What I Tell My Patients:
New Treatments and Clinical Trial Options

Part 2 of a 2-Part Complimentary NCPD Webinar Series

Hodgkin and Non-Hodgkin Lymphomas

Tuesday, June 14, 2022
5:00 PM – 6:00 PM ET

Faculty

Christopher R Flowers, MD, MS
Robin Klebig, APRN, CNP, AOCNP

Moderator

Neil Love, MD

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

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

Robin Klebig, APRN, CNP, AOCNP
Nurse Practitioner
Assistant Professor of Medicine
Division of Hematology
Mayo Clinic
Rochester, Minnesota

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Commercial Support

This activity is supported by educational grants from ADC Therapeutics, Incyte Corporation, and Seagen Inc.

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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 NCPD 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 Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, the parent company of GHI, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, 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, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Mersana Therapeutics Inc, 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, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

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Dr Flowers — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Bristol-Myers Squibb Company, Celgene Corporation, Curio Science, Denovo Biopharma, Epizyme Inc, Foresight Diagnostics, Genentech, a member of the Roche Group, Genmab, Incyte Corporation, Janssen Biotech Inc, MEI Pharma Inc, MorphoSys, Pharmacyclics LLC, an AbbVie Company, Seagen Inc
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Ms Klebig— Disclosures

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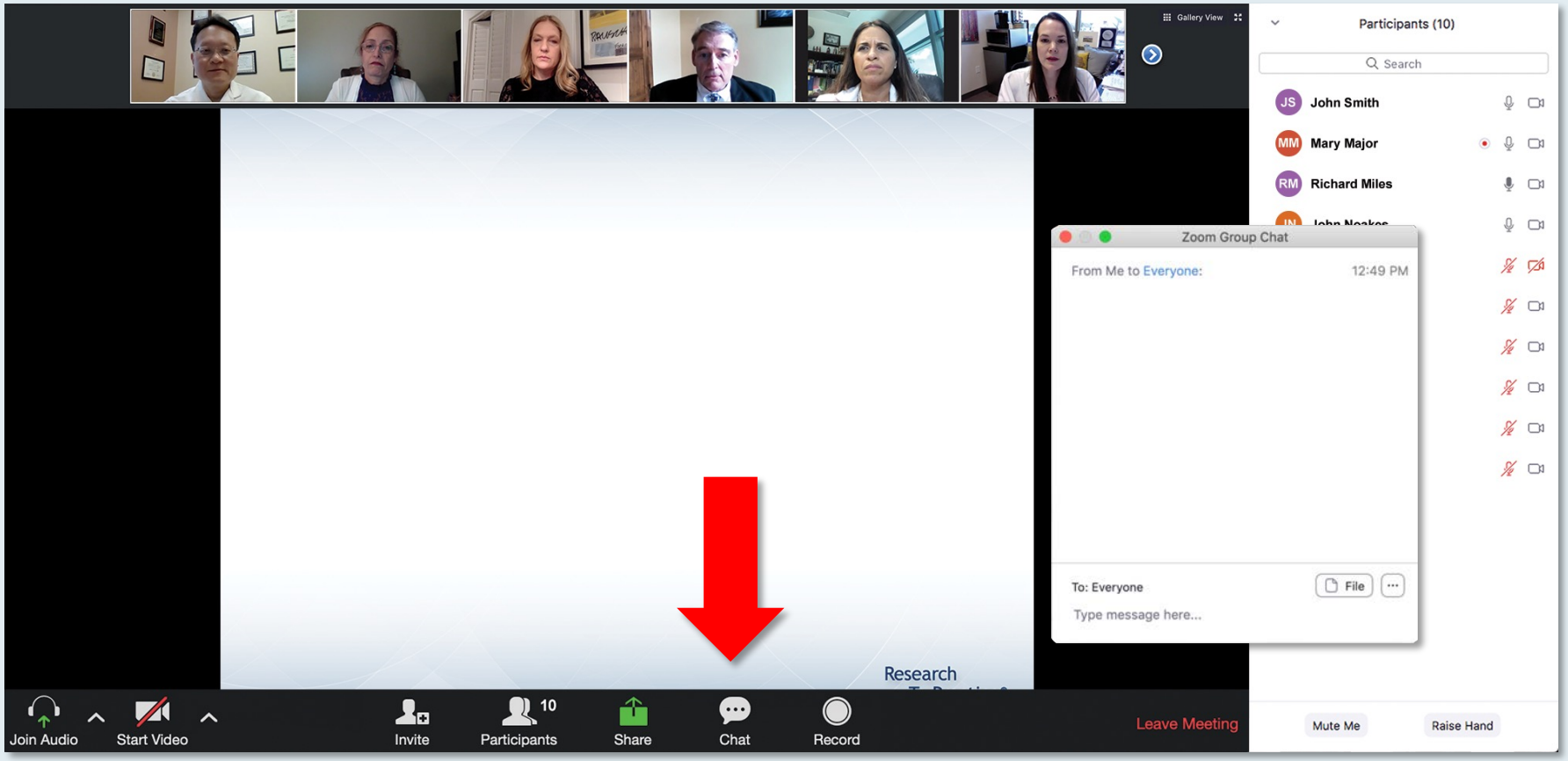
We Encourage Clinicians in Practice to Submit Questions



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

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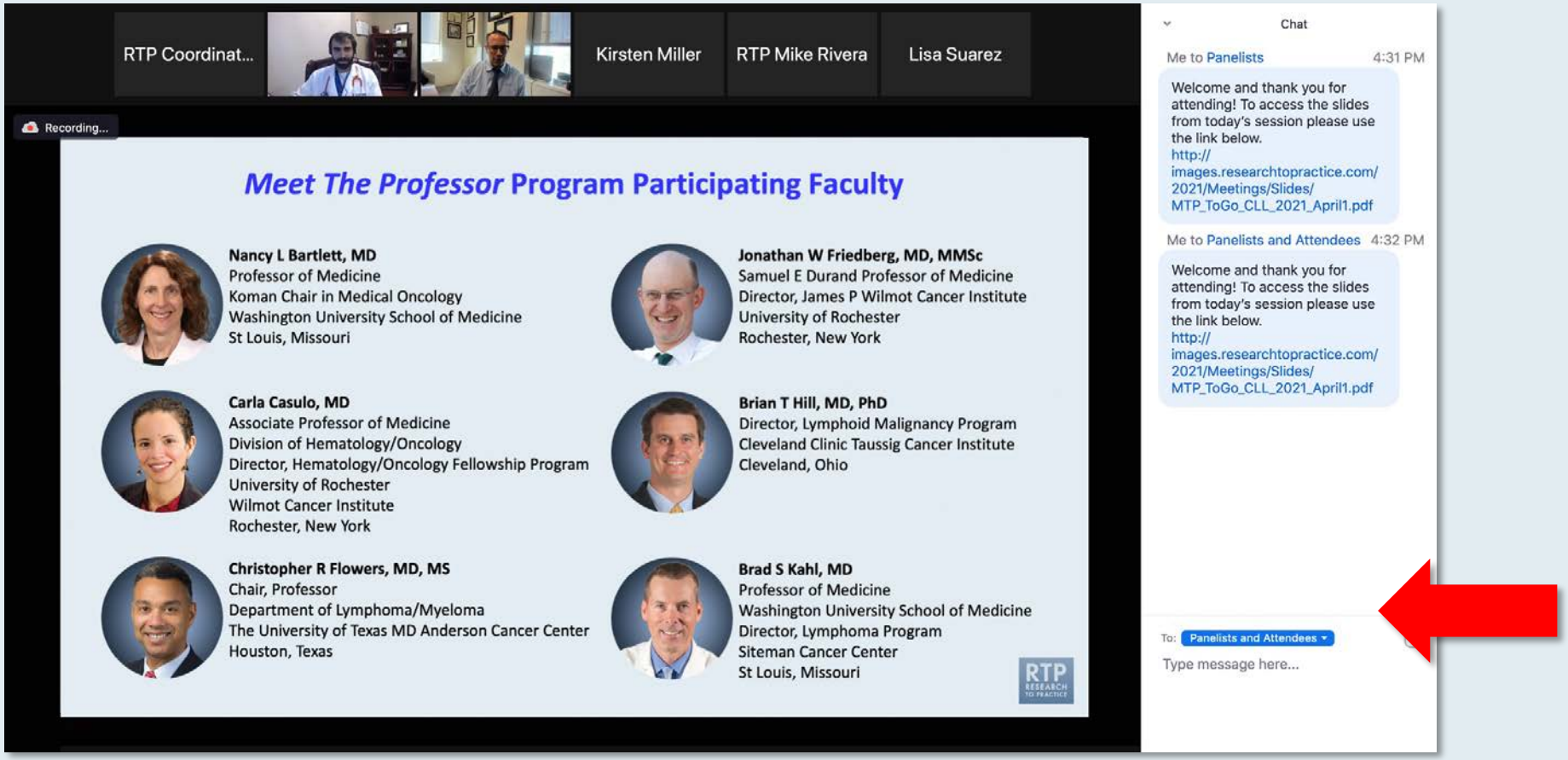
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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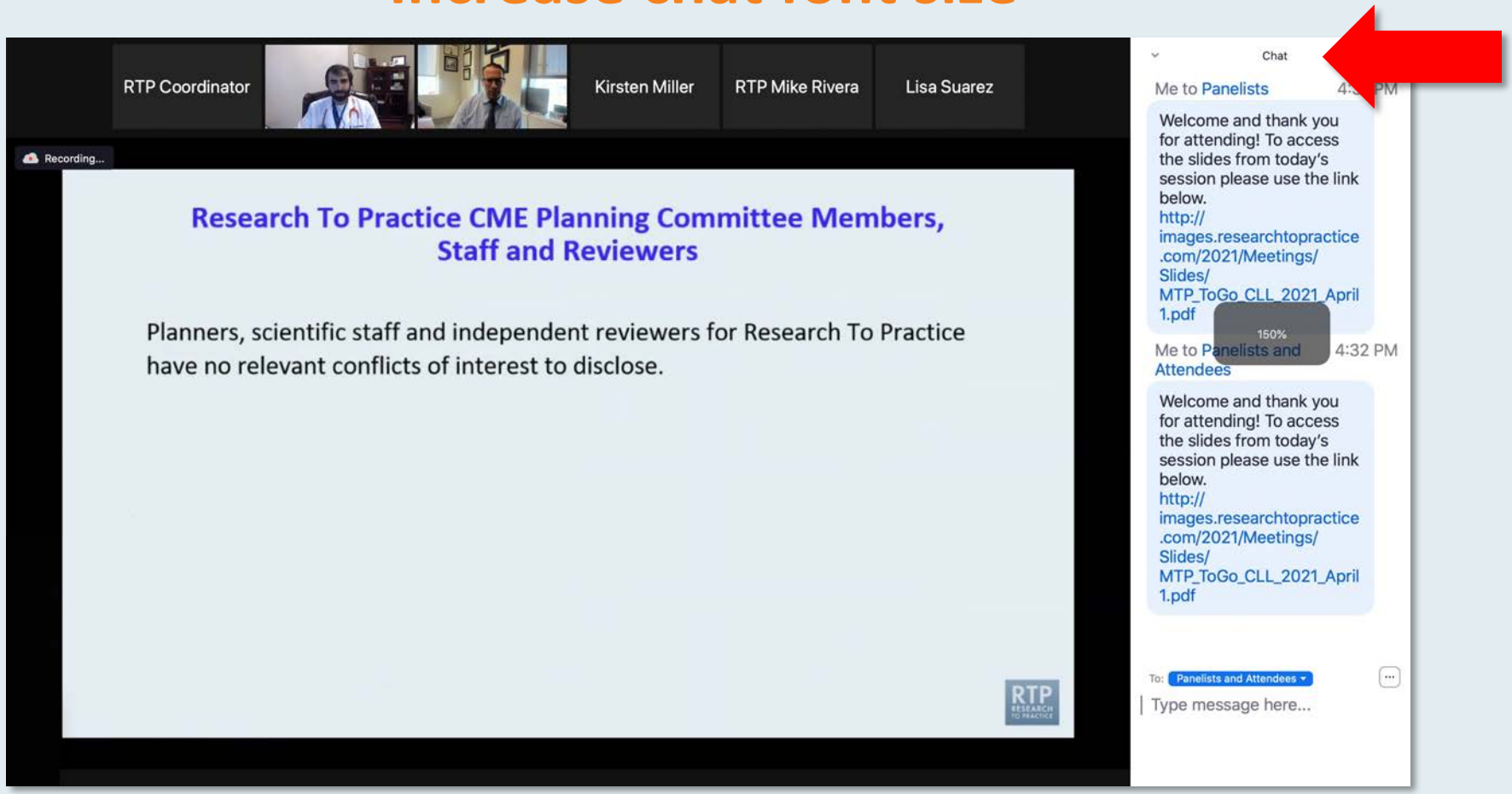
Familiarizing Yourself with the Zoom Interface

Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Advances in the Treatment of Hodgkin and Non-Hodgkin Lymphomas from ASH 2021

DR MATTHEW LUNNING
UNIVERSITY OF NEBRASKA
MEDICAL CENTER

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Spotify

Listen on Google Podcasts

Meet The Professor

Non-Small Cell Lung Cancer with an Actionable Target Beyond EGFR

Thursday, June 16, 2022
5:00 PM – 6:00 PM ET

Faculty

Melissa Johnson, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Ovarian Cancer

Tuesday, June 21, 2022
5:00 PM – 6:00 PM ET

Faculty

Shannon N Westin, MD, MPH

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Wednesday, June 22, 2022
5:00 PM – 6:00 PM ET

Faculty

Manish A Shah, MD

Moderator

Neil Love, MD

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PARP Inhibition in the Management of Prostate Cancer — Where We Are and Where We're Headed

Thursday, June 23, 2022
5:00 PM – 6:00 PM ET

Faculty

Johann S de Bono, MB ChB, MSc, PhD, FMedSci
Fred Saad, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Management of Chronic Myeloid Leukemia

Tuesday, June 28, 2022
5:00 PM – 6:00 PM ET

Faculty

Jorge E Cortes, MD

Moderator

Neil Love, MD

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Meet The Professor

Current and Future Management of Non-Small Cell Lung Cancer with an EGFR Mutation

Thursday, June 30, 2022
5:00 PM – 6:00 PM ET

Faculty

Joel W Neal, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

NCPD credit information will be emailed to each participant within 5 business days.

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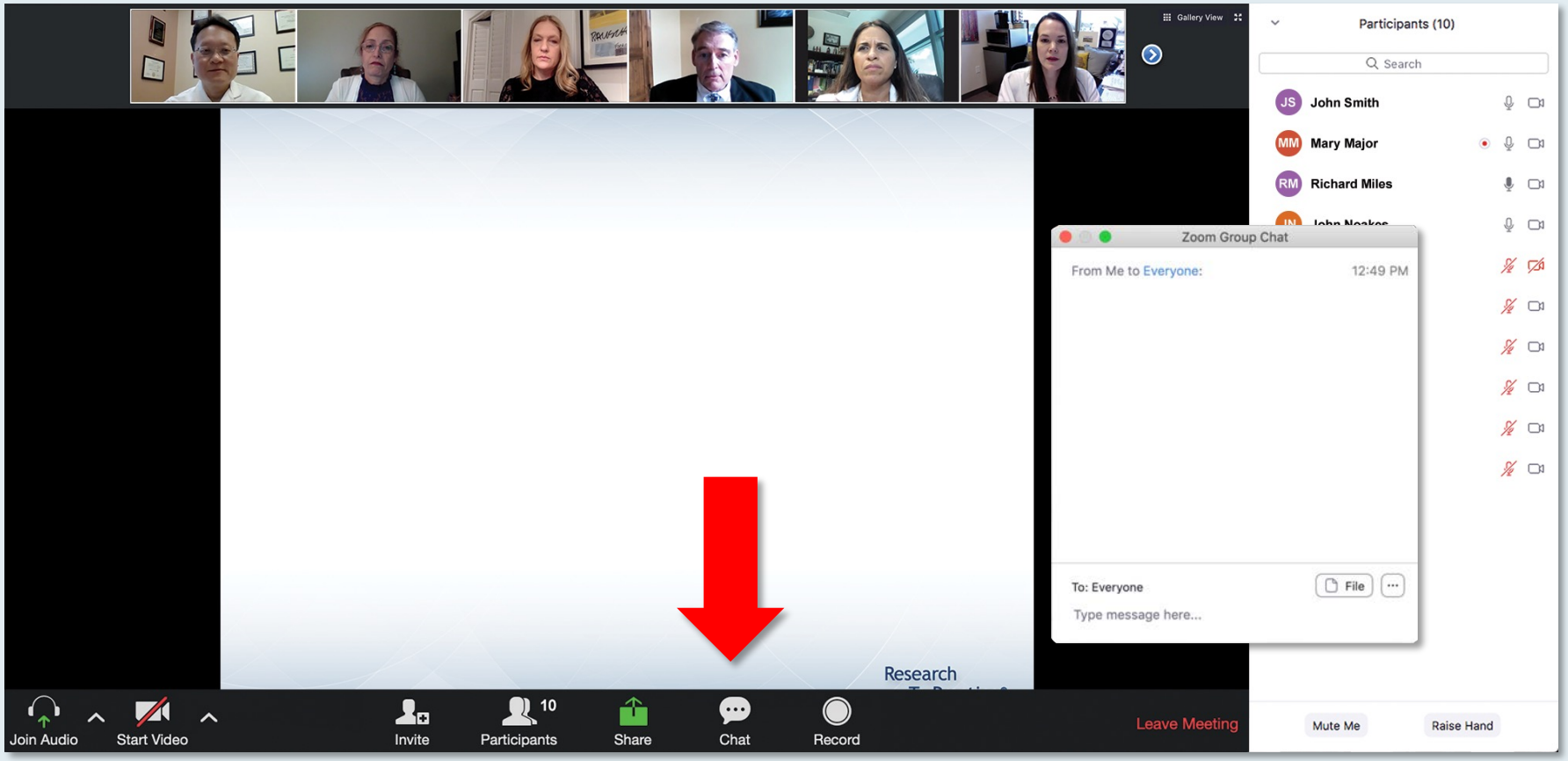

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Mantle Cell Lymphoma

Wrestle Mania

Matthew Lunning D.O. FACP
Associate Professor

A National Cancer Institute
Designated Cancer Center

FRED & PAMELA
BUFFETT CANCER CENTER

Shine 2022

FRED & PAMELA
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The Core Oncology Triad
Developing an Individualized Oncology Strategy

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Agenda
Management of Hodgkin and Non-Hodgkin Lymphomas

Module 1 – Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2 – Hodgkin Lymphoma (HL)

Module 3 – Follicular Lymphoma (FL)

Module 4 – Mantle Cell Lymphoma (MCL)

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Agenda
Management of Hodgkin and Non-Hodgkin Lymphomas

Module 1 – Diffuse Large B-Cell Lymphoma (DLBCL)

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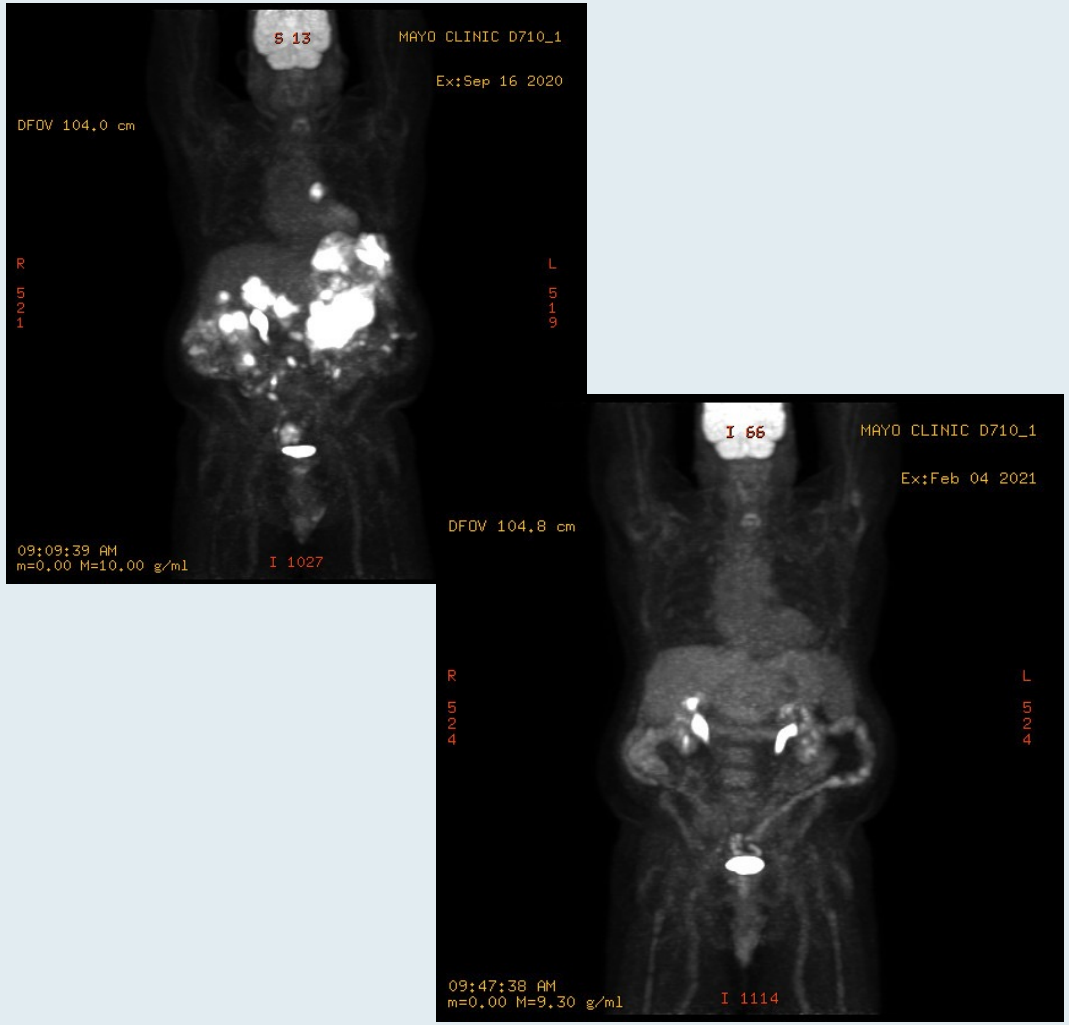
Case 1 — Robin Klebig, APRN, CNP, AOCNP

- 77 yo male
- Lives 6 hours from Mayo Clinic
- Farmer, insurance, real estate
- Wife w/ depression/dementia
- DLBCL-DE, stage IVB
- Dx 9/2020 – treatment during COVID – challenging
- R-CHOP x 6
- Interim & EOT PET/CT – Deauville 1



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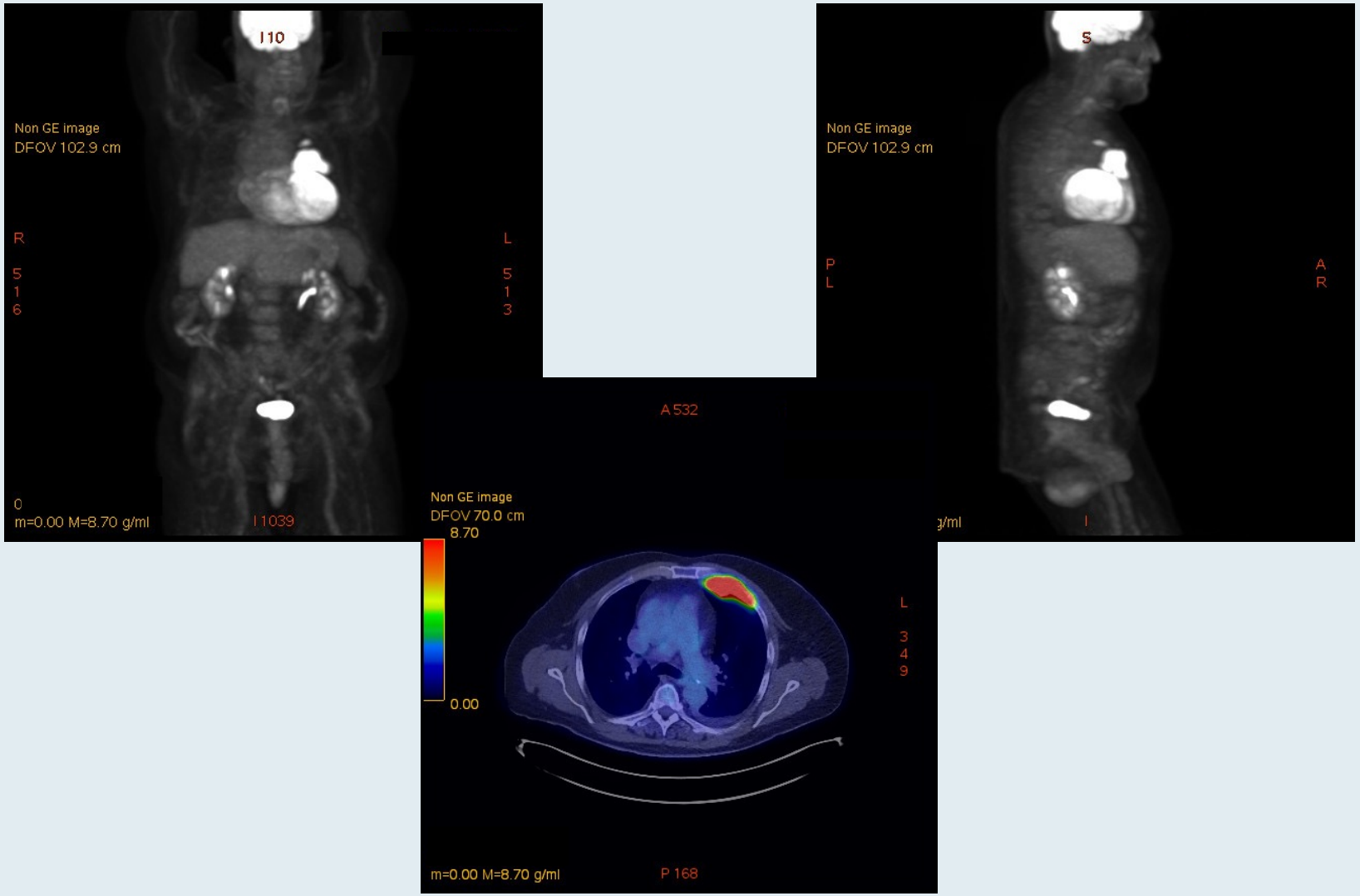
Case 1 — Robin Klebig, APRN, CNP, AOCNP

DLBCL relapse

- **6 months later:**



Case 1 — Robin Klebig, APRN, CNP, AOCNP

- **August 2021**
- **Initiated tafasitamab/lenalidomide**
  - **Tolerated tafasitamab well**
  - **Pruritic rash on scalp with initiation of lenalidomide**
    - **Intolerable to patient**
      - **despite topical and oral corticosteroids and diphenhydramine**
  - **Received only 2 doses of lenalidomide with each cycle**
- **October 2021: Chest pain – ED for CT angio**
  - **Negative for PE**
  - **Demonstrated progression of chest wall mass**

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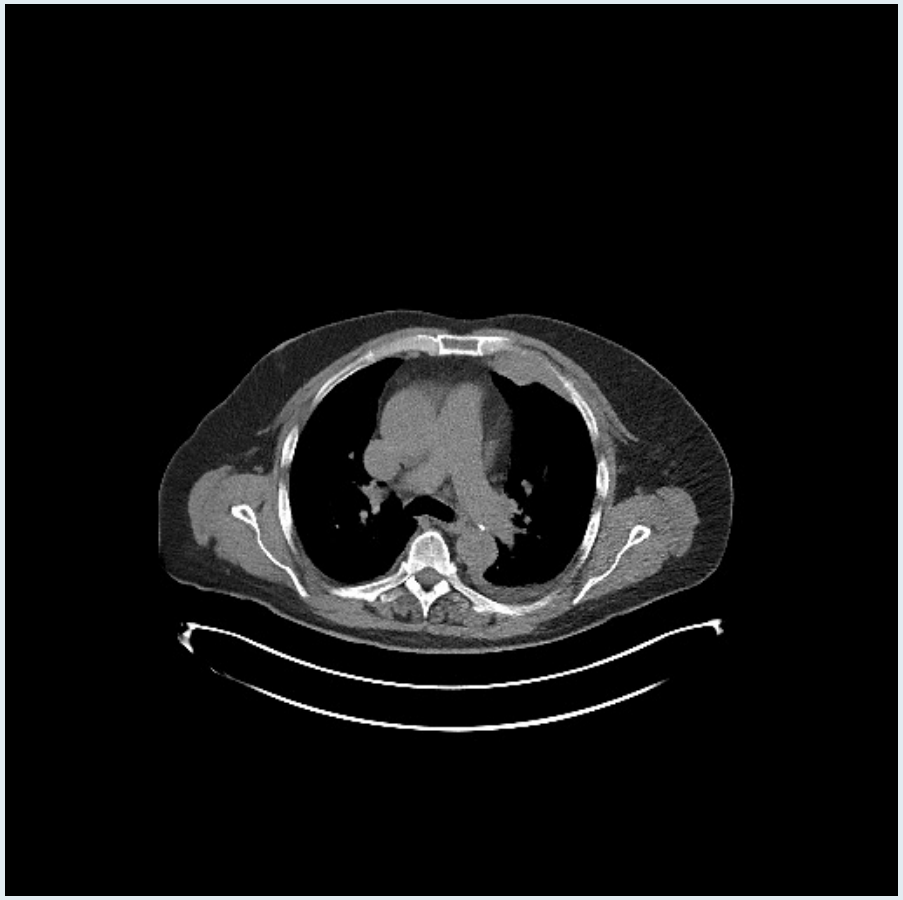
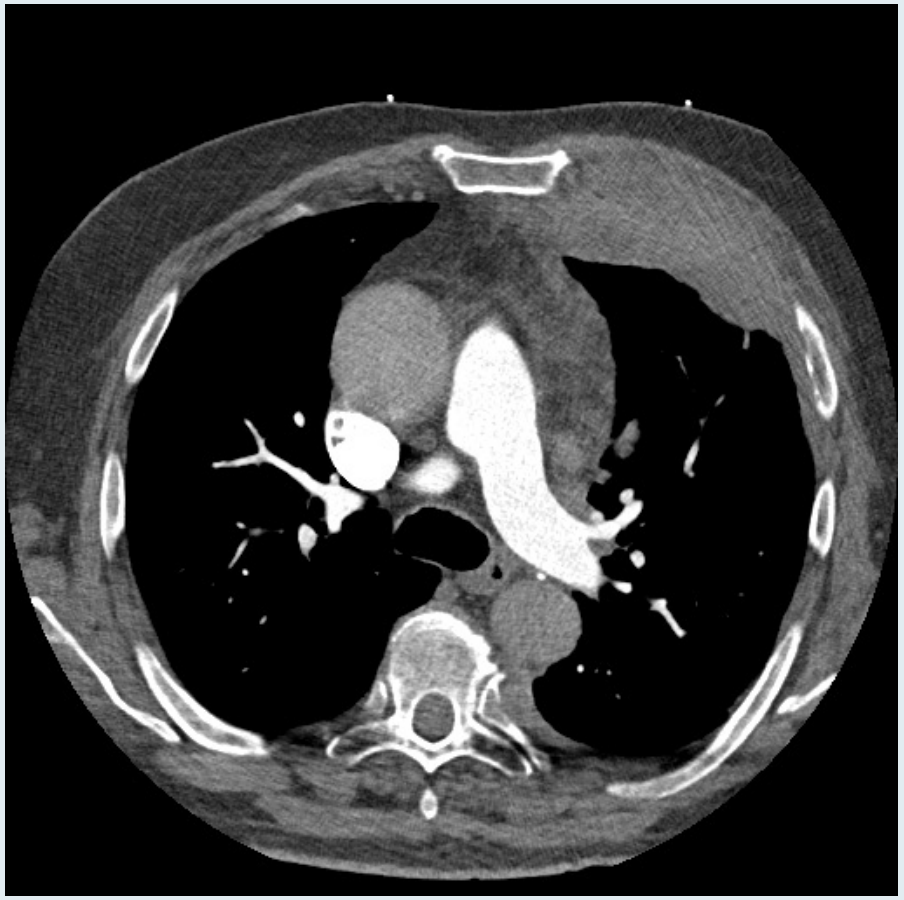
Case 1 — Robin Klebig, APRN, CNP, AOCNP

August 2021



October 2021



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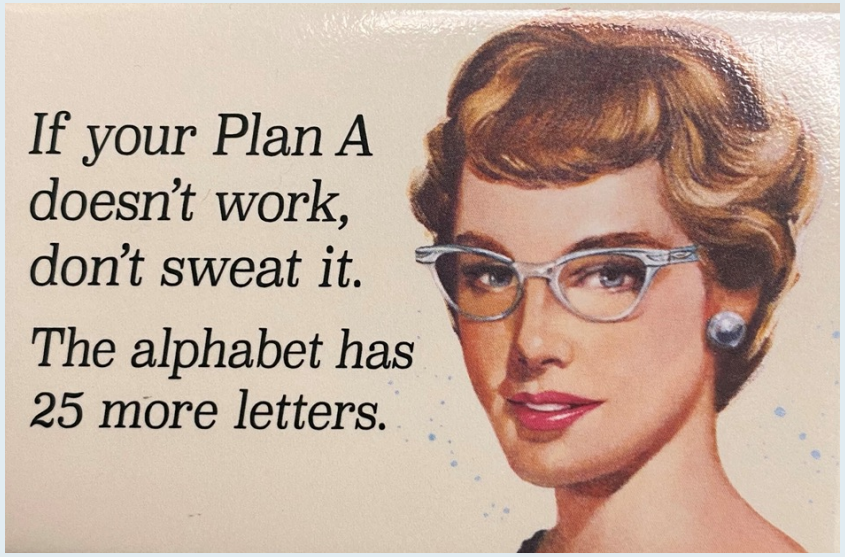
Case 1 — Robin Klebig, APRN, CNP, AOCNP

DLBCL – Plan C



- **Polatuzumab + BR**
- **5 cycles**
- **Discontinued due to complications**
  - **Fatigue**
  - **Bone pain related to pegfilgrastim**
  - **Hospitalizations**
    - **Chest pain/Afib/cardiomyopathy r/t previous anthracycline**
    - **Dehydration/diarrhea/rash**
  - **Diarrhea**
    - **Found to be due to IBD – resolved with mesalamine**
  - **Rash (sulfamethoxazole-trimethoprim)**
  - **Anorexia/weight loss**
- **Remains in CR (Deauville 1) 6 months later…**

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Novel Agents Recently Approved for Relapsed/Refractory DLBCL

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

ADC = antibody-drug conjugate

Courtesy of Laurie H Sehn MD, MPH

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Blood Rev 2022 Apr 22;[Online ahead of print].

Contents lists available at ScienceDirect

Blood Reviews

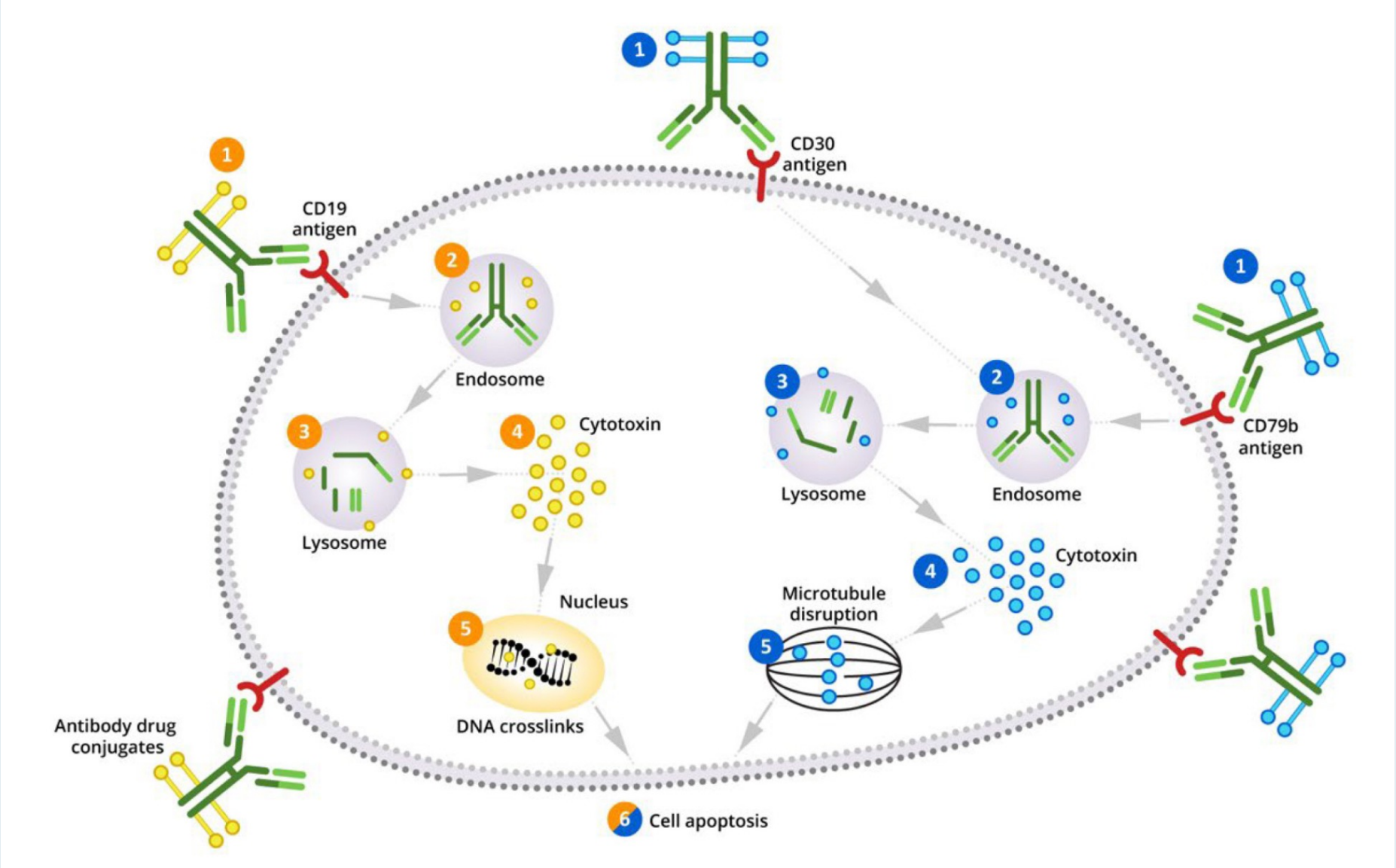
journal homepage: www.elsevier.com/locate/issn/0268960X

Review

ABCs of ADCs in management of relapsed/refractory diffuse large B-cell lymphoma

Juan Pablo Alderuccio [a,*], Jeff P. Sharman [b]

Antibody-Drug Conjugate Mechanism of Action in DLBCL



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

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

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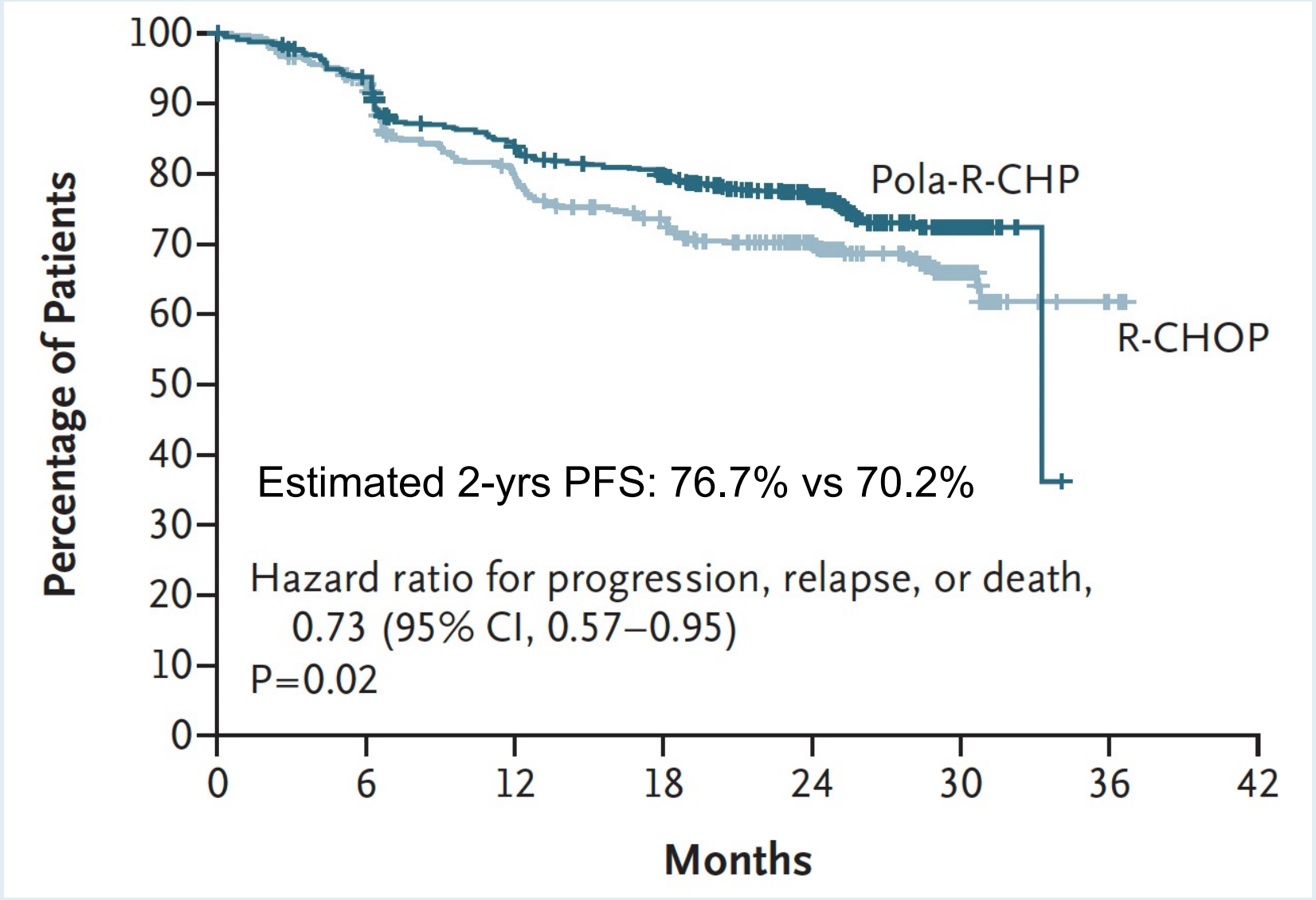
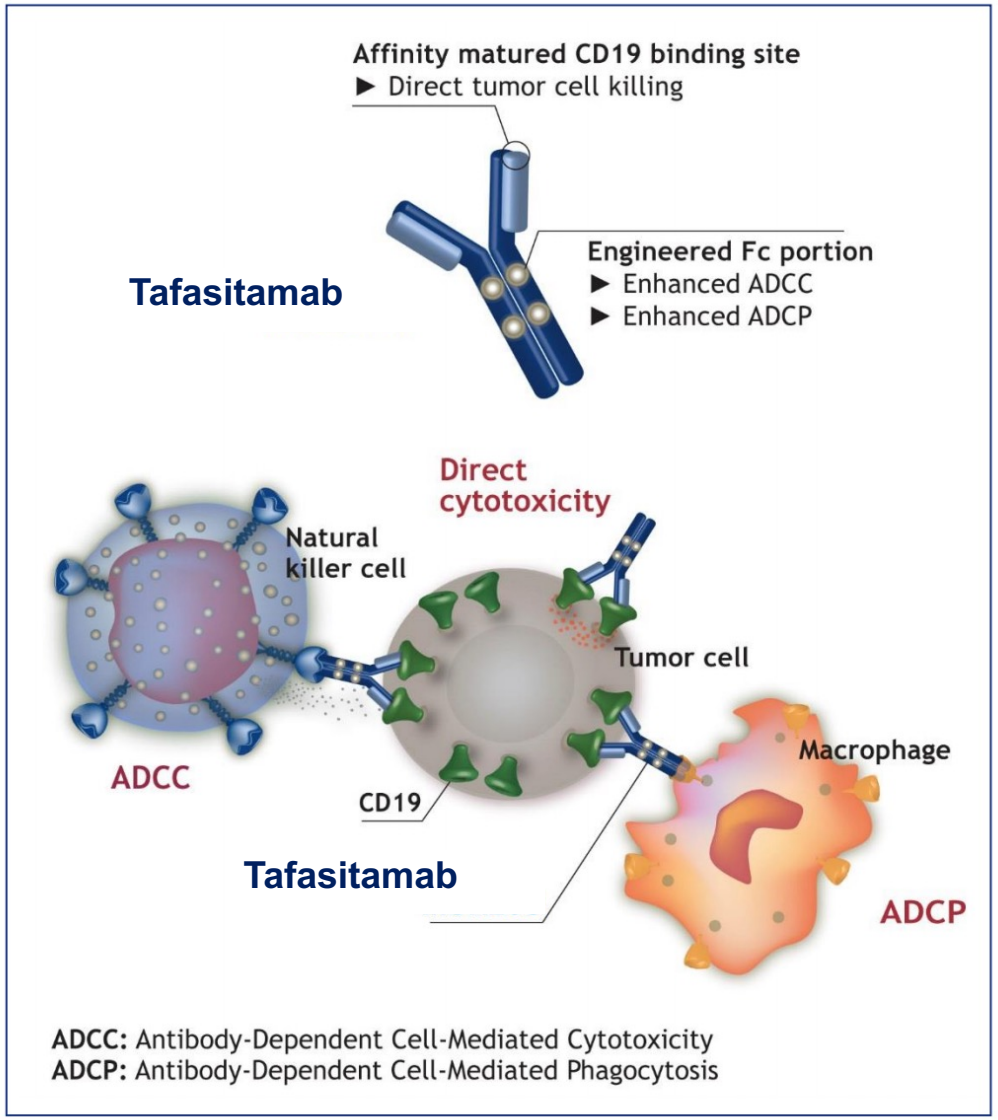
POLARIX: Investigator-Assessed Progression-Free Survival (Primary Endpoint)



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

Tafasitamab (MOR208)



Lenalidomide enhances NK function with enhanced ADCC in vitro

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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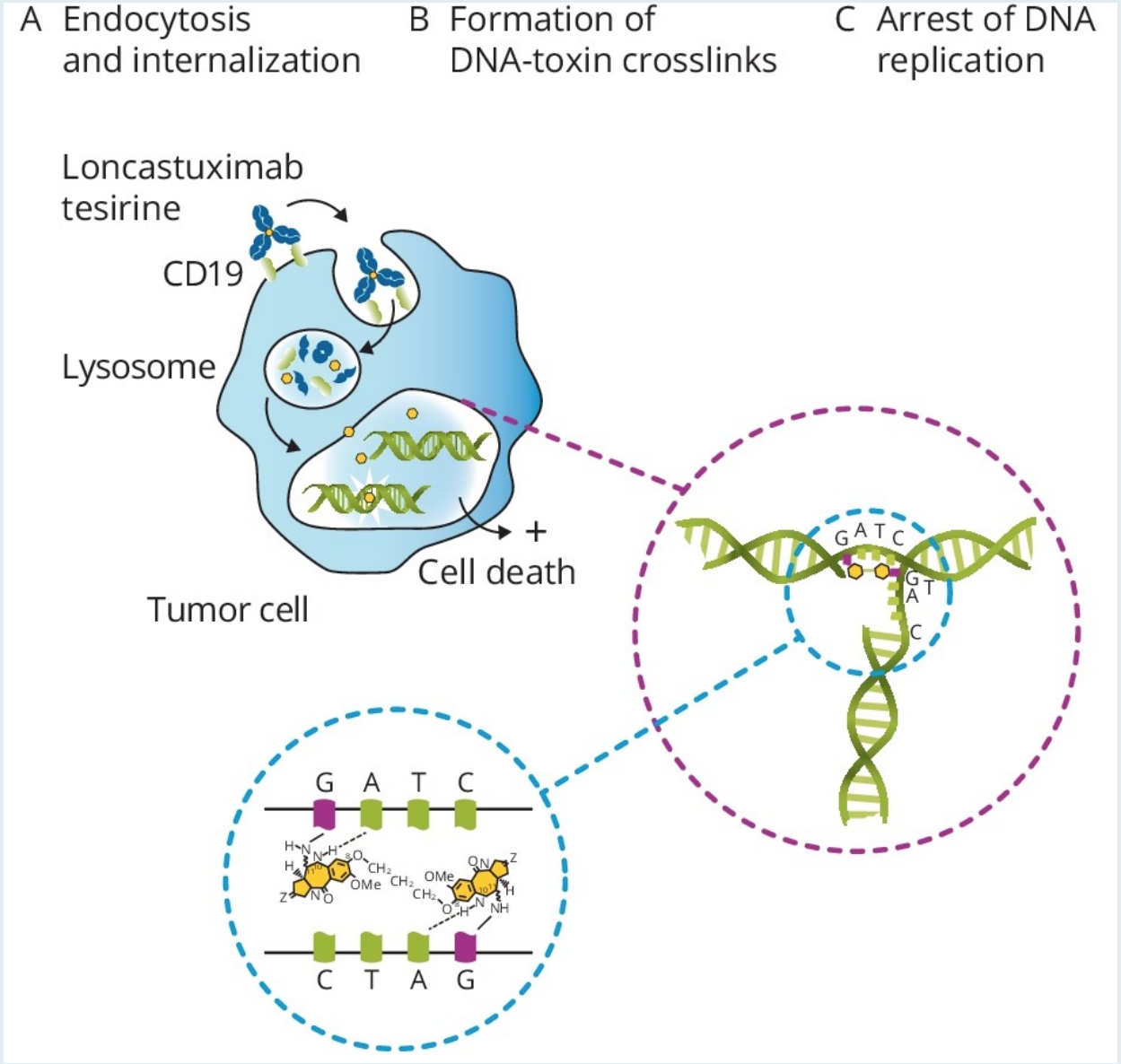
Mechanism of Action of Loncastuximab Tesirine



Hamadani M et al. ASCO 2021; Abstract TPS7574.

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

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

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

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

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

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

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

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

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Randomized Trials of CAR T-Cells vs SOC in 2nd Line Transplant-Eligible DLBCL with Primary Refractory Disease or Relapse within 1 Year of 1st Line Therapy

	ZUMA-7	TRANSFORM	BELINDA
CAR T-cell	Axicabtagene ciloleucel	Lisocabtagene maraleucel	Tisagenlecleucel
n	359	184	322
% 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 months	6 months	10 months
CR rate	65% vs 32%	66% vs 39%	28% vs 28%
Grade ≥3 CRS/NT	6%/21%	1%/4%	5%/3%
	Locke, et al. Abstract 2	Kamdar, et al. Abstract 91	Bishop, et al. Abstract LBA-6

Courtesy of Jeremy Abramson, MD

RTP RESEARCH TO PRACTICE

An 88-year-old woman with newly diagnosed DLBCL who developed pneumonia after the first dose of R-CHOP

Dr Erik Rupard (West Reading, Pennsylvania)

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Agenda
Management of Hodgkin and Non-Hodgkin Lymphomas

Module 1 – Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2 – Hodgkin Lymphoma (HL)

Module 3 – Follicular Lymphoma (FL)

Module 4 – Mantle Cell Lymphoma (MCL)

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Case 2 — Robin Klebig, APRN, CNP, AOCNP

- 75 yo female
- Dx 6/2021: Stage IVA cHL – lymphadenopathy & bone lesions
- PMH: Afib, CHF – apixaban & multiple cardiac meds – cleared by CV; idiopathic PN on duloxetine & gabapentin, chronic diarrhea
- Rx plan: Sequential BV & AVD for older pts with untreated cHL
  - BV x 2 – AVD x 6 – BV x 4
  - C1 BV: E coli enteritis, dehydration, pneumonia despite adequate ANC (delayed C2 by 3 weeks)
  - C2 BV: Dx DM. Prolonged hospitalization for respiratory failure w/ hypoxia requiring intubation and pressor support (due to fluid overload w/ h/o Afib)

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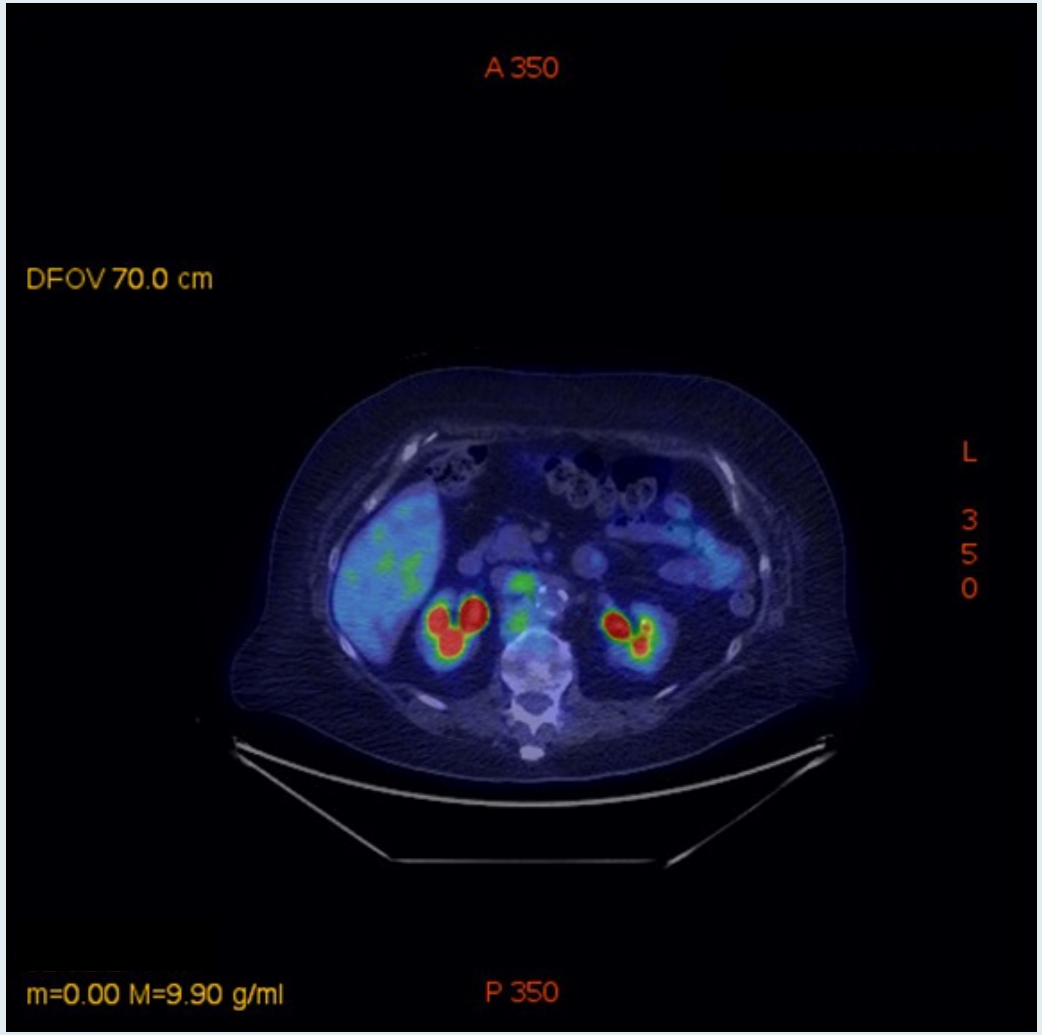
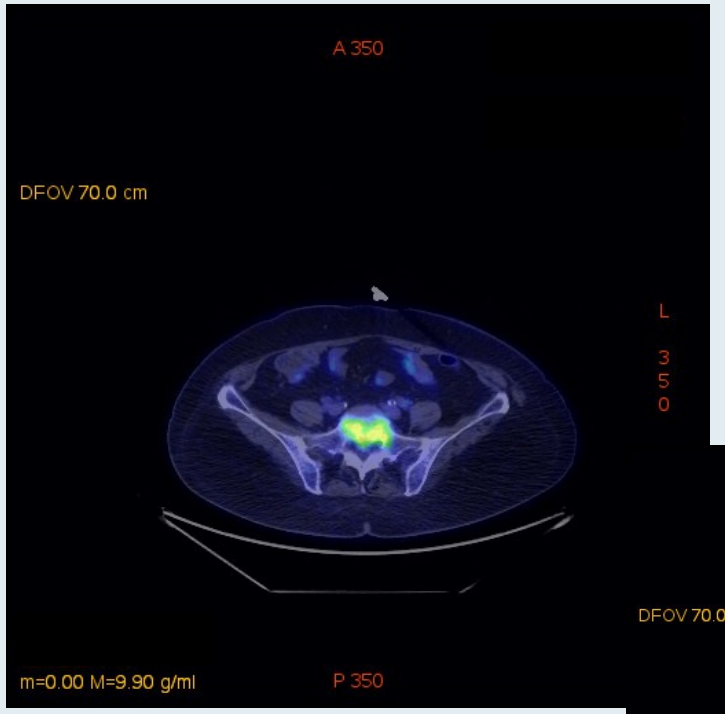
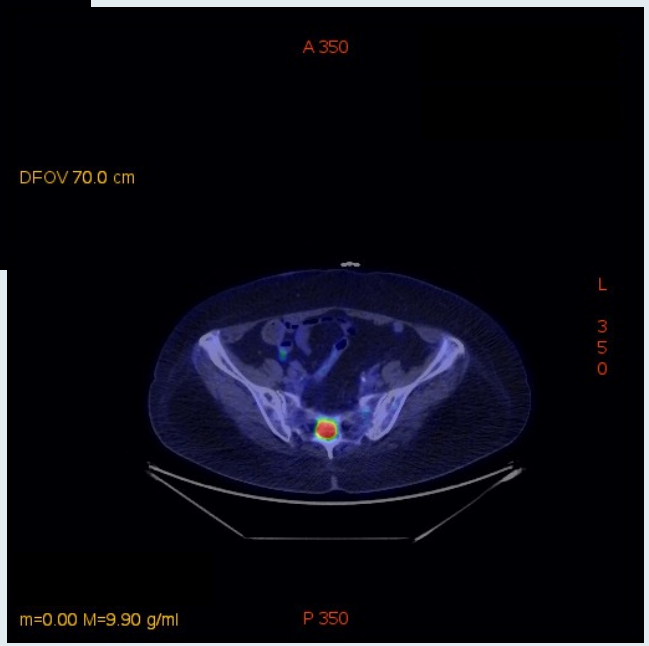
Case 2 — Robin Klebig, APRN, CNP, AOCNP

Baseline PET/CT



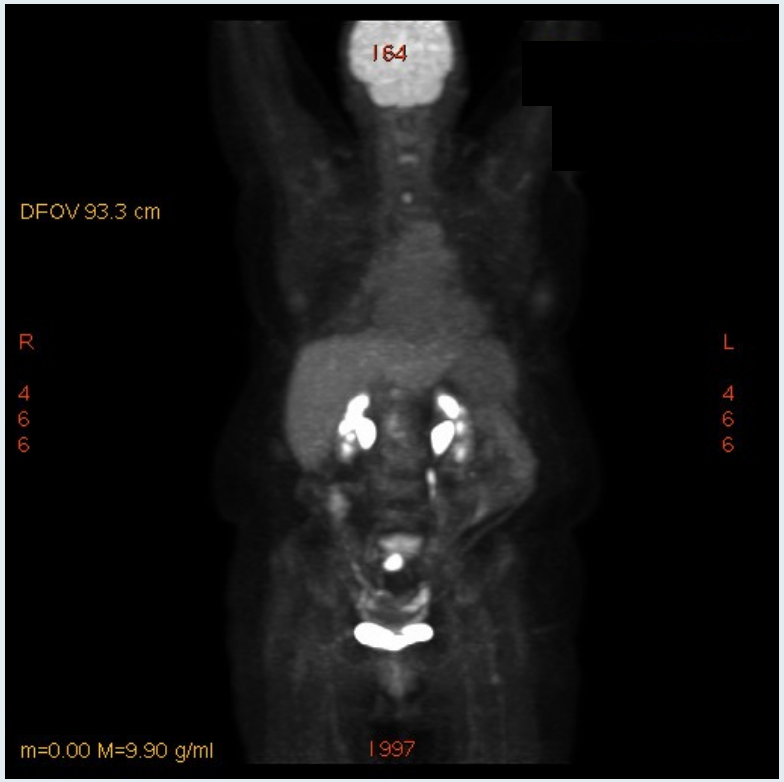




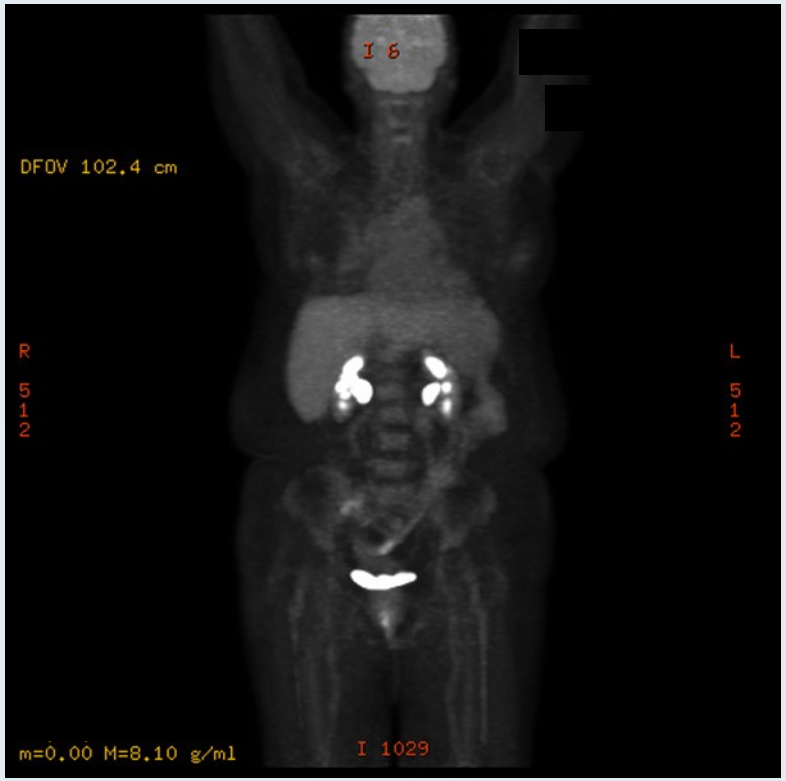
Case 2 — Robin Klebig, APRN, CNP, AOCNP

Response to 2 cycles of BV

6/29/2021



9/30/2021



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Case 2 — Robin Klebig, APRN, CNP, AOCNP

Chemo plan continued

- **C1 AVD (delayed 1 week)**
  - **Had "unexpected alopecia"**
  - **Dose reductions**
    - **50% doxorubicin due to drug interactions and PS**
    - **25% vinblastine due to peripheral neuropathy**
    - **25% dacarbazine due to PS**
- **Complications requiring dose delays due to**
  - **Diarrhea, hypomagnesemia, dehydration, Afib/RVR requiring hospitalization**
  - **Recurrence of perirectal fistula & abscess**
  - **Sudden death of daughter**
- **No further dose reductions**

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Case 2 — Robin Klebig, APRN, CNP, AOCNP

- **AVD completed – FINALLY!**
- **PET/CT – Deauville 1**

- **C3 BV resumed 5/17/2021 still at full dose**
- **C4 BV dose reduced to 1.2 mcg/kg due to progressive PN**

- **Should be completing chemotherapy 7/18/2022 if all goes well…**

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2022 ASCO® ANNUAL MEETING

Abstract 7503

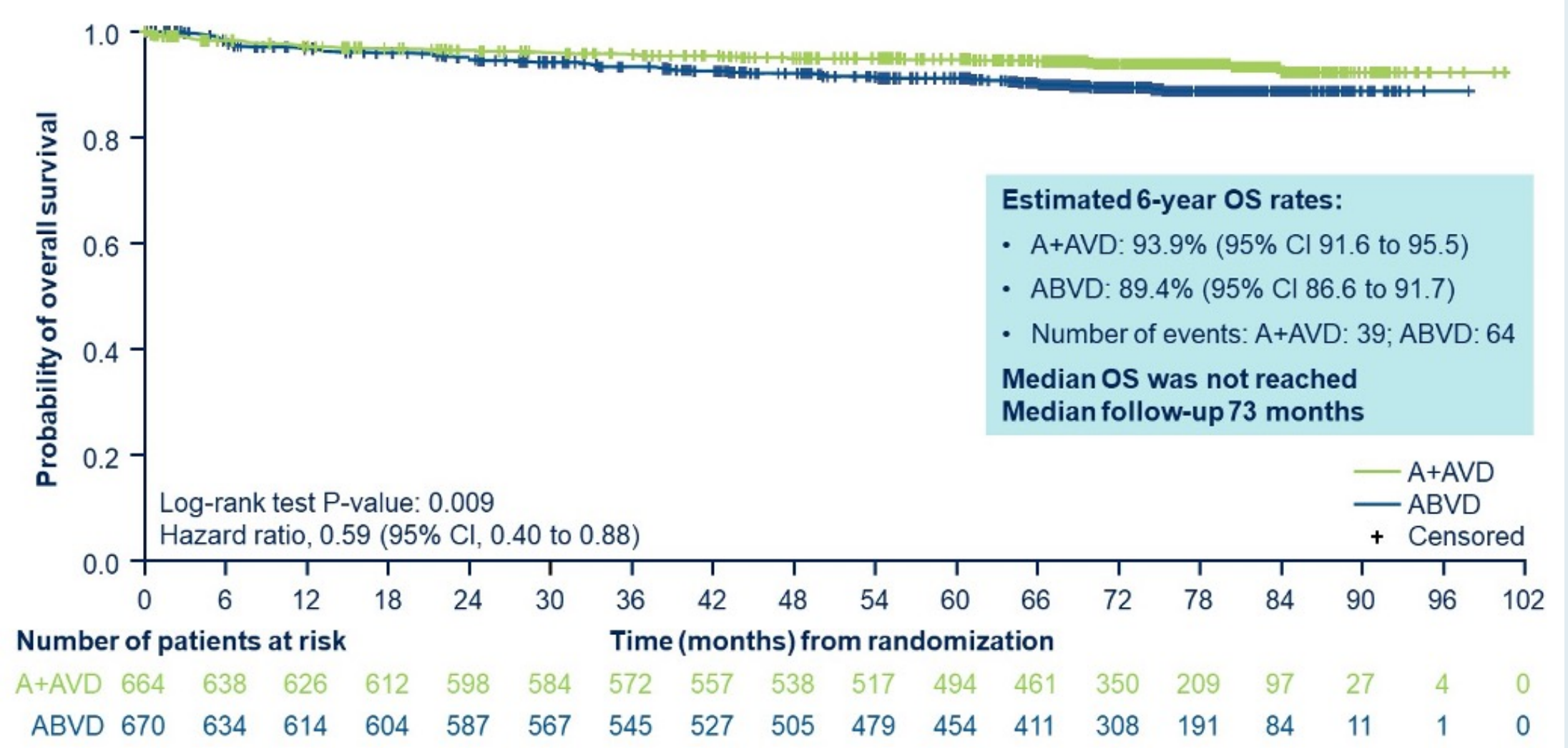
FIRST-LINE BRENTUXIMAB VEDOTIN PLUS CHEMOTHERAPY IMPROVES OVERALL SURVIVAL IN PATIENTS WITH STAGE III/IV CLASSICAL HODGKIN LYMPHOMA: AN UPDATED ANALYSIS OF ECHELON-1

Stephen M. Ansell, John Radford, Joseph M. Connors, Won-Seog Kim, Andrea Gallamini, Radhakrishnan Ramchandren, Jonathan W. Friedberg, Ranjana Advani, Martin Hutchings, Andrew M. Evens, Piotr Smolewski, Kerry J. Savage, Nancy L. Bartlett, Hyeon-Seok Eom, Jeremy S. Abramson, Cassie Dong, Frank Campana, Keenan Fenton, Markus Puhlmann, and David J. Straus, for the ECHELON-1 Study Group

Stephen M. Ansell

Division of Hematology, Mayo Clinic, Rochester, MN, USA

ECHELON-1: Prespecified OS Analysis After Approximately 6 Years Follow-Up



A + AVD = brentuximab vedotin and doxorubicin/vinblastine/dacarbazine; ABVD = doxorubicin/bleomycin/vinblastine/dacarbazine

Ansell SM et al. ASCO 2022;Abstract 7503.

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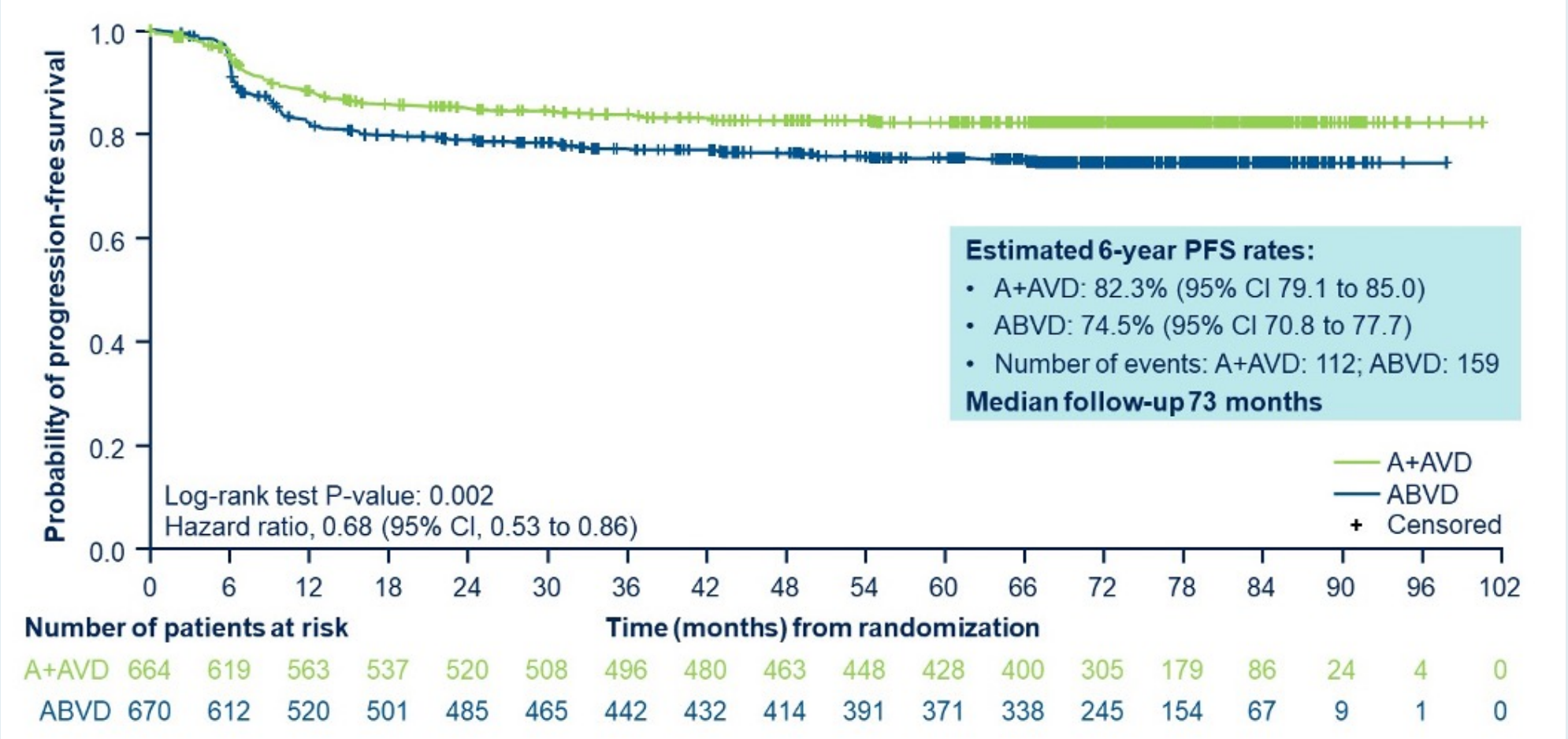
ECHELON-1: Updated PFS Analysis After Approximately 6 Years Follow-Up



- In patients with peripheral neuropathy (PN) in the A + AVD and ABVD arms after 6-year follow-up, treatment-emergent PN either resolved or continued to improve in 86% and 87% (median time to resolution was 16 and 10 weeks).

Ansell SM et al. ASCO 2022;Abstract 7503.

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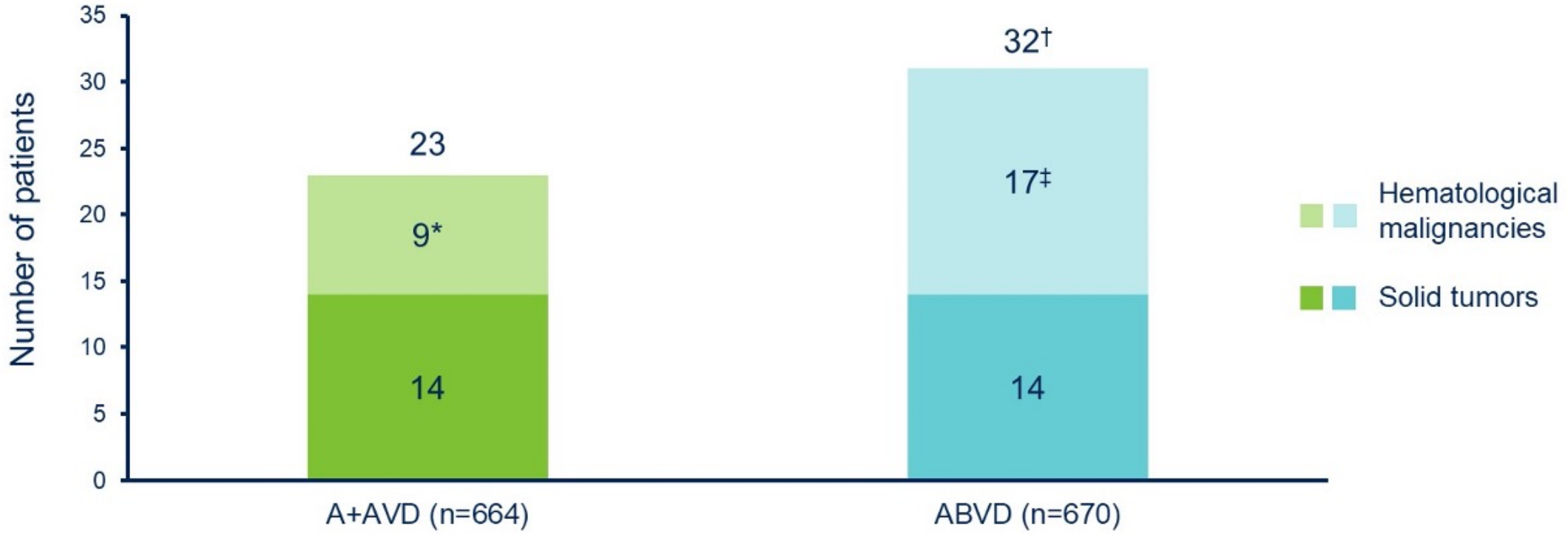
ECHELON-1: Incidence of Secondary Cancer



*Includes 2 cases of acute myeloid leukemia and 6 cases of B- or T-cell lymphomas; †Includes 1 unknown malignancy; ‡Includes 1 case each of acute myeloid leukemia, acute promyelocytic leukemia, and myelodysplastic syndrome, and 13 cases of B- or T-cell lymphomas.

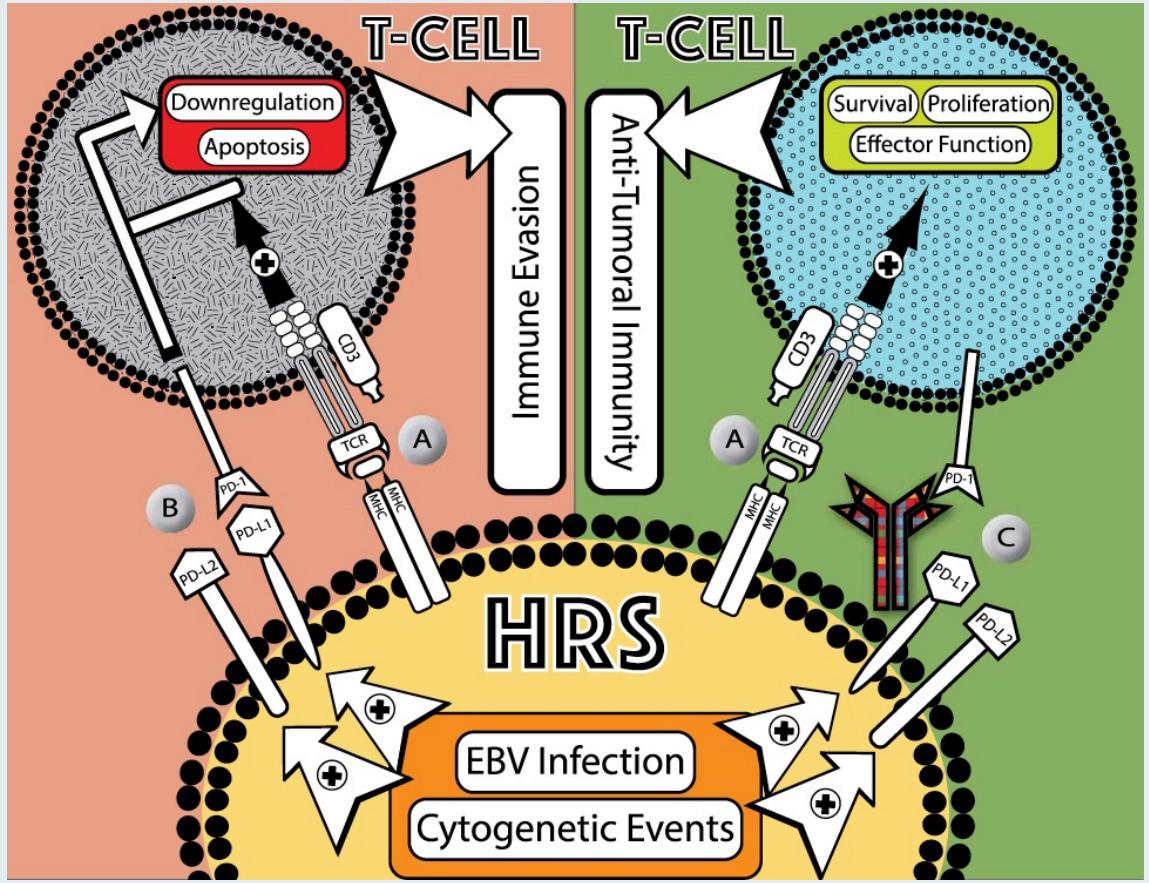
Among patients with second malignancies:

- Two patients on each arm received transplant
- Three patients on the ABVD arm received prior radiation (none with A+AVD)

Ansell SM et al. ASCO 2022;Abstract 7503.

RTP RESEARCH TO PRACTICE

Targeting the PD-1/PD-L1 Axis in HL



- **HL characterized by small number of malignant Hodgkin Reed-Sternberg cells (HRS) surrounded by normal immune cells**
- 9p24.1 chromosomal abnormalities frequently observed in HRS cells
- **More than 90% of HRS cells have alterations in PD-L1 and PD-L2 loci**
- Malignant Hodgkin and RS cells overexpress PD-L1/L2 ligands (due to cytogenetic events, infection with EBV)

Villasboas JC, Ansell SA. *Cancer J* 2016;22(1):17-22; Roemer MGM et al. *J Clin Oncol* 2016;34(23):2690-7.

RTP RESEARCH TO PRACTICE

ICML Virtual Congress 2021;Abstract 075.

Camidanlumab tesirine efficacy and safety in an open-label, multicenter, Phase 2 study of patients with relapsed or refractory classical Hodgkin lymphoma (R/R cHL)

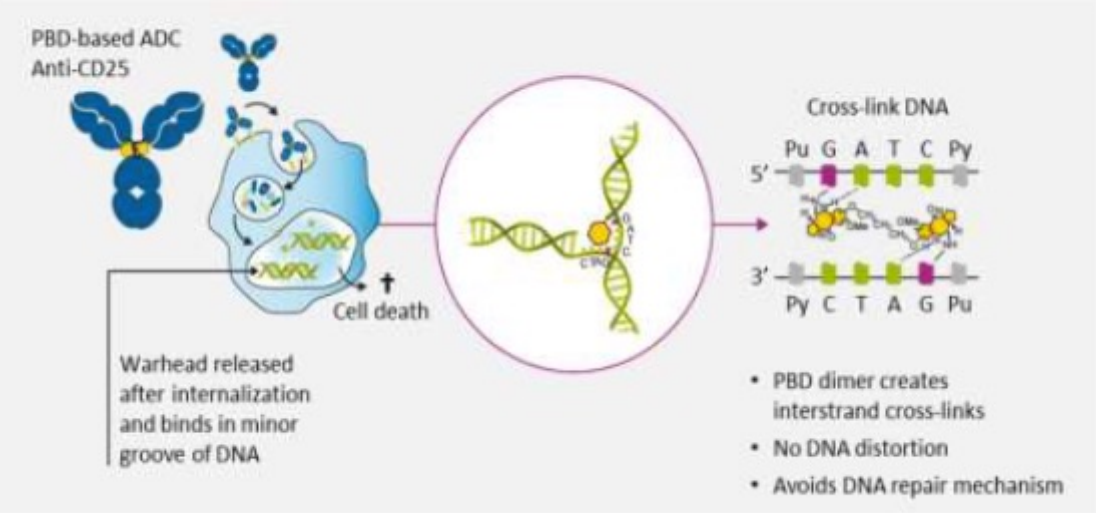
Pier Luigi Zinzani[1], Carmelo Carlo-Stella[2], Mehdi Hamadani[3], Alex F. Herrera[4], Stephen M. Ansell[5], John Radford[6], Kami Maddocks[7], Justin Kline[8], Kerry J. Savage[9], Nancy L. Bartlett[10], Paolo F. Caimi[11], Yanina Negievich[12], Hans G. Cruz[12], Luqiang Wang[13], Jens Wuerthner[12], Graham P. Collins[14]

RTP RESEARCH TO PRACTICE

Camidanlumab Tesirine: Mechanism of Action and Study Rationale

Limited therapeutic options are available for patients with R/R cHL who are unresponsive to, or whose disease progresses after, BV and PD-1 blockade therapy.[1–5] Novel treatments are required to address this unmet need

Camidanlumab tesirine (Cami) is an Ab-drug conjugate comprising a human IgG1 anti-CD25 monoclonal Ab conjugated to a potent PBD dimer warhead[6]



Treatment with Cami demonstrated encouraging antitumor activity and manageable toxicity:

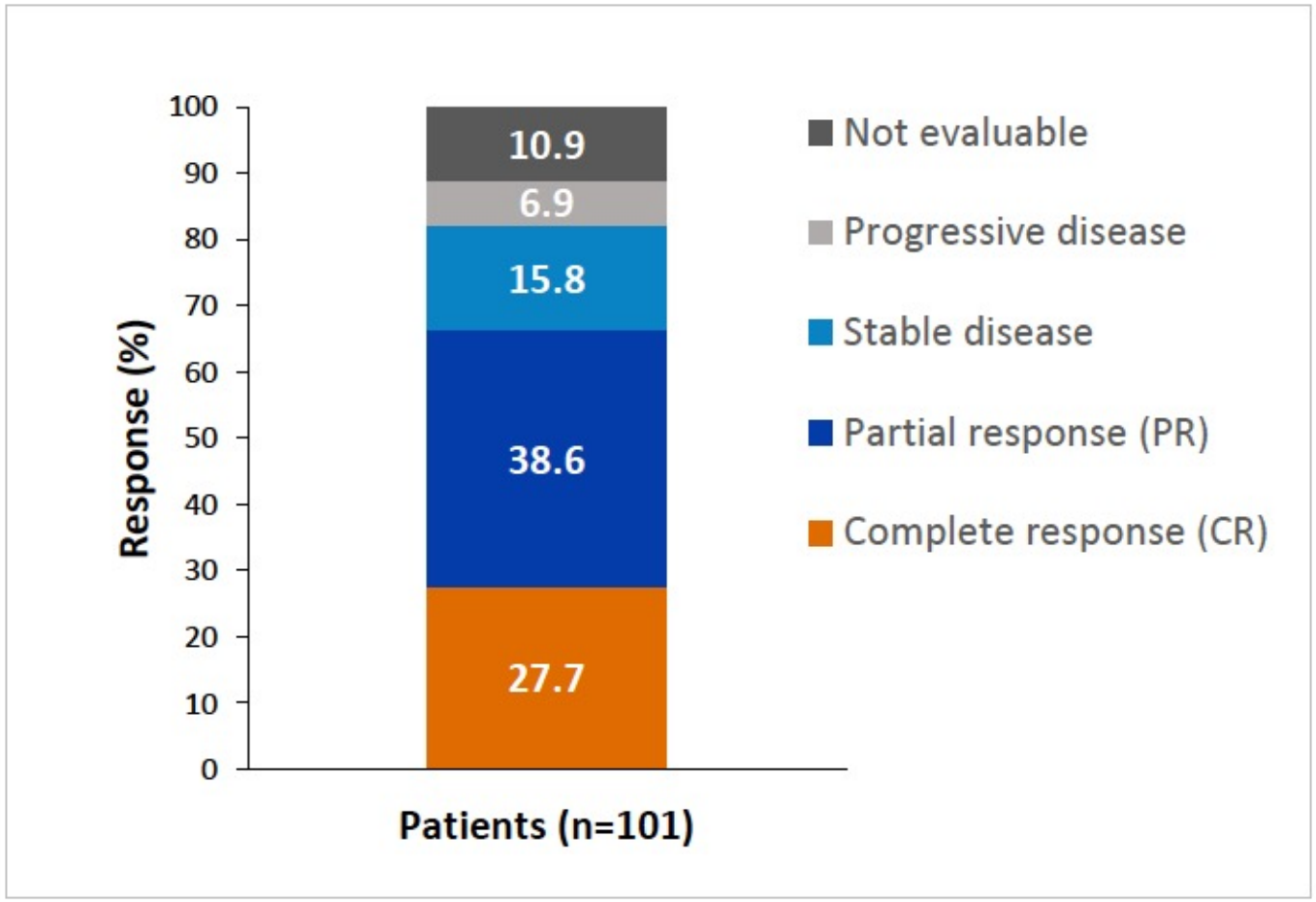
- In a Phase 1 trial that included patients with R/R cHL who received Cami at a dose of 45 µg/kg and achieved an overall response rate (ORR; CR + PR) of 86.5%[7]
- In the initial findings of this Phase 2 study of patients with R/R cHL, who achieved an ORR of 83.0%[8]

Here, we present preliminary results from this Phase 2 study of patients with R/R cHL (NCT04052997) after meeting target enrollment (100 patients)

Zinzani PL et al. ICML Virtual Congress 2021;Abstract 075.

RTP RESEARCH TO PRACTICE

Response to Camidanlumab Tesirine for R/R cHL (Primary Study Endpoint)



ORR (CR + PR)
66.3% (67/101)
95% CI: 56.2, 75.4

No. of patients with CR
28 (27.7%)

No. of patients with PR
39 (38.6%)

No. of patients reporting HSCT as reason for discontinuation
9 (7.7%)[b]

Zinzani PL et al. ICML Virtual Congress 2021;Abstract 075.

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Most Common Treatment-Related Adverse Events (TEAEs) with Camidanlumab Tesirine

All-grade TEAEs in ≥20% of patients	Total (N=117)
Any TEAE of any grade	116 (99.1)
Fatigue	43 (36.8)
Maculopapular rash	33 (28.2)
Nausea	32 (27.4)
Pyrexia	31 (26.5)
Anemia	24 (20.5)

Grade ≥3 TEAEs in ≥5% of patients	Total (N=117)
Any TEAE Grade ≥3	62 (53.0)
Hypophosphatemia	9 (7.7)
Maculopapular rash	8 (6.8)
Thrombocytopenia	8 (6.8)
Anemia	7 (6.0)
Lymphopenia	7 (6.0)

All-grade TEAEs leading to dose delay, reduction or discontinuation	Total (N=117)
Dose delay or reduction	56 (47.9)
Discontinuation	16 (13.7)

Zinzani PL et al. ICML Virtual Congress 2021;Abstract 075.

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Incidence of Guillain-Barré Syndrome (GBS) and Polyradiculopathy with Camidanlumab Tesirine

Total: 7/117 (6.0%) patients. All events were deemed related or probably related to treatment

AE by preferred term	Study day event start–stop	Max grade	Grade at last assessment	Outcome at last assessment
Radiculopathy	Days 41–206	2	-	Recovered/resolved
GBS	Days 164–283	2	-	Recovered/resolved
GBS	Day 48–ongoing[b]	3	2	Not recovered/not resolved
Polyneuropathy (assessed as polyradiculopathy by Sponsor)[a]	Day 64–ongoing[b]	3	3	Recovering/resolving
GBS	Day 137–ongoing[b]	3	3	Not recovered/not resolved
GBS	Day 24–ongoing[b]	4	3	Not recovered/not resolved
GBS	Day 101–ongoing[b]	4	4	Not recovered/not resolved

[a] Additional events reported in the same patient included Grade 3 meningitis aseptic, which was recovering/resolving at last assessment; Grade 3 facial paralysis, not recovered/not resolved; and Grade 4 inappropriate antidiuretic hormone secretion, which recovered/resolved; all 3 events were considered related to treatment; [b] At last assessment prior to data cutoff.

Zinzani PL et al. ICML Virtual Congress 2021;Abstract 075.

RTP RESEARCH TO PRACTICE

Agenda
Management of Hodgkin and Non-Hodgkin Lymphomas

Module 1 – Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2 – Hodgkin Lymphoma (HL)

Module 3 – Follicular Lymphoma (FL)

Module 4 – Mantle Cell Lymphoma (MCL)

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Case 3 — Robin Klebig, APRN, CNP, AOCNP

- **66 yo female**
- **RN at Mayo Clinic**
- **Dx 2009 (age 53) with follicular NHL grade 1, stage IVA**
- **Rx: R-CHOP x 8 to PR**
  - **Notable side effects:**
    - **Hoarseness r/t GERD +/- vincristine**
    - **Painful plantar erythema, blisters & desquamation r/t doxorubicin**
  - **PET/CT showed PR after 6 cycles**
    - **Give additional 2 cycles of R-CHOP**
  - **CT at EOT:** *"given the limited information in regard to the meaning of the PET scan in follicular lymphoma that we will hold off on a PET"*

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Case 3 — Robin Klebig, APRN, CNP, AOCNP

Round 2

- **2013 (4 years later, age 57)**
- **Progressive bilateral pelvic lymphadenopathy (inguinal/femoral)**
- **Bx: FL grade 1**
- **Rx: ^{90}Y-ibritumomab tiuxetan**
  - **Notable side effects:**
    - **Platelet nadir 53K at 5 weeks**
    - **ANC nadir 0.93 at 7 weeks**
    - **No transfusions or infections**
- **EOT PET/CT: CR**

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Case 3 — Robin Klebig, APRN, CNP, AOCNP

Round 3

- **2017 (3 years later, age 60)**
- **Progression left femoral and bilateral inguinal nodes**
- **Bx: FL grade 1-2**
- **Rx: Rituximab monotherapy/maintenance x 2 years**
- **EOT CT: PR**

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Case 3 — Robin Klebig, APRN, CNP, AOCNP

Round 4

- **2020 (4 years later, age 64)**
- **Significant progression of abdominopelvic lymphadenopathy concerning for transformation, SUV max 12**
- **Bx: FL grade 1-2**
- **BR x 6**
  - **COVID era: 10/2020-2/2021**
  - **Notable side effects: Chemobrain – decided to retire**
- **EOT PET/CT: CR (Deauville 1)**

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Case 3 — Robin Klebig, APRN, CNP, AOCNP

- **Still doing well**
- **Watching for late effects**
  - **Cardiotoxicity**
  - **Secondary malignancies**
  - **Bone marrow failure (t-MNs)**

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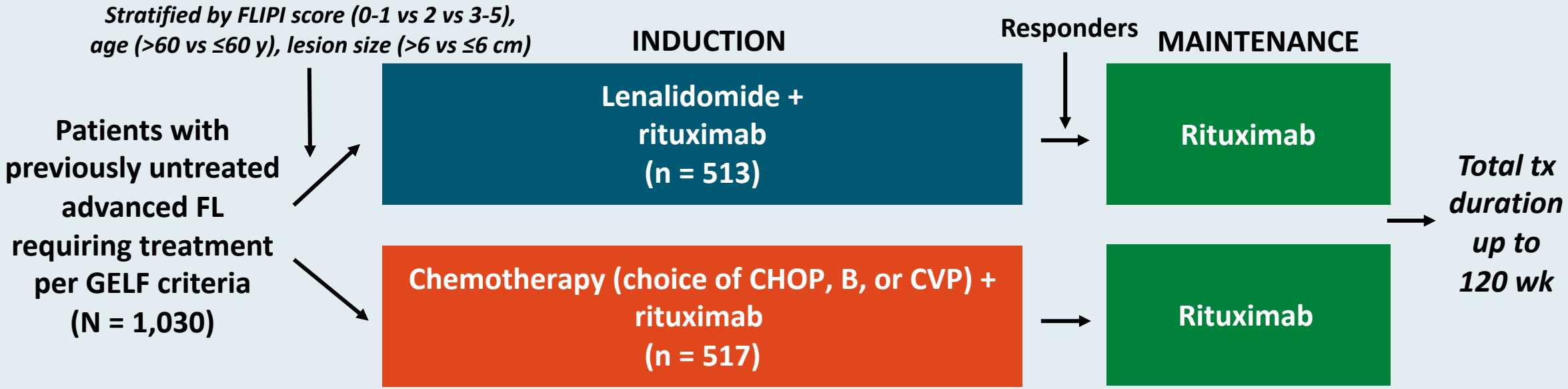
RELEVANCE: Study Design

- **International, open-label, randomized Phase III study**
  - **Lenalidomide: immunomodulatory agent with MoA complementary to rituximab**



- **Coprimary endpoints (superiority): Confirmed/unconfirmed complete response (CR/CRu) at 120 wk, PFS**

Morschhauser et al. *N Engl J Med* 2018;379:934. Fowler et al. *Lancet Oncol* 2014;15:1315.
Gribben et al. *J Clin Oncol* 2015;33:2803.

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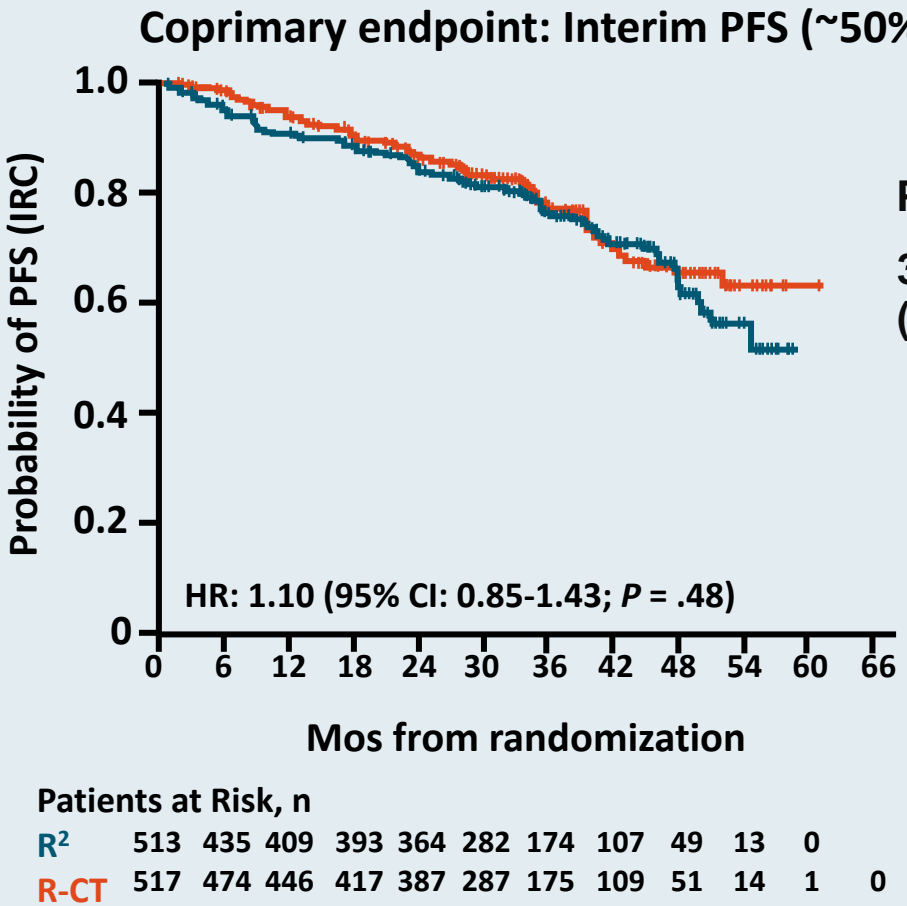
RELEVANCE: PFS by IRC



	R²	R-CT
Patients, n	513	517
3-y PFS, % (95% CI)	77 (72-80)	78 (74-82)

- **Interim PFS at median follow-up of 37.9 mo was similar in both arms**
- **PFS benefit observed across prespecified subgroups**

Morschhauser et al. *N Engl J Med* 2018;379:934.

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American Society of Hematology
Helping hematologists conquer blood diseases worldwide
2021; Abstract 815

Long Term Follow Up of RESORT – Rituximab Extended Schedule Or Retreatment Trial (E4402):

Brad Kahl, Fangxin Hong, Yemi Jegede, Christopher Peterson, Lode Swinnen, Thomas Habermann, Stephen Schuster, Matthias Weiss, Paul Fishkin, Christopher Ehmann, Tim Fenske, Michael Williams

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Original Conclusions *Kahl et al, JCO 2014*

- Rituximab retreatment was as effective as maintenance rituximab for time to treatment failure
- MR was superior of RR for time to cytotoxic therapy
- Both strategies appeared to delay time to chemotherapy compared to historical controls
- 4x more drug administered with MR strategy
- No benefit in QOL or anxiety with MR (Wagner et al, JCO 2015)

- Rituximab retreatment is our recommended strategy if opting for single agent rituximab in LTB FL

American Society *of* Hematology

63rd ASH® Annual Meeting and Exposition

Kahl B et al. ASH 2021;Abstract 815.

RTP RESEARCH TO PRACTICE

LTFU Conclusions

- Time to treatment failure outcomes unchanged with LTFU due to data lock
  - No difference between RR and MR
- Time to first cytotoxic therapy MR benefit increased over time
  - …but 63% of patients on RR strategy remained chemo-free at 7 years
- Duration of response favored MR
  - …but 30% of RR patients remained in 1st remission at 10 years
- No long-term safety signals with prolonged MR (2nd CA, Ig levels)
- ***No OS benefit for MR***
- 4x less drug utilized with the RR strategy
- A rituximab retreatment strategy remains our recommendation

American Society *of* Hematology

63rd ASH® Annual Meeting and Exposition

LTFU = long-term follow-up

Kahl B et al. ASH 2021;Abstract 815.

Obinutuzumab Short Duration Infusion Is Preferred by Healthcare Providers and Has Minimal Impact on Patient-Reported Symptoms Among Patients with Untreated, Advanced Follicular Lymphoma

Trask P et al.

ASH 2021;Abstract 1345.

Background: *The GAZELLE study is a prospective open label, multicenter, single arm, Phase IV study, which evaluated the safety of obinutuzumab (G) administered as a 90-minute short-duration infusion (SDI) from Cycle 2 (C2) onwards in patients with previously untreated advanced FL.*

Author conclusions: *Untreated, advanced FL patients had no or mild symptom severity and interference at baseline regardless of risk group. These low levels were maintained during G SDI administration. Additionally, SDI administration was preferred by providers for the time it saved, convenience, and comfort for patients, suggesting that G SDI administration can be a beneficial treatment option for untreated, advanced FL patients by minimizing patient treatment burden with no impact on health-related quality of life.*

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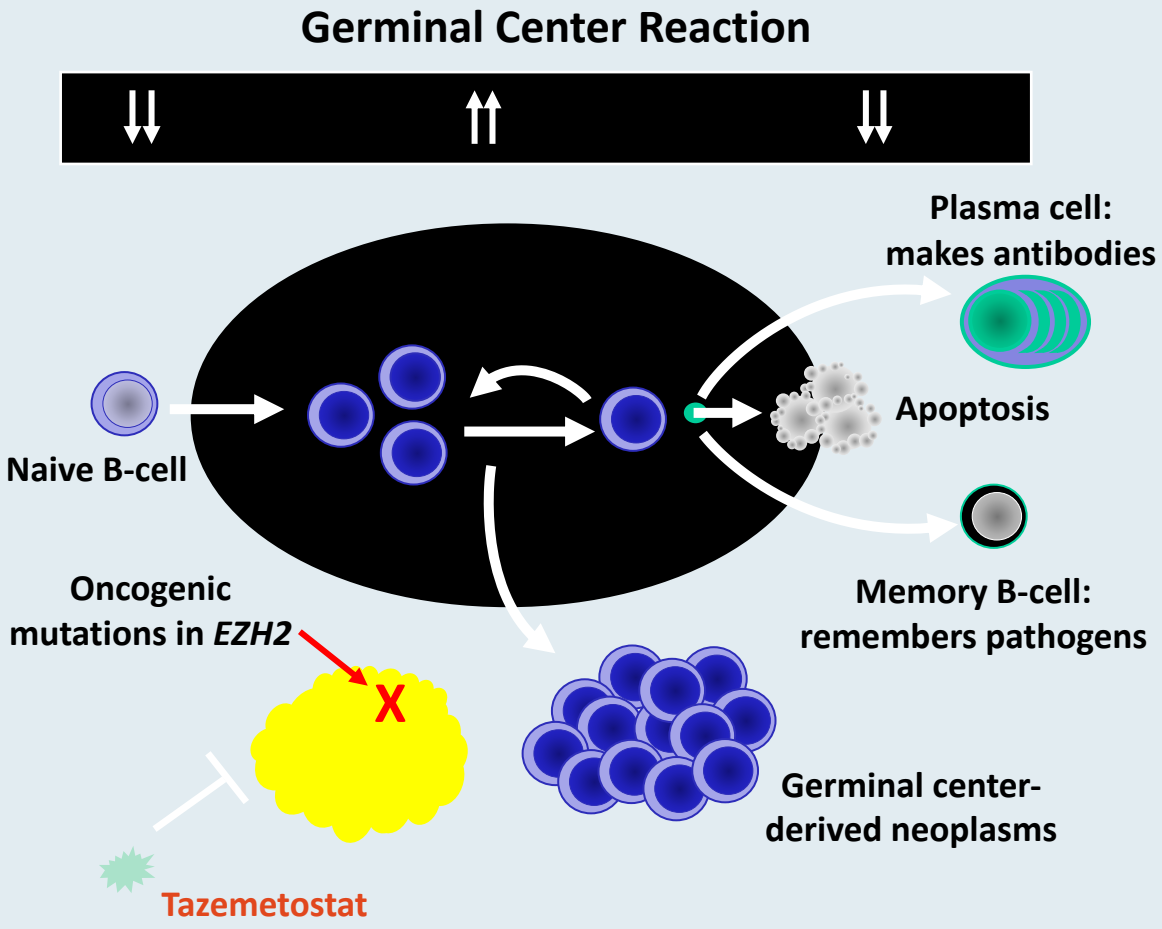
EZH2, a Histone Methyltransferase, in FL

- In normal B-cell biology, EZH2 regulates germinal center formation
- *EZH2* mutations can lead to oncogenic transformation by locking B-cells in germinal state and preventing terminal differentiation
- *EZH2*-activating mutations found in ~20% of patients with FL
- Tazemetostat: Selective, oral, first-in-class EZH2 inhibitor
- Whether WT or mutant, *EZH2* biology relevant to FL



Morschhauser. ICML 2019. Abstr 105.

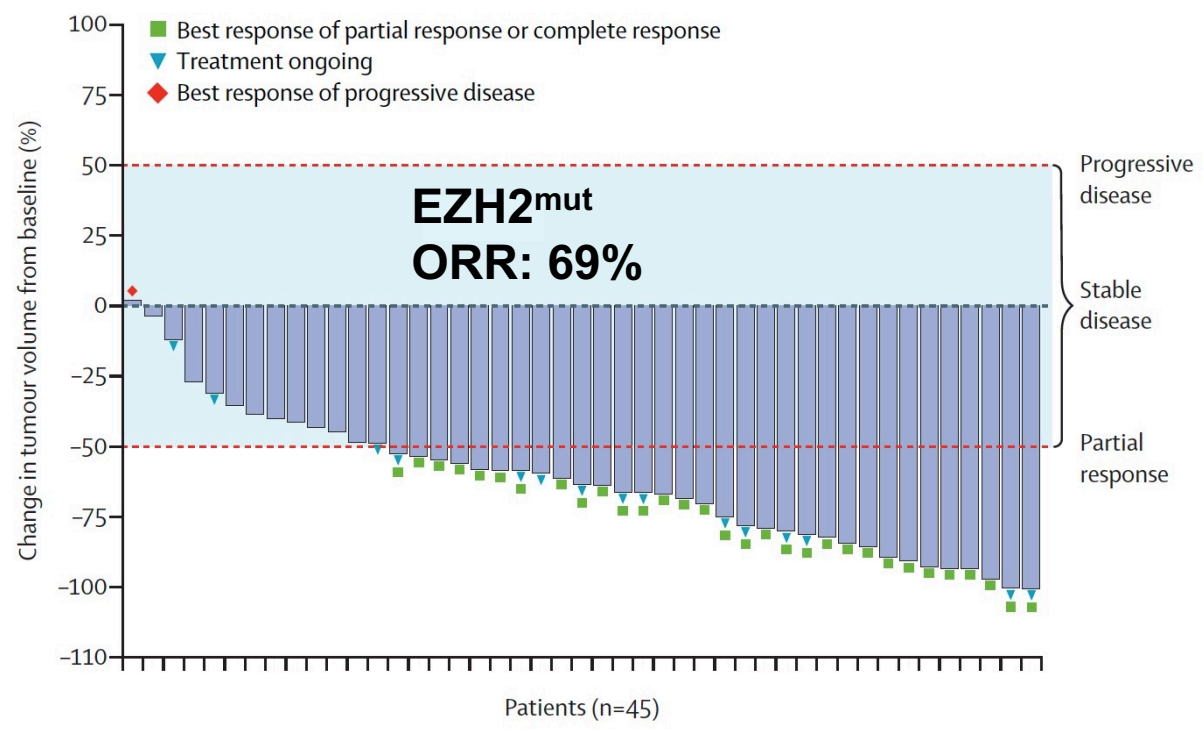
RTP RESEARCH TO PRACTICE

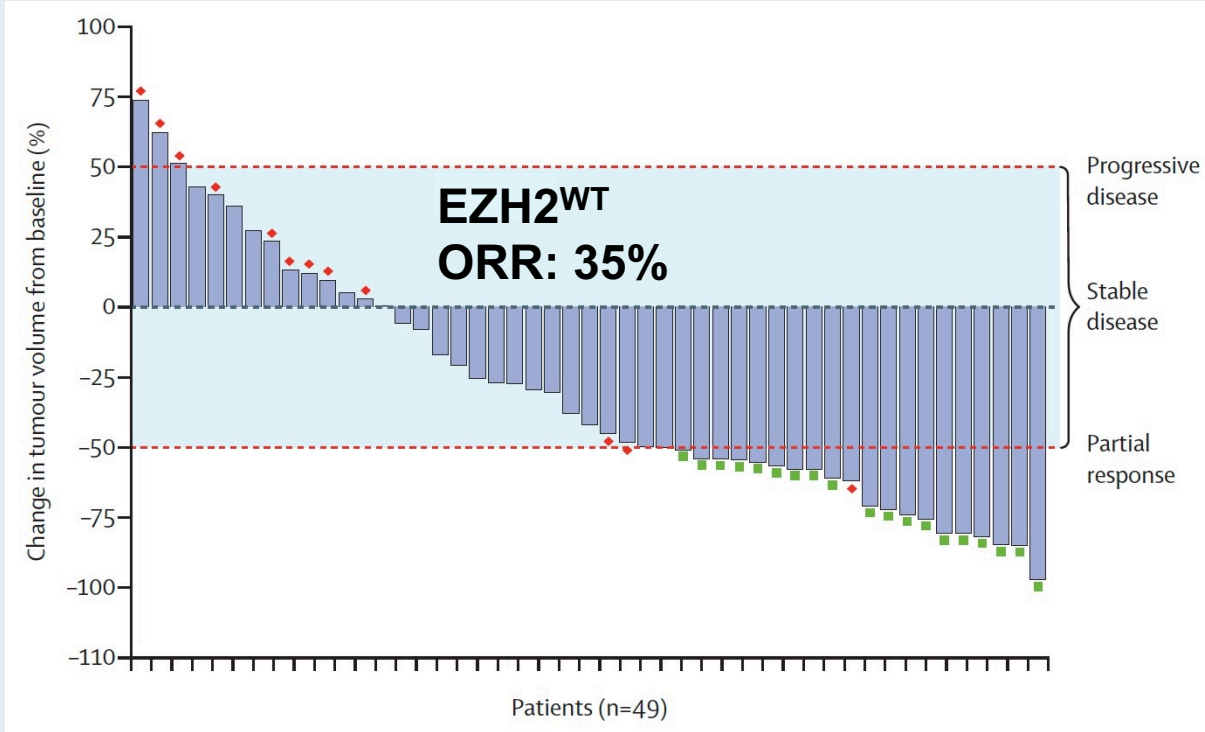
Lancet Oncol 2020;21(11):1433-42.

Tazemetostat for patients with relapsed or refractory follicular lymphoma: an open-label, single-arm, multicentre, phase 2 trial

Franck Morschhauser, Hervé Tilly, Aristeidis Chaidos, Pamela McKay, Tycel Phillips, Sarit Assouline, Connie Lee Batlevi, Phillip Campbell, Vincent Ribrag, Gandhi Laurent Damaj, Michael Dickinson, Wojciech Jurczak, Maciej Kazmierczak, Stephen Opat, John Radford, Anna Schmitt, Jay Yang, Jennifer Whalen, Shefali Agarwal, Deyaa Adib, Gilles Salles

Response to Tazemetostat in Patients with R/R FL and an EZH2 Mutation or EZH2 Wild-Type Tumors

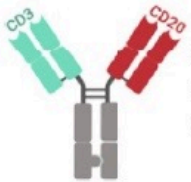
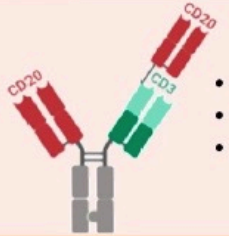
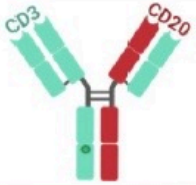




Morschhauser F et al. *Lancet Oncol* 2020;21(11):1433-42.

RTP RESEARCH TO PRACTICE

Structure of Selected Bispecific Antibodies

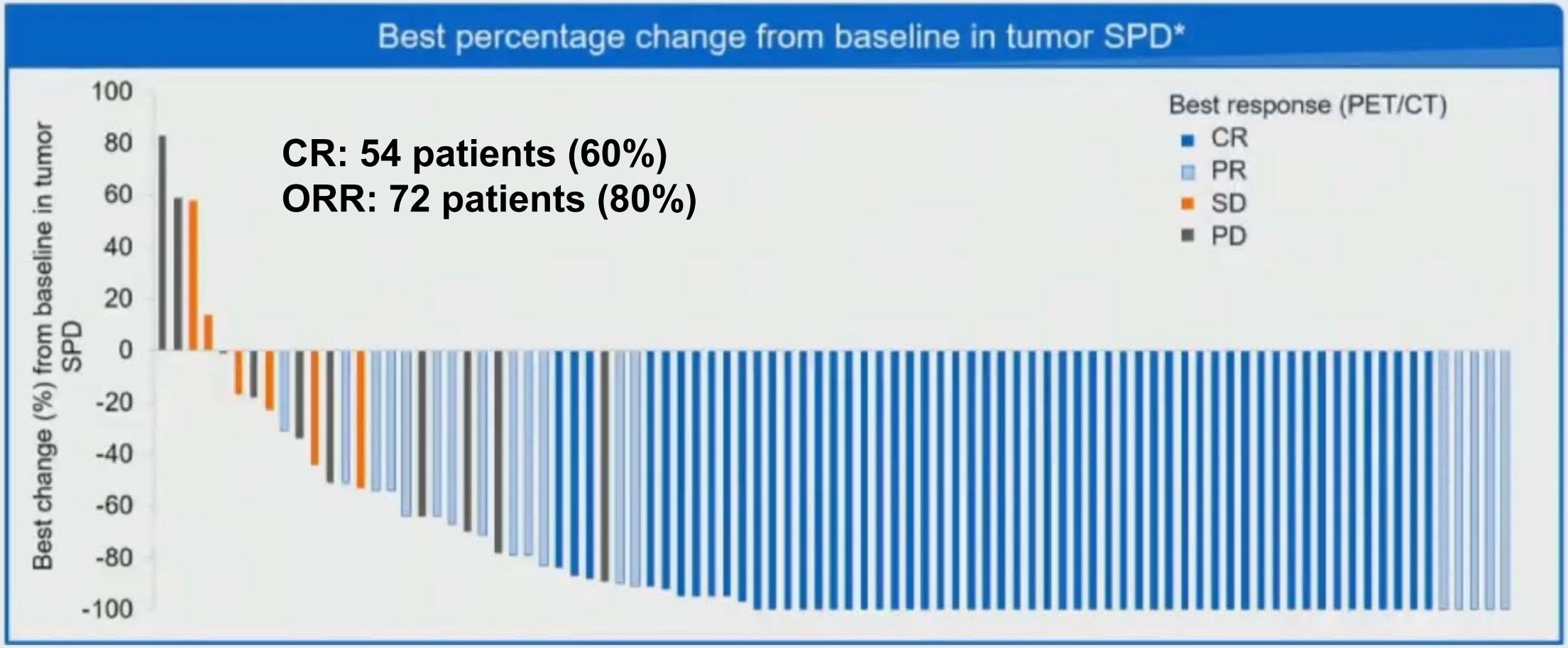
Bi-Specific Antibody	Targets	Design	Ig Fragment Formats
blinatumomab	CD19 x CD3		• two murine scFv joined by a glycine-serine linker • monovalent CD19 and monovalent CD3 binding • cloned from anti-CD19 (clone HD37) and anti-CD3 (clone L2K-07) murine mAbs
mosunetuzumab	CD20 x CD3		• humanized mouse heterodimeric IgG1-based antibody • monovalent CD20 and monovalent CD3ε binding • modified Fc devoid of FcγR and complement binding
glofitamab	$(CD20)_2$ x CD3		• humanized mouse IgG1-based antibody • bivalent CD20 and monovalent CD3ε binding • modified Fc devoid of FcγR and complement binding
odronextamab	CD20 x CD3		• fully human IgG4-based heterodimeric antibody • monovalent CD20 and monovalent CD3ε binding • Fc-dependent effector function-minimized antibody with Fc of the anti-CD3ε heavy chain modified to reduce Protein A binding • common κ light chain from anti-CD3ε mAb
epcoritamab	CD20 x CD3		• humanized mouse IgG1-based heterodimeric antibody • monovalent CD20 and monovalent CD3 binding • IgG1 Fc modified to minimize Fc-dependent effector functions and to control Fab-arm exchange of mAb half-molecules, resulting in high bispecific product yield

Ig, immunoglobulin; scFv, single-chain variable fragment; mAb, monoclonal antibody; Fc, fragment crystallizable; FcγR, Fc gamma receptor

Schuster SJ. *Hematol Oncol* 2021;39(S1):113-16.

RTP RESEARCH TO PRACTICE

Response to Mosunetuzumab Monotherapy in Patients with R/R FL Who Have Received ≥2 Lines of Therapy

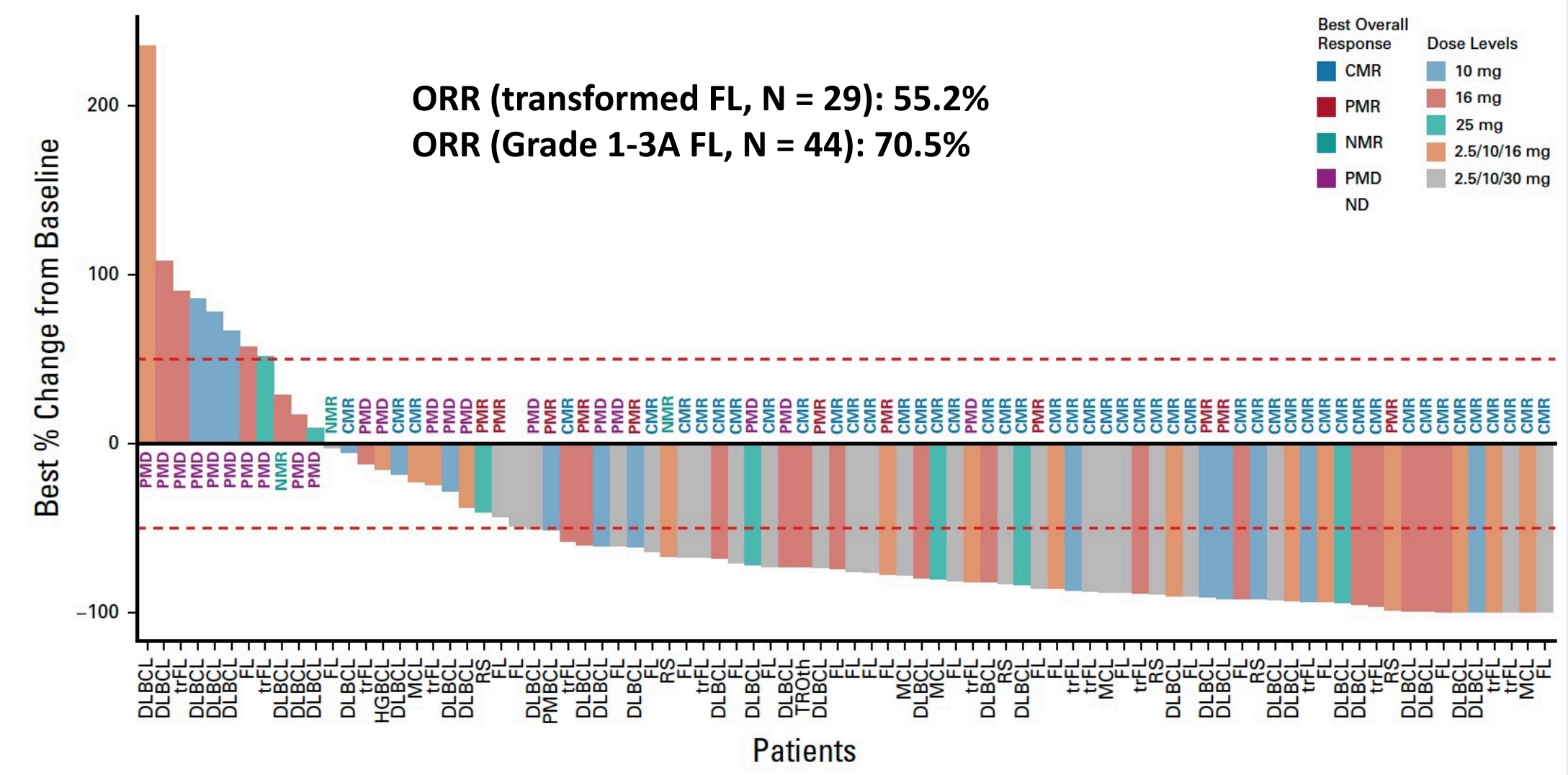


- Median DoR: 22.8 months
- Median PFS: 17.9 months

Budde EL et al. ASH 2021;Abstract 127.

RTP RESEARCH TO PRACTICE

Response to Glofitamab in Patients with R/R B-Cell Lymphomas



Hutchings M et al. *J Clin Oncol* 2021;39:1959-70.

Agenda
Management of Hodgkin and Non-Hodgkin Lymphomas

Module 1 – Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2 – Hodgkin Lymphoma (HL)

Module 3 – Follicular Lymphoma (FL)

Module 4 – Mantle Cell Lymphoma (MCL)

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TO PRACTICE

Case 4 — Robin Klebig, APRN, CNP, AOCNP

- 76 yo male
- Retired engineer
- Very active, Florida snowbird; plays better pickleball than 50-year-olds
- Dx 2014 (age 69): Stage IVA mantle cell with splenomegaly, lymphadenopathy, colon, marrow & peripheral blood involvement
- PMH: Melanoma, SCC, BPH
- Rx: BR x 6 to CR
    - Rituximab maintenance x 12 cycles completed June 2017

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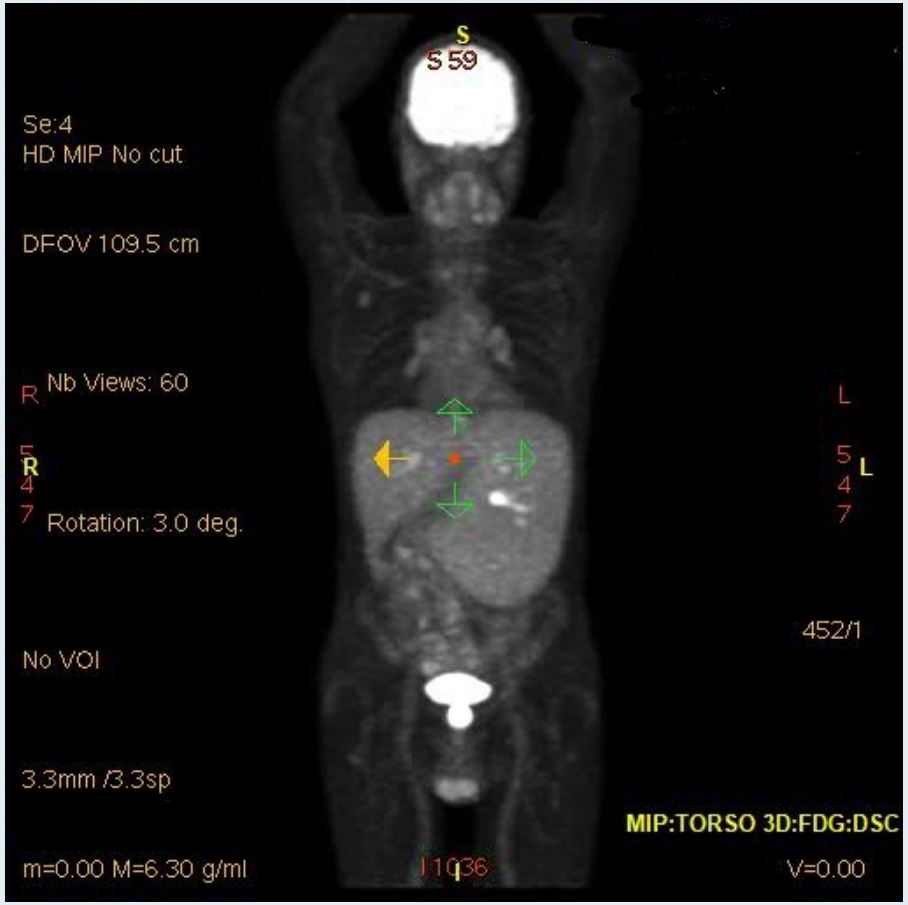
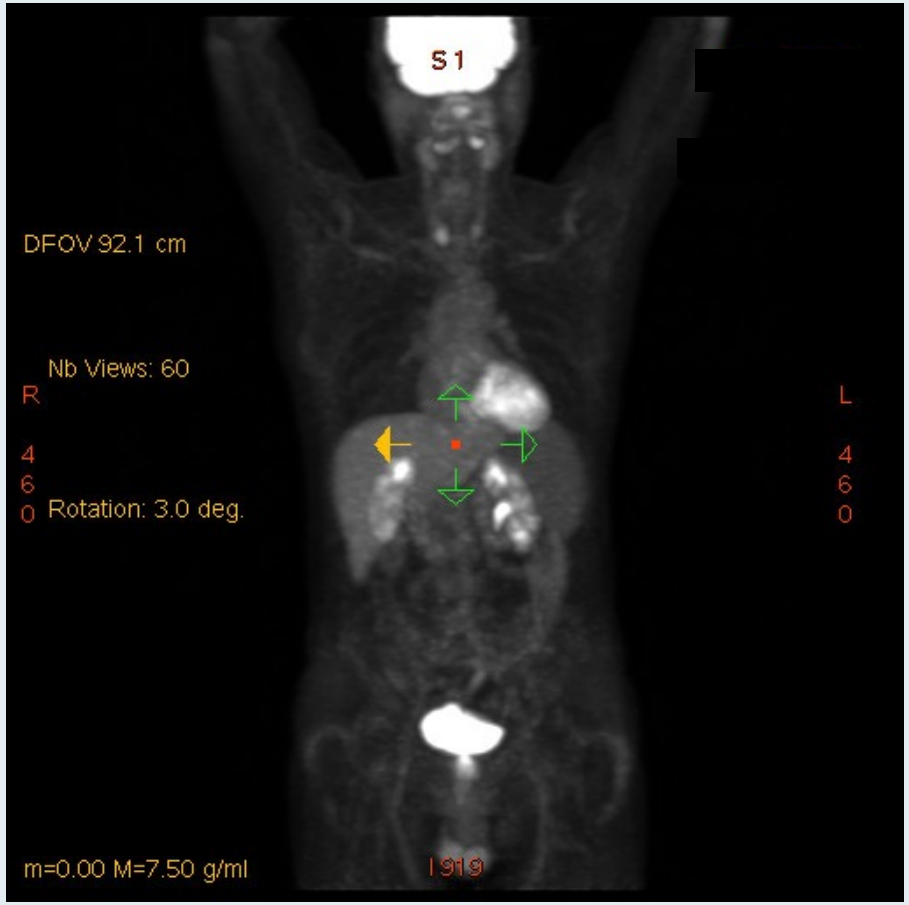
Case 4 — Robin Klebig, APRN, CNP, AOCNP

PET/CT before & after

January 9, 2015



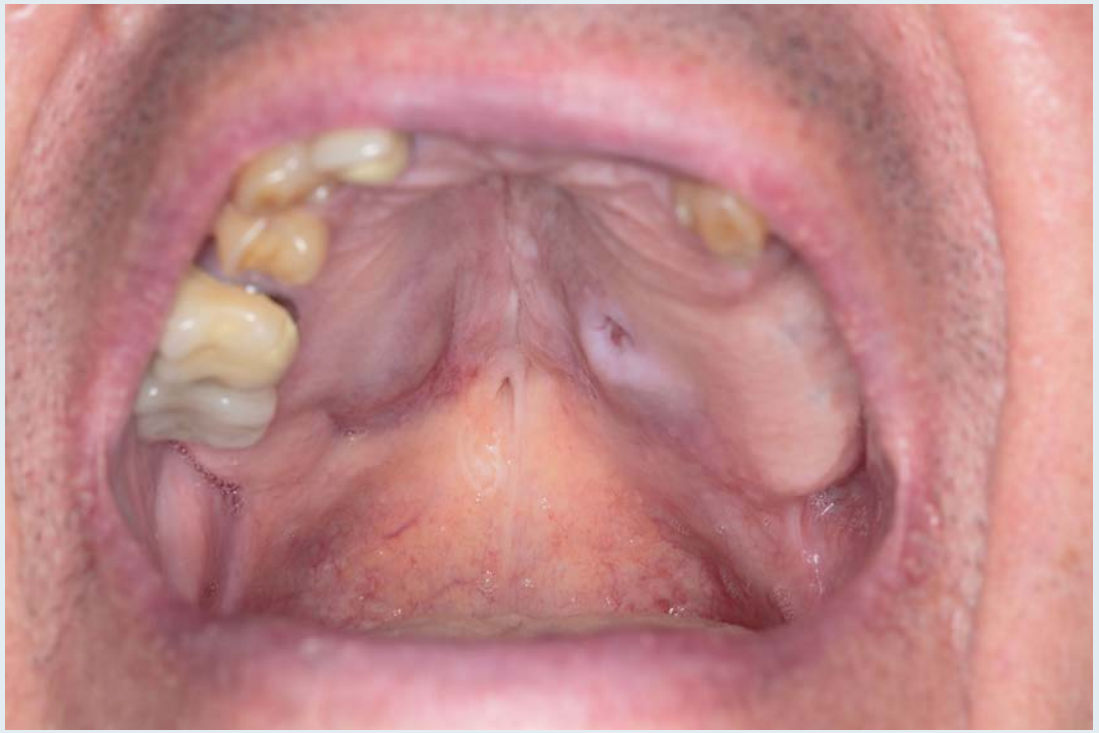
August 27, 2015



Case 4 — Robin Klebig, APRN, CNP, AOCNP

Relapsed MCL

- **December 2020 (5 years after BR, age 75)**
- **Upper denture rubbing against palate**
- **Bx: Recurrent MCL**
- **PET/CT: Involvement of palate, possible right posterior nasopharynx**



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Case 4 — Robin Klebig, APRN, CNP, AOCNP

BTKi for relapsed MCL

- **December 2020 – initiated acalabrutinib**
  - **Notable side effects: Headaches**
  - **1 month on treatment: Palate lesion resolved**
- **PET/CT – difficult area to assess for CMR due to physiologic uptake in palate**
- **Continues on therapy**

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TO PRACTICE

Primary Results From the Double-Blind, Placebo-Controlled, Phase III SHINE Study of Ibrutinib in Combination With Bendamustine-Rituximab and Rituximab Maintenance as a First-Line Treatment for Older Patients With Mantle Cell Lymphoma

Michael L. Wang,[1] Wojciech Jurczak,[2] Mats Jerkeman,[3] Judith Trotman,[4] Pier Luigi Zinzani,[5] Jan Walewski,[6] Jun Zhu,[7] Stephen E. Spurgeon,[8] Andre Goy,[9] Paul A. Hamlin,[10] David Belada,[11] Muhit Özcan,[12] John M. Storring,[13] David Lewis,[14] José-Ángel Hernández-Rivas,[15] Todd Henninger,[16] Sanjay Deshpande,[16] Rui Qin,[16] Steven Le Gouill*,[17] Martin Dreyling*[18]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Maria Sklodowska-Curie National Research Institute of Oncology, Kraków, Poland; [3]Skane University Hospital and Lund University, Lund, Sweden; [4]Concord Repatriation General Hospital, University of Sydney, Sydney, NSW, Australia; [5]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale Università di Bologna, Bologna, Italy; [6]Maria Sklodowska-Curie National Research Institute of Oncology, Warszawa, Poland; [7]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Lymphoma, Peking University Cancer Hospital & Institute (Beijing Cancer Hospital), Beijing, China; [8]Division of Hematology and Medical Oncology, Oregon Health & Science University, Portland, OR, USA; [9]John Theurer Cancer Center, Hackensack, NJ, USA; [10]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [11]4th Department of Internal Medicine - Haematology, Charles University, Hospital and Faculty of Medicine, Hradec Králové, Czech Republic; [12]Ankara University School of Medicine, Ankara, Turkey; [13]The Research Institute of the McGill University Health Centre, McGill University, Montreal, Quebec, Canada; [14]University Hospitals Plymouth NHS Trust, Plymouth, United Kingdom; [15]Department of Hematology, Hospital Universitario Infanta Leonor, Universidad Complutense, Madrid, Spain; [16]Janssen Research & Development, Raritan, NJ, USA; [17]Institut Curie Comprehensive Cancer Center, Paris, France; Hospitalier Universitaire de Nantes at the time of the present work; [18]Klinikum der Universität München, LMU, Munich, Germany.

*Professors Le Gouill and Dreyling contributed equally.

Presented at ASCO 2022 Annual Meeting; June 3-7, 2022; Chicago, IL, USA.

Abstract LBA7502

https://www.congresshub.com/Oncology/AM2022/Ibrutinib/Wang

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The NEW ENGLAND JOURNAL of MEDICINE

Published on 3rd June 2022

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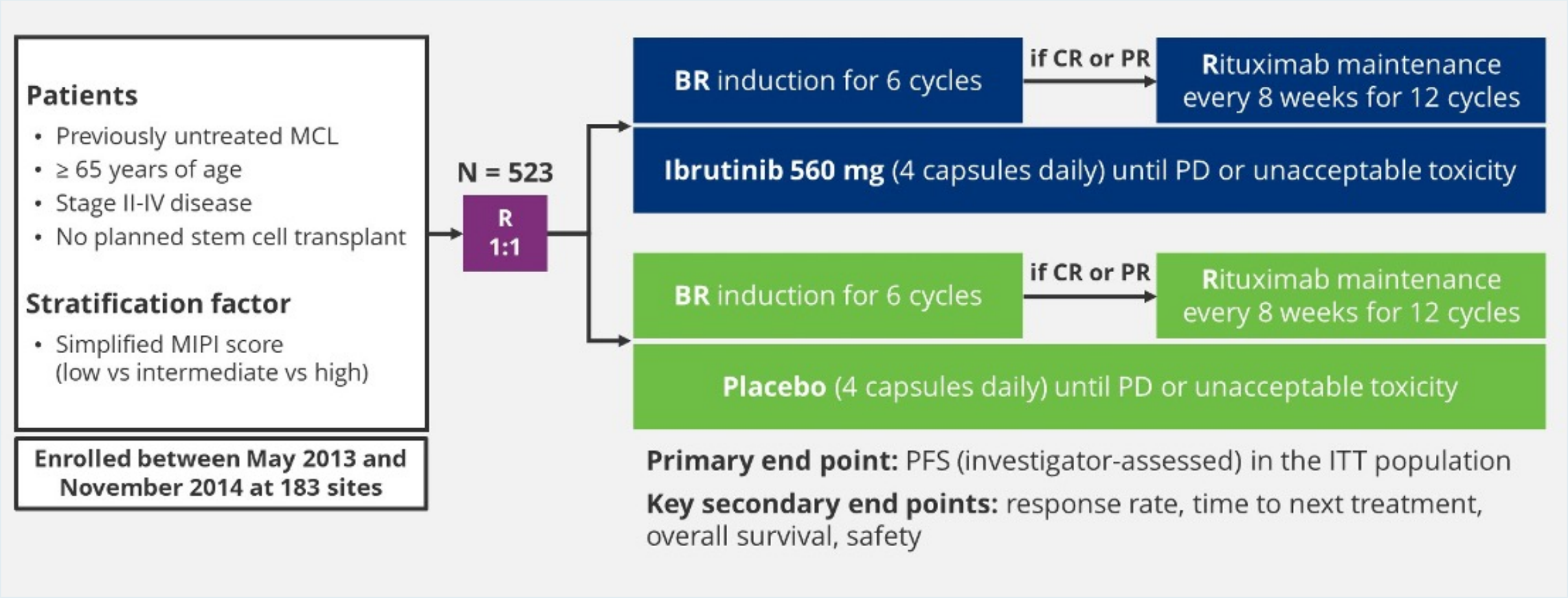
ORIGINAL ARTICLE

Ibrutinib plus Bendamustine and Rituximab in Untreated Mantle-Cell Lymphoma

Michael L. Wang, M.D., Wojciech Jurczak, M.D., Ph.D., Mats Jerkeman, M.D., Ph.D., Judith Trotman, F.R.A.C.P., Pier L. Zinzani, M.D., Ph.D., David Belada, M.D., Ph.D., Carola Boccomini, M.D., Ian W. Flinn, M.D., Ph.D., Pratyush Giri, F.R.A.C.P., Andre Goy, M.D., Paul A. Hamlin, M.D., Olivier Hermine, M.D., Ph.D., José-Ángel Hernández-Rivas, M.D., Ph.D., Xiaonan Hong, M.D., Seok Jin Kim, M.D., Ph.D., David Lewis, F.R.C.Path., Ph.D., Yuko Mishima, M.D., Ph.D., Muhit Özcan, M.D., Guilherme F. Perini, M.D., Christopher Pocock, M.D., Ph.D., Yuqin Song, M.D., Ph.D., Stephen E. Spurgeon, M.D., John M. Storring, M.D., Jan Walewski, M.D., Jun Zhu, M.D., Ph.D., Rui Qin, Ph.D., Todd Henninger, Ph.D., Sanjay Deshpande, M.D., Angela Howes, Ph.D., Steven Le Gouill, M.D., Ph.D., and Martin Dreyling, M.D., for the SHINE Investigators*

RTP RESEARCH TO PRACTICE

SHINE: Phase III Study Design



BR = bendamustine/rituximab

Wang ML et al. ASCO 2022;Abstract LBA7502.

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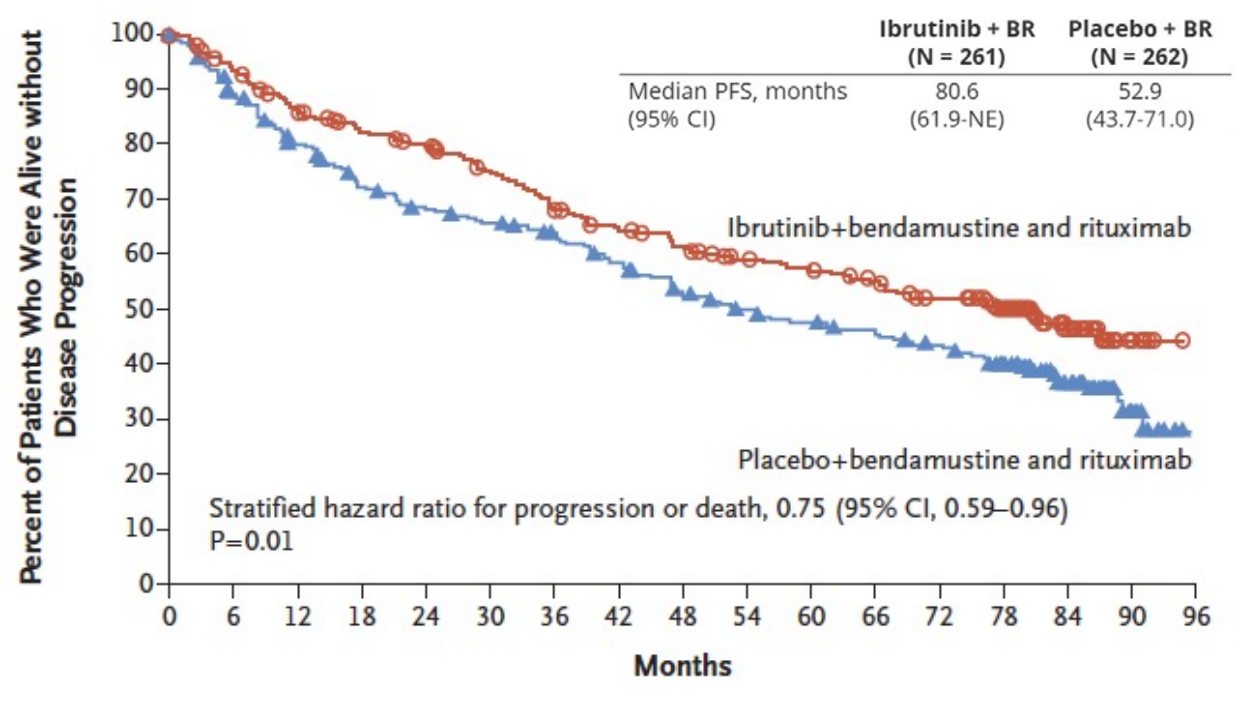
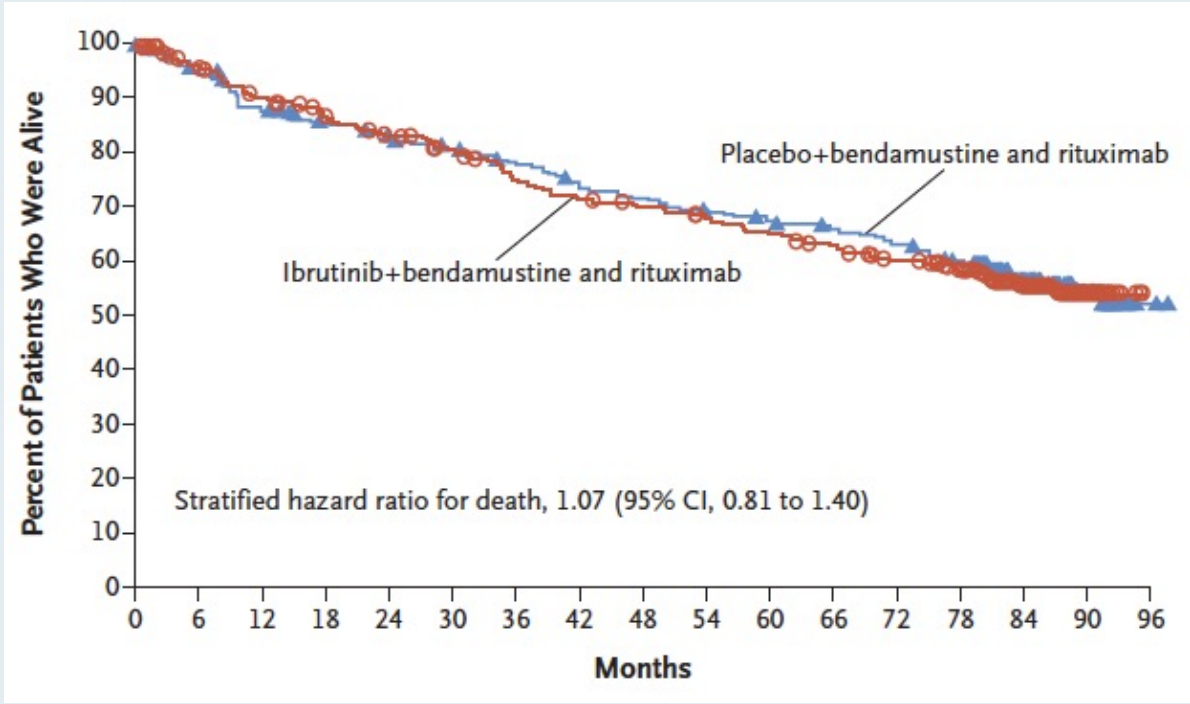
SHINE: Survival Outcomes

Progression-free survival (primary endpoint)



Overall survival (secondary endpoint)



Wang ML et al. *N Engl J Med* 2022;[Online ahead of print]; ASCO 2022;Abstract LBA7502.

RTP RESEARCH TO PRACTICE

SHINE: Adverse Events of Clinical Interest

	Ibrutinib + BR (N = 259)		Placebo + BR (N = 260)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Any bleeding	42.9%	3.5%	21.5%	1.5%
Major bleeding	5.8%	–	4.2%	–
Atrial fibrillation	13.9%	3.9%	6.5%	0.8%
Hypertension	13.5%	8.5%	11.2%	5.8%
Arthralgia	17.4%	1.2%	16.9%	0

Wang ML et al. *N Engl J Med* 2022;[Online ahead of print]; ASCO 2022;Abstract LBA7502.

RTP RESEARCH TO PRACTICE

N Engl J Med 2020;382(14):1331-42.

The NEW ENGLAND JOURNAL of MEDICINE

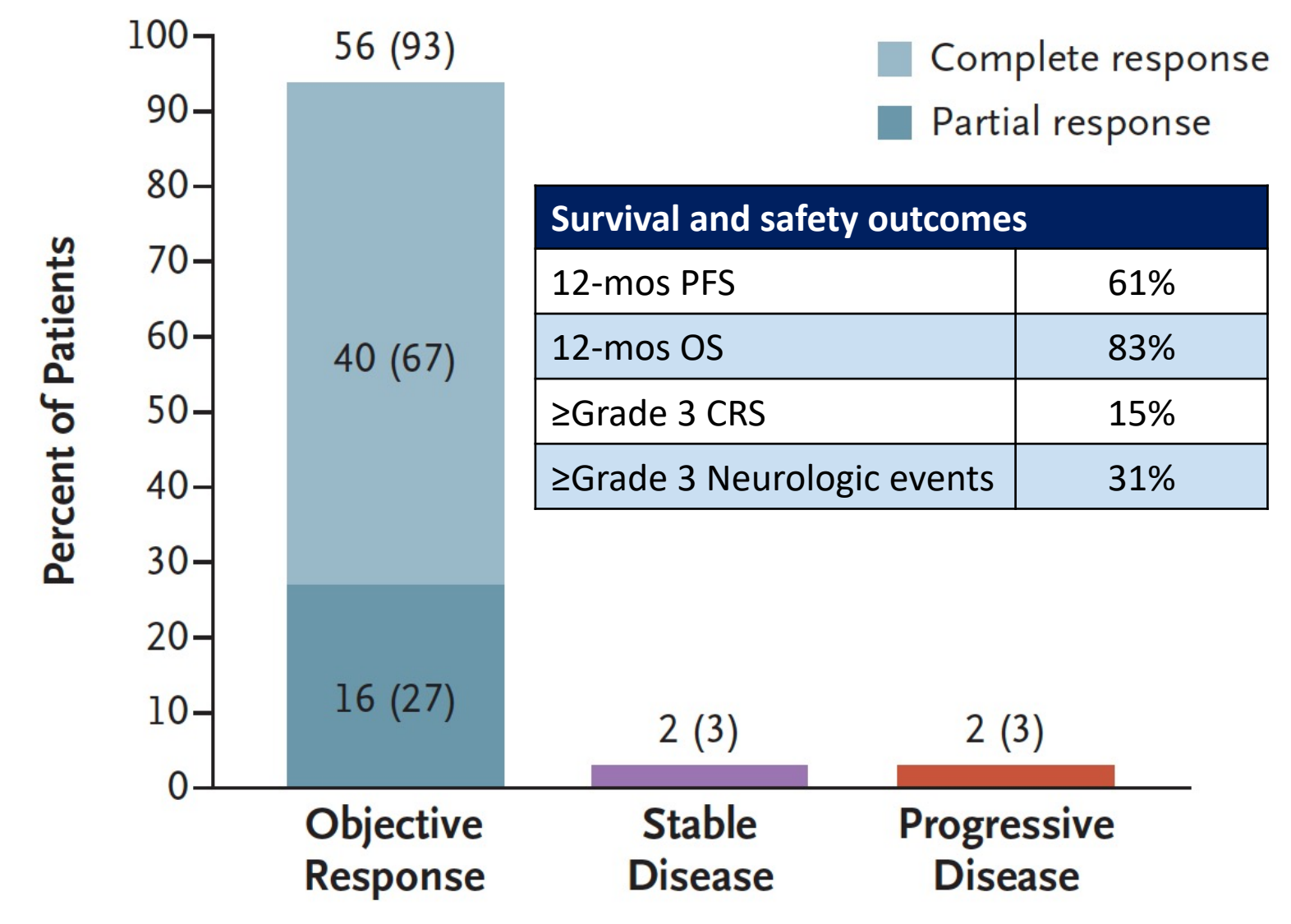
ORIGINAL ARTICLE

KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma

M. Wang, J. Munoz, A. Goy, F.L. Locke, C.A. Jacobson, B.T. Hill, J.M. Timmerman, H. Holmes, S. Jaglowski, I.W. Flinn, P.A. McSweeney, D.B. Miklos, J.M. Pagel, M.-J. Kersten, N. Milpied, H. Fung, M.S. Topp, R. Houot, A. Beitinjaneh, W. Peng, L. Zheng, J.M. Rossi, R.K. Jain, A.V. Rao, and P.M. Reagan

RTP RESEARCH TO PRACTICE

ZUMA-2: Response Rates, Survival and Select Safety Outcomes with Brexucabtagene Autoleucel for Mantle Cell Lymphoma



Survival and safety outcomes	
12-mos PFS	61%
12-mos OS	83%
≥Grade 3 CRS	15%
≥Grade 3 Neurologic events	31%

Wang M et al. *N Engl J Med* 2020;382(14):1331-42.

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Appendix of Recent Data Sets

Diffuse Large B-Cell Lymphoma

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TO PRACTICE

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]

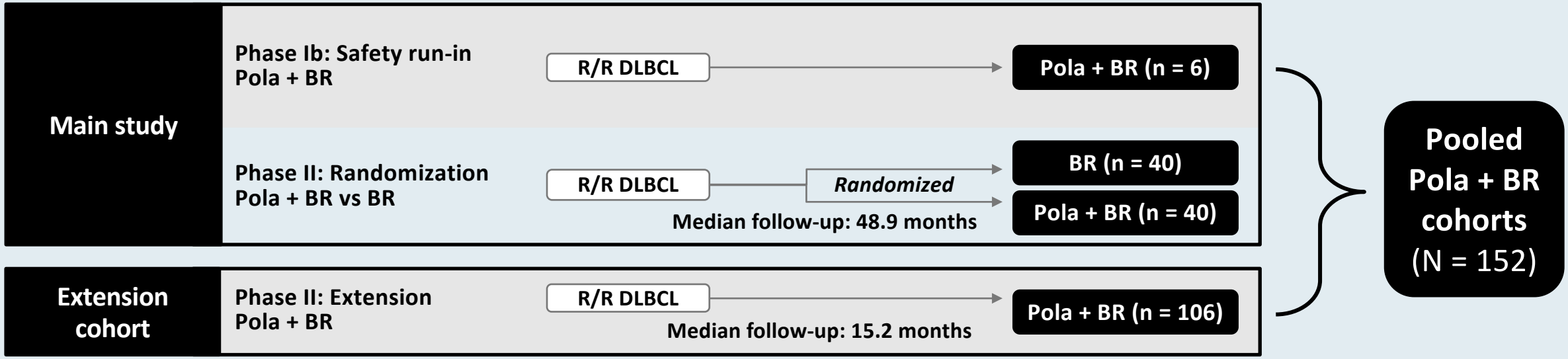
***Blood Adv* 2022;6(2):533-43.**

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

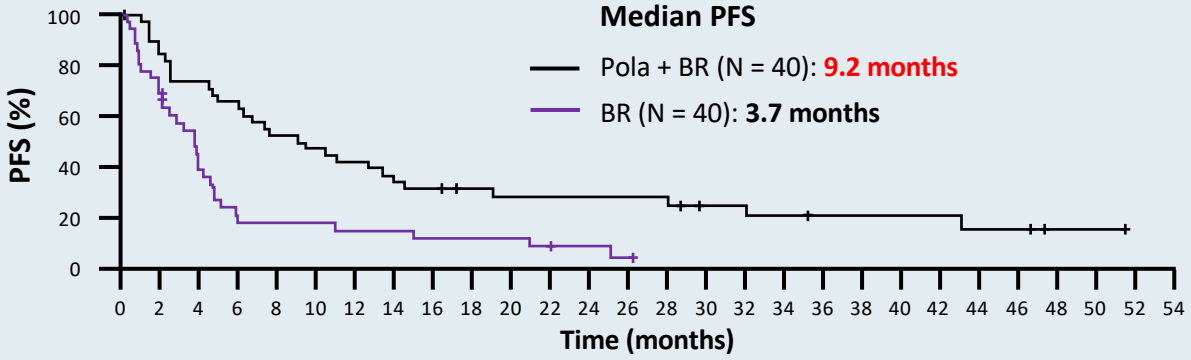
Pola 1.8 mg/kg on day 1 of each cycle of BR; up to 6 cycles at 3-weekly interval

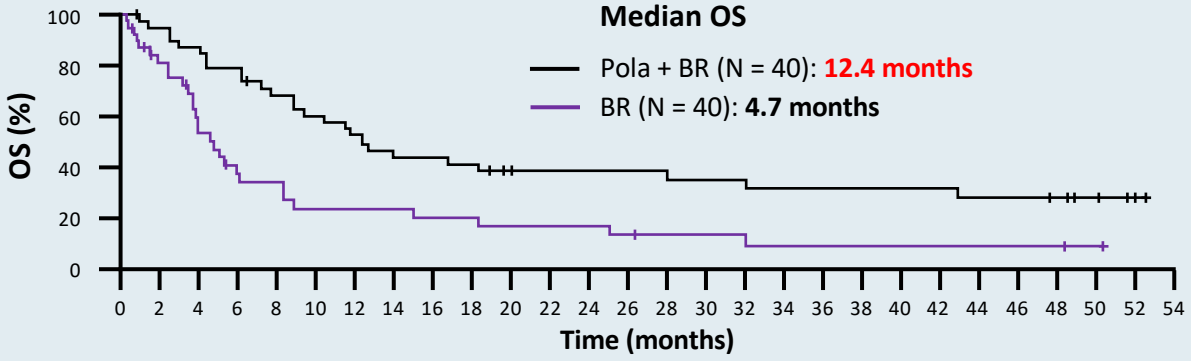
Sehn LH et al. *Blood Adv* 2022;6(2):533-43.

RTP RESEARCH TO PRACTICE

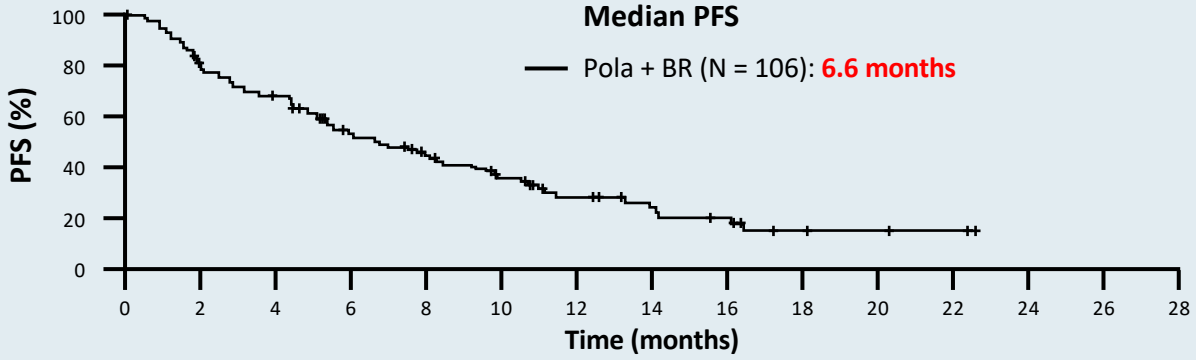
GO29365: PFS and OS in Randomized and Extension Cohorts

Randomized

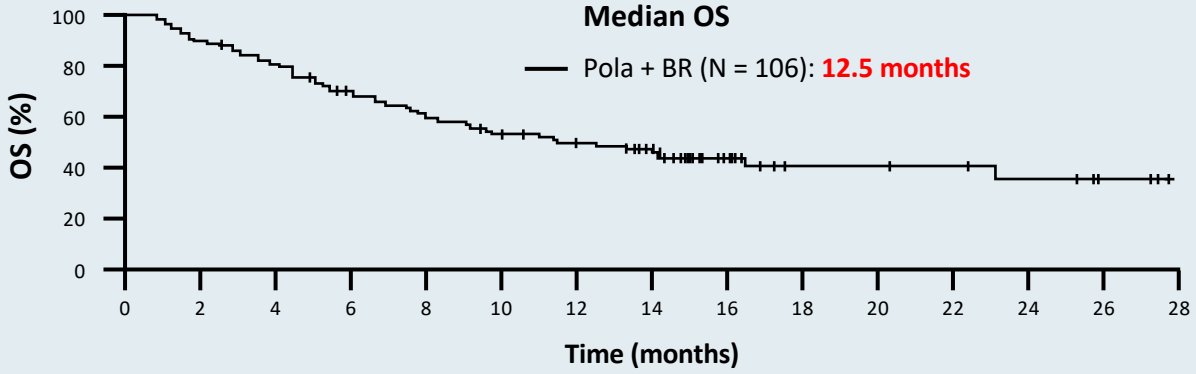




Extension cohort



Pola+BR



Randomized cohort:

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

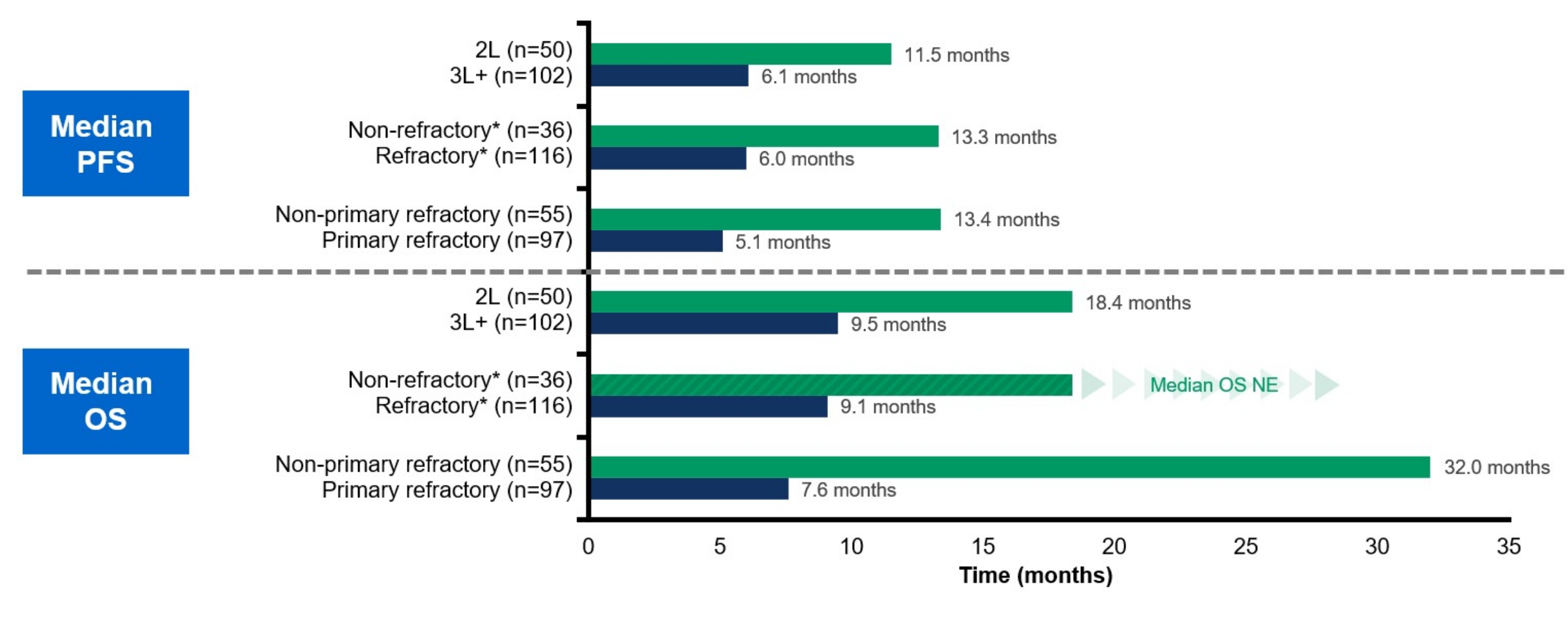
Pooled cohort

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

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

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.

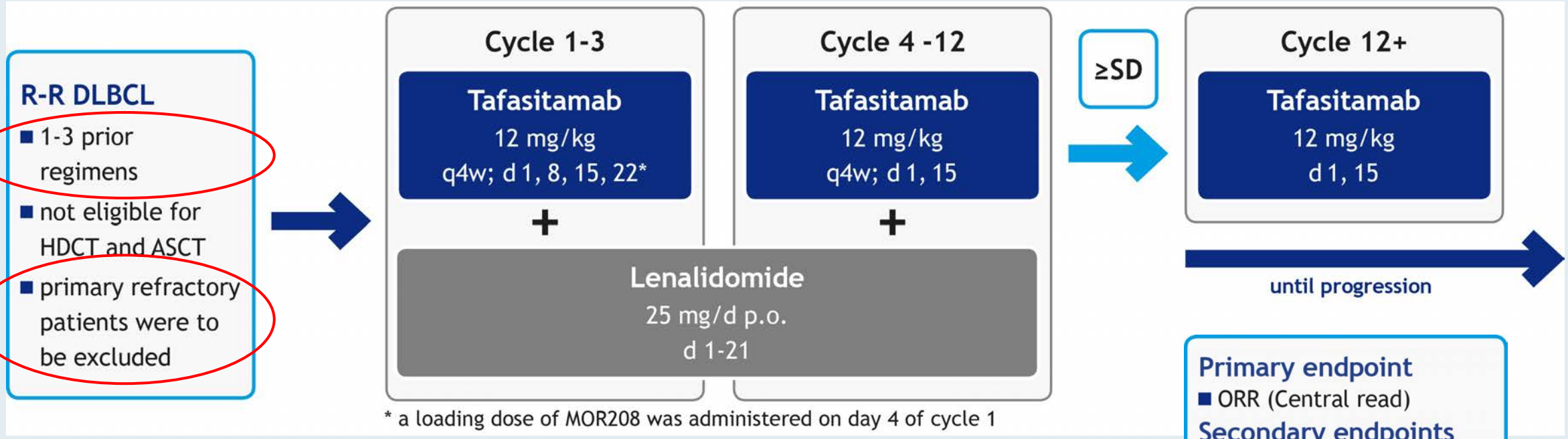
Lancet Oncol 2020;21(7):978-88.

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

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

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

L-MIND: Phase II Study Design



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

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

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

RTP RESEARCH TO PRACTICE

FDA Grants Accelerated Approval to Loncastuximab Tesirine-lpyl for Large B-Cell Lymphoma

Press Release – April 23, 2021

"The Food and Drug Administration granted accelerated approval to loncastuximab tesirine-lpyl, a CD19-directed antibody and alkylating agent conjugate, for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma.

Approval was based on LOTIS-2 (NCT03589469), an open-label, single-arm trial in 145 adult patients with relapsed or refractory DLBCL or high-grade B-cell lymphoma after at least two prior systemic regimens. Patients received loncastuximab tesirine-lpyl 0.15 mg/kg every 3 weeks for 2 cycles, then 0.075 mg/kg every 3 weeks for subsequent cycles. Patients received treatment until progressive disease or unacceptable toxicity."

www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-loncastuximab-tesirine-lpyl-large-b-cell-lymphoma

RTP RESEARCH TO PRACTICE

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

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

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

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

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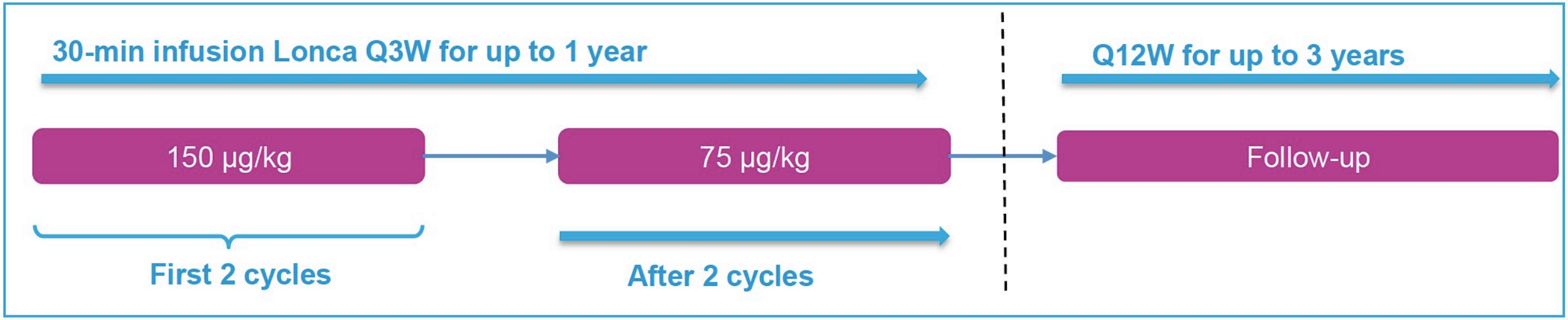
LOTIS-2: Phase II Trial Design

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

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



ORR = overall response rate; Lonca = loncastuximab tesirine

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

RTP RESEARCH TO PRACTICE

FDA Approves Lisocabtagene Maraleucel for R/R Large B-Cell Lymphoma

Press Release – February 5, 2021

"The Food and Drug Administration approved lisocabtagene maraleucel for the treatment of adult patients with relapsed or refractory (R/R) large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B.

Lisocabtagene maraleucel is a CD19-directed chimeric antigen receptor (CAR) T cell immunotherapy. It consists of autologous T cells that are genetically modified to produce a CAR protein, allowing the T cells to identify and eliminate CD19-expressing normal and malignant cells.

Efficacy was evaluated in TRANSCEND (NCT02631044), a single-arm, open label, multicenter trial that evaluated lisocabtagene maraleucel, preceded by lymphodepleting chemotherapy, in adults with R/R large B-cell lymphoma after at least two lines of therapy."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-lisocabtagene-maraleucel-relapsed-or-refractory-large-b-cell-lymphoma

RTP RESEARCH TO PRACTICE

Characteristics of Pivotal Trials of Axi-cel and Tisagenlecleucel

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

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

RTP RESEARCH TO PRACTICE

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

CRS — May be mild or life-threatening

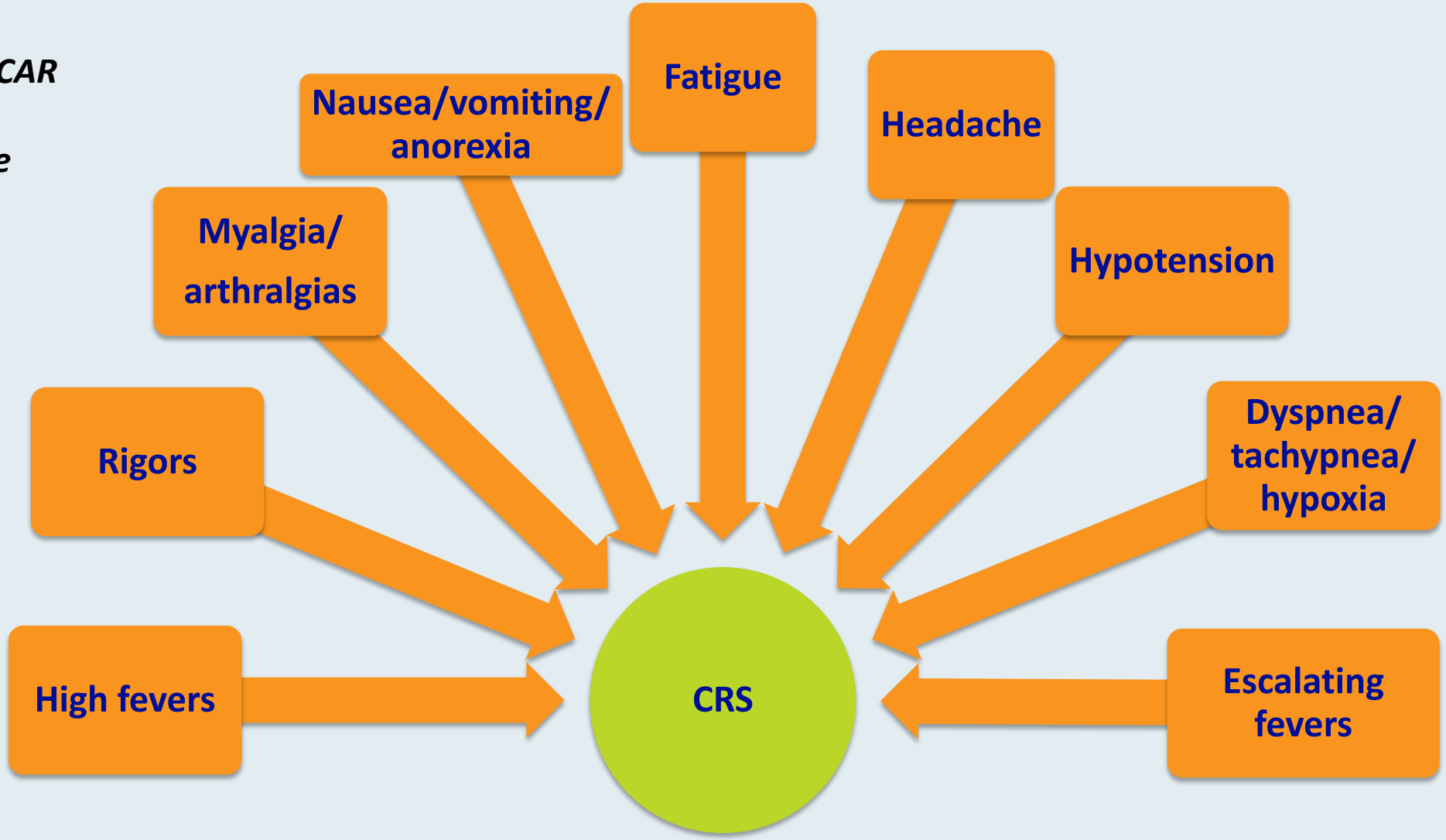
- Occurs with CART19 activation and expansion
- Dramatic cytokine elevations (IL-6, IL10, IFNɣ, CRP, ferritin)
- Fevers initially (can be quite high: 105˚F)
- Myalgias, fatigue, nausea/anorexia
- Capillary leak, headache, hypoxia and hypotension
- CRS-related mortality 3% to 10%

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

RTP RESEARCH TO PRACTICE

Cytokine Release Syndrome (CRS): Common Symptoms

Based on CAR T-cell experience



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

RTP RESEARCH TO PRACTICE

CAR T-Cell Therapy-Associated Neurologic Toxicity

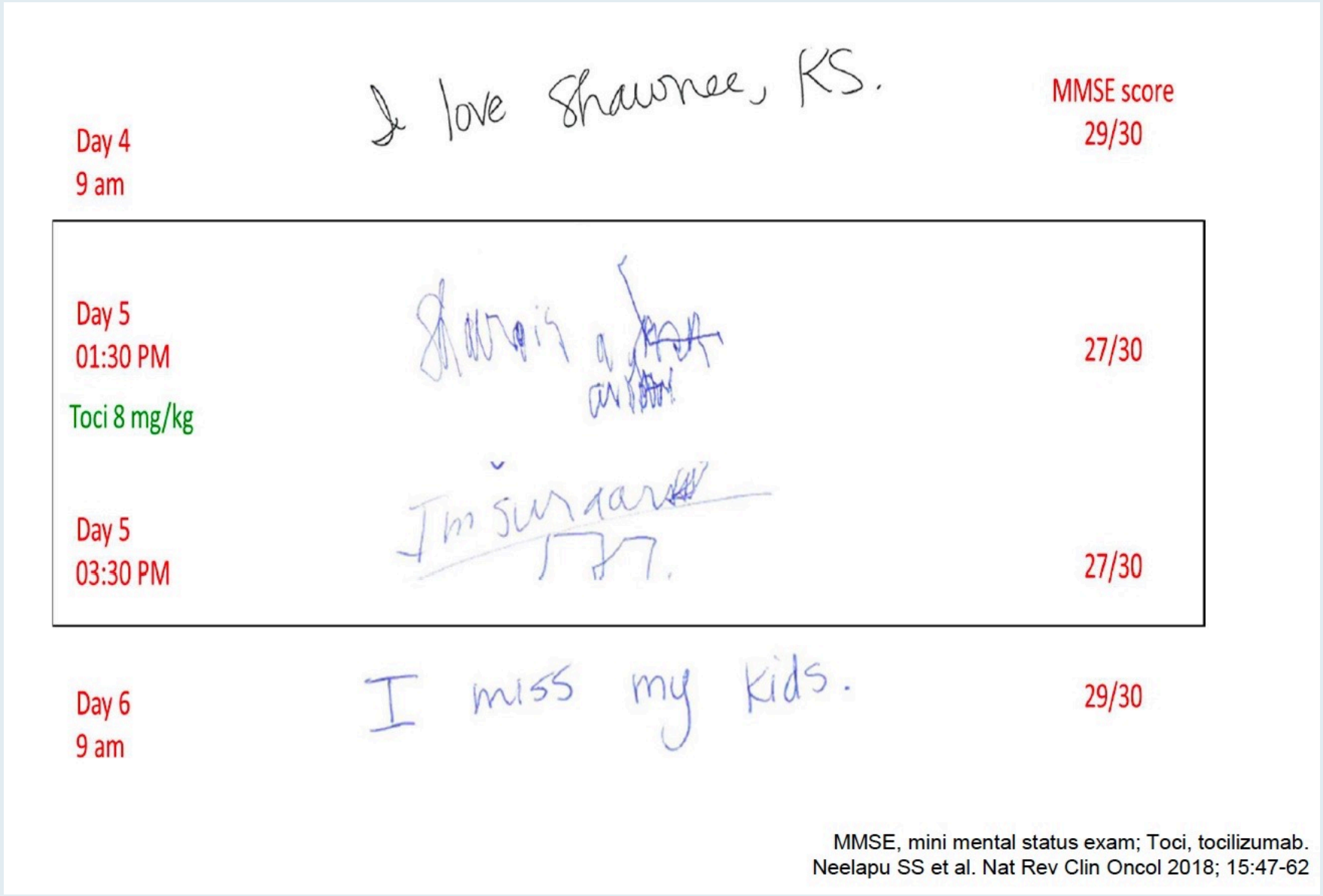
Neurologic toxicity — May be mild or life-threatening

- 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.

RTP RESEARCH TO PRACTICE

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



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

RTP RESEARCH TO PRACTICE

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

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Nat Med 2022;[Online ahead of print].

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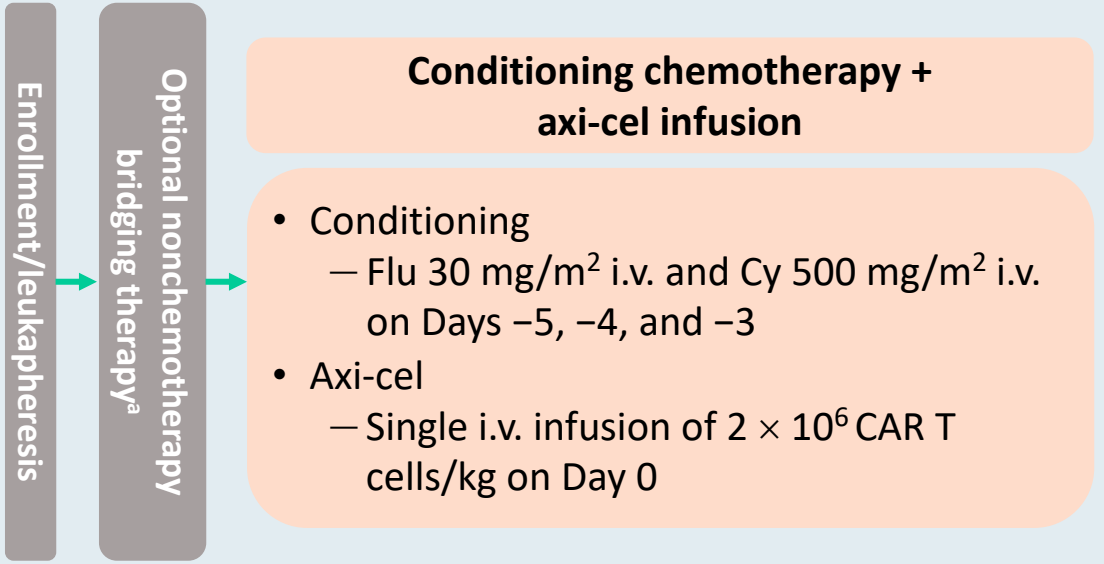
Multicenter Phase II ZUMA-12 Schema: First-Line Therapy

Eligibility criteria

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



Primary endpoint

- CR (complete response)[b]

Key secondary endpoints

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

Neelapu SS et al. ASH 2020;Abstract 405.

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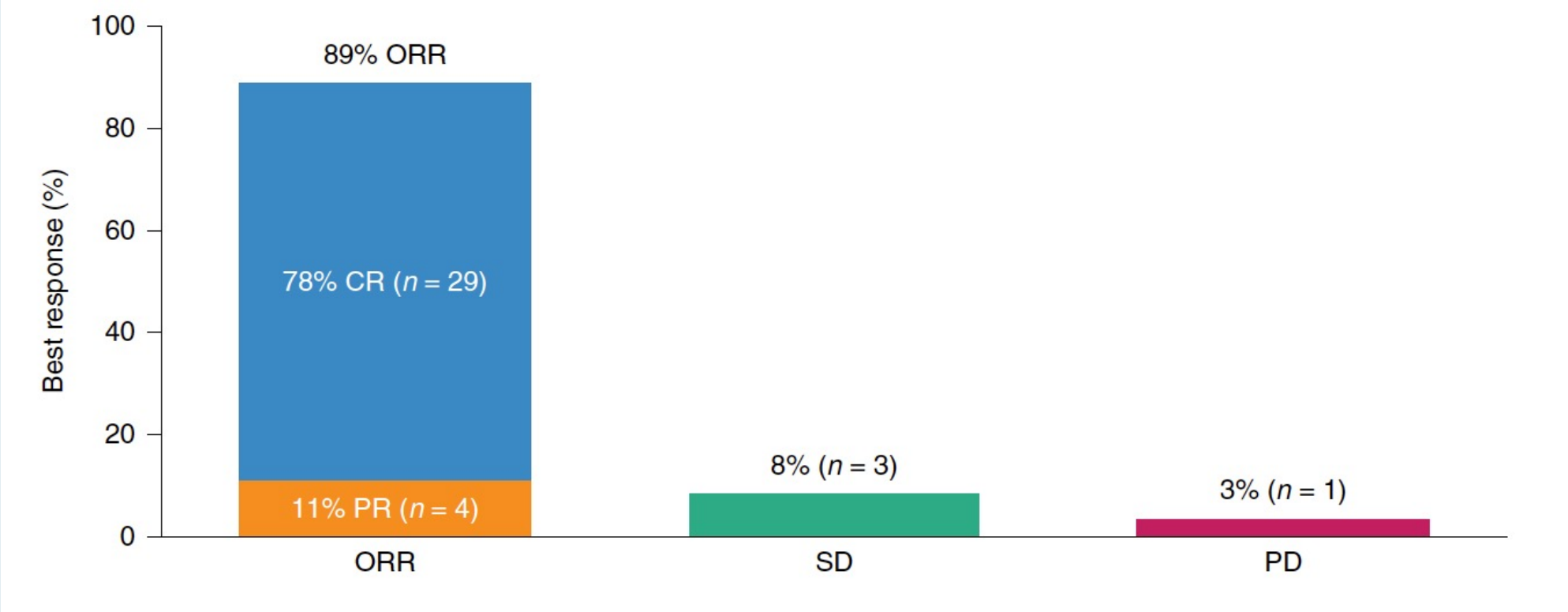
ZUMA-12: Efficacy Results with Axi-cel as First-Line Treatment

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;[Online ahead of print].

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

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

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

Neelapu SS et al. *Nat Med* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

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

Jacobson C et al.

ASH 2021;Abstract 1764.

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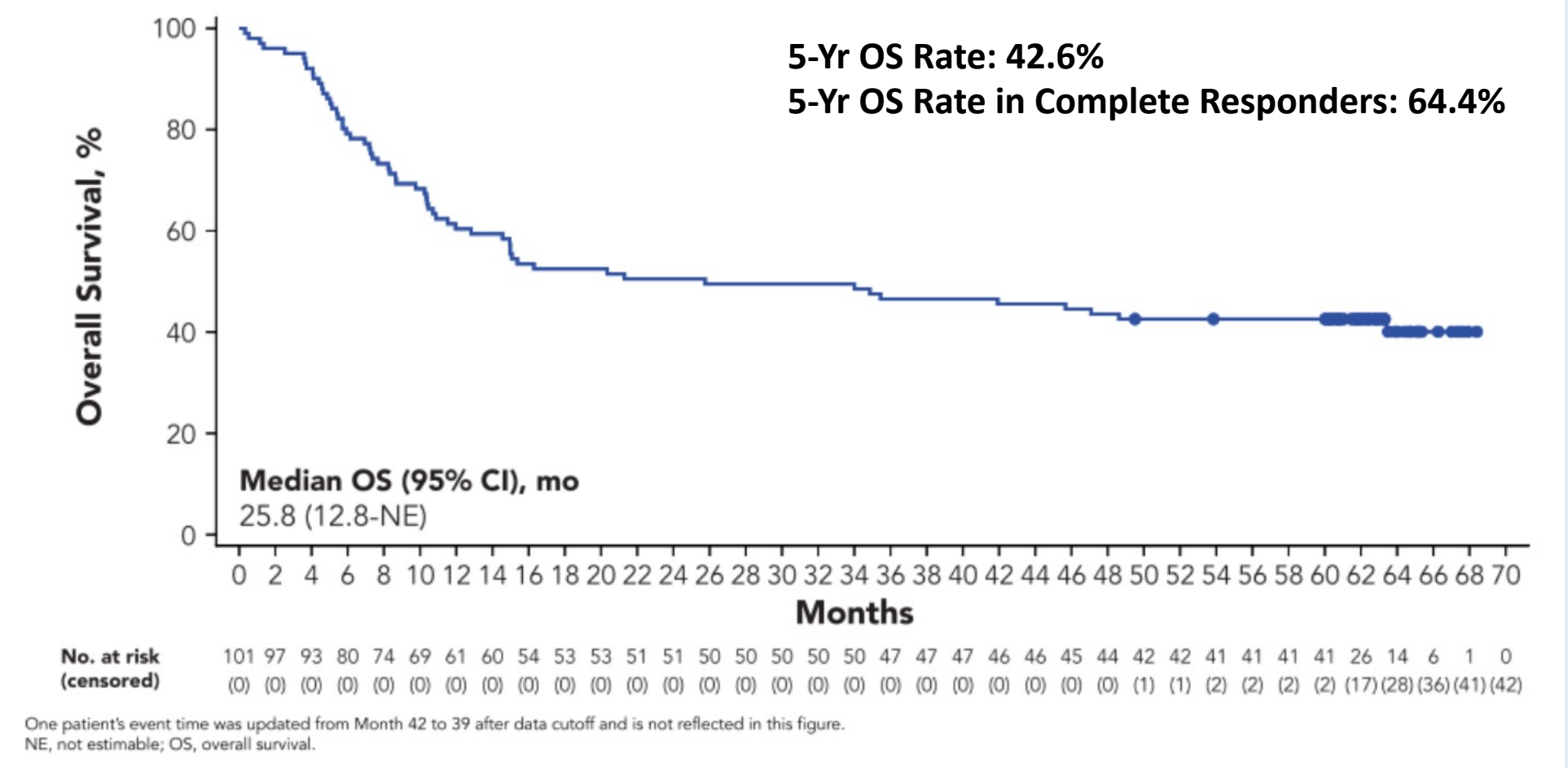
ZUMA-1: Five-Year Update



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

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

Jacobson C et al. ASH 2021;Abstract 1764.

RTP RESEARCH TO PRACTICE

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

The NEW ENGLAND JOURNAL of MEDICINE

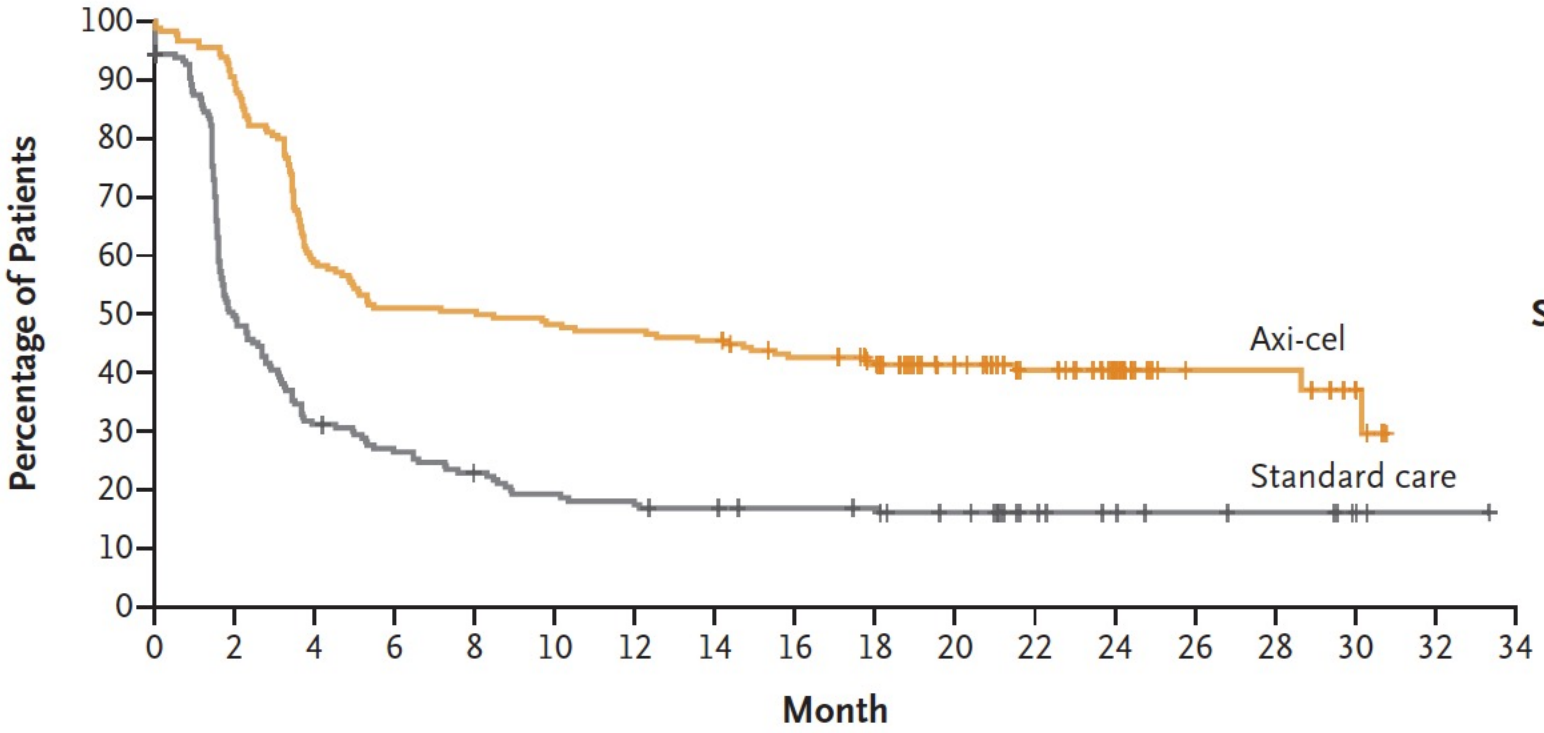
ORIGINAL ARTICLE

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*

RTP RESEARCH TO PRACTICE

ZUMA-7: Event-Free Survival

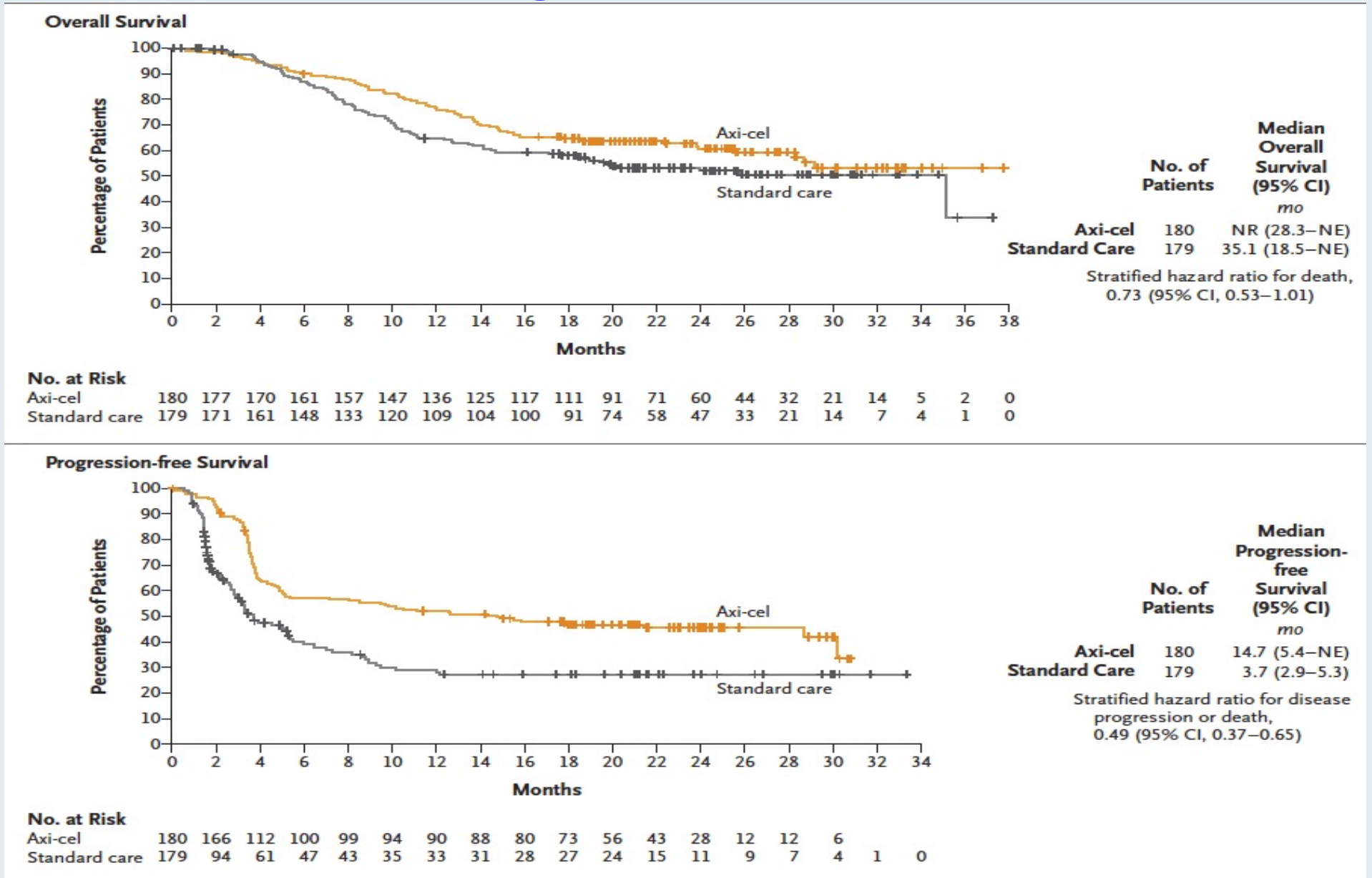


	No. of Patients	Median Event-free Survival (95% CI)
		mo
Axi-cel	180	8.3 (4.5–15.8)
Standard Care	179	2.0 (1.6–2.8)

Stratified hazard ratio for event or death, 0.40 (95% CI, 0.31–0.51)
P<0.001

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

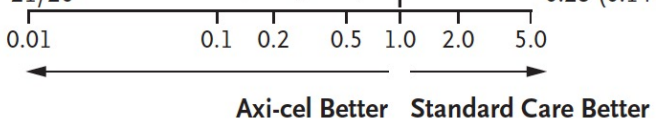
ZUMA-7: Overall and Progression-Free Survival



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

ZUMA-7: Event-Free Survival Subgroup Analysis

Subgroup	Axi-cel	Standard Care	Hazard Ratio for Event or Death (95% CI)
	no. of patients with event/total no.		
Overall	108/180	144/179	0.40 (0.31–0.51)
Age			
<65 yr	81/129	96/121	0.49 (0.36–0.67)
≥65 yr	27/51	48/58	0.28 (0.16–0.46)
Response to first-line therapy at randomization			
Primary refractory disease	85/133	106/131	0.43 (0.32–0.57)
Relapse ≤12 mo after initiation or completion of first-line therapy	23/47	38/48	0.34 (0.20–0.58)
Second-line age-adjusted IPI			
0 or 1	54/98	73/100	0.41 (0.28–0.58)
2 or 3	54/82	71/79	0.39 (0.27–0.56)
Prognostic marker according to central laboratory			
HGBL, double- or triple-hit	15/31	21/25	0.28 (0.14–0.59)
Double-expressor lymphoma	35/57	50/62	0.42 (0.27–0.67)
Molecular subgroup according to central laboratory			
Germinal center B-cell–like	64/109	80/99	0.41 (0.29–0.57)
Activated B-cell–like	11/16	9/9	0.18 (0.05–0.72)
Unclassified	8/17	12/14	—
Disease type according to investigator			
DLBCL, not otherwise specified	68/110	97/116	0.37 (0.27–0.52)
Large-cell transformation from follicular lymphoma	10/19	24/27	0.35 (0.16–0.77)
HGBL, including rearrangement of *MYC* with *BCL2* or *BCL6* or both	23/43	18/27	0.47 (0.24–0.90)
Disease type according to central laboratory			
DLBCL	79/126	95/120	0.44 (0.32–0.60)
HGBL, including rearrangement of *MYC* with *BCL2* or *BCL6* or both	15/31	21/26	0.28 (0.14–0.59)



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

ZUMA-7: Select Grade ≥3 Adverse Events

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

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

RTP RESEARCH TO PRACTICE

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

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

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

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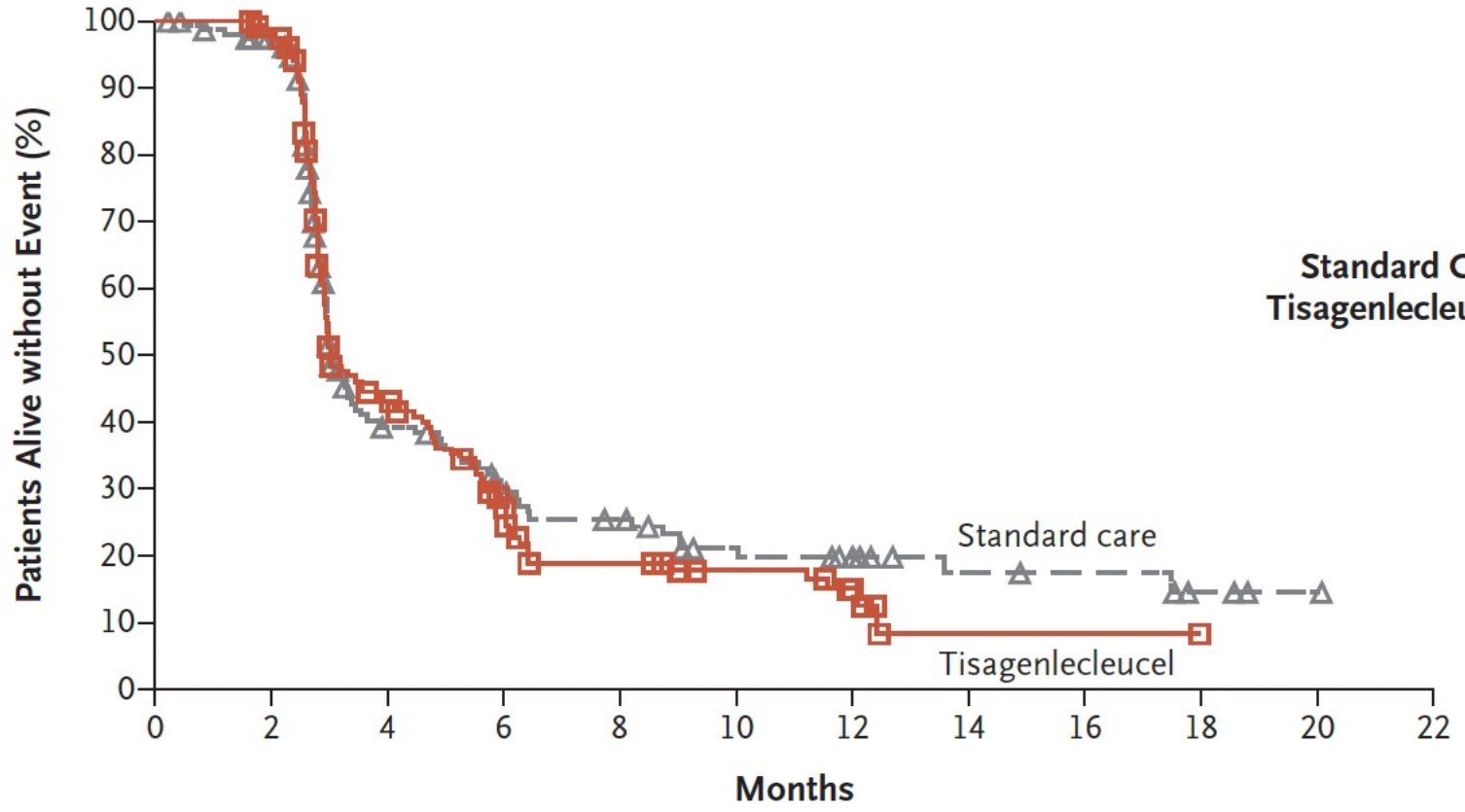
BELINDA: Event-Free Survival (Primary Endpoint)



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

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

No. at Risk

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

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

RTP RESEARCH TO PRACTICE

BELINDA: Select Grade ≥3 Adverse Events

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

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

RTP RESEARCH TO PRACTICE

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

Manali Kamdar,[1] Scott R. Solomon,[2] Jon Arnason,[3] Patrick B. Johnston,[4] Bertram Glass,[5] Veronika Bachanova,[6] Sami Ibrahimi,[7] Stephan Mielke,[8] Pim Mutsaers,[9] Francisco Hernandez-Ilizaliturri,[10] Koji Izutsu,[11] Franck Morschhauser,[12] Matthew Lunning,[13] David G. Maloney,[14] Alessandro Crotta,[15] Sandrine Montheard,[15] Alessandro Previtali,[15] Lara Stepan,[16] Ken Ogasawara,[16] Timothy Mack,[16] Jeremy S. Abramson[17]

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ASH 2021, Presentation Number 91

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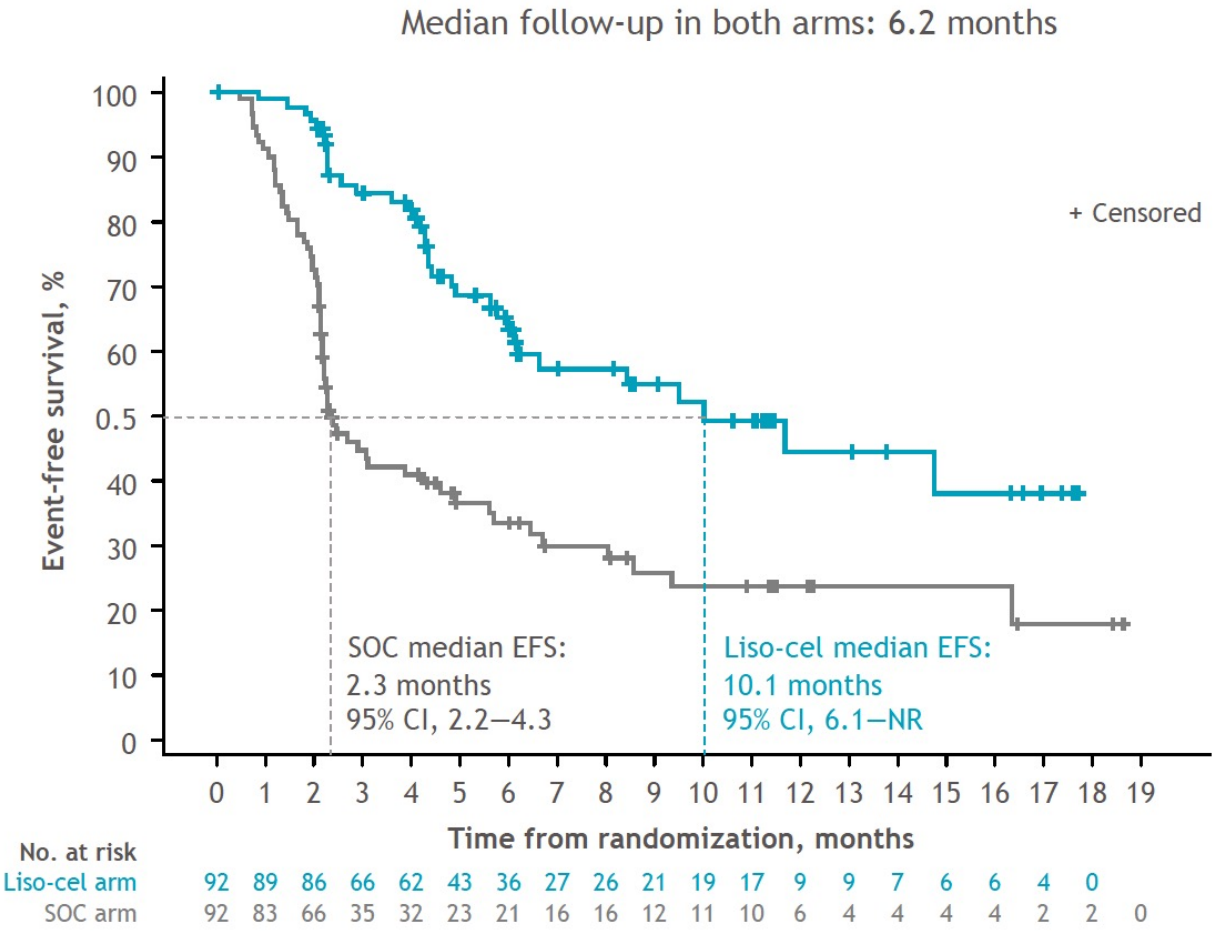
TRANSFORM: Event-Free Survival per Independent Review Committee (ITT, Primary Endpoint)



	Liso-cel arm (n = 92)	SOC arm (n = 92)
Patients with events, n	35	63
Stratified HR (95% CI)	**0.349** (0.229–0.530) *P* < 0.0001	
6-month EFS rate, % (SE)	63.3 (5.77)	33.4 (5.30)
Two-sided 95% CI	52.0–74.7	23.0–43.8
12-month EFS rate, % (SE)	44.5 (7.72)	23.7 (5.28)
Two-sided 95% CI	29.4–59.6	13.4–34.1

One-sided *P* value significance threshold to reject the null hypothesis was < 0.012

Kamdar M et al. ASH 2021;Abstract 91.

Hodgkin Lymphoma

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original reports

Limited, But Not Eliminated, Excess Long-Term Morbidity in Stage I-IIA Hodgkin Lymphoma Treated With Doxorubicin, Bleomycin, Vinblastine, and Dacarbazine and Limited-Field Radiotherapy

Ingemar Lagerlöf, MD[1]; Helena Fohlin, PhD[2]; Gunilla Enblad, MD, PhD[1]; Bengt Glimelius, MD, PhD[1]; Christina Goldkuhl, MD[3]; Marzia Palma, MD, PhD[4]; Lisa Åkesson, BS[2]; Ingrid Glimelius, MD, PhD[1]; and Daniel Molin, MD, PhD[1]

J Clin Oncol 2022;40(13):1487-96.

AUTHOR CONCLUSIONS: Compared with toxicity from earlier RT techniques, excess morbidity was not eliminated, but lower than previously reported. The elevated risk of diseases of the respiratory system was driven by diagnosis of asthma, which could in part be explained by misdiagnosis of persisting pulmonary toxicity.

RTP RESEARCH TO PRACTICE

original reports

Brentuximab Vedotin Combined With Chemotherapy in Patients With Newly Diagnosed Early-Stage, Unfavorable-Risk Hodgkin Lymphoma

Anita Kumar, MD[1]; Carla Casulo, MD[2]; Ranjana H. Advani, MD[3]; Elizabeth Budde, MD[4]; Paul M. Barr, MD[2]; Connie L. Batlevi, MD, PhD[1]; Philip Caron, MD[1]; Louis S. Constine, MD[2]; Savita V. Dandapani, MD[4]; Esther Drill, MD[1]; Pamela Drullinsky, MD[1]; Jonathan W. Friedberg, MD[2]; Clare Grieve, BA[1]; Audrey Hamilton, MD[1]; Paul A. Hamlin, MD[1]; Richard T. Hoppe, MD[3]; Steven M. Horwitz, MD[1]; Ashlee Joseph, BA[1]; Niloufer Khan, MD[1]; Leana Laraque, BA[1]; Matthew J. Matasar, MD[1]; Alison J. Moskowitz, MD[1]; Ariela Noy, MD[1]; Maria Lia Palomba, MD[1]; Heiko Schöder, MD[1]; David J. Straus, MD[1]; Shreya Vemuri, BA[1]; Joanna Yang, MD[5]; Anas Younes, MD[6]; Andrew D. Zelenetz, MD, PhD[1]; Joachim Yahalom, MD[1]; and Craig H. Moskowitz, MD[7]

J Clin Oncol 2021;39(20):2257-65.

RTP RESEARCH TO PRACTICE

Multicenter Pilot Study of Brentuximab Vedotin (BV) and AVD with or without Consolidative Radiation Therapy for Early-Stage, Unfavorable-Risk Hodgkin Lymphoma

- Patients who achieved a negative end-of-therapy (EOT) PET-4 scan after 4 cycles of BV + AVD were studied with de-escalating radiation dose and field.

Clinical endpoint	Cohort 1 30-Gy ISRT (n = 29)	Cohort 2 20-Gy ISRT (n = 29)	Cohort 3 30-Gy CVRT (n = 29)	Cohort 4 No radiation (n = 29)	All patients (n = 114)
EOT CR rate	27 (93%)	29 (100%)	27 (93%)	28 (97%)	111 (96%)
2-year PFS rate	93.1%	96.6%	89.7%	96.6%	94%

"BV + AVD x four cycles is a highly active and well-tolerated treatment program for ES, unfavorable-risk Hodgkin lymphoma, including bulky disease. The efficacy of BV + AVD supports the safe reduction or elimination of consolidative radiation among PET-4–negative patients."

Kumar A et al. *J Clin Oncol* 2021;39(20):2257-65.

RTP RESEARCH TO PRACTICE

Follicular Lymphoma

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TO PRACTICE

Long-Term Follow-Up Analysis of ZUMA-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

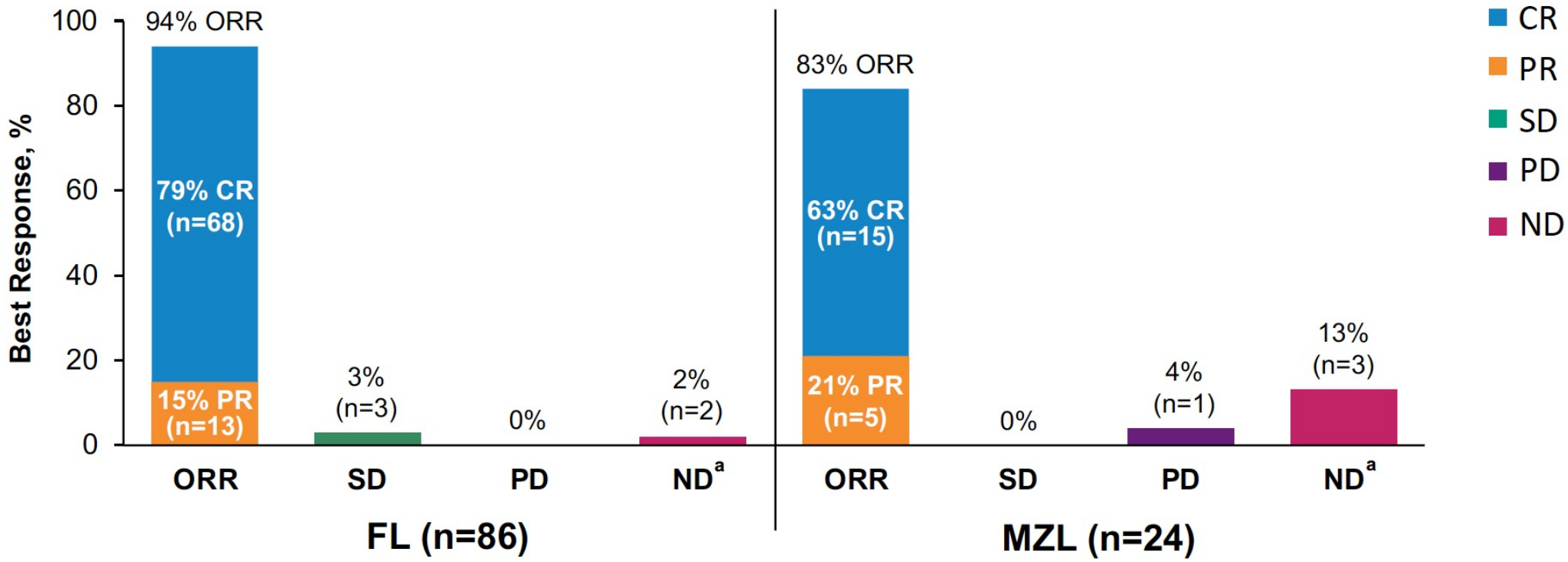
Sattva S. Neelapu, MD[1]*; Julio C. Chavez, MD[2]*; Alison R. Sehgal, MD[3]; Narendranath Epperla, MD, MS[4]; Matthew Ulrickson, MD[5]; Emmanuel Bachy, MD, PhD[6]; Pashna N. Munshi, MD[7]; Carla Casulo, MD[8]; David G. Maloney, MD, PhD[9]; Sven de Vos, MD, PhD[10]; Ran Reshef, MD[11]; Lori A. Leslie, MD[12]; Olalekan O. Oluwole, MD, MPH, MBBS[13]; Ibrahim Yakoub-Agha, MD, PhD[14]; Rashmi Khanal, MD[15]; Joseph Rosenblatt, MD[16]; Marika Sherman, MSHS[17]; Jinghui Dong, PhD[17]; Alessandro Giovanetti, BSc[17]; Yin Yang, MD, PhD[17]; Christine Lui, MS[17]; Zahid Bashir, MBBS; MS[17]; A. Scott Jung, MD[17]; and Caron A. Jacobson, MD[18]

[1]The University of Texas MD Anderson Cancer Center, Houston, Texas, USA; [2]University of South Florida H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [3]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [4]The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [5]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [6]Centre Hospitalier Lyon Sud, Pierre-Bénite, France; [7]Georgetown Lombardi Comprehensive Cancer Center, Washington, DC, USA; [8]University of Rochester Medical Center - James P. Wilmot Cancer Center, Rochester, NY, USA; [9]Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [10]Ronald Reagan University of California Los Angeles Medical Center, Santa Monica, CA, USA; [11]Columbia University Herbert Irving Comprehensive Cancer Center, New York City, NY, USA; [12]John Theurer Cancer Center, Hackensack, NJ, USA; [13]Vanderbilt University Medical Center, Nashville, TN, USA; [14]CHU de Lille, Univ Lille, INSERM U1286, Infinite, 59000 Lille, France; [15]Fox Chase Cancer Center, Philadelphia, PA, USA [16]University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA; [17]Kite, a Gilead Company, Santa Monica, CA, USA; and [18]Dana-Farber Cancer Institute, Boston, MA, USA
**Equal contributors*

ASH 2021;Abstract 93.

RTP RESEARCH TO PRACTICE

ZUMA-5: Overall Response Rate (ORR) by Central Review

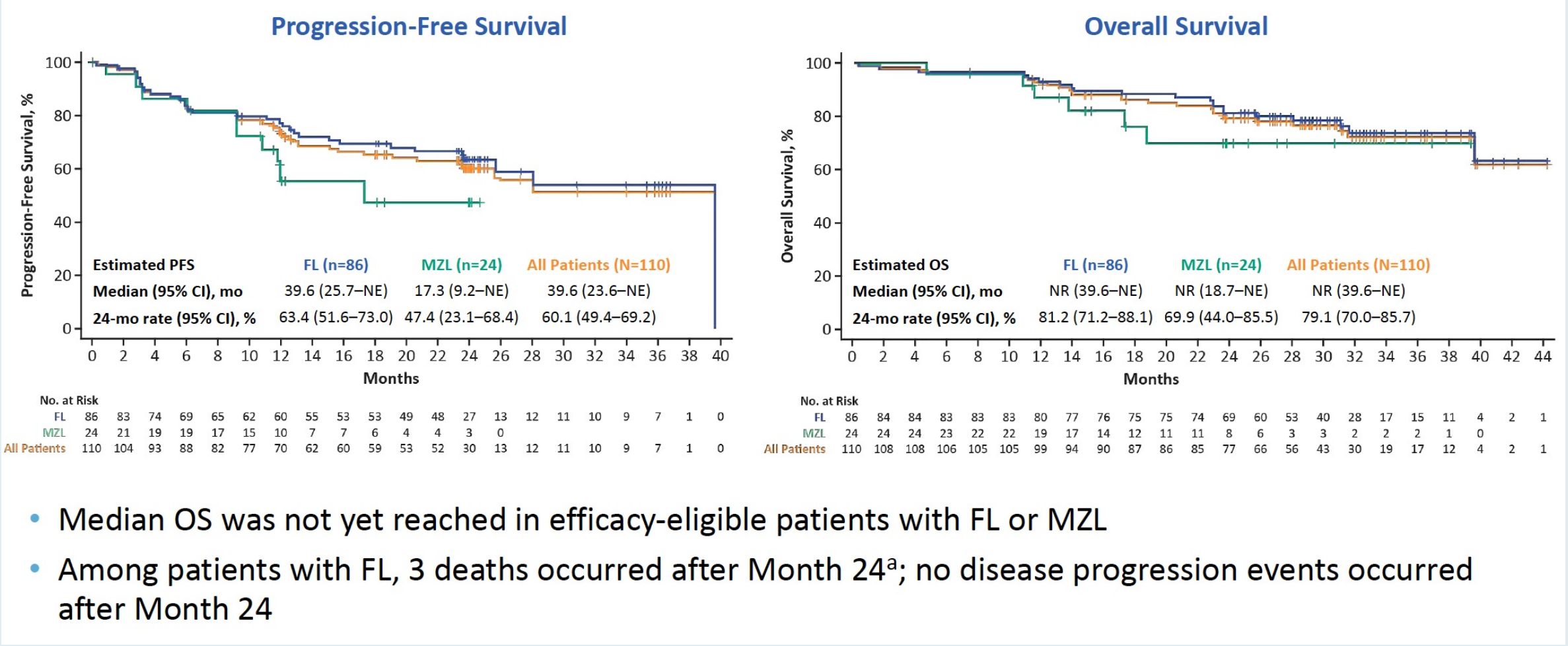


- Among efficacy-eligible patients with iNHL (n=110), the ORR was 92% (95% CI, 85–96), with a 75% CR rate
- Among all treated patients with iNHL (n=149), the ORR was 92% (95% CI, 86–96), with a 77% CR rate

Neelapu SS et al. ASH 2021;Abstract 93.

RTP RESEARCH TO PRACTICE

ZUMA-5: PFS and Overall Survival



- Median OS was not yet reached in efficacy-eligible patients with FL or MZL
- Among patients with FL, 3 deaths occurred after Month 24[a]; no disease progression events occurred after Month 24

Neelapu SS et al. ASH 2021;Abstract 93.

RTP RESEARCH TO PRACTICE

ZUMA-5: AEs with First Occurrence After Primary Analysis Data Cutoff

AE, n (%)	Follicular Lymphoma (N=124)		Marginal Zone Lymphoma (N=25)		All Patients (N=149)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any AE	27 (22)	14 (11)	11 (44)	6 (24)	38 (26)	20 (13)
Serious AE	11 (9)	11 (9)	4 (16)	4 (16)	15 (10)	15 (10)
Cytopenia	8 (6)	4 (3)	3 (12)	3 (12)	11 (7)	7 (5)
Infection	18 (15)	7 (6)	7 (28)	4 (16)	25 (17)	11 (7)
CRS	0 (0)	0 (0)	2 (8)	0 (0)	2 (1)	0 (0)
Neurologic event	0 (0)	0 (0)	2 (8)	0 (0)	2 (1)	0 (0)
Hypogammaglobulinemia	2 (2)	0 (0)	2 (8)	0 (0)	4 (3)	0 (0)
Tumor lysis syndrome	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

- Grade 5 AEs occurred in 6 patients after the data cutoff of the primary analysis[b]
  - Grade 5 infectious AEs occurred in 5 patients: 1 COVID-19 (FL, Day 717, unrelated), 1 COVID-19 pneumonia (FL, Day 780, related to axi-cel), 1 PML[c] (FL, Day 697, related to axi-cel and CC) and 2 sepsis (FL, Day 1204; MZL, Day 139; both unrelated)
  - Acute bilineal leukemia occurred in 1 patient (FL, Day 623, CC related)

[a] Includes all AEs that occurred after the primary analysis data cutoff date (March 12, 2020) and by the data cutoff date of the current analysis (March 31, 2021). [b] No Grade 5 AEs were due to progressive disease.
[c] The Grade 5 PML event occurred after axi-cel retreatment.

Neelapu SS et al. ASH 2021;Abstract 93.

RTP RESEARCH TO PRACTICE

FDA Approves Tisagenlecleucel for Relapsed or Refractory Follicular Lymphoma

Press Release: May 27, 2022

"On May 27, 2022, the Food and Drug Administration granted accelerated approval to tisagenlecleucel for adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

The approval was based on the ELARA trial (NCT03568461), a multicenter, single-arm, open-label trial evaluating tisagenlecleucel, a CD19-directed chimeric antigen receptor (CAR) T cell therapy, in adult patients who were refractory or relapsed within 6 months after completion of two or more lines of systemic therapy (including an anti-CD20 antibody and an alkylating agent) or relapsed after autologous hematopoietic stem cell transplant."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tisagenlecleucel-relapsed-or-refractory-follicular-lymphoma

RTP RESEARCH TO PRACTICE

Efficacy of Tisagenlecleucel in Adult Patients with High-Risk Relapsed/Refractory Follicular Lymphoma: Subgroup Analysis of the Phase II ELARA Study

Catherine Thieblemont,[1] Michael Dickinson,[2] Joaquin Martinez-Lopez,[3] Arne Kolstad,[4] Jason P. Butler,[5] Monalisa Ghosh,[6] Leslie L. Popplewell,[7] Julio C. Chavez,[8] Emmanuel Bachy,[9] Koji Kato,[10] Hideo Harigae,[11] Marie José Kersten,[12] Charalambos Andreadis,[13] Peter A. Riedell,[14] P. Joy Ho,[15] José Antonio Pérez-Simón,[16] Andy I. Chen,[17] Loretta J. Nastoupil,[18] Bastian von Tresckow,[19] Andrés José María Ferreri,[20] Takanori Teshima,[21] Piers EM Patten,[22] Joseph P. McGuirk,[23] Andreas Petzer,[24] Fritz Offner,[25] Andreas Viardot,[26] Pier Luigi Zinzani,[27] Ram Malladi,[28] Aiesha Zia,[29] Chiara Lobetti Bodoni,[29] Aisha Masood,[30] Stephen J. Schuster,[31] Nathan H. Fowler,[32] Martin H. Dreyling,[33]

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Thieblemont C et al. ASH 2021;Abstract 131.

RTP RESEARCH TO PRACTICE

ELARA: Efficacy Analysis with Extended Follow-Up

- As of March 29, 2021, 97 patients received tisagenlecleucel and 94 were evaluable for efficacy
- CR rates are consistent and durable for the interim, primary analyses, and this extended follow-up analysis
- Complete response correlated with durability and prolonged PFS
  - **Among patients who achieved CR, 12-month PFS was 85.5% (95% CI, 74-92) and estimated DOR rate at 9 months was 86.5% (95% CI, 75-93)**

Efficacy Results of Extended Follow-up Analysis

Endpoint	% (95% CI)
ORR[a]	**86.2** (77.5-92.4)
CRR[a]	**69.1** (58.8-78.3)
12-mo PFS	**67.0** (56.0-75.8)
9-mo DOR	**76.0** (64.6-84.2)

[a]ORR and CRR were comparable with the primary efficacy analysis (ORR 86.2% and CRR 66.0%).

Thieblemont C et al. ASH 2021;Abstract 131.

RTP RESEARCH TO PRACTICE

Mosunetuzumab Monotherapy is an Effective and Well-Tolerated Treatment Option for Patients with Relapsed/ Refractory (R/R) Follicular Lymphoma (FL) who have Received ≥2 Prior Lines of Therapy: Pivotal Results from a Phase I/II Study

L Elizabeth Budde,[1] Laurie H Sehn,[2] Matthew Matasar,[3] Stephen J Schuster,[4] Sarit Assouline,[5] Pratyush Giri,[6] John Kuruvilla,[7] Miguel Canales,[8] Sascha Dietrich,[9] Keith Fay,[10] Matthew Ku,[11] Loretta Nastoupil,[12] Michael C Wei,[13] Shen Yin,[13] Michelle Y Doral,[13] Chi-Chung Li,[13] Huang Huang,[14] Raluca Negricea,[15] Elicia Penuel,[13] Carol O'Hear,[13] Nancy L Bartlett[16]

[1]*City of Hope, Duarte, CA, USA;* [2]*BC Cancer Centre for Lymphoid Cancer and University of British Columbia, Vancouver, BC, Canada;* [3]*Memorial Sloan Kettering Cancer Center, New York, NY, USA;* [4]*Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA;* [5]*Jewish General Hospital, Montreal, QC, Canada;* [6]*Royal Adelaide Hospital, Adelaide, Australia;* [7]*Princess Margaret Cancer Centre, Toronto, ON, Canada;* [8]*Hospital Universitario La Paz, Madrid, Spain;* [9]*Universitat Heidelberg, Heidelberg, Germany;* [10]*St Vincent's Hospital and Royal North Shore Hospital, Sydney, Australia;* [11]*St Vincent's Hospital, University of Melbourne, Melbourne, Australia;* [12]*MD Anderson Cancer Center, Houston, TX, USA;* [13]*Genentech, Inc., South San Francisco, CA, USA;* [14]*Hoffmann-La Roche Ltd, Mississauga, ON, Canada;* [15]*Roche Products Ltd, Welwyn Garden City, United Kingdom;* [16]*Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, USA*

Accepted as an Oral Presentation at the 63rd ASH Annual Meeting and Exposition

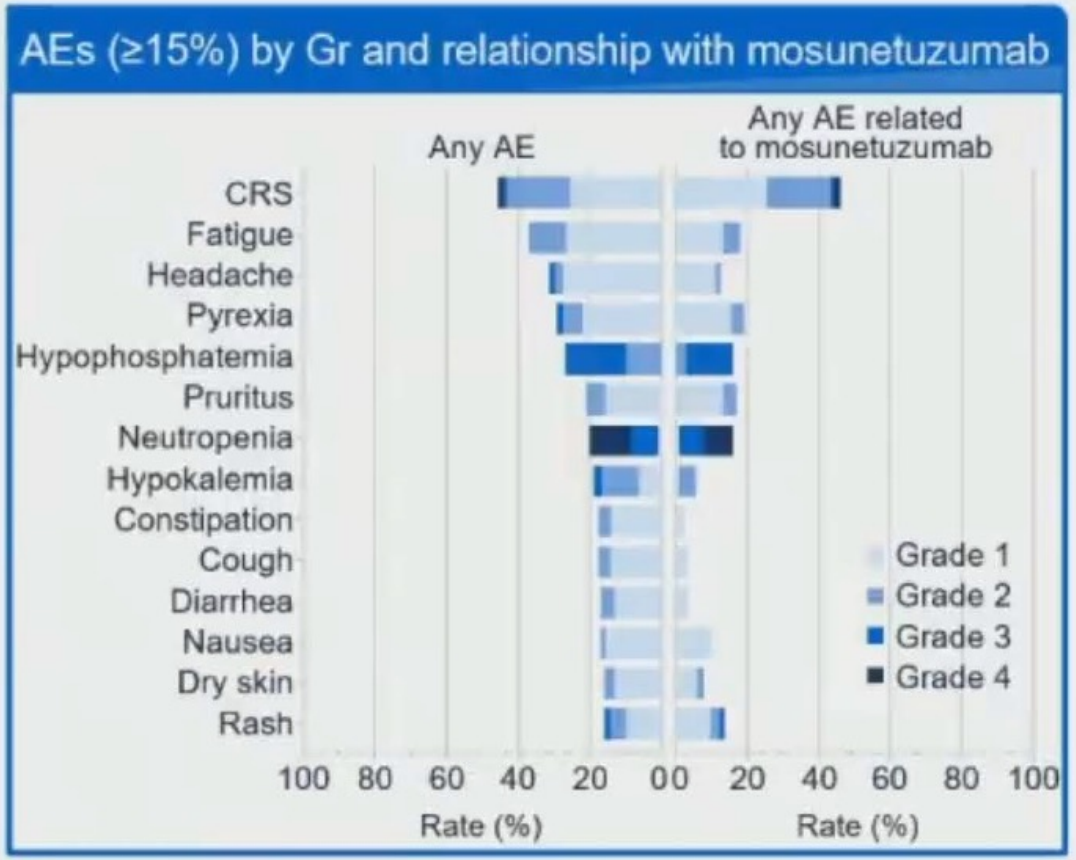
63rd ASH® Annual Meeting and Exposition

ASH 2021;Abstract 127.

RTP RESEARCH TO PRACTICE

Safety Profile of Mosunetuzumab Monotherapy for Patients with R/R FL Who Have Received ≥2 Lines of Therapy

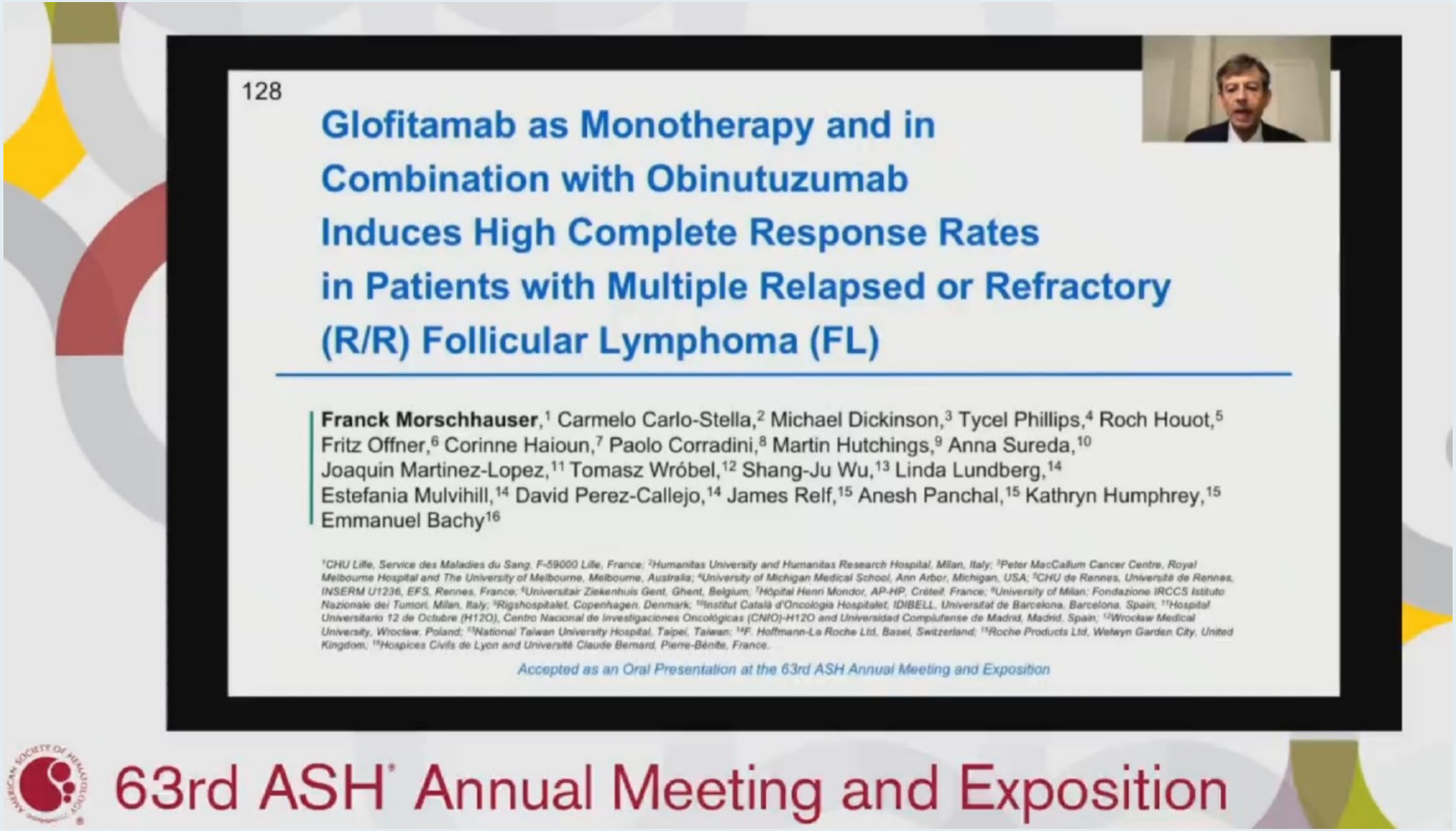
N (%)	N=90
AE	90 (100%)
Mosunetuzumab related*	83 (92.2%)
Grade 3–4 AE	63 (70.0%)
Mosunetuzumab related*	46 (51.1%)
Serious AE	42 (46.7%)
Mosunetuzumab related*	30 (33.3%)
Grade 5 (fatal) AE	2 (2.2%)†
Mosunetuzumab related*	0
AE leading to discontinuation of treatment	4 (4.4%)‡
Mosunetuzumab related*	2 (2.2%)‡



*AE considered related to treatment by the investigator; †mosunetuzumab unrelated: malignant neoplasm progression and unexplained death (1 patient each); ‡mosunetuzumab related: CRS (2 patients); mosunetuzumab unrelated: Esptein-Barr viremia and Hodgkin's disease (1 patient each); AE, adverse event; Gr, Grade

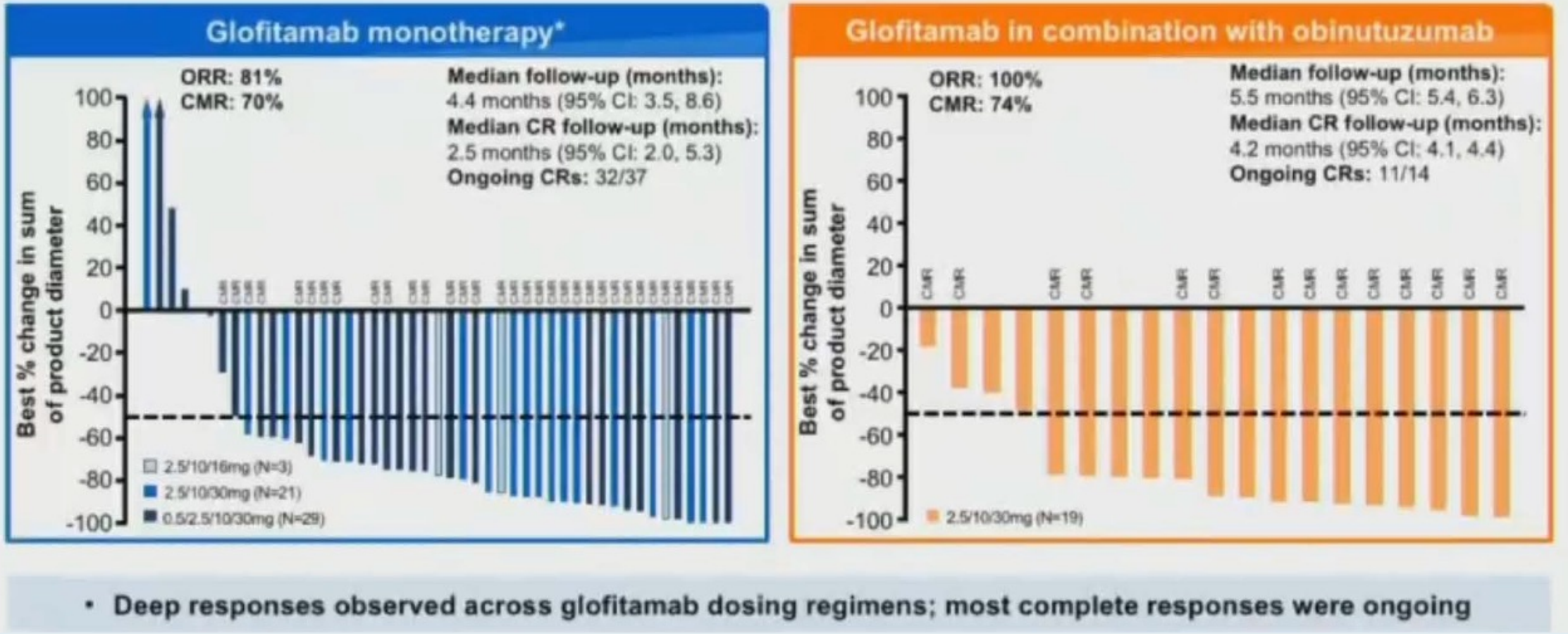
Budde EL et al. ASH 2021;Abstract 127.

RTP RESEARCH TO PRACTICE



ASH 2021;Abstract 128.

Phase I/II Study of Glofitamab as Monotherapy or in Combination with Obinutuzumab for R/R FL



- Myelosuppression was more common with the combination
- Cytokine release syndrome rates were high and comparable, and cases were mainly low grade

Morschhauser F et al. ASH 2021;Abstract 128.

RTP RESEARCH TO PRACTICE

Mantle Cell Lymphoma

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original reports

Ibrutinib With Rituximab in First-Line Treatment of Older Patients With Mantle Cell Lymphoma

Preetesh Jain, MD, DM, PhD[1]; Shuangtao Zhao, PhD[2]; Hun Ju Lee, MD[1]; Holly A. Hill, MPH[1]; Chi Young Ok, MD[3]; Rashmi Kanagal-Shamanna, MD[3]; Fredrick B. Hagemeister, MD[1]; Nathan Fowler, MD[1]; Luis Fayad, MD[1]; Yixin Yao, PhD[1]; Yang Liu, PhD[1]; Omar B. Moghrabi, BS[1]; Lucy Navsaria, MBBS[1]; Lei Feng, MS[4]; Graciela M. Nogueras Gonzalez, MPH[4]; Guofan Xu, MD[5]; Selvi Thirumurthi, MD[6]; David Santos, MD[7]; Cezar Iliescu, MD[8]; Guilin Tang, MD, PhD[3]; L. Jeffrey Medeiros, MD[3]; Francisco Vega, MD, PhD[3]; Michelle Avellaneda, BS[1]; Maria Badillo, BS[1]; Christopher R. Flowers, MD[1]; Linghua Wang, PhD[2]; and Michael L. Wang, MD[1]

J Clin Oncol 2021;40:202-12.

RTP RESEARCH TO PRACTICE

Phase II Trial of Ibrutinib with Rituximab for Older Patients with MCL

Clinical endpoint	N = 48
Best overall response rate	100%
Complete metabolic response (CMR) by PET*	74%
3-year PFS	87%
3-year OS	94%

* In 26 patients who achieved CMR, 21 (81%) had bone marrow negative for MCL

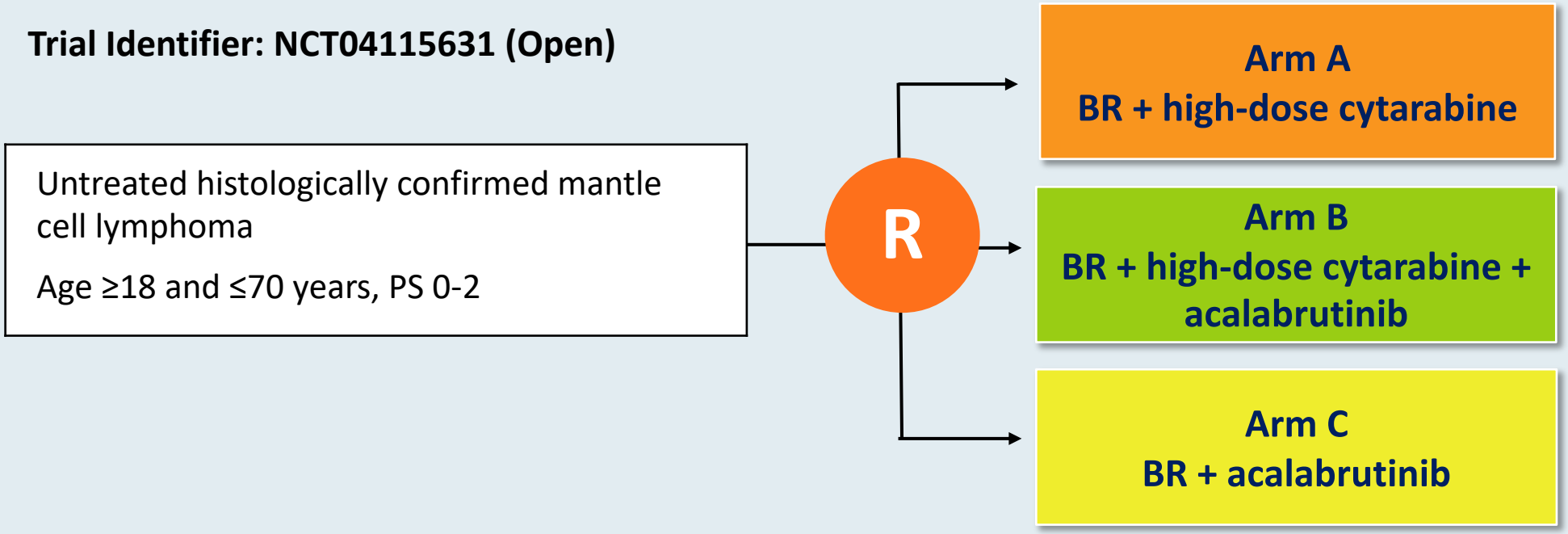
- 0 deaths were reported on study
- 11 (22%) patients had Grade 3 atrial fibrillation
- Grade 3-4 myelosuppression was seen in <5% of patients

Jain P et al. *J Clin Oncol* 2021;40:202-12.

RTP RESEARCH TO PRACTICE

ECOG-EA4181: A Phase II Study of BR with High-Dose Cytarabine with or without Acalabrutinib, and BR with Acalabrutinib as Initial Treatment for Patients ≤70 Years Old with MCL

Trial Identifier: NCT04115631 (Open)



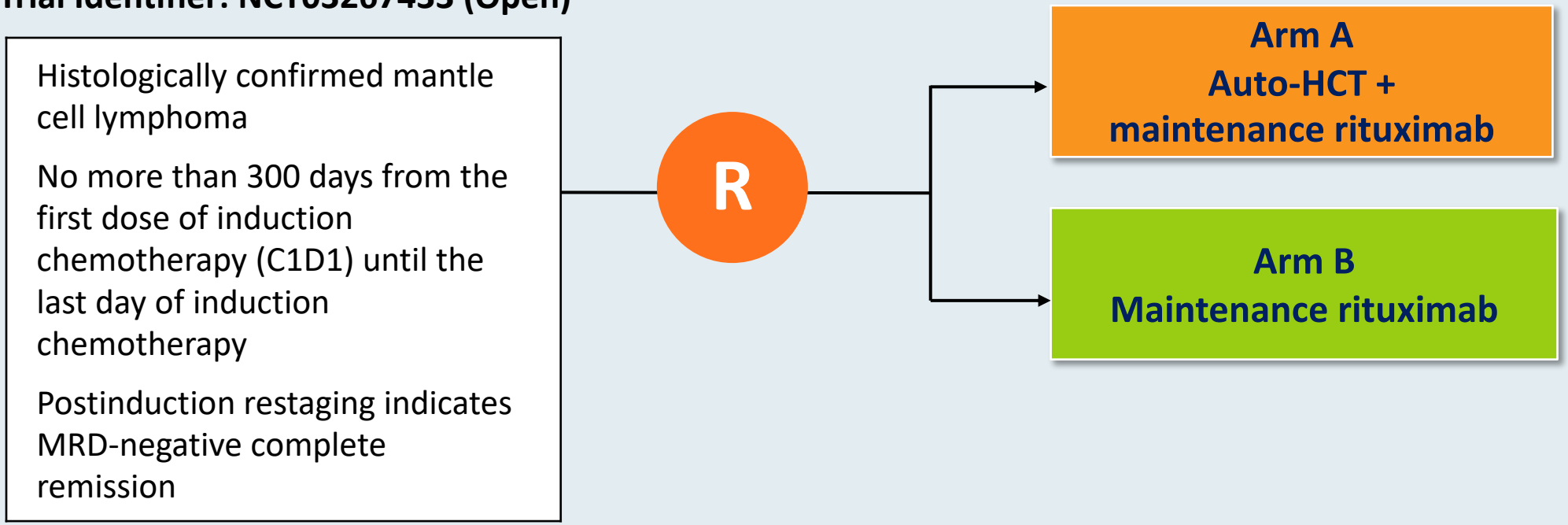
Primary endpoint: PET/CT complete response and peripheral blood minimal residual disease (MRD)-negative rate

www.clinicaltrials.gov. Accessed April 2022; https://ecog-acrin.org/clinical-trials/ea4181-educational-materials/

RTP RESEARCH TO PRACTICE

ECOG-EA4151: A Phase III Trial of Consolidation Therapy with Autologous Hematopoietic Cell Transplantation (HCT) Followed by Maintenance Rituximab versus Maintenance Rituximab Alone for Patients with MCL in MRD-Negative First Complete Remission

Trial Identifier: NCT03267433 (Open)



Primary endpoint: Overall survival for patients in MRD-negative first remission who undergo auto-HCT followed by rituximab versus maintenance rituximab alone

www.clinicaltrials.gov. Accessed April 2022; https://ecog-acrin.org/clinical-trials/ea4151-educational-materials/

RTP RESEARCH TO PRACTICE

Wang *et al. J Hematol Oncol* (2021) 14:179
https://doi.org/10.1186/s13045-021-01188-x

Journal of Hematology & Oncology

RAPID COMMUNICATION

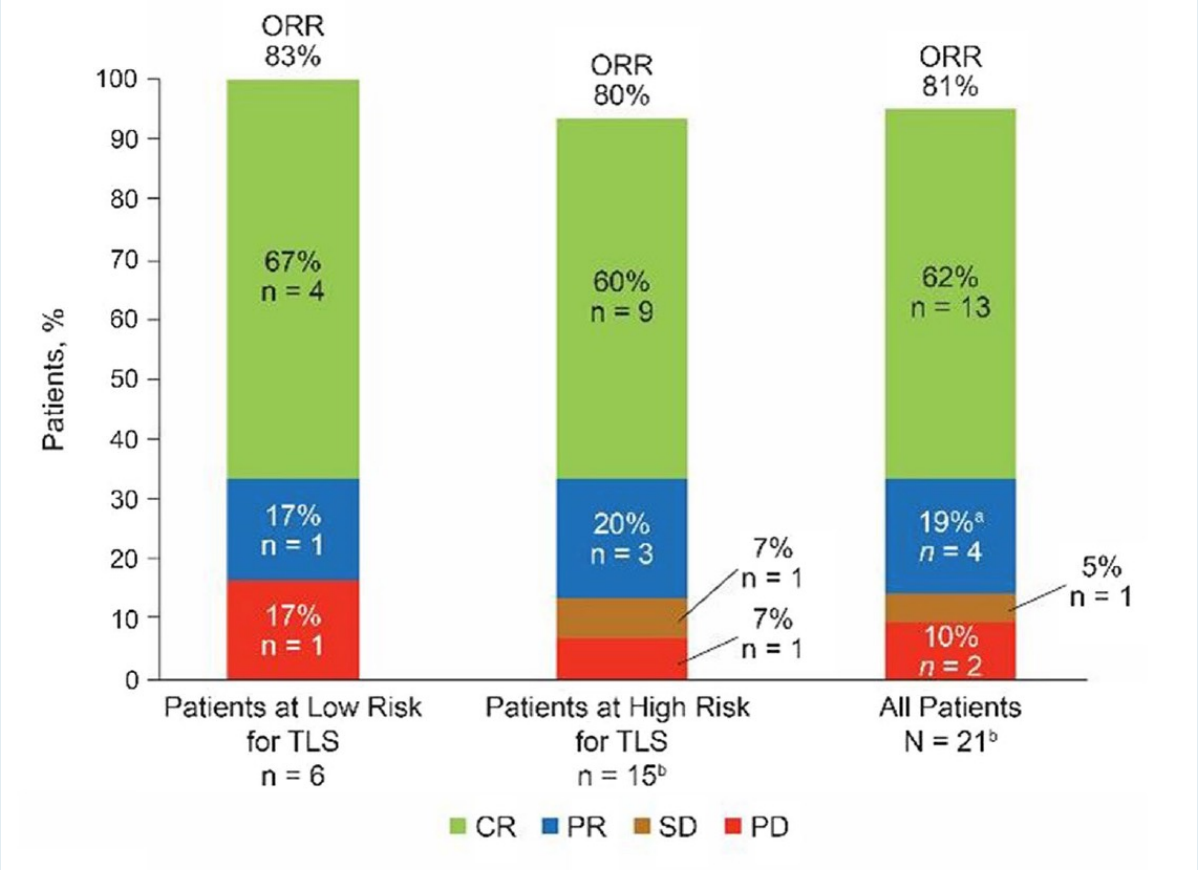
Open Access

Concurrent ibrutinib plus venetoclax in relapsed/refractory mantle cell lymphoma: the safety run-in of the phase 3 SYMPATICO study

Michael Wang[1*], Radhakrishnan Ramchandren[2], Robert Chen[3], Lionel Karlin[4], Geoffrey Chong[5], Wojciech Jurczak[6], Ka Lung Wu[7], Mark Bishton[8], Graham P. Collins[9], Paul Eliadis[10], Frédéric Peyrade[11], Yihua Lee[12], Karl Eckert[12], Jutta K. Neuenburg[12] and Constantine S. Tam[13]

RTP RESEARCH TO PRACTICE

SYMPATICO: Efficacy Outcomes with Concurrent Ibrutinib and Venetoclax for Relapsed/Refractory MCL



- Median duration of response was 32.3 months
- Median PFS was 35.0 months
- Median OS was also 35.0 months

ORR = overall response rate

Wang M et al. *J Hematol Oncol* 2021;14(1):179.

RTP RESEARCH TO PRACTICE

REGULAR ARTICLE

blood advances

Zanubrutinib for the treatment of relapsed or refractory mantle cell lymphoma

Constantine S. Tam,[1-4] Stephen Opat,[5,6] David Simpson,[7,8] Gavin Cull,[9,10] Javier Munoz,[11] Tycel J. Phillips,[12] Won Seog Kim,[13] Simon Rule,[14] Siminder Kaur Atwal,[8] Rachel Wei,[8] William Novotny,[8] Jane Huang,[8] Michael Wang,[15,*] and Judith Trotman[16,*]

Blood Adv 2021;5(12):2577-85.

RTP RESEARCH TO PRACTICE

Phase I/II Study of Zanubrutinib for Relapsed/Refractory MCL

Response assessment	Investigator-assessed response (N = 32)	IRC-assessed response (N = 32)
ORR 95% CI*	29 (90.6) (75.0-98.0)	27 (84.4) (67.2-94.7)
Best response		
CR	10 (31.3)	8 (25.0)
PR	19 (59.4)	19 (59.4)
Stable disease	1 (3.1)	2 (6.3)
PD	2 (6.3)	2 (6.3)
Unknown†	0	1 (3.1)

Unless otherwise noted, data are n (%).
*Two-sided Clopper-Pearson 95% CIs.
†Patient had discontinued treatment and died before signing an updated informed consent to allow scan collection for IRC review.

- Median duration of response was 18.5 months
- Median PFS was 21.1 months

ORR = overall response rate

Tam CS et al. *Blood Adv* 2021;5(12):2577-85.

RTP RESEARCH TO PRACTICE

Pirtobrutinib, a Next Generation, Highly Selective, Non-Covalent BTK Inhibitor in Previously Treated Mantle Cell Lymphoma: Updated Results from the Phase 1/2 BRUIN Study

Wang M et al.

ASH 2021;Abstract 381.

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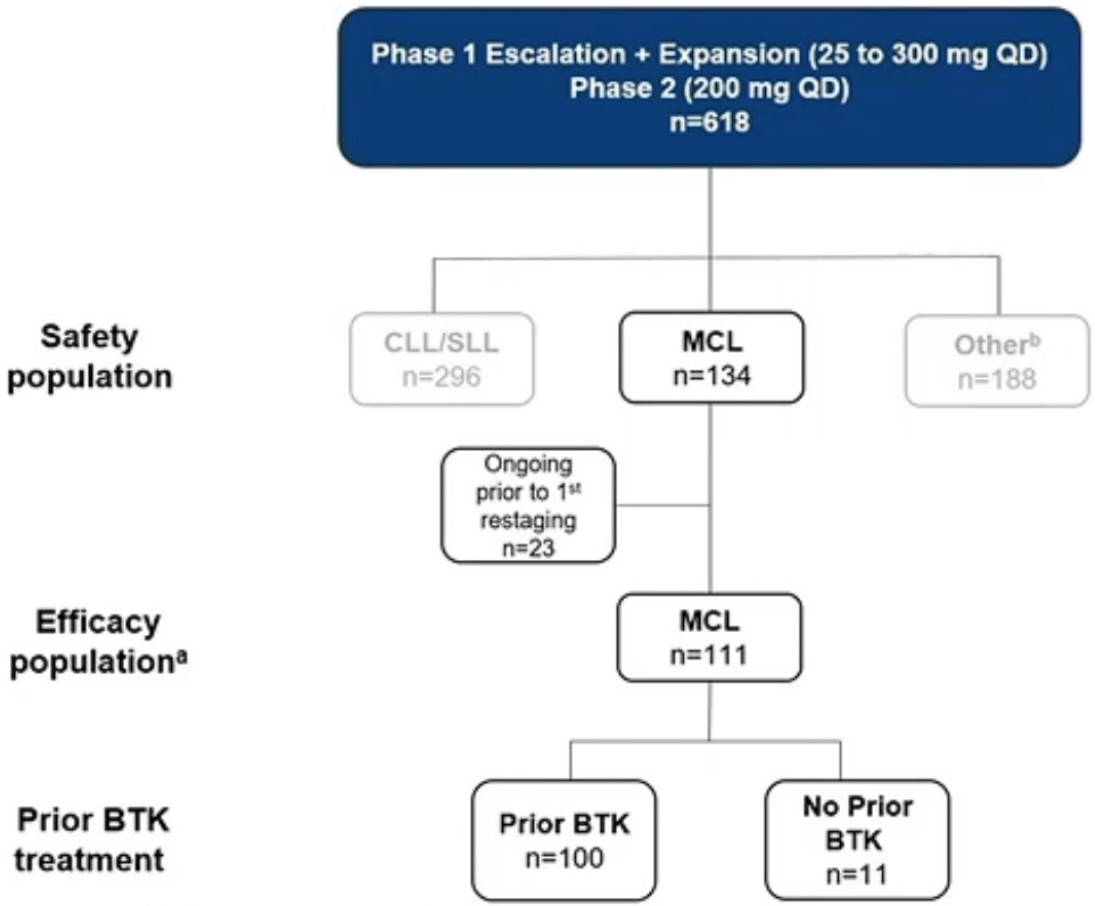
BRUIN: Phase I/II Trial Schema



Phase 1 3+3 design

- 28-day cycles
- Intra-patient dose escalation allowed
- Cohort expansion permitted at doses deemed safe

Eligibility

- Age ≥18
- ECOG 0-2
- CLL or other B-cell NHL
- Active disease and in need of treatment
- Previously treated

Key endpoints

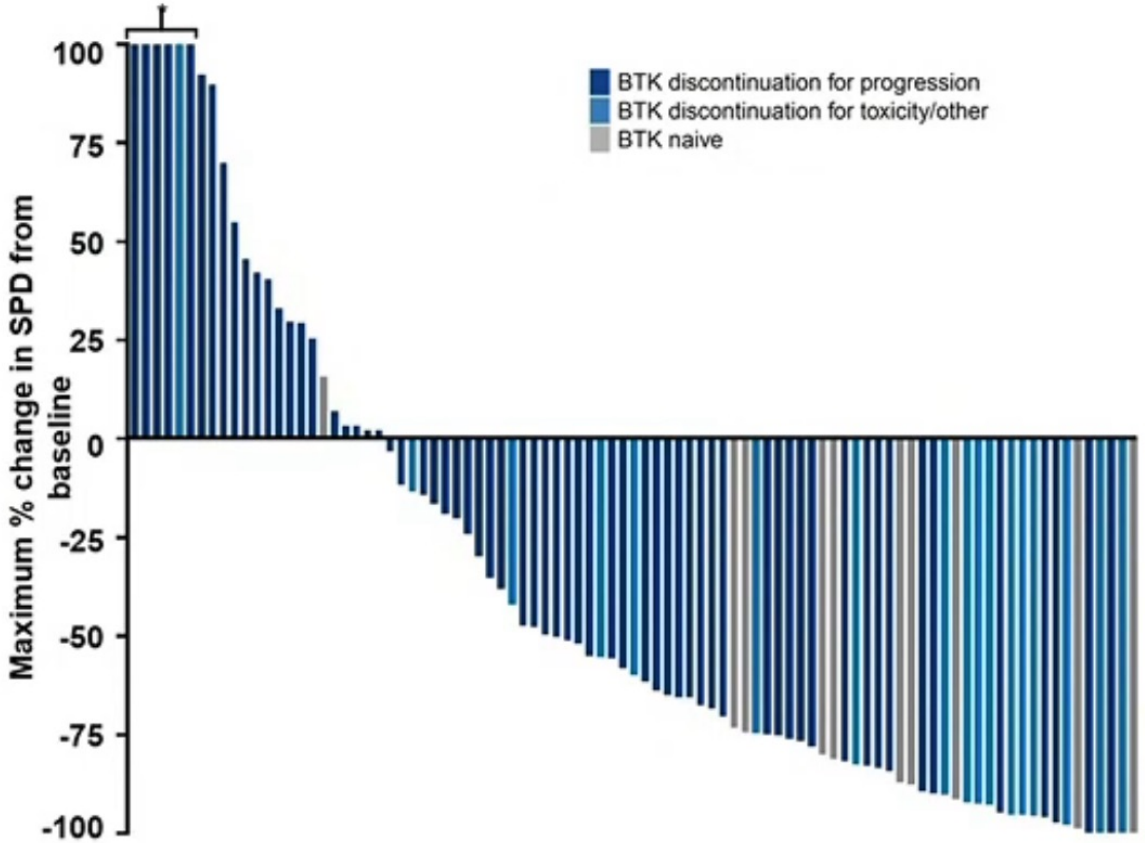
- Safety/tolerability
- Determine MTD & recommended phase 2 dose
- Pharmacokinetics
- Efficacy according to ORR & DoR based on disease criteria (Lugano, iwCLL, IWWM)

Data cutoff date of 16 July 2021. [a]Efficacy evaluable patients are those who had at least one post-baseline response assessment or had discontinued treatment prior to first post-baseline response assessment. [b]Other includes DLBCL, WM, FL, MZL, Richter's transformation, B-PLL, Hairy Cell Leukemia, PCNSL, and other transformation.

Wang M et al. ASH 2021;Abstract 381.

RTP RESEARCH TO PRACTICE

BRUIN: A Phase I/II Study of Pirtobrutinib — MCL Cohort



BTK Pre-Treated MCL Patients[a]	n=100
Overall Response Rate[b], % (95% CI)	**51% (41-61)**
Best Response	
CR, n (%)	25 (25)
PR, n (%)	26 (26)
SD, n (%)	16 (16)
BTK Naive MCL Patients[a]	**n=11**
Overall Response Rate[b], % (95% CI)	**82% (48-98)**
Best Response	
CR, n (%)	2 (18)
PR, n (%)	7 (64)
SD, n (%)	1 (9)

Efficacy also seen in patients with prior:

- Stem cell transplant (n=28): ORR 64% (95% CI: 44-81)
- CAR-T therapy (n=6): ORR 50% (95% CI: 12-88)

Data cutoff date of 16 July 2021. Data for 20 MCL patients are not shown in the waterfall plot due to no measurable target lesions identified by CT at baseline, discontinuation prior to first response assessment, or lack of adequate imaging in follow-up. *Indicates patients with >100% increase in SPD. [a]Efficacy evaluable patients are those who had at least one post-baseline response assessment or had discontinued treatment prior to first post-baseline response assessment. [b]ORR includes patients with a best response of CR and PR. Response status per Lugano 2014 criteria based on investigator assessment. Total % may be different than the sum of the individual components due to rounding.

Wang M et al. ASH 2021;Abstract 381.

RTP RESEARCH TO PRACTICE

Efficacy and Safety of Parsaclisib in Patients with Relapsed or Refractory Mantle Cell Lymphoma Not Previously Treated with a BTK Inhibitor: Primary Analysis from a Phase 2 Study (CITADEL-205)

Mehta A et al.

ASH 2021;Abstract 382.

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CITADEL-205: Response per Independent Review Committee

	WG (n=31)	DG (n=77)	Total (N=108)
ORR, n (%)	20 (64.5)	54 (70.1)	74 (68.5)
95% CI	45.4–80.8	58.6–80.0	58.9–77.1
Complete response, n (%)	7 (22.6)	12 (15.6)	19 (17.6)
Partial response, n (%)	13 (41.9)	42 (54.5)	55 (50.9)

Author conclusions: *Parsaclisib monotherapy demonstrated a rapid and durable response, had an acceptable safety profile, and was generally well tolerated in BTK inhibitor–naive pts with R/R MCL. These data suggest that parsaclisib could be a potential treatment option for pts with R/R MCL.*

WG = weekly dosing group; DG = daily dosing group; ORR = objective response rate

Mehta A et al. ASH 2021;Abstract 382.

RTP RESEARCH TO PRACTICE

Meet The Professor

Non-Small Cell Lung Cancer with an Actionable Target Beyond EGFR

Thursday, June 16, 2022
5:00 PM – 6:00 PM ET

Faculty

Melissa Johnson, MD

Moderator

Neil Love, MD

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Thank you for joining us!

NCPD credit information will be emailed to each participant within 5 business days.