Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Lymphoma

Tuesday, February 13, 2024
5:00 PM – 6:00 PM ET

Faculty

Andrew M Evens, DO, MBA, MSc
Sonali M Smith, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Faculty

Andrew M Evens, DO, MBA, MSc
Associate Director for Clinical Services
Rutgers Cancer Institute of New Jersey
Associate Vice Chancellor, Clinical Innovation
and Data Analytics
Rutgers Health
System Director of Medical Oncology and Oncology Lead
for RWJBarnabas-Rutgers Medical Group
RWJBarnabas Health
Professor of Medicine, Rutgers Robert Wood Johnson
Medical School
New Brunswick, New Jersey

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
Miami, Florida

RTP Year in Review 2024

Commercial Support

This activity is supported by educational grants from ADC Therapeutics, AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, Incyte Corporation, and Seagen Inc.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI Biopharma, a Sobi company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Grail Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Kronos Bio Inc, Legend Biotech, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc, and Zymeworks Inc.

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Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Evens — Disclosures

Advisory Committees and Consulting Agreements	Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Incyte Corporation, Pfizer Inc
Data and Safety Monitoring Boards/Committees	Novartis, Pharmacyclics LLC, an AbbVie Company

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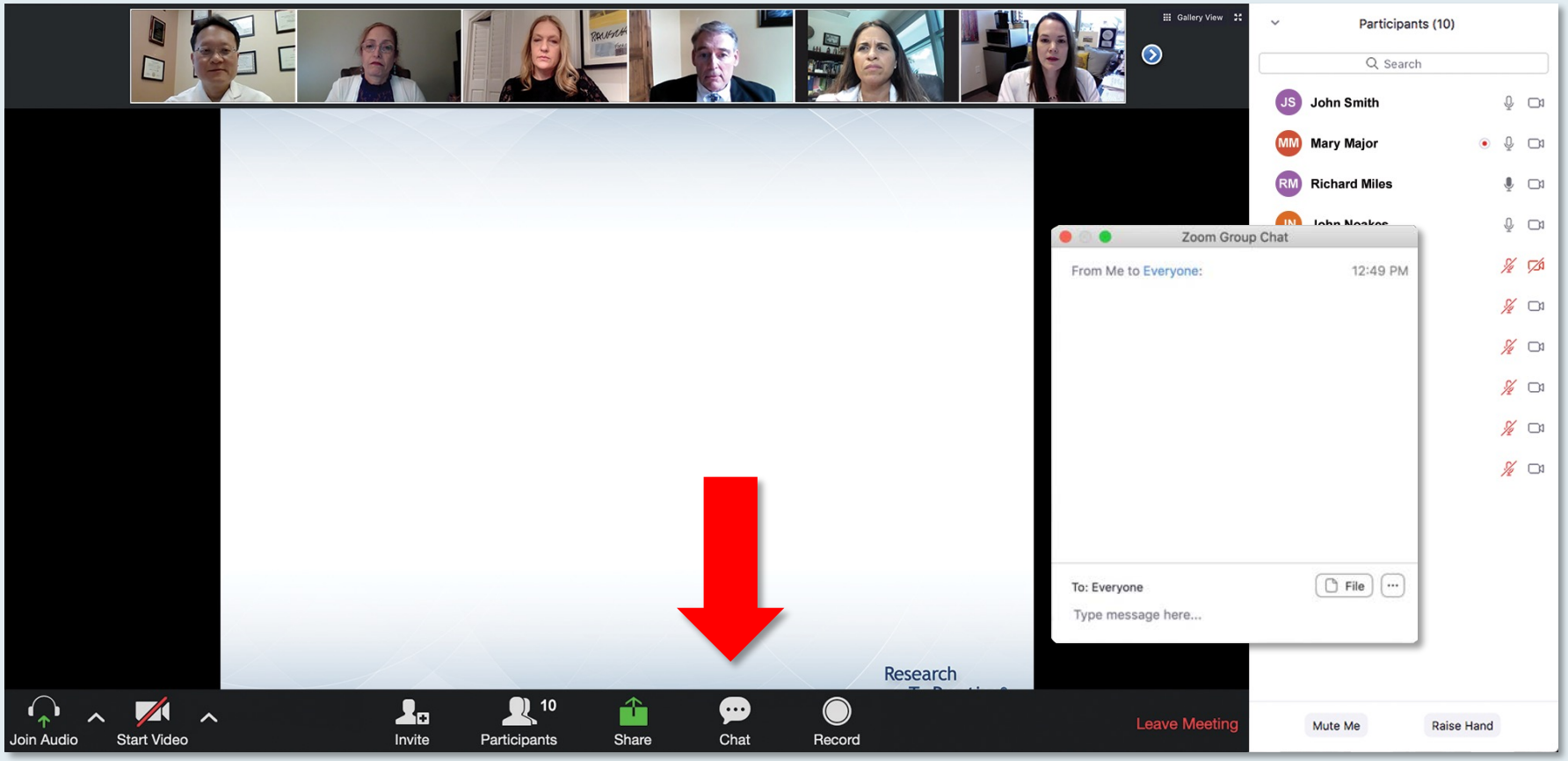
Nonrelevant Financial Relationship	Spouse is employed at Caris Life Sciences

We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

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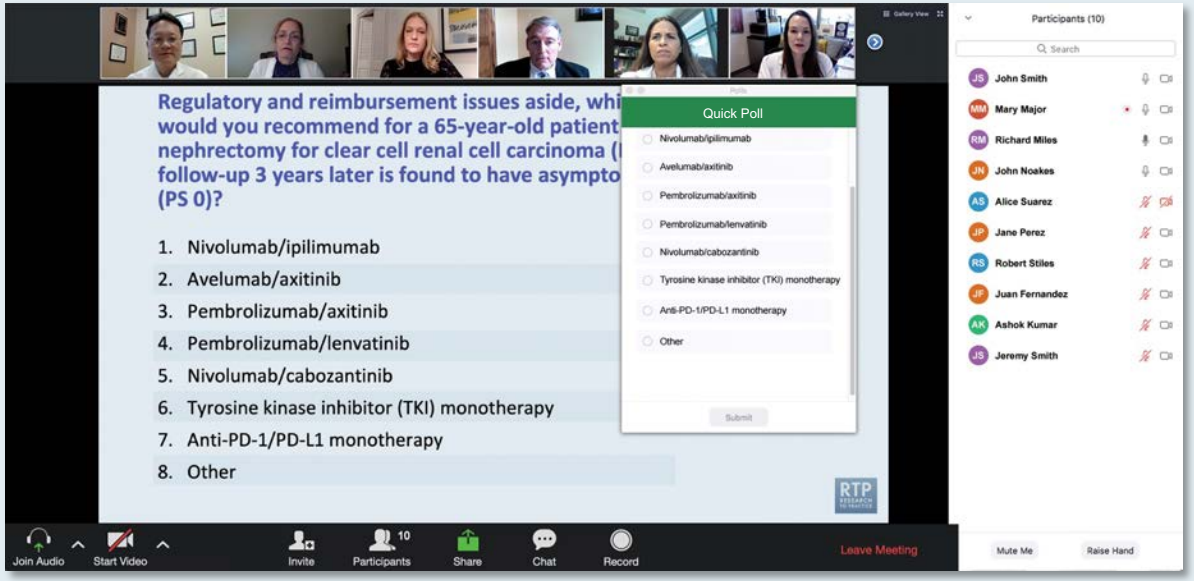
Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

What Clinicians Want to Know About the Management of Relapsed/Refractory Mantle Cell Lymphoma

DR TOBY A EYRE

OXFORD UNIVERSITY HOSPITALS
NHS FOUNDATION TRUST

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Consensus or Controversy? Investigator Perspectives on the Current and Future Role of Immune Checkpoint Inhibitors in the Management of Hepatobiliary Cancers — A 2024 Post-ASCO Gastrointestinal Cancers Symposium Review

A CME-Accredited Virtual Event

Thursday, February 15, 2024
5:00 PM – 6:00 PM ET

Faculty

Robin (Katie) Kelley, MD
Mark Yarchoan, MD

Moderator

Neil Love, MD

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TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Urothelial Bladder Cancer

Thursday, February 22, 2024
5:00 PM – 6:00 PM ET

Faculty

Shilpa Gupta, MD

Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

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Prostate Cancer

Wednesday, February 28, 2024
5:00 PM – 6:00 PM ET

Faculty

Andrew J Armstrong, MD, ScM

Maha Hussain, MD, FACP, FASCO

Moderator

Neil Love, MD

RTP Year in Review 2024

Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Management of Ovarian Cancer

Part 1 of a 2-Part CME Symposium Series Held in Conjunction with the 2024 Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer®

Monday, March 18, 2024

6:30 AM – 8:00 AM PT (9:30 AM – 11:00 AM ET)

Faculty

Joyce F Liu, MD, MPH

Mansoor Raza Mirza, MD

David M O'Malley, MD

Moderator

Kathleen N Moore, MD, MS

RTP RESEARCH TO PRACTICE

Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Management of Endometrial Cancer

Part 2 of a 2-Part CME Symposium Series Held in Conjunction with the 2024 Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer®

Monday, March 18, 2024

12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

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RTP RESEARCH TO PRACTICE

JOIN US IN MARCH FOR THE RETURN OF

The Annual
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MARCH 22-24, 2024

JW Marriott Miami Turnberry

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Agenda

INTRODUCTION: CD3-Based Bispecific Antibodies and the General Medical Oncologist: Lymphomas, Multiple Myeloma … and Solid Tumors?

MODULE 1: Follicular and Mantle Cell Lymphoma

MODULE 2: Diffuse Large B-Cell Lymphoma and Hodgkin Lymphoma

Thank you for joining us!

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

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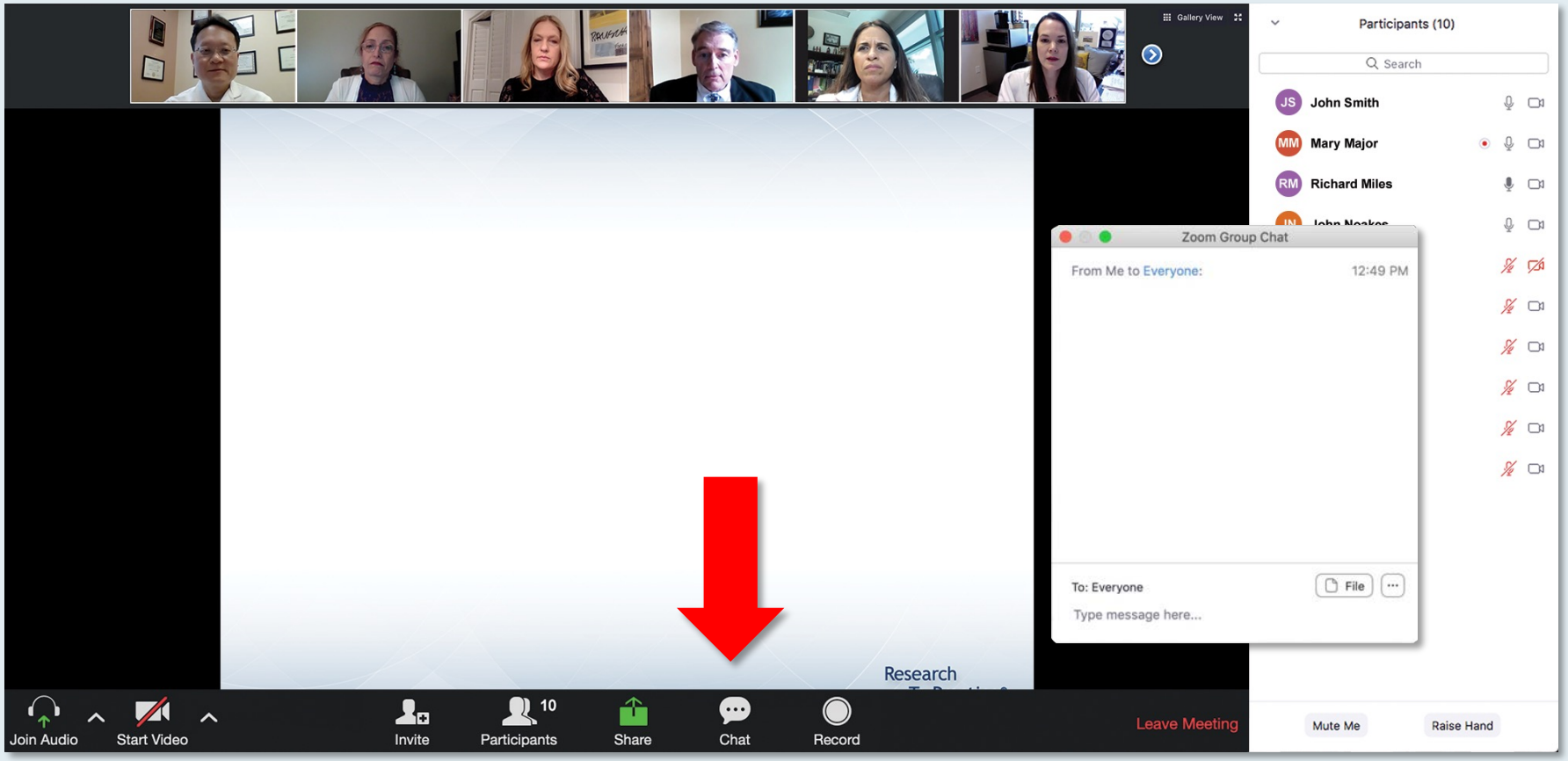

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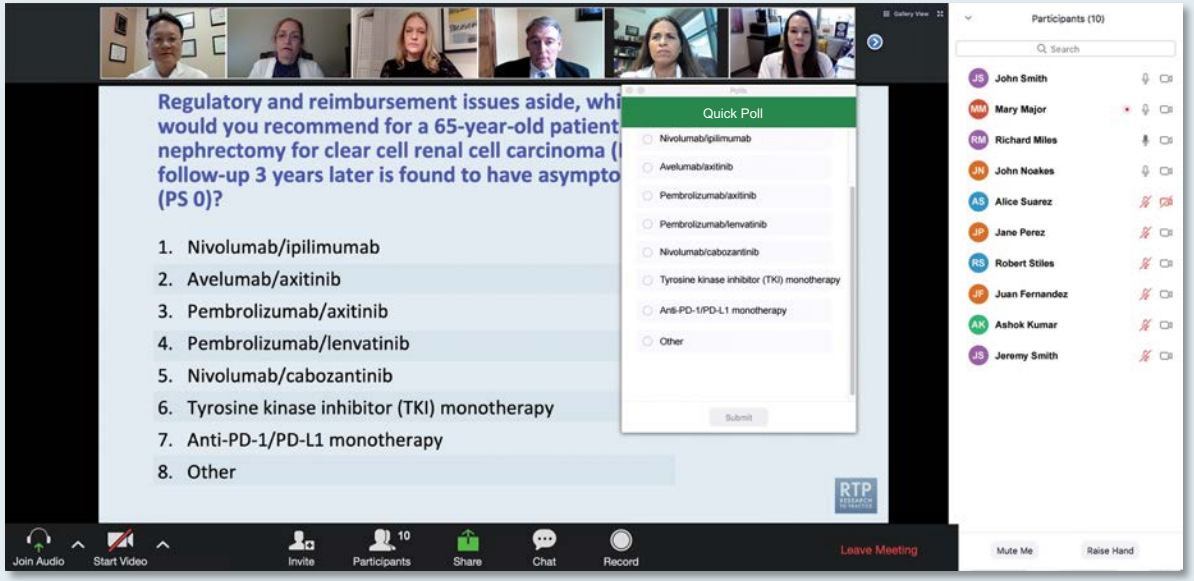

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Third Annual **National General Medical Oncology Summit**

Friday, March 22, 2024

6:30 PM – 7:00 PM

Welcome Reception

7:00 PM – 9:00 PM

Keynote Session: ER-Positive Metastatic Breast Cancer

Erika Hamilton, MD
Kevin Kalinsky, MD, MS
Joyce O'Shaughnessy, MD
Hope S Rugo, MD

Special Feature: Clinicians with Breast Cancer

Third Annual **National General Medical Oncology Summit**

Saturday, March 23, 2024

7:30 AM – 9:10 AM

Hodgkin and Non-Hodgkin Lymphoma

Ann S LaCasce, MD, MMSc
Matthew Lunning, DO
Kami Maddocks, MD
Andrew D Zelenetz, MD, PhD

9:30 AM – 10:20 AM

Gynecologic Cancers

Bradley J Monk, MD
David M O'Malley, MD

10:20 AM – 11:10 AM

Localized Breast Cancer; SABCS 2023 Review

Virginia Kaklamani, MD, DSc
Kevin Kalinsky, MD, MS
Joyce O'Shaughnessy, MD

11:10 AM – 12:00 PM

Metastatic Breast Cancer, Triple-Negative Breast Cancer, HER2-Positive Breast Cancer; SABCS 2023 Review

Erika Hamilton, MD
Virginia Kaklamani, MD, DSc
Hope S Rugo, MD

Third Annual **National General Medical Oncology Summit**

Saturday, March 23, 2024

12:30 PM – 1:20 PM

Prostate Cancer

Emmanuel S Antonarakis, MD
Rana R McKay, MD

1:20 PM – 2:10 PM

Urothelial Bladder Cancer

Matthew D Galsky, MD
Jonathan E Rosenberg, MD

2:10 PM – 3:00 PM

Renal Cell Carcinoma

Eric Jonasch, MD
Brian Rini, MD

3:20 PM – 4:10 PM

Targeted Therapy for Non-Small Cell Lung Cancer

Ibiayi Dagogo-Jack, MD
Helena Yu, MD

4:10 PM – 5:00 PM

Nontargeted Treatments for Lung Cancer

Edward B Garon, MD, MS
Corey J Langer, MD

Third Annual **National General Medical Oncology Summit**

Sunday, March 24, 2024

7:30 AM – 8:20 AM

Multiple Myeloma

Natalie S Callander, MD
Paul G Richardson, MD

8:20 AM – 9:10 AM

Gastroesophageal Cancers

Yelena Y Janjigian, MD
Samuel J Klempner, MD

9:30 AM – 10:20 AM

Hepatobiliary Cancers

Ghassan Abou-Alfa, MD, MBA
Richard S Finn, MD

10:20 AM – 11:10 AM

Colorectal Cancer

Kristen K Ciombor, MD, MSCI
John Strickler, MD

11:10 AM – 12:00 PM

Pancreatic Cancer

Andrew H Ko, MD
Eileen M O'Reilly, MD

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Nonrelevant Financial Relationship	Spouse is employed at Caris Life Sciences

AT THE FOREFRONT
UChicago Medicine

Year in Review: Follicular lymphoma and Mantle cell lymphoma

Sonali Smith, MD FASCO
Elwood V. Jensen Professor of Medicine
Chief, Section of Hematology/Oncology
Co-Leader, Cancer Service Line

2023 Year-in-Review: Updates in the Management of Diffuse Large B-Cell Lymphoma and Hodgkin Lymphoma

Andrew M. Evens, DO, MBA, MSc
Deputy Director for Clinical Services, Rutgers Cancer Institute of New Jersey
Associate Vice Chancellor, Clinical Innovation & Data Analytics, Rutgers Health
System Director of Medical Oncology, and Oncology Lead for RWJBarnabas-Rutgers Medical Group, RWJBarnabas Health
Professor of Medicine, Rutgers Robert Wood Johnson Medical School

Key Data Sets

Sonali M Smith, MD

- Townsend W et al. **Obinutuzumab** versus **Rituximab** Immunochemotherapy in **Previously Untreated** iNHL: **Final Results** from the **GALLIUM** Study. *Hemasphere* 2023;7(7):e919.
- Neelapu S et al. **Axicabtagene Ciloleucel** (Axi-Cel) in Patients with **Relapsed/Refractory Indolent Non-Hodgkin Lymphoma**: **4-Year Follow-Up** from the **Phase 2 ZUMA-5 Trial**. ASH 2023;Abstract 4868.
- Schuster SJ et al. **Clinical Outcomes** of Patients with **Relapsed/Refractory Follicular Lymphoma** Treated with **Tisagenlecleucel: Phase 2 Elara 3-Year Follow-Up**. ASH 2023;Abstract 601.
- Morschhauser F et al. **TRANSCEND FL: Phase 2** Study **Results** of **Lisocabtagene Maraleucel** (Liso-cel) in Patients (Pts) with **Relapsed/Refractory** (R/R) **Follicular Lymphoma** (FL). ICML 2023;Abstract LBA4.
- Morschhauser F et al. **TRANSCEND FL: Phase 2** Study **Primary Analysis** of **Lisocabtagene Maraleucel** as **Second-Line Therapy** in Patients with **High-Risk Relapsed or Refractory Follicular Lymphoma**. ASH 2023;Abstract 602.

Key Data Sets

Sonali M Smith, MD (continued)

- Schuster SJ et al. **Mosunetuzumab Monotherapy** Continues to Demonstrate Durable Responses in Patients with **Relapsed and/or Refractory Follicular Lymphoma** After ≥2 Prior Therapies**: 3-Year Follow-Up** from a Pivotal **Phase II** Study. ASH 2023;Abstract 603.
- Linton K et al. **Epcoritamab SC** Monotherapy Leads to Deep and Durable Responses in Patients with **Relapsed or Refractory Follicular Lymphoma**: First Data Disclosure from the **Epcore NHL-1** Follicular Lymphoma Dose-Expansion Cohort. ASH 2023;Abstract 1655.
- Villasboas JC et al. Results of a Second, Prespecified Analysis of the Phase 2 Study **ELM-2** Confirm High Rates of Durable Complete Response with **Odronextamab** in Patients with **Relapsed/Refractory** (R/R) **Follicular Lymphoma** (FL) with Extended Follow-Up. ASH 2023;Abstract 3041.
- Wang M et al. **Ibrutinib** Combined with **Venetoclax** in Patients with **Relapsed/Refractory Mantle Cell Lymphoma**: **Primary Analysis** Results from the Randomized **Phase 3 Sympatico** Study. ASH 2023;Abstract LBA-2.

Key Data Sets

Sonali M Smith, MD (continued)

- Wang M et al. **Ibrutinib-Rituximab** and **Venetoclax** (IRV) Followed by Risk-Stratified R-HyperCVAD/MTX in Young Patients with **Untreated Mantle Cell Lymphoma** – Phase II **WINDOW-2** Trial. ICML 2023;Abstract 101.
- Le Gouill S et al. Final Results and Overall Survival Data from a Phase II Study of **Acalabrutinib** Monotherapy in Patients with **Relapsed/Refractory Mantle Cell Lymphoma**, Including Those with Poor Prognostic Factors. *Haematologica* 2024;109(1):343-50.
- Hawkes E et al. A Window Study of **Acalabrutinib & Rituximab**, Followed by Chemotherapy & Autograft (**ASCT**) in Fit Patients with **Treatment Naïve Mantle Cell Lymphoma** (MCL): First Report of the Investigator-Initiated Australasian Leukaemia & Lymphoma Group **NHL33 'Wamm'** Trial. ASH 2023;Abstract 735.
- Kumar A et al. A Multicenter Phase 2 Trial of **Zanubrutinib, Obinutuzumab**, and **Venetoclax** (BOVen) in Patients with **Treatment-Naïve, TP53-Mutant Mantle Cell Lymphoma**. ASH 2023;Abstract 738.

Key Data Sets

Sonali M Smith, MD (continued)

- Portell C et al. Primary Analysis and Results of **Bendamustine, Rituximab**, and **Venetoclax** (BR-VEN) **for Initial Treatment** of **Mantle Cell Lymphoma** in Subjects over 60 Years of Age (**PrE0405**). ASH 2023;Abstract 733.
- Cohen JB et al. **Pirtobrutinib** in **Relapsed/Refractory** (R/R) **Mantle Cell Lymphoma** (MCL) Patients with Prior cBTKi: Safety and Efficacy Including High-Risk **Subgroup Analyses** from the Phase 1/2 **BRUIN** Study. ASH 2023;Abstract 981.
- Goy A et al. Outcomes of Patients with Relapsed/Refractory Mantle Cell Lymphoma **(R/R MCL)** Treated with **Brexucabtagene Autoleucel** (Brexu-cel) in **ZUMA-2** and **ZUMA-18**, an Expanded Access Study. ASH 2023;Abstract 106.
- Wang M et al. **Lisocabtagene Maraleucel** in **Relapsed/Refractory Mantle Cell Lymphoma**: Primary Analysis of the Mantle Cell Lymphoma Cohort from **TRANSCEND NHL 001**, a Phase I Multicenter Seamless Design Study. *J Clin Oncol* 2023;[Online ahead of print].

Key Data Sets

Andrew M Evens, DO, MBA, MSc

- Morschhauser F et al. Deciphering the Clinical Benefit of **Pola-R-CHP** versus R-CHOP in **Different Genetic Subtypes** Beyond Cell of Origin in the **POLARIX** Study. ASH 2023;Abstract 3000.
- Jerkeman M et al. Initial Safety Data from the **Phase 3 POLAR BEAR** Trial in Elderly or Frail Patients with **Diffuse Large Cell Lymphoma**, Comparing **R-pola-mini-CHP** and R-mini-CHOP. EHA 2023;Abstract S227.
- Duell J et al. **Tafasitamab** for Patients with **Relapsed or Refractory Diffuse Large B-Cell Lymphoma**: **Final 5-Year** Efficacy and Safety in the Phase II **L-MIND Study**. *Haematologica* 2024 Feb 1;109(2):553-66.
- Belada D et al. Safety and Efficacy of **Tafasitamab** with or without **Lenalidomide** Added to First-Line R-CHOP for **DLBCL**: The Phase 1b **First-MIND** Study. *Blood* 2023;142(16):1348-58.
- Caimi PF et al. **Loncastuximab Tesirine** in **Relapsed/Refractory Diffuse Large B-Cell Lymphoma**: Long-Term Efficacy and Safety from the Phase 2 **LOTIS-2** Study. *Haematologica* 2023;[Online ahead of print].

Key Data Sets

Andrew M Evens, DO, MBA, MSc (continued)

- Neelapu S et al. **Five-Year** Follow-Up of **ZUMA-1** Supports the Curative Potential of **Axicabtagene Ciloleucel** in Refractory Large B-Cell Lymphoma. *Blood* 2023;141(19):2307-15.
- Westin JR et al. Survival with **Axicabtagene Ciloleucel** in Large B-Cell Lymphoma. *N Engl J Med* 2023;389(2):148-57.
- Chavez J et al. **3-Year** Analysis of **ZUMA-12**: A Phase 2 Study of Axicabtagene Ciloleucel **(Axi-cel)** as **First-Line** Therapy in Patients with **High-Risk** Large B-Cell Lymphoma **(LBCL)**. ASH 2023;Abstract 894.
- Abramson JS et al. **Lisocabtagene Maraleucel** as **Second-Line** Therapy for Large B-Cell Lymphoma: Primary Analysis of the **Phase 3 TRANSFORM Study**. *Blood* 2023;141(14):1675-84.
- Hutchings M et al. **Glofitamab Monotherapy** in Relapsed or Refractory Large B-Cell Lymphoma: **Extended Follow-Up** from a Pivotal Phase II Study and **Subgroup Analyses** in Patients with Prior Chimeric Antigen Receptor T-Cell Therapy and by Baseline Total Metabolic Tumor Volume. ASH 2023;Abstract 433.

Key Data Sets

Andrew M Evens, DO, MBA, MSc (continued)

- Karimi Y et al. Effect of Follow-Up Time on the Ability of **Subcutaneous Epcoritamab** to Induce Deep and Durable Complete Remissions in Patients with Relapsed/Refractory Large B-Cell Lymphoma: **Updated Results** from the Pivotal **EPCORE NHL-1** Trial. ASCO 2023;Abstract 7525.
- Ayyappan S et al. **Final Analysis** of the Phase 2 **ELM-2** Study: **Odronextamab** in Patients with Relapsed/Refractory **(R/R)** Diffuse Large B-Cell Lymphoma **(DLBCL)**. ASH 2023;Abstract 436.
- Crombie J et al. **Odronextamab** Demonstrates Durable Complete Responses in Patients with Diffuse Large B-Cell Lymphoma (**DLBCL**) Progressing after CAR-T Therapy: Outcomes from the **ELM-1 Study**. ASH 2023;Abstract 4461.
- Herrera AF et al. **SWOG S1826**, a Randomized Study of **Nivolumab(N)-AVD** versus **Brentuximab Vedotin(BV)-AVD** in **Advanced Stage** (AS) **Classic Hodgkin Lymphoma** (HL). ASCO 2023;Abstract LBA4.
- Rutherford SC et al. **Nivolumab-AVD** Is Better Tolerated and Improves Progression-Free Survival Compared to **BV-AVD** in Older Patients (Aged ≥60 Years) with **Advanced Stage Hodgkin Lymphoma** Enrolled on **SWOG S1826**. ASH 2023;Abstract 181.

Key Data Sets

Andrew M Evens, DO, MBA, MSc (continued)

- Fornecker L et al. **Brentuximab Vedotin** plus **AVD** for **First-Line** Treatment of **Early-Stage** Unfavorable **Hodgkin Lymphoma (BREACH):** A Multicenter, Open-Label, Randomized, Phase II Trial. *J Clin Oncol* 2023;41(2):327-35.
- Abramson JS et al. **Brentuximab Vedotin** plus **Doxorubicin** and **Dacarbazine** in Nonbulky **Limited-Stage** Classical **Hodgkin Lymphoma**. *Blood Adv* 2023;7(7):1130-6.
- Abramson J et al. Brentuximab Vedotin, Nivolumab, Doxorubicin, and Dacarbazine **(AN+AD)** for **Early-Stage** Classical **Hodgkin Lymphoma (SGN35-027 Part C)**. ASH 2023;Abstract 611.
- Lee H et al. **Brentuximab Vedotin, Nivolumab, Doxorubicin**, and **Dacarbazine** for **Advanced Stage** Classical **Hodgkin Lymphoma**: Efficacy and Safety Results from the Single Arm Phase 2 Study. ASH 2023;Abstract 608.
- Henderson TO et al. **AHOD2131**: A Randomized **Phase 3** Response-Adapted Trial Comparing **Standard Therapy** with **Immuno-Oncology Therapy** for Children and Adults with Newly Diagnosed **Stage I and II** Classic **Hodgkin Lymphoma**. ASH 2023;Abstract 3084.

Agenda

INTRODUCTION: CD3-Based Bispecific Antibodies and the General Medical Oncologist: Lymphomas, Multiple Myeloma … and Solid Tumors?

MODULE 1: Follicular and Mantle Cell Lymphoma

MODULE 2: Diffuse Large B-Cell Lymphoma and Hodgkin Lymphoma

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Previously Untreated Indolent Non-Hodgkin Lymphoma

- Townsend W et al. **Obinutuzumab** versus **Rituximab** Immunochemotherapy in **Previously Untreated** iNHL: **Final Results** from the **GALLIUM** Study. *Hemasphere* 2023;7(7):e919.

Frequently Asked Clinical Questions About Follicular Lymphoma (FL)

- What factors do you evaluate to determine the long-term prognosis for a patient with FL?
- How do you define and care for patients with “POD-24”?

Frequently Asked Clinical Questions About FL

- What is the mechanism of action of bendamustine, and how does the agent affect T-cell function? How much of a concern is this in FL?
- Do you currently utilize obinutuzumab as a component of up-front therapy for FL in any situations?
- What about rituximab as maintenance?

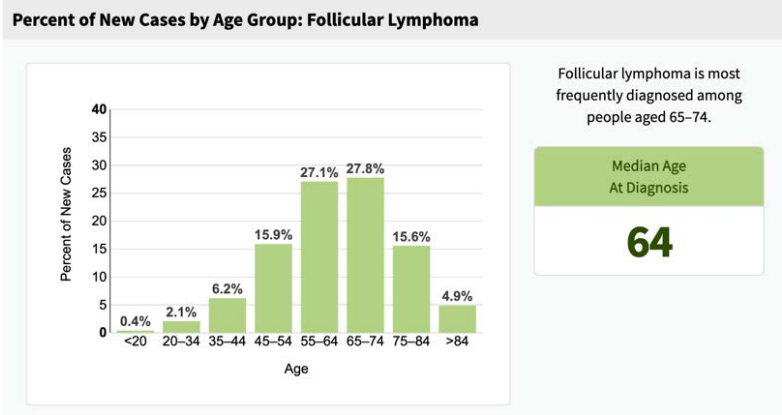
Frequently Asked Clinical Questions About FL

- How do you manage recurrent FL, and what do you observe in terms of efficacy with successive lines of treatment?

- In general, what is your usual second-line treatment?

Follicular lymphoma: key principles

- Indolent, incurable
  - Long life expectancy for most patients
  - 90% 5-year survival after diagnosis
- More common in older adults
  - Median age 6th decade
  - 25% pts under 40y



- No ability to determine *individual* prognosis at diagnosis
  - Grade, FLIPI and FLIPI-2, molecular assessments all lack precision
- Treatment is based on symptoms and not stage or biology
- Event-based outcomes determine prognosis (i.e. POD24)
- Limited data regarding optimal sequencing
  - Many new regimens and modalities
- Lifelong risk of transformation

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Courtesy of Sonali M Smith, MD

Relapsed/Refractory Follicular Lymphoma: CAR T-Cell Therapies

- Neelapu S et al. **Axicabtagene Ciloleucel** (Axi-Cel) in Patients with **Relapsed/Refractory Indolent Non-Hodgkin Lymphoma**: **4-Year Follow-Up** from the **Phase 2 ZUMA-5 Trial**. ASH 2023;Abstract 4868.
- Schuster SJ et al. **Clinical Outcomes** of Patients with **Relapsed/Refractory Follicular Lymphoma** Treated with **Tisagenlecleucel: Phase 2 Elara 3-Year Follow-Up**. ASH 2023;Abstract 601.
- Morschhauser F et al. **TRANSCEND FL: Phase 2** Study **Results** of **Lisocabtagene Maraleucel** (Liso-cel) in Patients (pts) with **Relapsed/Refractory** (R/R) **Follicular Lymphoma** (FL). ICML 2023;Abstract LBA4.
- Morschhauser F et al. **TRANSCEND FL: Phase 2** Study **Primary Analysis** of **Lisocabtagene Maraleucel** as **Second-Line Therapy** in Patients with **High-Risk Relapsed or Refractory Follicular Lymphoma**. ASH 2023;Abstract 602.

Frequently Asked Clinical Questions About FL

- **What is the global efficacy and tolerability of CAR T-cell therapy in FL?**

- **In general, how are you sequencing CAR T-cell therapy and bispecific antibodies for patients with R/R FL?**

Where does CAR-T fit into FL management? Two FDA-approved products: axi-cel and tisa-cel

ZUMA-5: axi-cel

Patients with R/R FL (grade 1-3a) or MZL;
≥2 prior lines of therapy including anti-CD20 mAb + alkylating agent
(N = 104; n = 84 FL)

Conditioning CT: **Fludarabine** 30 mg/m^2 + **Cyclophosphamide** 500 mg/m^2 Days -5, -4, -3

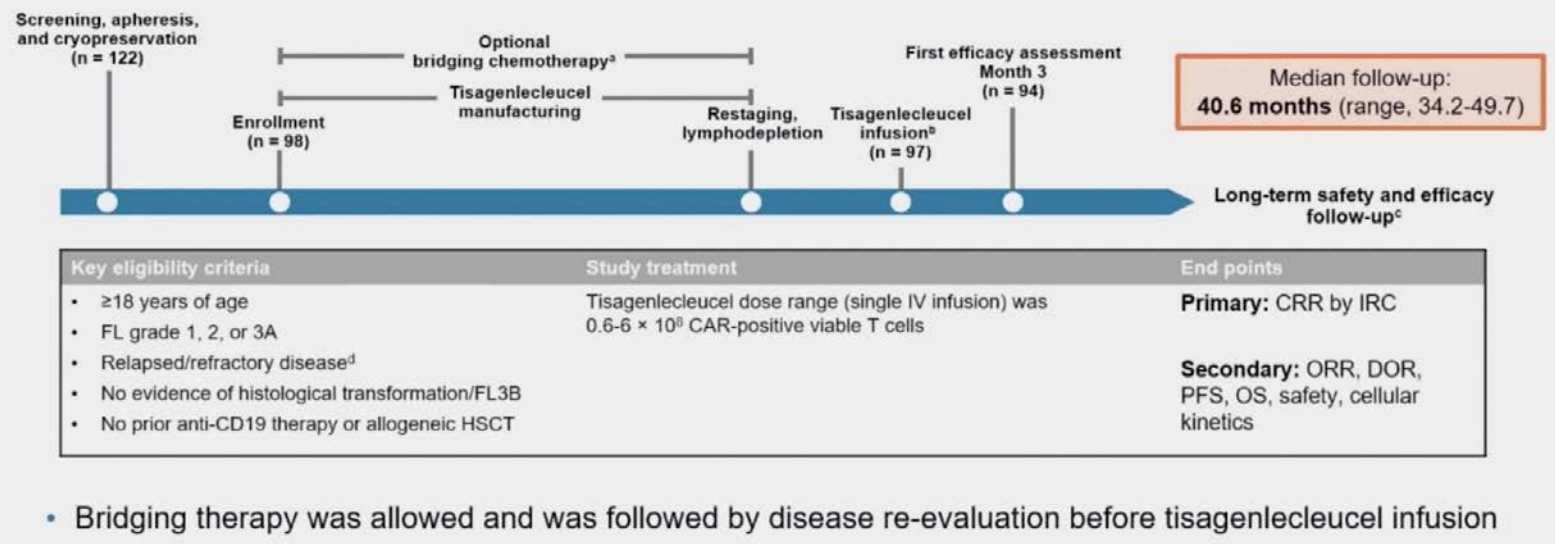
CAR T-Cells: **Axi-Cel** 2 x 10^6 cells/kg Day 0

Followed for safety up to 15 yr

Patients with SD but no relapse >1 yr from completion of last therapy ineligible. Single-agent anti-CD20 mAb not counted as line of therapy for eligibility. Median time to delivery of axi-cel: 17 days following leukapheresis.

- Primary endpoint: ORR

ELARA: tisa-cel



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Neelapu ASH 2023;Abstract 4868; Schuster ASH 2023;Abstract 601

FDA Investigating Serious Risk of T-Cell Cancer After BCMA-Directed or CD19-Directed Autologous Chimeric Antigen Receptor (CAR) T-Cell Immunotherapies

Press Release: November 28, 2023

"The Food and Drug Administration (FDA) has received reports of T-cell malignancies, including chimeric antigen receptor CAR-positive lymphoma, in patients who received treatment with BCMA- or CD19-directed autologous CAR T cell immunotherapies. Reports were received from clinical trials and/or postmarketing adverse event (AE) data sources.

FDA has determined that the risk of T-cell malignancies is applicable to all currently approved BCMA-directed and CD19-directed genetically modified autologous CAR T cell immunotherapies. T-cell malignancies have occurred in patients treated with several products in the class.

Although the overall benefits of these products continue to outweigh their potential risks for their approved uses, FDA is investigating the identified risk of T cell malignancy with serious outcomes, including hospitalization and death, and is evaluating the need for regulatory action."

https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-investigating-serious-risk-t-cell-malignancy-following-bcma-directed-or-cd19-directed-autologous

nature medicine

2024 January 24; Online ahead of print

Accelerated Article Preview

T-cell Lymphoma and Secondary Primary Malignancy Risk After Commercial CAR T-cell Therapy

Guido Ghilardi, Joseph A. Fraietta, James N. Gerson, Vivianna M. Van Deerlin, Jennifer J.D. Morrissette, Gabriel C. Caponetti, Luca Paruzzo, Jaryse C. Harris, Elise A. Chong, Sandra P. Susanibar Adaniya, Jakub Svoboda, Sunita D. Nasta, Ositadimma H. Ugwuanyi, Daniel J. Landsburg, Eugenio Fardella, Adam J. Waxman, Emeline R. Chong, Vrutti Patel, Raymone Pajarillo, Irina Kulikovskaya, David B. Lieberman, Adam D. Cohen, Bruce L. Levine, Edward A. Stadtmauer, Noelle V. Frey, Dan T. Vogl, Elizabeth O. Hexner, Stefan K. Barta, David L. Porter, Alfred L. Garfall, Stephen J. Schuster, Carl H. June & Marco Ruella

Author Conclusions: *The observed very low incidence of secondary T-cell lymphomas should provide reassurance to the scientific community regarding the safety of commercially available CART products. This aligns with the FDA's assertion that "…the overall benefits of these products continue to outweigh their potential risks for their approved uses."*

Relapsed/Refractory Follicular Lymphoma: Bispecific Antibodies

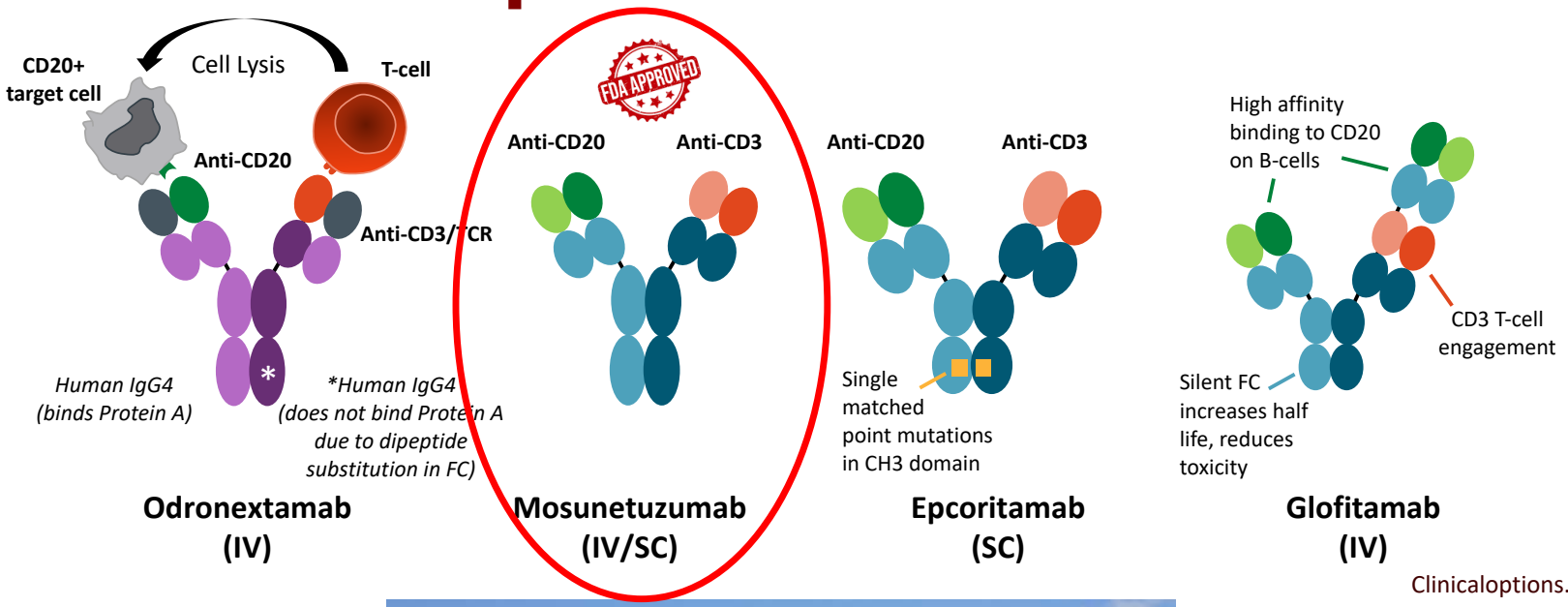
- Linton K et al. **Epcoritamab SC** Monotherapy Leads to Deep and Durable Responses in Patients with **Relapsed or Refractory Follicular Lymphoma**: First Data Disclosure from the **Epcore NHL-1** Follicular Lymphoma Dose-Expansion Cohort. ASH 2023;Abstract 1655.
- Schuster SJ et al. **Mosunetuzumab Monotherapy** Continues to Demonstrate Durable Responses in Patients with **Relapsed and/or Refractory Follicular Lymphoma** After ≥2 Prior Therapies**: 3-Year Follow-Up** from a Pivotal **Phase II** Study. ASH 2023;Abstract 603.
- Villasboas JC et al. Results of a Second, Prespecified Analysis of the Phase 2 Study **ELM-2** Confirm High Rates of Durable Complete Response with **Odronextamab** in Patients with **Relapsed/Refractory** (R/R) **Follicular Lymphoma** (FL) with Extended Follow-Up. ASH 2023;Abstract 3041.

Frequently Asked Clinical Questions About FL

- **What is the global efficacy and tolerability of mosunetuzumab in FL?**

- **From a clinical point of view, do you believe any of the other CD20 x CD3 bispecific antibodies (eg, glofitamab, epcoritamab and odronextamab) offer advantages over mosunetuzumab in FL?**

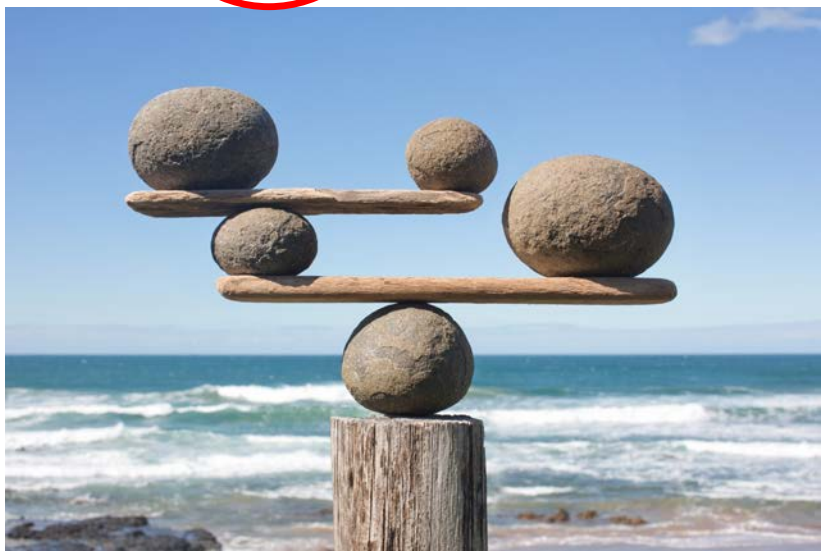
CD20xCD3 bispecific antibodies in FL



Clinicaloptions.com*

Bispecifics

- Off the shelf
- Lower CRS
- Need for longer treatment



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CAR-T

- Requires manufacturing
- Higher CRS, ICANS
- "one and done"

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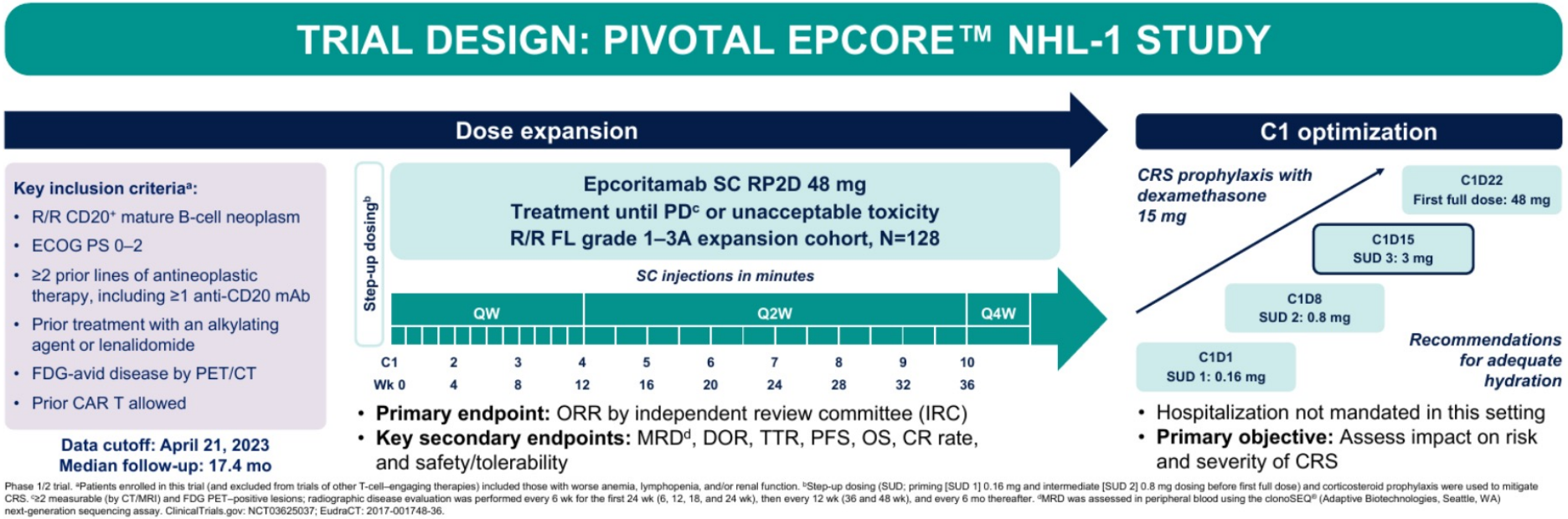
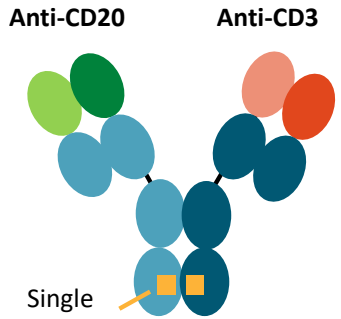
Castaneda-Puglianni. Drugs Context. 2021;10:2021; Bannerji. ASH 2020. Abstr 42; Budde. ASH 2018. Abstr 399; Hutchings. Lancet. 2021;398:1157; Engelberts. eBioMedicine. 2020;52:102625; Hutchings. JCO. 2021;39:1959.

EPCORE NHL-1: epco in r/r FL



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



Epcoritamab (SC)

Key clinical features:

- Med age 65y
- FLIPI 3-5 61%
- Med prior Rx = 3
- POD24 42%
- Double refractory 70%
- Primary refractory 54%
- Refractory to last Rx 69%

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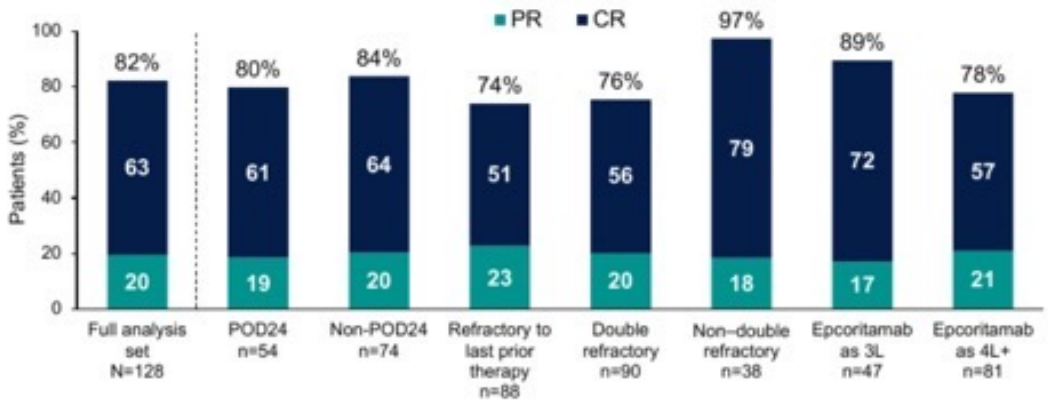
Courtesy of Sonali M Smith, MD

Linton ASH 2023;Abstract 1655.

EPCORE NHL-1: epco in r/r FL results

Efficacy Results

ORRs and CR Rates Were High Regardless of Subgroup



C1 Optimization Reduced Risk and Severity of CRS

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

[a]Data cutoff: September 21, 2023. Median follow-up: 3.8 mo (range, 1.9–8.7). [b]Graded by Lee et al 2019 criteria.[13]

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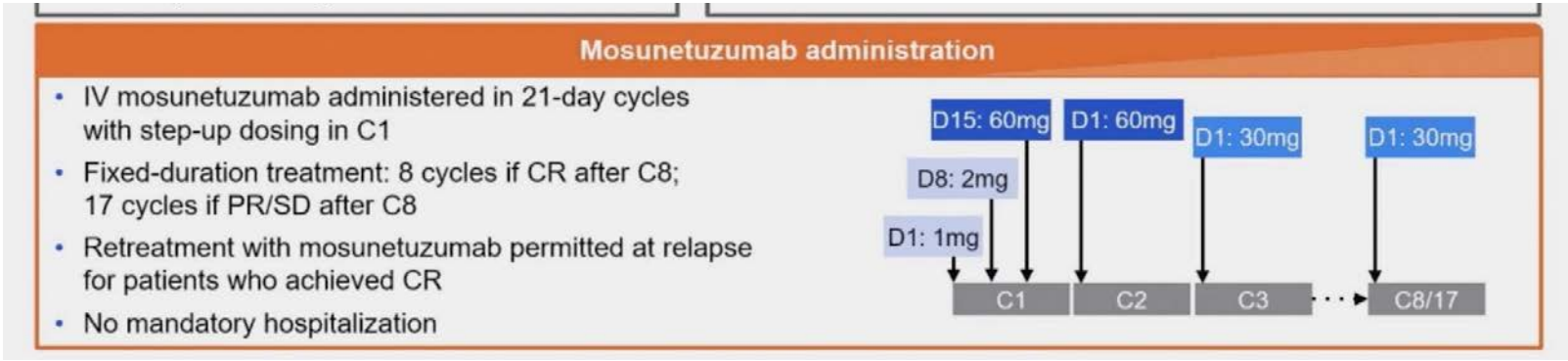
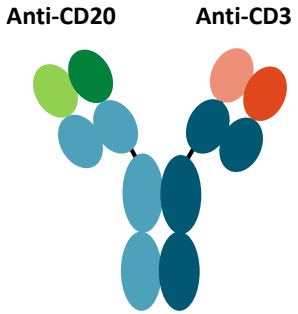
Linton ASH 2023;Abstract 1655.

Mosun in FL





Mosunetuzumab (IV/SC)

Baseline patient characteristics

n, unless stated	N=90
Median age, years (range)	60 (29–90)
Male	55 (61%)
ECOG PS 0 1	 53 (59%) 37 (41%)
Ann Arbor stage I/II III/IV	 21 (23%) 69 (77%)
Median lines of prior therapy, (range)	3 (2–10)
Prior autologous stem cell transplant	28 (31%)*
Refractory to last prior therapy	62 (69%)
Refractory to any prior anti-CD20 therapy	71 (79%)
POD24	47 (52%)
Double refractory to prior anti-CD20 and alkylator therapy	48 (53%)

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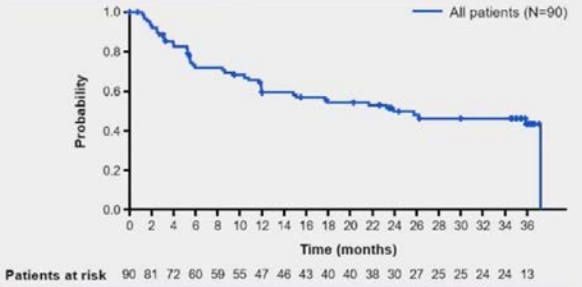
Courtesy of Sonali M Smith, MD

Schuster ASH 2023;Abstract 603.

Mosun in r/r FL: 3-year follow up

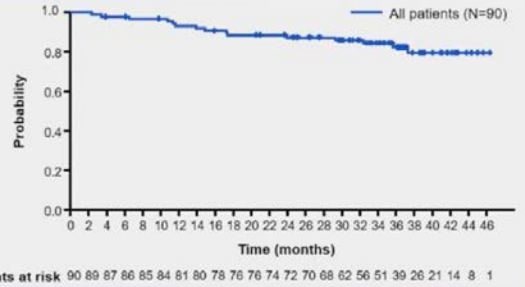
PFS and OS; median follow-up >36 months

PFS



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

OS

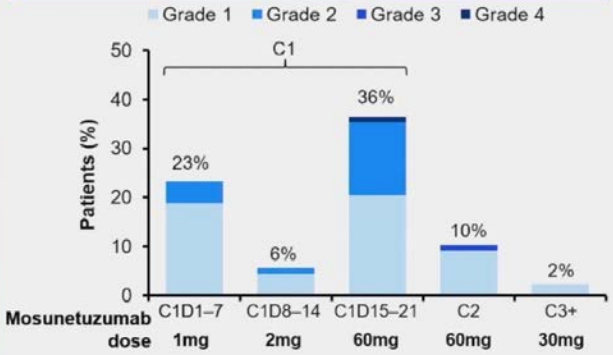


	N=90
Median OS, months (95% CI)	**NR** (NE–NE)
36-month OS, months (95% CI)	**82.4%** (73.8–91.0)

CRS summary

CRS by ASTCT criteria[1]	N=90
CRS (any grade), n	40 (44%)
Grade 1	23 (26%)
Grade 2	15 (17%)
Grade 3	1 (1%)
Grade 4	1 (1%)
Median time to CRS onset, hours (range)	
C1D1	5 (1–24)
C1D15	27 (0–391)
Median CRS duration, days (range)	3 (1–29)
Corticosteroids for CRS management, n	10 (11%)*
Tocilizumab for CRS management, n	7 (8%)*
Events resolved	100%

CRS by cycle and grade



CRS was predominantly low-grade and occurred during C1
All CRS events resolved; no new events have been reported in this extended follow-up

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Schuster ASH 2023;Abstract 603.

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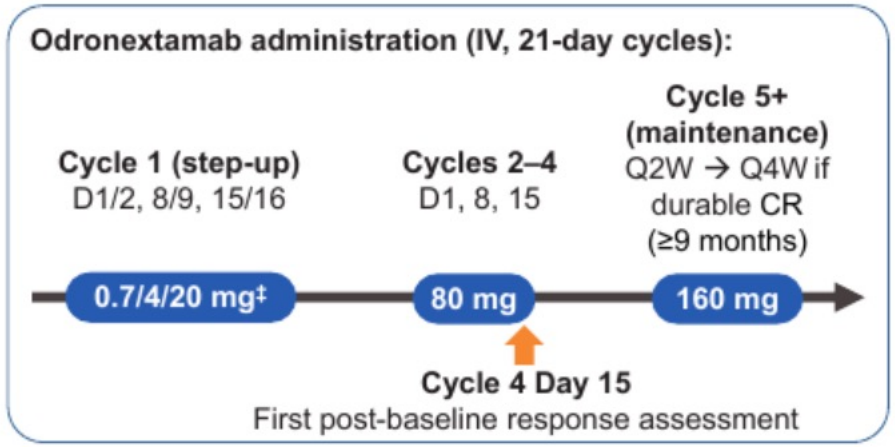
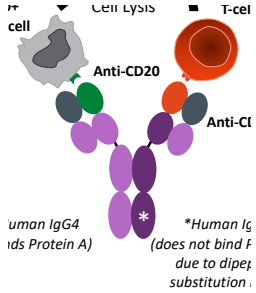
Odronextamab (ELM-2 trial)





Primary endpt: ORR

Patient and disease characteristics		N=128
Median age, years (range)		61.0 (22–84)
Age ≥75 years, %		9.4
Male, %		53.1
Race, %	White / Asian / other / unknown / not reported	61.7 / 26.6 / 0.8 / 1.6 / 9.4
ECOG PS, %	0 / 1 / 2	50.8 / 48.4 / 0.8
Ann Arbor stage III–IV, %		85.2
FLIPI risk score, %	0–1 / 2 / 3–5	16.4 / 25.8 / 57.8
Bulky disease, investigator assessment, %		14.1
Median prior lines, n (range)		3 (2–13)
Prior PI3K inhibitor, %		14.1
Prior R², %		13.3
Prior ASCT, %		30.5
Refractory to last line of therapy, %		71.9
Refractory to anti-CD20 antibody, %		74.2
Double refractory to alkylator/anti-CD20 antibody, %		41.4
POD24, %		49.2

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Courtesy of Sonali M Smith, MD

Villasboas ASH 2023;Abstract 3041.

ELM-2: Outcomes with Odronextamab in r/r FL

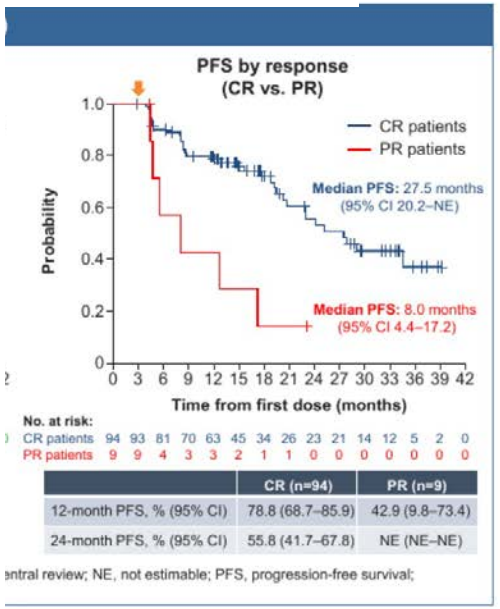
Table 5. CRS

		0.7/4/20 mg N=60
Any grade, n (%)		34 (56.7)
Grade 1 / 2		27 (45.0) / 6 (10.0)
Grade 3 / 4		1 (1.7) / 0
Median time to CRS onset, hours (range)		19.7 (0.7–159.0)
Median CRS duration, days (range)		2.00 (1.0–10.0)
CRS management, n (%)	Systemic steroids / tocilizumab	20 (33.3) / 10 (16.7)

CRS per Lee 2019 criteria[5]. CRS, cytokine release syndrome.

Conclusions

- **Heavily pretreated patients with R/R FL achieved deep and durable responses with continued odronextamab treatment**
  - ORR, 81%; CR, 73%; 2-year CR rate, 49%
  - Median PFS, 20.7 months; median OS, NR
  - PROs were maintained from baseline to Week 50
- **The safety profile of odronextamab was generally manageable**
  - CRS was mostly Grade 1/2 and one low-grade ICANS event was reported with 0.7/4/20 mg Cycle 1 step-up
  - Any-grade infection TEAEs were reported in 80% of patients, and over a third of patients had COVID-19 infection, reflective of a study conducted during the pandemic in a patient population with increased underlying risk for infections
- **Phase 3 randomized trials are ongoing in FL patients in earlier lines of therapy**
  - OLYMPIA-1 (NCT06091254), OLYMPIA-2 (NCT06097364), OLYMPIA-5



	CR (n=94)	PR (n=9)
12-month PFS, % (95% CI)	78.8 (68.7–85.9)	42.9 (9.8–73.4)
24-month PFS, % (95% CI)	55.8 (41.7–67.8)	NE (NE–NE)

ntral review; NE, not estimable; PFS, progression-free survival;

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Villasboas ASH 2023;Abstract 3041.

Treatment Naïve Mantle Cell Lymphoma

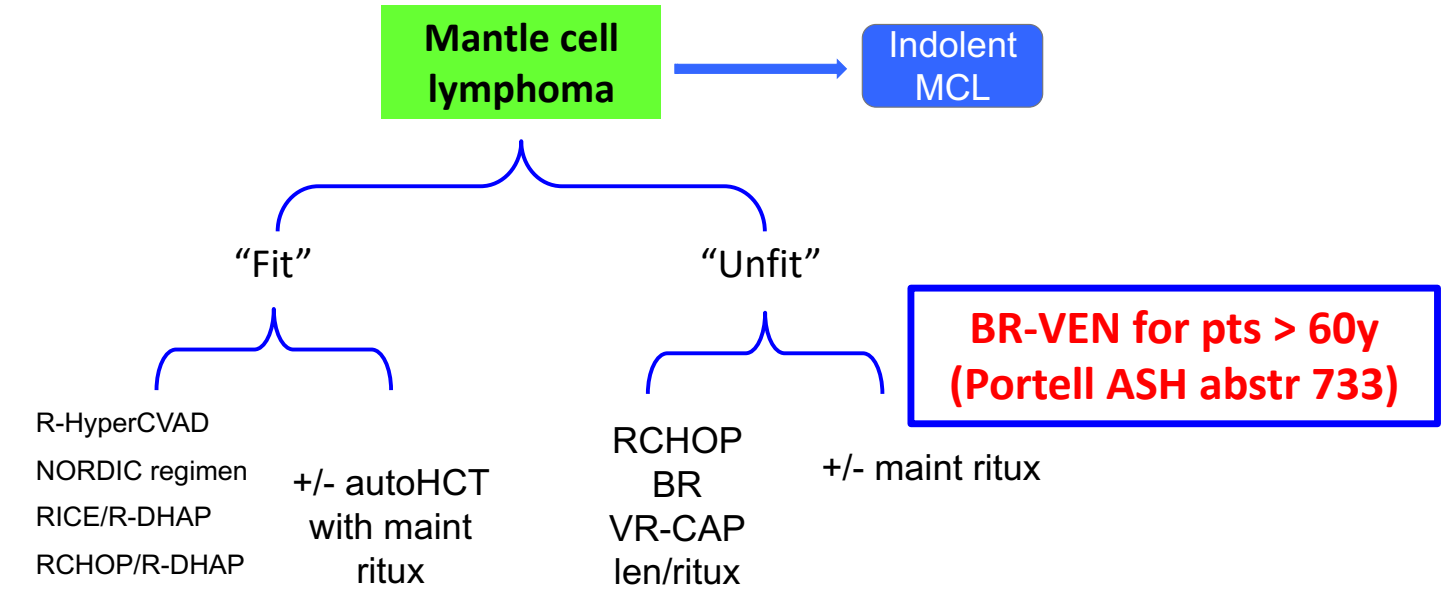
- Wang M et al. **Ibrutinib-Rituximab** and **Venetoclax** (IRV) Followed by Risk-Stratified R-HyperCVAD/MTX in Young Patients with **Untreated Mantle Cell Lymphoma** – Phase II **WINDOW-2** Trial. ICML 2023;Abstract 101.
- Hawkes E et al. A Window Study of **Acalabrutinib & Rituximab**, Followed by Chemotherapy & Autograft (**ASCT**) in Fit Patients with **Treatment Naïve Mantle Cell Lymphoma** (MCL): First Report of the Investigator-Initiated Australasian Leukaemia & Lymphoma Group **NHL33 'Wamm'** Trial. ASH 2023;Abstract 735.
- Kumar A et al. A Multicenter Phase 2 Trial of **Zanubrutinib, Obinutuzumab**, and **Venetoclax** (BOVen) in Patients with **Treatment-Naïve, TP53-Mutant Mantle Cell Lymphoma**. ASH 2023;Abstract 738.
- Portell C et al. Primary Analysis and Results of **Bendamustine, Rituximab**, and **Venetoclax** (BR-VEN) **for Initial Treatment** of **Mantle Cell Lymphoma** in Subjects over 60 Years of Age (**PrE0405**). ASH 2023;Abstract 733.

Frequently Asked Clinical Questions About Mantle Cell Lymphoma (MCL)

- **What is your current approach to first-line treatment for younger patients with MCL? What about older patients? If regulatory and reimbursement issues were removed, would your choices change in any way?**

- **How do you approach first-line treatment for patients with p53-mutated or blastoid MCL?**

General approach to TN MCL



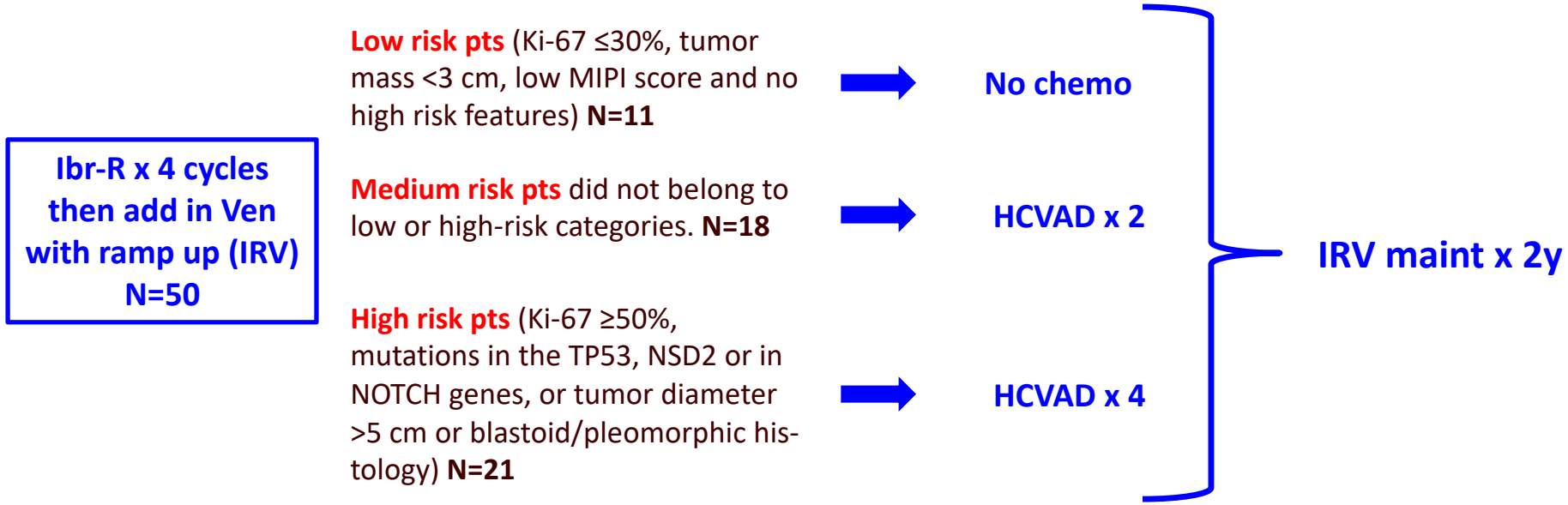
Ibr-R-ven→risk stratified RHCVAD (Wang ICML 2023 abstr 101)

Acala-R→chemo/HCT (Hawkes ASH abstr 735)

BOVen for *TP53*-mut MCL (Kumar ASH abstr 738)

Courtesy of Sonali M Smith, MD

Young/fit TN MCL: IRV → risk adapted HCVAD



Results:

- Med f/u 41m
- ORR and CR 100% to IRV induction
- 3 year PFS 85% and OS 86%
- PFS and OS not significantly different in pts with high and low Ki-67% or with/without TP53 aberrations or among pts with low, medium or high-risk categories.

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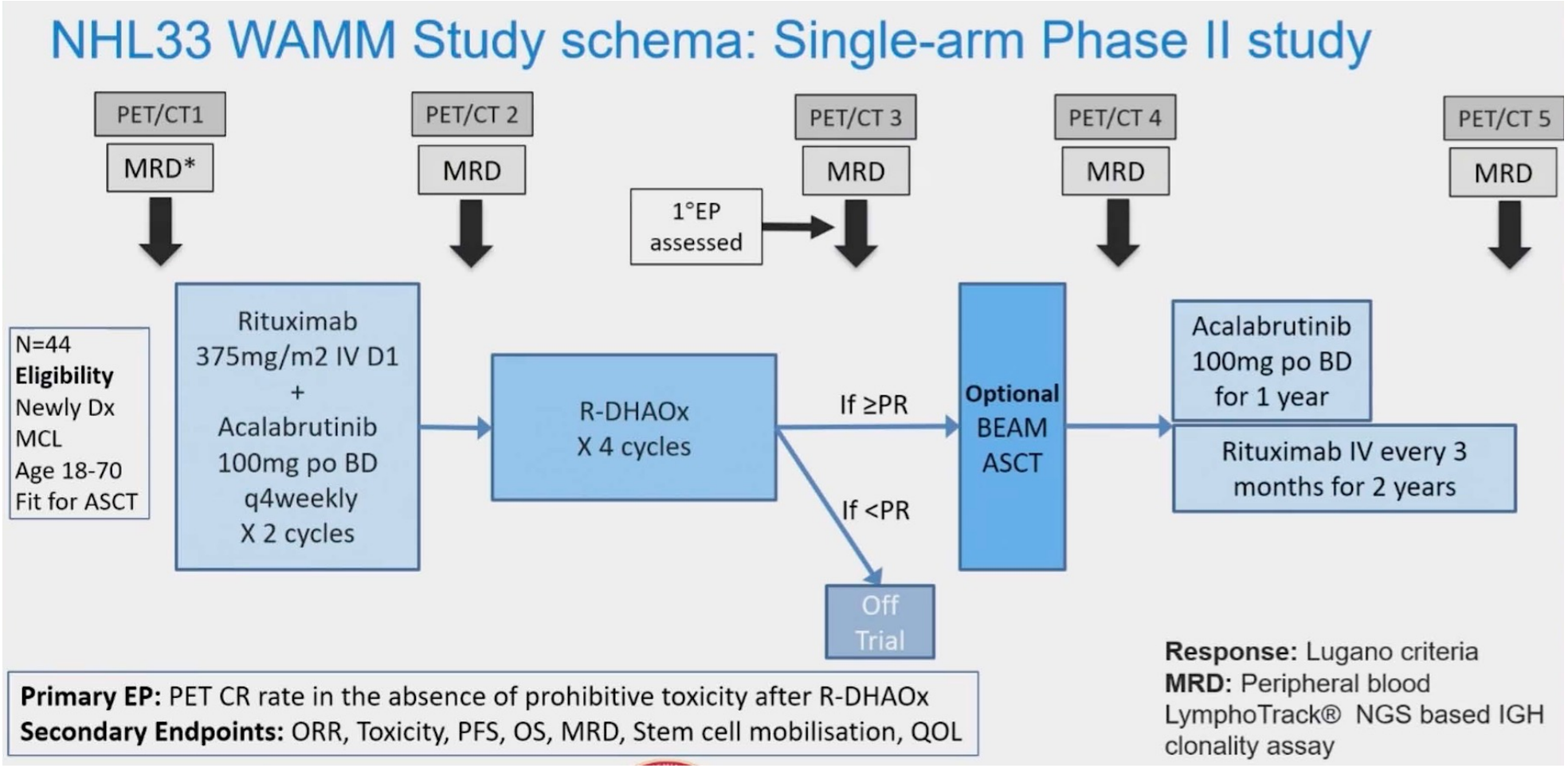
Wang ICML 2023;Abstract 101.

Young/fit MCL: Acala-R→chemo/ASCT



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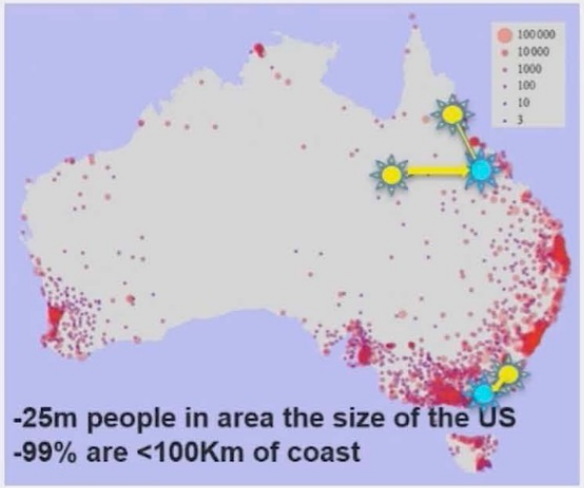
Hawkes ASH 2023;Abstract 735.

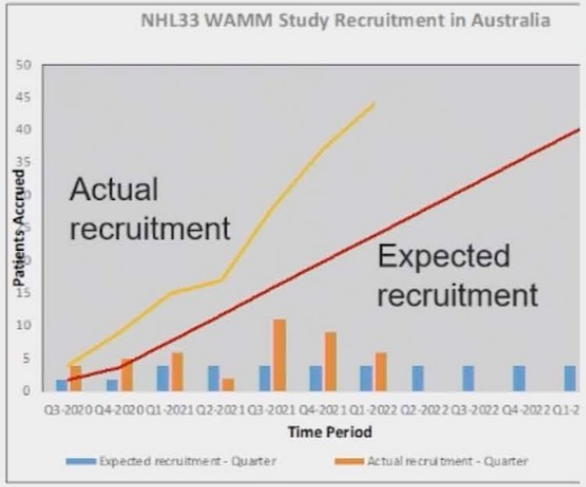
Rapid accrual in rural and remote areas

NHL33 WAMM study: Hub & Spoke trial model

- The ALLG cooperative group employed a **unique telehealth, 'hub and spoke' design** for non-transplant sites and remote locations.
  - ➢ *'Hub' site* — Delivered ASCT +/- R-DHAOX; provides trial management; receives & manages IMP.
  - ➢ *'Spoke' site* — Provided local patient care & dispensed medications.

➢Some of these were >1000km apart….
- ✓**Recruitment of a rare disease in half the expected time**
- ✓**Rural/remote patients gained access to novel therapies**





ALLG Australasian Leukaemia & Lymphoma Group — Better treatments… Better lives.

50th Anniversary ALLG 1973 – 2023

ALLG NHL33 WAMM study primary report.
ASH 2023 San Diego Abstr # 735

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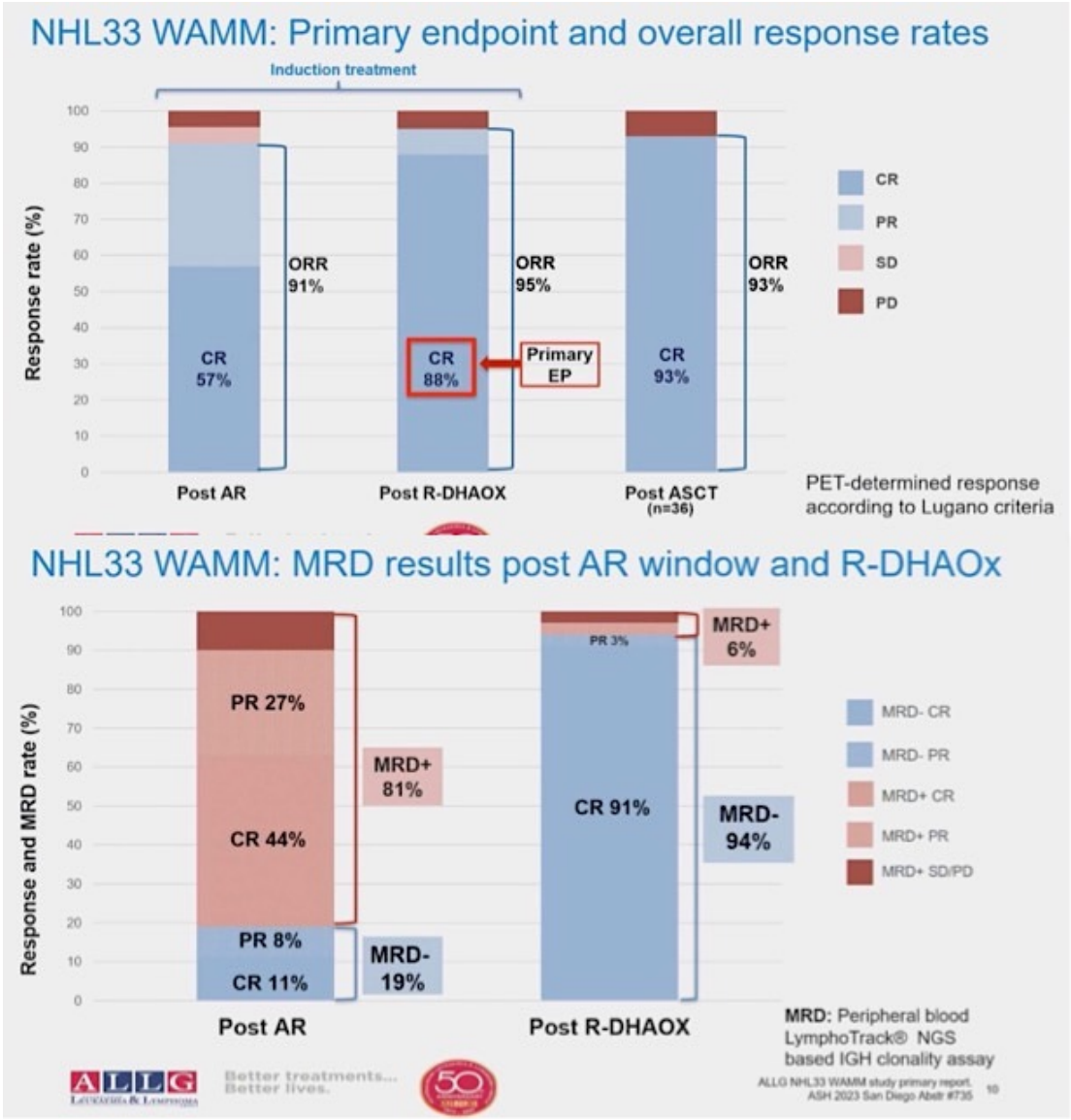
Courtesy of Sonali M Smith, MD

Hawkes ASH 2023;Abstract 735.

Young/fit TN MCL: Acala-R→chemo/ASCT



Results:

- Med f/u 25m
- CR after AR: 57%
- CR after chemo 88%
- Higher MRD neg after chemo
- 2-yr PFS: 73%
- 2-yr OS: 79%

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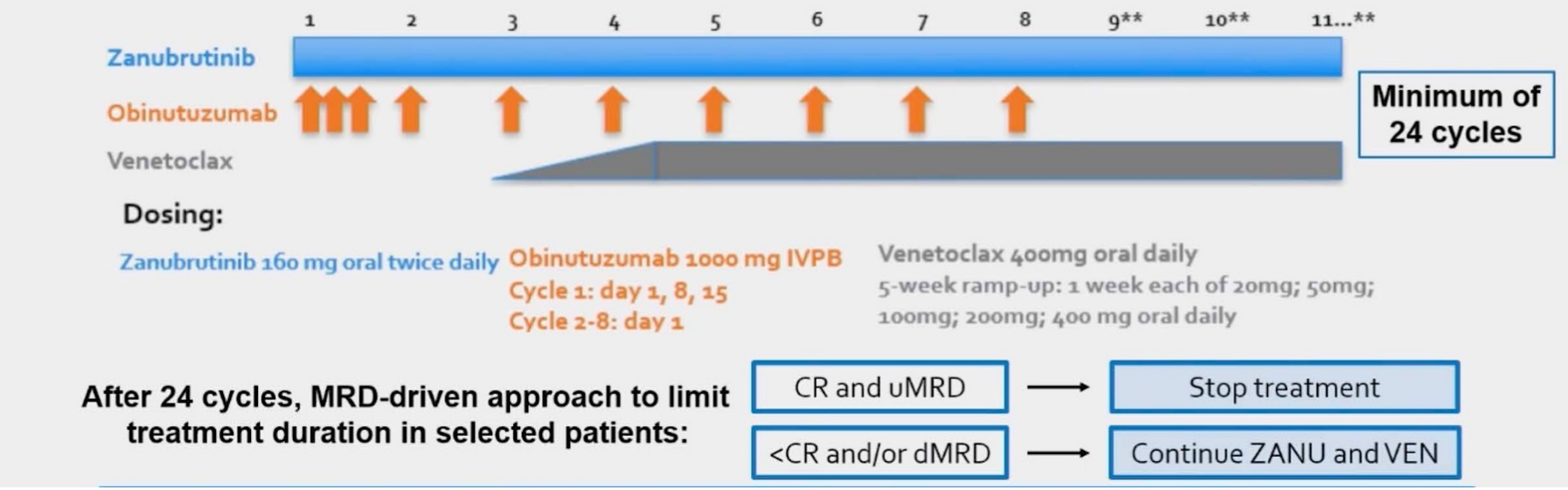
Courtesy of Sonali M Smith, MD

Hawkes ASH 2023;Abstract 735.

Treatment-naïve *TP53* mut MCL: zanu-obin-ven



Patient Characteristics:

N=25

Blastoid/pleomorphic 20%

Ki67 >30% 62% (incl 33% over 50%)

High MIPI 68%

TP53 overexpression by IHC 86%

17p del via FISH 44%

Toxicity:

Well-tolerated

Grade 3 neutropenia

Grade 1 diarrhea (60%)

COVID infections—2 fatal

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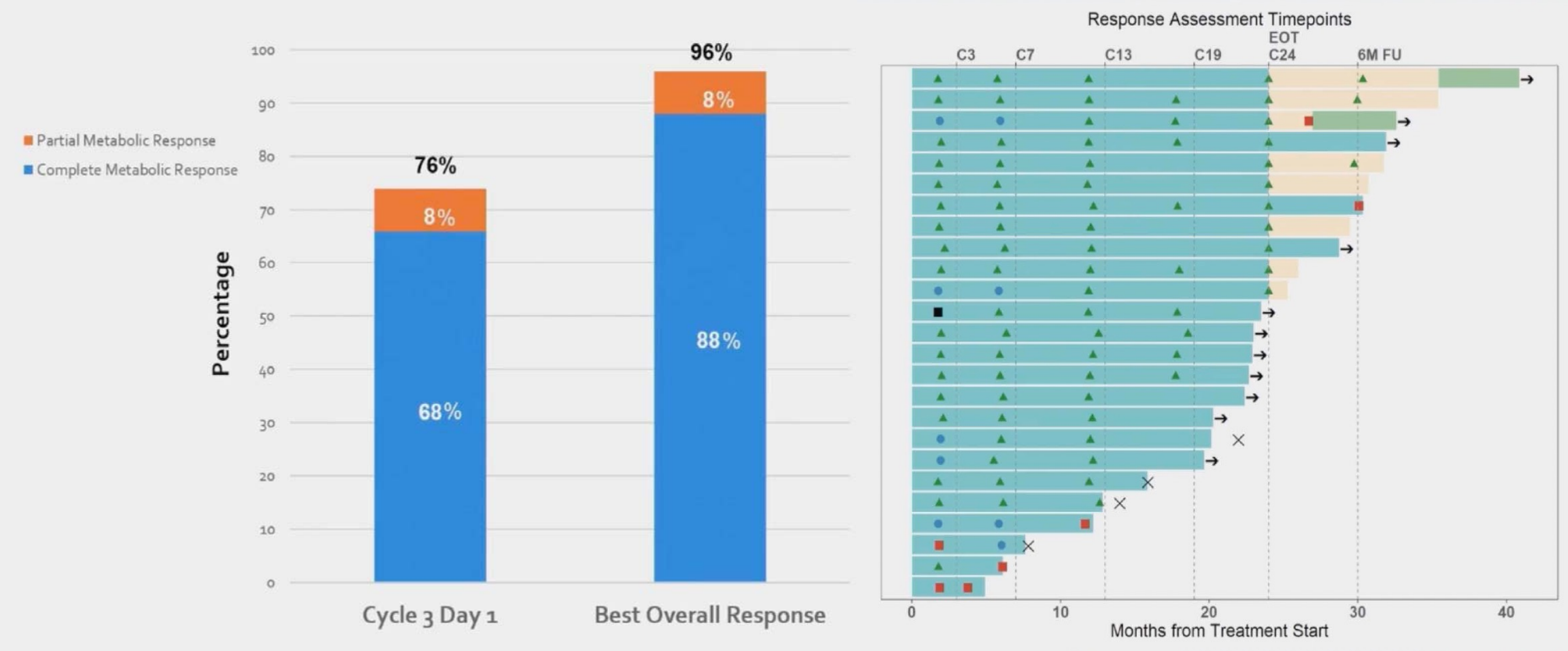
Courtesy of Sonali M Smith, MD

Kumar ASH 2023;Abstract 738.

Treatment-naïve *TP53* mut MCL: zanu-obin-ven



Median f/u 23m

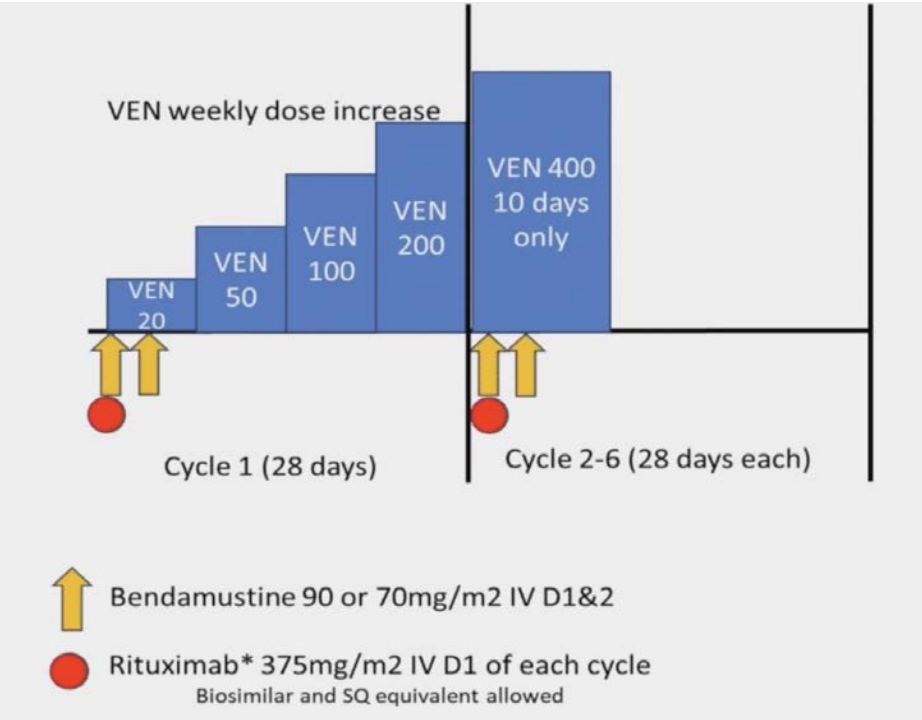
9 events:

- 5 PD
- 4 deaths (all infectious)

Courtesy of Sonali M Smith, MD

Kumar ASH 2023;Abstract 738.

Older pts with MCL: BR-ven



N=33		
Age median years (range)	71	(61,80)
	N	(%)
Male	25	76%
Female	8	24%
MIPI		
Low	2	6%
Intermediate	9	27%
High	22	67%
Median MIPI Score (range)	6.3	(2.8,8.3)
Blastoid Histology		
Yes	9	27%
No	21	64%
Unknown	3	9%
Ki-67		
Median % (range)	30%	(10,90)
N Missing	8	

Primary endpt: CR

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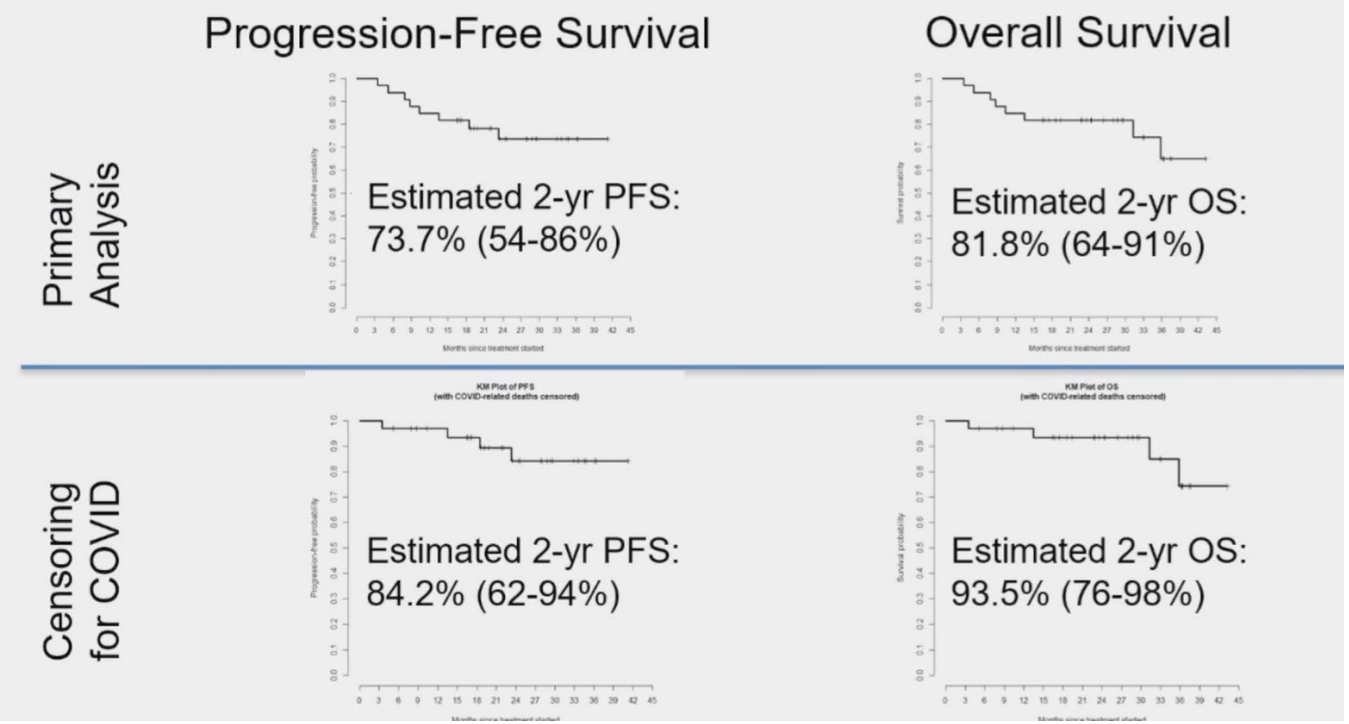
Courtesy of Sonali M Smith, MD

Portell ASH 2023;Abstract 733.

BR-ven in older adults with MCL

End of Induction Response*		
Overall Response	97%	32/33
PET and BM confirmed CR EOT*	85%	28/33
MRD by NGS at EOT	Under analysis	
*Met primary endpoint (≥ 23 with CR)		



- AE's: cytopenias
- 8 deaths on study (4 from COVID, 1 influenza)

Courtesy of Sonali M Smith, MD

Portell ASH 2023;Abstract 733.

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Relapsed/Refractory Mantle Cell Lymphoma

- Wang M et al. **Ibrutinib** Combined with **Venetoclax** in Patients with **Relapsed/Refractory Mantle Cell Lymphoma**: **Primary Analysis** Results from the Randomized **Phase 3 Sympatico** Study. ASH 2023;Abstract LBA-2.
- Le Gouill S et al. Final Results and Overall Survival Data from a Phase II Study of **Acalabrutinib** Monotherapy in Patients with **Relapsed/Refractory Mantle Cell Lymphoma**, Including Those with Poor Prognostic Factors. *Haematologica* 2024;109(1):343-50.
- Cohen JB et al. **Pirtobrutinib** in **Relapsed/Refractory** (R/R) **Mantle Cell Lymphoma** (MCL) Patients with Prior cBTKi: Safety and Efficacy Including High-Risk **Subgroup Analyses** from the Phase 1/2 **BRUIN** Study. ASH 2023;Abstract 981.
- Goy A et al. Outcomes of Patients with Relapsed/Refractory Mantle Cell Lymphoma **(R/R MCL)** Treated with **Brexucabtagene Autoleucel** (Brexu-cel) in **ZUMA-2** and **ZUMA-18**, an Expanded Access Study. ASH 2023;Abstract 106.
- Wang M et al. **Lisocabtagene Maraleucel** in **Relapsed/Refractory Mantle Cell Lymphoma**: Primary Analysis of the Mantle Cell Lymphoma Cohort from **TRANSCEND NHL 001**, a Phase I Multicenter Seamless Design Study. *J Clin Oncol* 2023;[Online ahead of print].

Frequently Asked Clinical Questions About MCL

- What is your usual second-line treatment for patients with MCL who experience relapse after first-line bendamustine/rituximab?
- Which BTK inhibitor (BTKi) do you normally employ for MCL and why?
- What is your experience with the efficacy and tolerability of pirtobrutinib, and how do you integrate this agent into your practice?

Frequently Asked Clinical Questions About MCL

- **Given recently presented research, are there situations in which you would like to combine a BTKi with a Bcl-2 inhibitor for your patients with MCL? If so, what regimen would you use and when?**
- **Reimbursement aside, what do you consider the optimal use of first-line combinations containing a BTKi, an anti-CD20 antibody and venetoclax?**

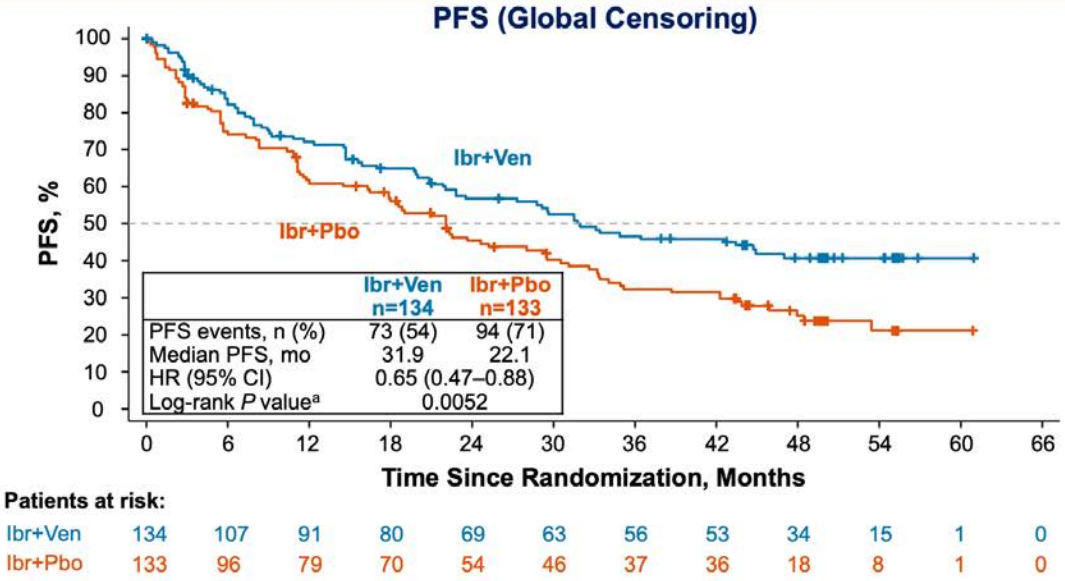
Frequently Asked Clinical Questions About MCL

- How do you incorporate CAR T-cell therapy into the management of MCL?

- How do the responses and toxicity with CAR T-cell therapy in MCL compare to what is seen in DLBCL and FL?

SYMPATICO: RP3 ibr-ven vs. ibr-pbo x 24m→ibr maintenance

Primary Endpoint: Investigator-Assessed PFS Was Significantly Improved With Ibrutinib + Venetoclax Versus Ibrutinib + Placebo



Median PFS, mo	Global Censoring[b]				US FDA Censoring[c]			
	Ibr+Ven n=134	Ibr+Pbo n=133	HR (95% CI)	Log-rank *P* value[a]	Ibr+Ven n=134	Ibr+Pbo n=133	HR (95% CI)	Log-rank *P* value[a]
Investigator assessment	31.9	22.1	0.65 (0.47–0.88)	0.0052	42.6	22.1	0.60 (0.44–0.83)	0.0021
IRC assessment	31.8	20.9	0.67 (0.49–0.91)	0.0108	43.5	22.1	0.63 (0.45–0.87)	0.0057

No unexpected toxicity

No sig diff in OS (?trend)

Courtesy of Sonali M Smith, MD

Wang ASH 2023;Abstract LBA-2

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Acalabrutinib monotherapy in rel/ref MCL (n=124)

Pt Characteristics:

Med age 68y

37.1% bulky

21% blastoid morphology

Ki67 > 50% in 25% of pts

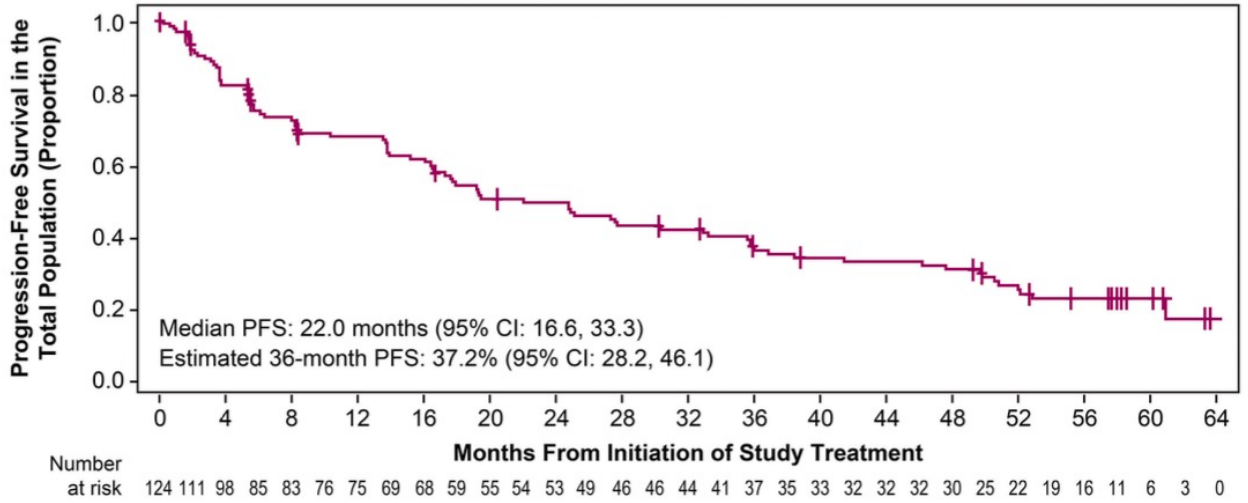
Results:

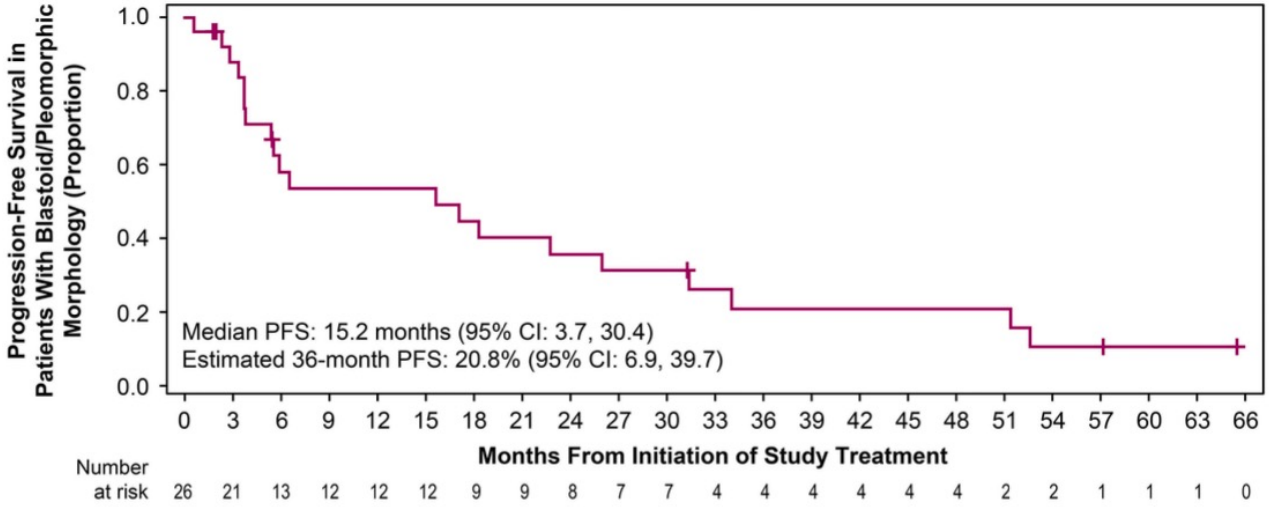
ORR 81%

CR 47.6%

DoR 28m

Low risk and CR pts had the best outcomes





Courtesy of Sonali M Smith, MD

Le Gouill Haematologica 2024;109(1):343-50.

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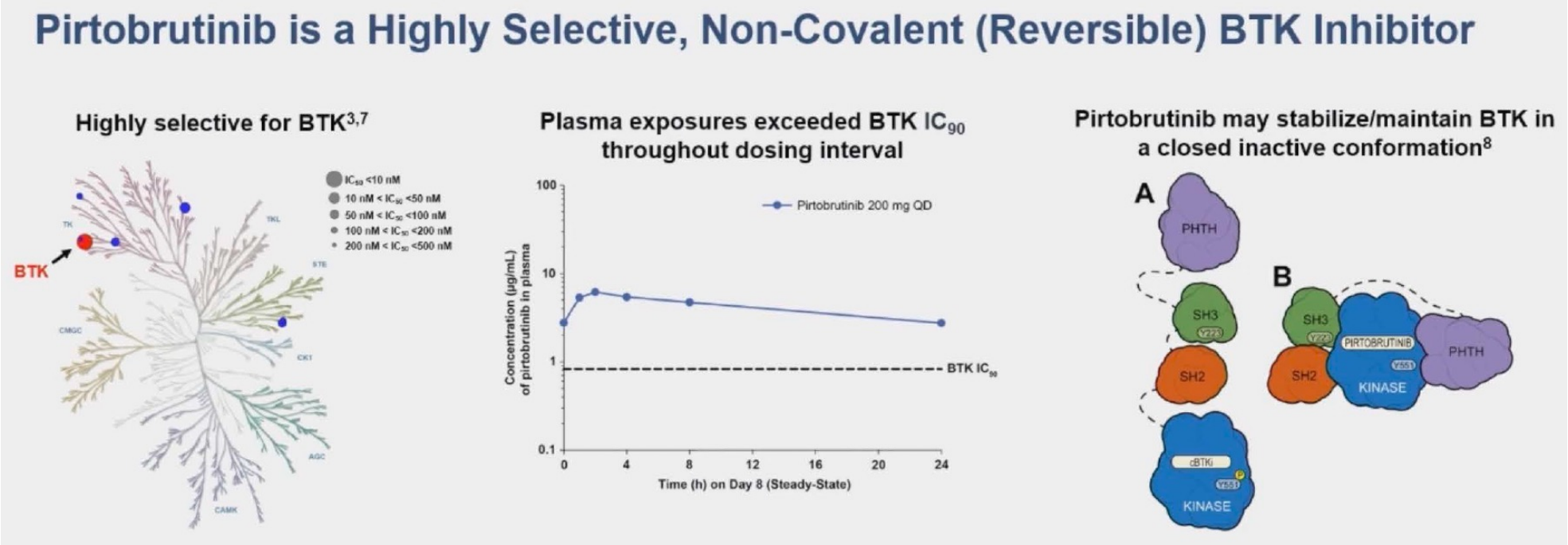
BRUIN Phase I/II trial of pirtobrutinib monotherapy (MCL cohort=166, with 14 naïve to prior BTKi)



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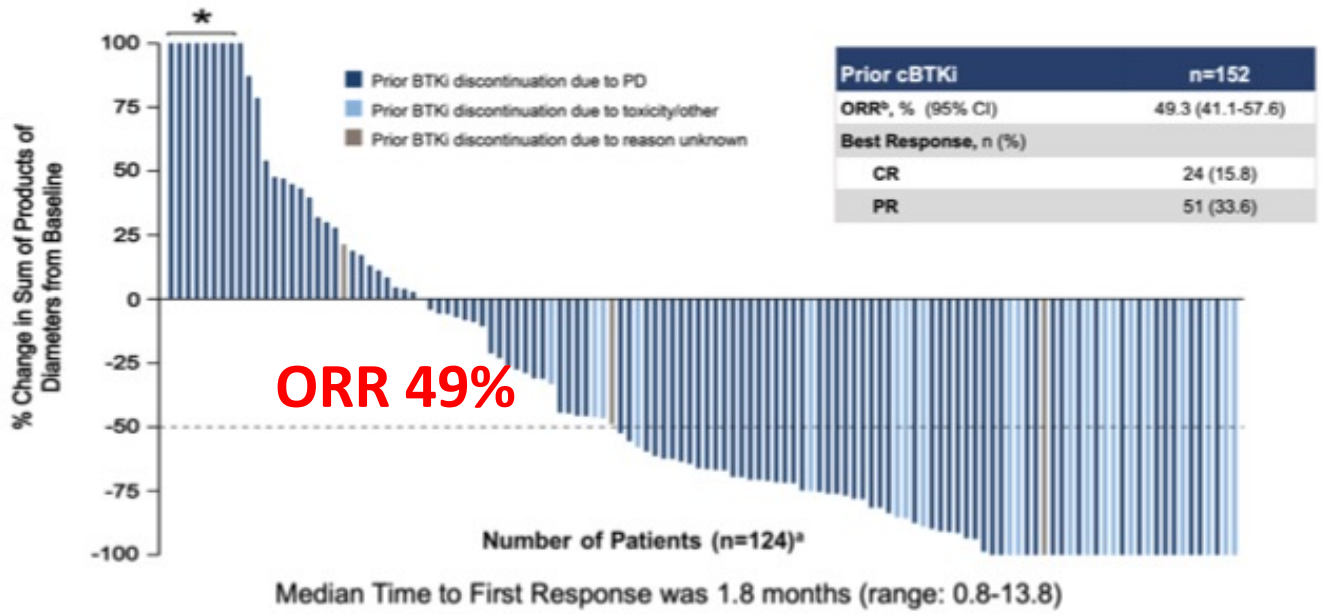
Courtesy of Sonali M Smith, MD

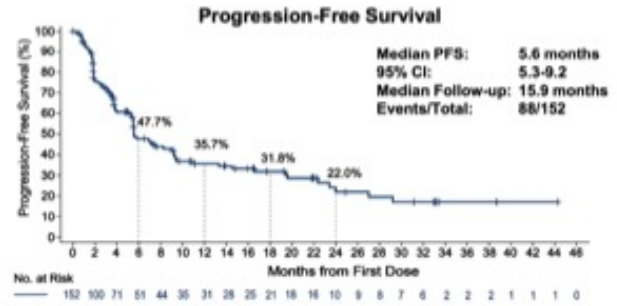
Cohen ASH 2023;Abstract 981.

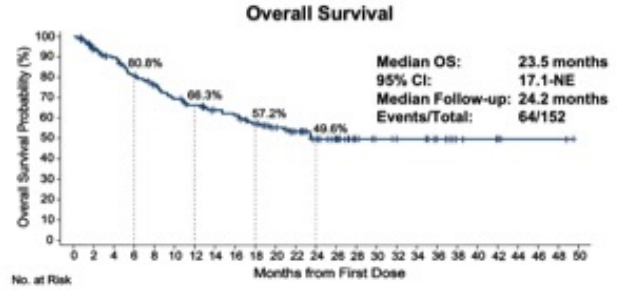
Pirtobrutinib in rel/ref MCL



Prior cBTKi	n=152
ORR[b], % (95% CI)	49.3 (41.1-57.6)
Best Response, n (%)	
CR	24 (15.8)
PR	51 (33.6)

Med DoR 21m





Courtesy of Sonali M Smith, MD

Cohen ASH 2023;Abstract 981.

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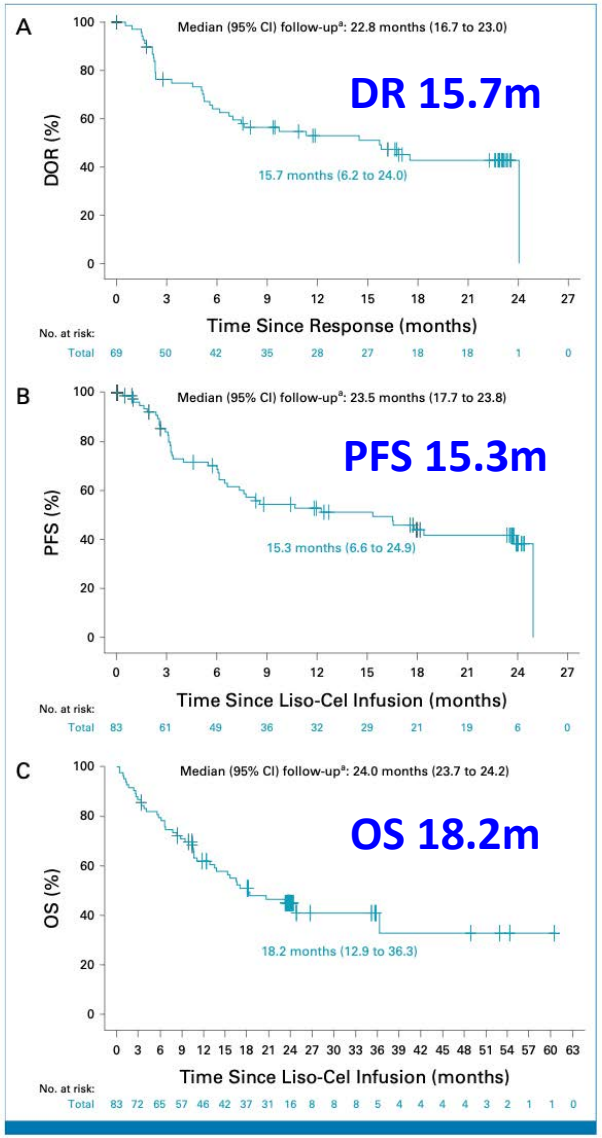
CAR-T for MCL: Liso-cel (104 pts→88 received product)

Patient Characteristics:

- Med age 68.5y
- 20% over age 75y
- 75% with Ki67 over 30%
- 31% blastoid morphology
- 23% with TP53 mutation
- Med prior Rx 3 (range, 1-11)
- 69% refractory disease

ORR and CR: 86.5% and 74.3%



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Courtesy of Sonali M Smith, MD

Wang J Clin Oncol 2023

Liso-cel in rel/ref MCL: Results

	Liso-Cel–Treated Set (N = 88)	
TEAE	Any Grade	Grade ≥3
Any TEAE,[a] No. (%)	88 (100)	76 (86)
Most common TEAEs (≥15%), No. (%)		
CRS	54 (61)	1 (1)
Neutropenia	52 (59)	49 (56)
Anemia	39 (44)	33 (37.5)
Fatigue	31 (35)	2 (2)
Thrombocytopenia	26 (30)	22 (25)
Hypokalemia	21 (24)	7 (8)
Headache	20 (23)	0
Decreased appetite	18 (20)	4 (5)
Nausea	16 (18)	2 (2)
Diarrhea	15 (17)	0
Hypophosphatemia	15 (17)	8 (9)
Peripheral edema	15 (17)	1 (1)
Pyrexia	15 (17)	0
Confusional state	14 (16)	2 (2)

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Wang J Clin Oncol 2023

Brexu-cel in rel/ref MCL: 4y f/u ZUMA-2 and primary analysis of ZUMA-18 expanded access study

Baseline Characteristic	N=23
Median age (range), years	69.0 (43-79)
Intermediate or high risk Simplified MIPI, n (%)	13 (57)
Blastoid or pleomorphic morphologic characteristics of MCL, n (%)	6 (26)
Extranodal disease, n (%)	9 (39)
Elevated LDH levels (ULN to >1.5 ULN), n (%)	
ULN ≤ LDH <1.5 ULN	4 (17)
1.5 ULN ≥ LDH meant	2 (9)
Median tumor burden (SPD) by central read, mm^2 (range)	874.8 (6-9469)
Received bridging therapy, n (%)	5 (22)
ECOG PS of 1, n (%)	13 (57)
Median no. of prior therapies, n (range)	4 (1-10)
Prior BTKi therapy, n (%)	21 (91)
Ibrutinib	16 (70)
Acalabrutinib	8 (35)
Both	3 (13)
Relapsed or refractory disease, n (%)	
Relapse after autologous SCT	6 (26)
Refractory to last MCL therapy	1 (4)
Relapsed after last MCL	16 (70)

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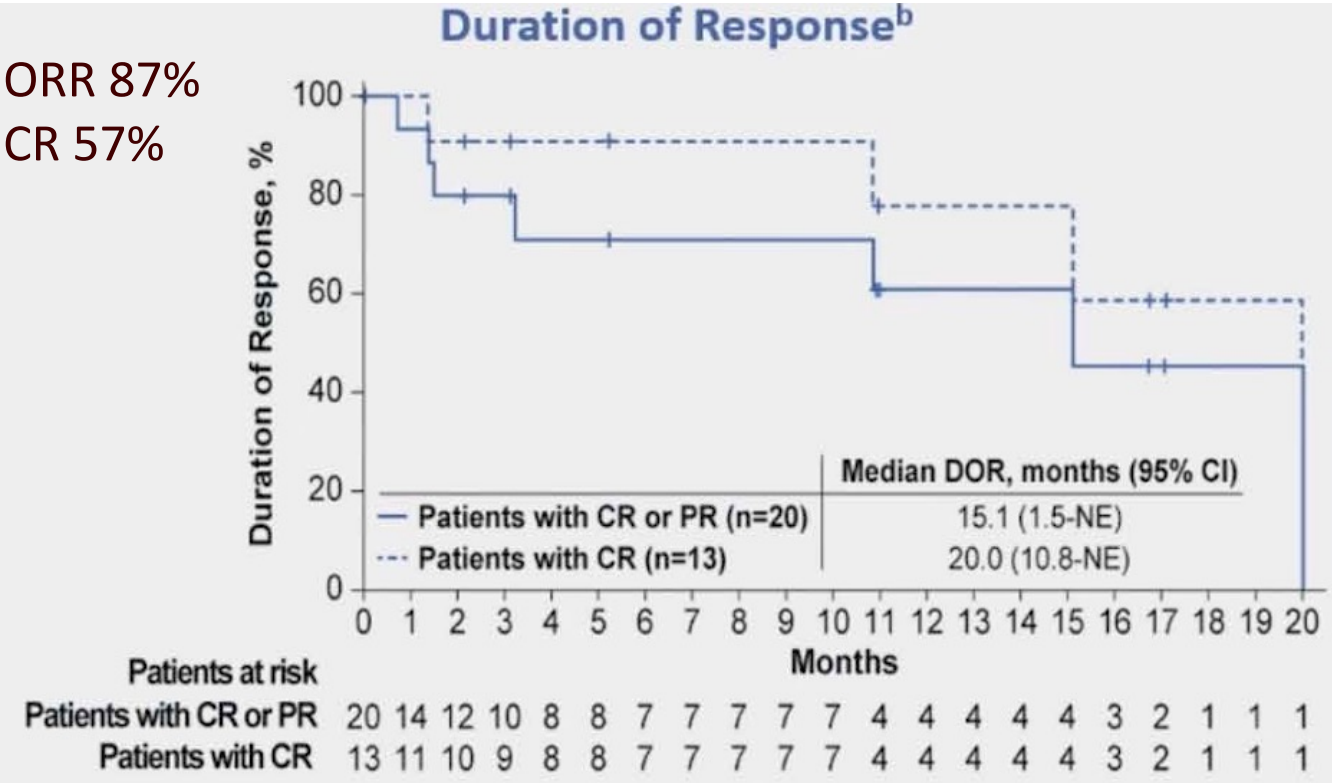
Courtesy of Sonali M Smith, MD

Goy ASH 2023;Abstract 106.

ZUMA-18 Results

ORR 87%
CR 57%



MedDRA Preferred Term	Overall (N=23)
Any brexu-cel–related AE, n (%)	23 (100)
Worst Grade ≥3	18 (78)
Grade ≥3 CRS	1 (4)
Grade ≥3 NEs	8 (35)
Grade ≥3 hematologic TEAE occurring in ≥3 patients, n (%)	15 (65)
Anemia	10 (43)
Neutropenia	6 (26)
Leukopenia	4 (17)
Febrile neutropenia	3 (13)
Thrombocytopenia	3 (13)

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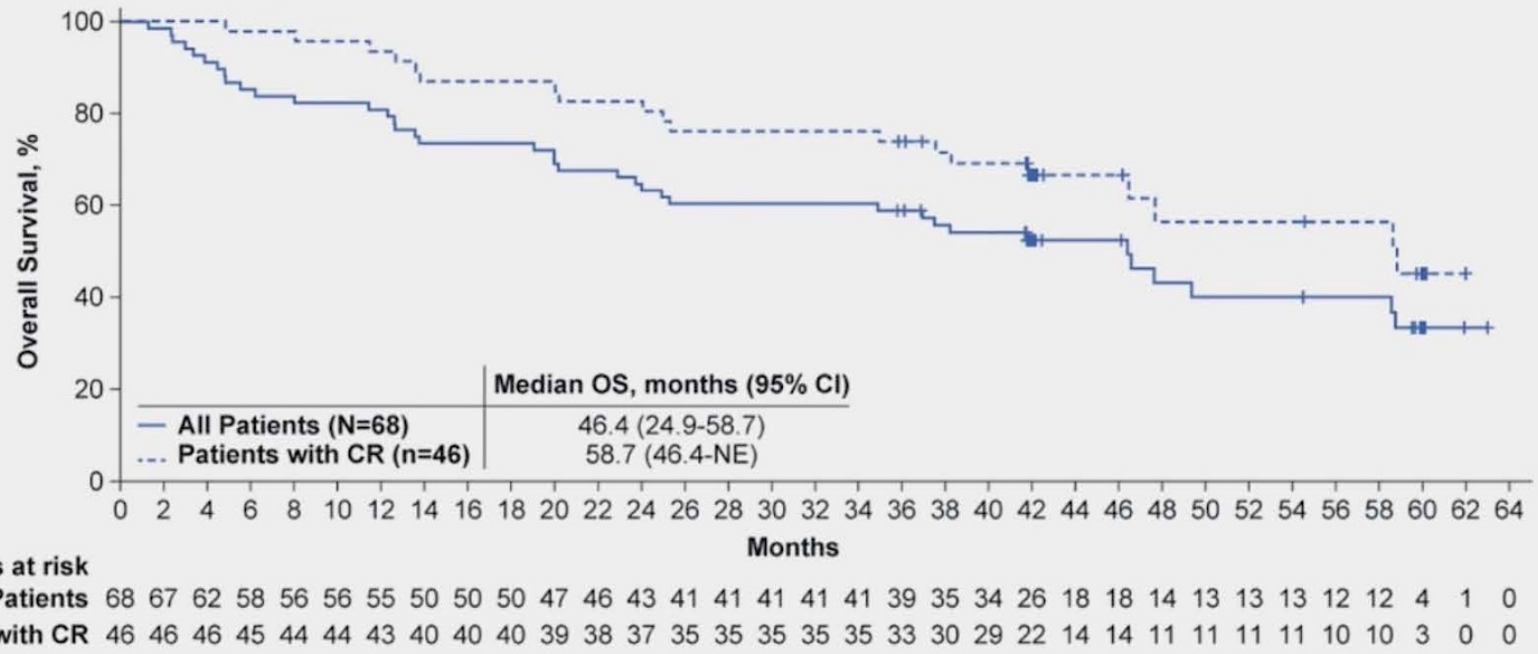
Goy ASH 2023;Abstract 106.

ZUMA-2 4y results

Overall Survival in ZUMA-2 at 4 years (N=68)



- As of July 23, 2022, median follow-up in ZUMA-2 was 47.5 months (N=68; range, 37.9-68.3)
- Median OS in ZUMA-2 was **58.7 months for patients with a CR** (n=46)
- After almost 4 years of median follow-up, **30 patients (45%) were still alive, 27 of which had achieved a CR**

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Courtesy of Sonali M Smith, MD

Goy ASH 2023;Abstract 106.

Agenda

INTRODUCTION: CD3-Based Bispecific Antibodies and the General Medical Oncologist: Lymphomas, Multiple Myeloma … and Solid Tumors?

MODULE 1: Follicular and Mantle Cell Lymphoma

MODULE 2: Diffuse Large B-Cell Lymphoma and Hodgkin Lymphoma

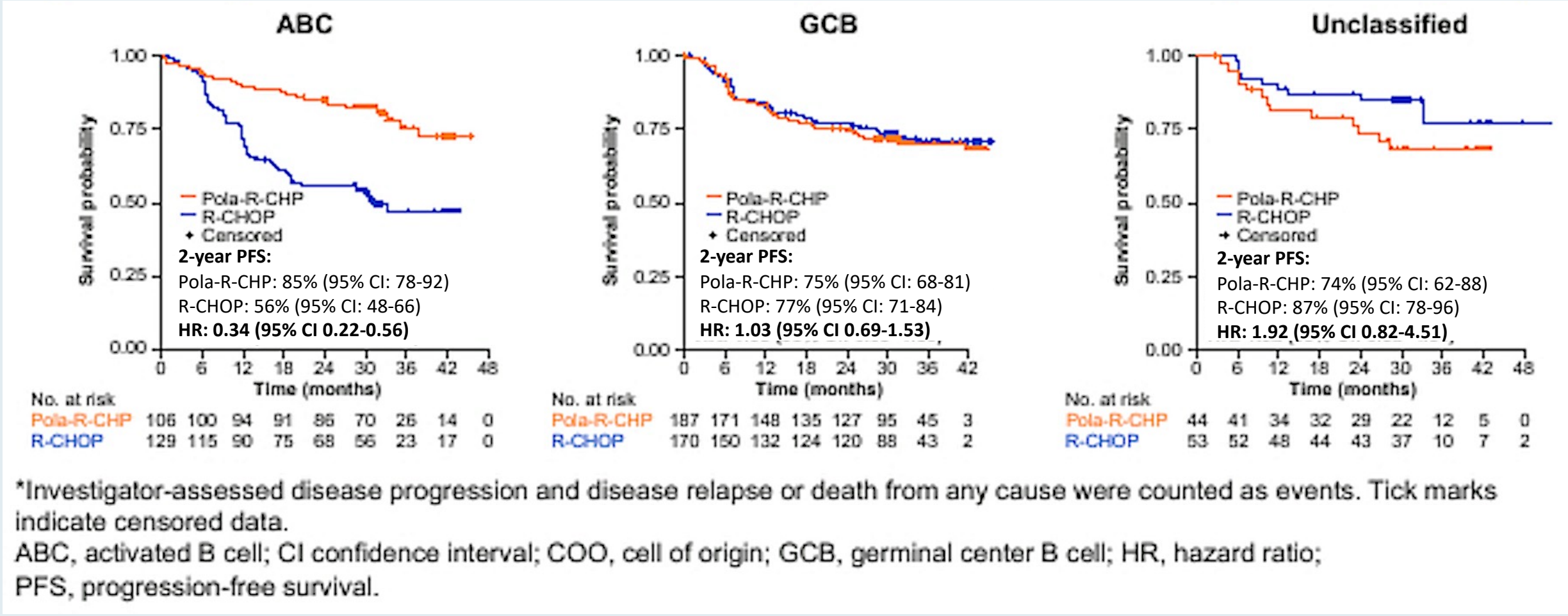
Diffuse Large B-Cell Lymphoma: Polatuzumab Vedotin

- Morschhauser F et al. Deciphering the Clinical Benefit of **Pola-R-CHP** versus R-CHOP in **Different Genetic Subtypes** Beyond Cell of Origin in the **POLARIX** Study. ASH 2023;Abstract 3000.
- Jerkeman M et al. Initial Safety Data from the **Phase 3 POLAR BEAR** Trial in Elderly or Frail Patients with **Diffuse Large Cell Lymphoma**, Comparing **R-pola-mini-CHP** and R-mini-CHOP. EHA 2023;Abstract S227.

Frequently Asked Clinical Questions About DLBCL

- Do community-based physicians have access to reliable cell-of-origin assays?
- Should cell of origin be used to determine eligibility for polatuzumab/R-CHP (pola-R-CHP)?
- For older patients, can an “R-mini-CHOP-like” approach be used with the POLARIX regimen?

POLARIX: PFS by Cell of Origin



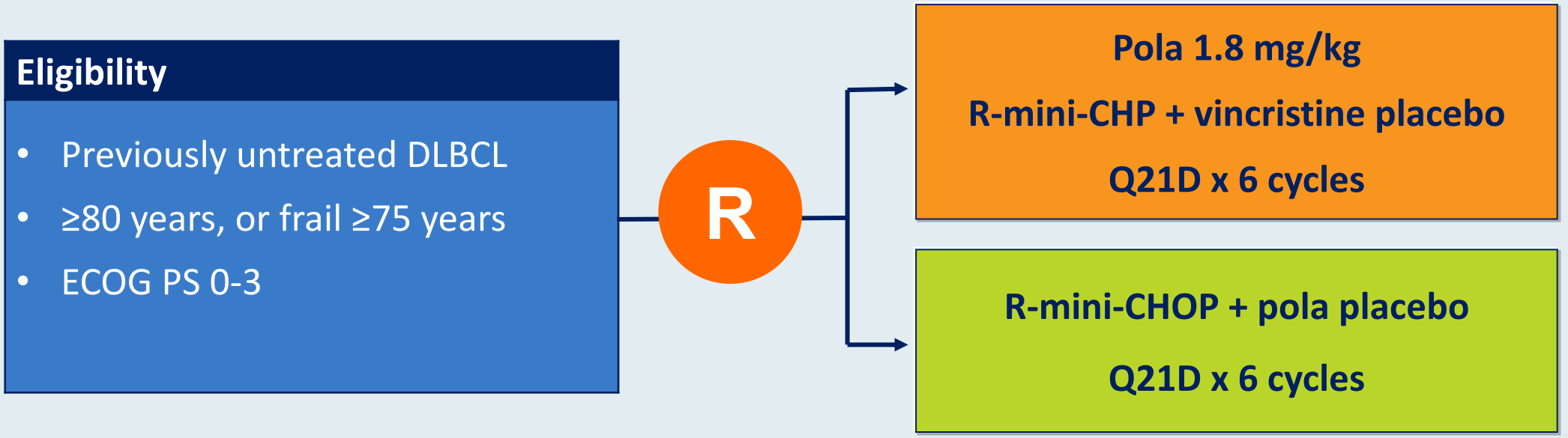
*Investigator-assessed disease progression and disease relapse or death from any cause were counted as events. Tick marks indicate censored data.

ABC, activated B cell; CI confidence interval; COO, cell of origin; GCB, germinal center B cell; HR, hazard ratio; PFS, progression-free survival.

Morschhauser F et al. ASH 2023;Abstract 3000.

POLAR BEAR: Phase III Trial of Polatuzumab Vedotin with R-mini-CHP versus R-mini-CHOP as Initial Therapy for Older Patients with DLBCL

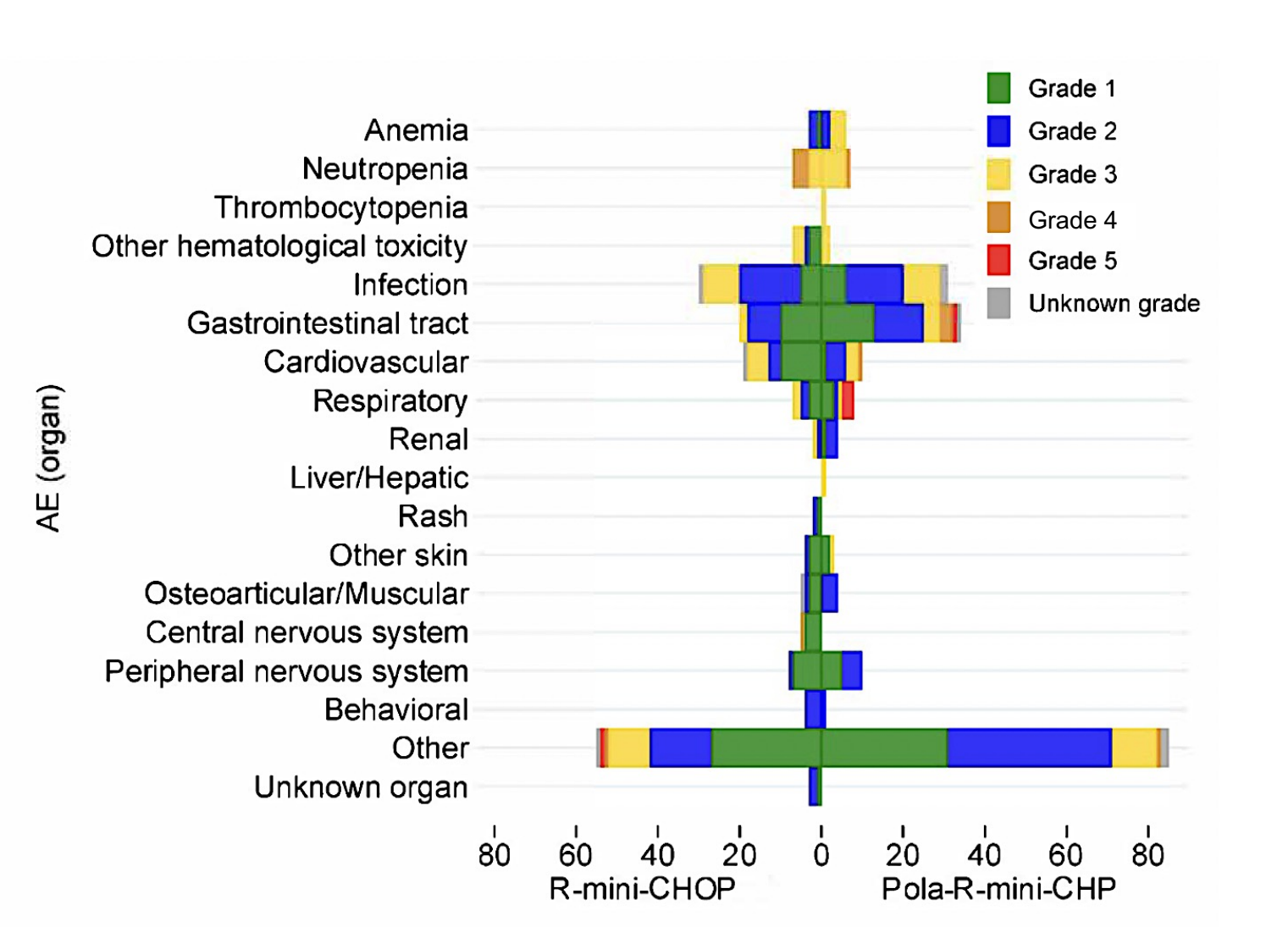
Trial identifier: NCT04332822 (Open)
Estimated enrollment: 200



Primary endpoint: Progression-free survival

www.clinicaltrials.gov. Accessed February 2024.

POLAR BEAR: Initial Safety Data with R-pola-mini-CHP versus R-mini-CHOP for Older or Frail Patients with DLBCL



Jerkeman M et al. EHA 2023;Abstract S227.

Diffuse Large B-Cell Lymphoma: Tafasitamab; Loncastuximab Tesirine

- Duell J et al. **Tafasitamab** for Patients with **Relapsed or Refractory Diffuse Large B-Cell Lymphoma**: **Final 5-Year** Efficacy and Safety in the Phase II **L-MIND Study**. *Haematologica* 2024 February 1;109(2):553-66.
- Belada D et al. Safety and Efficacy of **Tafasitamab** with or without **Lenalidomide** Added to First-Line R-CHOP for **DLBCL**: The Phase 1b **First-MIND** Study. *Blood* 2023;142(16):1348-58.
- Caimi PF et al. **Loncastuximab Tesirine in Relapsed/Refractory Diffuse Large B-Cell Lymphoma**: Long-Term Efficacy and Safety from the Phase 2 **LOTIS-2** Study. *Haematologica* 2023;[Online ahead of print].

Frequently Asked Clinical Questions About DLBCL

- What is the global efficacy, including duration of response, of tafasitamab/lenalidomide?
- How are you employing this regimen in the management of recurrent DLBCL?
- Do you believe tafasitamab will one day become a standard part of first-line treatment for DLBCL?

Frequently Asked Clinical Questions About DLBCL

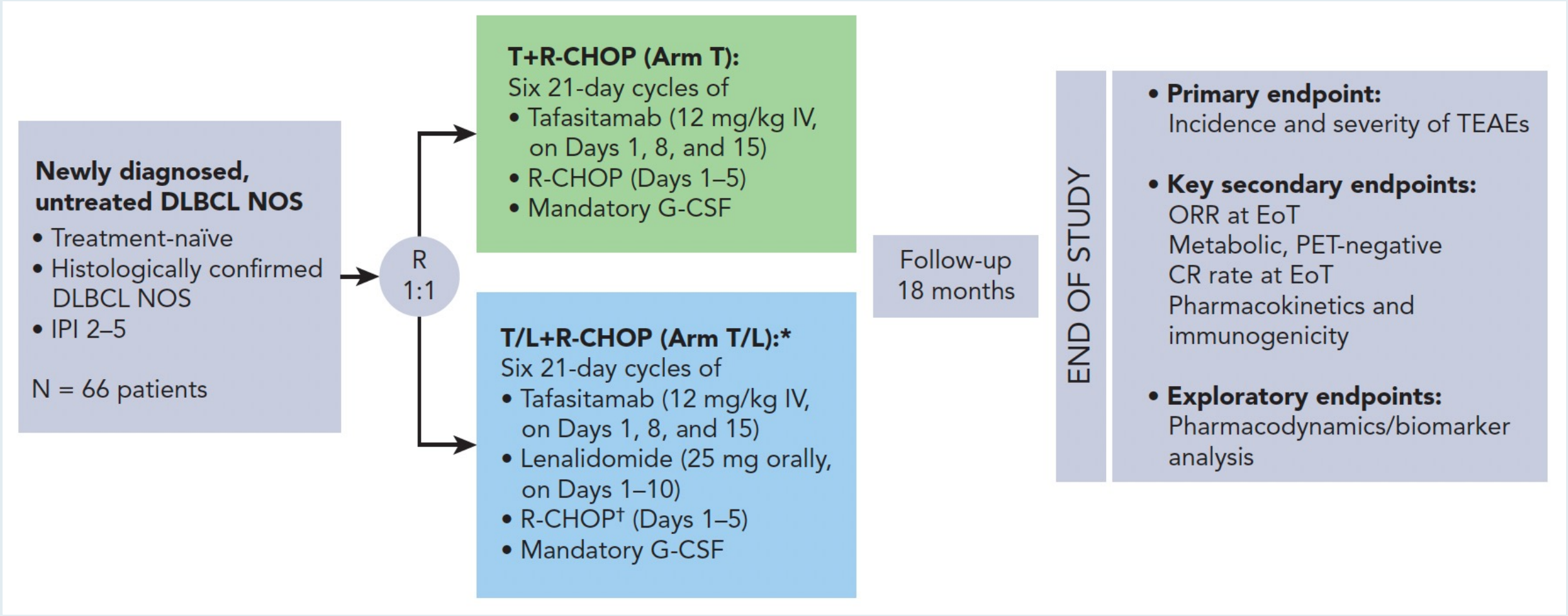
- What is the global efficacy, including duration of response, of loncastuximab tesirine?
- How are you employing this regimen in the management of recurrent DLBCL?
- What has been your experience with the tolerability of this agent, particularly as it relates to the risk of effusions?

L-MIND: Tafasitamab + Lenalidomide — Response Data

Characteristics	Primary analysis	3-year follow-up	Final 5-year data	5-year data for patients with 1 prior line of therapy, N=40	5-year data for patients with ≥2 prior lines of therapy, N=40
Data cut-off date	Nov 30, 2018	Oct 30, 2020	Nov 14, 2022	Nov 14, 2022	Nov 14, 2022
Best ORR, N (%) [95% CI]	48 (60.0) [48.4-70.9]	46 (57.5) [45.9-68.5]	46 (57.5) [45.9-68.5]	27 (67.5) [50.9-81.4]	19 (47.5) [31.5-63.9]
CR rate, N (%) [95% CI]	34 (42.5) [32.0-54.0]	32 (40.0) [29.2-51.6]	33 (41.3) [30.4-52.8]	21 (52.5) [36.1-68.5]	12 (30.0) [16.6-46.5]
PR rate, N (%) [95% CI]	14 (17.5) [10.0-28.0]	14 (17.5) [9.9-27.6]	13 (16.3) [8.9-26.2]	6 (15.0) [5.7-29.8]	7 (17.5) [7.3-32.8]
Median DoR in months [95% CI]	21.7 [21.7-NR]	43.9 [26.1-NR]	NR [33.8-NR]	NR [9.1-NR]	NR [26.1-NR]
Median PFS in months [95% CI]	12.1 [5.7-NR]	11.6 [6.3-45.7]	11.6 [5.7-45.7]	23.5 [7.4-NR]	7.6 [2.7-45.5]
Median OS in months [95% CI]	NR [18.3-NR]	33.5 [18.3-NR]	33.5 [18.3-NR]	NR [24.6-NR]	15.5 [8.6-45.5]

Duell J et al. *Haematologica* 2023 August 31;[Online ahead of print].

First-MIND: R-CHOP + Tafasitamab ± Lenalidomide



Belada D et al. *Blood* 2023;142(16):1348-58.

First-MIND: R-CHOP + Tafasitamab ± Lenalidomide (continued)

Table 2. Efficacy outcomes after ≥18 months' follow-up

Event	Arm T (n = 33)	Arm T/L (n = 33)	Arm T/L IPI 3–5 (n = 22)
ORR, n (%) (95% CI)			
CR or PR (at EoT)	25 (75.8) (57.7-88.9)	27 (81.8) (64.5-93.0)	18 (81.8) (59.7-94.8)
CR or PR (best response across all visits)	30 (90.9) (75.7-98.1)	31 (93.9) (79.8-99.3)	20 (90.9) (70.8-98.9)
18-mo DoR rate, % (95% CI)	72.7 (52.7-85.3)	78.7 (58.5-89.9)	76.6 (48.8-90.5)
18-mo DoCR rate, % (95% CI)	74.5 (53.8-87.0)	86.5 (63.8-95.5)	80.0 (50.0-93.1)
24-mo PFS rate, % (95% CI)	72.7 (52.7-85.3)	76.8 (57.1-88.3)	73.6 (47.3-88.2)
24-mo OS rate, % (95% CI)	90.3 (72.9-96.8)	93.8 (77.3-98.4)	95.2 (70.7-99.3)

Belada D et al. *Blood* 2023;142(16):1348-58.

LOTIS-2: Loncastuximab Tesirine (N = 145)

- R/R DLBCL (≥2 prior therapies)
- ECOG PS 0-2

↓

Loncastuximab tesirine Q3W
- 150 µg/kg for the first two cycles
- 75 µg/kg for subsequent cycles

↓

Continue until 1 year, disease relapse/progression, or unacceptable toxicity

	All-treated population (N=145)	Best response of CR (n=36)
Median DOR, months (95% CI)	13.4 (6.9, —)	NR
Probability of maintaining response at 12 months	54.7% (37.9-68.8)	82.8% (59.9-93.3)
Probability of maintaining response at 24 months	44.6% (27.9-60.0)	72.4% (48.1-86.8)
Median PFS, months (95% CI)	4.9 (2.9-8.3)	NR
Probability of maintaining PFS at 12 months	33.5% (23.3-44.0)	82.9% (60.0-93.3)
Probability of maintaining PFS at 24 months	25.9% (16.2-36.7)	72.5% (48.2-86.8)
Median OS, months (95% CI)	9.5 (6.7-11.5)	NR
Probability of maintaining OS at 12 months	39.0% (30.7-47.1)	77.1% (59.4-87.9)
Probability of maintaining OS at 24 months	29.5% (22.0-37.4)	68.2% (50.0-81.0)
Median RFS, months (95% CI)	—	NR
Probability of maintaining RFS at 12 months	—	83.2% (60.5-93.5)
Probability of maintaining RFS at 24 months	—	72.8% (48.5-87.0)

Caimi PF et al. *Haematologica* 2023 August 31;[Online ahead of print].

Diffuse Large B-Cell Lymphoma: CAR T-Cell Therapies

- Neelapu S et al. **Five-Year** Follow-Up of **ZUMA-1** Supports the Curative Potential of **Axicabtagene Ciloleucel** in Refractory Large B-Cell Lymphoma. *Blood* 2023;141(19):2307-15.
- Westin JR et al. Survival with **Axicabtagene Ciloleucel** in Large B-Cell Lymphoma*. N Engl J Med* 2023;389(2):148-57.
- Chavez J et al. **3-Year** Analysis of **ZUMA-12**: A Phase 2 Study of Axicabtagene Ciloleucel **(Axi-cel)** As **First-Line** Therapy in Patients with **High-Risk** Large B-Cell Lymphoma **(LBCL)**. ASH 2023;Abstract 894.
- Abramson JS et al. **Lisocabtagene Maraleucel** as **Second-Line** Therapy for Large B-Cell Lymphoma: Primary Analysis of the **Phase 3 TRANSFORM Study**. *Blood* 2023;141(14):1675-84.

Frequently Asked Clinical Questions About DLBCL

- How is the timing of leukapheresis, reinfusion, etc, managed for patients in your center scheduled to receive CAR T-cell therapy?

- Can this be done in an outpatient setting?

Frequently Asked Clinical Questions About DLBCL

- How do you incorporate liso-cel into the management of R/R DLBCL?

- Are there patients who cannot receive axi-cel or ASCT for whom you recommend liso-cel?

Frequently Asked Clinical Questions About DLBCL

- How do you approach bridging therapy for patients (eg, significant tumor bulk 6 months after R-CHOP) scheduled to receive CAR T-cell therapy?

- Do you approach this any differently for a patient who received pola-R-CHP as first-line therapy?

Frequently Asked Clinical Questions About DLBCL

- How do you view the recent FDA-mandated black box warning regarding the risk of secondary cancer with CD19- and BCMA-directed CAR T-cell therapies?

- How do you discuss this with your patients?

ZUMA-1: 5-Year Efficacy Outcomes

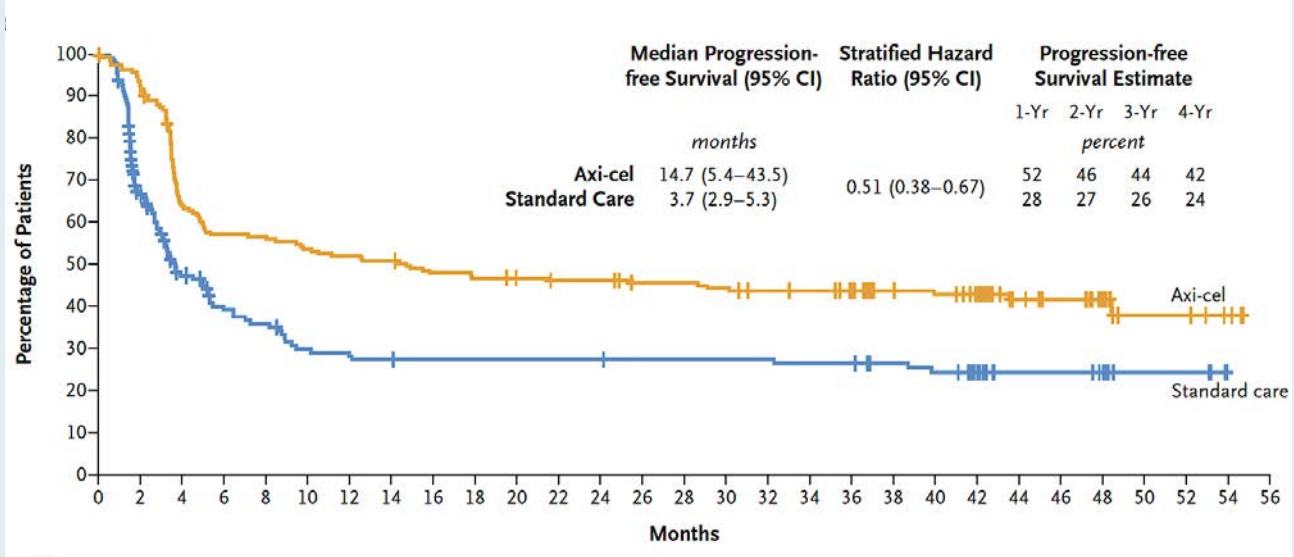
	N = 101
Best response, n (%, 95% CI)	
Objective response	84 (83, 74-90)
CR	59 (58, 48-68)
PR	25 (25, 17-34)
SD	10 (10, 5-17)
PD	5 (5, 2-11)
Not done	2 (2, 0-7)
Ongoing response, n (%)	31 (31)
CR	30 (30)
PR	1 (1)
DOR (95% CI)	
Median DOR, mos	11.1 (4.2-51.3)
Median duration of CR, mos	62.2 (12.9-NE)
Median duration of PR, mos	1.9 (1.3-2.1)

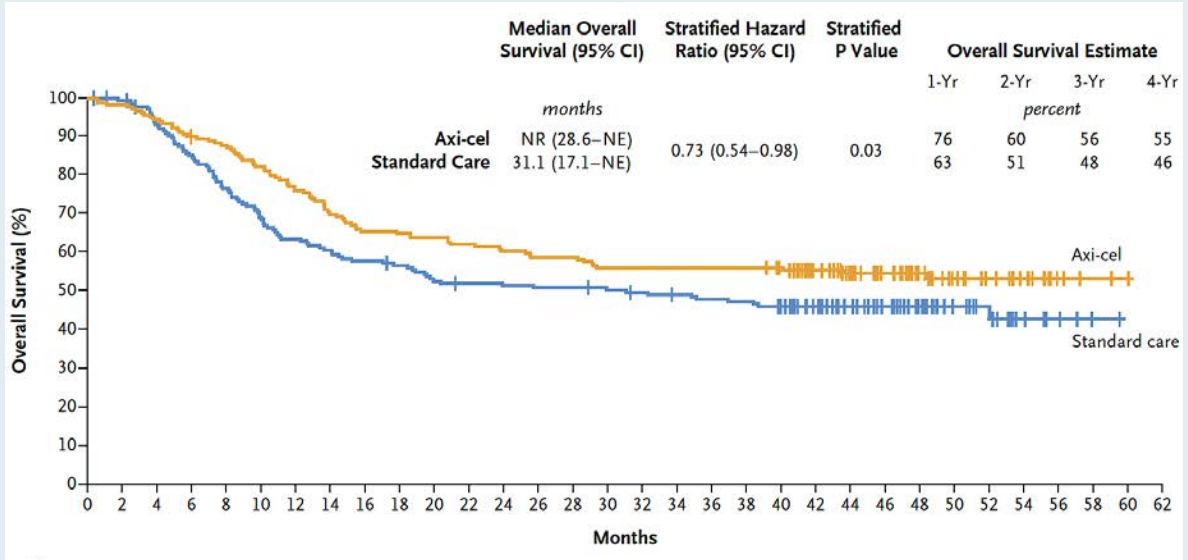
	Median	95% CI
EFS	5.7 months	(3.1 to 13.9)
PFS	5.9 months	(3.3 to 15.0)
OS	25.8 months	(12.8 to NE)

- CRS (cytokine release syndrome) occurred in 94 patients (93%) with Grade ≥3 cases in 11 patients (11%). Neurologic events occurred in 65 patients (64%) with Grade ≥3 events in 30 patients (30%).
- No new safety signals were reported in patients who received axi-cel (n = 101), and no new serious adverse events related to axi-cel were reported after the 2-year analysis. No secondary cancer related to axi-cel has been reported thus far.

Neelapu SS et al. *Blood* 2023;141(19):2307-15.

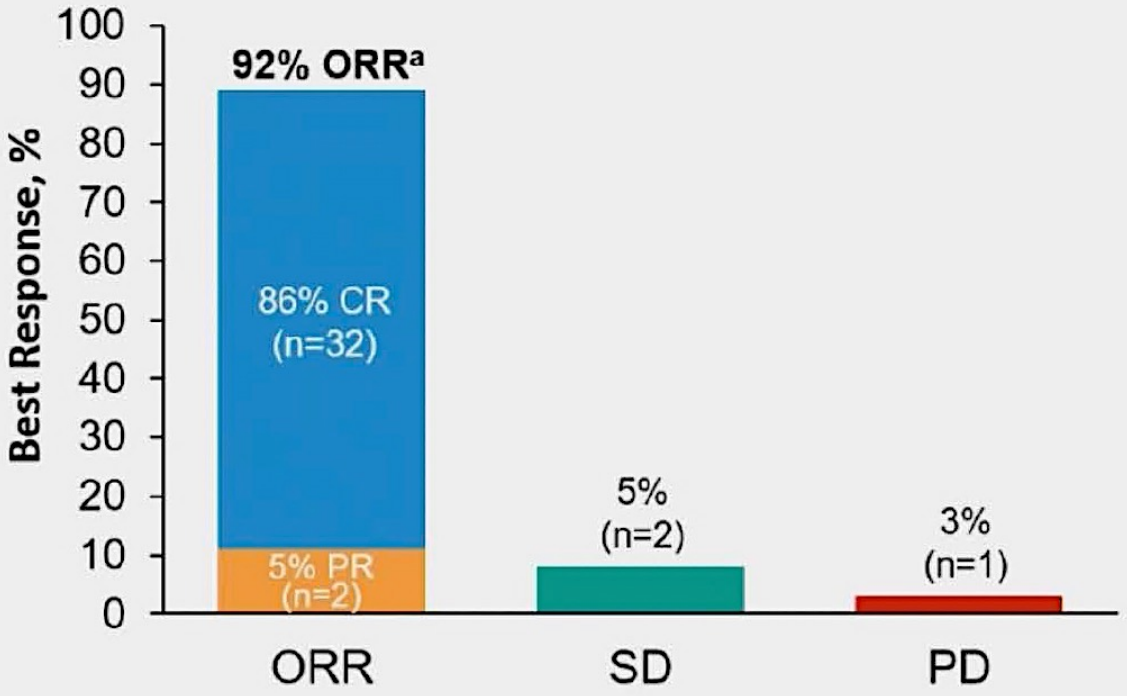
ZUMA-7: Progression-Free and Overall Survival





Westin JR et al. *N Engl J Med* 2023;389(2):148-57.

ZUMA-12: 3-Year Response Data



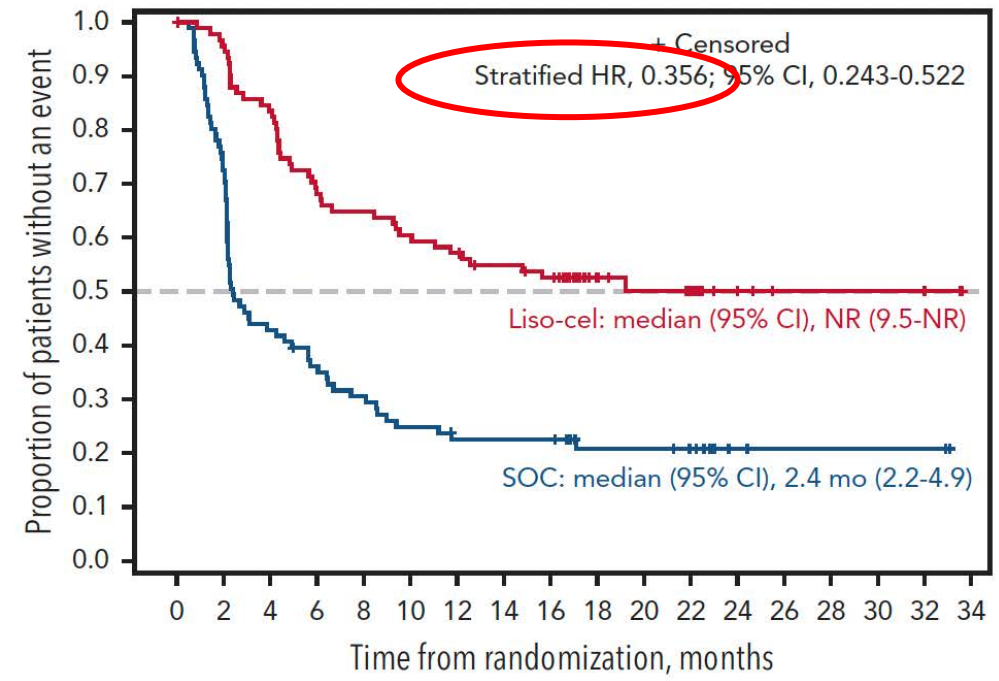
	Efficacy Evaluable n=37[b]
Overall CR rate, % (95% CI)	86 (71-95)
DHL/THL and IPI score ≥3 (n/N)	4/4 100 (40-100)
DHL/THL only (n/N)	5/6 83 (36-100)
IPI score ≥3 only (n/N)	23/27 85 (66-96)
Patients converted from PR/SD to CR, n (%)	9 (24)
PR to CR	8 (22)
SD to CR	1 (3)

Secondary endpoints (median EFS/PFS/OS) have not been reached.

Chavez JC et al. ASH 2023;Abstract 894.

TRANSFORM: Efficacy Outcomes

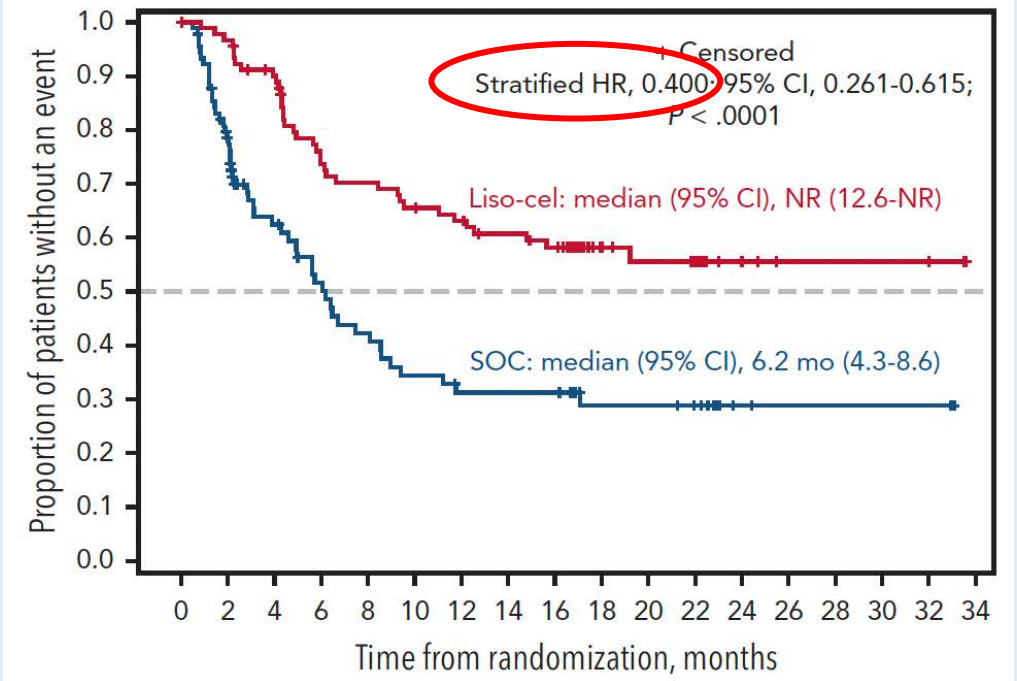
EFS



No. at risk

SOC	92	66	39	32	27	22	19	19	19	12	12	10	3	2	2	2	2	0
Liso-cel	92	87	76	62	59	55	52	48	45	24	20	17	5	3	3	3	3	0

PFS



No. at risk

SOC	92	66	42	33	27	22	19	19	19	12	12	10	3	2	2	2	2	0
Liso-cel	92	88	79	63	60	56	53	49	46	25	21	18	6	3	3	3	3	0

- The most common TEAEs of any grade were neutropenia, anemia, thrombocytopenia and nausea. The most common Grade ≥3 AEs in both arms were neutropenia, thrombocytopenia and anemia.
- The rates of any-grade CRS and NEs were 49% and 11%, respectively, with Grade 3 CRS and NEs in only 1% and 4%, respectively; there were no Grade 4 or 5 events.

No significant improvement in OS (HR, 0.724; 95% CI, 0.443-1.183; *P* = 0.0987)

EFS = event-free survival; PFS = progression-free survival; TEAEs = treatment-emergent adverse events; AEs = adverse events; CRS = cytokine release syndrome; NEs = neurologic events

Nastoupil LJ et al. ASCO 2023;Abstract 7526.

Diffuse Large B-Cell Lymphoma: Bispecific Antibodies

- Hutchings M et al. **Glofitamab Monotherapy** in Relapsed or Refractory Large B-Cell Lymphoma: **Extended Follow-Up** from a Pivotal Phase II Study and **Subgroup Analyses** in Patients with Prior Chimeric Antigen Receptor T-Cell Therapy and by Baseline Total Metabolic Tumor Volume. ASH 2023;Abstract 433.
- Karimi Y et al. Effect of Follow-Up Time on the Ability of **Subcutaneous Epcoritamab** to Induce Deep and Durable Complete Remissions in Patients with Relapsed/Refractory Large B-Cell Lymphoma: **Updated Results** from the Pivotal **EPCORE NHL-1** Trial. ASCO 2023;Abstract 7525.
- Ayyappan S et al. **Final Analysis** of the Phase 2 **ELM-2** Study: **Odronextamab** in Patients with Relapsed/Refractory **(R/R)** Diffuse Large B-Cell Lymphoma **(DLBCL)**. ASH 2023;Abstract 436.
- Crombie J et al. **Odronextamab** Demonstrates Durable Complete Responses in Patients with Diffuse Large B-Cell Lymphoma (**DLBCL**) Progressing after CAR-T Therapy: Outcomes from the **ELM-1 Study**. ASH 2023;Abstract 4461.

Frequently Asked Clinical Questions About DLBCL

- **Globally how are you sequencing CD20 x CD3 bispecific antibodies and CAR T-cell therapy for your patients with R/R DLBCL, and which are you generally recommending first?**

- **How does prior exposure to CAR T-cell therapy impact the effectiveness of bispecific antibodies? What about the converse?**

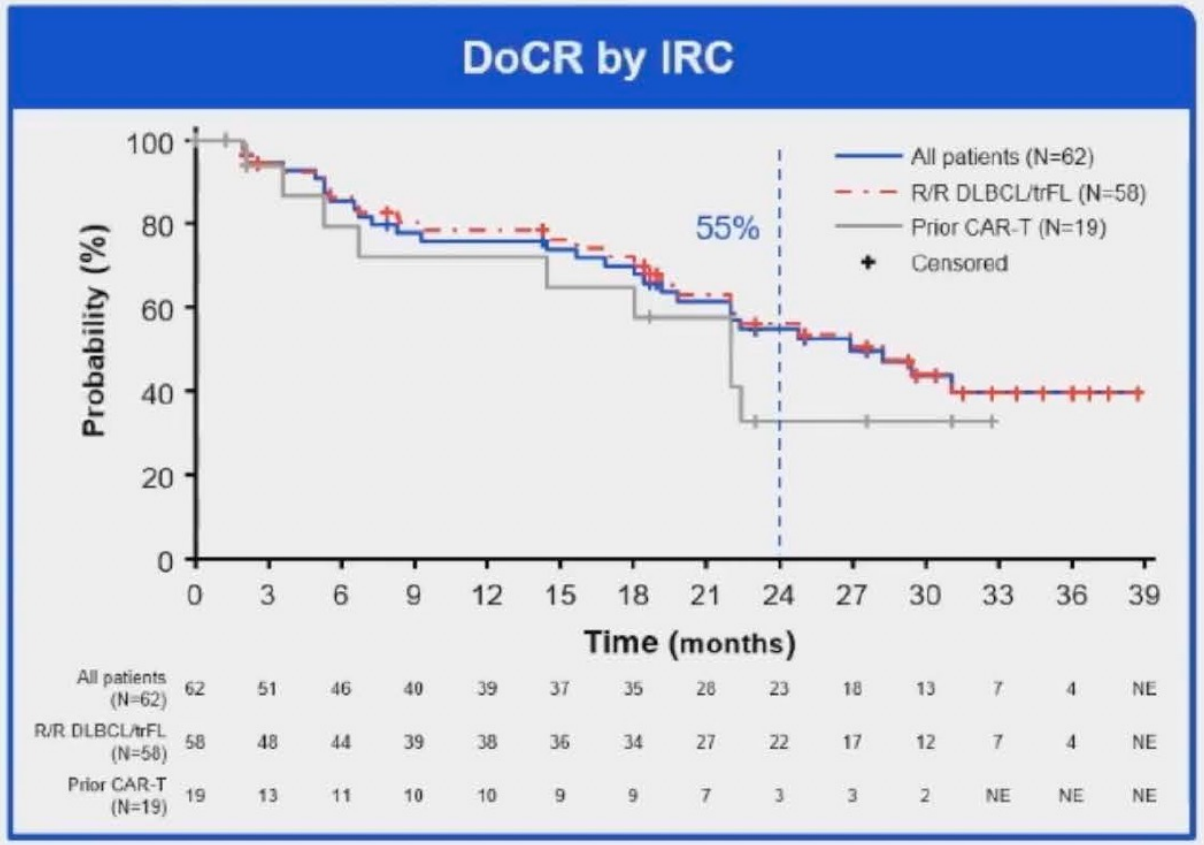
Frequently Asked Clinical Questions About DLBCL

- **Currently, what is the optimal method to integrate the use of bispecifics in the community setting?**

- **From a clinical point of view (eg, efficacy, tolerability, convenience) how, if at all, do you distinguish glofitamab, epcoritamab and odronextamab?**

Phase II Study of Glofitamab Monotherapy

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



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

The most common AE was CRS in 64% of patients, mostly Grade 1-2.

Hutchings M et al. ASH 2023;Abstract 433.

EPCORE NHL-1: Subcutaneous Epcoritamab

Dose escalation → **Dose expansion data cutoff: November 18, 2022; Median follow-up: 20.0 mo**

B-NHL:
- ✓ No DLTs
- ✓ MTD not reached
- ✓ RP2D identified
- ✓ Manageable safety profile
- ✓ Encouraging antitumor activity

Key inclusion criteria:
- R/R CD20+ mature B-cell neoplasm
- ECOG PS 0–2
- ≥2 prior lines of antineoplastic therapy, including ≥1 anti-CD20 mAb
- FDG PET–avid and measurable disease by CT/MRI
- Prior CAR T allowed

Step-up dosing[a]

Epcoritamab SC RP2D 48 mg
Treatment until PD[b,c] or unacceptable toxicity
LBCL cohort, N=157
DLBCL & HGBCL, n=148; PMBCL, n=4; FL G3B, n=5

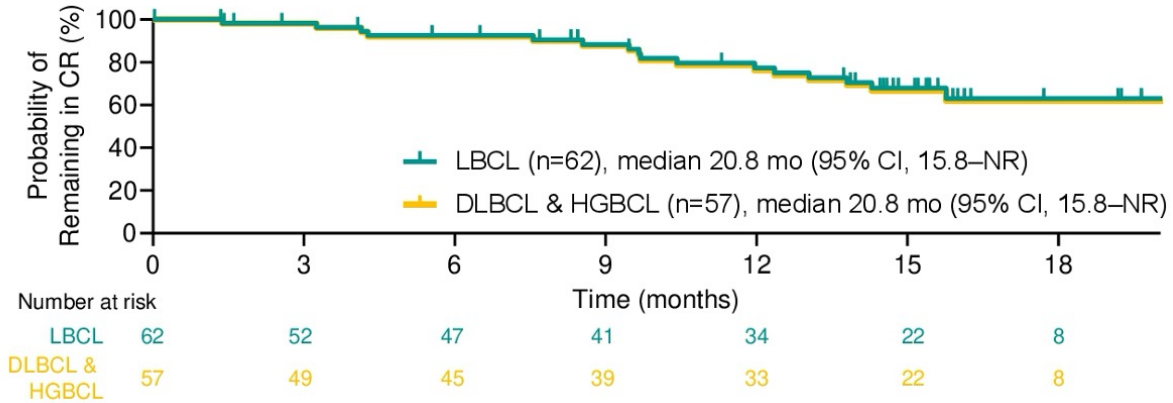
SC injections in minutes

QW				Q2W					Q4W
C1	2	3	4	5	6	7	8	9	10
Wk 0	4	8	12	16	20	24	28	32	36

- **Primary endpoint:** ORR by independent review committee (IRC)
- **Key secondary endpoints:** DOR, TTR, PFS, OS, CR rate, and safety/tolerability

[a]Step-up dosing (SUD; priming [SUD 1] 0.16 mg and intermediate [SUD 2] 0.8 mg dosing before first full dose) and corticosteroid prophylaxis were used to mitigate CRS. [b]Radiographic disease evaluation was performed every 6 wk for the first 24 wk (6, 12, 18, and 24 wk), then every 12 wk (36 and 48 wk), and every 6 mo thereafter. [c]≥2 measurable (by CT/MRI) and FDG PET–positive lesions. ClinicalTrials.gov: NCT03625037. EudraCT: 2017-001748-36.

Durable Complete Responses



Best Overall Response, n (%)	DLBCL & HGBCL, n=148[a]	LBCL, N=157[a]
Overall response	90 (61) [95% CI, 53–69]	99 (63) [95% CI, 55–71]
Complete response	57 (39) [95% CI, 31–47]	62 (39) [95% CI, 32–48]
Partial response	33 (22)	37 (24)
Stable disease	5 (3)	5 (3)
Progressive disease	37 (25)	37 (24)

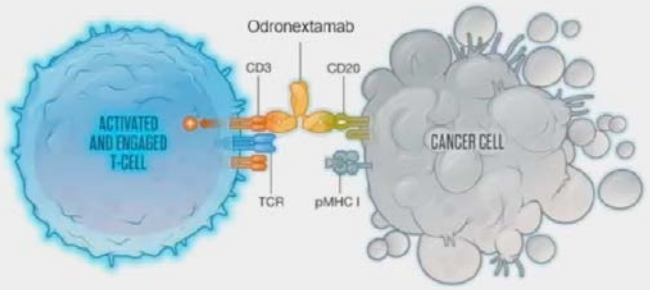
Based on IRC per Lugano criteria. [a]16 patients were not evaluable.

- The most common AE was CRS in 51% of patients (mostly Grade 1-2), followed by neutropenia in 25% of patients.

Karimi Y et al. ASCO 2023;Abstract 7525.

ELM-2: Odronextamab for R/R DLBCL

Odronextamab mechanism of action
Fc-silenced, human, CD20×CD3 bispecific antibody



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

Key eligibility criteria
- DLBCL per WHO 2016 classification[1]
- ECOG PS 0 or 1
- Refractory to or relapsed after ≥2 prior lines of therapy, including an anti-CD20 antibody and an alkylator

Primary endpoint: ORR* by ICR

Secondary endpoints:
- ORR* by local investigator
- CR*, DOR*, PFS*, and OS
- Safety and tolerability
- Patient-reported outcomes

Key exploratory endpoint: MRD

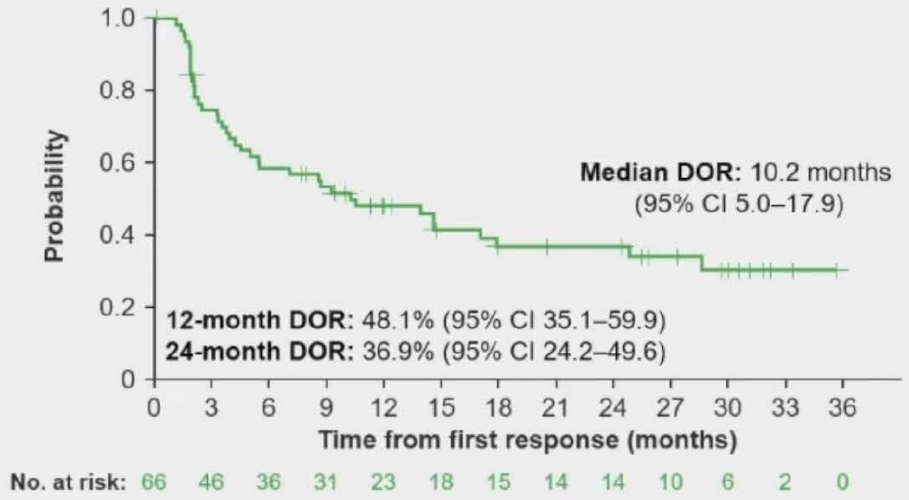
Odronextamab administration (IV, 21-day cycles)

Cycle 1 (step up)	Cycles 2–4	Cycle 5+ (maintenance)
D1/2, 8/9, 15/16	D1, 8, 15	Q2W → Q4W if durable CR (≥9 mos)
0.7/4/20 mg†	160 mg	320 mg

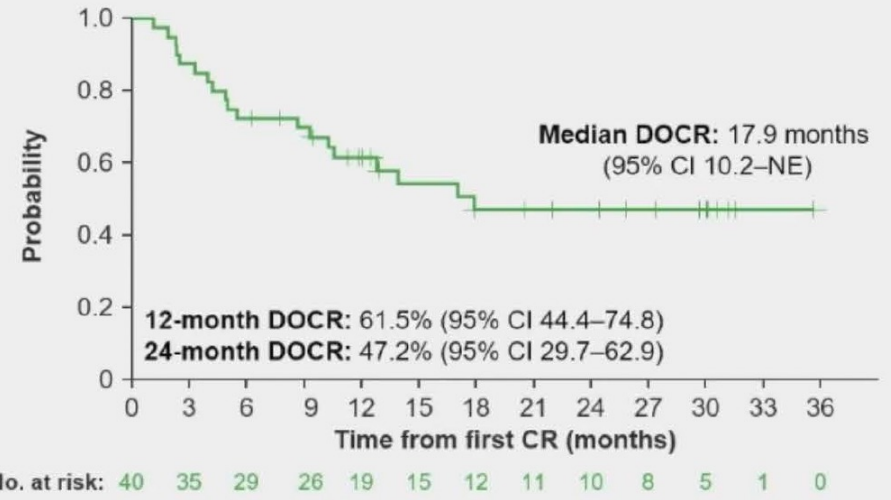
Cycle 4 Day 15
First post-baseline response assessment

ORR = 52.0%; CR = 31.5%

DOR



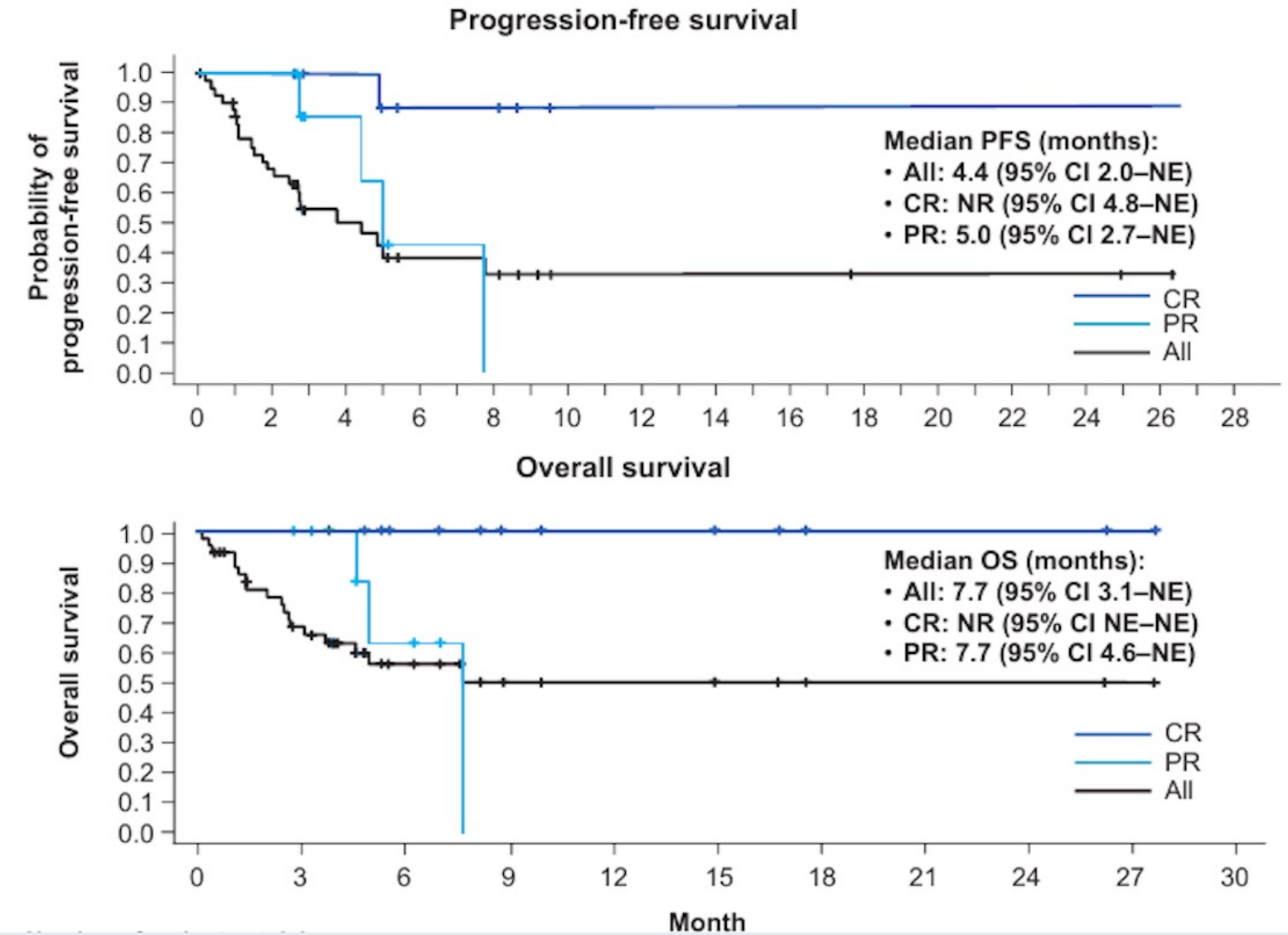
DOCR



- The most common AE was CRS in 55.1% of patients, mostly Grade 1-2.

Ayyappan S et al. ASH 2023;Abstract 436.

ELM-1: Odronextamab After CAR T-Cell Therapy



Response data	
ORR	47.7%
CR	29.5%

- The most common AE was CRS occurring in 52.3% of patients. All events were Grade 1-2 and resolved with a median time to resolution of 2 days.

Crombie J et al. ASH 2023;Abstract 4461.

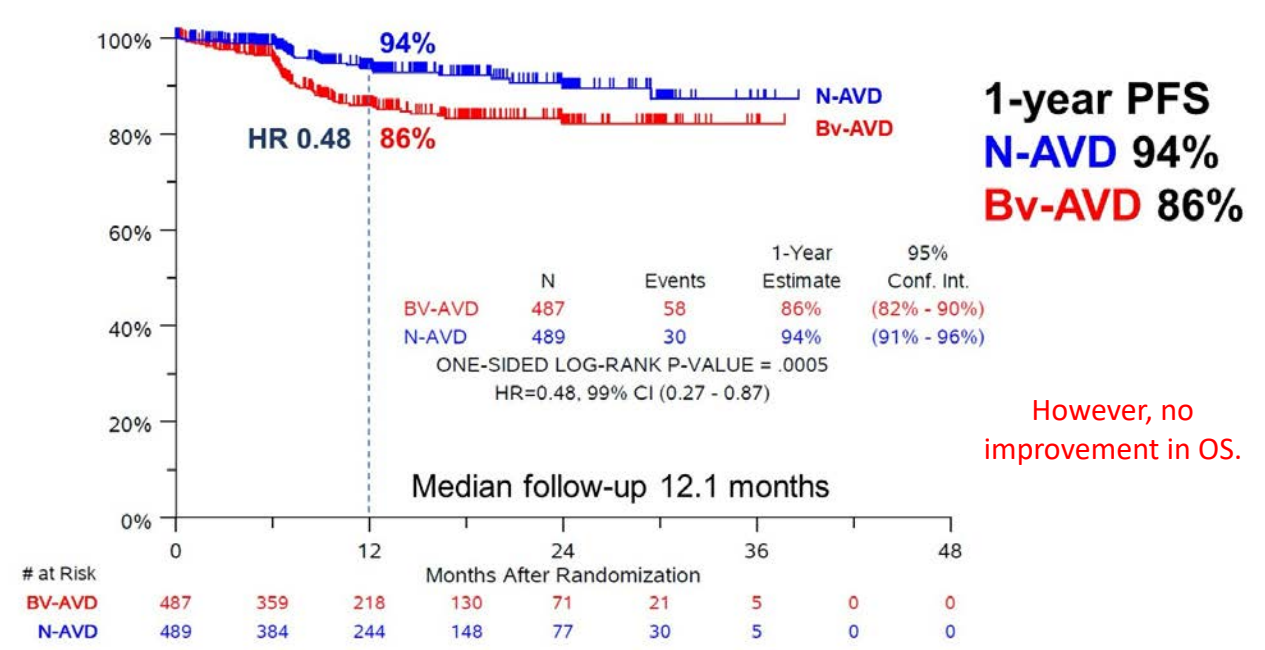
Advanced Stage Hodgkin Lymphoma

- Herrera AF et al. **SWOG S1826**, a Randomized Study of **Nivolumab(N)-AVD** versus **Brentuximab Vedotin(BV)-AVD** in **Advanced Stage** (AS) **Classic Hodgkin lymphoma** (HL). ASCO 2023;Abstract LBA4.
- Rutherford SC et al. **Nivolumab-AVD** Is Better Tolerated and Improves Progression-Free Survival Compared to **BV-AVD** in Older Patients (Aged ≥60 Years) with **Advanced Stage Hodgkin Lymphoma** Enrolled on **SWOG S1826**. ASH 2023;Abstract 181.
- Lee H et al. **Brentuximab Vedotin, Nivolumab, Doxorubicin**, and **Dacarbazine** for **Advanced Stage** Classical **Hodgkin Lymphoma**: Efficacy and Safety Results from the Single Arm Phase 2 Study. ASH 2023;Abstract 608.

Frequently Asked Clinical Questions About Hodgkin Lymphoma (HL)

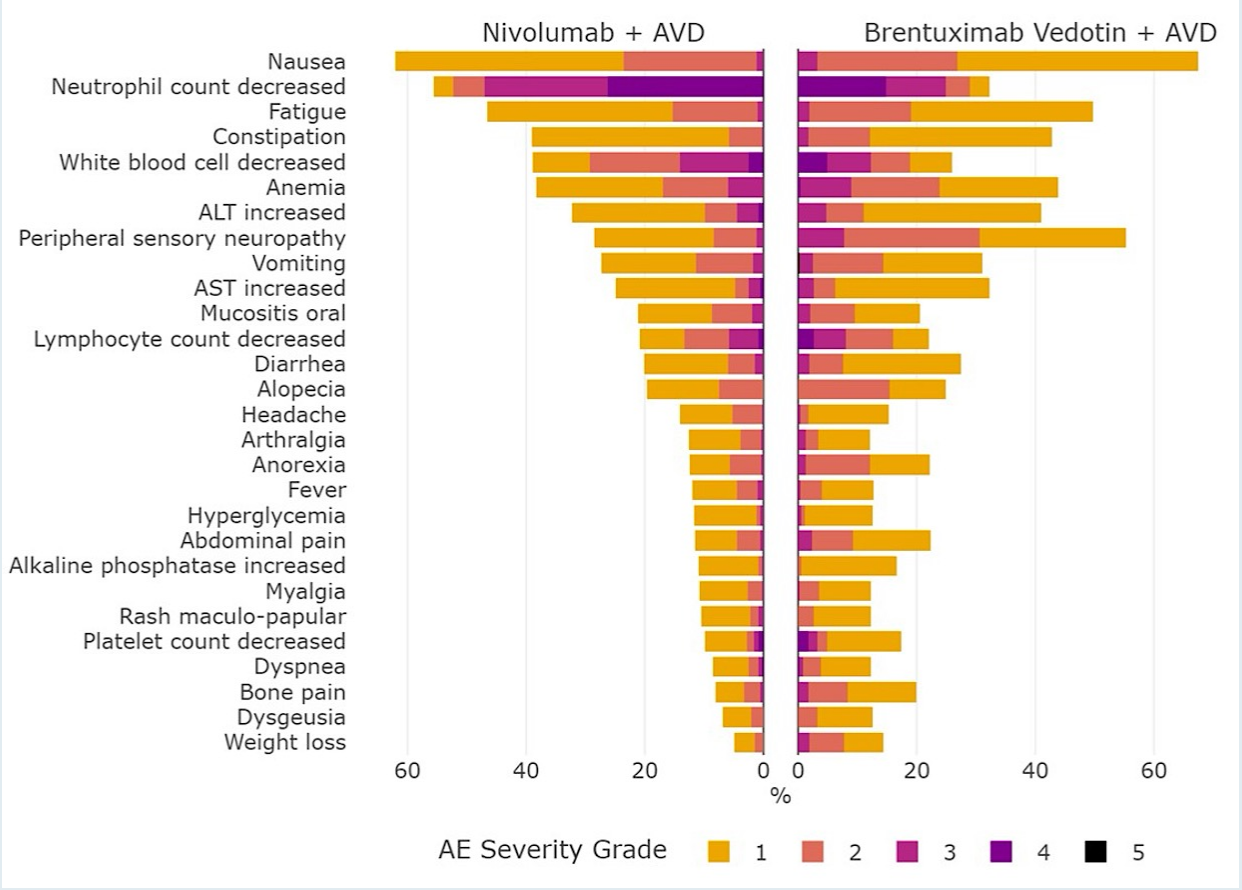
- Regulatory and reimbursement aside, what is your preferred first-line treatment for a patient with advanced-stage HL?
- What medical history (eg, autoimmune disease, solid organ transplant) would exclude a patient from receiving nivolumab/AVD?
- How do you approach the use of this regimen for older patients with comorbidities?

SWOG-S1826: Nivolumab/AVD vs BV-AVD — Efficacy and Safety



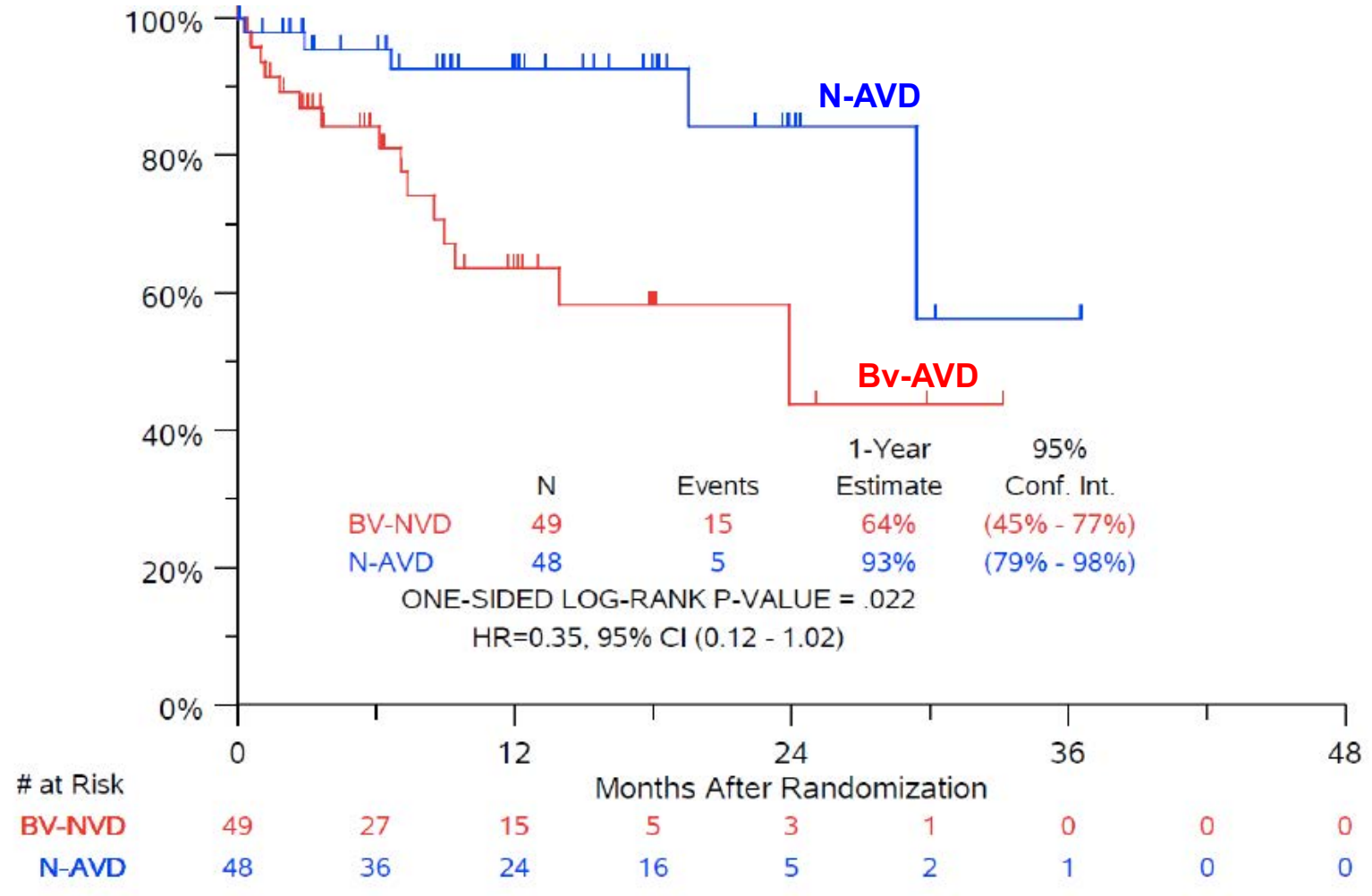
However, no improvement in OS.

1-year OS estimates	
BV-AVD	98%
Nivo-AVD	99%



Herrera AF et al. ASCO 2023;Abstract LBA4.

N-AVD markedly improves PFS over Bv-AVD in older patients with cHL



1-year PFS
N-AVD 93%
Bv-AVD 64%

Median follow-up
12.1 months

p-value = 0.022
HR = 0.35,
95% CI (0.12-1.02)

Rutherford SC et al. ASH 2023;Abstract 181.

Courtesy of Andrew M Evens, DO, MBA, MSc

S1826 in Older Pts with cHL: Conclusions

- N-AVD is better tolerated than Bv-AVD
  - More GI AEs, sepsis/infections, and peripheral neuropathy with Bv-AVD
  - Low immune event rates with N-AVD, similar to whole study population
  - More pts discontinued Bv than Nivolumab

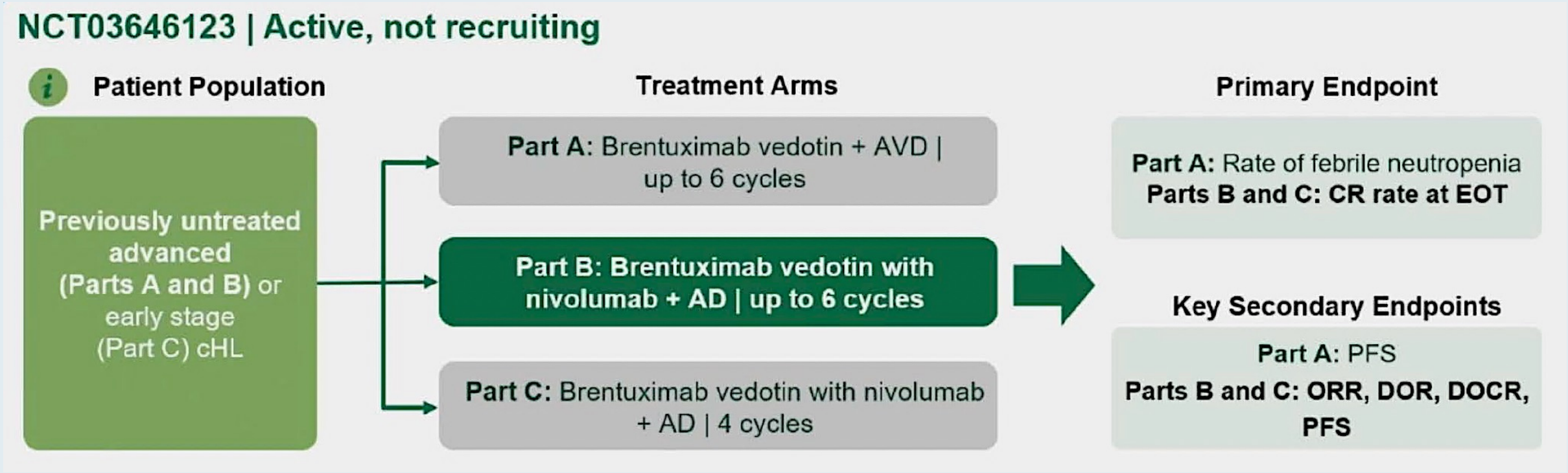
- **N-AVD substantially improves PFS compared to Bv-AVD in older pts**
  - **EFS is also improved, and fewer deaths occurred on N-AVD**

- Follow-up ongoing to confirm PFS durability, assess long-term safety, OS, and patient-reported outcomes

Rutherford SC et al. ASH 2023;Abstract 181.

Courtesy of Andrew M Evens, DO, MBA, MSc

SGN35-027 Part B: BV + Nivo + AD



Lee HJ et al. ASH 2023;Abstract 608.

SGN35-027 Part B: BV + Nivolumab + AD

Overall Response at EOT per Investigator, n (%)	All treated patients N = 57	Efficacy evaluable patients[a] N = 56
Objective response rate (complete + partial response)	**53 (93)**	**53 (95)**
95% CI	(83.0, 98.1)	(85.1, 98.9)
Complete response	**50 (88)**	**50 (89)**
95% CI	(76.3, 94.9)	(78.1, 96.0)
Partial response	3 (5)	3 (5)
Stable disease	0	0
Progressive disease	2 (4)	2 (4)
Indeterminate response[b]	1 (2)	1 (2)
Not evaluable[c]	1 (2)	0

- Best response of CR at any time point on treatment or in long-term follow-up was 95% (54/57) in all treated patients
- 88% (N=56) (95% CI, 75.7, 94.6) of patients had a **duration of response** beyond 24 months
- 88% (N=54) (95% CI, 76.0, 94.6) of patients had a **duration of complete response** beyond 24 months

Lee HJ et al. ASH 2023;Abstract 608.

Early-Stage Hodgkin Lymphoma

- Fornecker L et al. **Brentuximab Vedotin** Plus **AVD** for **First-Line** Treatment of **Early-Stage** Unfavorable **Hodgkin Lymphoma (BREACH):** A Multicenter, Open-Label, Randomized, Phase II Trial. *J Clin Oncol* 2023;41(2):327-35.
- Abramson J et al. Brentuximab Vedotin, Nivolumab, Doxorubicin, and Dacarbazine **(AN+AD)** for **Early-Stage** Classical **Hodgkin Lymphoma (SGN35-027 Part C)**. ASH 2023;Abstract 611.
- Henderson TO et al. **AHOD2131**: A Randomized **Phase 3** Response-Adapted Trial Comparing **Standard Therapy** with **Immuno-Oncology Therapy** for Children and Adults with Newly Diagnosed **Stage I and II** Classic **Hodgkin Lymphoma**. ASH 2023;Abstract 3084.

Frequently Asked Clinical Questions About HL

- Outside of a clinical trial, how do you currently manage Stage I and II HL? What are your thoughts about the AHOD 2131 trial, and are you actively recommending that eligible patients in your practice participate?
- What current first-line questions do you believe should be addressed in Phase III trials for advanced-stage HL?
- Is BV/nivolumab/AD a worthwhile regimen to evaluate?

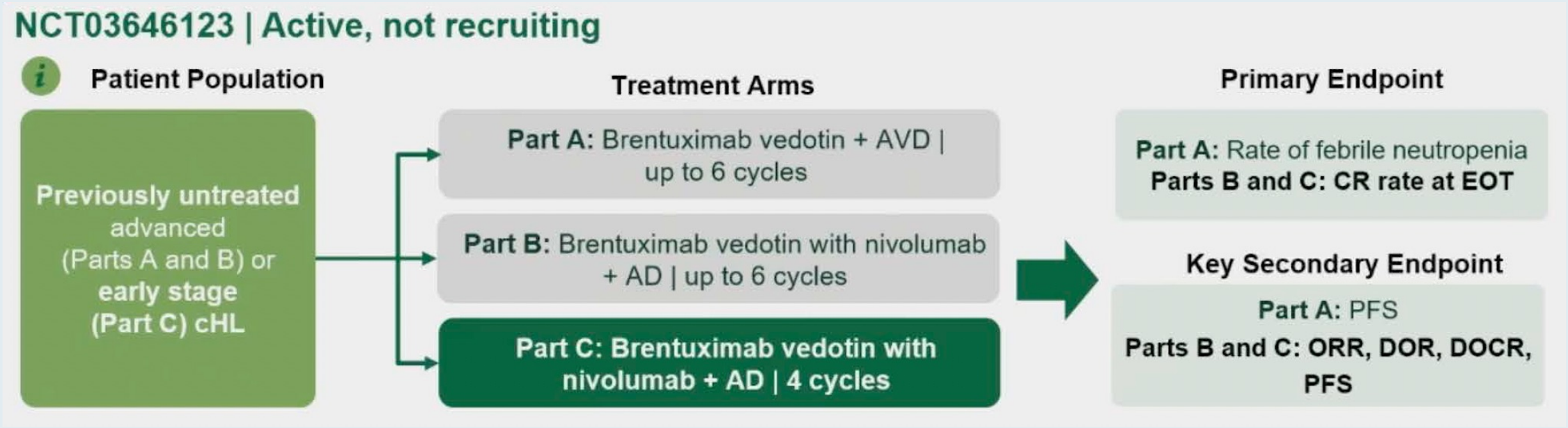
BREACH: BV-AVD vs ABVD — Response Data

Response	BV-AVD (n = 113)	ABVD (n = 57)
PET response after two cycles[a]		
Deauville 1	4 (4)	4 (7)
Deauville 2	34 (30)	22 (39)
Deauville 3	55 (49)	17 (30)
Deauville 4	13 (12)	8 (14)
Deauville 5	3 (3)	3 (5)
Not evaluated	4 (4)	3 (5)

Response	BV-AVD (n = 113)	ABVD (n = 57)
Response at EOT using 2007 Cheson criteria[b]		
Complete response	98 (87)	45 (79)
Partial response	5 (4)	1 (2)
Stable disease	1 (1)	1 (2)
Progressive disease	1 (1)	2 (4)
Missing	8 (7)	8 (14)
Response at EOT using 2014 Lugano criteria[c]		
CMR	99 (88)	44 (77)
Partial metabolic response	1 (1)	0 (0)
No metabolic response	1 (1)	1 (2)
Progressive metabolic disease	3 (3)	1 (2)
Missing	9 (8)	11 (19)

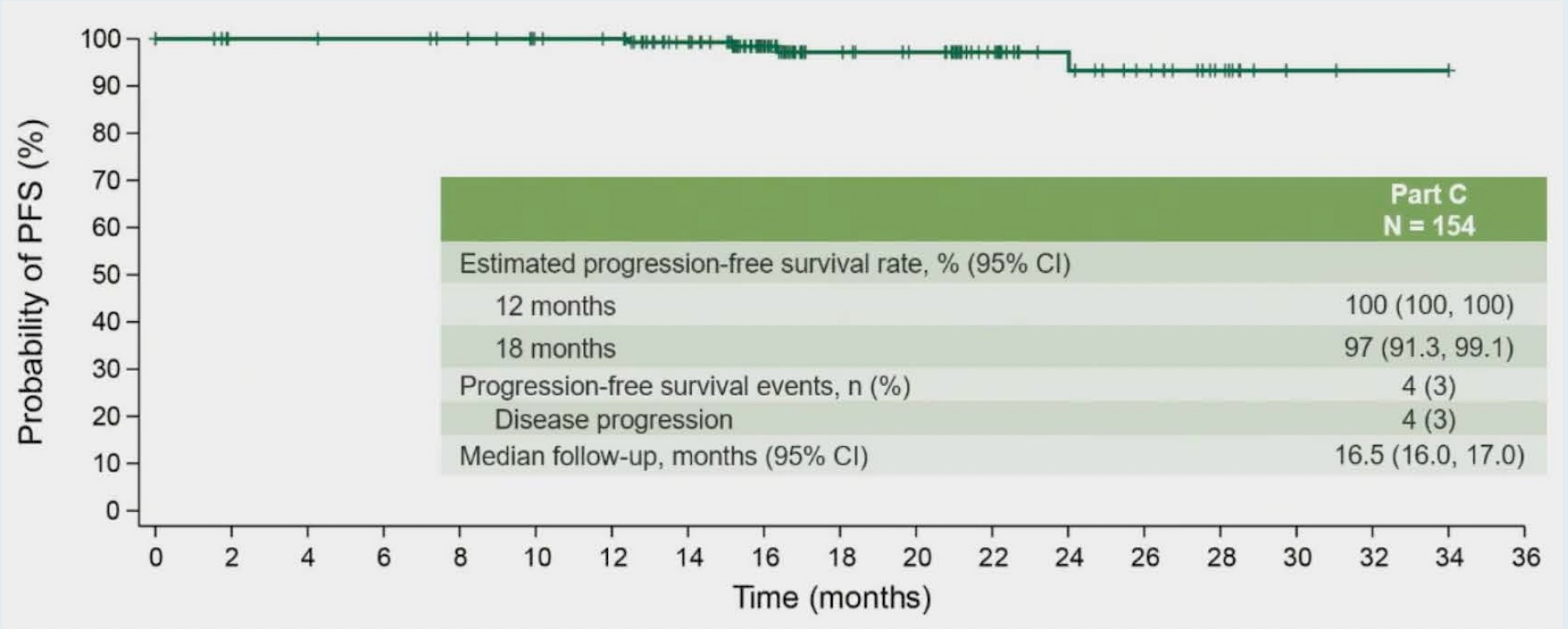
Fornecker L et al. *J Clin Oncol* 2023;41(2):327-35.

SGN35-027 Part C: BV + Nivolumab + AD



Abramson JS et al. ASH 2023;Abstract 611.

SGN35-027 Part C: BV + Nivolumab + AD — PFS Outcomes



	Part C N = 154
Estimated progression-free survival rate, % (95% CI)	
12 months	100 (100, 100)
18 months	97 (91.3, 99.1)
Progression-free survival events, n (%)	4 (3)
Disease progression	4 (3)
Median follow-up, months (95% CI)	16.5 (16.0, 17.0)

Abramson JS et al. ASH 2023;Abstract 611.

Are you familiar with AHOD 2132, a recently activated Phase III trial evaluating risk-adapted therapy for Stage I and II classic HL?

1. No
2. Yes, and it's a good alternative to present to my patients
3. Yes, but I would hesitate to present to my patients due to the scientific objective or design
4. Yes, but I would hesitate to present to my patients because it looks too complicated
5. Yes, other reason

RTP RESEARCH TO PRACTICE

Standard therapy vs. immuno-oncology for children and adults with newly diagnosed stage I and II classic HL: AHOD 2131

CHILDREN'S ONCOLOGY GROUP — The world's childhood cancer experts

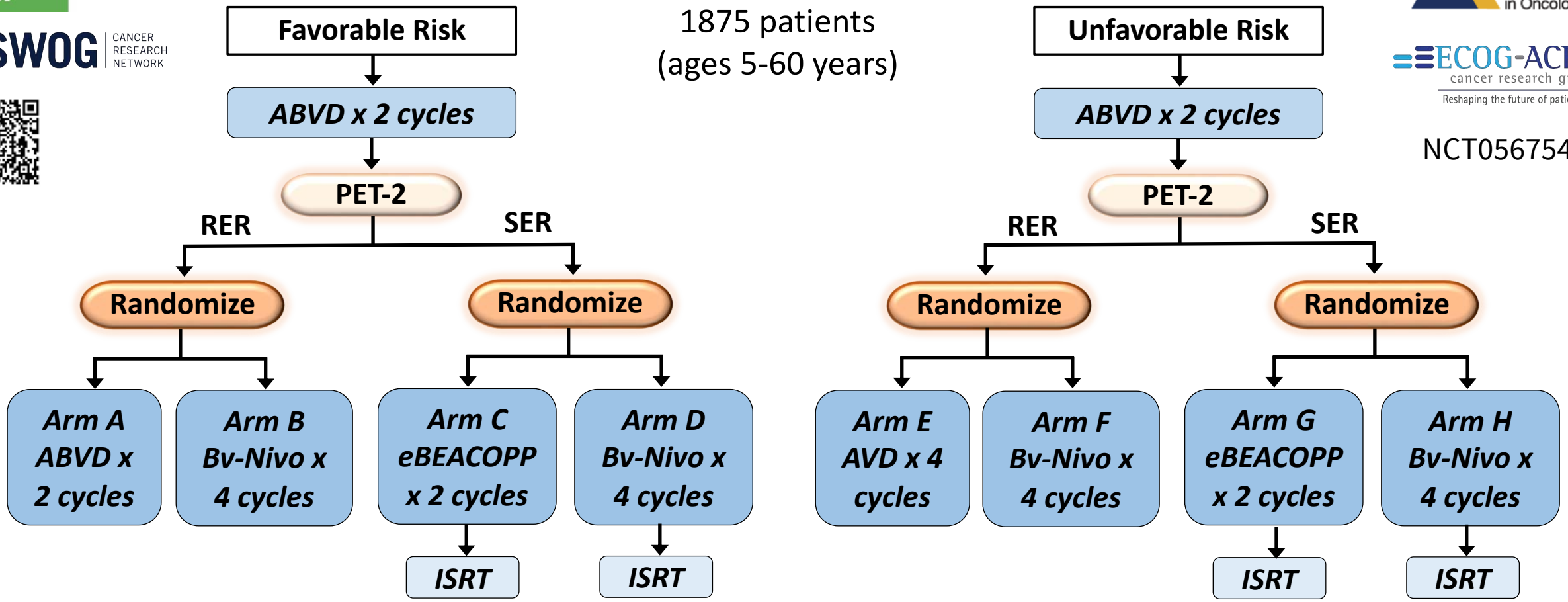
SWOG CANCER RESEARCH NETWORK

Alliance for Clinical Trials in Oncology

ECOG-ACRIN cancer research group — Reshaping the future of patient care

Planned enrollment
1875 patients
(ages 5-60 years)

NCT05675410



Courtesy of Andrew M Evens, DO, MBA, MSc

Standard therapy vs. immuno-oncology for children and adults with newly diagnosed stage I and II classic HL: AHOD 2131

- Large study (N=1875) in which the majority of ES patients will avoid radiation (N=1514 anticipated PET-).
  - Primary Endpoint: 3-year PFS superiority
  - Secondary Endpoint: 12-year OS non-inferiority
- Minority of patients will receive escBEACOPP (N=134, 5-7% overall)
- Harmonization of pediatric and adult cHL treatments
- Incorporation of reduced chemotherapy strategy in frontline
- Dedicated end point of long follow up (12-year OS) allows assessment of late-term effects of treatment
- Multitude of correlative studies planned (metabolic PET, ctDNA, quality of life, cost of care, post-acute and late effects, etc)

Courtesy of Andrew M Evens, DO, MBA, MSc

Are you familiar with AHOD 2132, a recently activated Phase III trial evaluating risk-adapted therapy for Stage I and II classic HL?

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RTP RESEARCH TO PRACTICE

Frequently Asked Clinical Questions About HL

- **What novel agents and strategies currently under investigation do you find most promising for the treatment of HL?**

Consensus or Controversy? Investigator Perspectives on the Current and Future Role of Immune Checkpoint Inhibitors in the Management of Hepatobiliary Cancers — A 2024 Post-ASCO Gastrointestinal Cancers Symposium Review

A CME-Accredited Virtual Event

Thursday, February 15, 2024
5:00 PM – 6:00 PM ET

Faculty

Robin (Katie) Kelley, MD
Mark Yarchoan, MD

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.

RTP Year in Review 2024