langer, MD
Prof Georgina Long, AO, BSc, PhD, MBBS
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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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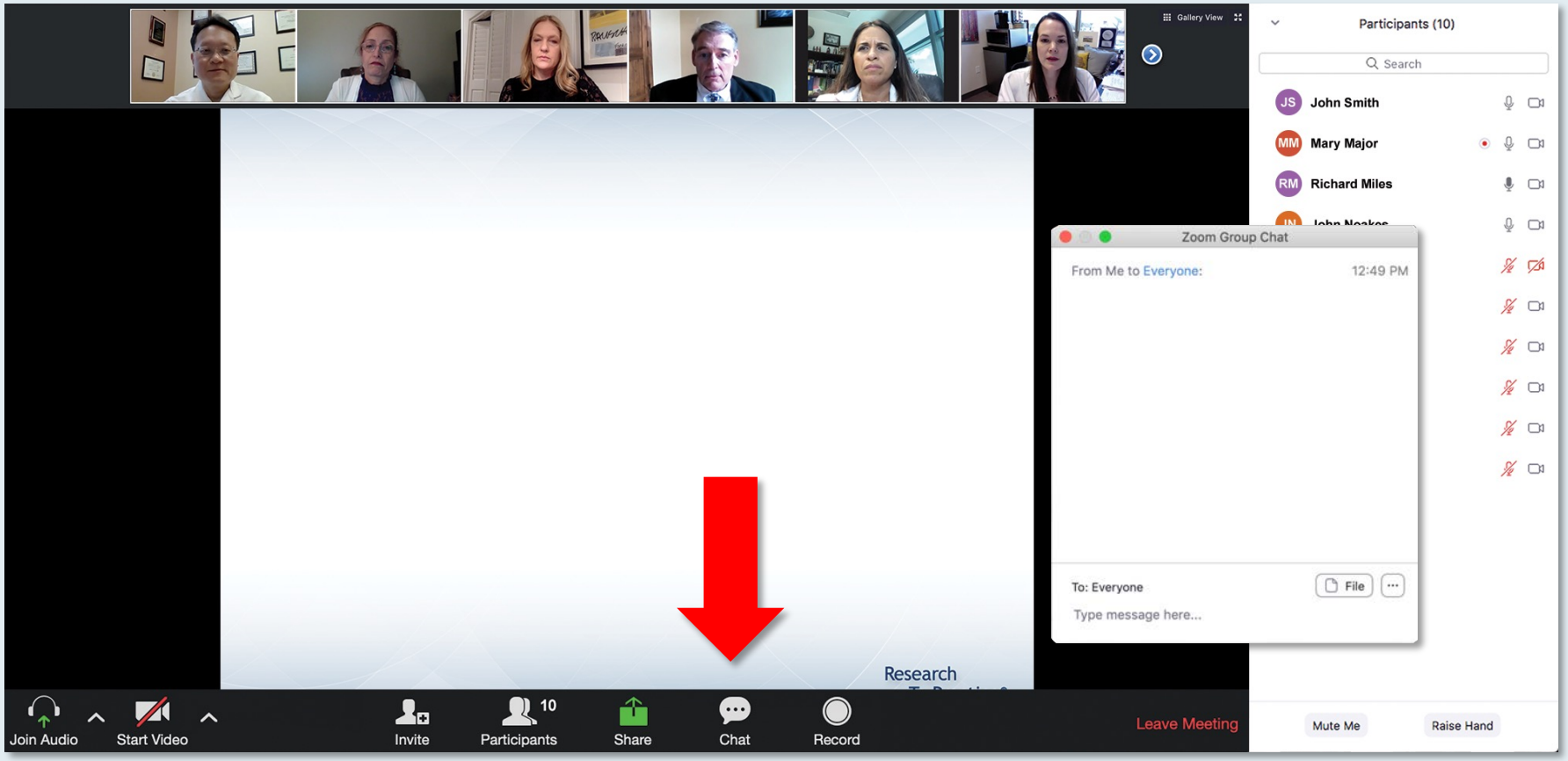

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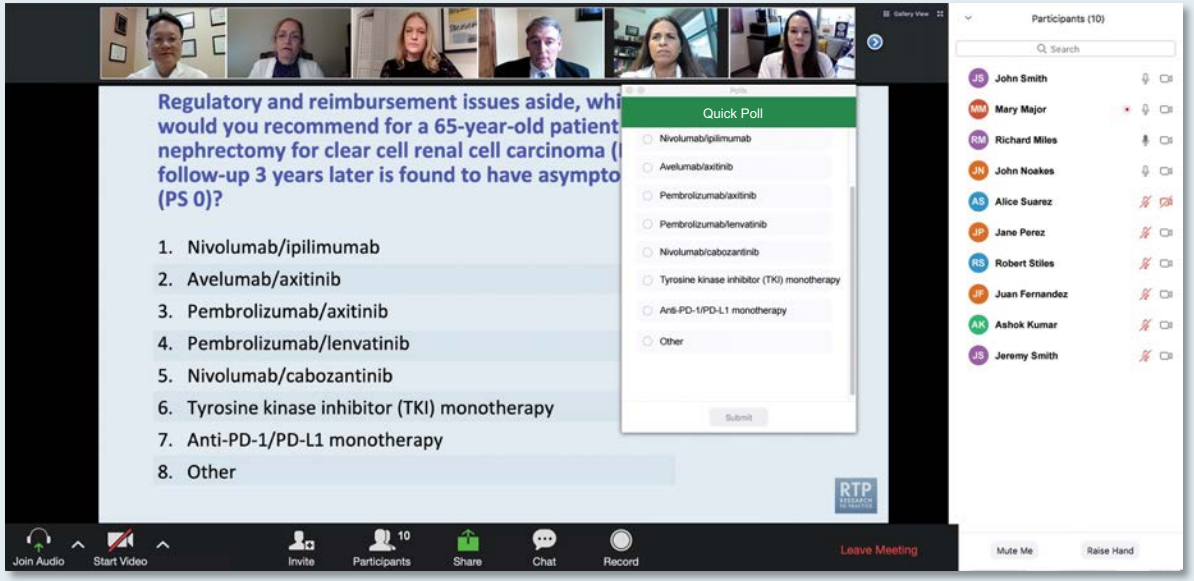

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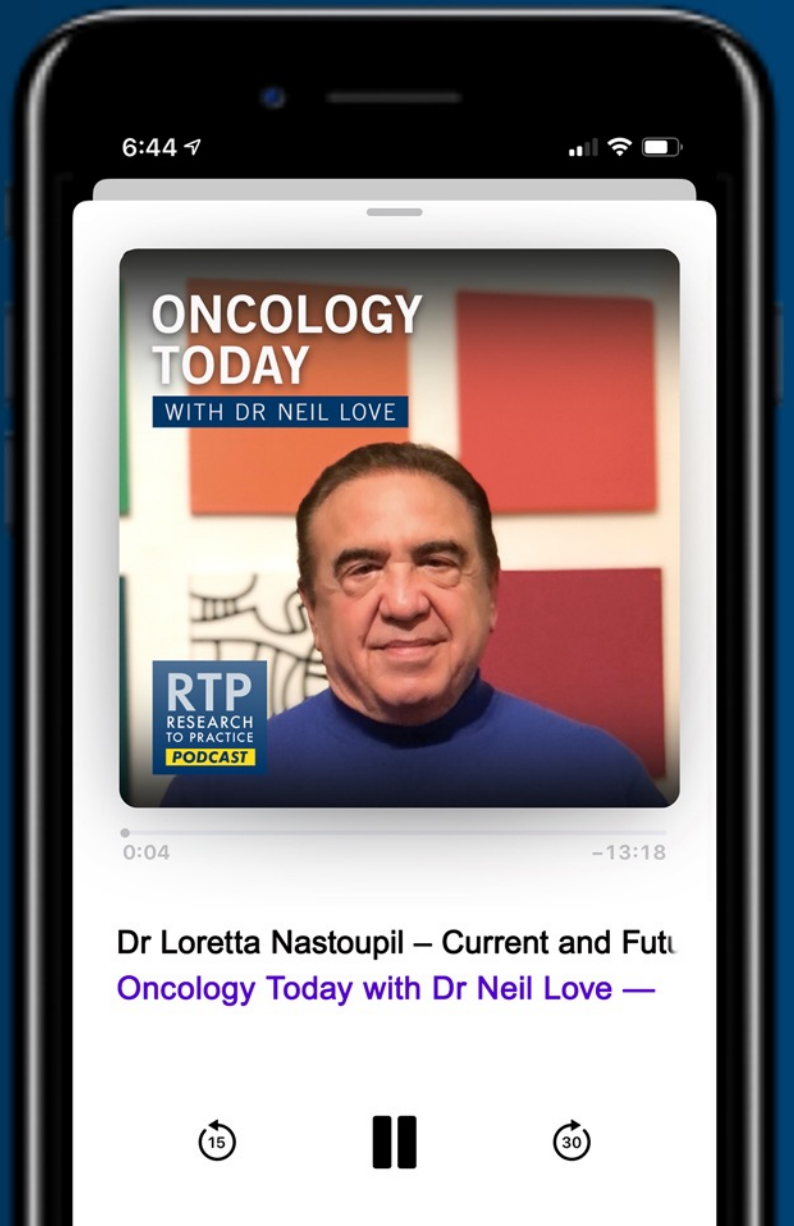

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Management of DLBCL
Where We Are, Where We're Headed

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Clinical Cases

Dr Morganstein: 43-year-old man with newly diagnosed GCB-subtype Stage III DLBCL

Dr Parsons: 59-year-old woman with Stage IV double-hit DLBCL and extensive bone involvement

Dr Choksi: 77-year-old symptomatic man with longstanding CLL and Richter's transformation

Dr Ku: 66-year-old woman with newly diagnosed nonbulky Stage II DLBCL

Dr Morganstein: 75-year-old man with a history of severe CHF with a pulmonary nodule and regional adenopathy that on biopsy is proven to be DLBCL

Dr Yang: 73-year-old woman with rapid relapse after R-CHOP then R-ICE/ASCT achieves a CR with CAR T-cell therapy but experiences severe pancytopenia

Dr Mushtaq: 45-year-old man with R-CHOP-refractory DLBCL receives polatuzumab vedotin as bridging therapy → CAR T-cell therapy on protocol

Dr Gupta: 68-year-old man with cardiac comorbidities and relapsed DLBCL while on R-CHOP receives second-line polatuzumab vedotin/BR

Accreditation Information

Target Audience

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Educational Objectives

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Management of DLBCL
Where We Are, Where We're Headed

PROLOGUE

MODULE 1: First-Line Treatment

MODULE 2: Bispecific Antibodies

MODULE 3: CAR T-Cell Therapy

MODULE 4: Sequencing of Novel Agents

MODULE 5: Appendix

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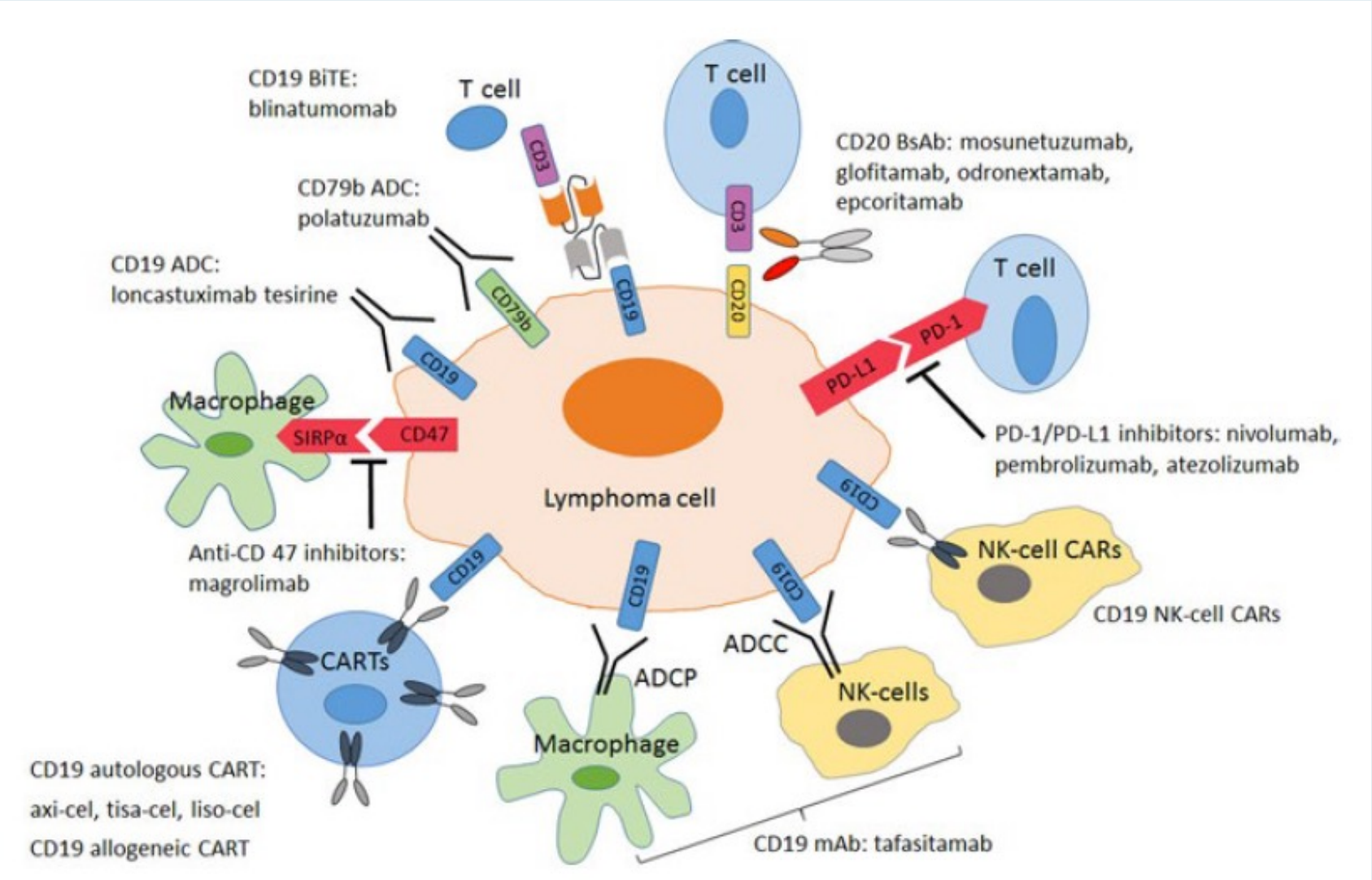
Randomized Phase III Trials Against R-CHOP for DLBCL

Trial	Comparator arm	N	Study population	PFS (experimental vs standard)
R-CHOP	R-CHOP14	602	60-80 y, aaIPI≥1	60% vs 62% (3y)
GOYA	G-CHOP	1,418	≥18 y, Stage II-IV	70% vs 67% (3y)
PHOENIX	R-CHOP + ibrutinib	838	≥18 y, Stage II-IV, non-GCB, IPI ≥2	71% vs 68% (3y)
ROBUST	R-CHOP + lenalidomide	570	≥18 y, Stage II-IV, non-GCB, IPI ≥2	67% vs 64% (3y)
CALGB-50203	DA-EPOCH-R	524	≥18 y, Stage II-IV	79% vs 76% (2y)
REMoDL-B	R-CHOP + bortezomib	918	≥18 y	75% vs 71% (2y)

Content Courtesy of Neha Mehta-Shah, MD, MSCI

Evolving Landscape of Customized Engineered and Off-the-Shelf Immunotherapies for Aggressive B-Cell Non-Hodgkin Lymphoma



ADCC = antibody-dependent cell cytotoxicity

ADCP = antibody-dependent cellular phagocytosis

BiTE = bispecific T-cell engager

PD-1 = programmed cell death 1

PD-L1 = programmed cell death ligand 1

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Important Recent Developments in DLBCL

- **POLARIX Phase III Trial**
  - Polatuzumab vedotin
- **CAR T-Cell Therapy in the Second-Line Setting**
  - Axicabtagene ciloleucel
  - Lisocabtagene maraleucel
  - Tisagenlecleucel
- **Bispecific Antibodies**
  - Glofitamab
  - Mosunetuzumab
  - Epcoritamab
  - Odronextamab

Management of DLBCL
Where We Are, Where We're Headed

PROLOGUE

MODULE 1: First-Line Treatment

Dr Morganstein: 43-year-old man with newly diagnosed GCB-subtype Stage III DLBCL

Dr Parsons: 59-year-old woman with Stage IV double-hit DLBCL and extensive bone involvement

Dr Choksi: 77-year-old symptomatic man with longstanding CLL and Richter's transformation

Dr Ku: 66-year-old woman with newly diagnosed nonbulky Stage II DLBCL

MODULE 2: Bispecific Antibodies

MODULE 3: CAR T-Cell Therapy

MODULE 4: Sequencing of Novel Agents

MODULE 5: Appendix

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Case Presentation: 43-year-old man with newly diagnosed GCB-subtype Stage III DLBCL

Dr Neil Morganstein (Summit, New Jersey)

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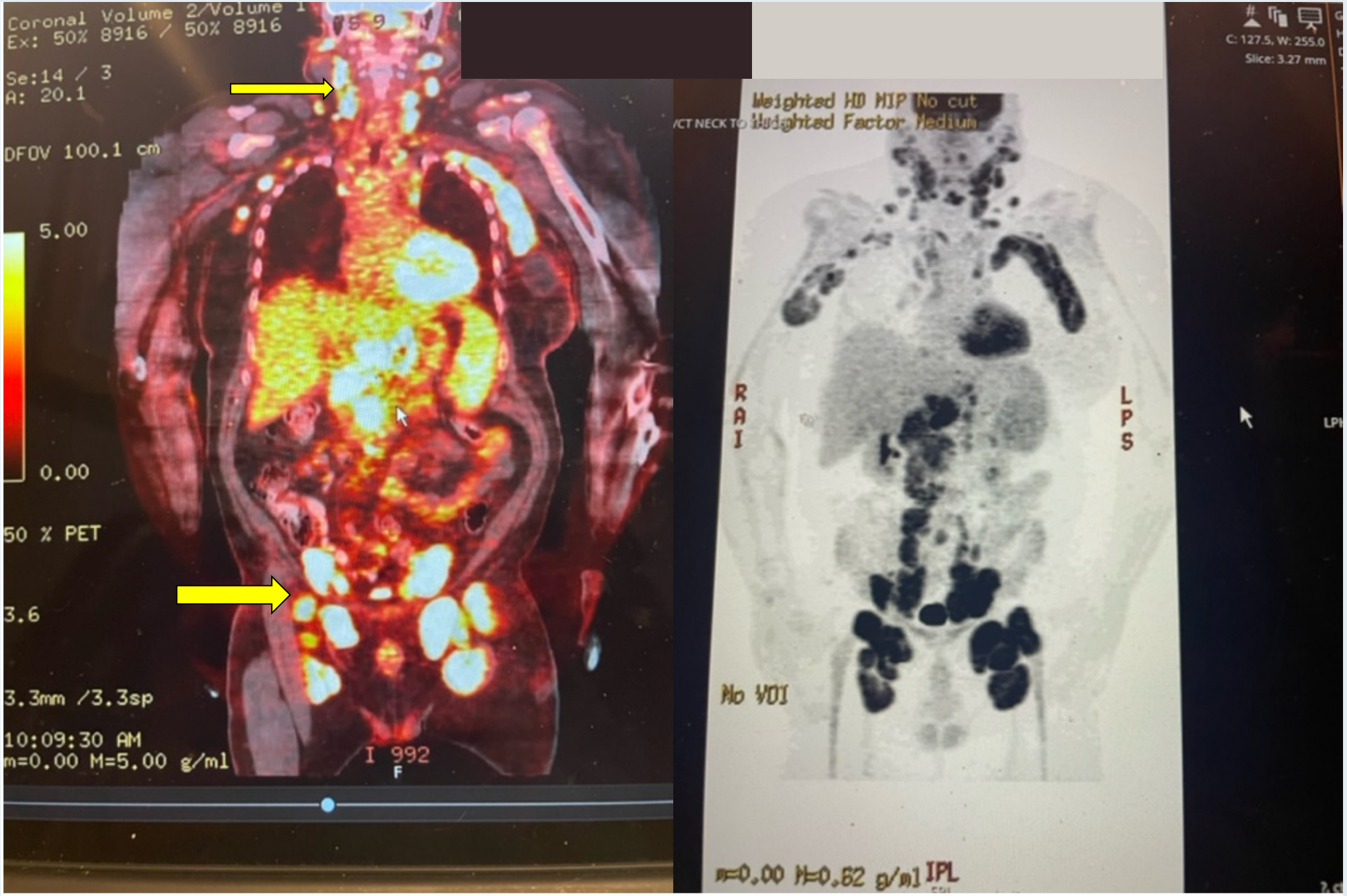
Coronal Volume 2/Volume 1
Ex: 50% 8916 / 50% 8916
Se:14 / 3
A: 20.1
DFOV 100.1 cm
5.00
0.00
50 % PET
3.6
3.3mm /3.3sp
10:09:30 AM
m=0.00 M=5.00 g/ml
I 992
F
Weighted HD MIP No cut
Weighted Factor Medium
R
A
I
L
P
S
No VOI
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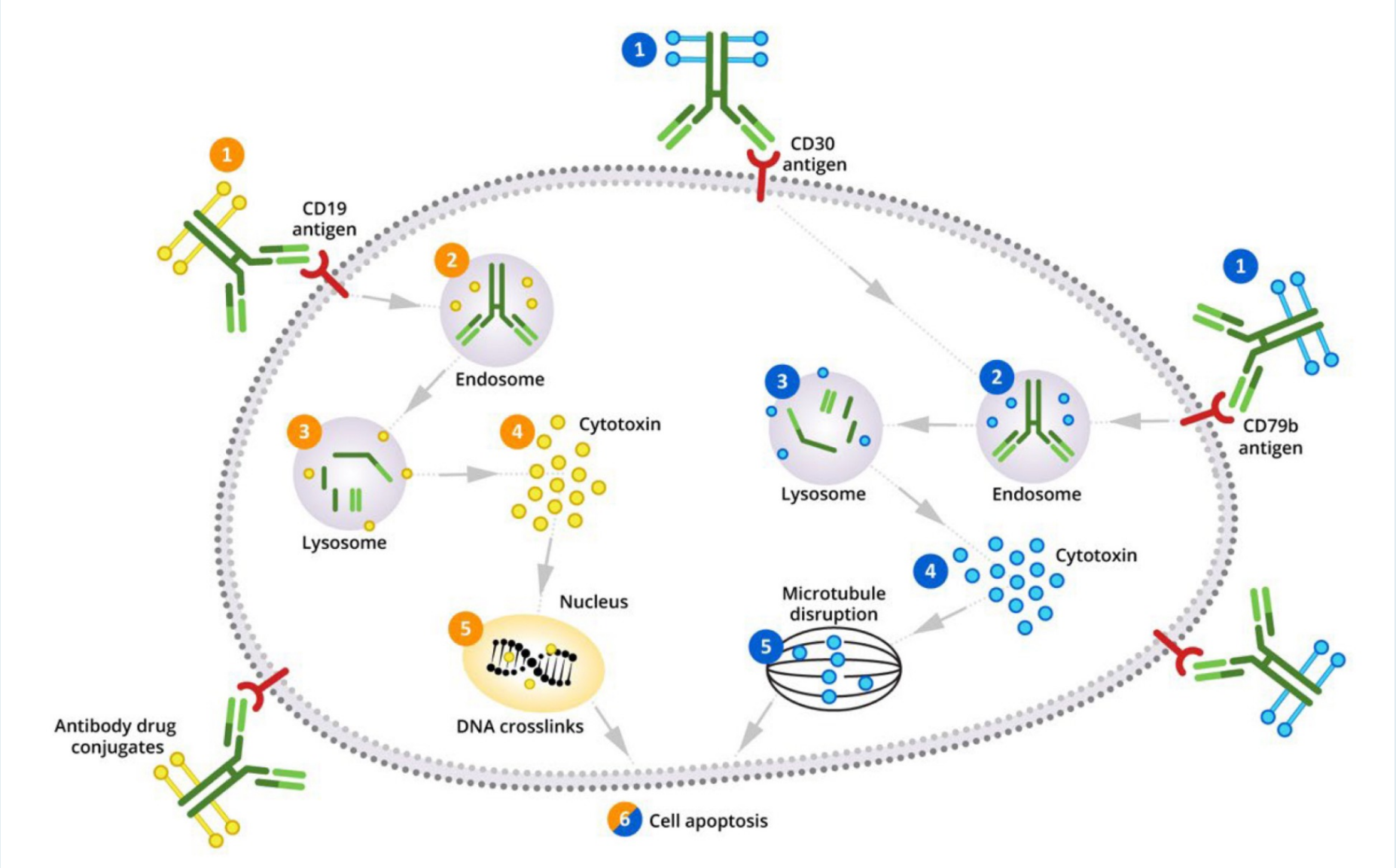
C: 127.5, W: 255.0
Slice: 3.27 mm

Antibody-Drug Conjugate Mechanism of Action in DLBCL



Alderuccio JP, Sharman JP. *Blood Rev* 2022;[Online ahead of print].

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N Engl J Med 2022;386(4):351-63.
The NEW ENGLAND JOURNAL of MEDICINE

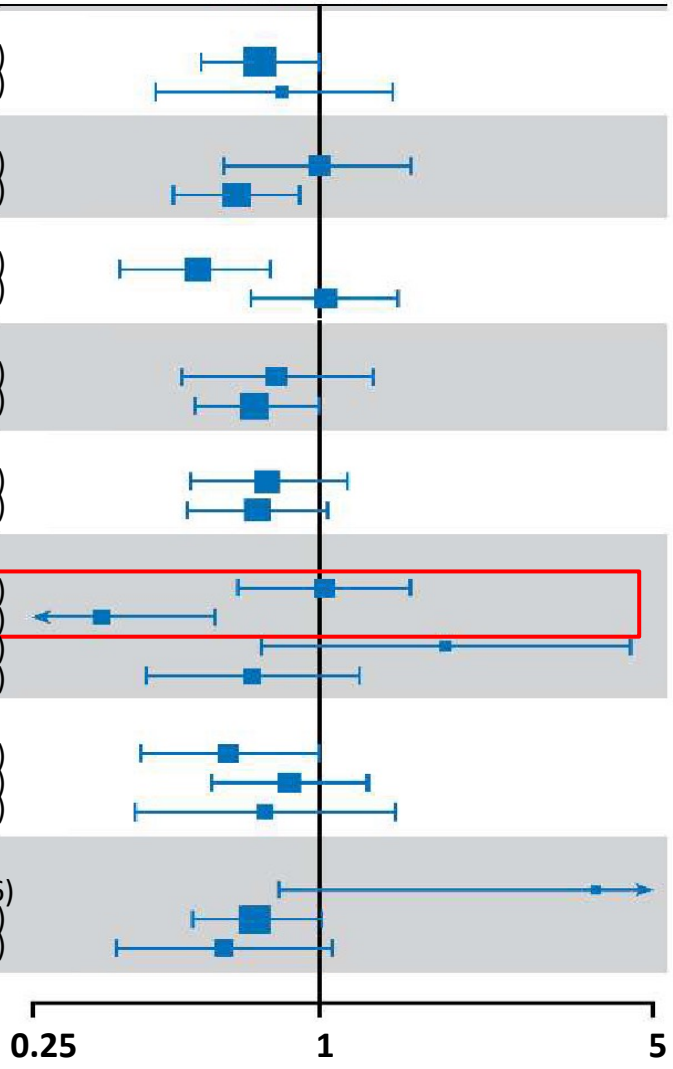
ORIGINAL ARTICLE

Polatuzumab Vedotin in Previously Untreated Diffuse Large B-Cell Lymphoma

H. Tilly, F. Morschhauser, L.H. Sehn, J.W. Friedberg, M. Trněný, J.P. Sharman, C. Herbaux, J.M. Burke, M. Matasar, S. Rai, K. Izutsu, N. Mehta-Shah, L. Oberic, A. Chauchet, W. Jurczak, Y. Song, R. Greil, L. Mykhalska, J.M. Bergua-Burgués, M.C. Cheung, A. Pinto, H.-J. Shin, G. Hapgood, E. Munhoz, P. Abrisqueta, J.-P. Gau, J. Hirata, Y. Jiang, M. Yan, C. Lee, C.R. Flowers, and G. Salles

POLARIX: Subgroup Analysis

Baseline Risk Factors	Total N	Pola-R-CHP (N=440) n	Pola-R-CHP (N=440) 2-year Rate	R-CHOP (N=439) n	R-CHOP (N=439) 2-year Rate	Hazard Ratio	95% Wald CI
ECOG PS							
0-1	737	374	78.4	363	71.2	0.8	(0.6 to 1.0)
2	141	66	67.2	75	65.0	0.8	(0.5 to 1.4)
IPI score							
IPI 2	334	167	79.3	167	78.5	1.0	(0.6 to 1.6)
IPI 3-5	545	273	75.2	272	65.1	0.7	(0.5 to 0.9)
Bulky disease							
Absent	494	247	82.7	247	70.7	0.6	(0.4 to 0.8)
Present	385	193	69.0	192	69.7	1.0	(0.7 to 1.5)
Baseline LDH							
≤ULN	300	146	78.9	154	75.6	0.8	(0.5 to 1.3)
>ULN	575	291	75.4	284	67.2	0.7	(0.5 to 1.0)
No. of extranodal sites							
0-1	453	227	80.2	226	74.5	0.8	(0.5 to 1.1)
≥2	426	213	73.0	213	65.8	0.7	(0.5 to 1.0)
Cell-of-origin							
GCB	352	184	75.1	168	76.9	1.0	(0.7 to 1.5)
ABC	221	102	83.9	119	58.8	0.4	(0.2 to 0.6)
Unclassified	95	44	73.0	51	86.2	1.9	(0.8 to 4.5)
Unkown	211	110	73.8	101	64.3	0.7	(0.4 to 1.2)
Double expressor by IHC							
DEL	290	139	75.5	151	63.1	0.6	(0.4 to 1.0)
Non DEL	438	223	77.7	215	75.7	0.9	(0.6 to 1.3)
Unknown	151	78	76.0	73	69.8	0.8	(0.4 to 1.5)
Double- or triple-hit lymphoma							
Yes	45	26	69.0	19	889	3.8	(0.8 to 17.6)
No	620	305	76.8	315	70.3	0.7	(0.5 to 1.0)
Unknown	214	109	78.5	105	66.4	0.6	(0.4 to 1.1)



Tilly H et al. *N Engl J Med* 2022;386(4):351-63.

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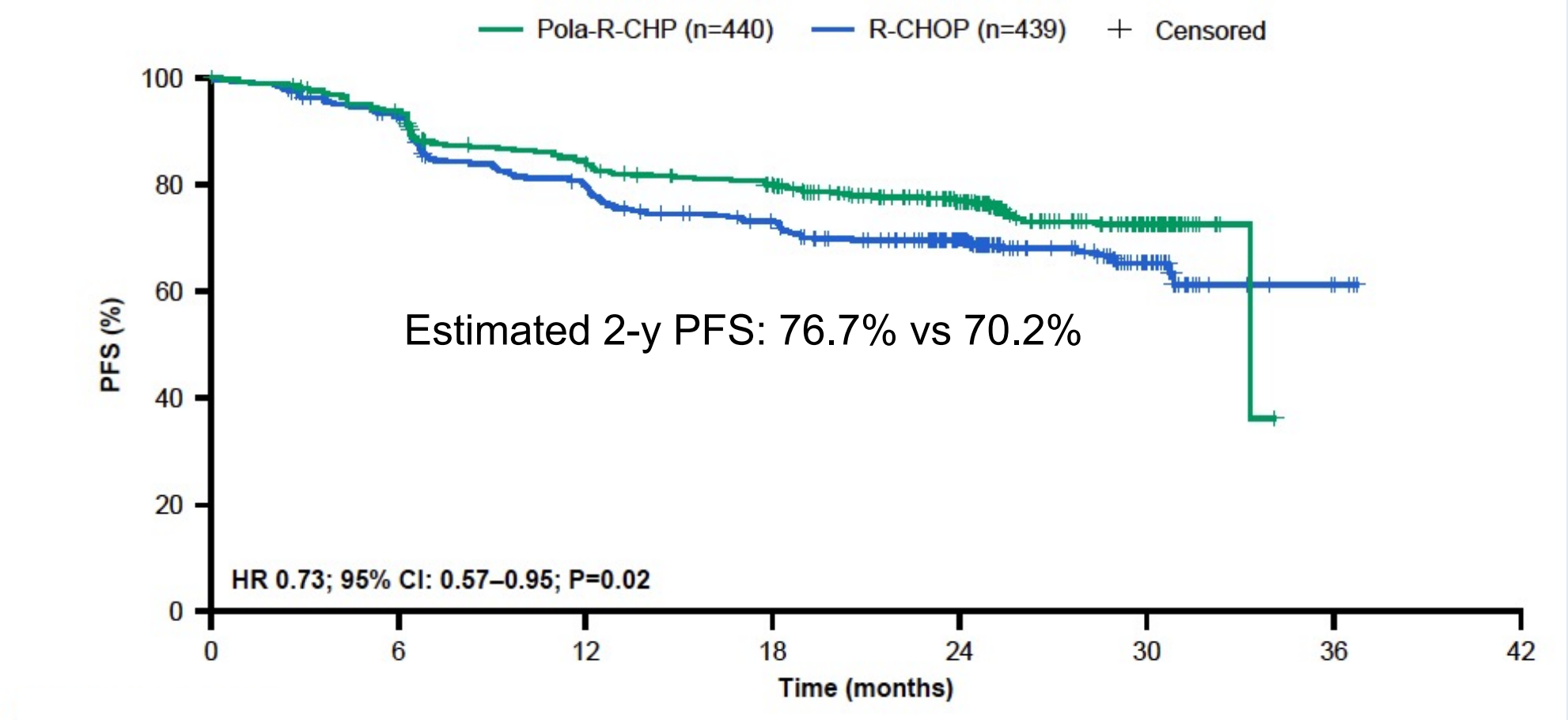
Polatuzumab Vedotin plus Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone (Pola-R-CHP) Versus Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (R-CHOP) Therapy in Patients with Previously Untreated Diffuse Large B-cell Lymphoma (DLBCL): Results from the Phase III POLARIX Study

Neha Mehta-Shah,[1] Hervé Tilly,[2] Franck Morschhauser,[3] Laurie H. Sehn,[4] Jonathan W. Friedberg,[5] Marek Trněný,[6] Jeff P. Sharman,[7] Charles Herbaux,[8] John M. Burke,[9] Matthew Matasar,[10] Shinya Rai,[11] Koji Izutsu,[12] Lucie Oberic,[13] Adrien Chauchet,[14] Wojciech Jurczak,[15] Yuqin Song,[16] Richard Greil,[17] Larysa Mykhalska,[18] Juan Miguel Bergua-Burgués,[19] Matthew C. Cheung,[20] Antonio Pinto,[21] Ho-Jin Shin,[22] Greg Hapgood,[23] Eduardo Munhoz,[24] Pau Abrisqueta,[25] Jyh-Pyng Gau,[26] Jamie Hirata,[27] Yanwen Jiang,[27] Mark Yan,[28] Calvin Lee,[27] Christopher Flowers,[29] Gilles Salles[30]

Pan Pacific Lymphoma Conference 2022

POLARIX: Investigator-Assessed Progression-Free Survival (PFS) — Primary Endpoint



Mehta-Shah N et al. Pan Pacific Lymphoma Conference 2022.

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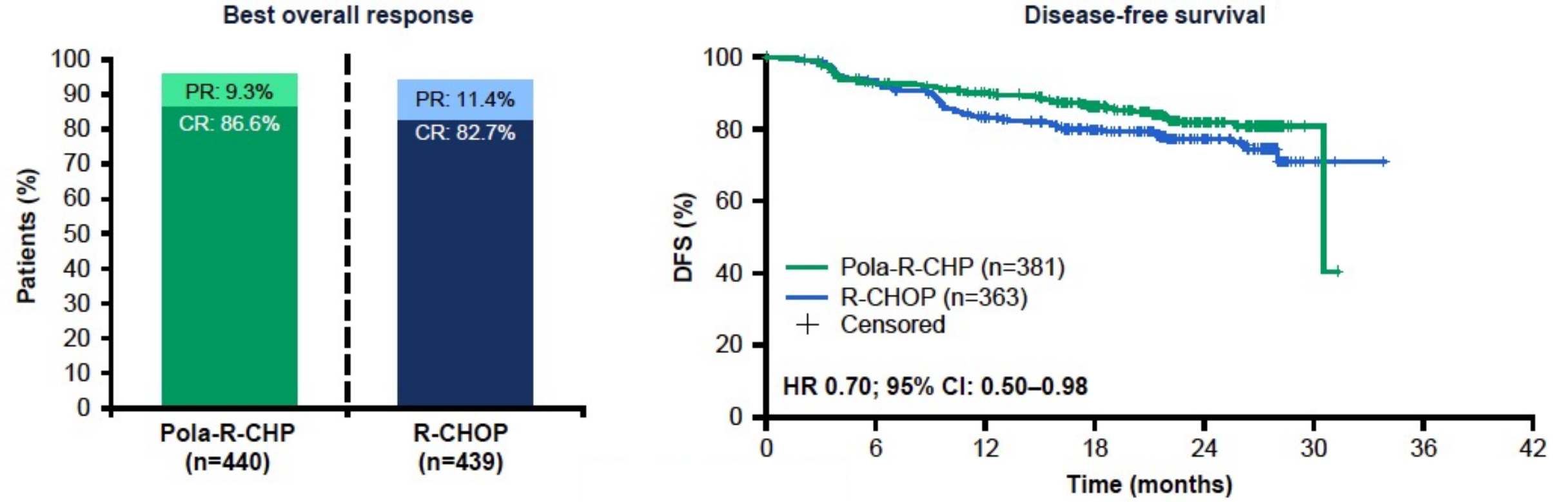
POLARIX: Key Secondary Endpoints



PR = partial response; CR = complete response

- There was no difference in overall survival between treatment arms

Mehta-Shah N et al. Pan Pacific Lymphoma Conference 2022.

P7517

ASCO 2022

Outcomes by BCL2 and MYC expression and rearrangements in untreated diffuse large B-cell lymphoma (DLBCL) from the POLARIX trial

Franck Morschhauser,[1] Yanwen Jiang,[2] Fabrice Jardin,[3] Alex F. Herrera,[4] Laurie H. Sehn,[5] Charles Herbaux,[6] Christopher Flowers,[7] Tycel Phillips,[8] Armando López Guillermo,[9] Catherine Diefenbach,[10] Gareth P. Gregory,[11] Austin Kim,[12] Anna Maria Barbui,[13] Sandhya Balasubramanian,[2] Will Harris,[2] Jamie Hirata,[2] Joseph N. Paulson,[2] Calvin Lee,[2] Georg Lenz[14]

Summary

POLARIX (NTC03274492) is a Phase III international study of Pola-R-CHP vs R-CHOP in patients with previously untreated DLBCL and IPI 2–5.

This is a **pre-specified exploratory analysis** of the prognostic significance of BCL2 and MYC protein expression, and *BCL2*, *BCL6*, and *MYC* gene rearrangements.

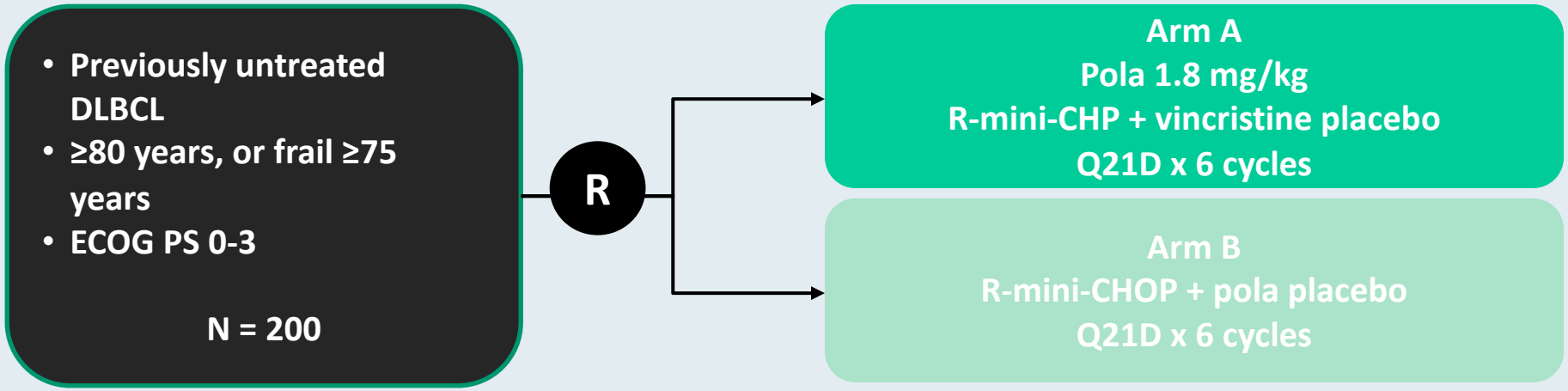
The **poor prognostic impact associated with DEL** appears reduced in patients receiving Pola-R-CHP vs R-CHOP.

DEL, double-expressor lymphoma

Multivariate analyses **support the benefit of Pola-R-CHP** in patients with DLBCL that has BCL2 or MYC protein overexpression.

Morschhauser F et al. ASCO 2022;Abstract 7517.

POLAR BEAR Study Design: Adding Polatuzumab Vedotin to R-Mini-CHOP as Initial Therapy for Older Patients with DLBCL



Primary endpoint: PFS

www.clinicaltrials.gov. NCT04332822. Accessed August 2022.

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Case Presentation: 59-year-old woman with Stage IV double-hit DLBCL and extensive bone involvement

Dr Benjamin Parsons (Madison, Wisconsin)

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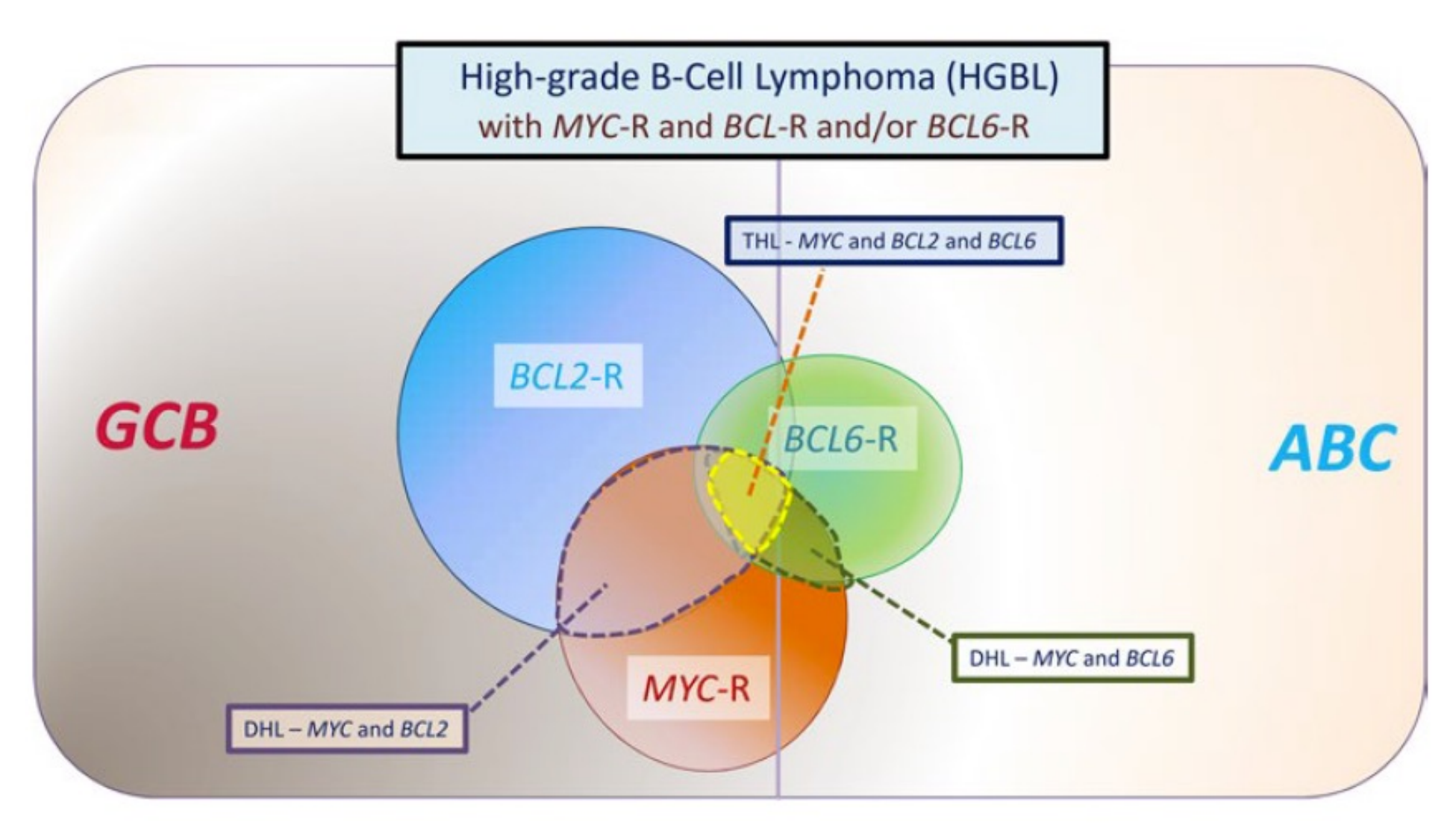
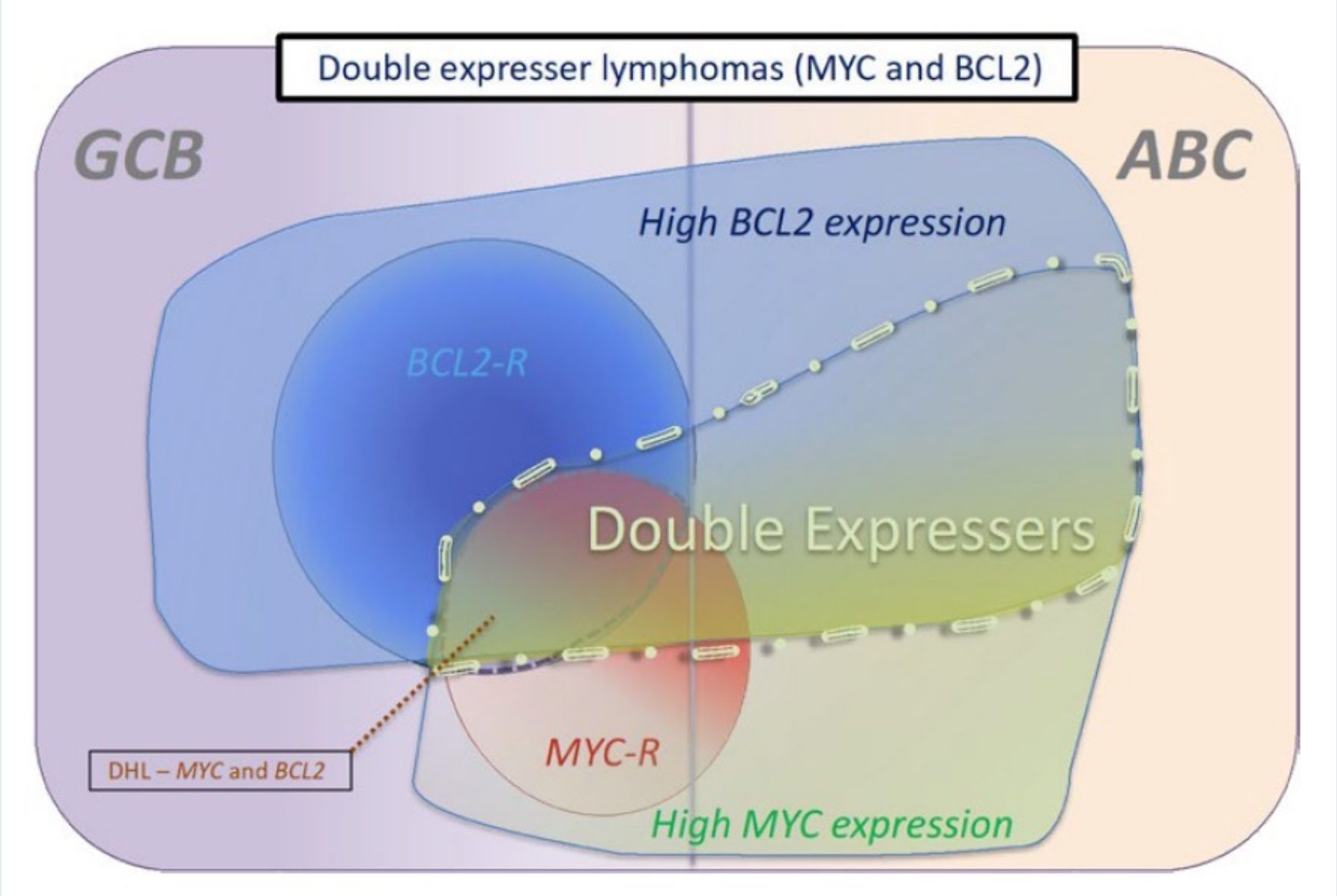
Categories of Aggressive B-Cell Lymphomas



Dunleavy K. ASH 2021 Education Program.

Categories of Double-Expressor Lymphomas



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Review Article

SOHO State of the Art Updates and Next Questions: Prophylaxis and Management of Secondary CNS Lymphoma

Jillian Simard, Mark Roschewski

Clin Lymphoma Myeloma Leuk 2022;[Online ahead of print].

“The prevention of SCNSL remains an unmet clinical need and the standard approaches of delivering MTX either as intrathecal therapy or as HD-MTX during frontline therapy are largely ineffective.”

Simard J and Roschewski M. *Clin Lymphoma Myeloma Leuk* 2022;[Online ahead of print].

nature medicine

FOCUS | ARTICLES

https://doi.org/10.1038/s41591-022-01731-4

OPEN

Axicabtagene ciloleucel as first-line therapy in high-risk large B-cell lymphoma: the phase 2 ZUMA-12 trial

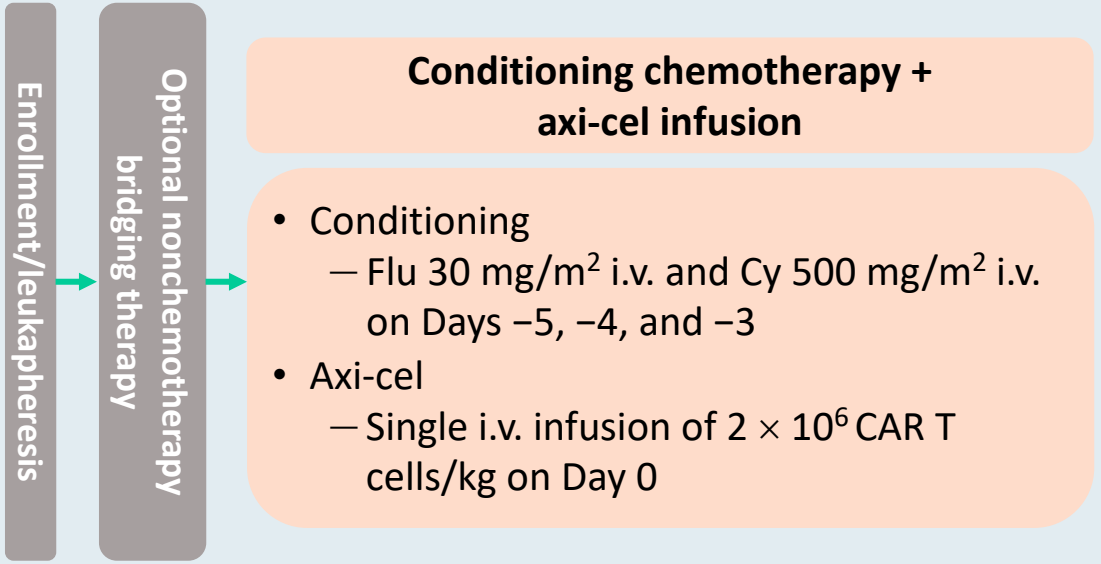
Sattva S. Neelapu[1]✉, Michael Dickinson[2], Javier Munoz[3], Matthew L. Ulrickson[3], Catherine Thieblemont[4,5], Olalekan O. Oluwole[6], Alex F. Herrera[7], Chaitra S. Ujjani[8], Yi Lin[9], Peter A. Riedell[10], Natasha Kekre[11], Sven de Vos[12], Christine Lui[13], Francesca Milletti[13], Jinghui Dong[13], Hairong Xu[13] and Julio C. Chavez[14]

Nat Med 2022 April;28(4):735-42.

Multicenter Phase II ZUMA-12 Schema: First-Line Therapy

Eligibility criteria

- Age ≥ 18 years
- High-risk LBCL
  - HGBCL, with *MYC* and *BCL2* and/or *BCL6* translocations, or
  - LBCL with IPI score ≥ 3 any time before enrollment
- 2 cycles of anti-CD20 plus anthracycline-containing regimen
- Positive interim PET (DS 4 or 5)
- ECOG PS score 0 or 1



Primary endpoint

- CR (complete response)

Key secondary endpoints

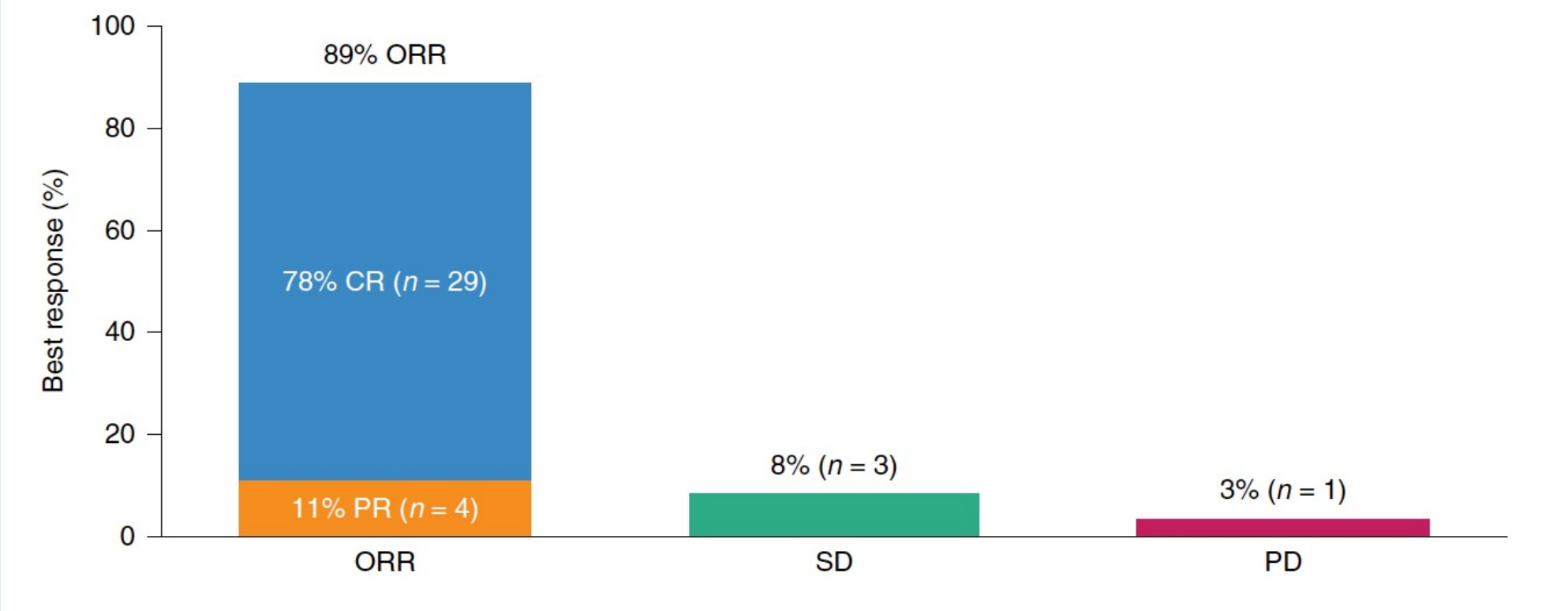
- ORR (objective response rate)
- DOR (duration of response)
- EFS (event-free survival)
- PFS
- OS
- Safety
- CAR T cells in blood and cytokine levels in serum

LBCL = large B-cell lymphoma; HGBCL = high-grade B-cell lymphoma

Neelapu SS et al. ASH 2020;Abstract 405.

ZUMA-12: Efficacy Results with Axi-Cel as First-Line Treatment

ORR and CR in efficacy-evaluable patients (N = 37)



- At median follow-up of 15.9 months, 73% of patients remained in objective response
- Median DOR, EFS and PFS were not reached

ORR = objective response rate; CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; DOR = duration of response; EFS = event-free survival; PFS = progression-free survival

Neelapu SS et al. *Nat Med* 2022 April;28(4):735-42.

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ZUMA-12: Adverse Events of Interest in ≥15% of Patients Receiving Treatment

Adverse event[a], *n* (%)	Grade 1	Grade 2	Grade ≥3	Total
Subjects with any CRS[a]	27 (68)	10 (25)	3 (8)	40 (100)
Pyrexia	8 (20)	28 (70)	4 (10)	40 (100)
Hypotension	7 (18)	5 (13)	0 (0)	12 (30)
Chills	9 (23)	1 (3)	0 (0)	10 (25)
Hypoxia	2 (5)	2 (5)	5 (13)	9 (23)
Sinus tachycardia	6 (15)	0 (0)	0 (0)	6 (15)
Subjects with any neurologic events	14 (35)	6 (15)	9 (23)	29 (73)
Confusional state	7 (18)	2 (5)	2 (5)	11 (28)
Encephalopathy	2 (5)	2 (5)	6 (15)	10 (25)
Tremor	8 (20)	2 (5)	0 (0)	10 (25)

[a]Adverse events include those with onset on or after axi-cel infusion date and coded using MedDRA v.23.1. Neurologic events were identified using the modified blinatumomab registrational study[35]. CRS was graded according to Lee et al.[36]. The severity of all adverse events, including neurologic events and symptoms of CRS, was graded according to CTCAE v.5.0.

Neelapu SS et al. *Nat Med* 2022 April;28(4):735-42.

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Case Presentation: 77-year-old symptomatic man with longstanding CLL and Richter's transformation

Dr Mamta Choksi (New Port Richey, Florida)

RTP RESEARCH TO PRACTICE

Case Presentation: 66-year-old woman with newly diagnosed nonbulky Stage II DLBCL

Dr Kimberly Ku (Bloomington, Illinois)

RTP RESEARCH TO PRACTICE

Management of DLBCL
Where We Are, Where We're Headed

PROLOGUE

MODULE 1: First-Line Treatment

MODULE 2: Bispecific Antibodies

Dr Morganstein: 75-year-old man with a history of severe CHF with a pulmonary nodule and regional adenopathy that on biopsy is proven to be DLBCL

MODULE 3: CAR T-Cell Therapy

MODULE 4: Sequencing of Novel Agents

MODULE 5: Appendix

Case Presentation: 75-year-old man with a history of severe CHF with a pulmonary nodule and regional adenopathy that on biopsy is proven to be DLBCL

Dr Neil Morganstein (Summit, New Jersey)

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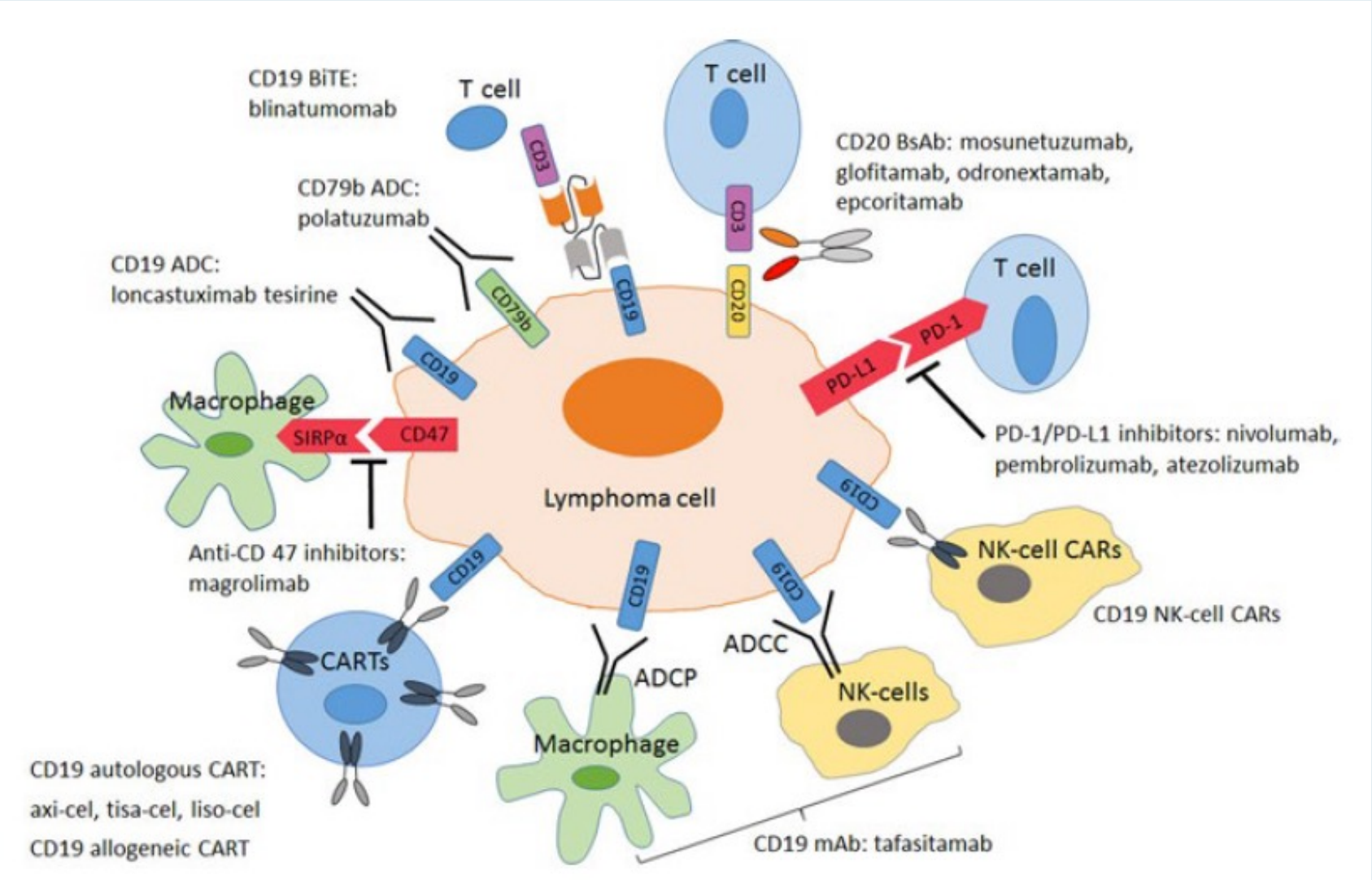
Evolving Landscape of Customized Engineered and Off-the-Shelf Immunotherapies for Aggressive B-Cell Non-Hodgkin Lymphoma



ADCC = antibody-dependent cell cytotoxicity

ADCP = antibody-dependent cellular phagocytosis

BiTE = bispecific T-cell engager

PD-1 = programmed cell death 1

PD-L1 = programmed cell death ligand 1

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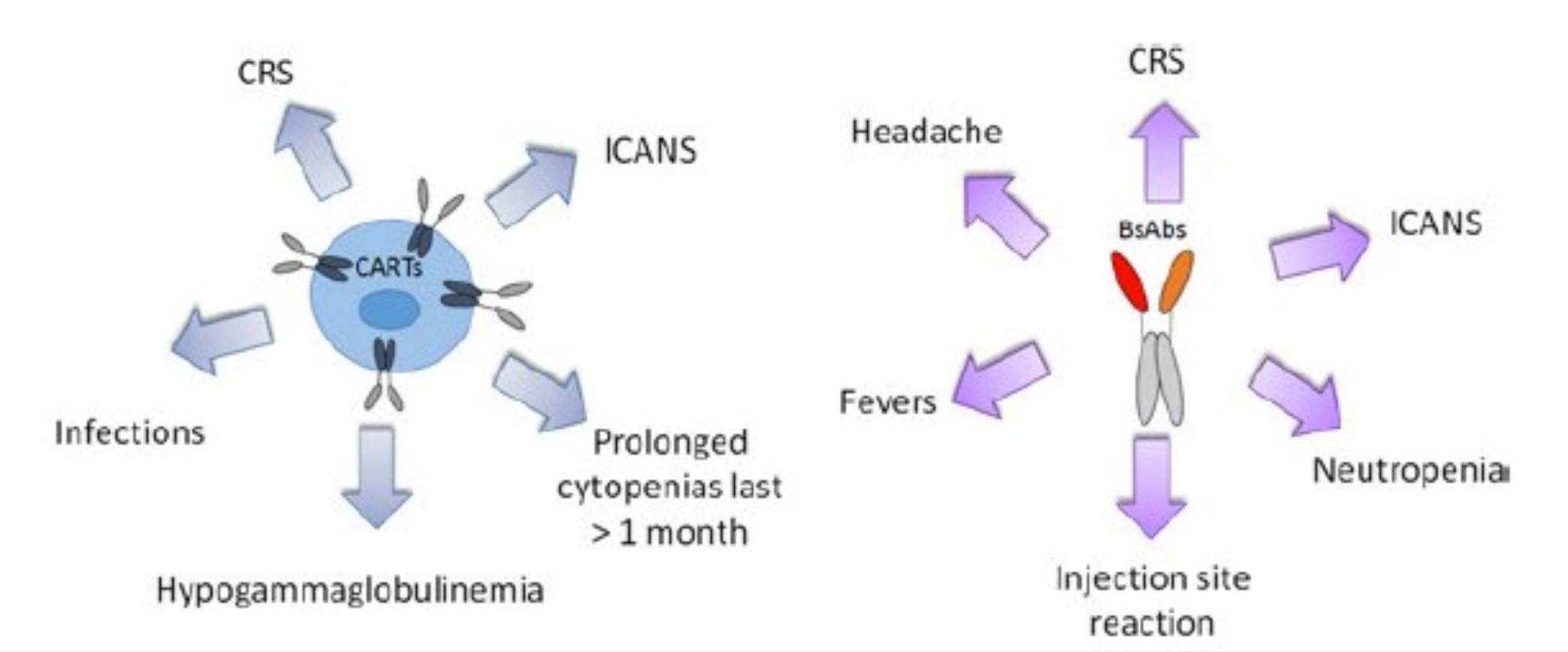
CAR T or Bispecific T-Cell-Engaging Antibody Treatment-Related Adverse Effects of Interest with an Incidence of ≥10% or ≥5%



BsAb = Bispecific T-cell-engaging antibody

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Emerging Bispecific Antibodies for DLBCL

Bispecific antibody	Construct	Administration
Glofitamab	CD3 (Fab) x CD20 (Fab x 2) Fc	IV
Mosunetuzumab	CD3 x CD20 Knobs-into-holes Fc	IV, SC
Epcoritamab	DuoBody®-CD3 x CD20	SC
Odronextamab	CD3 x CD20 common LC Fc	IV

IV = intravenous; SC = subcutaneous; LC = light chain

Content Courtesy of Jeremy Abramson, MD - adapted

Glofitamab in Patients with Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL) and ≥ 2 Prior Therapies: Pivotal Phase II Expansion Results

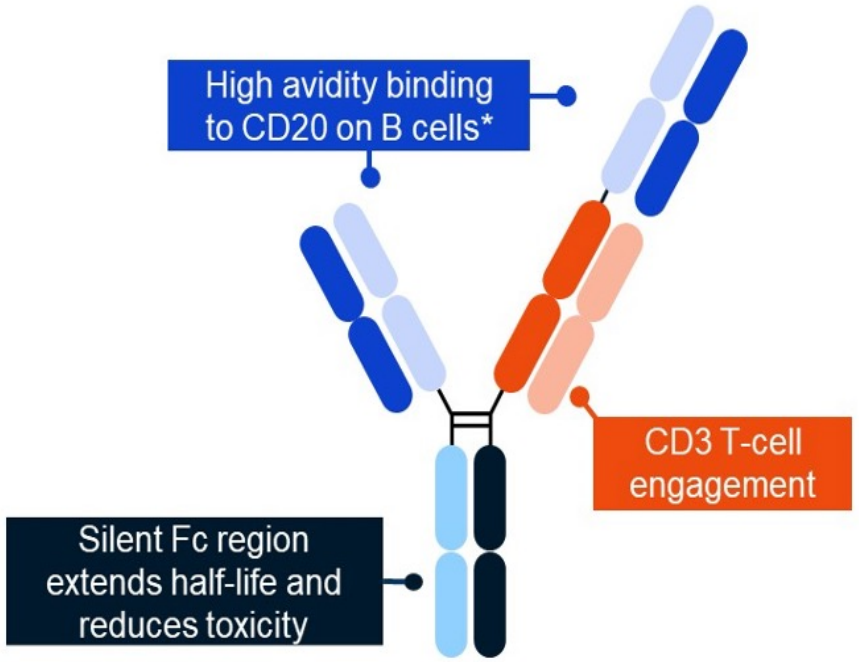
Dickinson M et al.

ASCO 2022;Abstract 7500.

Glofitamab: Background and Mechanism of Action

- **Patients with R/R DLBCL (≥2 prior therapies) have a poor prognosis[1,2]**
  - poor outcomes are reported in patients with treatment failure after R-CHOP, particularly in those with refractory disease[3]
  - CAR T-cell therapy is an option for patients with R/R DLBCL but its use may be limited by logistical challenges[4,5]
- **Glofitamab**
  - off-the-shelf and fixed duration treatment[6,7]
- **Phase I experience (NCT03075696)[7]**
  - encouraging efficacy and manageable safety with glofitamab monotherapy in patients with R/R B-cell NHL[6,7]
  - established a step-up dosing schedule and target dose (30mg) in patients with B-cell NHL in multiple cohorts[8]

Glofitamab: *CD20xCD3 bispecific monoclonal antibody with 2:1 format for increased potency vs 1:1 format[6]*



Dickinson M et al. ASCO 2022;Abstract 7500. Dickinson M et al. EHA 2022;Abstract S220.

RTP RESEARCH TO PRACTICE

Response Rates with Glofitamab in Patients with R/R DLBCL (≥2 Prior Therapies)

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

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

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

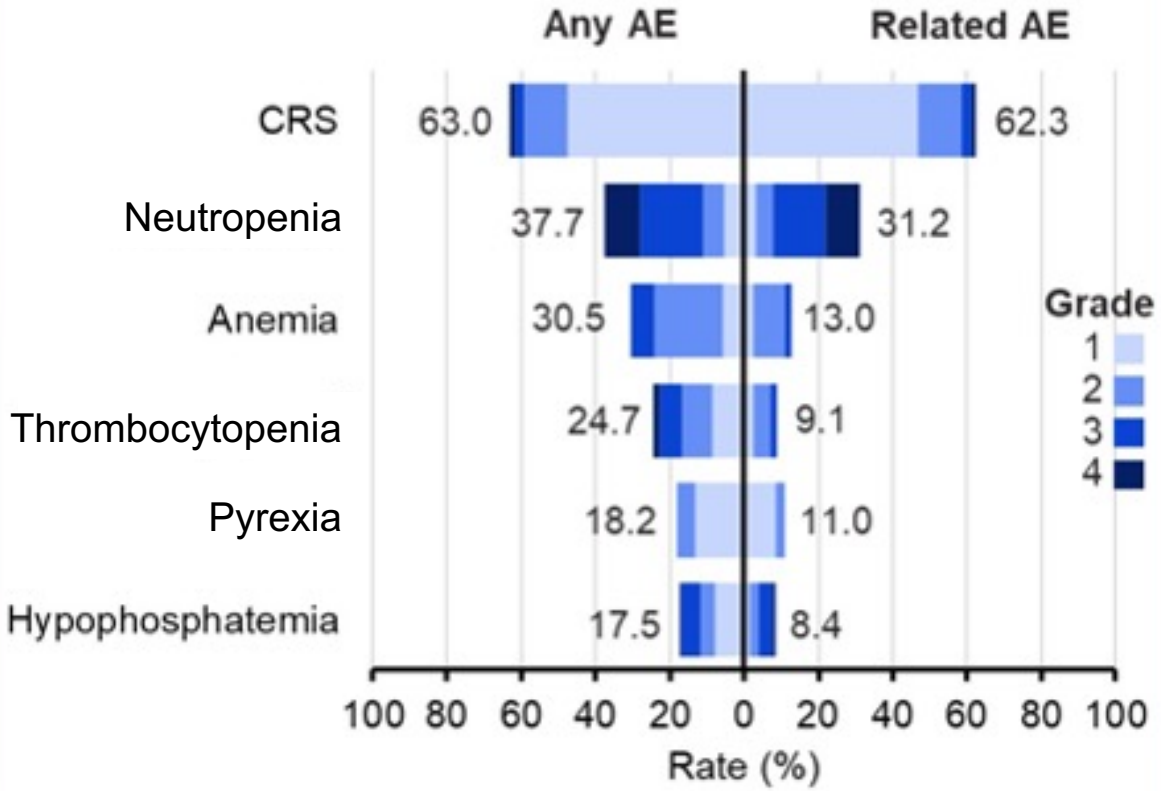
- **High CR/ORR rate at RP2D**

Dickinson M et al. ASCO 2022;Abstract 7500. Dickinson M et al. EHA 2022;Abstract S220.

Safety Profile of Glofitamab in Patients with R/R DLBCL (≥2 Prior Therapies)

n (%)	N=154
Median no. of cycles received (range)	5 (1–13)
Median relative dose intensity, % (range)	100 (94–100)
AE	152 (98.7)
Related AE	140 (90.9)
Grade 3–4 AE	87 (56.5)
Related AE	64 (41.6)
Serious AE	73 (47.4)
Related AE	46 (29.9)
Grade 5 (fatal AE)	8 (5.2)
Related AE	0
AE leading to treatment discontinuation	14 (9.1)
Related AE	5 (3.2)

AEs (≥15%) by grade and relationship with glofitamab



- **Glofitamab was well tolerated, with a favorable safety profile**

Dickinson M et al. ASCO 2022;Abstract 7500. Dickinson M et al. EHA 2022;Abstract S220.

RTP RESEARCH TO PRACTICE

Safety Profile of Glofitamab in Patients with R/R DLBCL (≥2 Prior Therapies) — Continued

n (%)	N=154
Infections (all grades)	59 (38.3)
Grade ≥3	23 (14.9)
Neutropenia (all grades)	58 (37.7)
Grade ≥3	41 (26.6)
Febrile neutropenia (all grades)	4 (2.6)
Grade ≥3	4 (2.6)
Tumor flare events (all grades)	17 (11.0)
Grade ≥3	4 (2.6)
Neurologic AEs (all grades)	59 (38.3)
Grade ≥3	5 (3.2)
ICANS (derived)	
All grades (CTCAE)	12 (7.8)
Grade ≥3 (CTCAE)	4 (2.6)

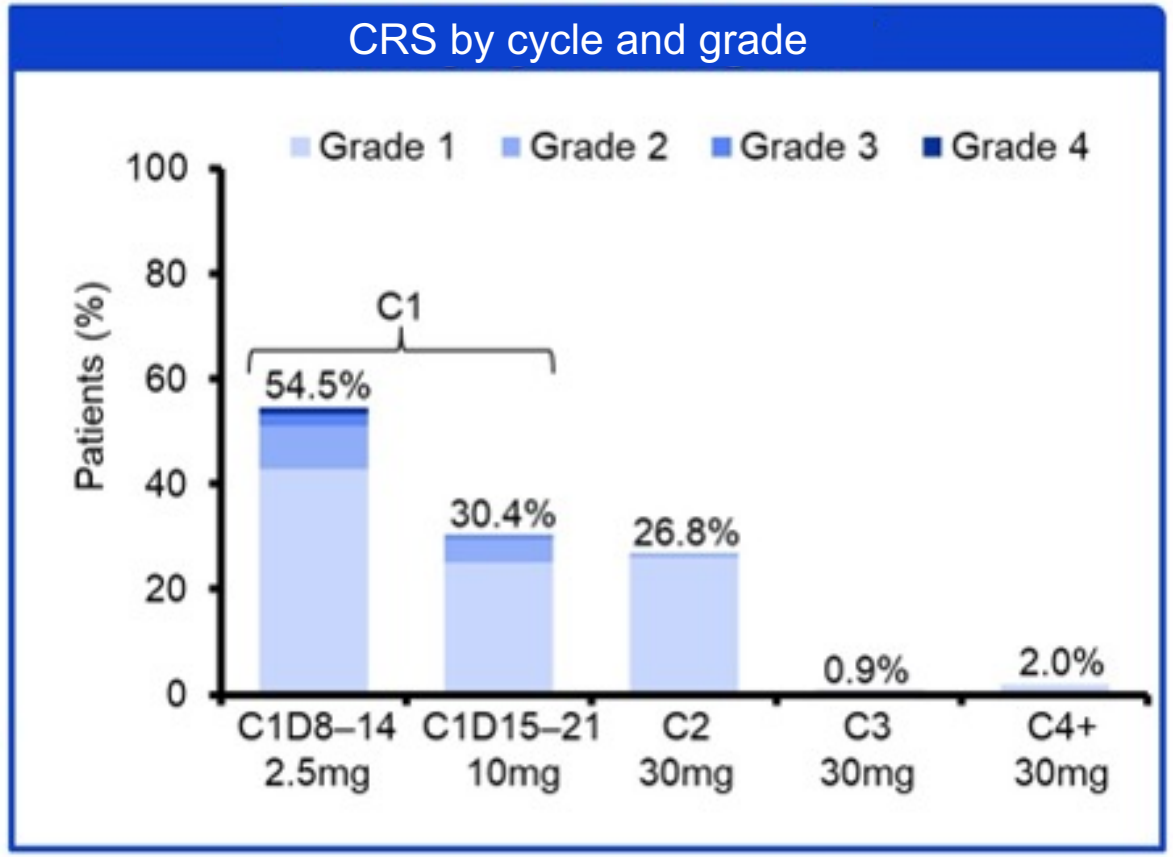
n (%)	N=154
AE leading to treatment discontinuation	14 (9.1)
Infections and infestations	6 (3.9)
Delirium	2 (1.3)
Neutropenia	2 (1.3)
Hepatobiliary disorders	1 (0.6)
Gastrointestinal hemorrhage	1 (0.6)
CRS	1 (0.6)
Melanoma recurrent	1 (0.6)

- **Low rate of treatment discontinuations due to AEs and low rate of ICANS events**

Dickinson M et al. ASCO 2022;Abstract 7500. Dickinson M et al. EHA 2022;Abstract S220.

Incidence of Cytokine Release Syndrome with Glofitamab in Patients with R/R DLBCL (≥2 Prior Therapies)

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

Dickinson M et al. ASCO 2022;Abstract 7500. Dickinson M et al. EHA 2022;Abstract S220.

original reports

Single-Agent Mosunetuzumab Shows Durable Complete Responses in Patients With Relapsed or Refractory B-Cell Lymphomas: Phase I Dose-Escalation Study

Lihua E. Budde, MD[1]; Sarit Assouline, MD[2]; Laurie H. Sehn, MD[3]; Stephen J. Schuster, MD[4]; Sung-Soo Yoon, MD, PhD[5]; Dok Hyun Yoon, MD, PhD[6]; Matthew J. Matasar, MD[7]; Francesc Bosch, MD, PhD[8]; Won Seog Kim, MD, PhD[9]; Loretta J. Nastoupil, MD[10]; Ian W. Flinn, MD, PhD[11]; Mazyar Shadman, MD, MPH[12]; Catherine Diefenbach, MD[13]; Carol O'Hear, MD, PhD[14]; Huang Huang, MSc[15]; Antonia Kwan, MBBS, PhD[14]; Chi-Chung Li, PhD[14]; Emily C. Piccione, PhD[14]; Michael C. Wei, MD, PhD[14]; Shen Yin, PhD[14]; and Nancy L. Bartlett, MD[16]

J Clin Oncol 2022 February 10;40(5):481-91.

Efficacy of Single-Agent Mosunetuzumab for Relapsed/Refractory B-Cell Lymphomas

Best Objective Response[a]	Aggressive NHL[b] (n = 129)	Indolent NHL[c] (n = 68)	Post–CAR-T Therapy (n = 19)
ORR, No. (%) [95% CI]	45 (34.9) [26.7 to 43.8]	45 (66.2) [53.7 to 77.2]	7[d] (36.8) [16.3 to 61.6]
Complete response, No. (%) [95% CI]	25 (19.4) [13.0 to 27.3]	33 (48.5) [36.2 to 61.0]	5 (26.3) [9.2 to 51.2]
Partial response, No. (%) [95% CI]	20 (15.5) [9.7 to 22.9]	12 (17.6) [9.5 to 28.8]	2 (10.5) [1.3 to 33.1]
Stable disease, No. (%) [95% CI]	9 (7.0) [3.2 to 12.8]	13 (19.1) [10.6 to 30.5]	0 (0) [0.0 to 17.7]
Progressive disease, No. (%) [95% CI]	70 (54.3) [45.3 to 63.1]	9 (13.2) [6.2 to 23.6]	12 (63.2) [38.4 to 83.7]
Duration of response, median [95% CI], months	7.6 [5.6 to 22.8]	16.8 [11.7 to NE]	Not reported due to small sample size (n = 7)[d]
Duration of response in patients with complete response, median [95% CI], months	22.8 [7.6 to NE]	20.4 [16.0 to NE]	Not reported due to small sample size (n = 5)

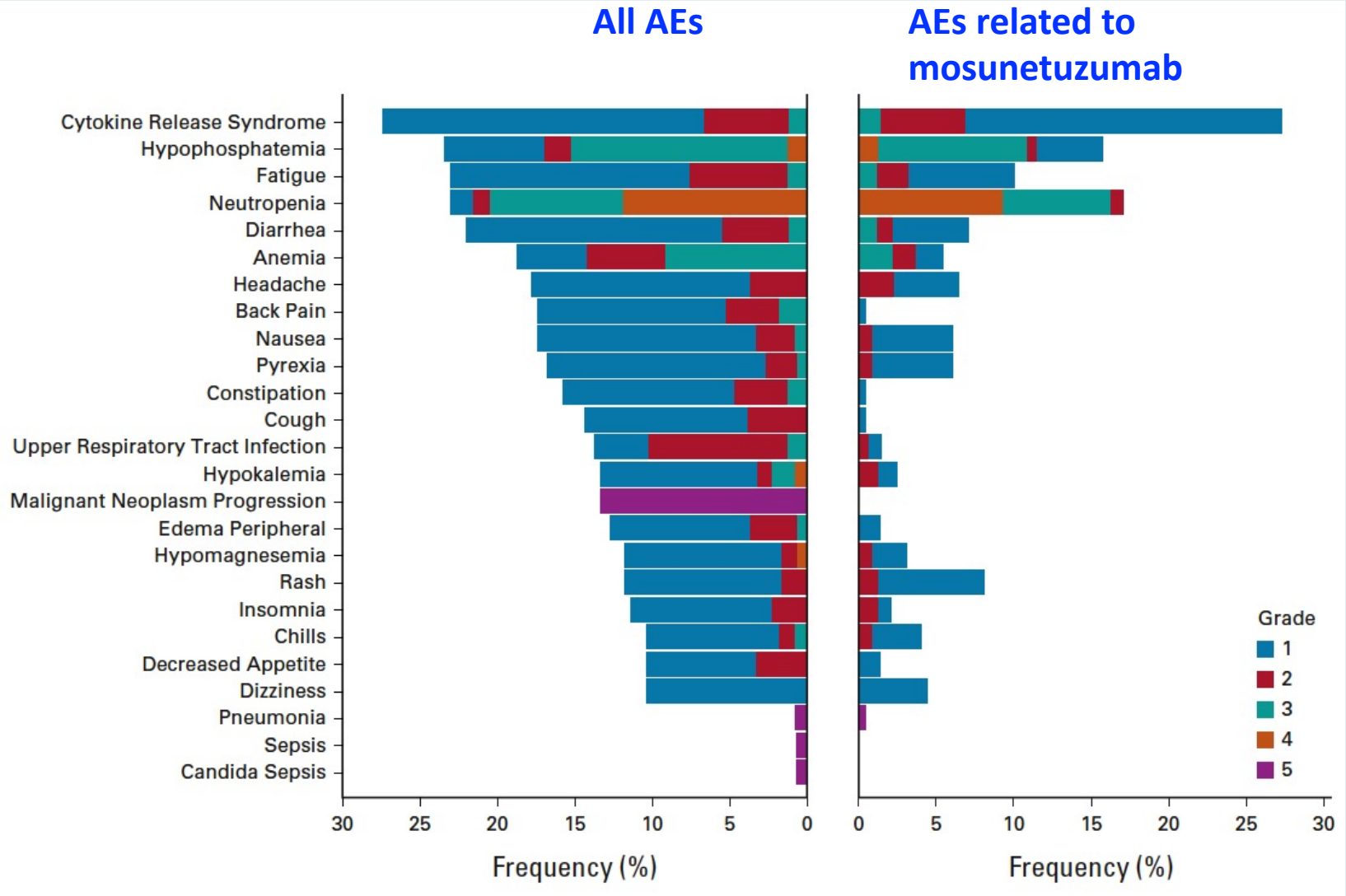
[a] Response by computed tomography with or without fluorodeoxyglucose positron emission tomography. At data cutoff, among patients who had at least one tumor assessment, 86% had at least one positron emission tomography scan performed.

[b] Includes patients with DLBCL (n = 82), transformed follicular lymphoma (FL; n = 26), mantle cell lymphoma (MCL; n = 13), Richter's transformation (n = 5), FL Grade IIIb (n = 1), transformed marginal zone lymphoma (MZL; n = 1) and mixed DLBCL and MCL (n = 1).

[c] Includes patients with FL (Grade I-IIIa; n = 68), MZL (n = 2) and small lymphocytic lymphoma (n = 1).

Budde LE et al. *J Clin Oncol* 2022 February 10;40(5):481-91.

Adverse Events (AEs) with Incidence of Greater than 10% or National Cancer Institute-Common Terminology Criteria for AEs Grade



Budde LE et al. *J Clin Oncol* 2022 February 10;40(5):481-91.

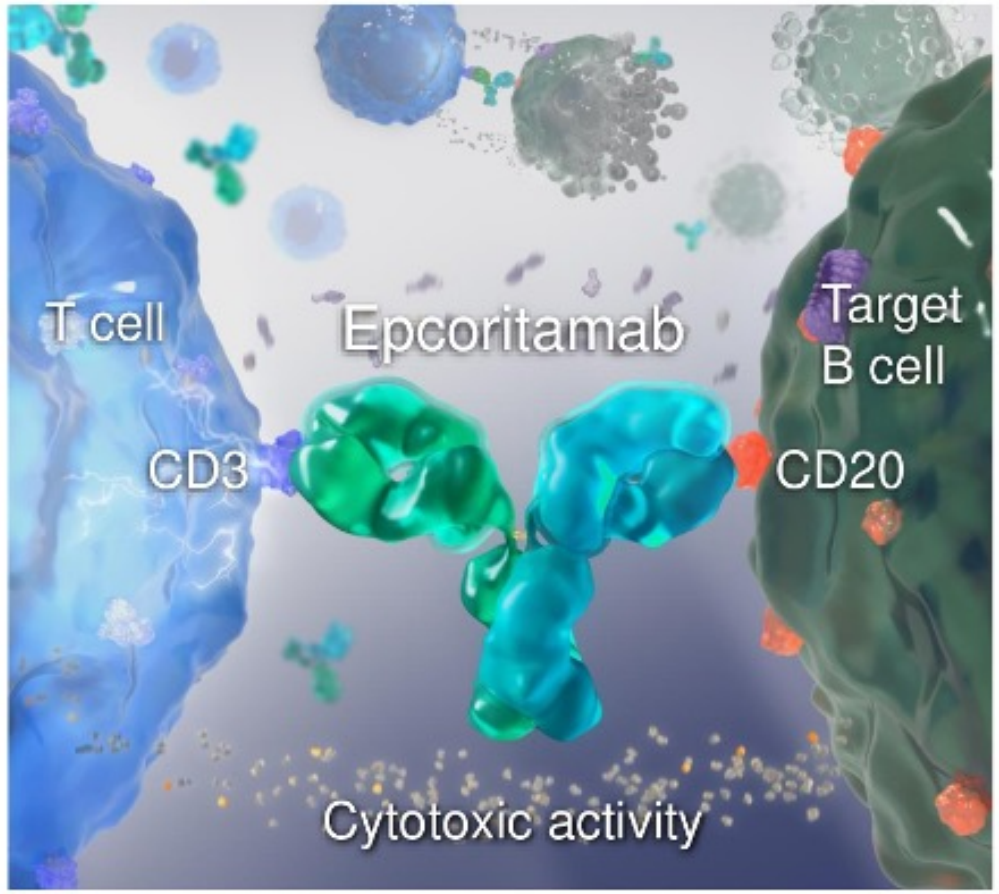
7523

ASCO 2022

First-line treatment (Tx) with subcutaneous (SC) epcoritamab (epco) + R-CHOP in patients (pts) with high-risk diffuse large B-cell lymphoma (DLBCL): phase 1/2 data update

Lorenzo Falchi, MD,[1*] Fritz Offner, MD, PhD,[2] David Belada, MD, PhD,[3] Joshua Brody, MD,[4] Kim M. Linton, MBChB, PhD,[5] Yasmin Karimi, MD,[6] Raul Cordoba, MD, PhD,[7] Sylvia Snauwaert, MD, PhD,[8] Aqeel Abbas, MS,[9] Liwei Wang, PhD,[9] Jun Wu, MD, MS,[10] Brian Elliott, MD,[9] Michael Roost Clausen, MD, PhD[11]

Epcoritamab: Background and Mechanism of Action

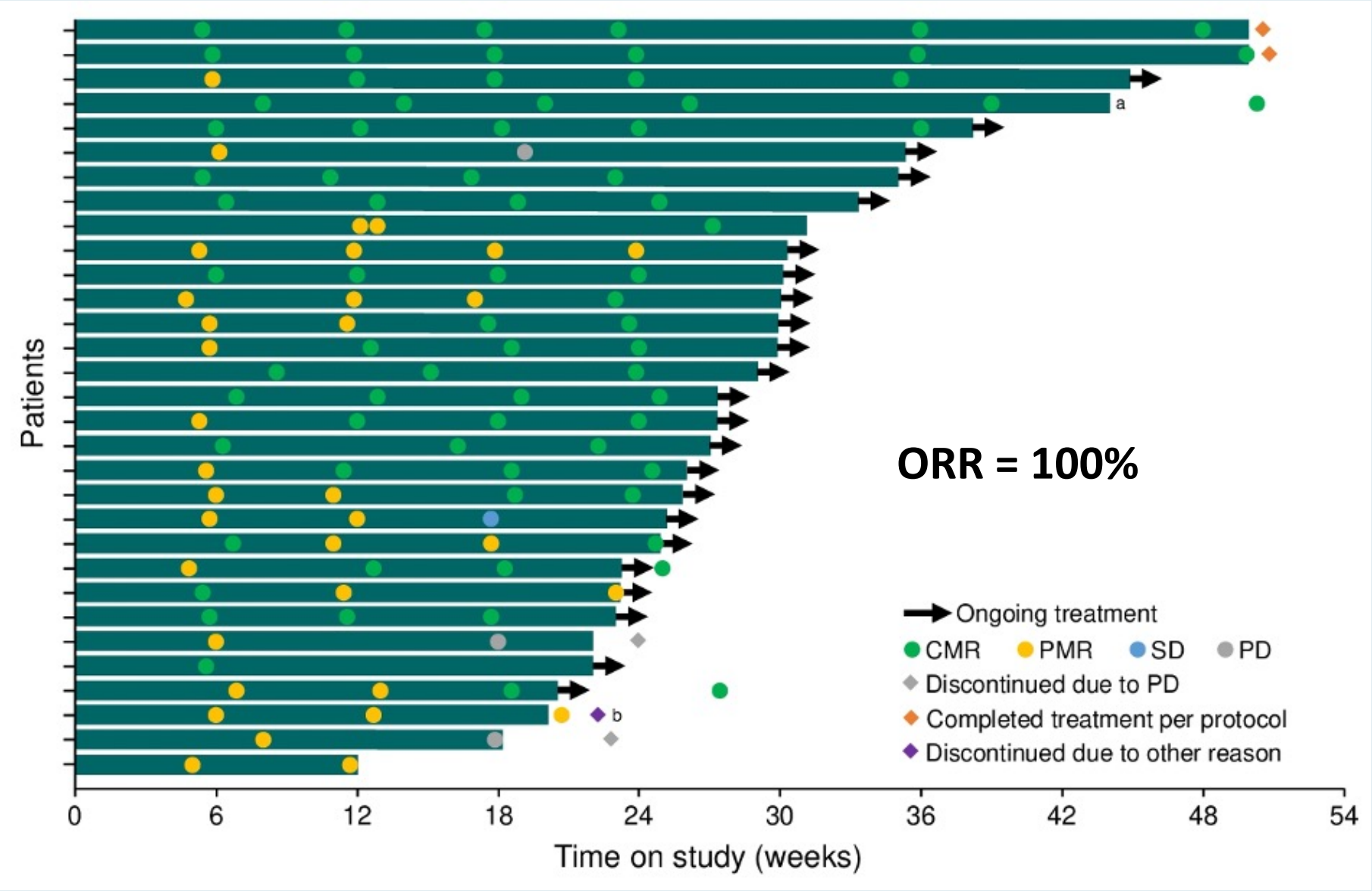


- Patients with DLBCL, particularly those considered high/poor risk (ie, with 3–5 risk factors, based on the revised IPI), have poor outcomes with standard first-line therapy (R-CHOP), with 55% overall survival at 4 years[1,2]
  - A significant unmet need remains in this population, and new approaches are needed
- Epcoritamab is a subcutaneously administered (SC) bispecific antibody that binds to CD3 on T cells and CD20 on B cells to induce T-cell–mediated killing of CD20+ malignant B cells[3,4]
- Epcoritamab-mediated T-cell cytotoxicity is maintained in combination with R-CHOP[3,5]
- In the dose-escalation part of the EPCORE NHL-1 phase 1/2 trial, single-agent epcoritamab had a manageable safety profile and substantial antitumor activity in patients with heavily pretreated B-cell NHL[6]
- Epcoritamab is well suited for combination therapy due to its mechanism of action, distinct from that of the components of standard of care R-CHOP[3,5,7]

Falchi L et al. ASCO 2022;Abstract 7523.

RTP RESEARCH TO PRACTICE

EPCORE NHL-2: Response Profile



Falchi L et al. ASCO 2022;Abstract 7523.

RTP RESEARCH TO PRACTICE

EPCORE NHL-2: Cytokine Release Syndrome (CRS)

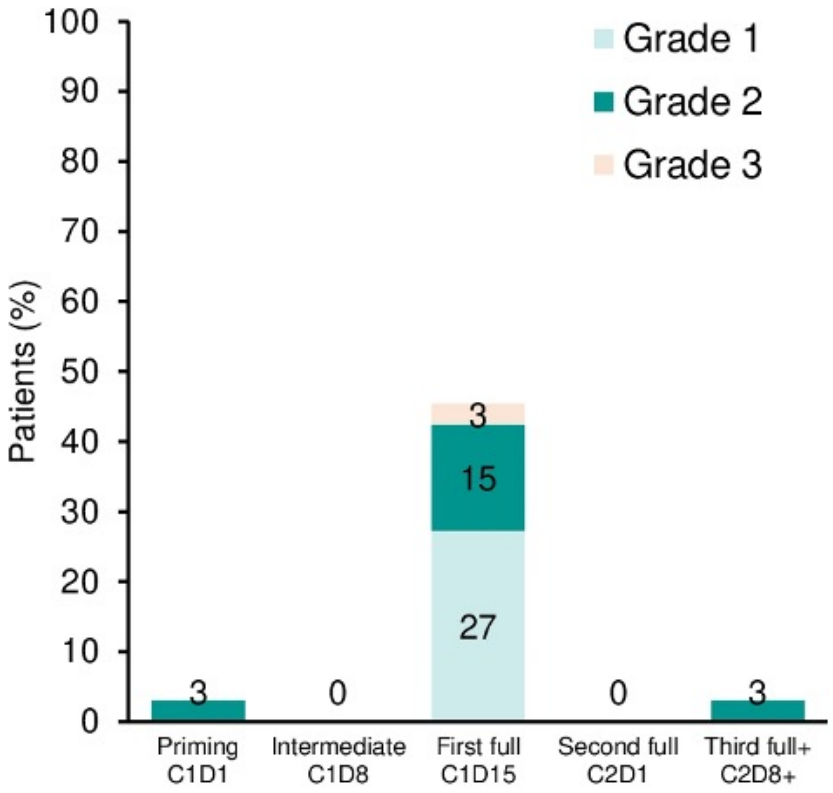
CRS Graded by Lee et al[9] 2019 Criteria

	Total N=33
CRS, n (%)	17 (52)
Grade 1	9 (27)
Grade 2	7 (21)
Grade 3	1 (3)
CRS resolution, n (%)	17 (100)
Median time to resolution, d (range)[a]	2 (1–11)
CRS leading to treatment discontinuation, n (%)	0
Tocilizumab use, n (%)	5 (15)

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 Events by Dosing Period

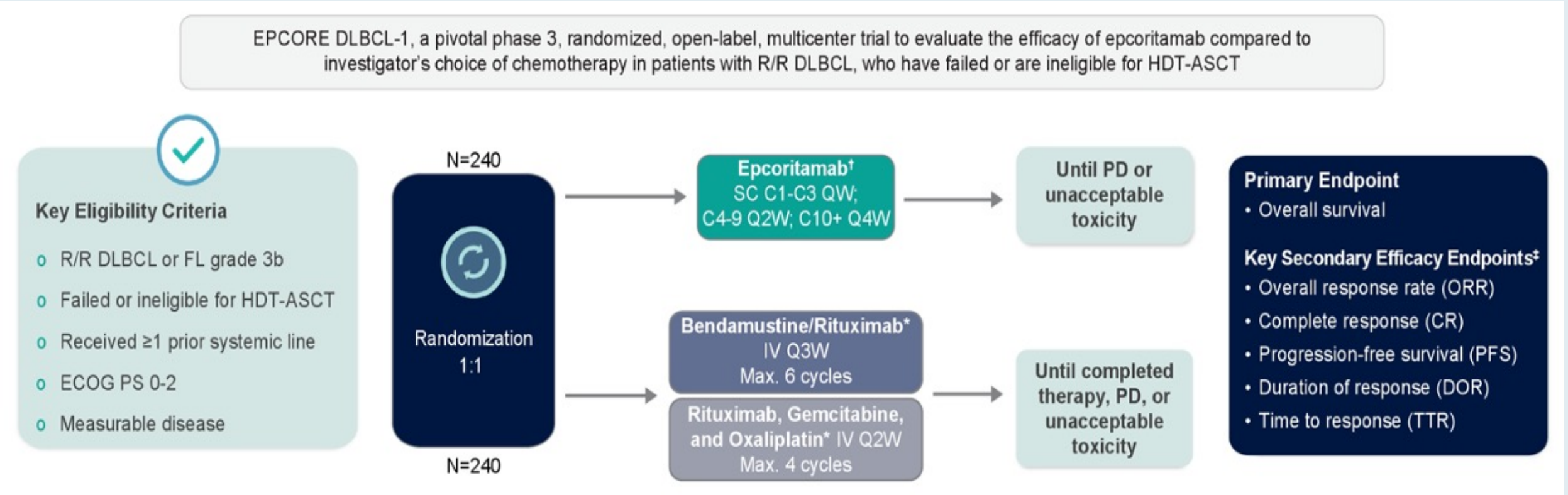


Data cutoff: March 25, 2022. Priming dose: n=33; intermediate dose: n=33; first full dose: n=33; second full dose: n=32; third full dose and later: n=32.

- CRS occurrence was predictable; most cases occurred following the first full dose with a median time to onset of 2 days (range, 1–4)

Falchi L et al. ASCO 2022;Abstract 7523.

EPCORE DLBCL-1: Phase III Study Design



Thieblemont C et al. ASCO 2021;Abstract TPS7569.

RTP RESEARCH TO PRACTICE

Management of DLBCL
Where We Are, Where We're Headed

PROLOGUE

MODULE 1: First-Line Treatment

MODULE 2: Bispecific Antibodies

MODULE 3: CAR T-Cell Therapy

Dr Yang: 73-year-old woman with rapid relapse after R-CHOP then R-ICE/ASCT achieves a CR with CAR T-cell therapy but experiences severe pancytopenia

Dr Mushtaq: 45-year-old man with R-CHOP-refractory DLBCL receives polatuzumab vedotin as bridging therapy → CAR T-cell therapy on protocol

MODULE 4: Sequencing of Novel Agents

MODULE 5: Appendix

RTP RESEARCH TO PRACTICE

Case Presentation: 73-year-old woman with rapid relapse after R-CHOP then R-ICE/ASCT achieves a CR with CAR T-cell therapy but experiences severe pancytopenia

Dr John Yang (Fall River, Massachusetts)

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TO PRACTICE

Notable CAR T-Cell Therapy-Associated Toxicities

- **Cytokine Release Syndrome**
- **Neurologic Toxicity**
  - CAR T-cell associated encephalopathy syndrome
  - ICANS (immune effector cell associated neurotoxicity syndrome
- **Prolonged Cytopenias**
- **B-Cell Aplasia**
- **Hypogammaglobulinemia**

Content Courtesy of Jeremy Abramson, MD - adapted

Case Presentation: 45-year-old man with R-CHOP-refractory DLBCL receives polatuzumab vedotin as bridging therapy → CAR T-cell therapy on protocol

Dr Rao Mushtaq (Thornton, Colorado)

RTP RESEARCH TO PRACTICE

Key Issues in CAR T-Cell Therapy Selection

- **Turnaround Time for Manufacturing**
- **Bridging for Symptomatic or Progressive Disease**
  - Radiation therapy
  - Polatuzumab vedotin
- **Referral to Center for CAR T-Cell Therapy**
  - Early referral is optimal – after first treatment failure before initiating salvage therapy

Content Courtesy of Jeremy Abramson, MD - adapted

Characteristics of Pivotal Trials of Axi-cel and Tisagenlecleucel

Variable	ZUMA-1 (axi-cel)	JULIET (tisagenlecleucel)	ZUMA-7 (axi-cel group)	BELINDA (tisagenlecleucel group)	ZUMA-7 (standard-care group)	BELINDA (standard-care group)
Primary end point	Overall response rate	Overall response rate	Event-free survival	Event-free survival after wk 12	Event-free survival	Event-free survival after wk 12
Histologic type						
DLBCL, NOS — no. (%)	77 (76)	88 (79)	126 (70)	101 (62)	120 (67)	112 (70)
HGBL, DH — no./total no. (%)	NR	19/70 (27)	31/180 (17)	32/162 (20)	25/179 (14)	19/160 (12)
HGBL, NOS — no. (%)	0	0	0	7 (4)	1 (1)	8 (5)
FL grade 3B — no. (%)	0	0	0	5 (3)	0	1 (1)
PMBL — no. (%)	8 (8)	0	0	12 (7)	0	13 (8)
Other or missing — no. (%)	0	2 (2)	23 (13)	5 (3)	33 (18)	7 (4)
Transformed lymphoma — no. (%)	16 (16)	21 (19)	19 (11)	27 (17)	27 (15)	22 (14)
Clinical outcomes						
Response — %	82	52 (efficacy cohort); 34 (ITT cohort)	83	46	50	42
Complete response — %	54	40 (efficacy cohort)	65	28	32	28
Median follow-up — mo	27.1	40.3	25	10	25	10
2-Yr progression-free survival — %	Approx. 40	Approx. 35	46	NR	27	NR
2-Yr progression-free survival among patients with complete response — %	72	Approx. 80	NR	NR	NR	NR
2-Yr overall survival — %	51	Approx. 45	61	NR	52	NR

Roschewski M et al. *N Engl J Med* 2022;386(7):692-96.

RTP RESEARCH TO PRACTICE

Recent FDA Approvals of CAR (Chimeric Antigen Receptor) T-Cell Therapy as Second-Line Treatment for Large B-Cell Lymphoma

June 24, 2022: "The FDA approved lisocabtagene maraleucel for adult patients with large B-cell lymphoma (LBCL) who have refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy; or refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age. It is not indicated for the treatment of patients with primary central nervous system lymphoma." Based on the TRANSFORM study

April 1, 2022: "The FDA approved axicabtagene ciloleucel for adult patients with large B-cell lymphoma (LBCL) that is refractory to first-line chemoimmunotherapy or relapses within 12 months of first-line chemoimmunotherapy. It is not indicated for the treatment of patients with primary central nervous system lymphoma." Based on the ZUMA-7 study

www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-lisocabtagene-maraleucel-second-line-treatment-large-b-cell-lymphoma
www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-axicabtagene-ciloleucel-second-line-treatment-large-b-cell-lymphoma

RTP RESEARCH TO PRACTICE

N Engl J Med 2022;386(7):640-54.
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma

F.L. Locke, D.B. Miklos, C.A. Jacobson, M.-A. Perales, M.-J. Kersten, O.O. Oluwole, A. Ghobadi, A.P. Rapoport, J. McGuirk, J.M. Pagel, J. Muñoz, U. Farooq, T. van Meerten, P.M. Reagan, A. Sureda, I.W. Flinn, P. Vandenberghe, K.W. Song, M. Dickinson, M.C. Minnema, P.A. Riedell, L.A. Leslie, S. Chaganti, Y. Yang, S. Filosto, J. Shah, M. Schupp, C. To, P. Cheng, L.I. Gordon, and J.R. Westin, for All ZUMA-7 Investigators and Contributing Kite Members*

Lancet 2022;399:2294-308.

Lisocabtagene maraleucel 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 (TRANSFORM): results from an interim analysis of an open-label, randomised, phase 3 trial

Manali Kamdar, Scott R Solomon, Jon Arnason, Patrick B Johnston, Bertram Glass, Veronika Bachanova, Sami Ibrahimi, Stephan Mielke, Pim Mutsaers, Francisco Hernandez-Ilizaliturri, Koji Izutsu, Franck Morschhauser, Matthew Lunning, David G Maloney, Alessandro Crotta, Sandrine Montheard, Alessandro Previtali, Lara Stepan, Ken Ogasawara, Timothy Mack, Jeremy S Abramson, for the TRANSFORM Investigators†*

N Engl J Med 2022;386(7):629-39.
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Second-Line Tisagenlecleucel or Standard Care in Aggressive B-Cell Lymphoma

M.R. Bishop, M. Dickinson, D. Purtill, P. Barba, A. Santoro, N. Hamad, K. Kato, A. Sureda, R. Greil, C. Thieblemont, F. Morschhauser, M. Janz, I. Flinn, W. Rabitsch, Y.-L. Kwong, M.J. Kersten, M.C. Minnema, H. Holte, E.H.L. Chan, J. Martinez-Lopez, A.M.S. Müller, R.T. Maziarz, J.P. McGuirk, E. Bachy, S. Le Gouill, M. Dreyling, H. Harigae, D. Bond, C. Andreadis, P. McSweeney, M. Kharfan-Dabaja, S. Newsome, E. Degtyarev, R. Awasthi, C. del Corral, G. Andreola, A. Masood, S.J. Schuster, U. Jäger, P. Borchmann, and J.R. Westin

Randomized Trials Comparing Second-Line CAR T-Cell to Standard Therapy for Patients with Transplant-Eligible DLBCL with Primary Refractory Disease or Relapse within 1 Year of First-Line Therapy

	ZUMA-7	TRANSFORM	BELINDA
CAR T-cell therapy	Axicabtagene ciloleucel	Lisocabtagene maraleucel	Tisagenlecleucel
n	359	184	322
Patients infused in CAR arm	94%	98%	96%
Median EFS	8.3 mo vs 2 mo	10.1 mo vs 2.3 mo	3 mo vs 3 mo
Hazard ratio	0.398 ($p < 0.0001$)	0.349 ($p < 0.0001$)	1.07 ($p = 0.69$)
Median follow-up	25 mo	6 mo	10 mo
CR rate	65% vs 32%	66% vs 39%	28% vs 28%
Grade ≥3 CRS/NT	6%/21%	1%/4%	5%/3%
	Locke et al. ASH 2021;Abstract 2.	Kamdar et al. ASH 2021;Abstract 91.	Bishop et al. ASH 2021;Abstract LBA-6.

Content Courtesy of Jeremy Abramson, MD

RTP RESEARCH TO PRACTICE

N Engl J Med 2022;386(7):640-54.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma

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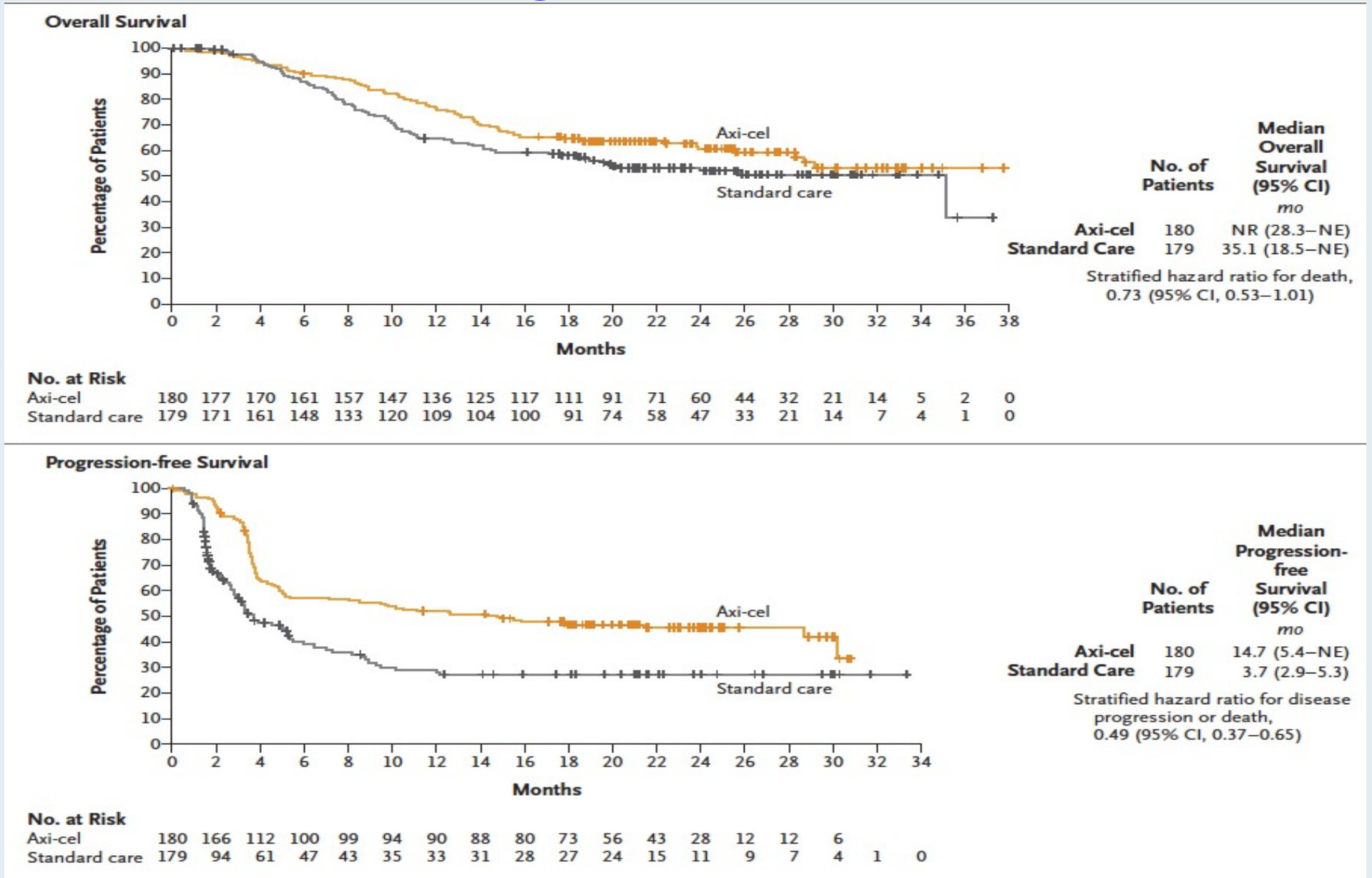
ZUMA-7: Overall and Progression-Free Survival



Locke FL et al. *N Engl J Med* 2022;386(7):640-54.

EHA EUROPEAN HEMATOLOGY ASSOCIATION

EHA2022 HYBRID JUNE 9-17 VIENNA

Clinical and Patient-Reported Outcomes in a Phase 3 Study of Axicabtagene Ciloleucel Versus Standard of Care in Elderly Patients With Relapsed/Refractory Large B-Cell Lymphoma (ZUMA-7)

Anna Sureda, MD, PhD[1]; Jason R. Westin, MD, MS, FACP[2]; Frederick L. Locke, MD[3]; Michael Dickinson, MBBS, DMEdSc[4]; Armin Ghobadi, MD[5]; Mahmoud Elsawy, MD, MSc[6]; Tom van Meerten, MD, PhD[7]; David B. Miklos, MD, PhD[8]; Matthew Ulrickson, MD[9]; Miguel-Angel Perales, MD[10]; Umar Farooq, MD[11]; Luciano Wannesson, MD[12]; Lori Leslie, MD[13]; Marie José Kersten, MD, PhD[14]; Caron A. Jacobson, MD, MMSc[15]; John M. Pagel, MD, PhD, DSc[16]; Gerald Wulf, MD, PhD[17]; Patrick Johnston, MD, PhD[18]; Aaron P. Rapoport, MD[19]; Leo I. Gordon, MD[20]; Yin Yang, MD, MS[21]; Andrew Peng, MS[21]; Linqiu Du, MS[21]; Julia T. Snider, PhD[21]; Jina Shah, MD, MPH[21*]; Marco Schupp, MD[21]; Paul Cheng, MD, PhD[21†]; Christina To, MD[21]; and Olalekan O. Oluwole, MBBS, MPH[22]

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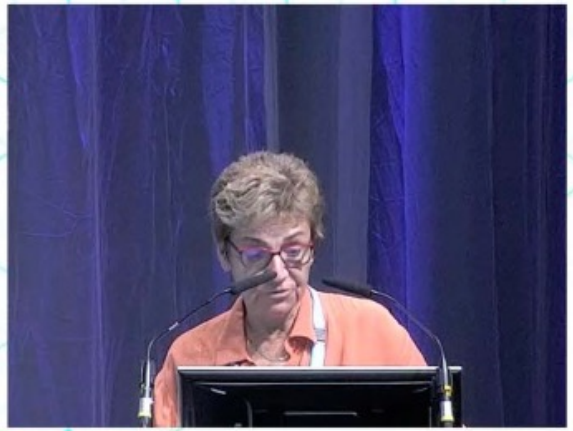


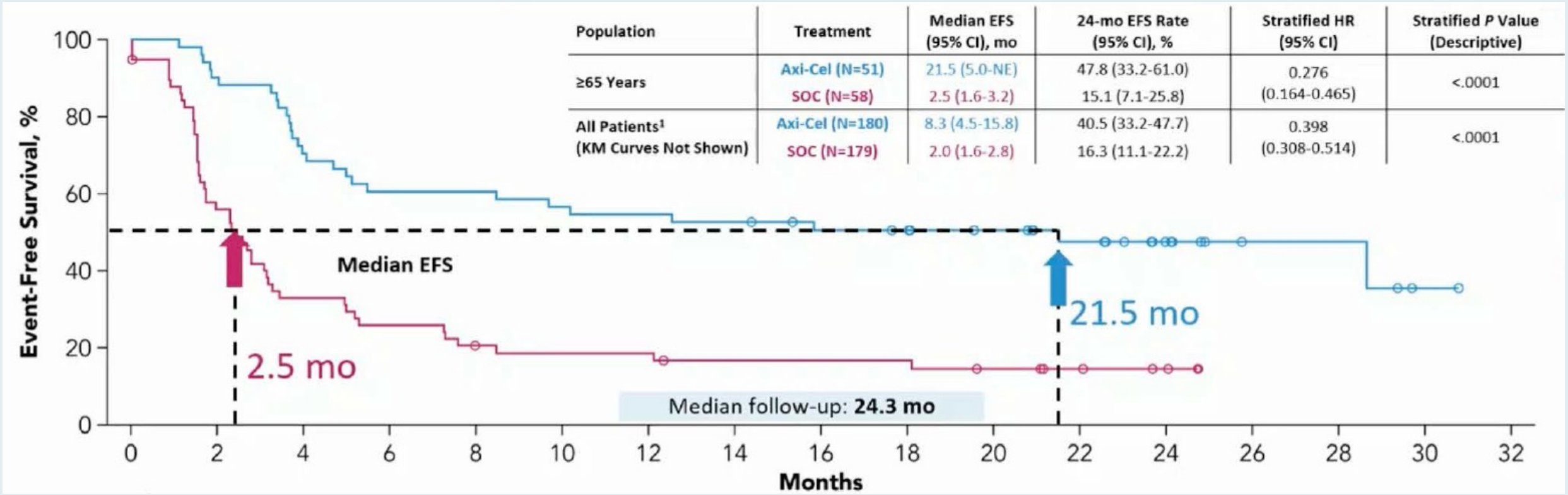
Anna Sureda

Abstract S211

RTP RESEARCH TO PRACTICE

ZUMA-7: Event-Free Survival per Blinded Central Review in Patients Aged ≥65 Years

Population	Treatment	Median EFS (95% CI), mo	24-mo EFS Rate (95% CI), %	Stratified HR (95% CI)	Stratified *P* Value (Descriptive)
≥65 Years	Axi-Cel (N=51)	21.5 (5.0-NE)	47.8 (33.2-61.0)	0.276 (0.164-0.465)	<.0001
	SOC (N=58)	2.5 (1.6-3.2)	15.1 (7.1-25.8)		
All Patients[1] (KM Curves Not Shown)	Axi-Cel (N=180)	8.3 (4.5-15.8)	40.5 (33.2-47.7)	0.398 (0.308-0.514)	<.0001
	SOC (N=179)	2.0 (1.6-2.8)	16.3 (11.1-22.2)		



Sureda A et al. EHA 2022;Abstract S211.

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ZUMA-7: Select Grade ≥3 Adverse Events

Adverse event	Axi-cel (N = 170)	SOC (N = 168)
Pyrexia	9%	1%
Neutropenia	69%	41%
Fatigue	6%	2%
Anemia	30%	39%
Thrombocytopenia	15%	57%
Febrile neutropenia	2%	27%
Cytokine release syndrome	6%	0
Neurologic event	21%	1%
Vomiting	0	1%

SOC = standard of care

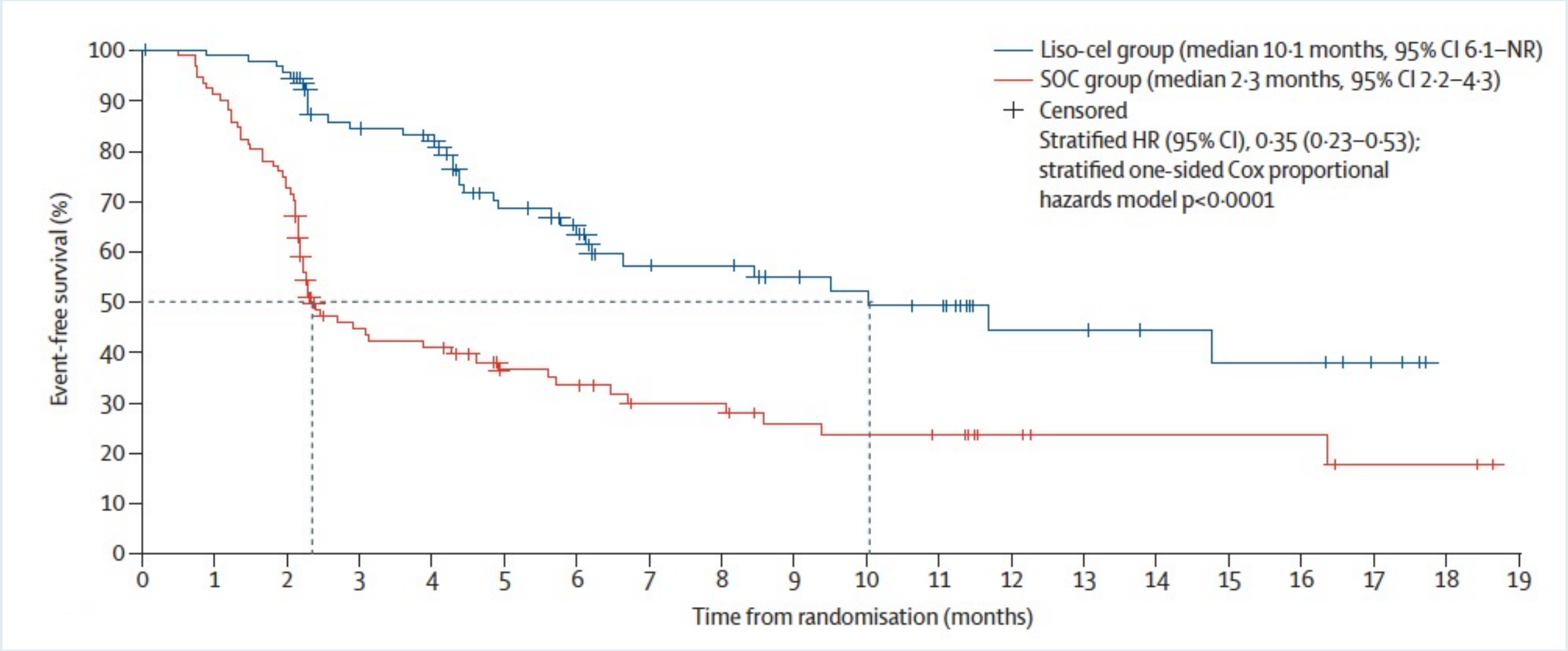
Sureda A et al. EHA 2022;Abstract S211.

Lisocabtagene maraleucel 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 (TRANSFORM): results from an interim analysis of an open-label, randomised, phase 3 trial

Manali Kamdar, Scott R Solomon, Jon Arnason, Patrick B Johnston, Bertram Glass, Veronika Bachanova, Sami Ibrahimi, Stephan Mielke, Pim Mutsaers, Francisco Hernandez-Ilizaliturri, Koji Izutsu, Franck Morschhauser, Matthew Lunning, David G Maloney, Alessandro Crotta, Sandrine Montheard, Alessandro Previtali, Lara Stepan, Ken Ogasawara, Timothy Mack, Jeremy S Abramson, for the TRANSFORM Investigators†*

Lancet 2022; 399: 2294–308

TRANSFORM: Event-Free Survival (ITT Population, Primary Endpoint)



Kamdar M et al. *Lancet* 2022;399:2294-308.

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N Engl J Med 2022;386(7):629-39.

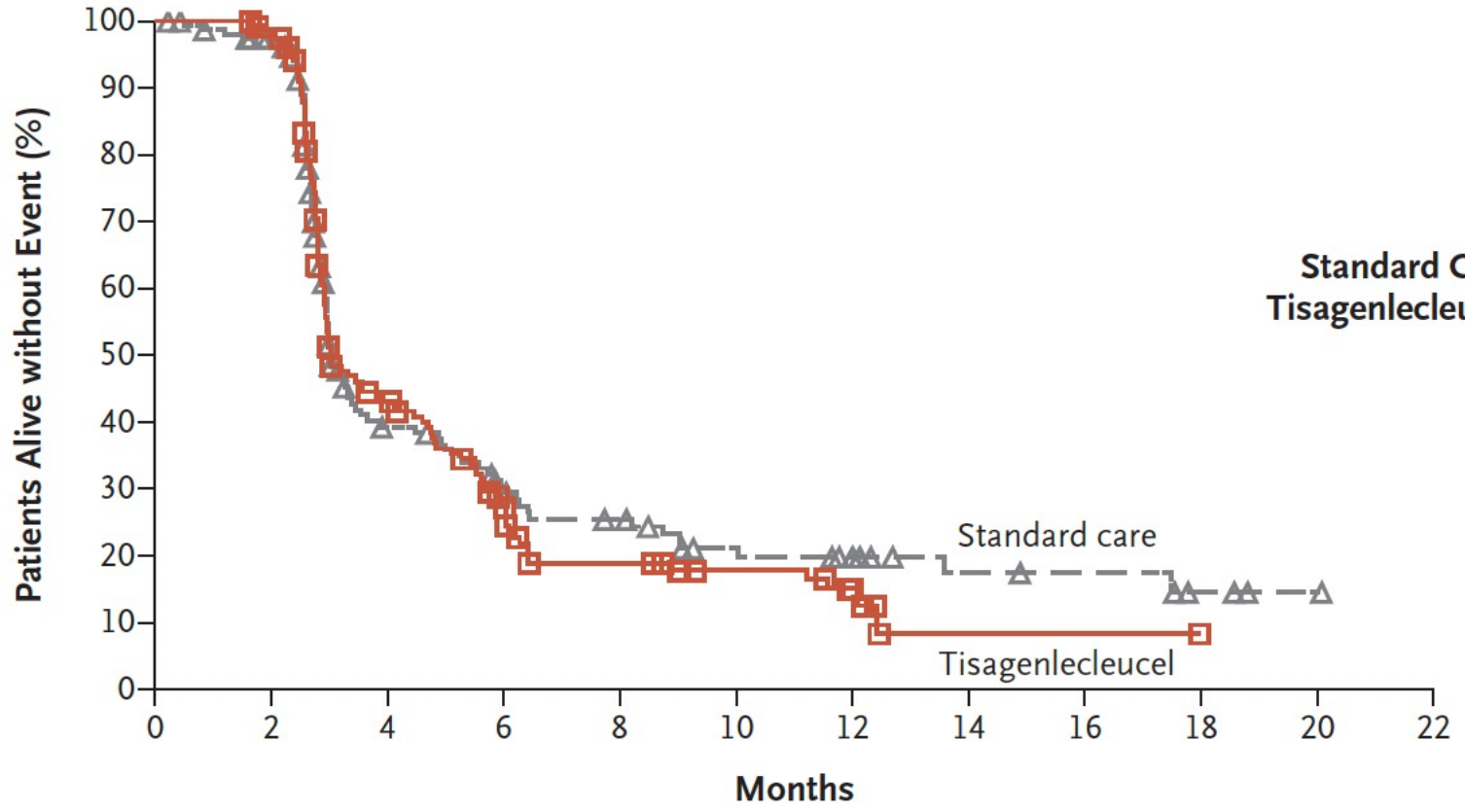
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Second-Line Tisagenlecleucel or Standard Care in Aggressive B-Cell Lymphoma

M.R. Bishop, M. Dickinson, D. Purtill, P. Barba, A. Santoro, N. Hamad, K. Kato, A. Sureda, R. Greil, C. Thieblemont, F. Morschhauser, M. Janz, I. Flinn, W. Rabitsch, Y.-L. Kwong, M.J. Kersten, M.C. Minnema, H. Holte, E.H.L. Chan, J. Martinez-Lopez, A.M.S. Müller, R.T. Maziarz, J.P. McGuirk, E. Bachy, S. Le Gouill, M. Dreyling, H. Harigae, D. Bond, C. Andreadis, P. McSweeney, M. Kharfan-Dabaja, S. Newsome, E. Degtyarev, R. Awasthi, C. del Corral, G. Andreola, A. Masood, S.J. Schuster, U. Jäger, P. Borchmann, and J.R. Westin

BELINDA: Event-Free Survival (Primary Endpoint)



	No. of Patients	No. of Events	Median Event-free Survival (95% CI)
			mo
Standard Care	160	104	3.0 (3.0–3.5)
Tisagenlecleucel	162	117	3.0 (2.9–4.2)

Hazard ratio for event or death (tisagenlecleucel vs. standard care), 1.07 (95% CI, 0.82–1.40)
P=0.61

No. at Risk

Standard care	160	148	45	31	25	17	12	7	6	3	1	0
Tisagenlecleucel	162	156	57	32	19	13	6	1	1	0	0	0

Bishop MR et al. *N Engl J Med* 2022;386(7):629-39.

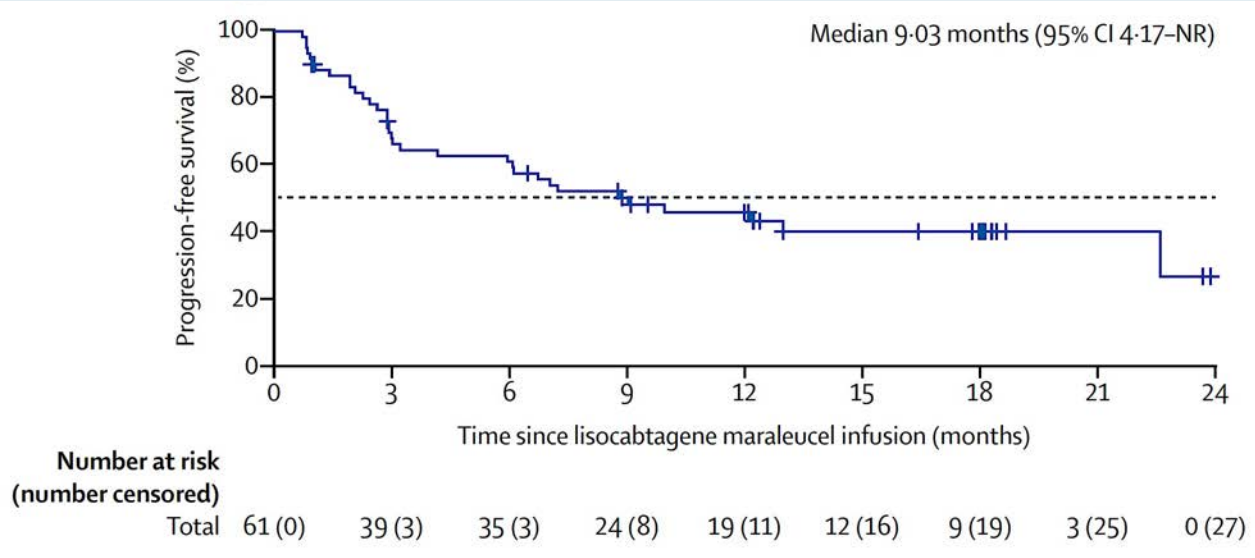
RTP RESEARCH TO PRACTICE

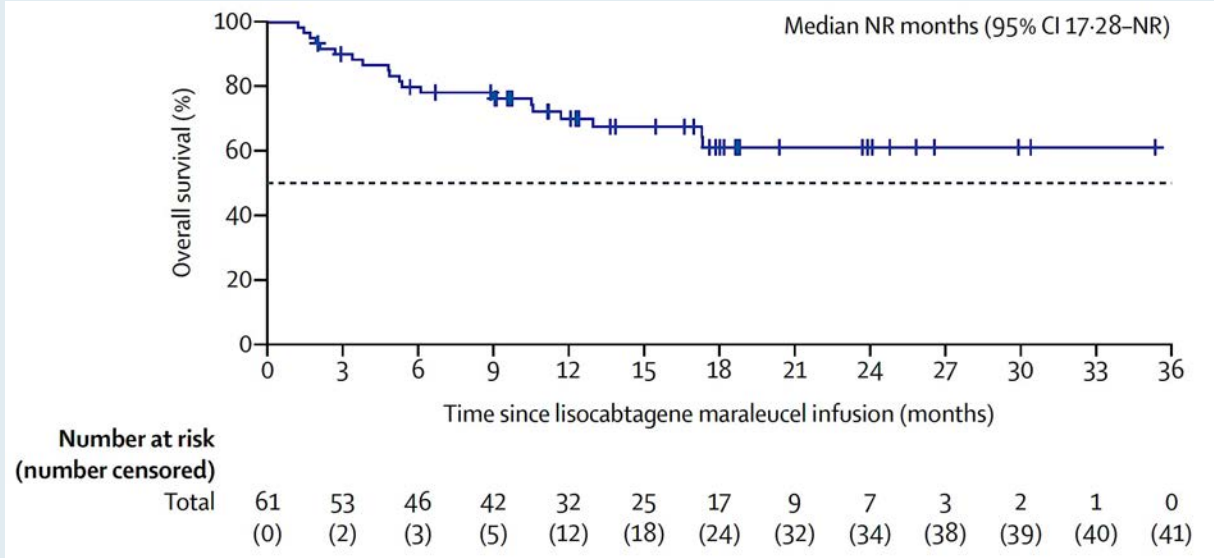
Lisocabtagene maraleucel as second-line therapy in adults with relapsed or refractory large B-cell lymphoma who were not intended for haematopoietic stem cell transplantation (PILOT): an open-label, phase 2 study

Alison Sehgal, Daanish Hoda, Peter A Riedell, Nilanjan Ghosh, Mehdi Hamadani, Gerhard C Hildebrandt, John E Godwin, Patrick M Reagan, Nina Wagner-Johnston, James Essell, Rajneesh Nath, Scott R Solomon, Rebecca Champion, Edward Licitra, Suzanne Fanning, Neel Gupta, Ronald Dubowy, Aleco D'Andrea, Lei Wang, Ken Ogasawara, Jerill Thorpe, Leo I Gordon

Lancet Oncology 2022;August;23(8):1066-77.

PILOT: Progression-Free and Overall Survival





Sehgal A et al. *Lancet Oncology* 2022;August;23(8):1066-77.

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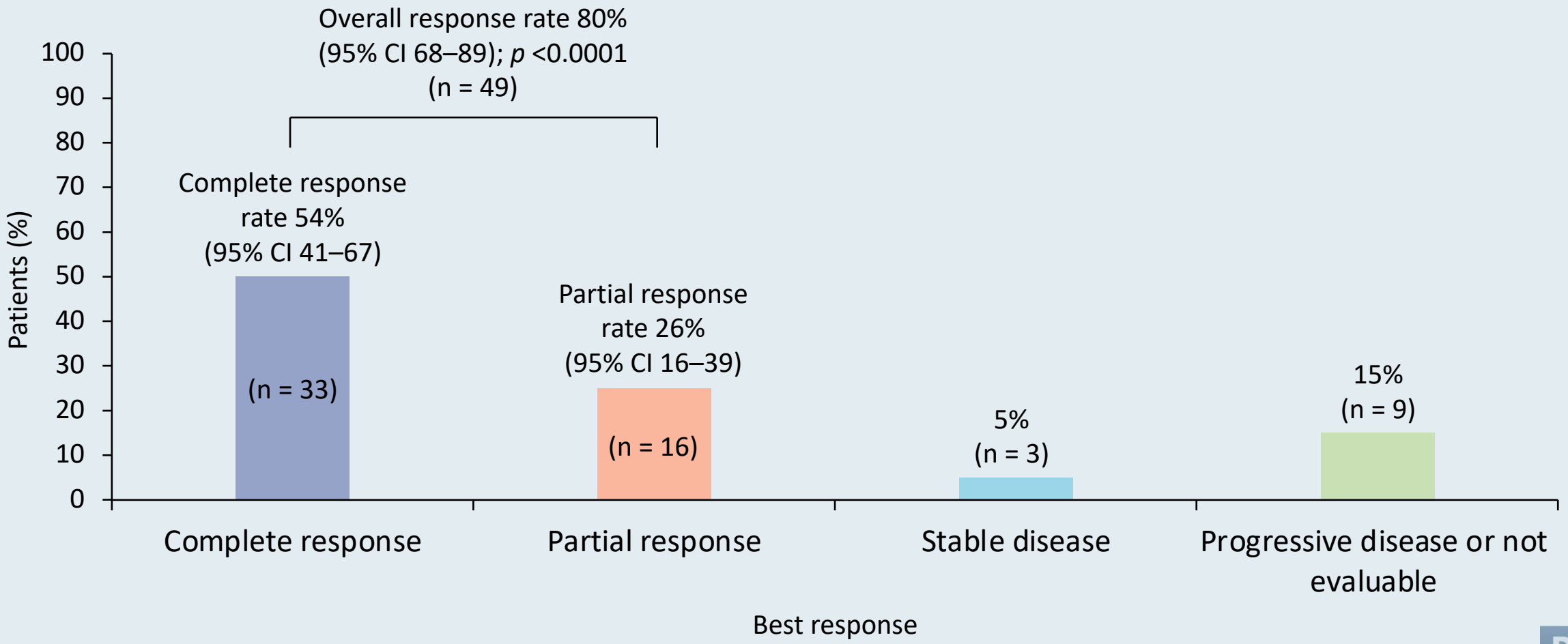
PILOT: Best Response by Independent Review Committee Assessment in the Efficacy Analysis Set



Sehgal A et al. *Lancet Oncology* 2022;August;23(8):1066-77.

PILOT: Patients Who Received Lisocabtagene Maraleucel (n = 61)

Transplantation not intended criteria	
Cytokine release syndrome	30 (49%)
Any grade	23 (38%)
Grade 1	11 (18%)
Grade 2	11 (18%)
Grade 3	1 (2%)
Grade 4 or 5	0
Time to onset,* days	4 (3-7)
Time to resolution,† days	4 (2-5)
Tocilizumab, corticosteroids, or both for cytokine release syndrome	16 (26%)
Tocilizumab only	6 (10%)
Tocilizumab and corticosteroids	10 (16%)
Corticosteroids only	0

* Time to onset was calculated from the lisocabtagene maraleucel infusion date to the first onset of cytokine release syndrome or a neurological event. Any cytokine release syndrome or a neurological event that started and stopped within 7 days was considered as a single episode.

† Time to resolution of cytokine release syndrome or a neurological event was defined as the number of days from onset to when the last event of the first episode ended. Patients with an unresolved event in the first episode were excluded from the summary.

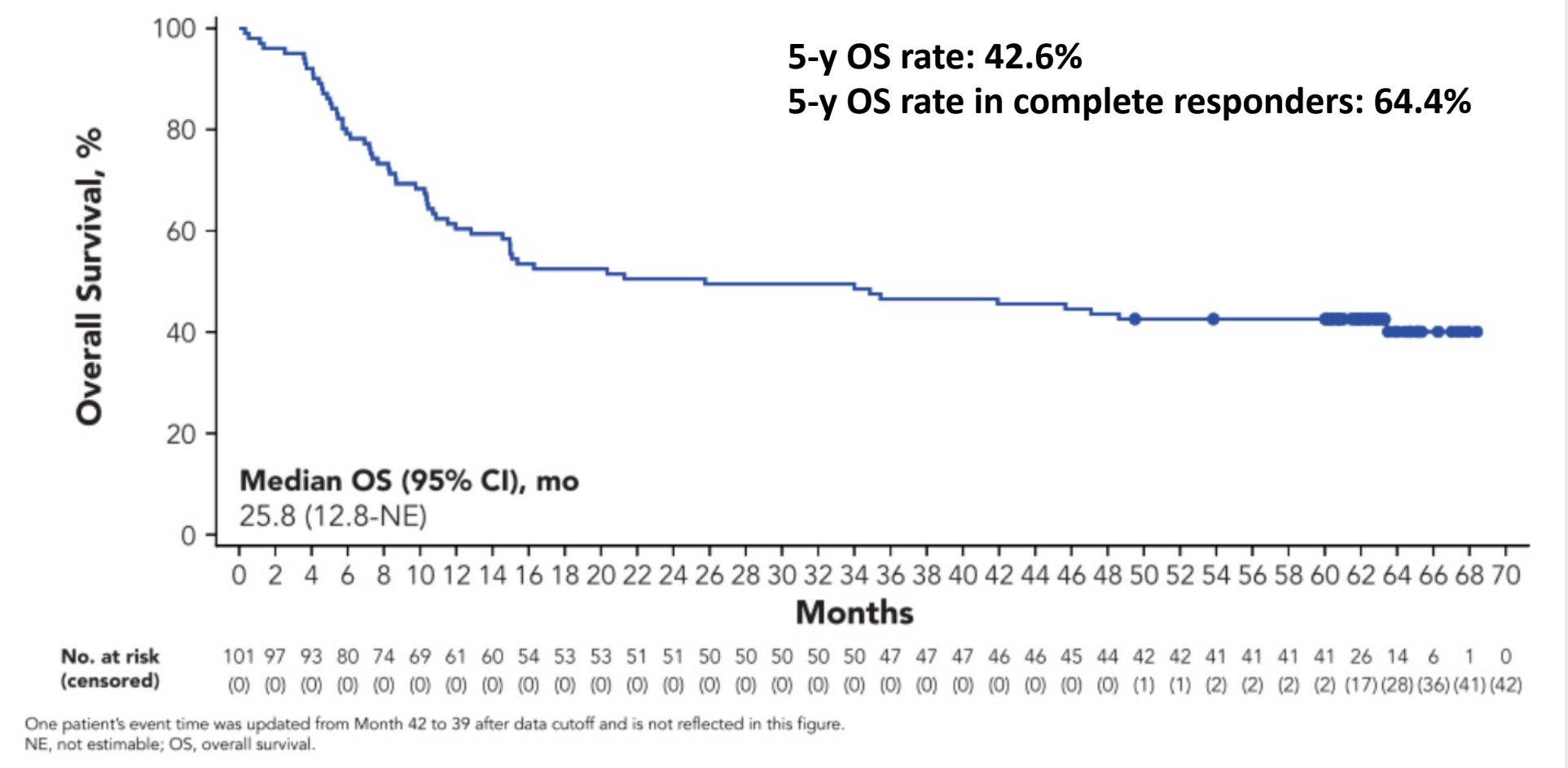
Sehgal A et al. *Lancet Oncology* 2022;August;23(8):1066-77.

Long-Term (4- and 5-Year) Overall Survival in ZUMA-1, the Pivotal Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients with Refractory Large B-Cell Lymphoma (LBCL)

Jacobson C et al.

ASH 2021;Abstract 1764.

ZUMA-1: Five-Year Update



One patient's event time was updated from Month 42 to 39 after data cutoff and is not reflected in this figure.
NE, not estimable; OS, overall survival.

- Median time to next cancer therapy: 8.7 months
- Safety findings were similar to those in previous reports

Jacobson C et al. ASH 2021;Abstract 1764.

RTP RESEARCH TO PRACTICE

Management of DLBCL
Where We Are, Where We're Headed

PROLOGUE

MODULE 1: First-Line Treatment

MODULE 2: Bispecific Antibodies

MODULE 3: CAR T-Cell Therapy

MODULE 4: Sequencing of Novel Agents

Dr Gupta: 68-year-old man with cardiac comorbidities and relapsed DLBCL while on R-CHOP receives second-line polatuzumab vedotin/BR

MODULE 5: Appendix

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Case Presentation: 68-year-old man with cardiac comorbidities and relapsed DLBCL while on R-CHOP receives second-line polatuzumab vedotin/BR

Dr Shaachi Gupta (Lake Worth, Florida)

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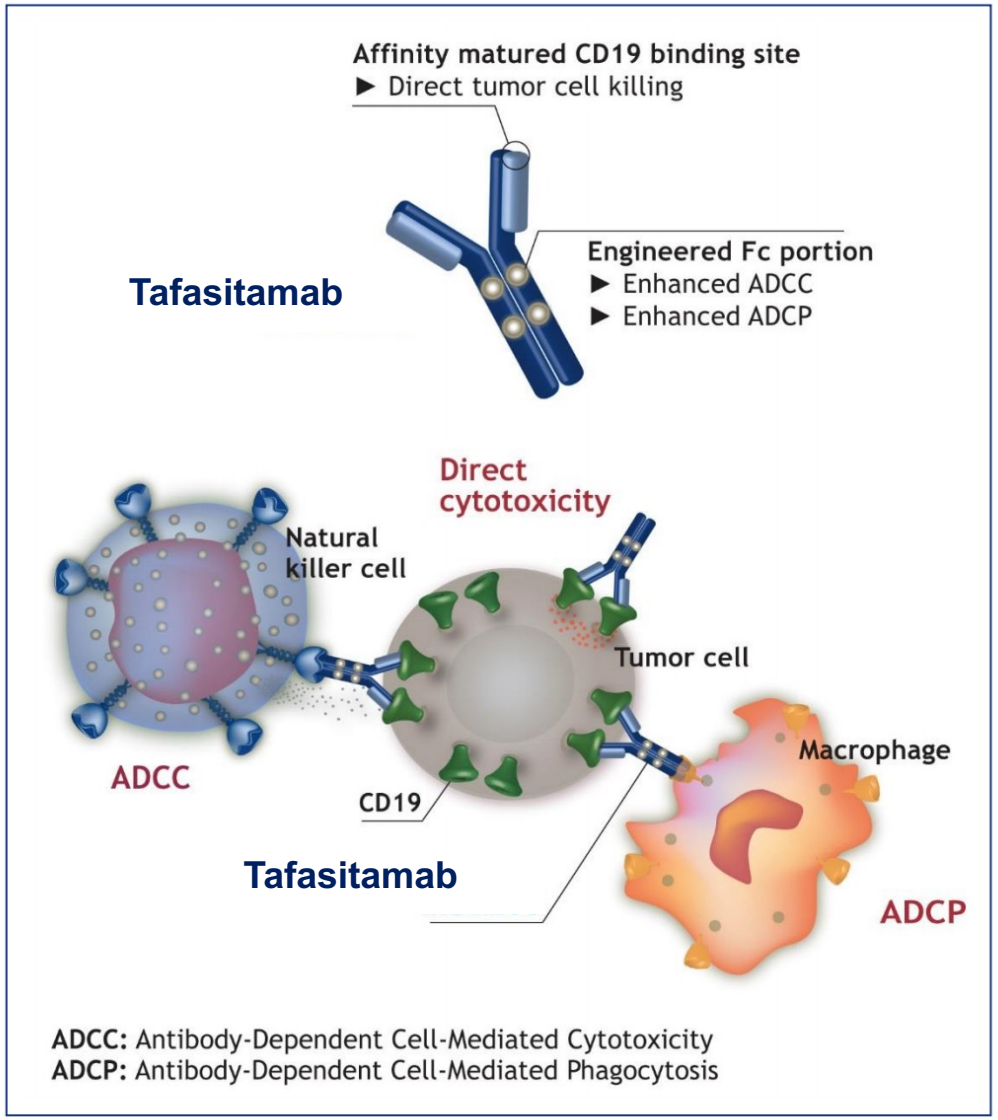
Novel Agents Recently Approved for Relapsed/Refractory DLBCL

	Pola-BR	Selinexor	Tafasitamab/ lenalidomide	Loncastuximab tesirine
Mechanism of action	Anti-CD79b ADC	XPO-1 inhibitor	Anti-CD19 MAb/immunomodulator	Anti-CD19 ADC
ORR	45%	28%	58%	48%
CR rate	40%	10%	40%	24%
PFS	9.2 mo	2.6 mo	11.6 mo	4.9 mo
DOR	12.6 mo	9.3 mo	43.9 mo	10.3 mo
OS	12.4 mo	NR	33.5 mo	9.9 mo

MAb = monoclonal antibody; ADC = antibody-drug conjugate

Content Courtesy of Laurie H Sehn MD, MPH

Tafasitamab (MOR208)



Lenalidomide enhances NK function with enhanced ADCC in vitro

Salles G et al. *Lancet Oncol* 2020;21(7):978-88.

RTP RESEARCH TO PRACTICE

Lancet Oncol 2020;21(7):978-88.

Tafasitamab plus lenalidomide in relapsed or refractory diffuse large B-cell lymphoma (L-MIND): a multicentre, prospective, single-arm, phase 2 study

Gilles Salles, Johannes Duell*, Eva González Barca, Olivier Tournilhac, Wojciech Jurczak, Anna Marina Liberati, Zsolt Nagy, Aleš Obr, Gianluca Gaidano, Marc André, Nagesh Kalakonda, Martin Dreyling, Johannes Weirather, Maren Dirnberger-Hertweck, Sumeet Ambarkhane, Günter Fingerle-Rowson, Kami Maddocks*

As a result of the L-MIND trial, tafasitamab in combination with lenalidomide was FDA approved for patients with relapsed or refractory DLBCL not otherwise specified, including DLBCL arising from low-grade lymphoma, who are not eligible for autologous stem cell transplant.

L-MIND: Best Objective Response According to Independent Radiology Committee or Clinical Review Committee

	Patients treated with tafasitamab plus lenalidomide (n=80)*
Best objective response	
Complete response	34 (43%; 32–54)
Partial response	14 (18%; 10–28)
Stable disease	11 (14%; 7–23)
Progressive disease	13 (16%; 9–26)
Not evaluable†	8 (10%; 4–19)
PET-confirmed complete response	30/34 (88%; 73–97)
Objective response‡	48 (60%; 48–71)
Disease control§	59 (74%; 63–83)

Data are n (%; 95% CI) or n/N (%). *One patient received tafasitamab only. †Patients had no valid postbaseline response assessments. ‡Complete response plus partial response. §Complete response plus partial response plus stable disease.

Salles G et al. *Lancet Oncol* 2020;21(7):978-88.

RTP RESEARCH TO PRACTICE

L-MIND: Select Adverse Events and Incidence of Infusion-Related Reactions

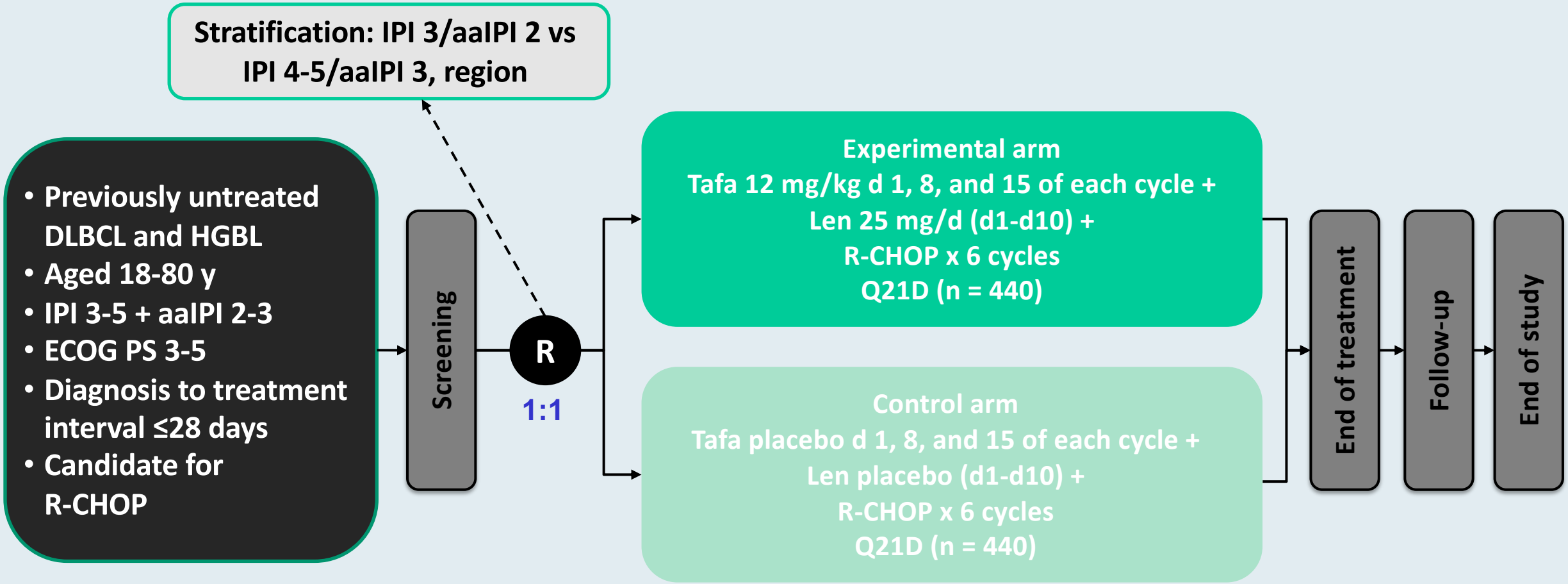
	Grade 1-2	Grade 3-4
Neutropenia	1 (1%)	39 (49%)
Anemia	22 (27%)	6 (7%)
Thrombocytopenia	11 (14%)	14 (18%)
Febrile neutropenia	0	10 (13%)
Pneumonia	1 (1%)	5 (6%)
Pulmonary embolism	0	4 (5%)

- Treatment-emergent adverse events that led to discontinuation of tafasitamab included pneumonia, bronchitis, deep vein thrombosis and allergic dermatitis.

- Infusion-related reactions (all Grade 1) were observed in 5 (6%) patients. All occurred once during the first infusion and no discontinuation of infusion was required.

Salles G et al. *Lancet Oncol* 2020;21(7):978-88.

frontMIND: Phase III Trial Design for Newly Diagnosed DLBCL



www.clinicaltrials.gov. NCT04824092. Accessed August 2022.

Lancet Oncol 2021;22(6):790-800.

Loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma (LOTIS-2): a multicentre, open-label, single-arm, phase 2 trial

Paolo F Caimi, Weiyun Ai, Juan Pablo Alderuccio, Kirit M Ardeshna, Mehdi Hamadani, Brian Hess, Brad S Kahl, John Radford, Melhem Solh, Anastasios Stathis, Pier Luigi Zinzani, Karin Havenith, Jay Feingold, Shui He, Yajuan Qin, David Ungar, Xiaoyan Zhang, Carmelo Carlo-Stella

As a result of the LOTIS-2 trial, loncastuximab tesirine was FDA approved for patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy, including DLBCL not otherwise specified, DLBCL arising from low-grade lymphoma and high-grade B-cell lymphoma.

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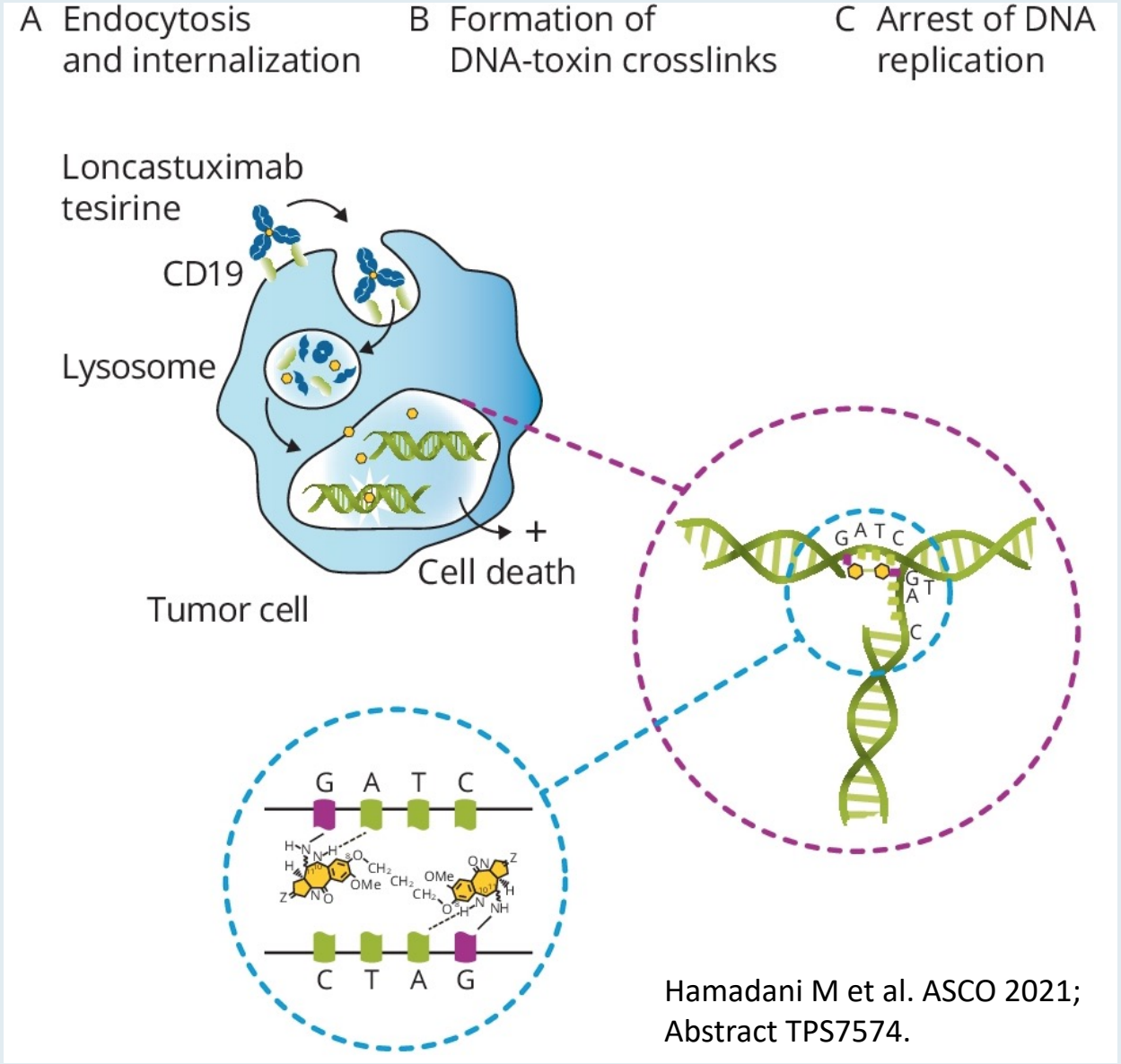
Mechanism of Action of Loncastuximab Tesirine



Hamadani M et al. ASCO 2021; Abstract TPS7574.

LOTIS-2: Response and Survival with Loncastuximab Tesirine for R/R DLBCL

Response	As-treated population (N = 145)
Overall response rate	70/145 (48.3%)
Complete response rate	35/145 (24.1%)
Complete response	35 (24%)
Partial response	35 (24%)
Stable disease	22 (15%)
Progressive disease	30 (21%)
Not evaluable	23 (16%)
Survival	**As-treated population (N = 145)**
Median progression-free survival	4.9 months
Median overall survival	9.9 months

Caimi PF et al. *Lancet Oncol* 2021;22(6):790-800.

LOTIS-2: Select Treatment-Emergent Adverse Events (AEs)

Treatment-emergent AEs	Grade 1-2	Grade 3-4
Peripheral edema*	19%	1%
Anemia	16%	10%
Thrombocytopenia	15%	18%
Neutropenia	14%	26%
Pleural effusion*	8%	2%
Leukopenia	6%	9%

* Treatment-emergent AEs considered likely to be related to the the agent's payload included edema or effusion, symptoms in the skin or nails and liver enzyme abnormalities

Caimi PF et al. *Lancet Oncol* 2021;22(6):790-800.

Polatuzumab vedotin plus bendamustine and rituximab in relapsed/refractory DLBCL: survival update and new extension cohort data

Laurie H. Sehn,[1] Mark Hertzberg,[2] Stephen Opat,[3] Alex F. Herrera,[4] Sarit Assouline,[5] Christopher R. Flowers,[6] Tae Min Kim,[7] Andrew McMillan,[8] Muhit Ozcan,[9] Violaine Safar,[10] Gilles Salles,[10] Grace Ku,[11] Jamie Hirata,[11] Yi Meng Chang,[12] Lisa Musick,[11] and Matthew J. Matasar[13]

***Blood Adv* 2022;6(2):533-43.**

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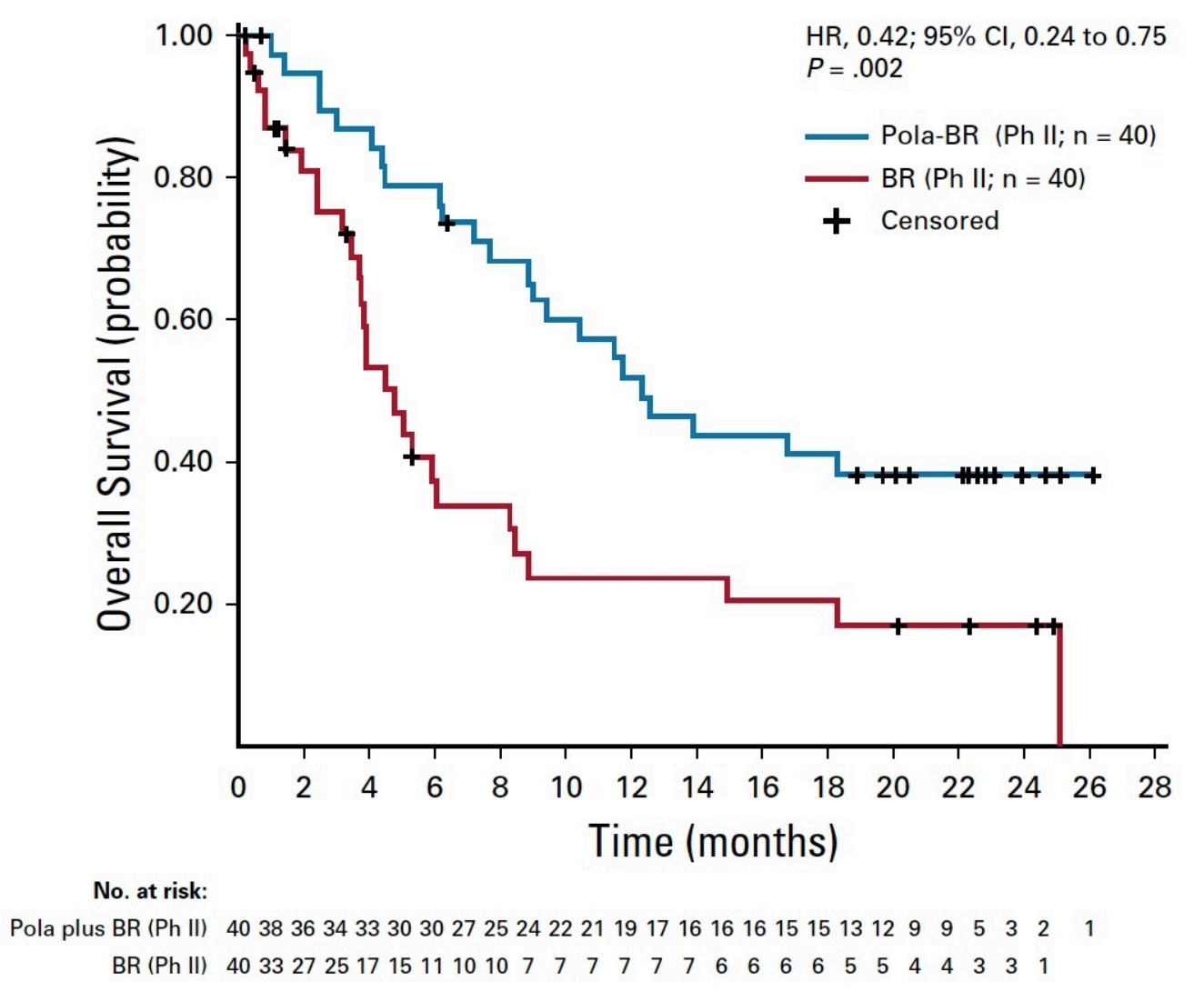
Polatuzumab Vedotin with BR for Transplant-Ineligible R/R DLBCL: Overall Survival



Sehn LH et al. *J Clin Oncol* 2020;38(2):155-65.

Management of DLBCL
Where We Are, Where We're Headed

PROLOGUE

MODULE 1: First-Line Treatment

MODULE 2: Bispecific Antibodies

MODULE 3: CAR T-Cell Therapy

MODULE 4: Sequencing of Novel Agents

MODULE 5: Appendix

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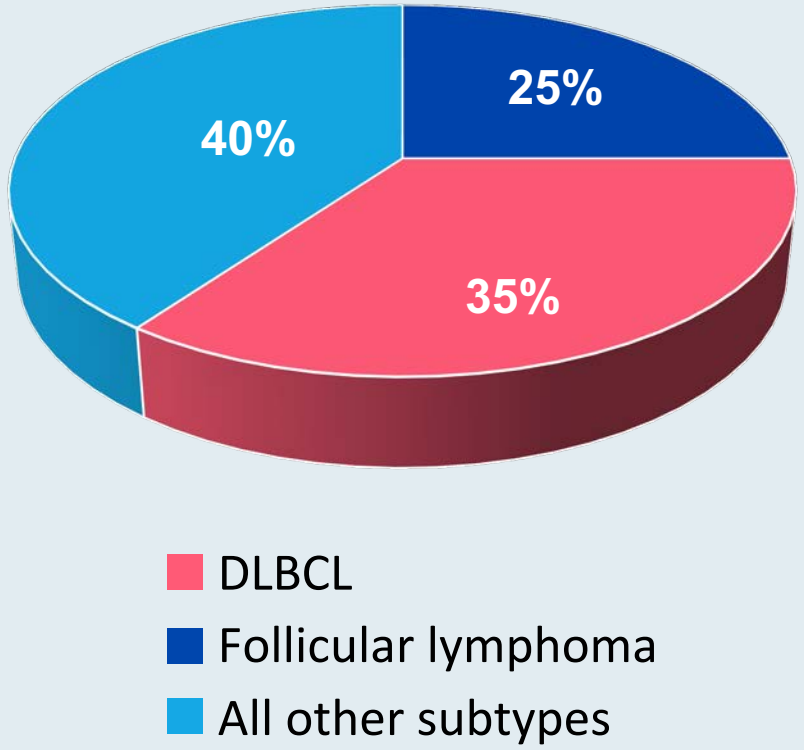
Overview of DLBCL

DLBCL Is the Most Common Non-Hodgkin Lymphoma (NHL) Subtype

United States patients with DLBCL

- Newly diagnosed ~28,000 per year
- Relapsed/refractory ~11,000 per year

NHL prevalence in the US



Teras et al. *CA Cancer J Clin* 2016;66(6):443-59.

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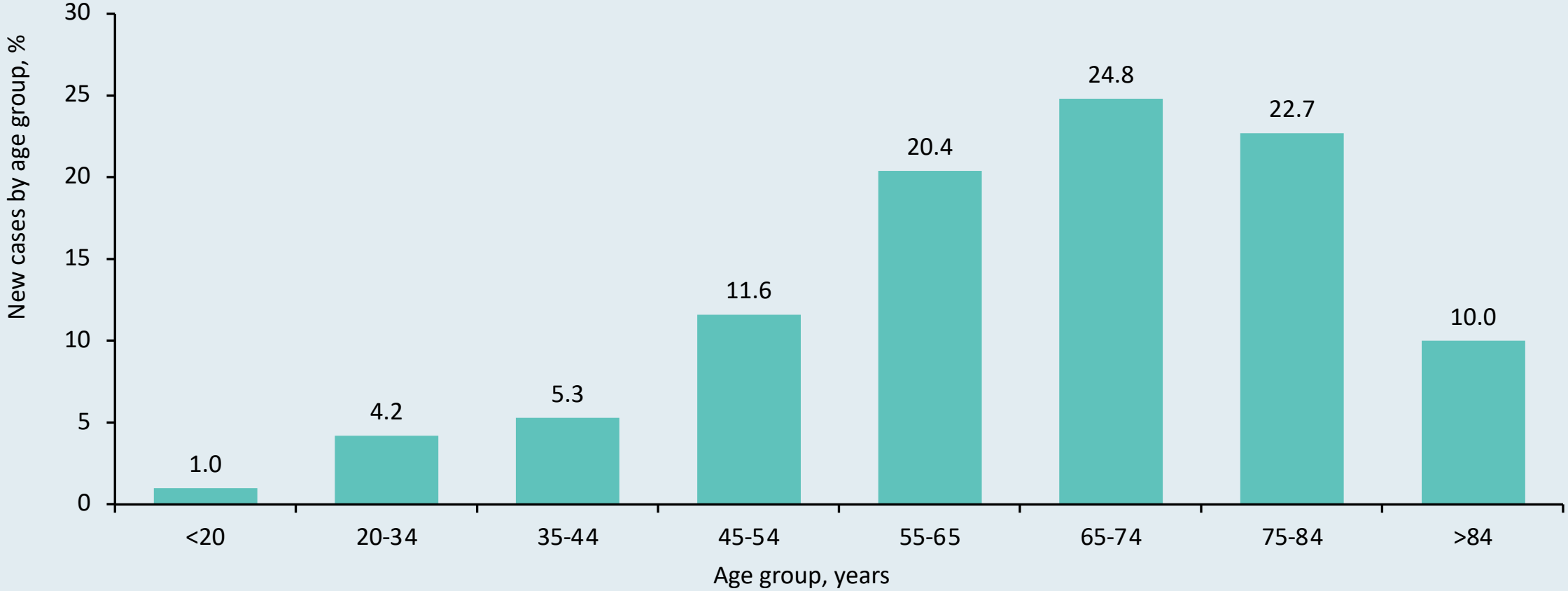
DLBCL Incidence Increases with Age

- **Average patient at diagnosis is 60-65 years of age (median age = 69 years), and most are not fit for high-dose chemotherapy/autologous stem cell transplant[1-4]**

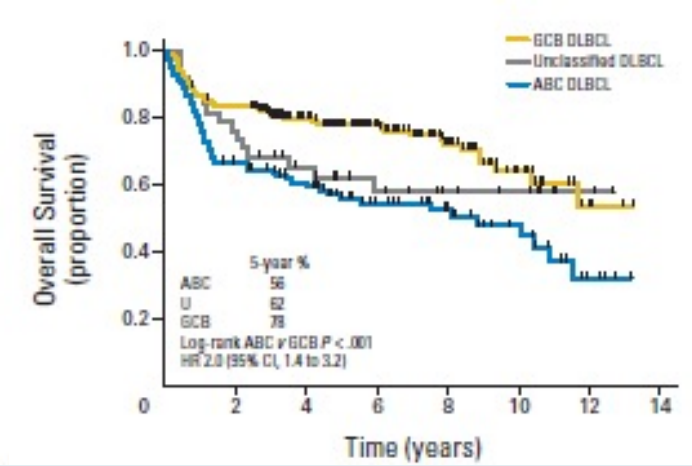


1. https://seer.cancer.gov/statfacts/html/dlbcl.html; 2. https://www.leukaemia.org.au/wp-content/uploads/2011/11/Factsheet-Lymphoma-DLBCL.pdf; 3. Martelli M et al. *Crit Rev Oncol Hematol* 2013;87(2):146-71; 4. Broccoli A et al. *Oncologist* 2019;24(9):1246-52.

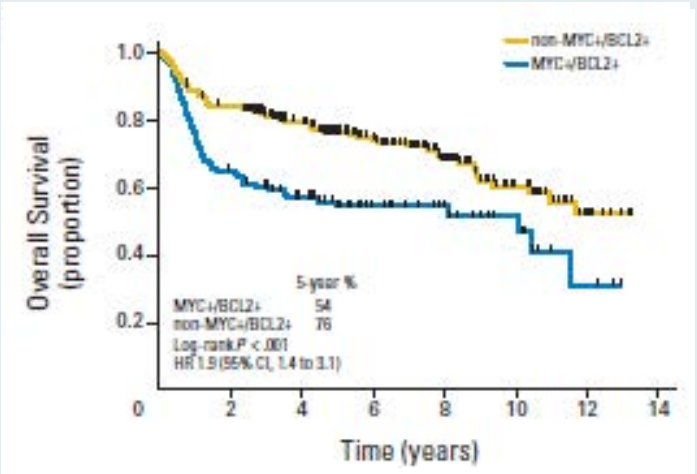
DLBCL: Prognosis

- **5-year overall survival**
  - Germinal center: 76%
  - Nongerminal center: 56%
  - "Double expressor": 54%
    - Overexpression of c-MYC and BCL2 or BCL6
  - Double hit: ~35%
    - Translocation of c-MYC and BCL2

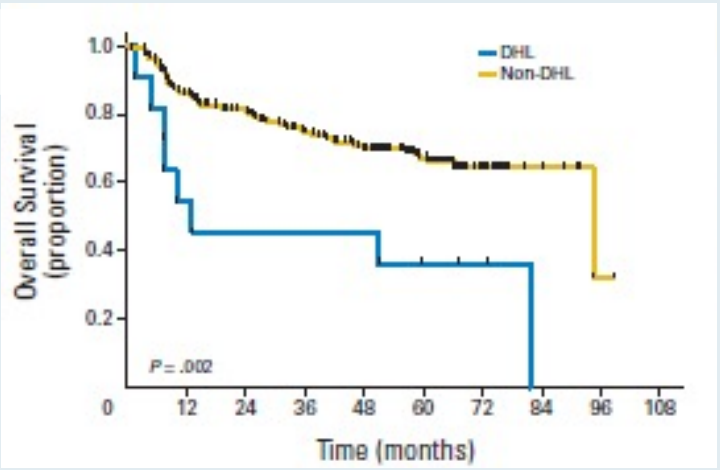
GCB vs non-GCB



Double expressor



Double hit



Hans et al. *Blood* 2004;103:275-82; Scott et al. *JCO* 2015; Green et al. *JCO* 2012.

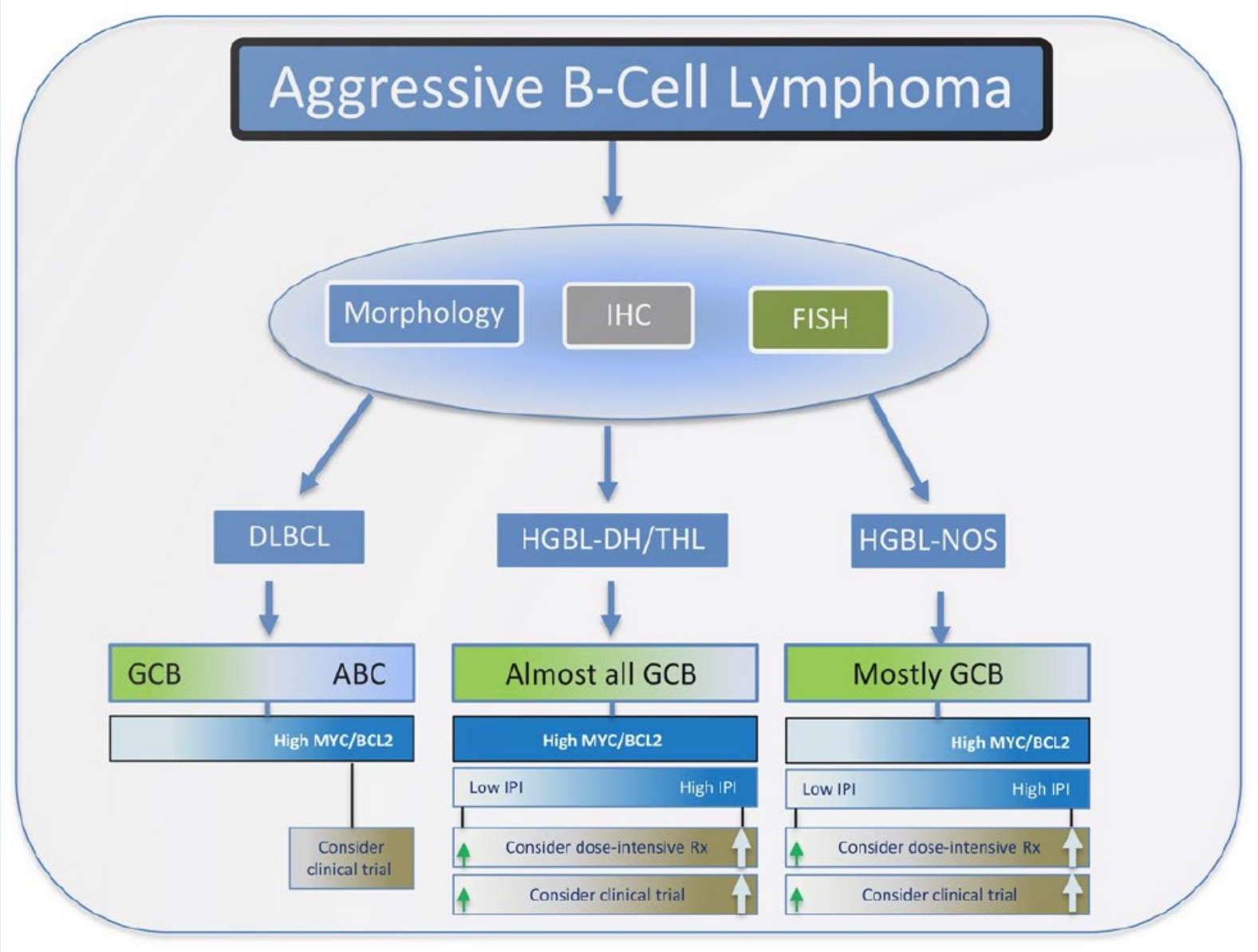
RTP RESEARCH TO PRACTICE

Double-hit lymphoma: optimizing therapy

Kieron Dunleavy
Division of Hematology and Oncology, Georgetown Lombardi Comprehensive Cancer Center, Georgetown University Hospital, Washington, DC

ASH 2021 Education Program.

Outline for Workup and Management of Aggressive B-Cell Lymphomas



Dunleavy K. ASH 2021 Education Program.

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R-CHOP Became the Standard Treatment >20 Years Ago

- **Three large randomized trials (n ≈ 2,000) in advanced-stage DLBCL for patients ≥60 years old show improved OS with R-CHOP versus CHOP:**
  - At 3 years: 70% versus 57%
  - At 5 years: 58% versus 45%
  - At 10 years: 44% versus 28%
- **Similar trial in advanced-stage DLBCL for patients <60 years old showed improved OS with R-CHOP versus CHOP (n = 824):**
  - At 3 years: 93% versus 84%
  - At 5 years: 90% versus 80%

Content Courtesy of Neha Mehta-Shah, MD, MSCI

Bispecific Antibodies

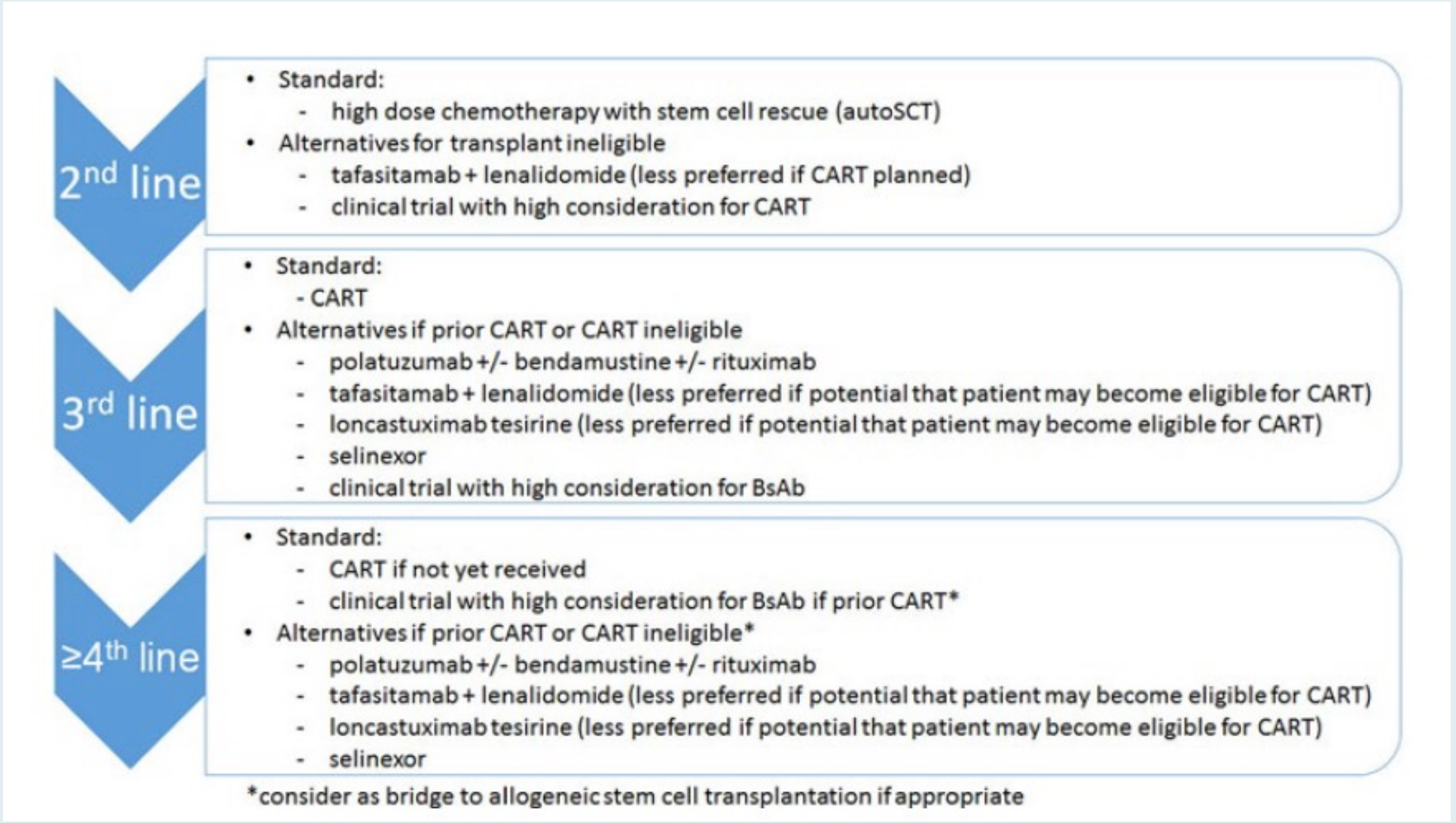
DEFEATING DIFFUSE, DOUBLE-HIT, AND DOGGED NON-HODGKIN LYMPHOMA

Relapsed disease: off-the-shelf immunotherapies vs customized engineered products

Reem Karmali
Northwestern University Feinberg School of Medicine, Chicago, IL

ASH 2021 Education Program.

Algorithm for Preferred and Alternative Treatment Options for R/R DLBCL



Karmali R. ASH 2021 Education Program.

RTP RESEARCH TO PRACTICE

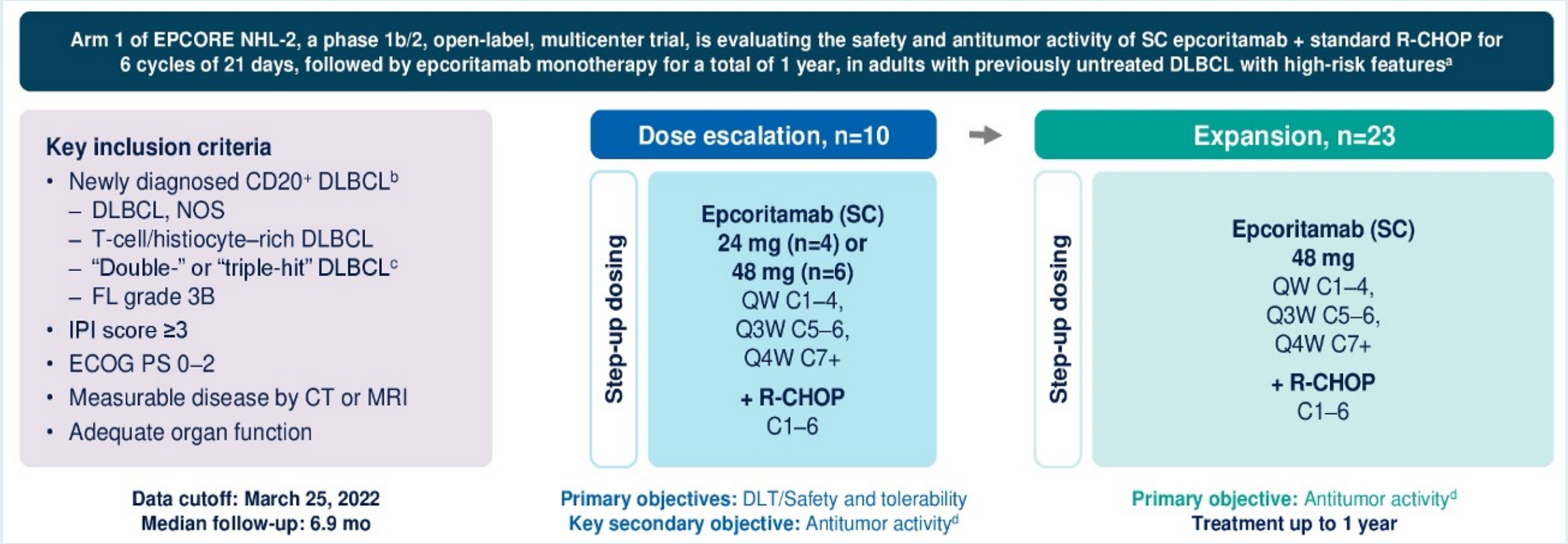
7523

ASCO 2022

First-line treatment (Tx) with subcutaneous (SC) epcoritamab (epco) + R-CHOP in patients (pts) with high-risk diffuse large B-cell lymphoma (DLBCL): phase 1/2 data update

Lorenzo Falchi, MD,[1*] Fritz Offner, MD, PhD,[2] David Belada, MD, PhD,[3] Joshua Brody, MD,[4] Kim M. Linton, MBChB, PhD,[5] Yasmin Karimi, MD,[6] Raul Cordoba, MD, PhD,[7] Sylvia Snauwaert, MD, PhD,[8] Aqeel Abbas, MS,[9] Liwei Wang, PhD,[9] Jun Wu, MD, MS,[10] Brian Elliott, MD,[9] Michael Roost Clausen, MD, PhD[11]

EPCORE NHL-2 Arm 1 Study Design



Falchi L et al. ASCO 2022;Abstract 7523.

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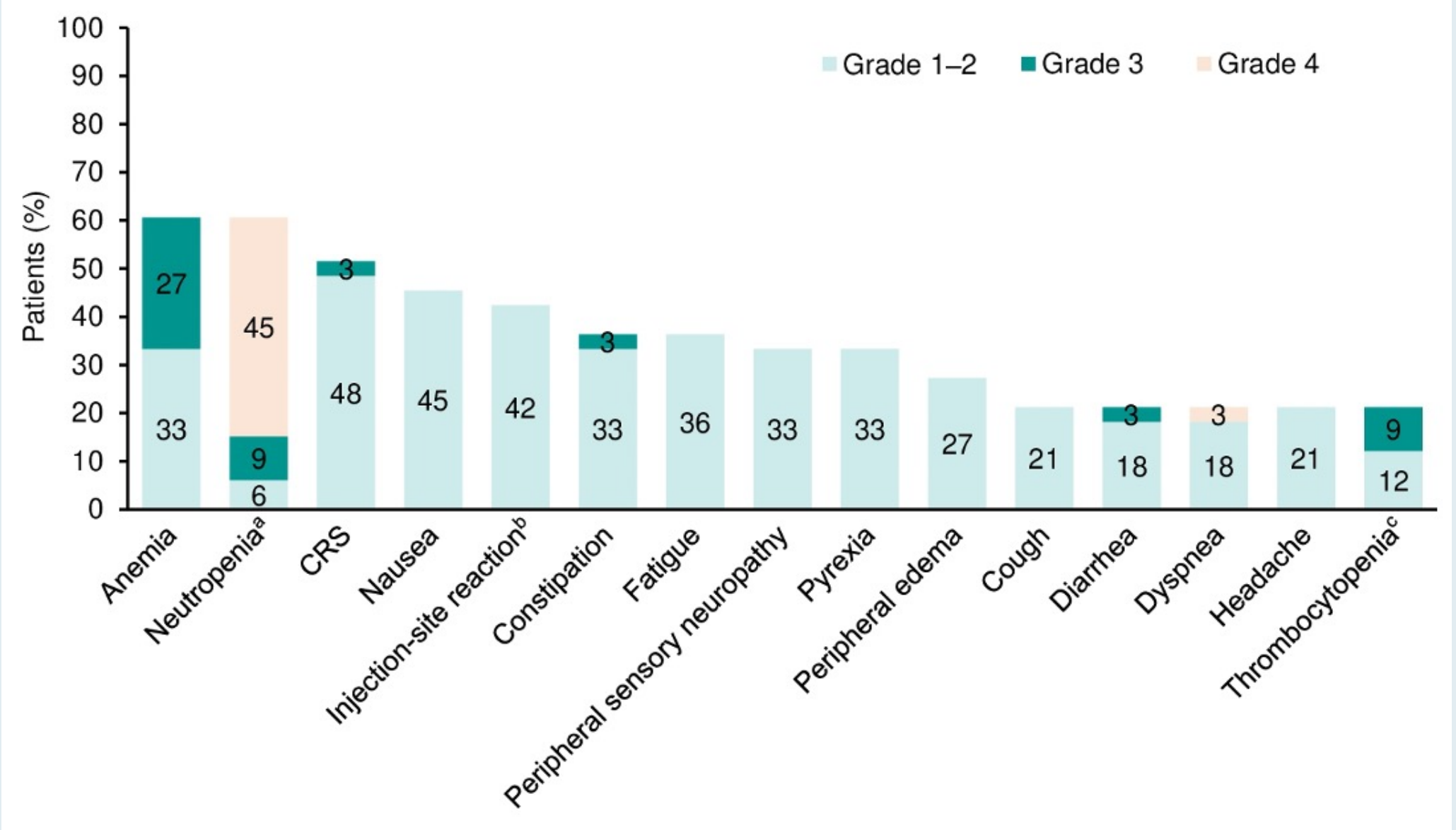
EPCORE NHL-2: Treatment-Emergent Adverse Events



Falchi L et al. ASCO 2022;Abstract 7523.

CAR T-Cell Therapy

Lisocabtagene maraleucel 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 (TRANSFORM): results from an interim analysis of an open-label, randomised, phase 3 trial

Manali Kamdar, Scott R Solomon, Jon Arnason, Patrick B Johnston, Bertram Glass, Veronika Bachanova, Sami Ibrahimi, Stephan Mielke, Pim Mutsaers, Francisco Hernandez-Ilizaliturri, Koji Izutsu, Franck Morschhauser, Matthew Lunning, David G Maloney, Alessandro Crotta, Sandrine Montheard, Alessandro Previtali, Lara Stepan, Ken Ogasawara, Timothy Mack, Jeremy S Abramson, for the TRANSFORM Investigators†*

Lancet 2022; 399: 2294–308

TRANSFORM: Summary of Primary and Key Secondary Endpoints

	Liso-cel group (n=92)	Standard-of-care group (n=92)	Stratified HR (95% CI)*	p value
Event-free survival based on IRC assessment (primary endpoint)				
Number of patients with events (%)	35 (38%)	63 (68%)	..	..
Median (95% CI), months†	10·1 (6·1–NR)	2·3 (2·2–4·3)	0·35 (0·23–0·53)	<0·0001
6-month rate (95% CI‡)	63·3% (52·0–74·7)	33·4% (23·0–43·8)	..	..
12-month rate (95% CI‡)	44·5% (29·4–59·6)	23·7% (13·4–34·1)	..	..
Complete response rate§ based on IRC assessment (key secondary endpoint)				
n (%, 95% CI)	61 (66%; 56–76)	36 (39%; 29–50)	..	<0·0001
Progression-free survival based on IRC assessment (key secondary endpoint)				
Number of patients with events (%)	28 (30%)	43 (47%)	..	..
Median (95% CI), months†	14·8 (6·6–NR)	5·7 (3·9–9·4)	0·41 (0·25–0·66)	0·0001
6-month rate (95% CI‡)	69·4% (58·1–80·6)	47·8% (35·0–60·6)	..	..
12-month rate (95% CI‡)	52·3% (36·7–67·9)	33·9% (20·1–47·7)	..	..
Overall survival (key secondary endpoint)				
Number of patients with events (%)	13 (14%)	24 (26%)	..	..
Median (95% CI), months	NR (15·8–NR)	16·4 (11·0–NR)	0·51 (0·26–1·00)	0·026
6-month rate (95% CI‡)	91·8% (85·4–98·2)	89·4% (82·9–96·0)	..	..
12-month rate (95% CI‡)	79·1% (67·1–91·1)	64·2% (50·5–77·9)	..	..
Overall response rate (secondary endpoint)				
n (%, 95% CI)	79 (86%; 77–92)	44 (48%; 37–59)	..	..

Kamdar M et al. *Lancet* 2022;399:2294-308.

TRANSFORM: Select Adverse Events

	Liso-cel group (n=92)		Standard-of-care group (n=91)	
	Grade 1–2	Grade ≥3	Grade 1–2	Grade ≥3
Any treatment-emergent adverse event	90 (98%)	85 (92%)	90 (99%)	79 (87%)
Any serious treatment-emergent adverse event	24 (26%)	31 (34%)	16 (18%)	39 (43%)
Deaths due to treatment-emergent adverse event	NA	1 (1%)*	NA	2 (2%)*
Most common treatment-emergent adverse events (occurring in ≥10% of patients in either group)				
Neutropenia	43 (47%)	74 (80%)	17 (19%)	46 (51%)
Anaemia	36 (39%)	45 (49%)	34 (37%)	45 (49%)
Thrombocytopenia	30 (33%)	45 (49%)	35 (38%)	58 (64%)
Nausea	49 (53%)	3 (3%)	52 (57%)	3 (3%)
Cytokine release syndrome	45 (49%)	1 (1%)	0	0
Prolonged cytopenia†	NA	40 (43%)	NA	3 (3%)
Headache	39 (42%)	4 (4%)	19 (21%)	1 (1%)
Fatigue	36 (39%)	0	34 (37%)	2 (2%)
Constipation	31 (34%)	2 (2%)	22 (24%)	0
Diarrhoea	23 (25%)	0	37 (41%)	3 (3%)

Kamdar M et al. *Lancet* 2022;399:2294-308.

RTP RESEARCH TO PRACTICE

N Engl J Med 2022;386(7):629-39.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Second-Line Tisagenlecleucel or Standard Care in Aggressive B-Cell Lymphoma

M.R. Bishop, M. Dickinson, D. Purtill, P. Barba, A. Santoro, N. Hamad, K. Kato, A. Sureda, R. Greil, C. Thieblemont, F. Morschhauser, M. Janz, I. Flinn, W. Rabitsch, Y.-L. Kwong, M.J. Kersten, M.C. Minnema, H. Holte, E.H.L. Chan, J. Martinez-Lopez, A.M.S. Müller, R.T. Maziarz, J.P. McGuirk, E. Bachy, S. Le Gouill, M. Dreyling, H. Harigae, D. Bond, C. Andreadis, P. McSweeney, M. Kharfan-Dabaja, S. Newsome, E. Degtyarev, R. Awasthi, C. del Corral, G. Andreola, A. Masood, S.J. Schuster, U. Jäger, P. Borchmann, and J.R. Westin

BELINDA: Select Grade ≥3 Adverse Events

Adverse event	Tisagenlecleucel (N = 162)	SOC (N = 160)
Anemia	33.3%	57.5%
Nausea	1.2%	6.3%
Thrombocytopenia	32.1%	47.5%
Neutropenia	40.1%	39.4%
Cytokine release syndrome	4.9%	0
Hypokalemia	4.9%	8.8%
Diarrhea	1.9%	3.8%
Pyrexia	0	1.9%
Vomiting	0.6%	1.9%

Bishop MR et al. *N Engl J Med* 2022;386(7):629-39.

CAR T-Cell Therapy-Associated Cytokine Release Syndrome (CRS)

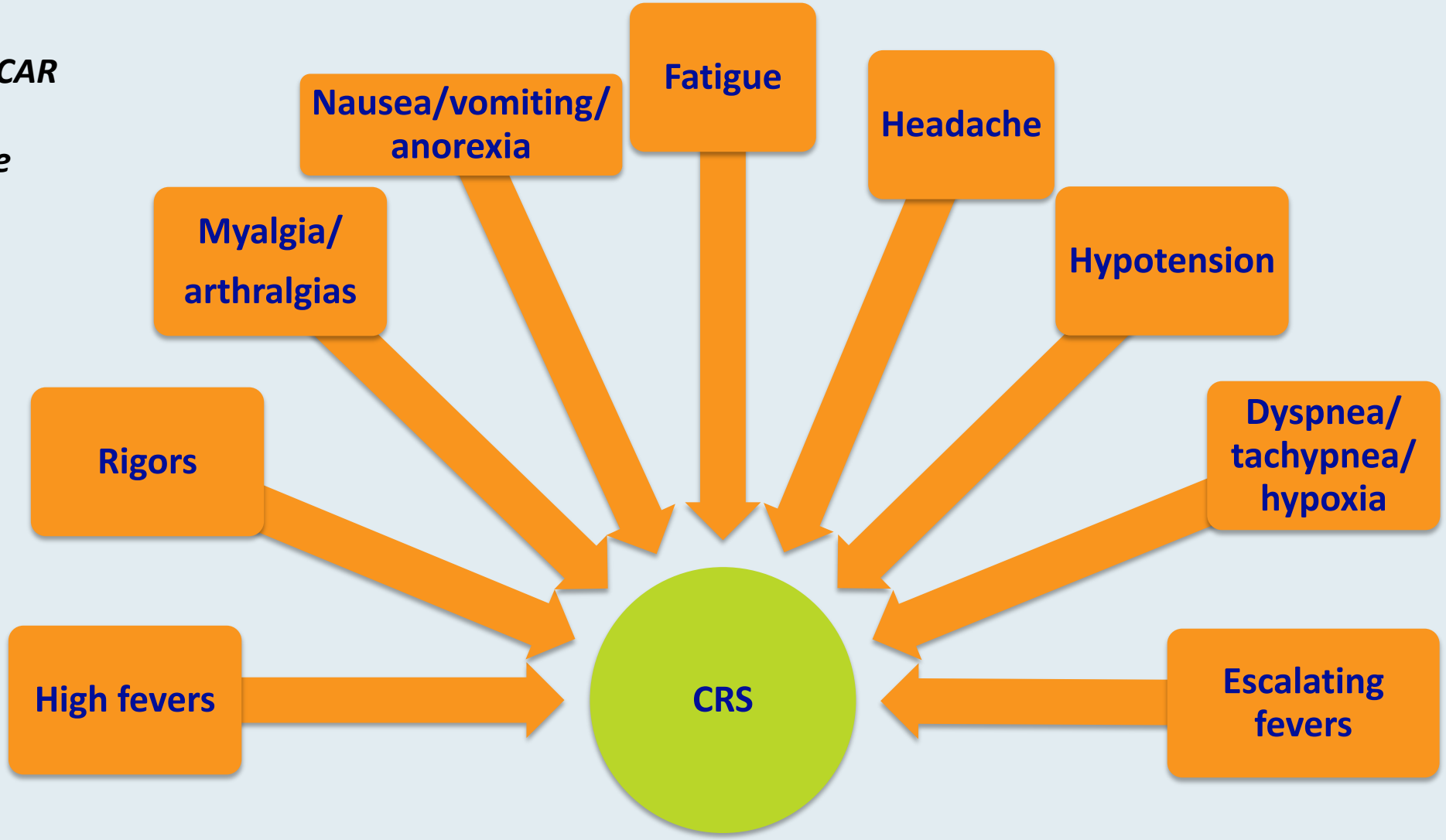
CRS — May be mild or life-threatening

- Occurs with CART19 activation and expansion
- Dramatic cytokine elevations (IL-6, IL10, IFNɣ, CRP, ferritin)
- Fevers initially (can be quite high: 105˚F)
- Myalgias, fatigue, nausea/anorexia
- Capillary leak, headache, hypoxia and hypotension
- CRS-related mortality 3% to 10%

Varadarajan I, Lee DW. *Cancer J* 2019;25(3):223-30.
Abramson JS et al. ASCO 2019 Education Book.

Cytokine Release Syndrome (CRS): Common Symptoms

Based on CAR T-cell experience



Diagnosis based on <u>clinical</u> symptoms and events

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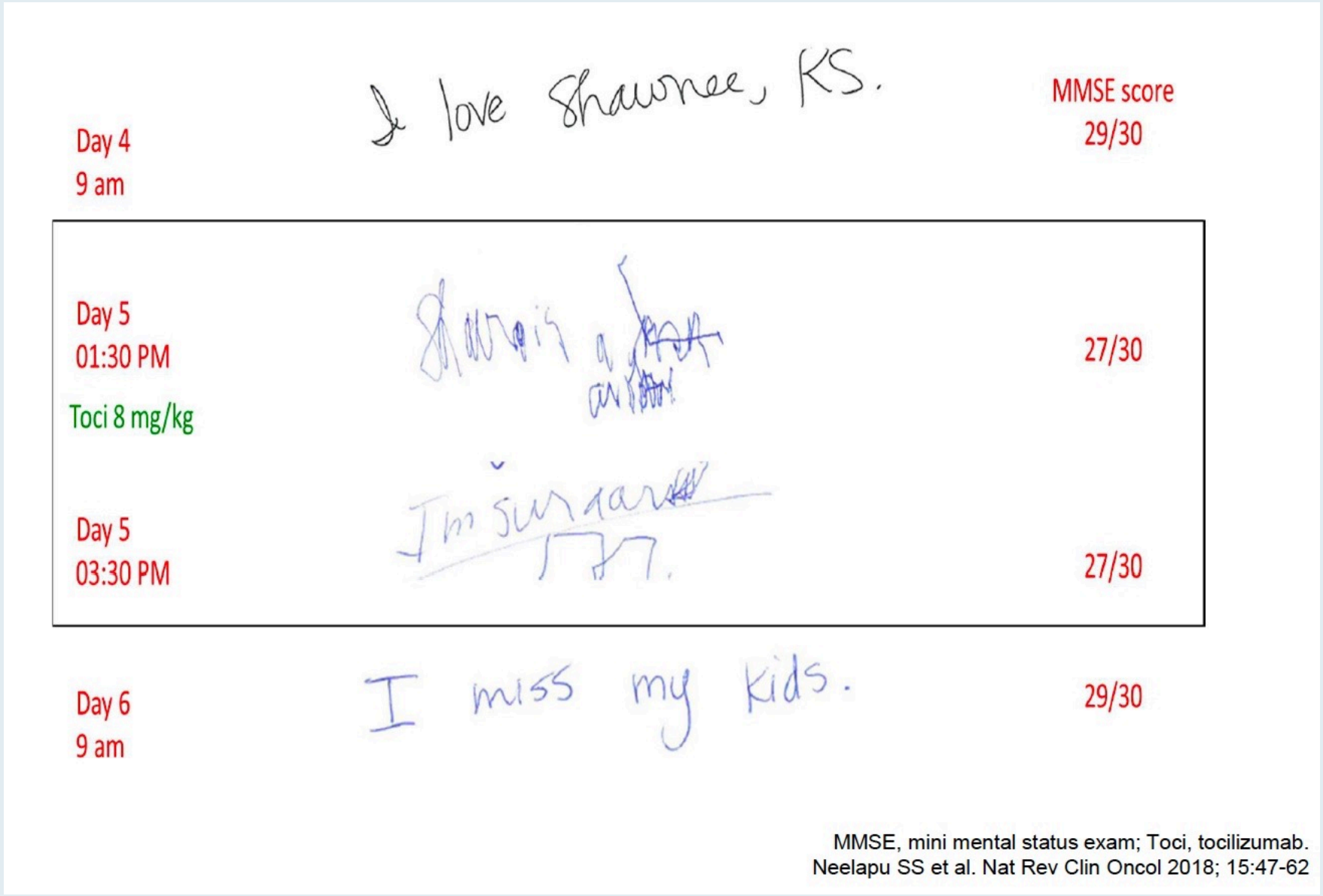
CAR T-Cell Therapy-Associated Neurologic Toxicity

Neurologic toxicity — May be mild or life-threatening

- Mechanism unclear, referred to as immune effector cell-associated neurotoxicity syndrome (ICANS)
- Encephalopathy
- Seizures
- Delirium, confusion, aphasia, agitation, sedation, coma

Varadarajan I, Lee DW. *Cancer J* 2019;25(3):223-30.
Abramson JS et al. ASCO 2019 Education Book.

Example of Handwriting Deterioration Associated with Neurotoxicity from CAR T-Cell Therapy



MMSE, mini mental status exam; Toci, tocilizumab.
Neelapu SS et al. Nat Rev Clin Oncol 2018; 15:47-62

Sequencing of Novel Agents

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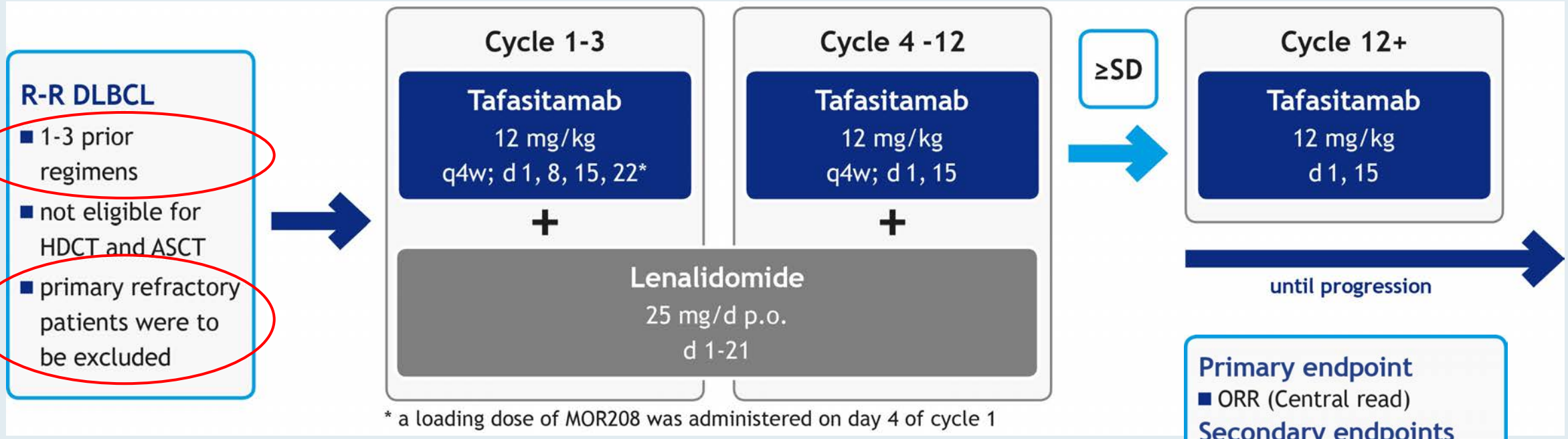
L-MIND: Phase II Study Design



- Sample size suitable to detect ≥15% absolute increase in ORR for tafasitamab/LEN combination versus LEN monotherapy at 85% power, 2-sided alpha of 5%
- Mature data: Primary endpoint analysis with data cutoff 30 Nov 2018; minimum follow-up 12 months, median follow-up 17.3 months

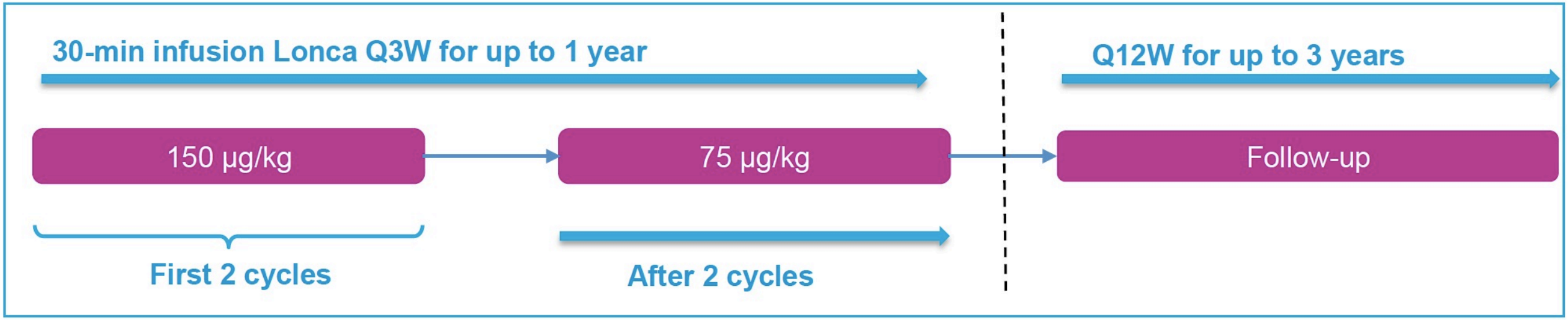
ORR = objective response rate; PFS = progression-free survival; DoR = duration of response; OS = overall survival

Salles G et al. *Lancet Oncol* 2020;21(7):978-88.

LOTIS-2: Phase II Trial Design

Patient population:
Patients with R/R DLBCL following ≥2 lines of prior systemic therapy

Primary objective:
Evaluate efficacy, **using ORR** (central review), and **safety** of the full Phase 2 study population



ORR = overall response rate; Lonca = loncastuximab tesirine

Caimi PF et al. *Lancet Oncol* 2021;22(6):790-800.

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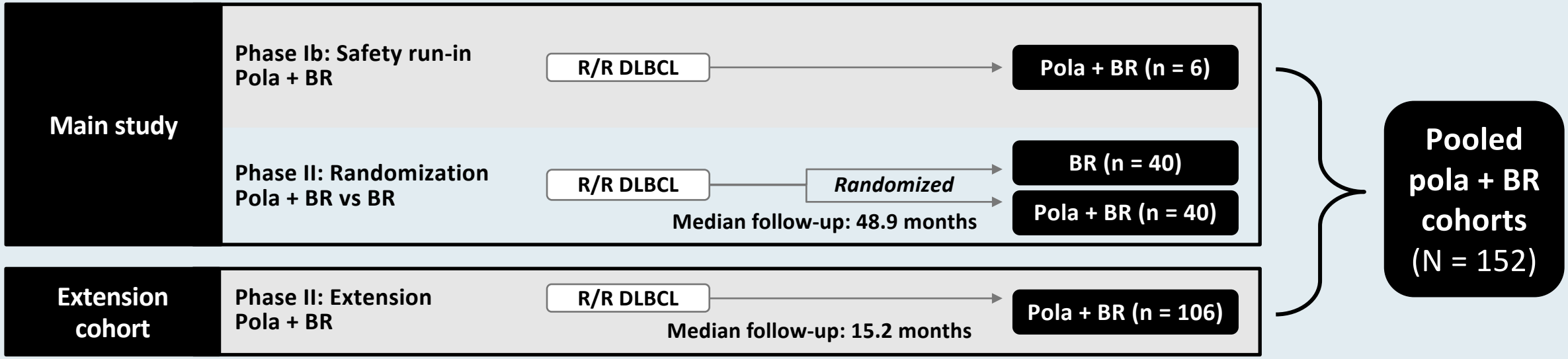
GO29365: Phase Ib/II Study Design

Inclusion: transplant-ineligible DLBCL, ≥1 line of therapy

Exclusion: prior allo-SCT, history of transformation, current Grade >1 peripheral neuropathy



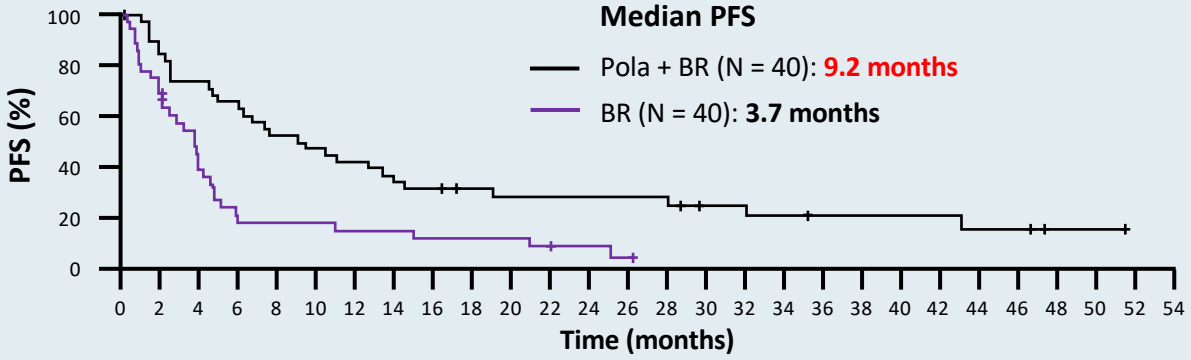
Pola = polatuzumab vedotin; BR = bendamustine/rituximab; R/R = relapsed/refractory

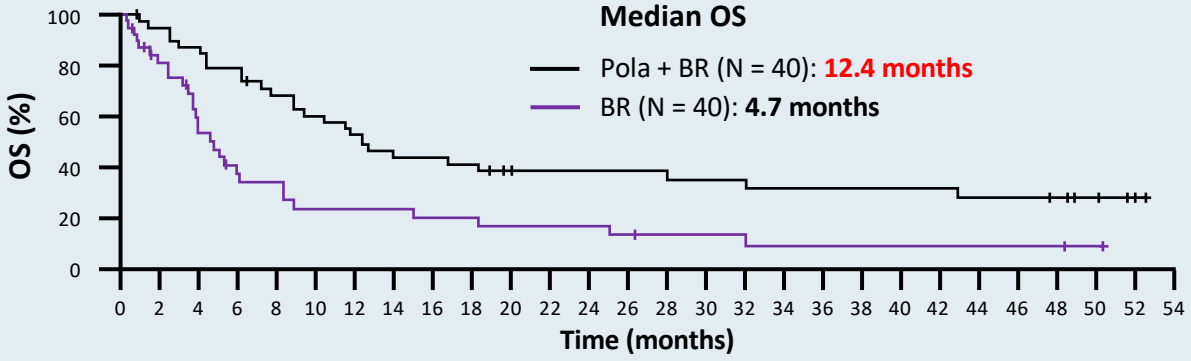
Pola 1.8 mg/kg on day 1 of each cycle of BR; up to 6 cycles at 3-weekly interval

Sehn LH et al. *Blood Adv* 2022;6(2):533-43.

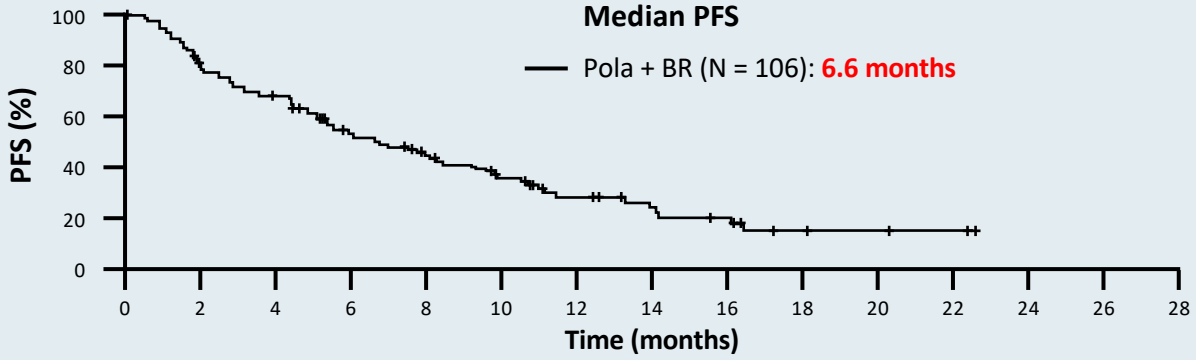
GO29365: PFS and OS in Randomized and Extension Cohorts

Randomized

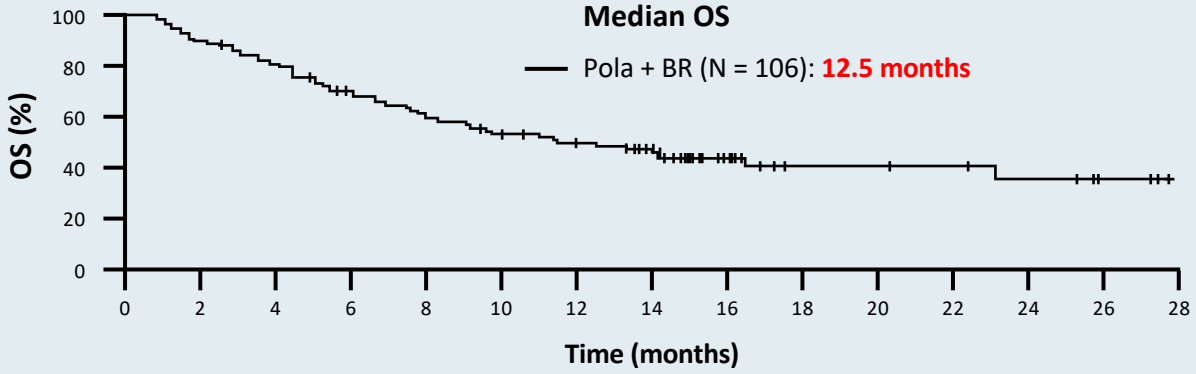




Extension cohort



Pola+BR



Randomized cohort:

- Survival benefit persists with longer follow-up
- 2-y PFS 28.4%, 2-y OS 38.2%

Pooled cohort

- Non-primary refractory:
  Median PFS 13.4 mo, median OS 32 mo

Sehn LH et al. *Blood Adv* 2022;6(2):533-43.

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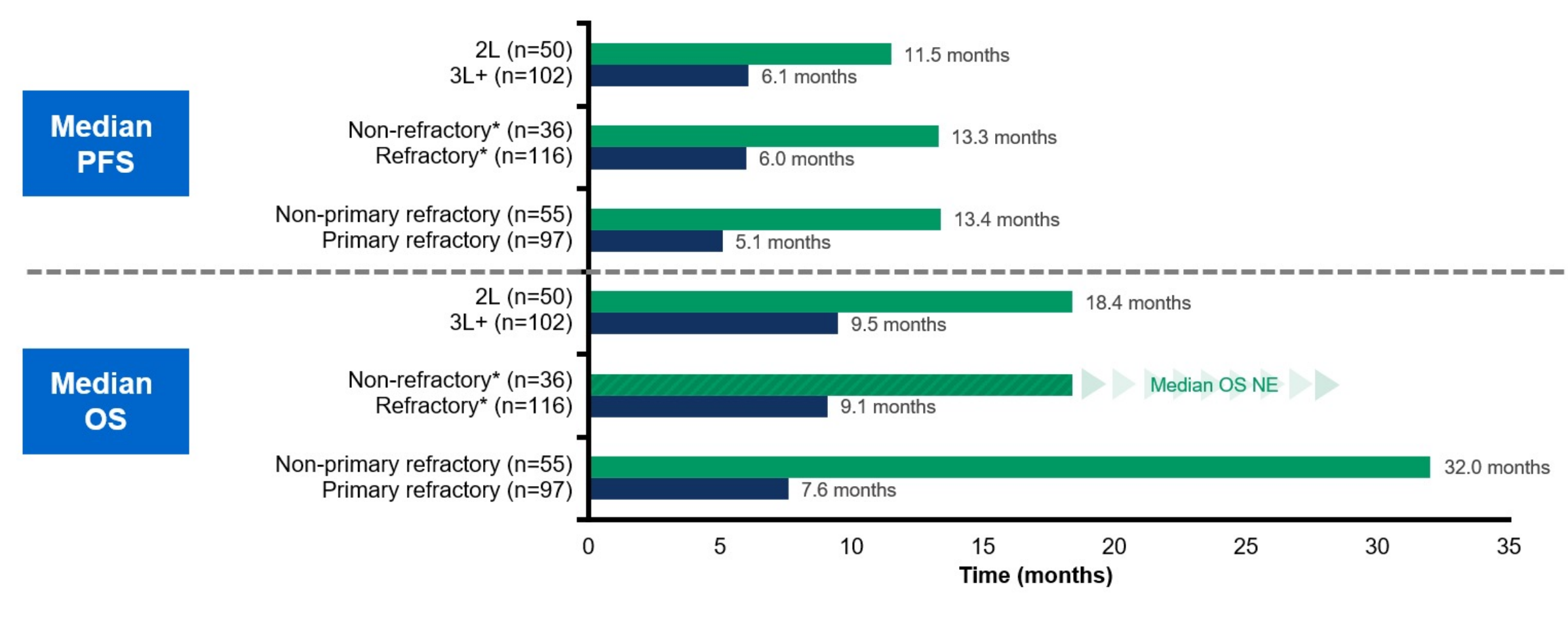
GO29365: Median PFS and OS in the Pooled Pola + BR Cohort According to Line of Therapy and Refractory Status



Sehn LH et al. *Blood Adv* 2022;6(2):533-43.

Oncology Today™ with Dr Neil Love — Management of Endometrial Cancer

A CME/MOC-Accredited Virtual Event

Wednesday, September 14, 2022
5:00 PM – 6:00 PM ET

Faculty

Michael J Birrer, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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