What I Tell My Patients:
Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Diffuse Large B-Cell Lymphoma

Thursday, April 27, 2023
6:00 AM – 7:30 AM

Faculty

Christopher R Flowers, MD, MS
Amy Goodrich, CRNP
Robin Klebig, APRN, CNP, AOCNP
Matthew Lunning, DO

Moderator

Neil Love, MD

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Faculty

Christopher R Flowers, MD, MS
Chair, Professor
Department of Lymphoma/Myeloma
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Amy Goodrich, CRNP
Nurse Practitioner
The Sidney Kimmel Comprehensive Cancer Center
Johns Hopkins Medicine
Baltimore, Maryland

Robin Klebig, APRN, CNP, AOCNP
Hematology Outpatient APP Supervisor
Assistant Professor of Medicine
Nurse Practitioner, Lymphoma Group
Division of Hematology
Mayo Clinic
Rochester, Minnesota

Matthew Lunning, DO
Associate Professor
Medical Director, Cellular Therapy
Assistant Vice Chair of Research, Department of Medicine
Assistant Vice Chancellor for Clinical Research
Fred and Pamela Buffett Cancer Center
University of Nebraska Medical Center
Omaha, Nebraska

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Dr Flowers — Disclosures

Consulting Agreements	AbbVie Inc, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Celgene Corporation, Denovo Biopharma, Epizyme Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Janssen Biotech Inc, Karyopharm Therapeutics, Pharmacyclics LLC, an AbbVie Company, Seagen Inc, Spectrum Pharmaceuticals Inc
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Nonrelevant Financial Relationship	Burroughs Wellcome Fund, Cancer Prevention and Research Institute of Texas (CPRIT Scholar in Cancer Research), Eastern Cooperative Oncology Group, National Cancer Institute

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Ms Goodrich — Disclosures

No relevant conflicts of interest to disclose

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Ms Klebig — Disclosures

No relevant conflicts of interest to disclose

Dr Lunning — Disclosures

Consulting Agreements	AbbVie Inc, Acrotech Biopharma, ADC Therapeutics, Astellas, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Caribou Biosciences Inc, CRISPR Therapeutics, Daiichi Sankyo Inc, EUSA Pharma, Fate Therapeutics, Genentech, a member of the Roche Group, Genmab US Inc, Instil Bio, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Kite, A Gilead Company, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Miltenyi Biotec, MorphoSys, Novartis, Nurix Therapeutics Inc, Pharmacyclics LLC, an AbbVie Company, Regeneron Pharmaceuticals Inc, Sanofi, Seagen Inc, Takeda Pharmaceuticals USA Inc, TG Therapeutics Inc
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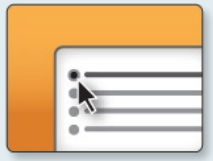
Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

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. Survey questions will be discussed throughout the meeting.

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.

Complete Your Evaluation: Tap the NCPD Evaluation button to complete your evaluation electronically to receive credit for your participation.

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

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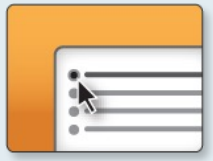
Clinicians Attending via Zoom

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. Survey questions will be discussed throughout the meeting.

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

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

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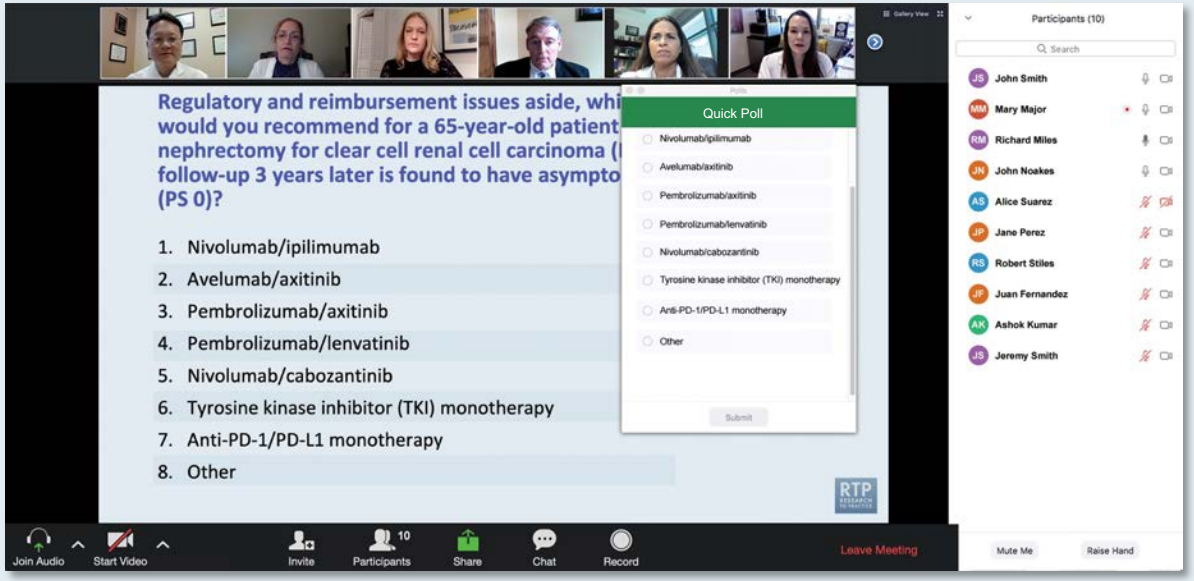
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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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.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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“What I Tell My Patients”
Fifteenth Annual RTP-ONS NCPD Symposium Series
ONS Congress, San Antonio, Texas — April 26 to 29, 2023

Wednesday April 26	**Cervical and Endometrial Cancer** 11:15 AM – 12:45 PM CT (12:15 PM – 1:45 PM ET)
	Breast Cancer 6:00 PM – 8:00 PM CT (7:00 PM – 9:00 PM ET)
Thursday April 27	**Diffuse Large B-Cell Lymphoma** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)
	Chronic Lymphocytic Leukemia 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)
	HER2-Targeted Antibody-Drug Conjugates 6:00 PM – 7:30 PM CT (7:00 PM – 8:30 PM ET)
Friday April 28	**Hepatobiliary Cancers** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)
	Ovarian Cancer 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)
	Lung Cancer 6:00 PM – 8:00 PM CT (7:00 PM – 9:00 PM ET)
Saturday April 29	**Acute Myeloid Leukemia, Myelodysplastic Syndromes and Myelofibrosis** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)
	Prostate Cancer 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)

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What I Tell My Patients

2023 ONS Congress

San Antonio, Texas

Symposia Themes

- New agents and therapies; ongoing trials related to specific clinical scenarios
- Patient education: Preparing to receive new therapies
- The bond that heals
- THANKS! (Great job)

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How was it different to take care of this patient versus another patient in the same oncologic setting?

What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Assistant Vice Chancellor for Clinical Research
Fred and Pamela Buffett Cancer Center
University of Nebraska Medical Center
Omaha, Nebraska

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Agenda

Module 1: POLARIX: Polatuzumab Vedotin/R-CHP for Previously Untreated DLBCL

Module 2: Polatuzumab Vedotin/BR and Selinexor for Relapsed Disease

Module 3: CD19-Directed Antibody-Drug Conjugate Loncastuximab Tesirine

Module 4: CD19-Directed Monoclonal Antibody Tafasitamab Combined with Lenalidomide

Module 5: CD20 x CD3 Bispecific Antibodies

Module 6: CAR T-Cell Therapy

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Module 6: CAR T-Cell Therapy

Robin Klebig, APRN, CNP, AOCNP

39-year-old man with DLBCL who received polatuzumab vedotin with R-CHP

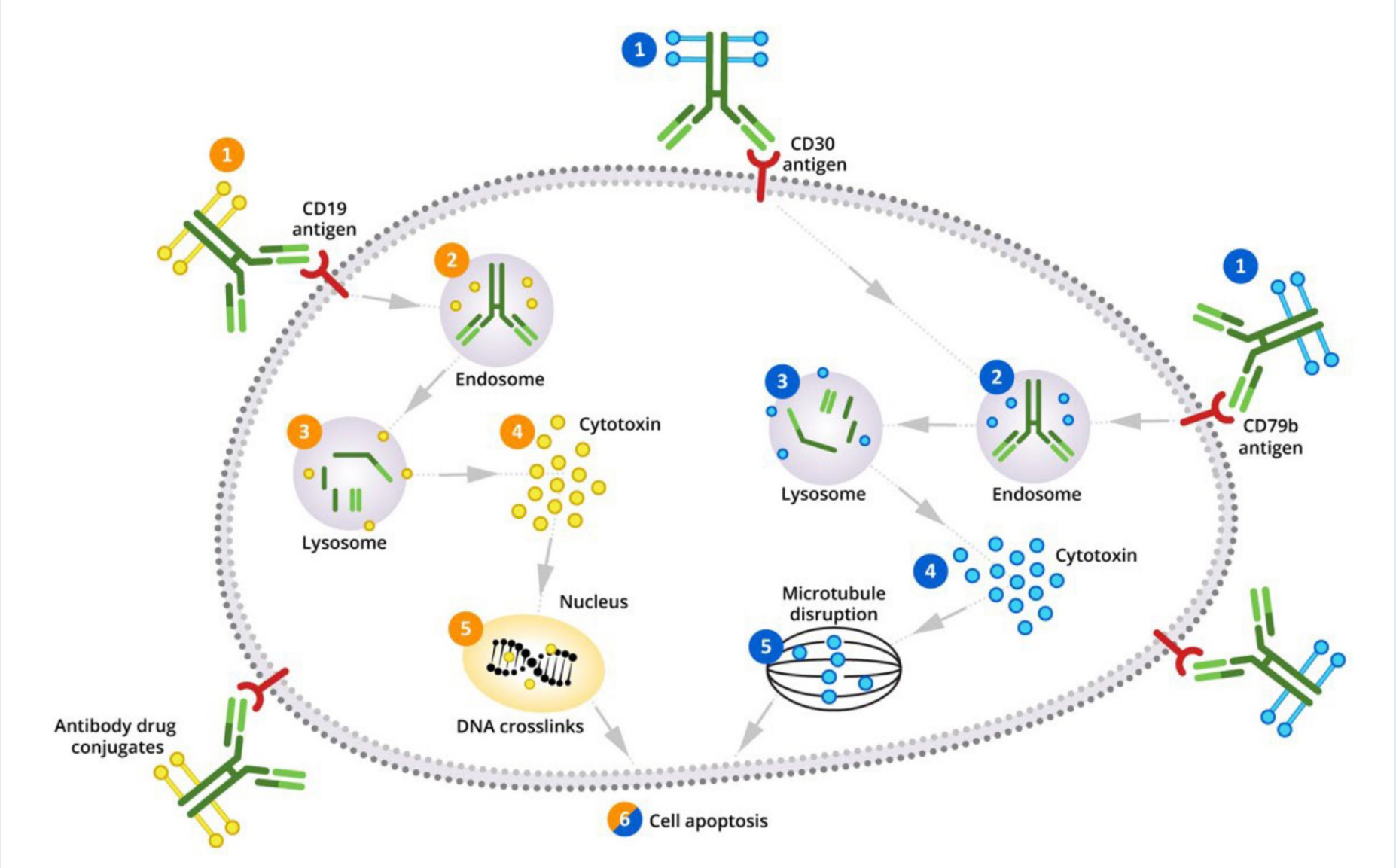
Dr Flowers
Houston, Texas

Clinical Research Background

Dr Lunning
Omaha, Nebraska

- **POLARIX: Polatuzumab vedotin/R-CHP for previously untreated DLBCL**

Antibody-Drug Conjugate Mechanism of Action in DLBCL



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

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Polatuzumab Vedotin

Mechanism of action

- **Antibody-drug conjugate directed against CD79b**

Indication

- **In combination with R-CHP for the treatment of previously untreated DLBCL not otherwise specified (NOS) or high-grade B-cell lymphoma in adult patients with an International Prognostic Index score of 2 or greater**
- **In combination with bendamustine/rituximab (BR) for the treatment of relapsed or refractory DLBCL NOS in adult patients after at least 2 prior therapies**

Recommended dose

- **1.8 mg/kg as an IV infusion q21d for 6 cycles**

Polatuzumab vedotin package insert, 4/2023.

FDA Grants Approval to Polatuzumab Vedotin in Combination with R-CHP for Diffuse Large B-Cell Lymphoma

Press Release – April 19, 2023

The Food and Drug Administration granted approval to polatuzumab vedotin-piiq in combination with rituximab, cyclophosphamide, doxorubicin and prednisone (R-CHP) for the treatment of adult patients who have previously untreated diffuse large B-cell lymphoma (DLBCL), not otherwise specified or high-grade B-cell lymphoma and who have an International Prognostic Index of 2 or greater.

The approval is based on positive results from the POLARIX trial, which demonstrated statistically significant improvement in progression-free survival compared to the current standard of care in patients with previously untreated DLBCL.

https://www.gene.com/media/news-features/fda-approves-genentech-medicine-for-people-with-previously-untreated-diffuse-large-b-cell-lymphoma

N Engl J Med 2022;386(4):351-63.

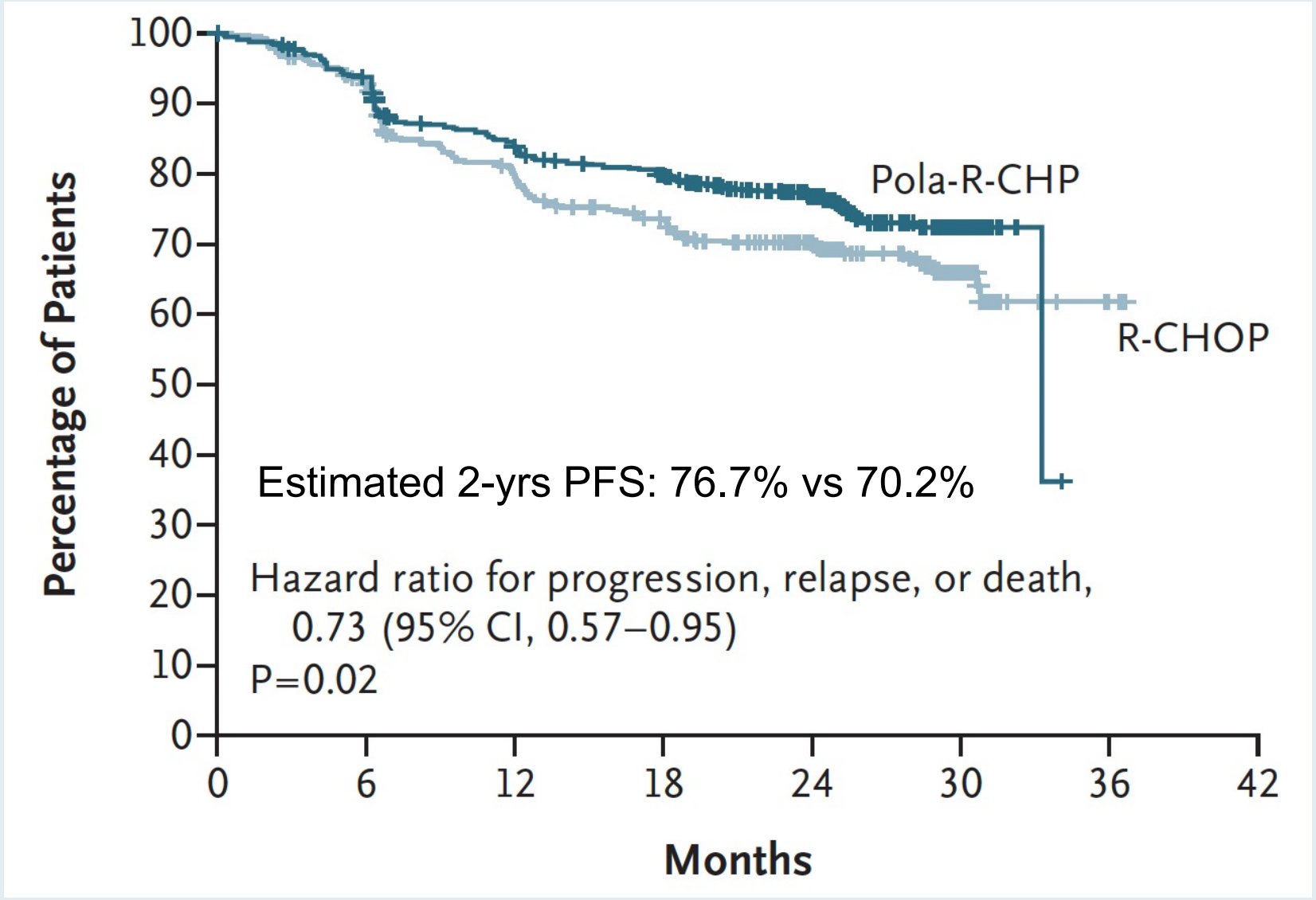
The NEW ENGLAND JOURNAL of MEDICINE

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

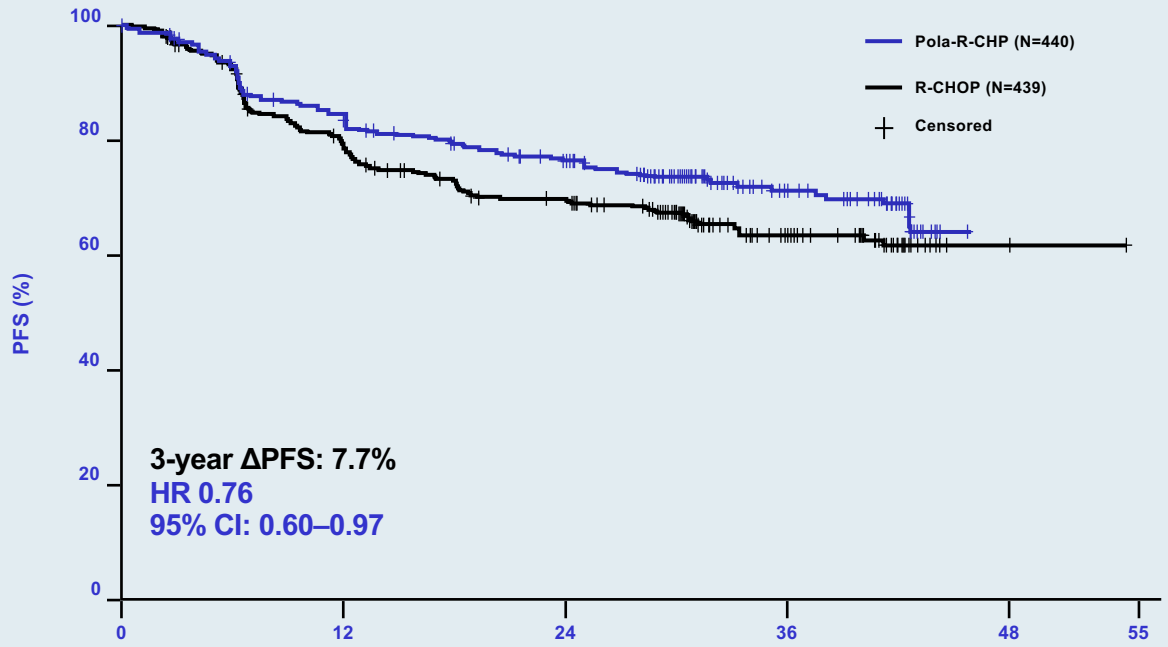
POLARIX: Investigator-Assessed Progression-Free Survival (Primary Endpoint)



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

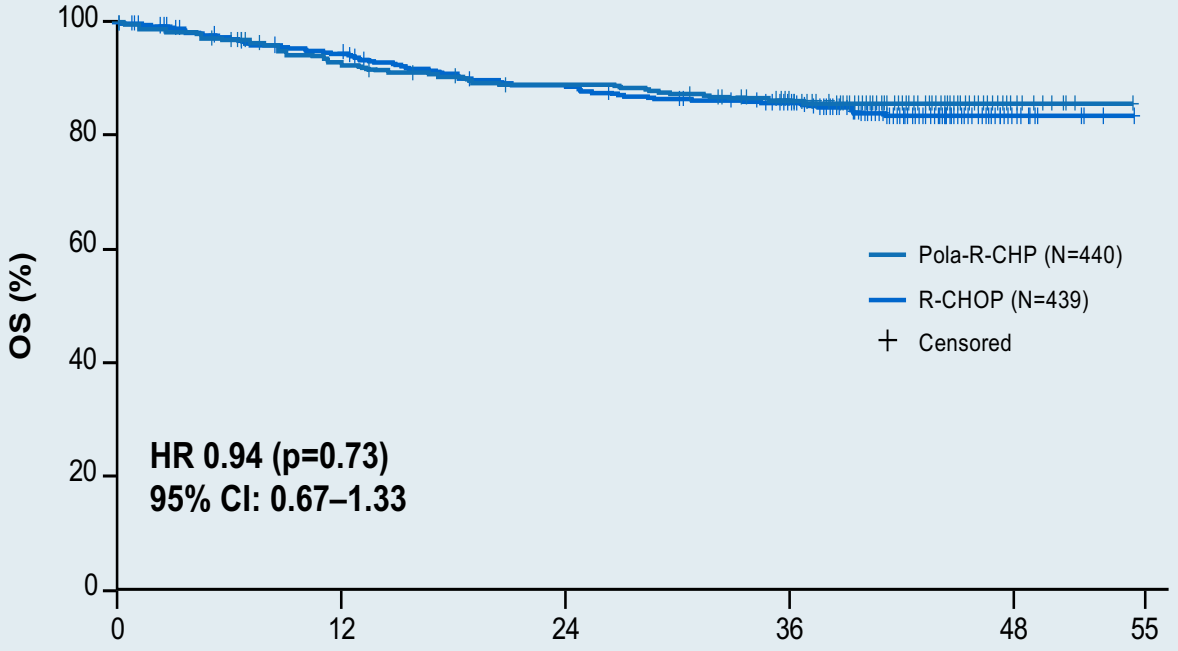
POLARIX: Updated Survival Analyses

PFS : Updated results
Median follow-up: 39.7 months



No. of patients at risk										
Pola-R-CHP	440	405	354	331	313	242	103	66	0	0
R-CHOP	439	390	331	300	284	222	94	59	2	1

Updated results (CCOD: June 15, 2022)
Median follow-up: 39.7 months



No. of patients at risk										
Pola-R-CHP	440	423	398	387	379	371	338	129	13	1
R-CHOP	439	415	403	382	372	361	329	124	18	1

Herrera AF et al. ASH 2022;Abstract 542.

Agenda

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Module 3: CD19-Directed Antibody-Drug Conjugate Loncastuximab Tesirine

Module 4: CD19-Directed Monoclonal Antibody Tafasitamab Combined with Lenalidomide

Module 5: CD20 x CD3 Bispecific Antibodies

Module 6: CAR T-Cell Therapy

Amy Goodrich, CRNP

66-year-old woman with relapsed DLBCL who received polatuzumab vedotin/BR

Dr Flowers
Houston, Texas

Clinical Research Background

Dr Lunning
Omaha, Nebraska

- **Polatuzumab vedotin/BR and selinexor for relapsed disease**

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

Pola-BR = polatuzumab vedotin with bendamustine/rituximab; ADC = antibody-drug conjugate; mAb = monoclonal antibody

Content courtesy of Laurie H Sehn, MD, MPH

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Module 5: CD20 x CD3 Bispecific Antibodies

Module 6: CAR T-Cell Therapy

Robin Klebig, APRN, CNP, AOCNP

70-year-old man with DLBCL who received loncastuximab tesirine

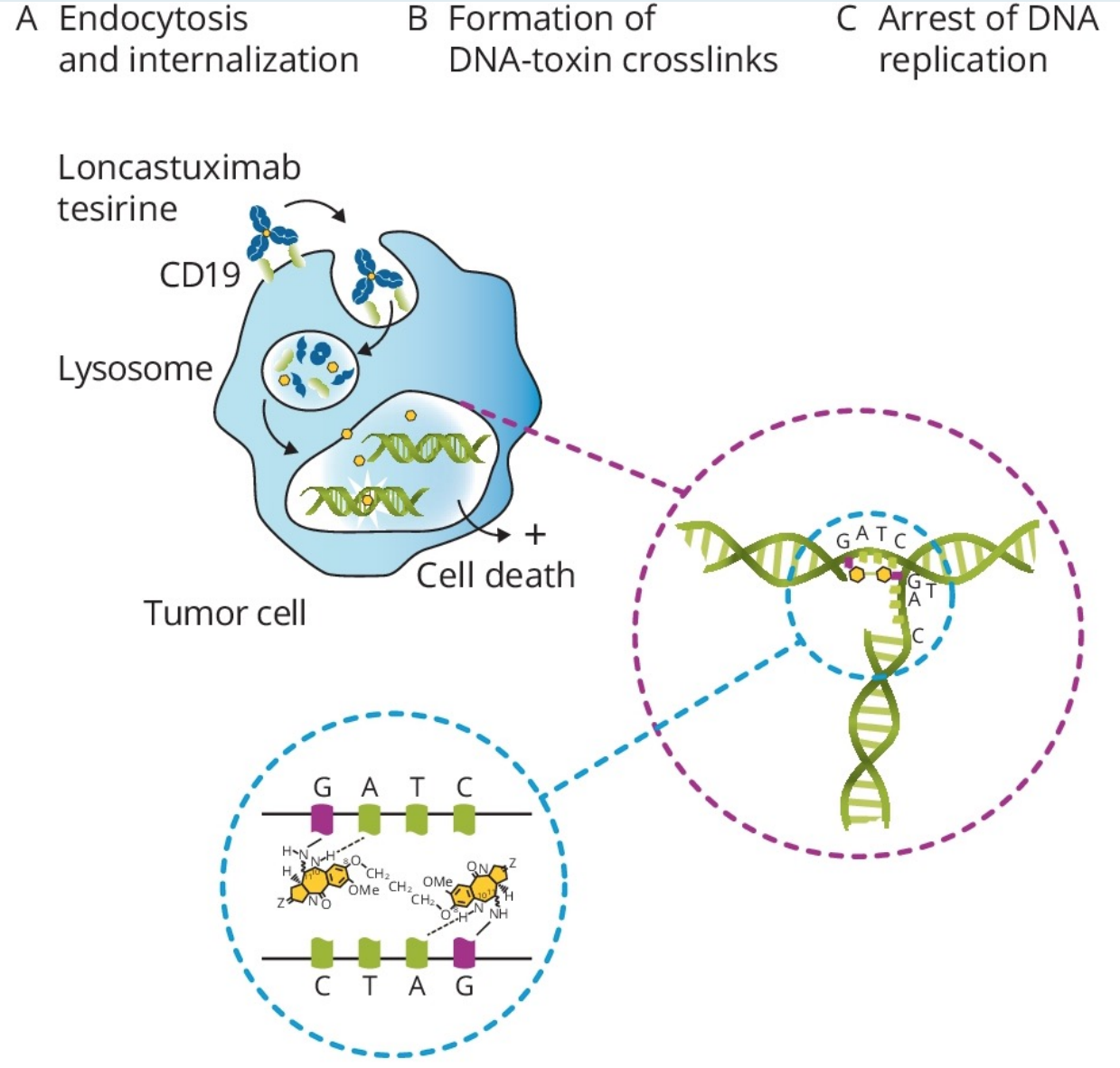
Dr Flowers
Houston, Texas

Clinical Research Background

Dr Lunning
Omaha, Nebraska

- **CD19-directed antibody-drug conjugate loncastuximab tesirine**

Mechanism of Action of Loncastuximab Tesirine



Hamadani M et al. ASCO 2021;Abstract TPS7574.

Loncastuximab Tesirine

Mechanism of action

- Antibody-drug conjugate directed against CD19

Indication

- For patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy, including those with DLBCL NOS, DLBCL arising from low-grade lymphoma and high-grade B-cell lymphoma

Recommended dose

- 0.15 mg/kg IV infusion on day 1 q3wk for the first 2 cycles, then 0.075 mg/kg IV infusion on day 1 q3wk for subsequent cycles

Loncastuximab tesirine package insert, 10/2022.

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Module 6: CAR T-Cell Therapy

Amy Goodrich, CRNP

58-year-old man and Jehovah's Witness with DLBCL who received tafasitamab/lenalidomide

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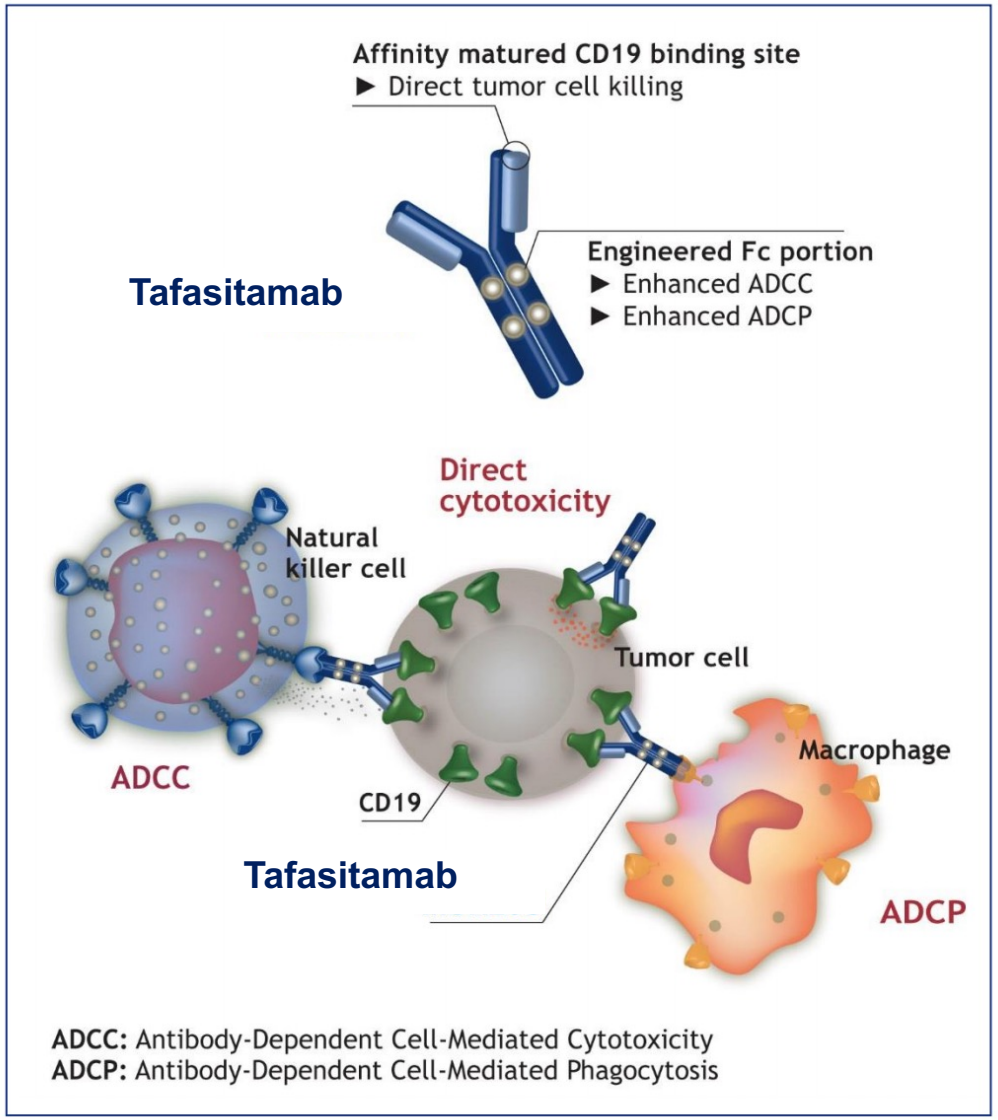
Dr Flowers
Houston, Texas

Clinical Research Background

Dr Lunning
Omaha, Nebraska

- **CD19-directed monoclonal antibody tafasitamab combined with lenalidomide**

Tafasitamab (MOR208)



Salles et al. *Lancet Onc* 2020

Lenalidomide enhances NK function with enhanced ADCC in vitro

Courtesy of Ann S LaCasce, MD, MMSc

Tafasitamab

Mechanism of action

- **Monoclonal antibody directed against CD19**

Indication

- **In combination with lenalidomide for the treatment of relapsed or refractory DLBCL NOS, including DLBCL arising from low grade lymphoma in adult patients who are not eligible for autologous stem cell transplant**

Recommended dose

- **12 mg/kg as an IV infusion as follows:**
  - **Cycle 1: Days 1, 4, 8, 15 and 22 of the 28-day cycle**
  - **Cycles 2 and 3: Days 1, 8, 15 and 22 of each 28-day cycle**
  - **Cycle 4 and beyond: Days 1 and 15 of each 28-day cycle**
- **Administered with lenalidomide for a maximum of 12 cycles, and then as monotherapy until toxicity or disease progression**

Tafasitamab package insert, 6/2021.

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Module 6: CAR T-Cell Therapy

Robin Klebig, APRN, CNP, AOCNP

63-year-old man with relapsed DLBCL who received odronextamab

Dr Flowers
Houston, Texas

Clinical Research Background

Dr Lunning
Omaha, Nebraska

- **CD20 x CD3 bispecific antibodies**
  - **Mechanism of action**
  - **Efficacy**
  - **Tolerability**

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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

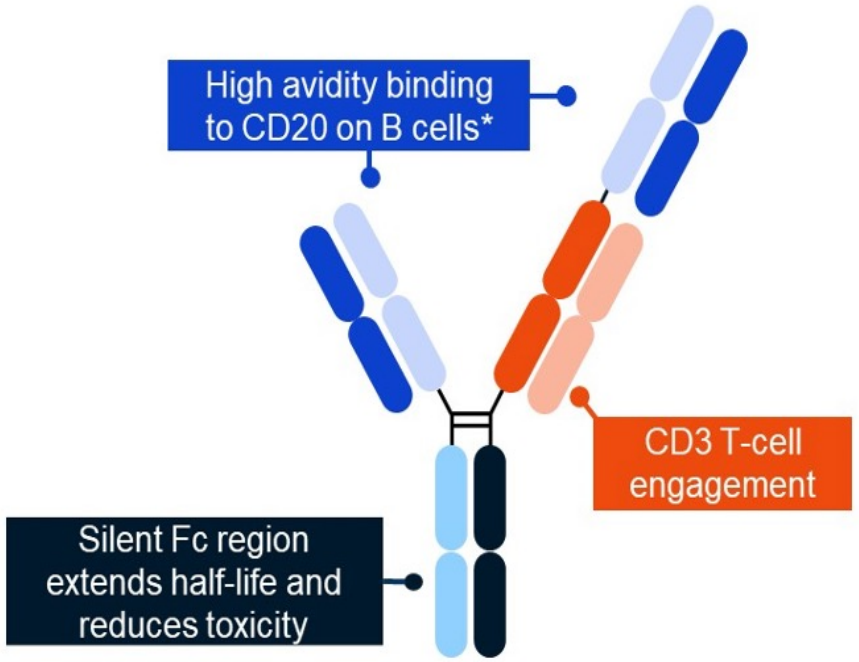
IV = intravenous; SC = subcutaneous; LC = light chain

Content courtesy of Jeremy Abramson, MD - adapted

Glofitamab: 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.

Glofitamab

Mechanism of action

- **Bispecific antibody directed against CD20 on B cells and CD3 on T cells**

Indication

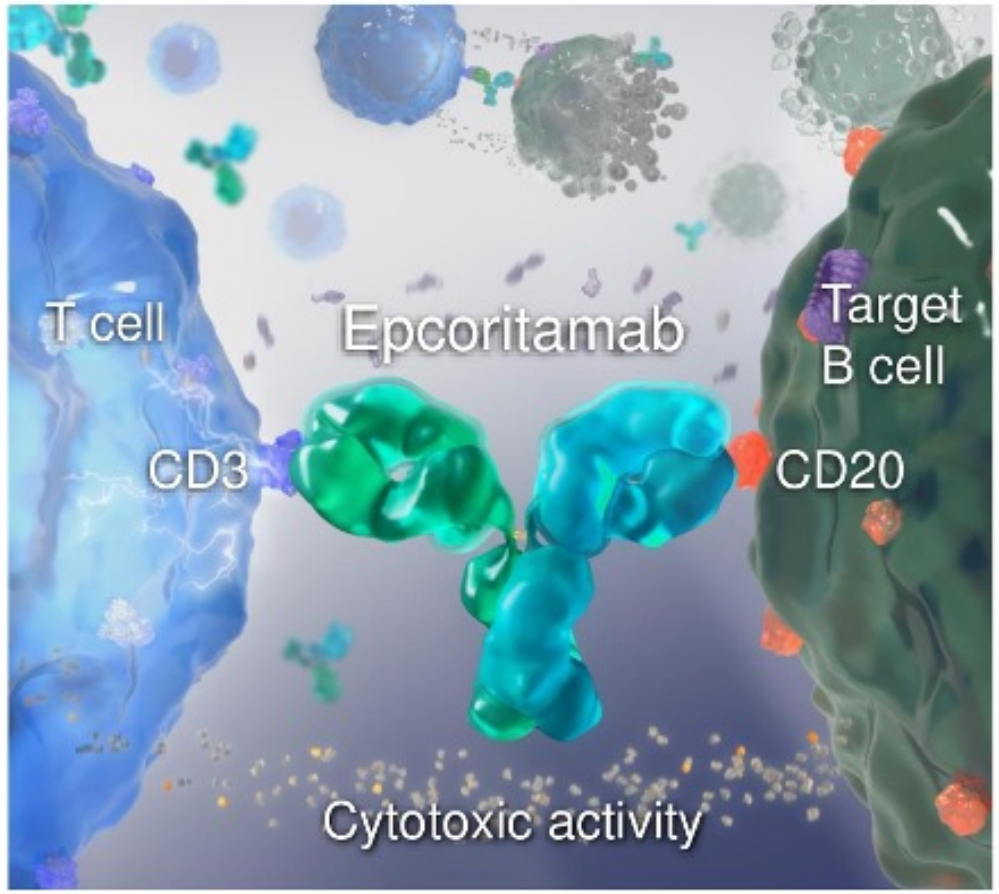
- **Investigational**

Key Trial Data

- **Phase I/II NP30179 study evaluating glofitamab in patients with relapsed or refractory large B-cell lymphoma**

Dickinson M et al. *N Engl J Med* 2022 Dec 15;387(24):2220-31.

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.

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Epcoritamab

Mechanism of action

- **Bispecific antibody directed against CD20 on B cells and CD3 on T cells**

Indication

- **Investigational**

Key Trial Data

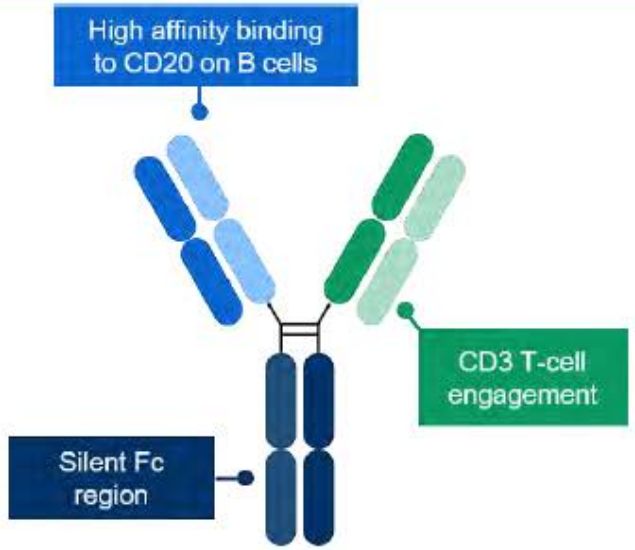
- **Phase I/II EPCORE NHL-1 study evaluating epcoritamab in patients with relapsed or refractory large B-cell lymphoma**

Thieblemont C et al. *J Clin Oncol* 2022;Dec 22;[Online ahead of print].

Study Background and Mechanism of Action of Mosunetuzumab

- DLBCL accounts for approximately 30% of all NHL[1]
  - Median age at diagnosis: 66 years[2]
- Poor outcomes have been reported for elderly/unfit patients with first-line DLBCL who receive R-mini-CHOP, R-CVP, R-benda, or no treatment[3]
- Mosunetuzumab monotherapy demonstrated promising efficacy and manageable safety in elderly/unfit patients with previously untreated DLBCL in early data from a Phase I/II study (NCT03677154)[4]

Mosunetuzumab: CD20xCD3 T cell engaging bispecific antibody that redirects T cells to engage and eliminate malignant B cells[5]



Olszewski AJ et al. ASH 2022;Abstract 738.

Mosunetuzumab

Mechanism of action

- **Bispecific antibody directed against CD20 on B cells and CD3 on T cells**

Indication

- **Investigational**

Key Trial Data

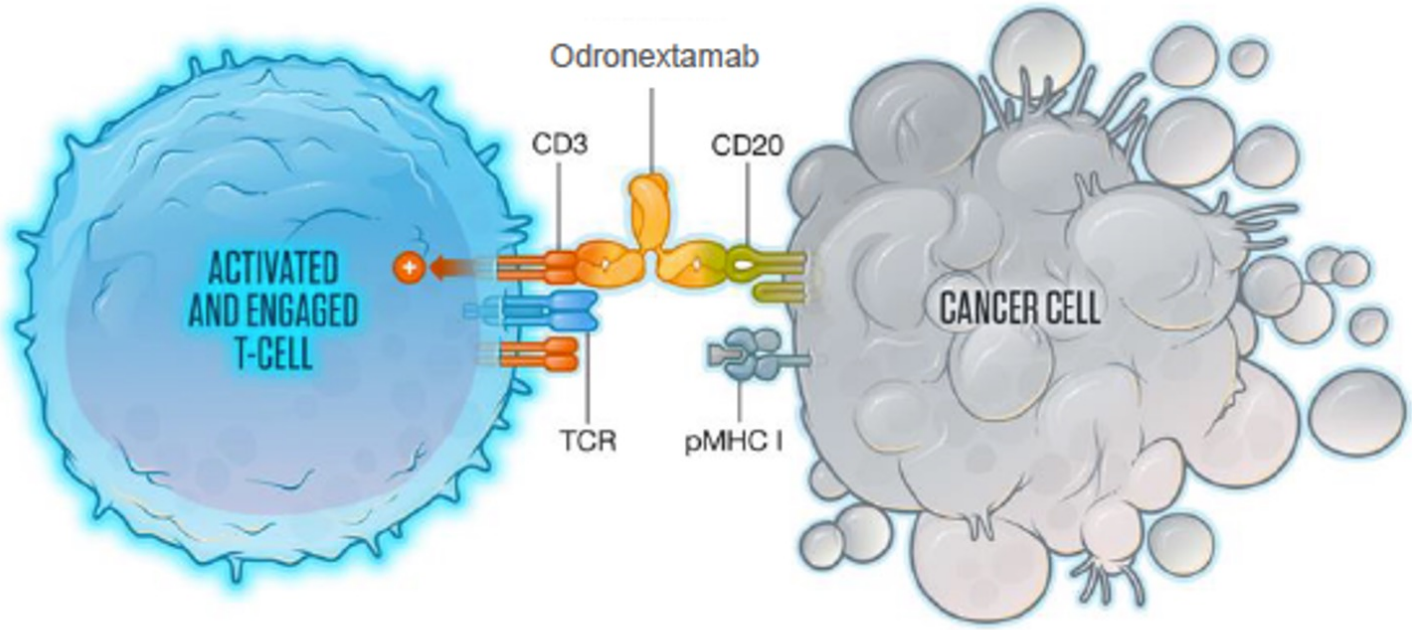
- **Phase I/II GO29781 study evaluating mosunetuzumab in patients with relapsed or refractory CD20-positive B-cell non-Hodgkin lymphoma**

Budde LE et al. *Lancet Oncol* 2022;23(8):1055-65.

Background and Mechanism of Action of Odronextamab

Odronextamab

Hinge-stabilized CD20×CD3 bispecific antibody



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

Kim WS et al. ASH 2022;Abstract 444.

Odronextamab

Mechanism of action

- **Bispecific antibody directed against CD20 on B cells and CD3 on T cells**

Indication

- **Investigational**

Key Trial Data

- **Phase II ELM-2 study evaluating odronextamab in patients with relapsed or refractory DLBCL**

Kim WS et al. ASH 2022;Abstract 444.

Agenda

Module 1: POLARIX: Polatuzumab Vedotin/R-CHP for Previously Untreated DLBCL

Module 2: Polatuzumab Vedotin/BR and Selinexor for Relapsed Disease

Module 3: CD19-Directed Antibody-Drug Conjugate Loncastuximab Tesirine

Module 4: CD19-Directed Monoclonal Antibody Tafasitamab Combined with Lenalidomide

Module 5: CD20 x CD3 Bispecific Antibodies

Module 6: CAR T-Cell Therapy

Amy Goodrich, CRNP

36-year-old woman with DLBCL receiving polatuzumab vedotin with rituximab while awaiting CAR T-cell therapy

Clinical Research Background

Dr Flowers
Houston, Texas

Dr Lunning
Omaha, Nebraska

- **CAR T-cell therapy**
  - **Mechanism of action**
  - **Efficacy**
  - **Tolerability**

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
Pts 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

CAR = chimeric antigen receptor; EFS = event-free survival; CR = complete response; CRS = cytokine release syndrome; NT = neurotoxicity

Content courtesy of Jeremy Abramson, MD

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

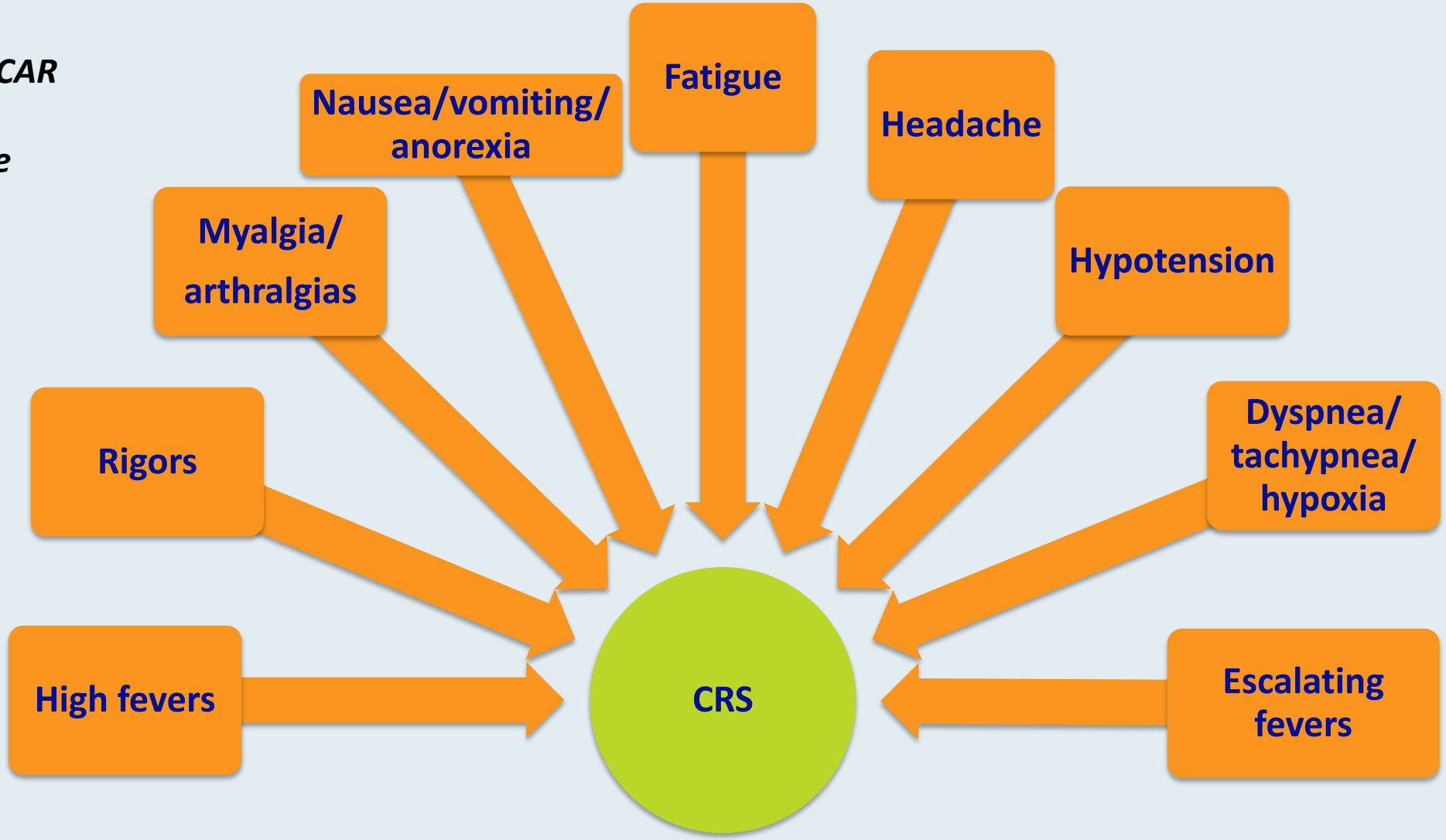
CRS — May be mild or life-threatening

- 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.

CRS: Common Symptoms

Based on CAR T-cell experience



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

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.

APPENDIX

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]

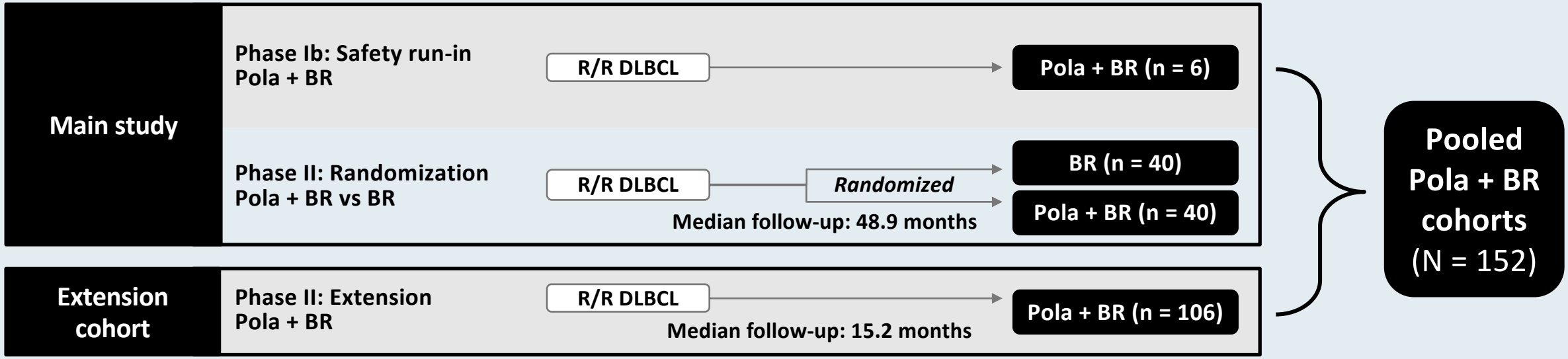
***Blood Adv* 2022;6(2):533-43.**

RTP RESEARCH TO PRACTICE

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



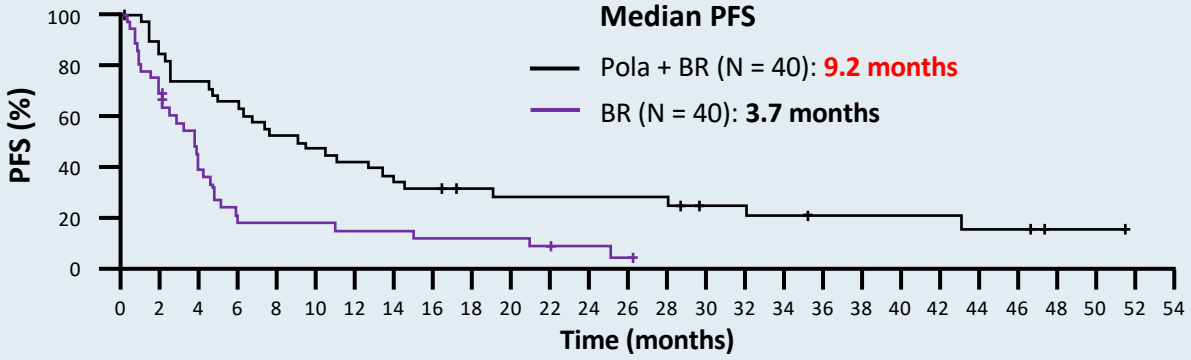
Pola = polatuzumab vedotin; BR = bendamustine/rituximab; R/R = relapsed/refractory

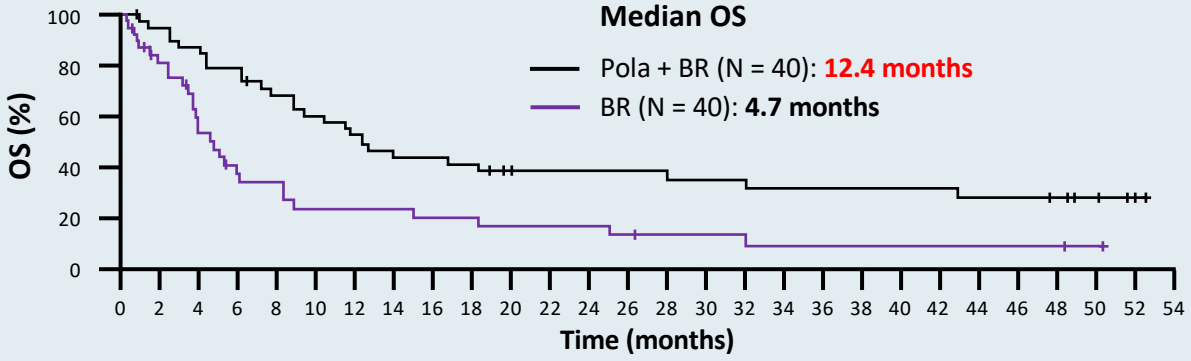
Pola 1.8 mg/kg on day 1 of each cycle of BR; up to 6 cycles at 3-week intervals

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

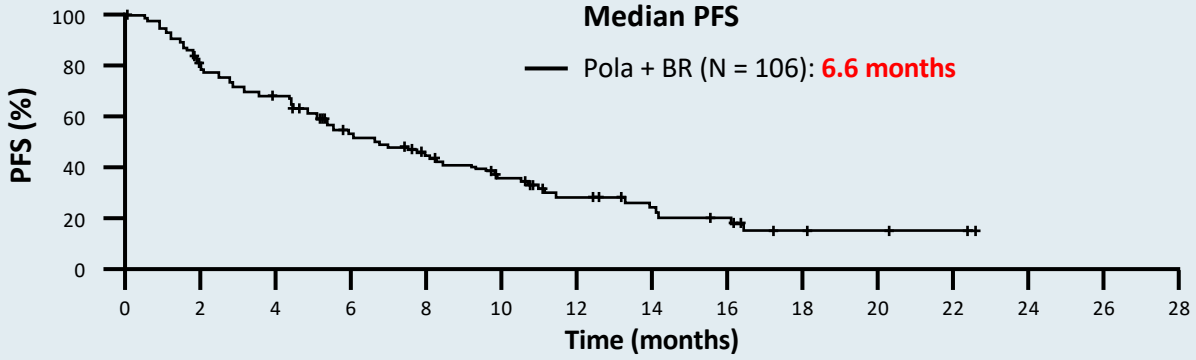
GO29365: PFS and OS in Randomized and Extension Cohorts

Randomized

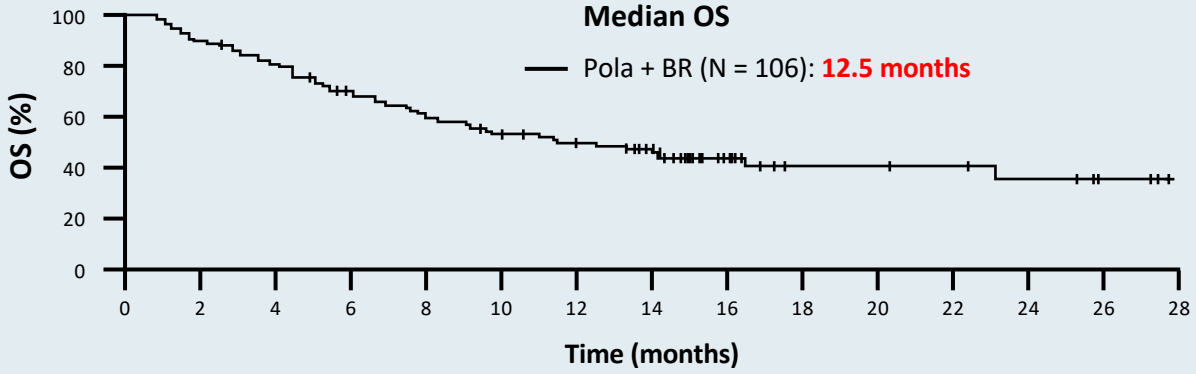




Extension cohort



Pola+BR



Randomized cohort:

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

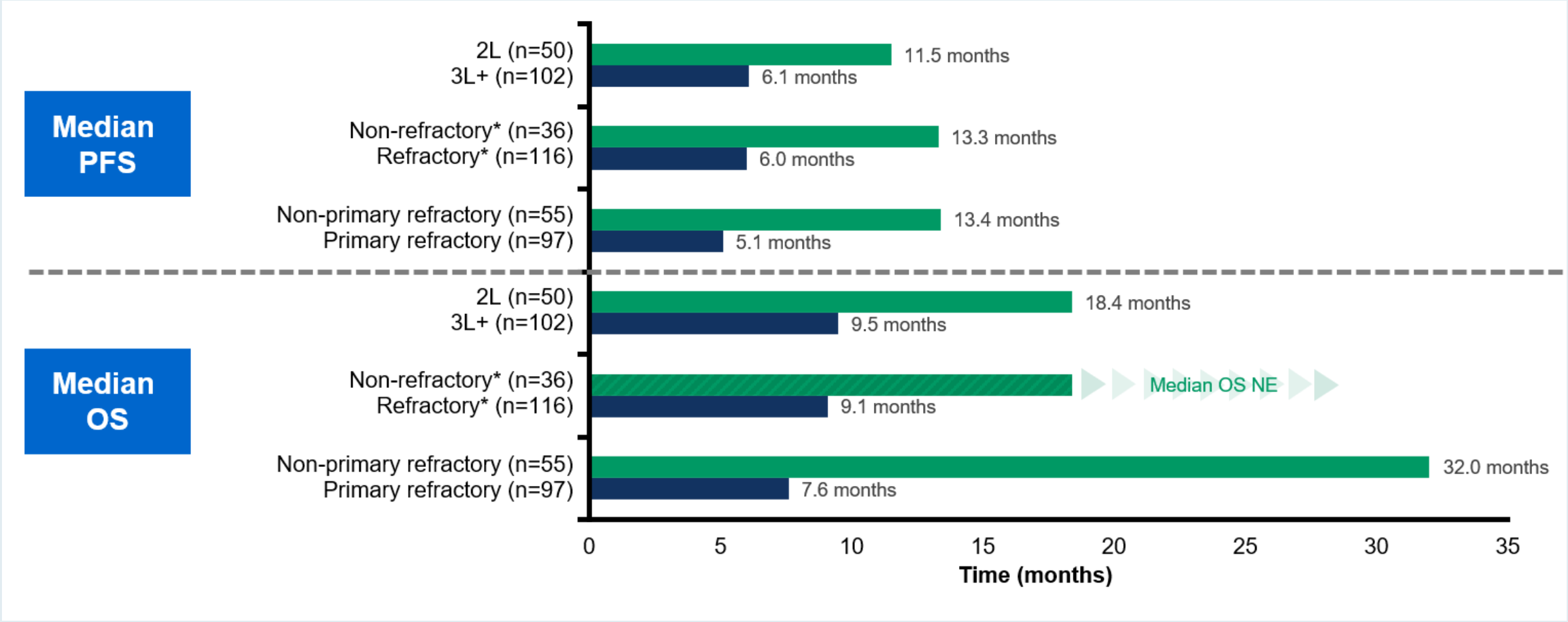
Pooled cohort

- Nonprimary refractory:
  Median PFS 13.4 mo, median OS 32 mo

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

RTP RESEARCH TO PRACTICE

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.

Emerging Bispecifics Antibodies Under Investigation for DLBCL

Agent	Patients	ORR (%)	CR Rate (%)	PFS (months)	Mode of Administration	Gr3-4 CRS %
Glofitamab[3,80]	aNHL (N = 127)	48	33	2.9	IV	4
	DLBCL (N = 107)	50	35	NR		
Mosunetuzumab[4]	aNHL (n = 129)	35	19	1.4	IV and SC	1
	DLBCL (n = 82)	33	20	NR		
Odronextamab[5]	DLBCL no prior CAR T (n = 49)	39	24	11.5	IV	7
	DLBCL prior CAR T (n = 33)	33	24	2.0		
Epcoritamab[6,79]	DLBCL (N = 157)	63	39	NA	SC	2
Blinatumomab[7,8]	DLBCL (n = 21)	43	19	NR	IV	4
	aNHL (n = 41)	37	22	NR	IV	2

ORR = objective response rate; CR = complete response; PFS = progression-free survival; Gr = grade; CRS = cytokine release syndrome; aNHL = aggressive non-Hodgkin lymphoma; DLBCL = diffuse large B-cell lymphoma; NR = not reached; IV = intravenous; SC = subcutaneous; CAR = chimeric antigen receptor; NA = not available

Nastoupil LJ, Bartlett NL. *J Clin Oncol* 2023 February 1;41(4):903-13.

ZUMA-12 Study Demonstrates 78% Complete Response Rate as Part of First-Line Treatment in Newly Diagnosed High-Risk Large B-Cell Lymphoma

Press Release: December 13, 2021

"Primary results [were announced] from ZUMA-12, a global, multicenter, single-arm, open-label Phase 2 study evaluating axicabtagene ciloleucel as part of first-line treatment in patients with high-risk large B-cell lymphoma (LBCL). This is the first study to evaluate CAR T-cell therapy as part of first-line therapy in high-risk LBCL. The study is based on the desire to utilize potential curative treatment as quickly as possible and the hypothesis that earlier use of CAR T-cell therapy when T cells are healthier may produce better outcomes. The data were presented in an oral session during the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition (Abstract #739).

After a single infusion of axicabtagene ciloleucel, 89% of evaluable patients achieved a response (ORR) (n=37 evaluable for efficacy), including 78% of patients with a complete response (CR) at a median follow-up of 15.9 months. CR rate was consistent among key subgroups. Among evaluable patients, median time to response was one month. At time of data cut-off, 73% of evaluable patients had ongoing responses. Medians for duration of response (DOR), event-free survival (EFS), and progression-free survival (PFS) were not yet reached, with 12-month estimates of 81%, 73%, and 75%, respectively, and an estimated 12-month OS rate of 91%."

https://www.gilead.com/news-and-press/press-room/press-releases/2021/12/yescarta-zuma12-study-demonstrates-78-complete-response-rate-as-part-of-firstline-treatment-in-newly-diagnosed-highrisk-large-bcell-lymphoma

RTP RESEARCH TO PRACTICE

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

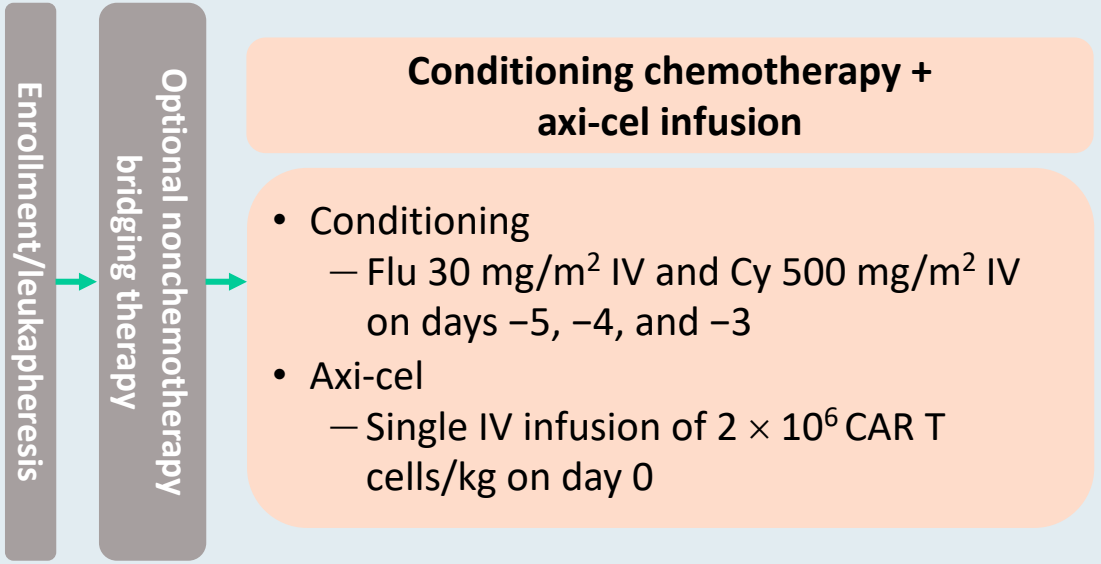
Sattva S. Neelapu[1]✉, Michael Dickinson[2], Javier Munoz[3], Matthew L. Ulrickson[3], Catherine Thieblemont[4,5], Olalekan O. Oluwole[6], Alex F. Herrera[7], Chaitra S. Ujjani[8], Yi Lin[9], Peter A. Riedell[10], Natasha Kekre[11], Sven de Vos[12], Christine Lui[13], Francesca Milletti[13], Jinghui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

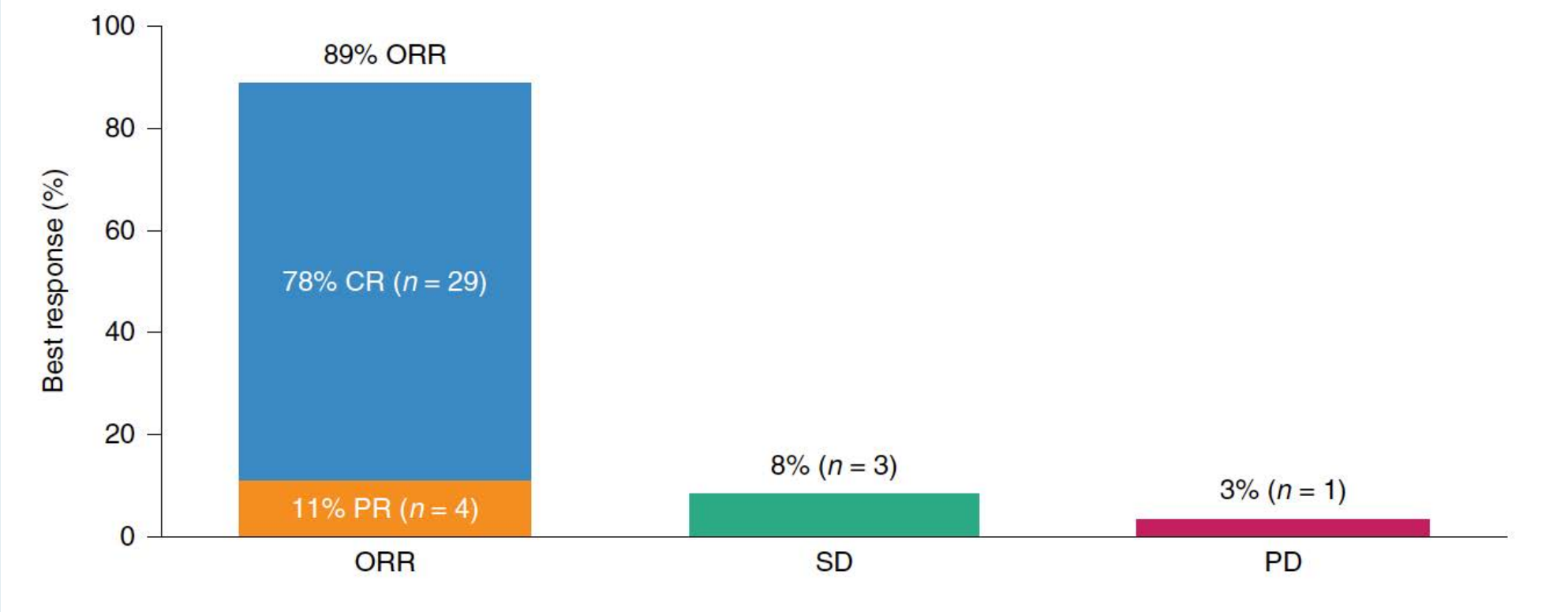
- ORR (objective response rate)
- DOR (duration of response)
- EFS (event-free survival)
- PFS
- Overall survival
- Safety
- CAR T cells in blood and cytokine levels in serum

LBCL = large B-cell lymphoma; HGBCL = high-grade B-cell lymphoma; axi-cel = axicabtagene ciloleucel; flu = fludarabine; cy = cyclophosphamide

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

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

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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

RTP RESEARCH TO PRACTICE

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

6-24-22: "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

4-01-22: "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

What I Tell My Patients:
Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Diffuse Large B-Cell Lymphoma

Thursday, April 27, 2023
6:00 AM – 7:30 AM

Faculty

Christopher R Flowers, MD, MS
Amy Goodrich, CRNP
Robin Klebig, APRN, CNP, AOCNP
Matthew Lunning, DO

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What I Tell My Patients:
Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Chronic Lymphocytic Leukemia

Thursday, April 27, 2023
12:15 PM – 1:45 PM

Faculty

John N Allan, MD
Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC
Corinne Hoffman, MS, APRN-CNP, AOCNP
Adam S Kittai, MD

Moderator

Neil Love, MD

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Virtual attendees: The NCPD credit link is posted in the chat room.

NCPD/ONCC credit information will be emailed to each participant within 1 to 2 business days.

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