Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Brian T Hill, MD, PhD
Director, Lymphoid Malignancy Program
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio

Commercial Support

This activity is supported by educational grants from ADC Therapeutics, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Genentech, a member of the Roche Group, Novartis 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 CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, Daiichi Sankyo Inc, Eisai Inc, Epizyme Inc, Exact Sciences Inc, 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, Natera Inc, Novartis, 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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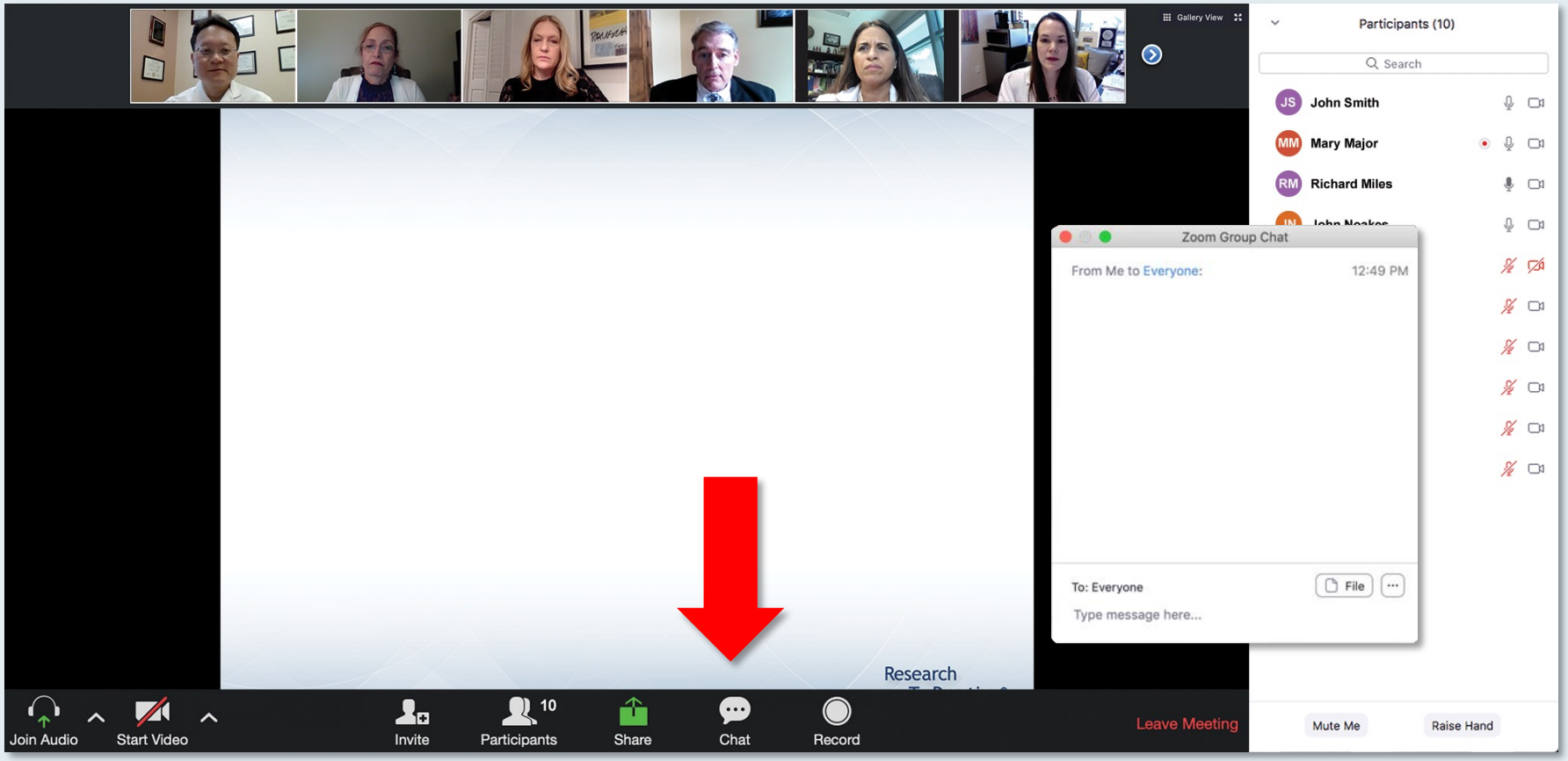
Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Dr Hill — Disclosures

No relevant conflicts of interest to disclose.

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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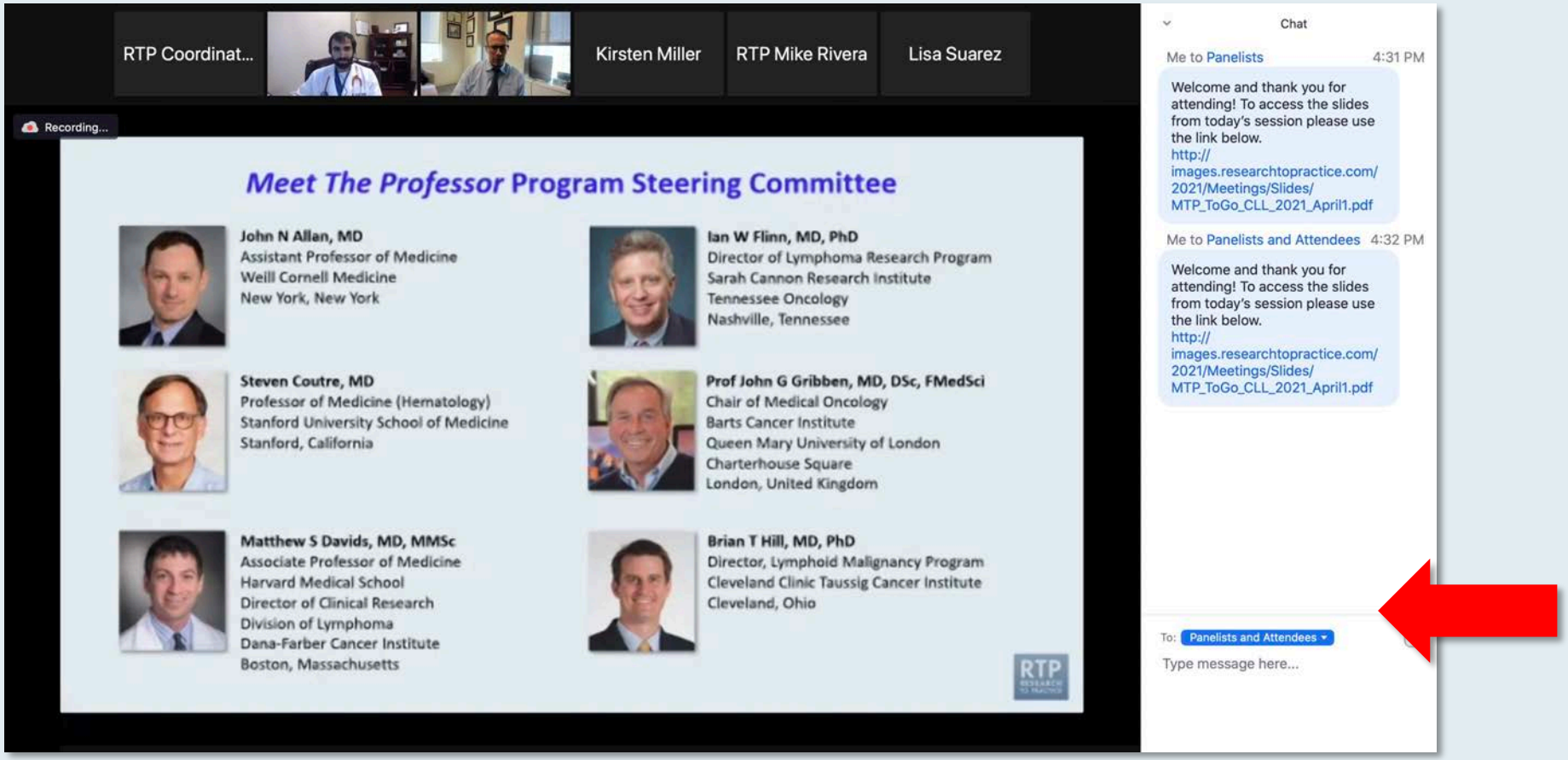
Expand chat submission box



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

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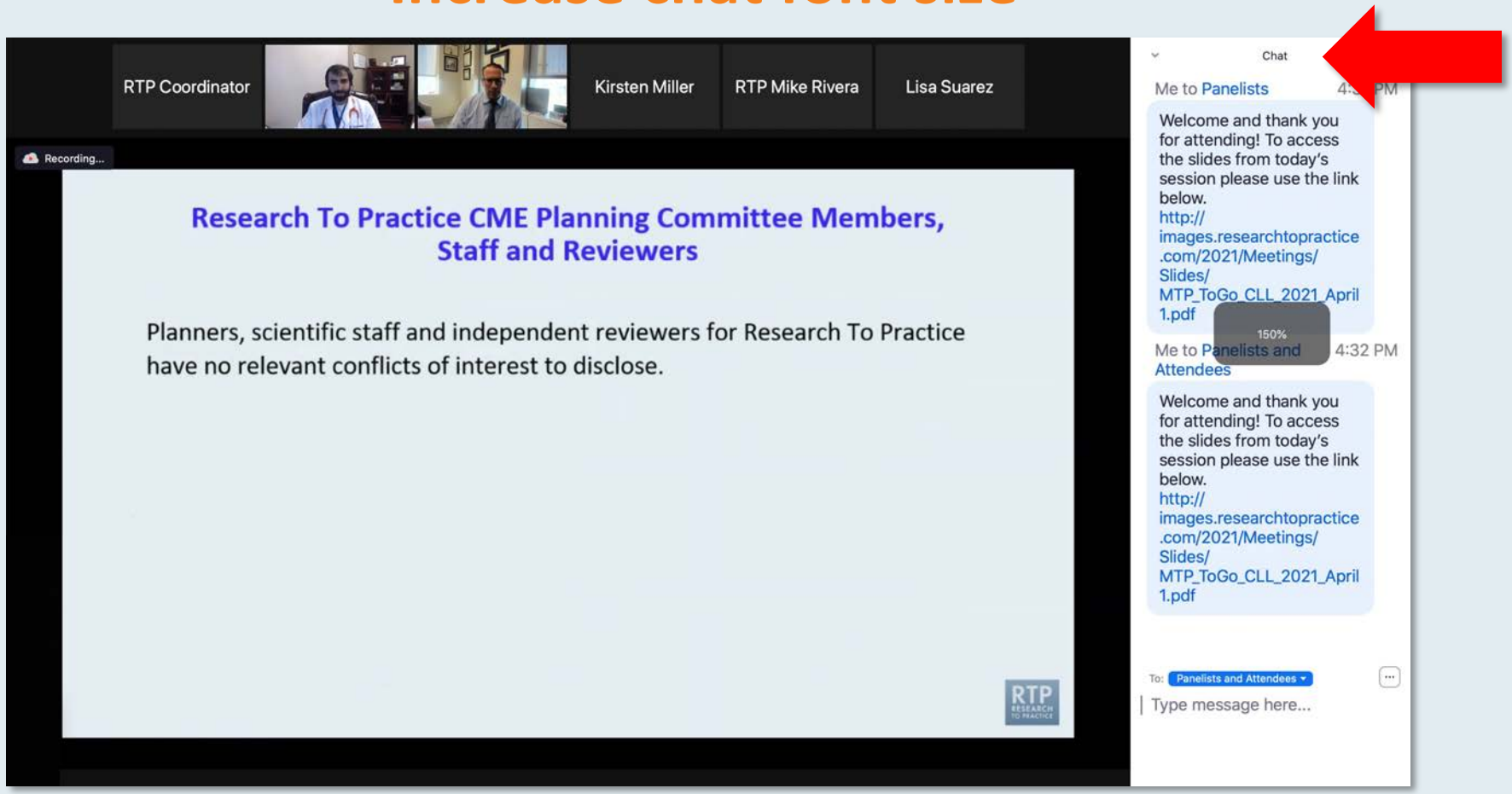

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Optimal Management of Hodgkin Lymphoma in Younger and Older Patients

DR ANDREW EVENS

RUTGERS CANCER INSTITUTE

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with ER-Positive Breast Cancer

Thursday, December 16, 2021
5:00 PM – 6:00 PM ET

Faculty

Ruth O'Regan, MD

Moderator

Neil Love, MD

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

Follicular Lymphoma

Tuesday, January 4, 2022
5:00 PM – 6:00 PM ET

Faculty

Laurie H Sehn, MD, MPH
Additional faculty to be announced.

Moderator

Neil Love, MD

RTP Year in Review 2022

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

Breast Cancer

Thursday, January 6, 2022
5:00 PM – 6:00 PM ET

Faculty

Harold J Burstein, MD, PhD
Additional faculty to be announced.

Moderator

Neil Love, MD

RTP Year in Review 2022

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Colorectal Cancer (Part 1 of a 3-Part Series)

Wednesday, January 19, 2022
10:15 PM – 11:45 PM ET

Faculty

Alan P Venook, MD

Additional faculty to be announced.

Moderator

To be announced.

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RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Gastroesophageal Cancers (Part 2 of a 3-Part Series)

Thursday, January 20, 2022
9:15 PM – 10:45 PM ET

Faculty

Yelena Y Janjigian, MD
Eric Van Cutsem, MD, PhD
Additional faculty to be announced.

Moderator

Samuel J Klempner, MD

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Hepatobiliary Cancers (Part 3 of a 3-Part Series)

Friday, January 21, 2022
9:15 PM – 10:45 PM ET

Faculty

Ghassan Abou-Alfa, MD, MBA
Richard S Finn, MD
Robin K Kelley, MD

Moderator

Tanios Bekaii-Saab, MD

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Thank you for joining us!

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

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Meet The Professor Program Participating Faculty

Nancy L Bartlett, MD
Professor of Medicine
Koman Chair in Medical Oncology
Washington University School of Medicine
St Louis, Missouri

Carla Casulo, MD
Associate Professor of Medicine
Division of Hematology/Oncology
Director, Hematology/Oncology Fellowship Program
University of Rochester
Wilmot Cancer Institute
Rochester, New York

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

Jonathan W Friedberg, MD, MMSc
Samuel E Durand Professor of Medicine
Director, James P Wilmot Cancer Institute
University of Rochester
Rochester, New York

Brian T Hill, MD, PhD
Director, Lymphoid Malignancy Program
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio

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Meet The Professor Program Participating Faculty

Brad S Kahl, MD
Professor of Medicine
Washington University School of Medicine
Director, Lymphoma Program
Siteman Cancer Center
St Louis, Missouri

Michael E Williams, MD, ScM
Byrd S Leavell Professor of Medicine
Chief, Hematology/Oncology Division
Physician Lead, Cancer Service Line
University of Virginia School of Medicine
Charlottesville, Virginia

Loretta J Nastoupil, MD
Associate Professor
Section Chief, Indolent Lymphoma
Section Chief, New Drug Development
Department of Lymphoma/Myeloma
The University of Texas MD Anderson Cancer Center
Houston, Texas

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

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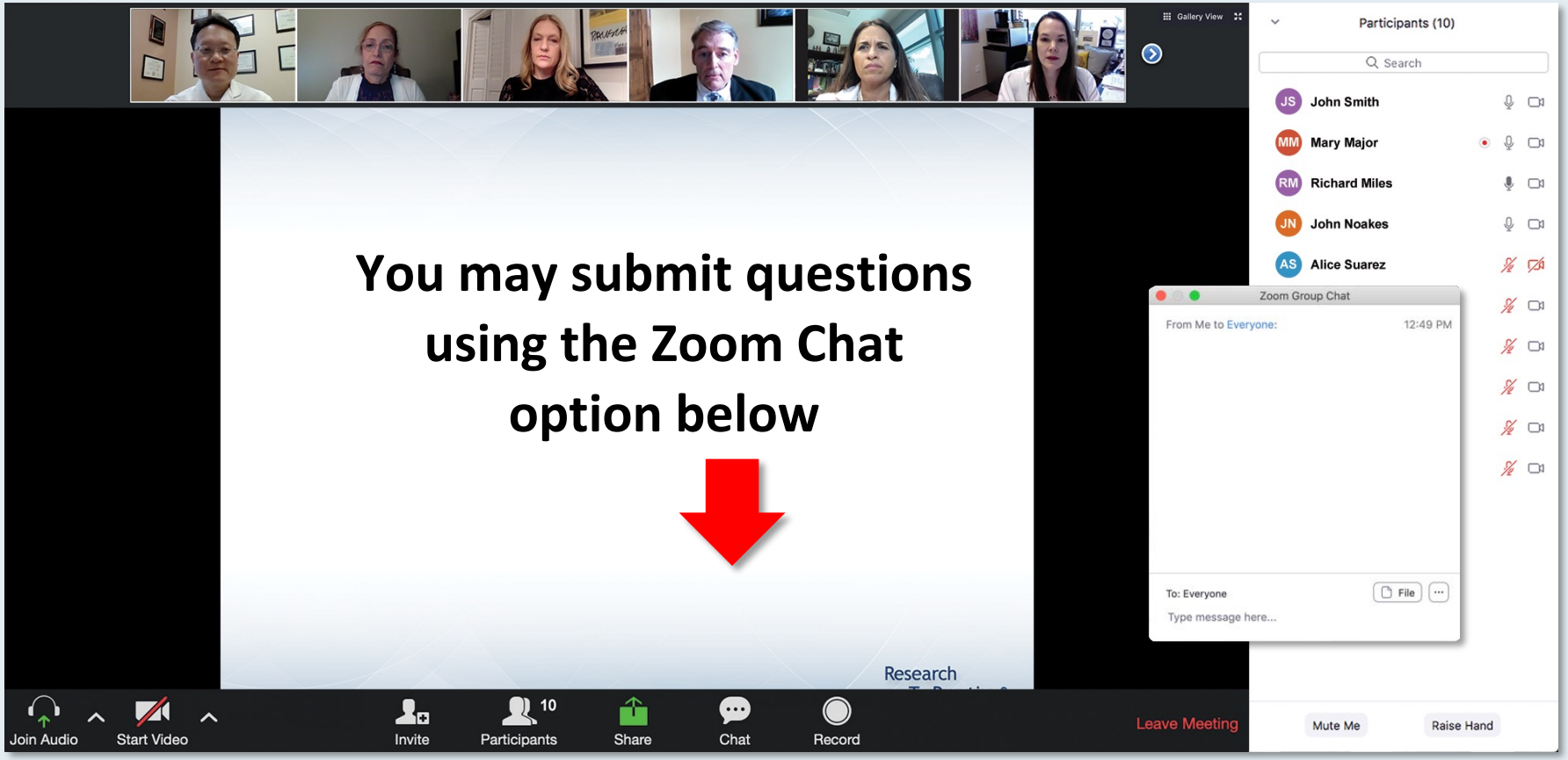

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Florida Cancer Specialists and
Research Institute
Lake Worth, Florida

Ferdy Santiago, MD
Florida Cancer Specialists and
Research Institute
Naples, Florida

Sulfi Ibrahim, MD
Reid Health
Richmond, Indiana

Syed F Zafar, MD
Florida Cancer Specialists and
Research Institute
Lee Health
Fort Myers, Florida

Laurie Matt-Amaral, MD, MPH
Northeast Ohio College of Medicine
Cleveland Clinic Akron General
Akron, Ohio

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A patient should be in adequate physical condition to undergo autologous stem cell transplant in order to be a suitable candidate for CAR T-cell therapy.

 Dr Bartlett	Disagree	 Dr Hill	Agree
 Dr Casulo	Agree	 Dr Kahl	Disagree
 Dr Flowers	Disagree	 Dr Nastoupil	Disagree
 Dr Friedberg	Agree	 Dr Williams	Disagree

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Hill

Introduction: ASH 2021 – Diffuse Large B-Cell Lymphoma (DLBCL)

MODULE 1: Case Presentations – DLBCL and Hodgkin Lymphoma

- Dr Zafar: A 77-year-old man with relapsed/refractory DLBCL
- Dr Gupta: A 68-year-old man with advanced DLBCL
- Dr Santiago: A 75-year-old woman with Hodgkin lymphoma

MODULE 2: Faculty Survey Results – Part 1

MODULE 3: ASH 2021 and Journal Club with Dr Hill – Part 1

MODULE 4: Case Presentations – Mantle Cell Lymphoma and Follicular Lymphoma

- Dr Ibrahim: A 60-year-old man with relapsed mantle cell lymphoma
- Dr Matt-Amaral: An 89-year-old man with Grade III follicular lymphoma

MODULE 5: Faculty Survey Results – Part 2

MODULE 6: ASH 2021 and Journal Club with Dr Hill – Part 2

MODULE 7: Appendix of Key Data Sets

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TO PRACTICE

N Engl J Med 2021;[Online ahead of print].

The NEW ENGLAND JOURNAL of MEDICINE

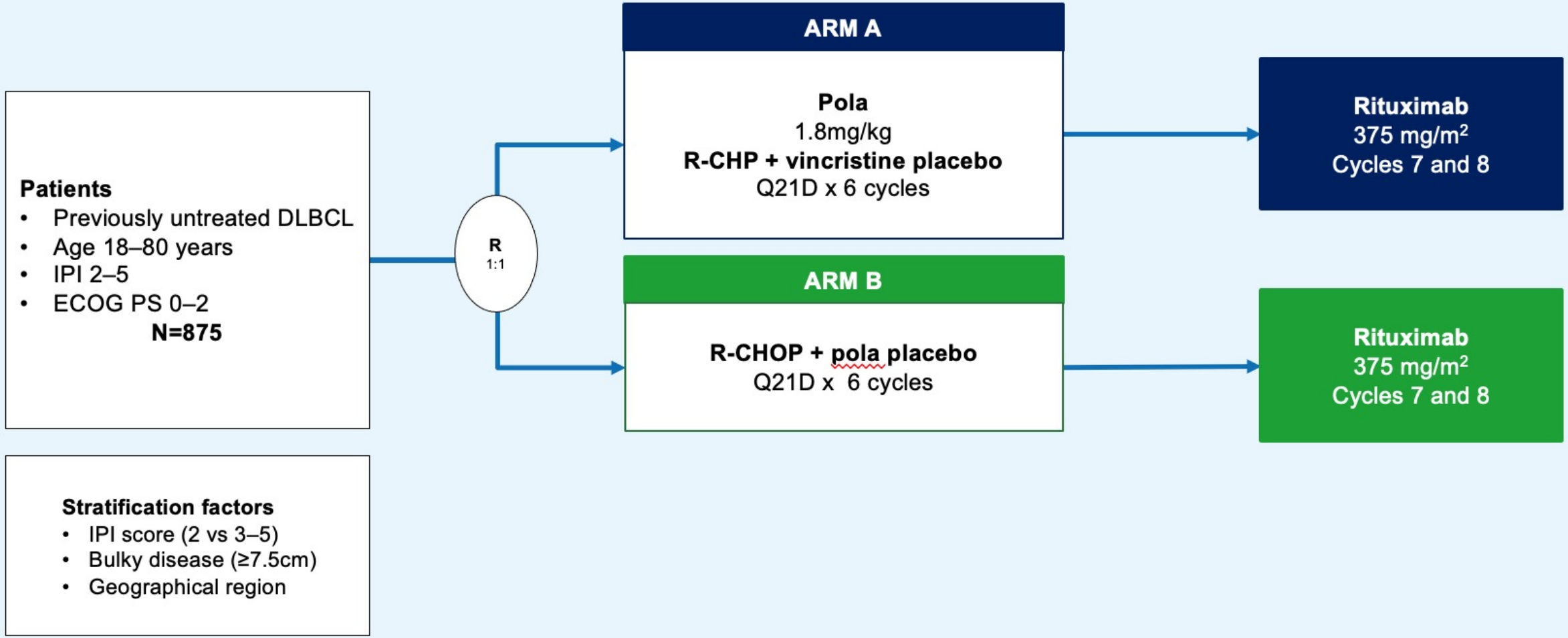
ORIGINAL ARTICLE

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

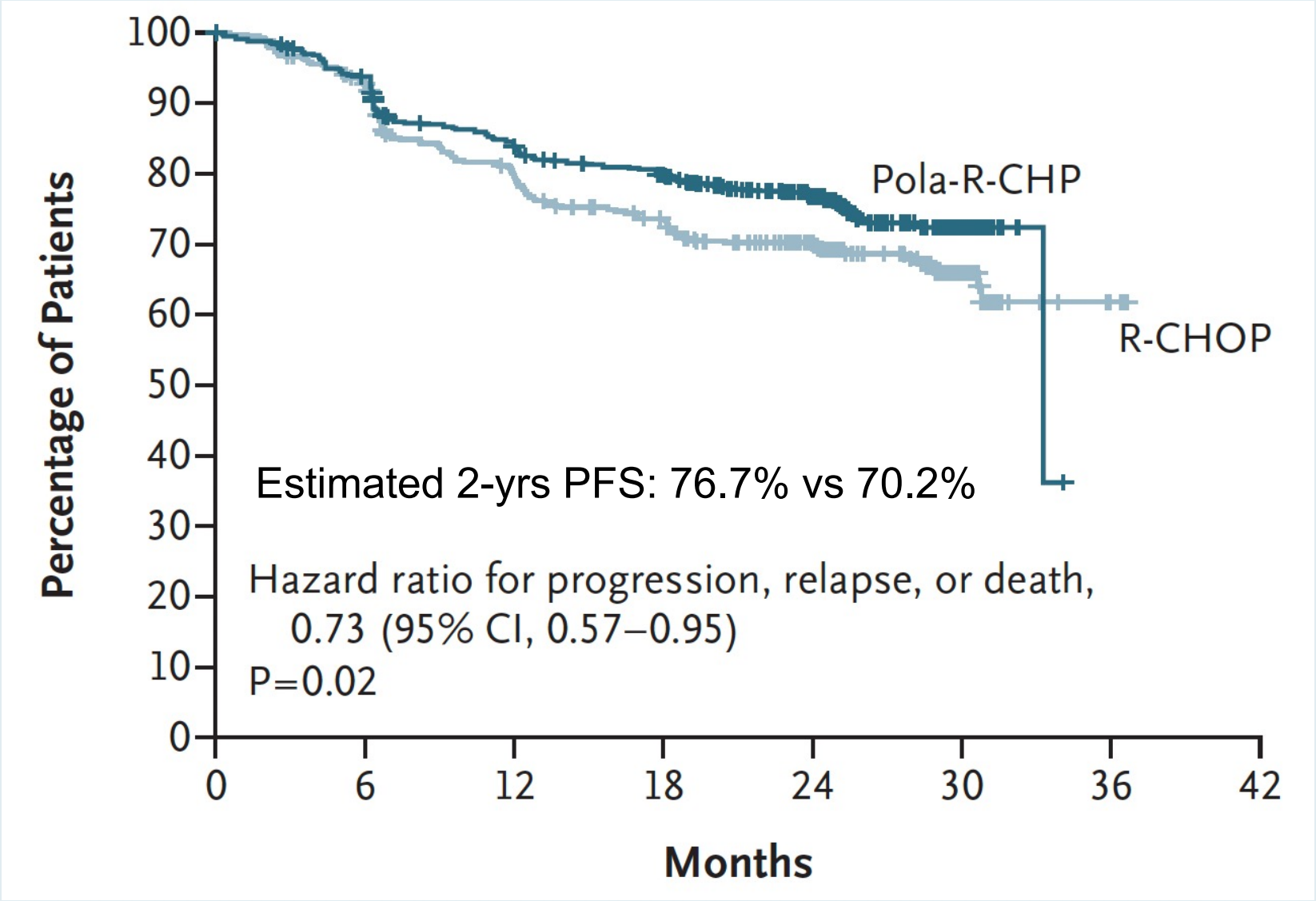
Tilly H et al. ASH 2021;LBA-1

POLARIX Phase III Trial Design



Courtesy of Gilles Salles MD, PhD

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



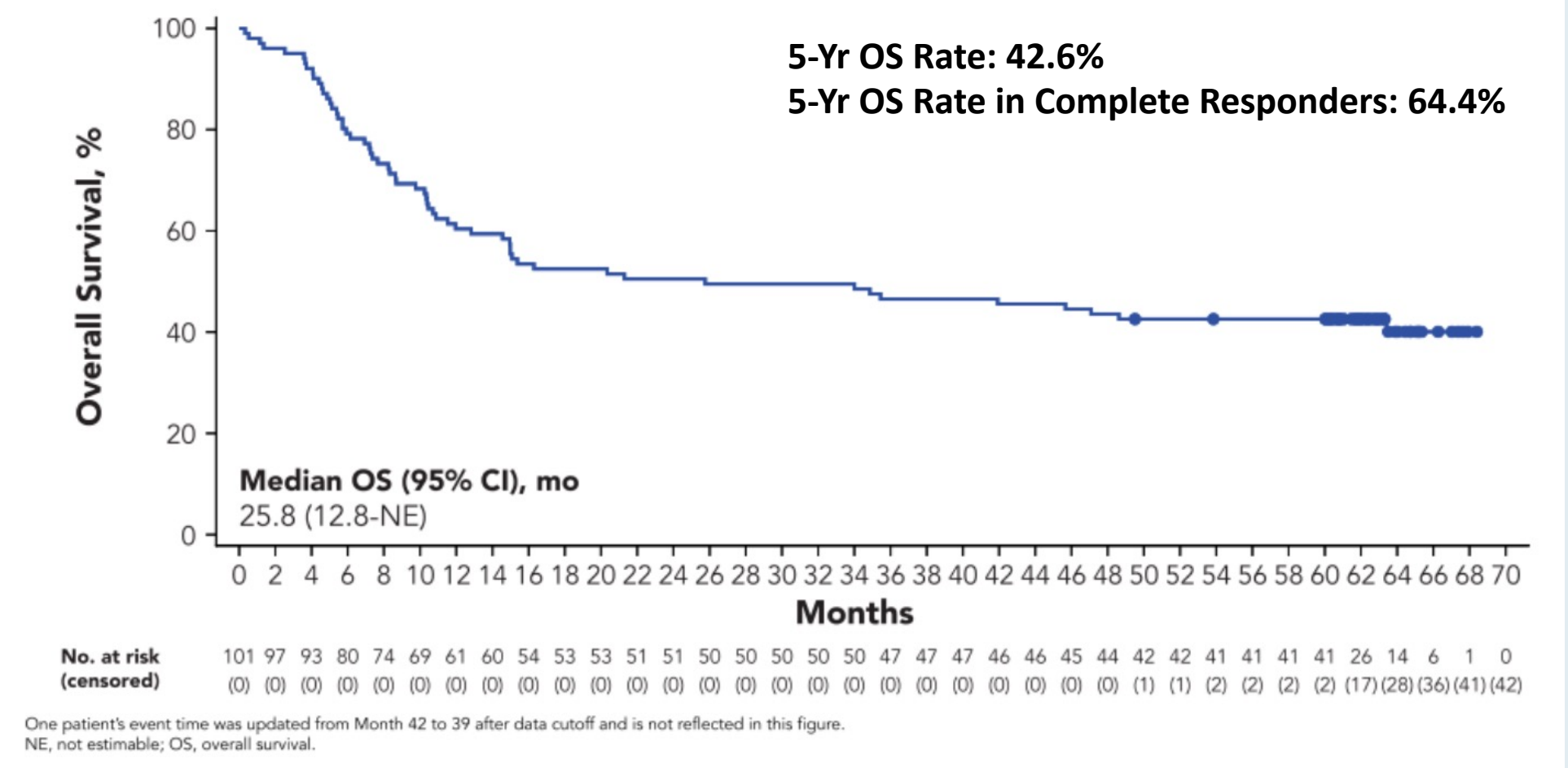
Tilly H et al. *N Engl J Med* 2021;[Online ahead of print].

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

Jacobson C et al.

ASH 2021;Abstract 1764.

ZUMA-1: Five-Year Update



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

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

Jacobson C et al. ASH 2021;Abstract 1764.

RTP RESEARCH TO PRACTICE

N Engl J Med 2021;[Online ahead of print].

The NEW ENGLAND JOURNAL of MEDICINE

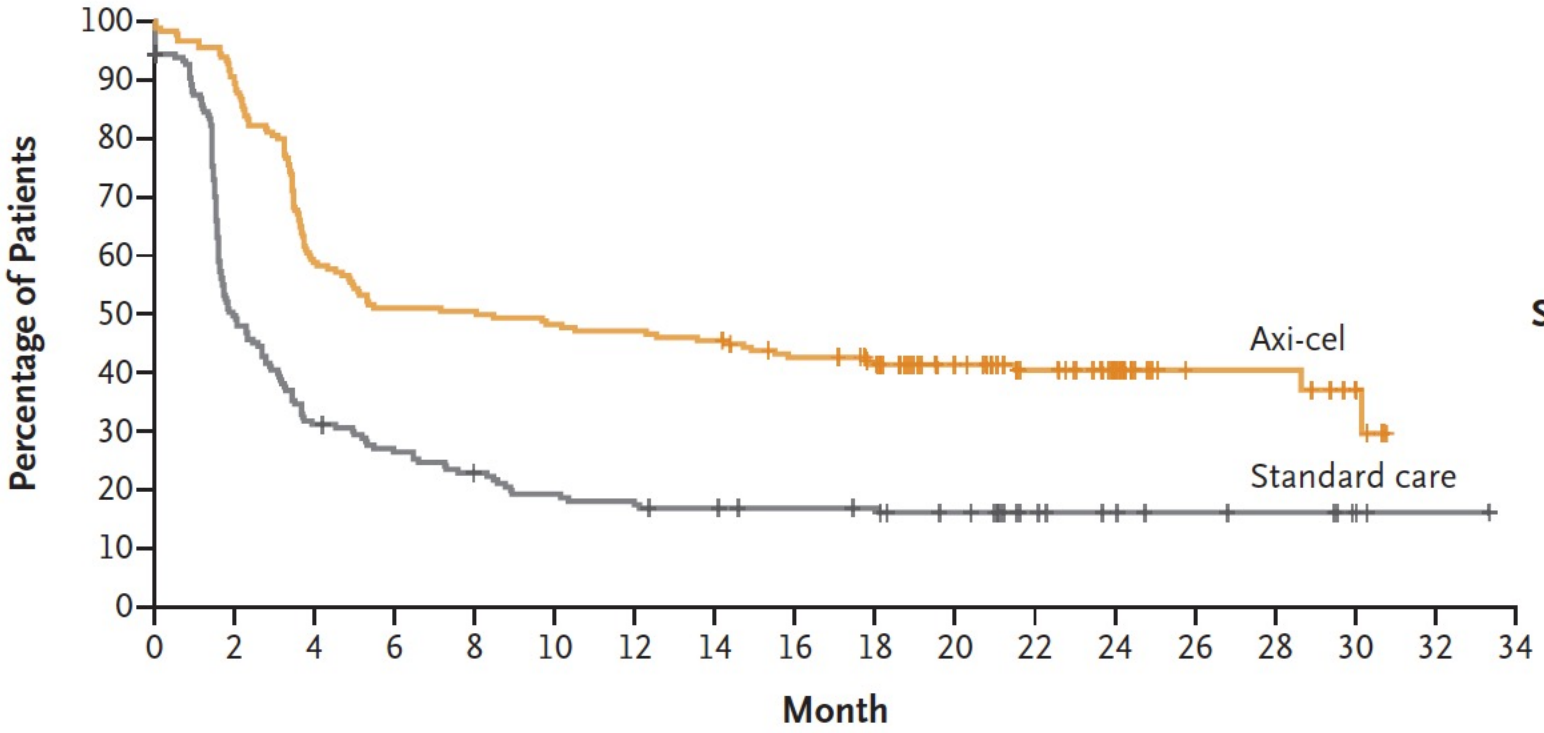
ORIGINAL ARTICLE

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*

Locke FL et al. ASH 2021;Abstract 2.

ZUMA-7: Event-Free Survival



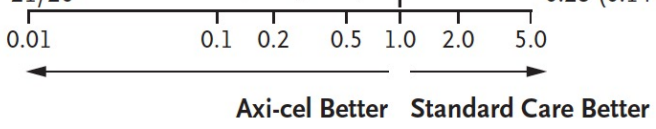
	No. of Patients	Median Event-free Survival (95% CI)
		mo
Axi-cel	180	8.3 (4.5–15.8)
Standard Care	179	2.0 (1.6–2.8)

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* 2021;[Online ahead of print].

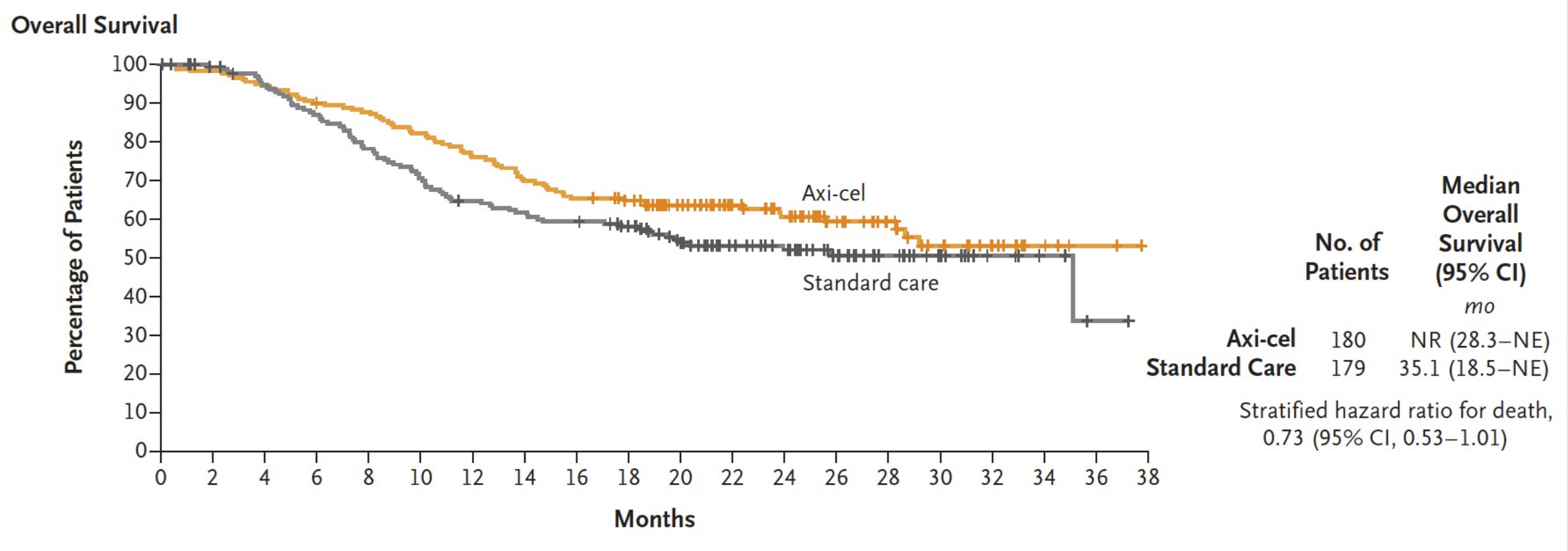
ZUMA-7: Event-Free Survival Subgroup Analysis

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)



Tilly H et al. *N Engl J Med* 2021;[Online ahead of print].

ZUMA-7: Overall Survival



Tilly H et al. *N Engl J Med* 2021;[Online ahead of print].

N Engl J Med 2021;[Online ahead of print].

The NEW ENGLAND JOURNAL of MEDICINE

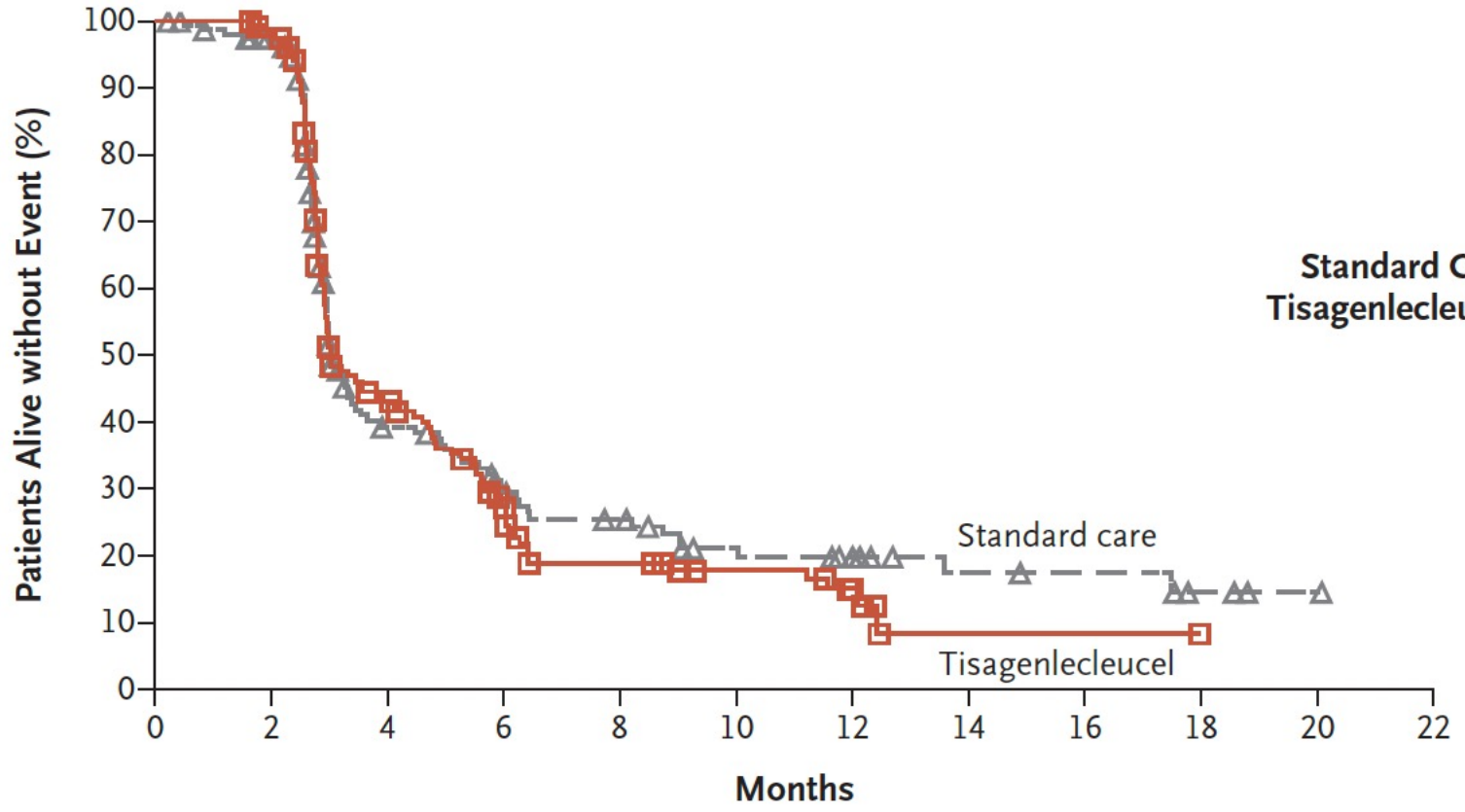
ORIGINAL ARTICLE

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

Bishop MR et al. ASH 2021;Abstract LBA-6.

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* 2021;[Epub ahead of print].

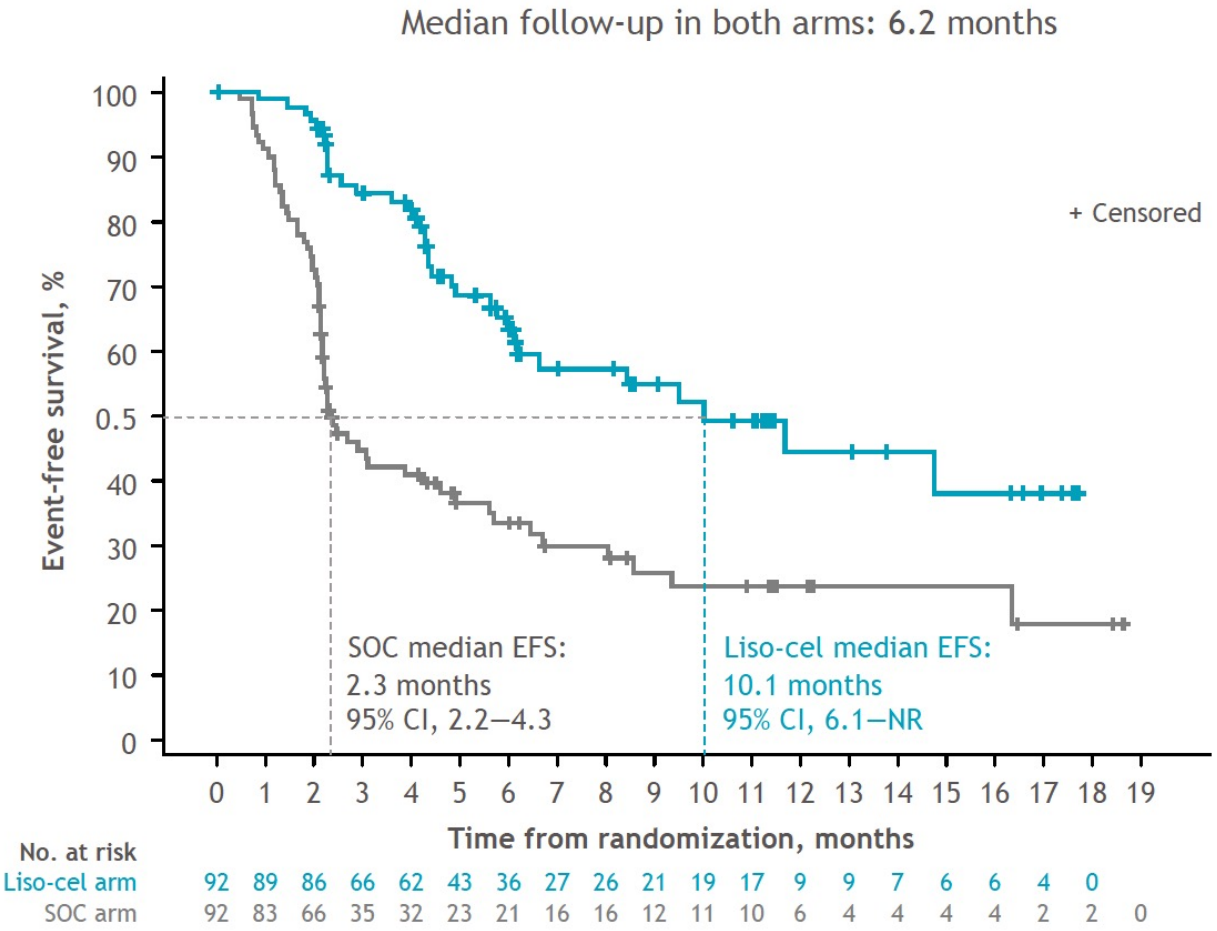
Lisocabtagene Maraleucel, a CD19-Directed Chimeric Antigen Receptor T Cell Therapy, Versus Standard of Care with Salvage Chemotherapy Followed by Autologous Stem Cell Transplantation as Second-Line Treatment in Patients with Relapsed or Refractory Large B-Cell Lymphoma: Results from the Randomized Phase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

[1]University of Colorado Cancer Center, Aurora, CO, USA; [2]Northside Hospital Cancer Institute, Atlanta, GA, USA; [3]Beth Israel Deaconess Medical Center, Boston, MA, USA; [4]Mayo Clinic, Rochester, MN, USA; [5]Helios Klinikum Berlin-Buch, Berlin, Germany; [6]University of Minnesota, Minneapolis, MN, USA; [7]University of Oklahoma Stephenson Cancer Center, Oklahoma City, OK, USA; [8]Center of Allogeneic Stem Cell Transplantation and Cellular Therapy (CAST), Karolinska Institutet and University Hospital, Stockholm, Sweden; [9]Erasmus University Medical Center, Rotterdam, The Netherlands, on behalf of HOVON/LLPC; [10]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [11]National Cancer Center Hospital, Tokyo, Japan; [12]Université de Lille, Centre Hospitalier Universitaire de Lille. ULR 7365, GRITA - Groupe de Recherche sur les formes Injectables et les Technologies Associées, Lille, France; [13]University of Nebraska Medical Center, Omaha, NE, USA; [14]Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [15]Celgene, a Bristol-Myers Squibb Company, Boudry, Switzerland; [16]Bristol Myers Squibb, Princeton, NJ, USA; [17]Massachusetts General Hospital Cancer Center, Boston, MA, USA

ASH 2021, Presentation Number 91

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.

N Engl J Med 2021;[Online ahead of print].

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

CAR T-Cell Therapy for Large B-Cell Lymphoma — Who, When, and How?

Mark Roschewski, M.D., Dan L. Longo, M.D., and Wyndham H. Wilson, M.D., Ph.D.

Meet The Professor with Dr Hill

Introduction: ASH 2021 – Diffuse Large B-Cell Lymphoma (DLBCL)

MODULE 1: Case Presentations – DLBCL and Hodgkin Lymphoma

- Dr Zafar: A 77-year-old man with relapsed/refractory DLBCL
- Dr Gupta: A 68-year-old man with advanced DLBCL
- Dr Santiago: A 75-year-old woman with Hodgkin lymphoma

MODULE 2: Faculty Survey Results – Part 1

MODULE 3: ASH 2021 and Journal Club with Dr Hill – Part 1

MODULE 4: Case Presentations – Mantle Cell Lymphoma and Follicular Lymphoma

- Dr Ibrahim: A 60-year-old man with relapsed mantle cell lymphoma
- Dr Matt-Amaral: An 89-year-old man with Grade III follicular lymphoma

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Case Presentation – Dr Zafar: A 77-year-old man with relapsed/refractory DLBCL

Dr Syed Zafar

- PMH: Grade 3A follicular lymphoma
- 2003: Diagnosed with Stage II DLBCL
  - R-CHOP, with a CR
- 2019: Relapse, with a renal mass and neck nodes → DLBCL, GCB-subtype, background of FL Grade 3A
- R-CEOP x 6, with CR
- 8/2021: B-symptoms, with imaging showing right iliac and retroperitoneal node, biopsy-proven DLBCL

Questions

- Would you recommend CAR T-cell therapy or autologous stem cell transplant?

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Case Presentation – Dr Gupta: A 68-year-old man with advanced DLBCL

Dr Saachi Gupta

- PMH: CAD and untreated obstructive ischemic cardiac disease
- Advanced DLBCL
- R-CHOP, with good response but relapse toward EOT
- Referred for clinical trial of second-line CAR T-cell therapy but ineligible due to cardiac issues

Question

- What treatment would you consider next?

Case Presentation – Dr Santiago: A 75-year-old woman with Hodgkin lymphoma

Dr Ferdy Santiago

- PMH: Long history of idiopathic thrombocytopenic purpura, HTN, diabetes
- Presented with right chest wall nodal conglomerate → Biopsy: Classic Hodgkin lymphoma
- ABVD, with significant disease response on PET after 2 cycles

Question

- Do you use brentuximab vedotin/AVD routinely instead of bleomycin with AVD to avoid the long-term side effects of bleomycin?

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Regulatory and reimbursement issues aside, which first-line therapy would you generally recommend for a 65-year-old patient with DLBCL?

 Dr Bartlett	R-CHOP	 Dr Hill	R-CHOP
 Dr Casulo	R-CHOP	 Dr Kahl	R-CHOP
 Dr Flowers	R-CHOP	 Dr Nastoupil	R-CHOP
 Dr Friedberg	R-CHOP	 Dr Williams	R-CHOP

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Do you generally use either tafasitamab/lenalidomide or loncastuximab tesirine in a patient who has experienced disease progression on or after CD19-directed CAR T-cell therapy?

 Dr Bartlett	Yes, either	 Dr Hill	Yes, tafasitamab/ lenalidomide
 Dr Casulo	Yes, either	 Dr Kahl	Yes, either
 Dr Flowers	Yes, either	 Dr Nastoupil	Yes, either
 Dr Friedberg	No	 Dr Williams	Yes, either

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What initial treatment would you recommend for a 26-year-old patient with classical Hodgkin lymphoma (HL) with anemia, diffuse adenopathy, hepatosplenomegaly and diffuse bone marrow involvement?

 Dr Bartlett	Brentuximab vedotin + AVD	 Dr Hill	ABVD
 Dr Casulo	Brentuximab vedotin + AVD	 Dr Kahl	Brentuximab vedotin + AVD
 Dr Flowers	Brentuximab vedotin + AVD	 Dr Nastoupil	Brentuximab vedotin + AVD
 Dr Friedberg	Brentuximab vedotin + AVD	 Dr Williams	Brentuximab vedotin + AVD

A = doxorubicin; V = vinblastine; D = dacarbazine; B = bleomycin

An 85-year-old frail patient with advanced-stage symptomatic HL is not a candidate for aggressive chemotherapy but is seeking active treatment. Regulatory and reimbursement issues aside, what would you recommend?

 Dr Bartlett	Brentuximab vedotin + nivolumab	 Dr Hill	Brentuximab vedotin
 Dr Casulo	Brentuximab vedotin/ dacarbazine	 Dr Kahl	Pembrolizumab
 Dr Flowers	Brentuximab vedotin + nivolumab	 Dr Nastoupil	Brentuximab vedotin + nivolumab
 Dr Friedberg	Brentuximab vedotin + nivolumab	 Dr Williams	Brentuximab vedotin

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Regulatory and reimbursement issues aside, in general, what would be your preferred bridge to transplant for a patient with HL who is experiencing disease relapse after up-front ABVD?

 Dr Bartlett	Ifosfamide/ carboplatin/etoposide	 Dr Hill	Ifosfamide/ carboplatin/etoposide
 Dr Casulo	Brentuximab vedotin + nivolumab	 Dr Kahl	Ifosfamide/ carboplatin/etoposide
 Dr Flowers	Ifosfamide/ carboplatin/etoposide	 Dr Nastoupil	Pembrolizumab + GVD
 Dr Friedberg	Brentuximab vedotin + nivolumab	 Dr Williams	Brentuximab vedotin + nivolumab

GND = gemcitabine/vinorelbine/liposomal doxorubicin

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ASH 2021 Lymphomas Review – Part 1

Diffuse Large B-Cell Lymphoma

- Locke FL et al. **Real world outcomes of axicabtagene ciloleucel (axi-cel) for the treatment of large B-cell lymphoma (LBCL): Impact of age and specific organ dysfunction.** ASH 2021; Abstract 530.
- Hill BT et al. **Impact of molecular features of diffuse large B-cell lymphoma on treatment outcomes with anti-CD19 chimeric antigen receptor (CAR) T-cell therapy.** ASH 2021;Abstract 165.
- Shouse G et al. **Impact of comorbidities on outcomes and toxicity in patients treated with CAR T-cell therapy for diffuse large B-cell lymphoma (DLBCL): A multicenter RWE study.** ASH 2021;Abstract 529.

ASH 2021 Lymphomas Review – Part 1 (Continued)

Diffuse Large B-Cell Lymphoma (Continued)

- Hutchings M et al. **Glofitamab (Glofit) in combination with polatuzumab vedotin (Pola): Phase Ib/II preliminary data support manageable safety and encouraging efficacy in relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL).** ASH 2021;Abstract 525.

- Carlo-Stella C et al. **Planned interim analysis of a Phase 2 study of loncastuximab tesirine plus ibrutinib in patients with advanced diffuse large B-cell lymphoma (LOTIS-3).** ASH 2021;Abstract 54.

Journal Club with Dr Hill – Part 1

- Hill BT et al. **Rapid tumor regression from PD-1 inhibition after anti-CD19 chimeric antigen receptor T-cell therapy in refractory diffuse large B-cell lymphoma.** *Bone Marrow Transplant* 2020;55(6):1184-7.
- Mian A et al. **Outcomes and factors impacting use of axicabtagene ciloleucel in patients with relapsed or refractory large B-cell lymphoma: Results from an intention-to-treat analysis.** *Leuk Lymphoma* 2021;62(6):1344-52.
- Spiegel JY et al. **Outcomes of patients with large B-cell lymphoma progressing after axicabtagene ciloleucel therapy.** *Blood* 2021;137(13):1832-5.
- Shah J et al. **Health-related quality of life and utility outcomes with selinexor in relapsed/refractory diffuse large B-cell lymphoma.** *Future Oncol* 2021;17(11):1295-310.
- Smith SD et al. **Polatuzumab vedotin for relapsed/refractory aggressive B-cell lymphoma: A multicenter post-marketing analysis.** *Clin Lymphoma Myeloma Leuk* 2021;21(3):170-5.
- Orellana-Noia VM et al. **Multicenter analysis of geriatric fitness and real-world outcomes in older patients with classical Hodgkin lymphoma.** *Blood Adv* 2021;5(18):3623-32.

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Case Presentation – Dr Ibrahim: A 60-year-old man with relapsed mantle cell lymphoma (MCL)

Dr Sulfi Ibrahim

- 2019: Diagnosed with MCL, s/p bendamustine/rituximab x 6, with CR
- Patient declined maintenance rituximab and follow-up
- Two years later: Symptomatic splenomegaly and LAD
- Zanubrutinib, with decline in spleen size, improvement in peripheral blood and symptoms
- Patient does not wish to continue indefinite zanubrutinib therapy

Questions

- Is there any difference in the clinical efficacy and tolerability of zanubrutinib versus the other BTK inhibitors approved in this disease?
- How would you decide between a BTK inhibitor therapy versus lenalidomide-based salvage therapy?
- Is it a reasonable option to stop the zanubrutinib and refer him for CAR T-cell therapy? How durable are the responses in MCL to CAR T-cell therapy?

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Case Presentation – Dr Matt-Amaral: An 89-year-old man with Grade III follicular lymphoma

Dr Laurie Matt-Amaral

- Presents with night sweats, right neck LAD; Biopsy: Grade 3 follicular lymphoma
- Staging PET scan and BMB under way
- EF > 60%, physically fit

Question

- What is the most appropriate treatment for this fit, elderly man – R-CHOP, mini-R-CHOP, bendamustine/rituximab, or some other regimen?

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In general, what would be your most likely treatment recommendation for a 70-year-old patient with mantle cell lymphoma who responds to BR and then ibrutinib on relapse but subsequently develops rapid tumor progression?

 Dr Bartlett	Brexucabtagene autoleucel	 Dr Hill	Brexucabtagene autoleucel
 Dr Casulo	Brexucabtagene autoleucel	 Dr Kahl	Brexucabtagene autoleucel
 Dr Flowers	Brexucabtagene autoleucel	 Dr Nastoupil	Brexucabtagene autoleucel
 Dr Friedberg	Brexucabtagene autoleucel	 Dr Williams	Venetoclax + rituximab as bridge to brexucabtagene autoleucel

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What treatment do you generally recommend for an otherwise healthy 65-year-old patient with symptomatic FL requiring treatment?

 Dr Bartlett	Bendamustine/ rituximab (BR)	 Dr Hill	BR
 Dr Casulo	BR	 Dr Kahl	BR
 Dr Flowers	BR	 Dr Nastoupil	BR
 Dr Friedberg	BR	 Dr Williams	BR

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Regulatory and reimbursement issues aside, what is your usual second-line therapy for a 65-year-old patient with FL who achieves a complete response to 6 cycles of bendamustine/rituximab (BR) but then experiences disease relapse 4 years later?

 Dr Bartlett	Lenalidomide/ rituximab	 Dr Hill	Lenalidomide/rituximab or rituximab alone
 Dr Casulo	Lenalidomide/ rituximab or R alone	 Dr Kahl	Lenalidomide/ rituximab
 Dr Flowers	Lenalidomide/ rituximab	 Dr Nastoupil	Lenalidomide/ rituximab
 Dr Friedberg	Lenalidomide/ obinutuzumab	 Dr Williams	Lenalidomide/ rituximab

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What is your usual third- and fourth-line treatment for a patient with FL (EZH2 wild type) who receives first-line BR, second-line lenalidomide/rituximab and then develops disease progression?

 Dr Bartlett	Duvelisib → tazemetostat	 Dr Hill	Tazemetostat → umbralisib
 Dr Casulo	Clin trial → tazemetostat	 Dr Kahl	Tazemetostat → umbralisib
 Dr Flowers	Tazemetostat → umbralisib	 Dr Nastoupil	Umbralisib → axi-cel
 Dr Friedberg	Umbralisib → tazemetostat	 Dr Williams	Umbralisib → tazemetostat

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What is your usual third- and fourth-line treatment for a patient with FL with an EZH2 mutation who receives first-line BR, second-line lenalidomide/rituximab and then develops disease progression?

Dr Bartlett

Duvelisib → tazemetostat

Dr Flowers

Tazemetostat → umbralisib

Dr Friedberg

Tazemetostat → umbralisib

Dr Hill

Tazemetostat → umbralisib

Dr Kahl

Tazemetostat → umbralisib

Dr Nastoupil

Tazemetostat → axi-cel

Dr Williams

Tazemetostat → umbralisib

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Which PI3K inhibitor do you use most commonly?

 Dr Bartlett	Duvelisib	 Dr Hill	Umbralisib
 Dr Casulo	Umbralisib	 Dr Kahl	Umbralisib
 Dr Flowers	Umbralisib	 Dr Nastoupil	Umbralisib
 Dr Friedberg	Umbralisib	 Dr Williams	Umbralisib

At what point in the treatment course are you referring patients with FL for consultation regarding CAR T-cell therapy?

 Dr Bartlett	Not referring for CAR T	 Dr Hill	At second relapse
 Dr Casulo	At third relapse	 Dr Kahl	At third relapse
 Dr Flowers	At second relapse	 Dr Nastoupil	At second relapse
 Dr Friedberg	At third relapse	 Dr Williams	At second relapse

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ASH 2021 Lymphomas Review – Part 2

Mantle Cell Lymphoma

- Wang M et al. **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.** ASH 2021;Abstract 381.
- Ribrag V et al. **Rituximab-lenalidomide (R^2) maintenance is superior to rituximab maintenance after first line immunochemotherapy in mantle cell lymphoma: Results of the MCL R2 Elderly clinical trial.** ASH 2021;Abstract 379.

ASH 2021 Lymphomas Review – Part 2 (Continued)

Follicular Lymphoma

- Kahl BS et al. **Long term follow up of the Resort study (E4402): A randomized phase III study comparing two different rituximab dosing strategies for low tumor burden follicular lymphoma.** ASH 2021;Abstract 815.
- Lansigan F et al. **Completed induction phase analysis of magnify: Phase 3b study of lenalidomide + rituximab (R^2) followed by maintenance in relapsed/refractory indolent non-Hodgkin lymphoma.** ASH 2021;Abstract 812.

ASH 2021 Lymphomas Review – Part 2 (Continued)

Follicular Lymphoma (Continued)

- Morschhauser F et al. **Glofitamab as monotherapy and in combination with obinutuzumab induces high complete response rates in patients (pts) with multiple relapsed or refractory (R/R) follicular lymphoma (FL).** ASH 2021;Abstract 128.
- Morschhauser F et al. **Mosunetuzumab in combination with lenalidomide has a manageable safety profile and encouraging activity in patients with relapsed/refractory follicular lymphoma: Initial results from a phase Ib study.** ASH 2021;Abstract 129.
- Budde LE et al. **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.** ASH 2021;Abstract 127.

Journal Club with Dr Hill – Part 2

- Mian A, Hill BT. **Brexucabtagene autoleucel for the treatment of relapsed/refractory mantle cell lymphoma.** *Expert Opin Biol Ther* 2021;21(4):435-41.
- Chakraborty R et al. **Late effects after chimeric antigen receptor T cell therapy for lymphoid malignancies.** *Transplant Cell Ther* 2021;27(3):222-9.
- Munshi PN et al. **ASTCT, CIBMTR, and EBMT clinical practice recommendations for transplant and cellular therapies in mantle cell lymphoma.** *Bone Marrow Transplant* 2021; [Online ahead of print].
- Munshi PN et al. **American Society of Transplantation and Cellular Therapy, Center of International Blood and Marrow Transplant Research, and European Society for Blood and Marrow Transplantation clinical practice recommendations for transplantation and cellular therapies in mantle cell lymphoma.** *Transplant Cell Ther* 2021;27(9):720-8.

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Journal Club with Dr Hill – Part 2 (Continued)

- Bond DA et al. **Early relapse identifies MCL patients with inferior survival after intensive or less intensive frontline therapy.** *Blood Adv* 2021;[Online ahead of print].
- Karmali R et al. **Multi-center analysis of practice patterns and outcomes of younger and older patients with mantle cell lymphoma in the rituximab era.** *Am J Hematol* 2021;96(11):1374-84.
- Riedell PA et al. **Effect of time to relapse on overall survival in patients with mantle cell lymphoma following autologous haematopoietic cell transplantation.** *Br J Haematol* 2021;195(5):757-63.

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Diffuse Large B-Cell Lymphoma

original reports

Polatuzumab Vedotin in Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Laurie H. Sehn, MD, MPH[1]; Alex F. Herrera, MD[2]; Christopher R. Flowers, MD, MSc[3]; Manali K. Kamdar, MD, MBBS[4]; Andrew McMillan, PhD[5]; Mark Hertzberg, MBBS, PhD[6]; Sarit Assouline, MDCM, MSc[7]; Tae Min Kim, MD[8]; Won Seog Kim, MD, PhD[9]; Muhit Ozcan, MD[10]; Jamie Hirata, PharmD[11]; Elicia Penuel, PhD[11]; Joseph N. Paulson, PhD[11]; Ji Cheng, PhD[12]; Grace Ku, MD[11]; and Matthew J. Matasar, MD[13]

J Clin Oncol 2020;38(2):155-65.

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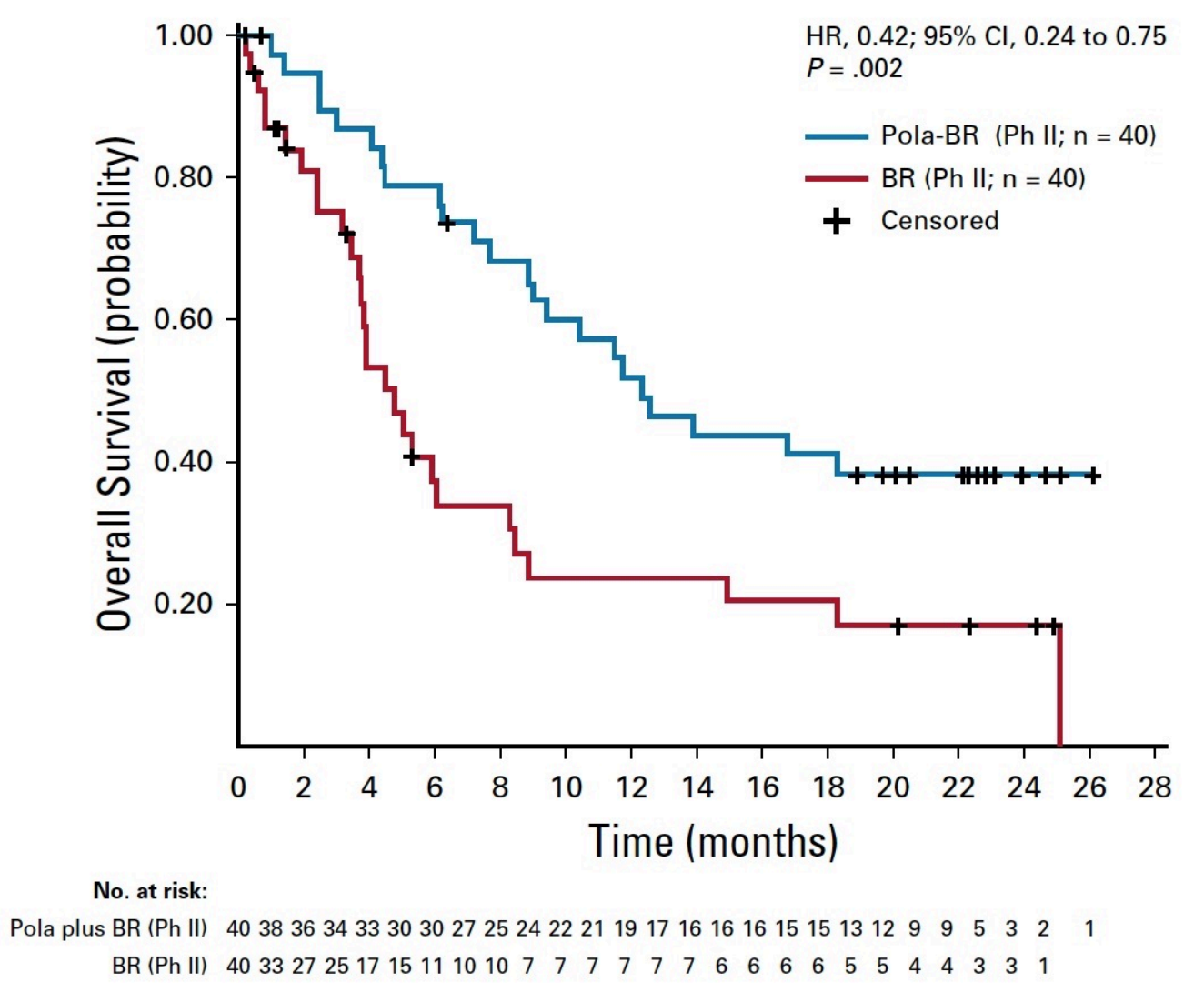
Polatuzumab Vedotin with Bendamustine/Rituximab for Transplant-Ineligible R/R DLBCL: End-of-Treatment CR Rate

Outcome	Phase II Randomized	
	Pola-BR (n = 40)	BR (n = 40)
End of treatment		
IRC, objective response	18 (45.0)	7 (17.5)
Complete response	16 (40.0)	7 (17.5)
Partial response	2 (5.0)	0
Stable disease	6 (15.0)	1 (2.5)
Progressive disease	8 (20.0)	10 (25.0)
Missing or unevaluable†	8 (20.0)	22 (55.0)

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

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



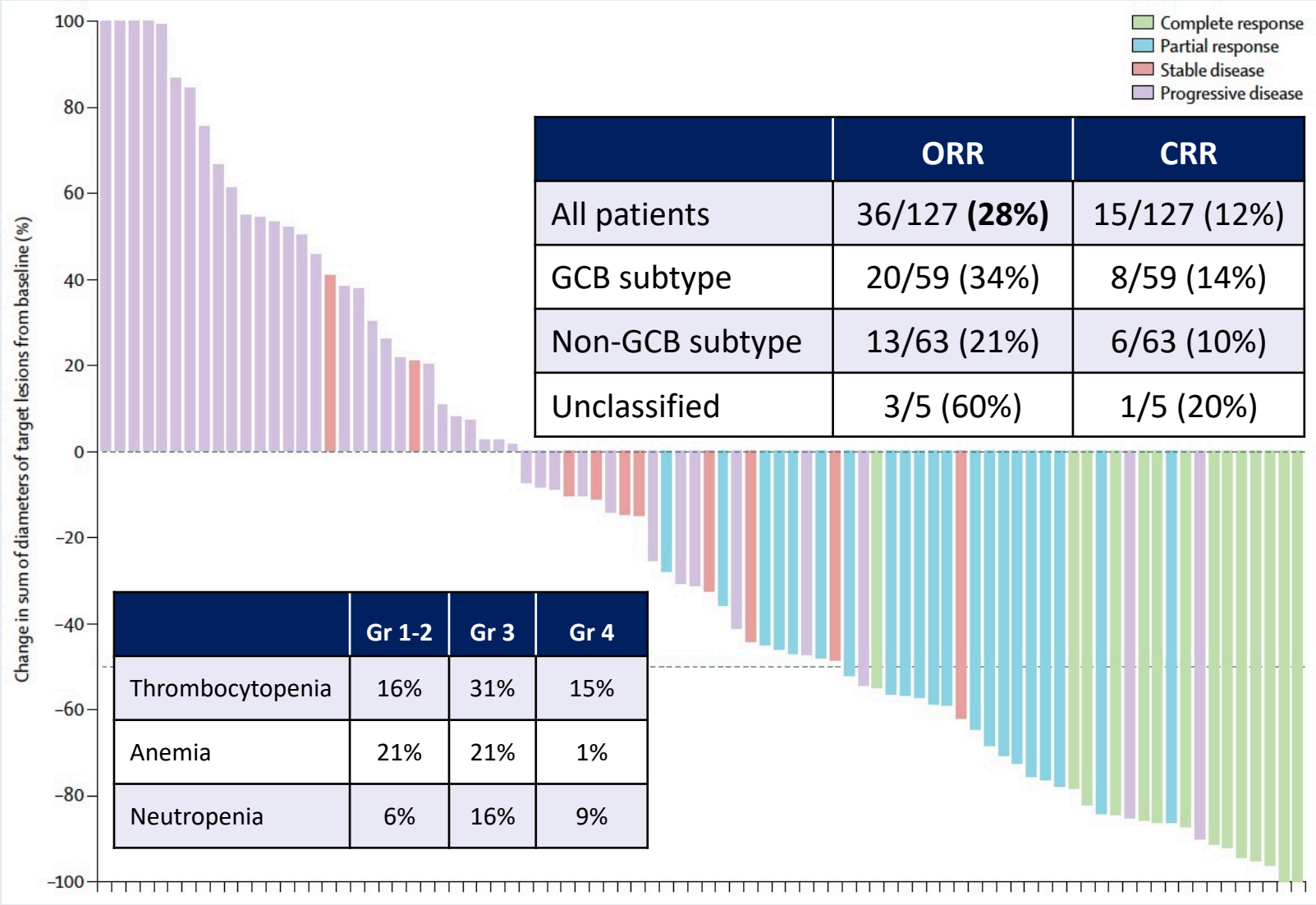
Sehn LH et al. *J Clin Oncol* 2020;38(2):155-65.

Lancet Haematol 2020;7:e511-22.

Selinexor in patients with relapsed or refractory diffuse large B-cell lymphoma (SADAL): a single-arm, multinational, multicentre, open-label, phase 2 trial

Nagesh Kalakonda, Marie Maerevoet*, Federica Cavallo, George Follows, Andre Goy, Joost S P Vermaat, Olivier Casasnovas, Nada Hamad, Josée M Zijlstra, Sameer Bakhshi, Reda Bouabdallah, Sylvain Choquet, Ronit Gurion, Brian Hill, Ulrich Jaeger, Juan Manuel Sancho, Michael Schuster, Catherine Thieblemont, Fátima De la Cruz, Miklos Egyed, Sourav Mishra, Fritz Offner, Theodoros P Vassilakopoulos, Krzysztof Warzocha, Daniel McCarthy, Xiwen Ma, Kelly Corona, Jean-Richard Saint-Martin, Hua Chang, Yosef Landesman, Anita Joshi, Hongwei Wang, Jatin Shah, Sharon Shacham, Michael Kauffman, Eric Van Den Neste, Miguel A Canales*

SADAL: Efficacy and Safety of Selinexor for R/R DLBCL After at Least 2 Previous Lines of Chemoimmunotherapy



	ORR	CRR
All patients	36/127 **(28%)**	15/127 (12%)
GCB subtype	20/59 (34%)	8/59 (14%)
Non-GCB subtype	13/63 (21%)	6/63 (10%)
Unclassified	3/5 (60%)	1/5 (20%)

	Gr 1-2	Gr 3	Gr 4
Thrombocytopenia	16%	31%	15%
Anemia	21%	21%	1%
Neutropenia	6%	16%	9%

Kalakonda N et al. *Lancet Haematol* 2020;7:e511-22.

FDA Grants Accelerated Approval to Tafasitamab-cxix for DLBCL

Press Release – July 31, 2020

"The Food and Drug Administration granted accelerated approval to tafasitamab-cxix, a CD19-directed cytolytic antibody, indicated in combination with lenalidomide for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low grade lymphoma, and who are not eligible for autologous stem cell transplant.

The efficacy of tafasitamab-cxix with lenalidomide was evaluated in L-MIND (NCT02399085), an open label, multicenter single-arm trial in 81 patients. Patients received tafasitamab-cxix 12 mg/kg intravenously with lenalidomide (25 mg orally on days 1 to 21 of each 28-day cycle) for maximum of 12 cycles, followed by tafasitamab-cxix as monotherapy."

www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-tafasitamab-cxix-diffuse-large-b-cell-lymphoma

Lancet Oncol 2020;21:978-88

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*

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;21:978-88.

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."

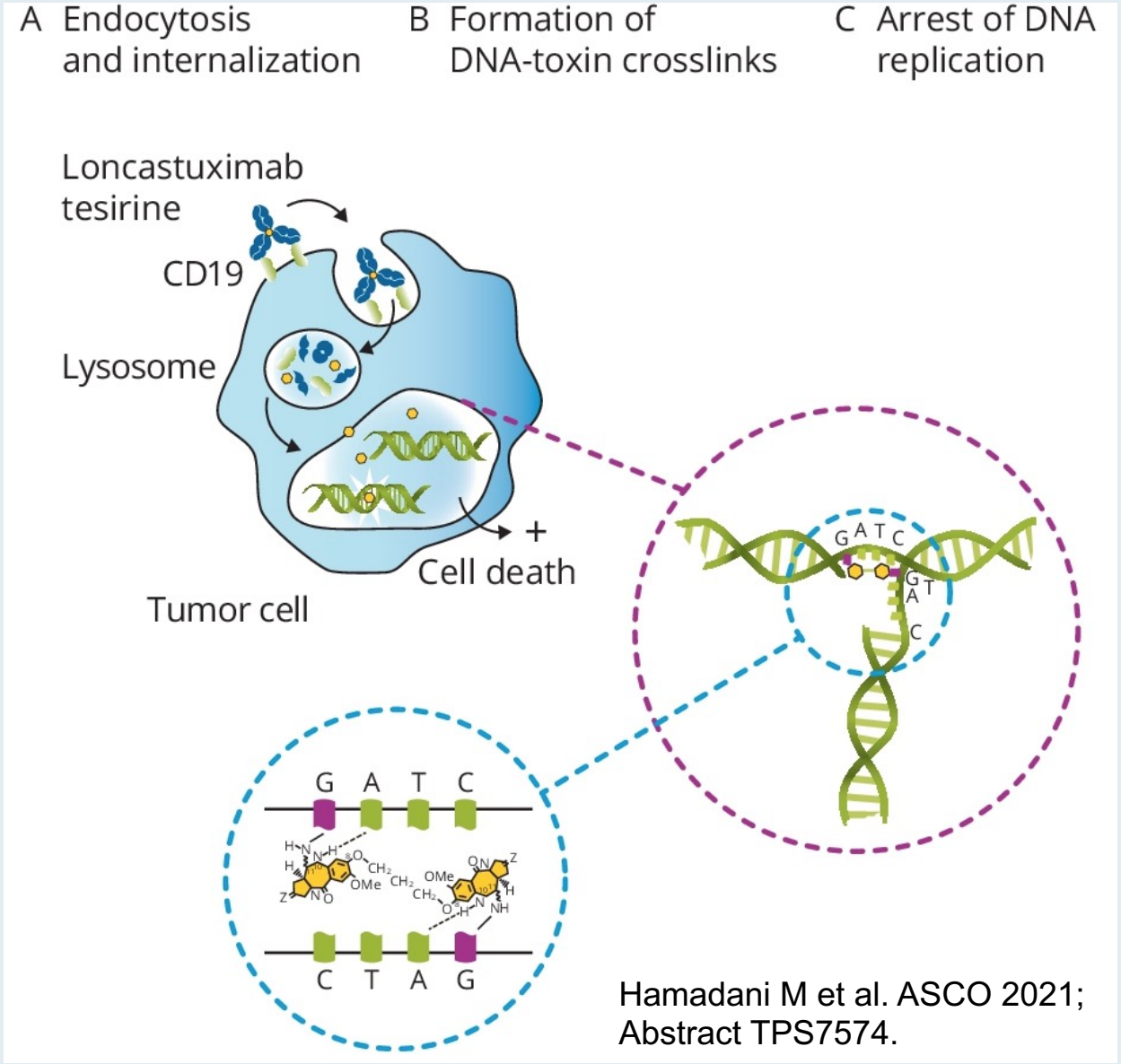
www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-loncastuximab-tesirine-lpyl-large-b-cell-lymphoma

Lancet Oncol 2021;22:790-800

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

Mechanism of Action of Loncastuximab Tesirine



Hamadani M et al. ASCO 2021; Abstract TPS7574.

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

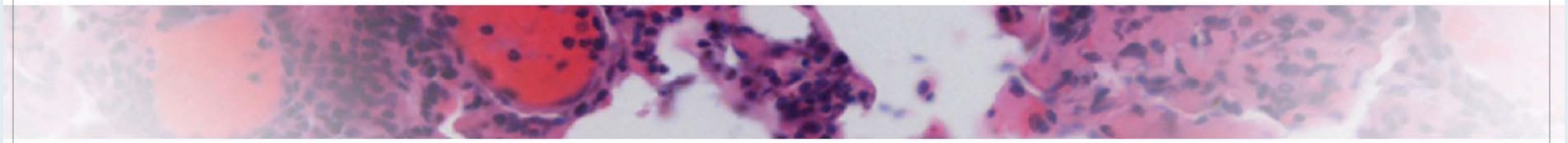
Response	As-treated population (N = 145)
Overall response rate	70/145 (48.3%)
Complete response rate	35/145 (24.1%)
Complete response	35 (24%)
Partial response	35 (24%)
Stable disease	22 (15%)
Progressive disease	30 (21%)
Not evaluable	23 (16%)
Survival	**As-treated population (N = 145)**
Median progression-free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

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

LOTIS-2: Common Treatment-Emergent Adverse Events

Treatment-Emergent AEs	Grade 1-2	Grade 3-4
Anemia	16%	10%
Thrombocytopenia	15%	18%
Neutropenia	14%	26%
Leukopenia	6%	9%

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



Planned Interim Analysis of a Phase 2 Study of Loncastuximab Tesirine Plus Ibrutinib in Patients with Advanced Diffuse Large B-Cell Lymphoma (LOTIS-3)

Oral Presentation, 63rd ASH Annual Meeting and Exposition, December 11–14, 2021

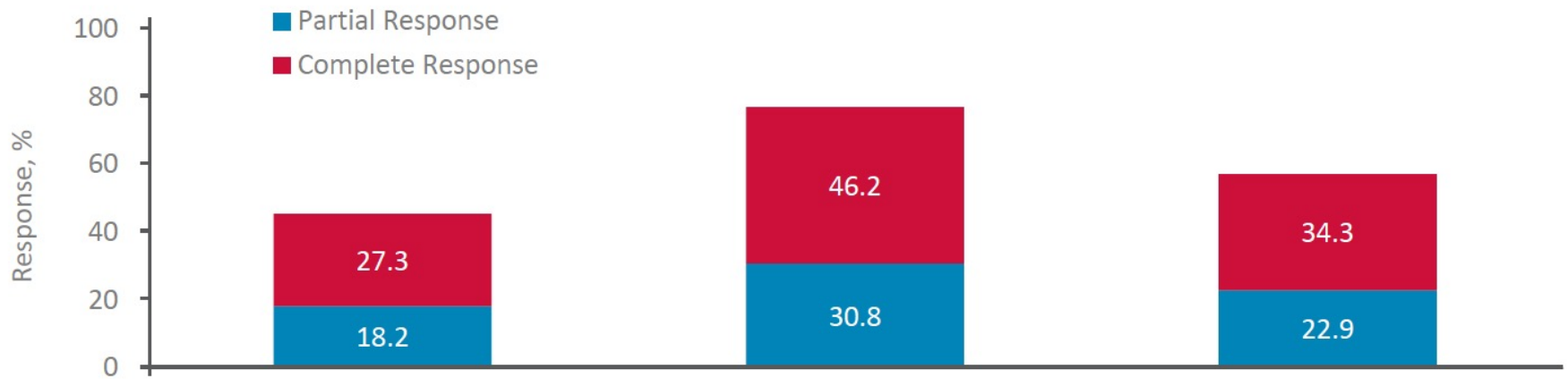
Carmelo Carlo-Stella, MD[1], Pier Luigi Zinzani, MD[2], Murali Janakiram, MD, MS[3], Vivian Dai, MD[4], Xiaomin He, PhD[4], Annette Ervin-Haynes, DO, MPA[4], Julien Depaus, MD[5]

[1]Department of Biomedical Sciences, Humanitas University, and Department of Oncology and Hematology, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Humanitas Research Hospital, Milan, Italy; [2]IRCCS Azienda Ospedaliero-Universitaria di Bologna Istituto di Ematologia "Seràgnoli," and Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale Università di Bologna, Bologna, Italy; [3]Division of Hematology, Oncology and Transplantation, University of Minnesota, Minneapolis, MN, USA; [4]Clinical Development, ADC Therapeutics America, Inc., Murray Hill, NJ, USA; [5]Department of Hematology, Centre Hospitalier Universitaire (CHU) Université Catholique de Louvain (UCL) Namur Site Godinne, Yvoir, Belgium

ASH 2021;Abstract 54

LOTIS-3: Phase II Study of Loncastuximab Tesirine with Ibrutinib for Advanced DLBCL

Efficacy: Response Rates[a]



	Non-GCB DLBCL (n=22)	GCB DLBCL (n=13)	All DLBCL (n=35)
ORR	**45.5%**	**76.9%**	**57.1%**
(n/N)	(10/22)	(10/13)	(20/35)
(95% CI)[b]	(24.4, 67.8)	(46.2, 95.0)	(39.4, 73.7)

Data cutoff: August 30, 2021. Efficacy analysis set consists of patients who received ≥1 dose of study drugs, have a valid BL radiological assessment(s), and have ≥1 valid post-BL radiological assessment.
[a]Overall response rates by IRC assessment; COO designation by local IHC assessment according to the Hans criteria. Patients who do not have a post-baseline radiological assessment due to early clinical progression or death (after receiving study drugs) were also included.
[b]The exact 95% CIs are two-sided and calculated using the Clopper–Pearson method.
BL, baseline; CI, confidence interval; COO, cell of origin; DLBCL, diffuse large B-cell lymphoma; GCB, germinal center B-cell; IHC, immunohistochemistry; IRC, independent review committee; ORR, overall response rate.

- Safety data were consistent with those reported previously

Carlo-Stella C et al. ASH 2021;Abstract 54.

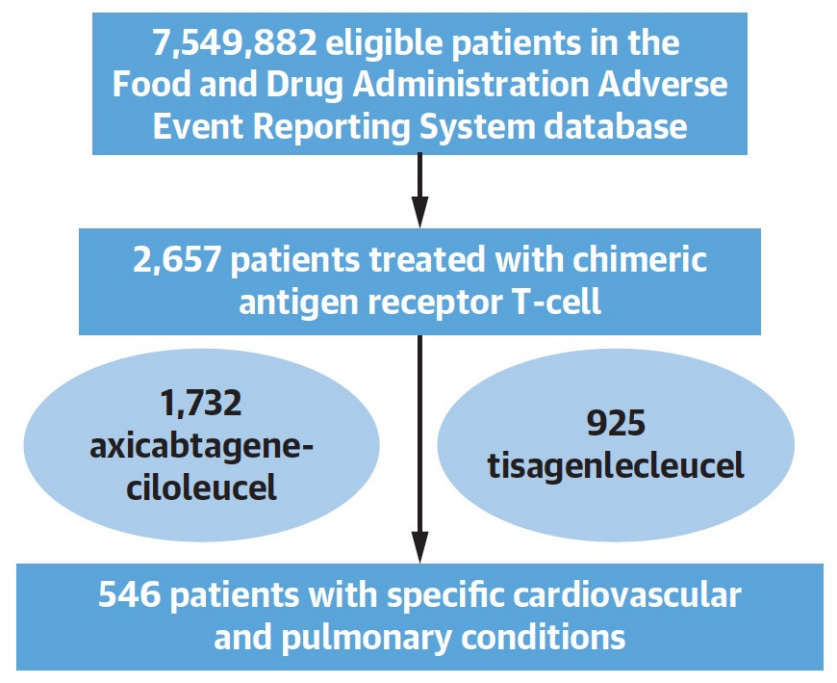
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 78, NO. 18, 2021

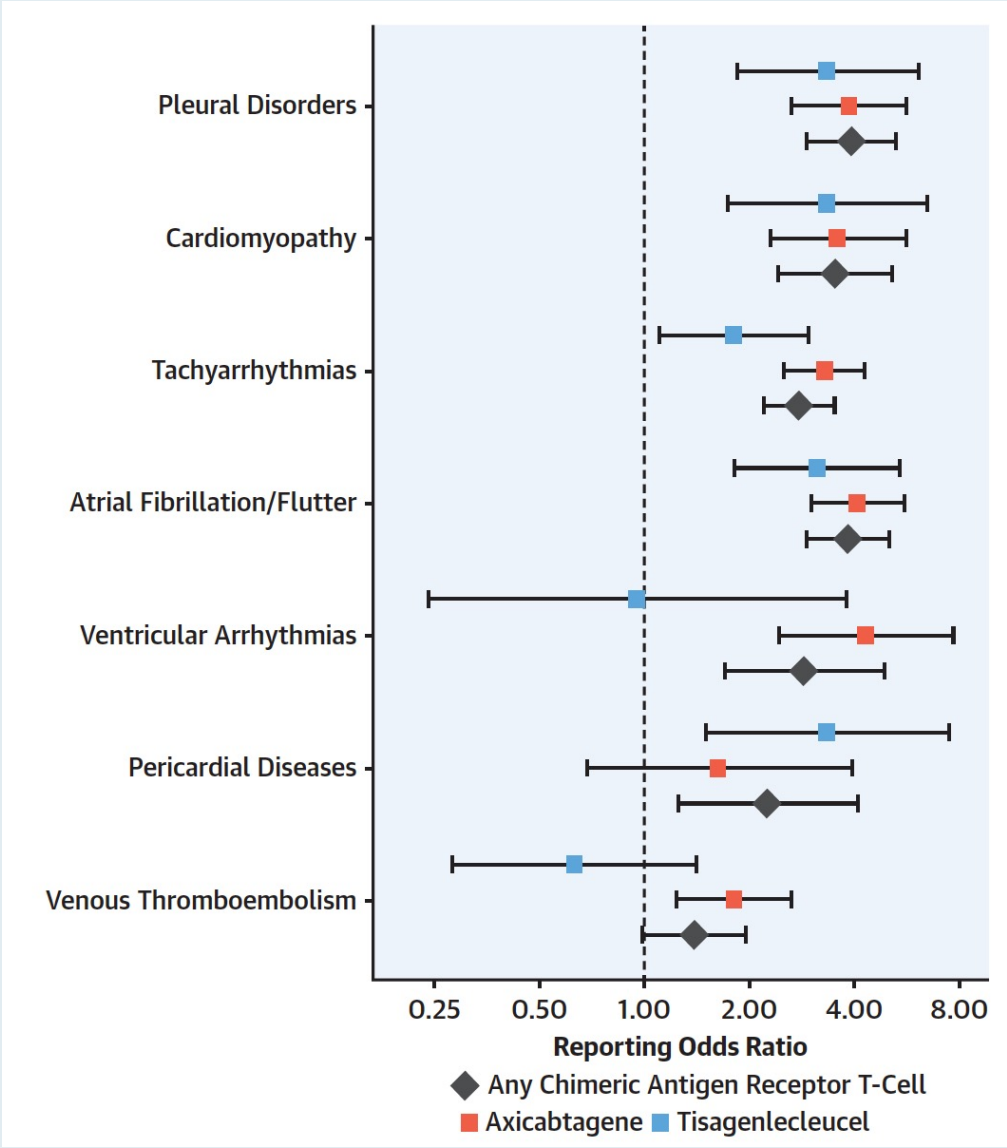
PUBLISHED BY ELSEVIER

Adverse Cardiovascular and Pulmonary Events Associated With Chimeric Antigen Receptor T-Cell Therapy

Adam Goldman, MD, MPH,[a,b] Elad Maor, MD, PhD,[a,b] David Bomze, MD, MPH, MSc,[b] Jennifer E. Liu, MD,[c,d] Joerg Herrmann, MD,[e] Joshua Fein, MD,[f] Richard M. Steingart, MD,[c,d] Syed S. Mahmood, MD, MPH,[g] Wendy L. Schaffer, MD, PhD,[c,d] Miguel-Angel Perales, MD,[d,h] Roni Shouval, MD, PhD[d,h]

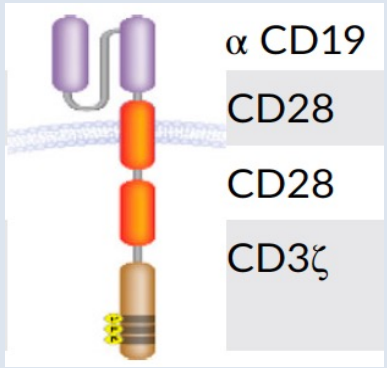
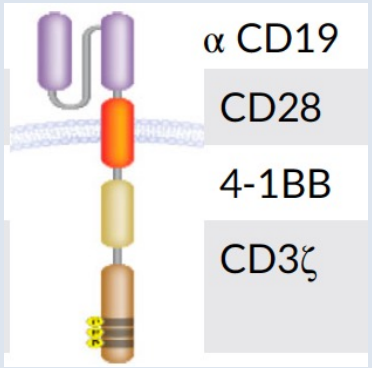
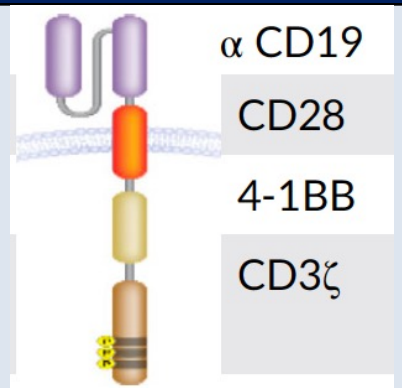
Cardiovascular and Pulmonary Toxicities of CAR T-Cell Therapy





Goldman A et al. *J Am Coll Cardiol* 2021;78(18):1800-13.

Summary of CAR T-Cell Pivotal Studies in DLBCL

	Axi-cel ZUMA-1 (N = 108 infused)	Tisagenlecleucel JULIET (N = 108 infused)	Liso-cel TRANSCEND (N = 294 infused)
CAR			
Transmembrane domain			
Co-stimulatory doman			
T-cell activation domain			
Leukapheresis	Fresh product	Cryopreserved product	Fresh product
Outpatient administration	Not allowed	Allowed	Allowed
Bridging therapy, %	Not allowed	92%	59%
Lymphodepletion chemotherapy	Cy/Flu 500/30 mg/m^2 × 3d	Cy/Flu 250/25 mg/m^2 x 3d Bendamustine 90 mg/m^2 x 2d	Cy/Flu 300/30 mg/m^2 x 3d

Westin JR et al. *Am J Hematol* 2021;[Online ahead of print].

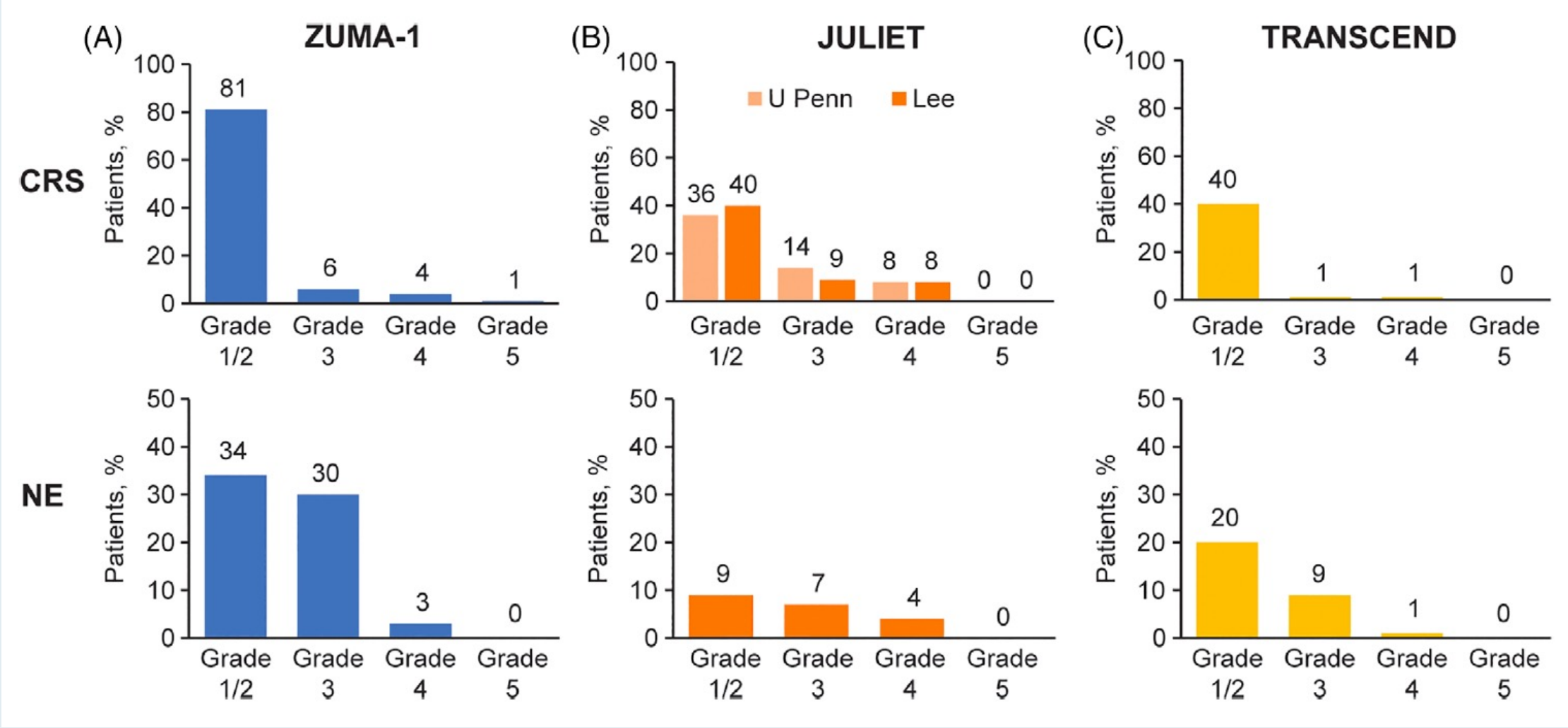
RTP RESEARCH TO PRACTICE

Summary of Efficacy Outcomes in Pivotal Studies of CAR T-Cell Therapy for DLBCL

	Axi-cel ZUMA-1 (N = 108 infused)	Tisagenlecleucel JULIET (N = 115 infused)	Liso-cel TRANSCEND (N = 294 infused)
Overall response rate	74%	52%	73%
Complete response rate	54%	40%	53%
24-month OS rate	50.5%	40.0%	44.9%
Indication	DLBCL, High grade, PMBCL, tFL	DLBCL, High grade, tFL	DLBCL, HGBCL, PMBCL, tFL, tIND

Westin JR et al. *Am J Hematol* 2021;[Online ahead of print].

Cytokine Release Syndrome and Neurologic Events in Pivotal Studies of CAR T-Cell Therapy for DLBCL



Westin JR et al. *Am J Hematol* 2021;[Online ahead of print].

RTP RESEARCH TO PRACTICE

CAR-T-Associated Cytokine Release Syndrome (CRS) and Neurologic Toxicity

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%

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.

ASCO special articles

Management of Immune-Related Adverse Events in Patients Treated With Chimeric Antigen Receptor T-Cell Therapy: ASCO Guideline

Bianca D. Santomasso, MD, PhD[1]; Loretta J. Nastoupil, MD[2]; Sherry Adkins, RN, MS[2]; Christina Lacchetti, MHSc[3]; Bryan J. Schneider, MD[4]; Milan Anadkat, MD[5]; Michael B. Atkins, MD[6]; Kelly J. Brassil, PhD, RN[2]; Jeffrey M. Caterino, MD, MPH[7]; Ian Chau, MD[8]; Marianne J. Davies, DNP[9]; Marc S. Ernstoff, MD[10]; Leslie Fecher, MD[4]; Pauline Funchain, MD[11]; Ishmael Jaiyesimi, DO, MS[12]; Jennifer S. Mammen, MD, PhD[13]; Jarushka Naidoo, MD[14]; Aung Naing, MD[2]; Tanyanika Phillips, MD[15]; Laura D. Porter, MD[16]; Cristina A. Reichner, MD[17]; Carole Seigel, MBA[18]; Jung-Min Song, MSN, RN, CNS[11]; Alexander Spira, MD, PhD[19]; Maria Suarez-Almazor, MD[2]; Umang Swami, MD[20]; John A. Thompson, MD[21]; Praveen Vikas, MD[22]; Yinghong Wang, MD[2]; Jeffrey S. Weber, MD, PhD[23]; Kathryn Bollin, MD[24]; and Monalisa Ghosh, MD[25]

J Clin Oncol 2021;39:3978-92

525

Glofitamab in Combination with Polatuzumab Vedotin: Phase Ib/II Preliminary Data Support Manageable Safety and Encouraging Efficacy in Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL)

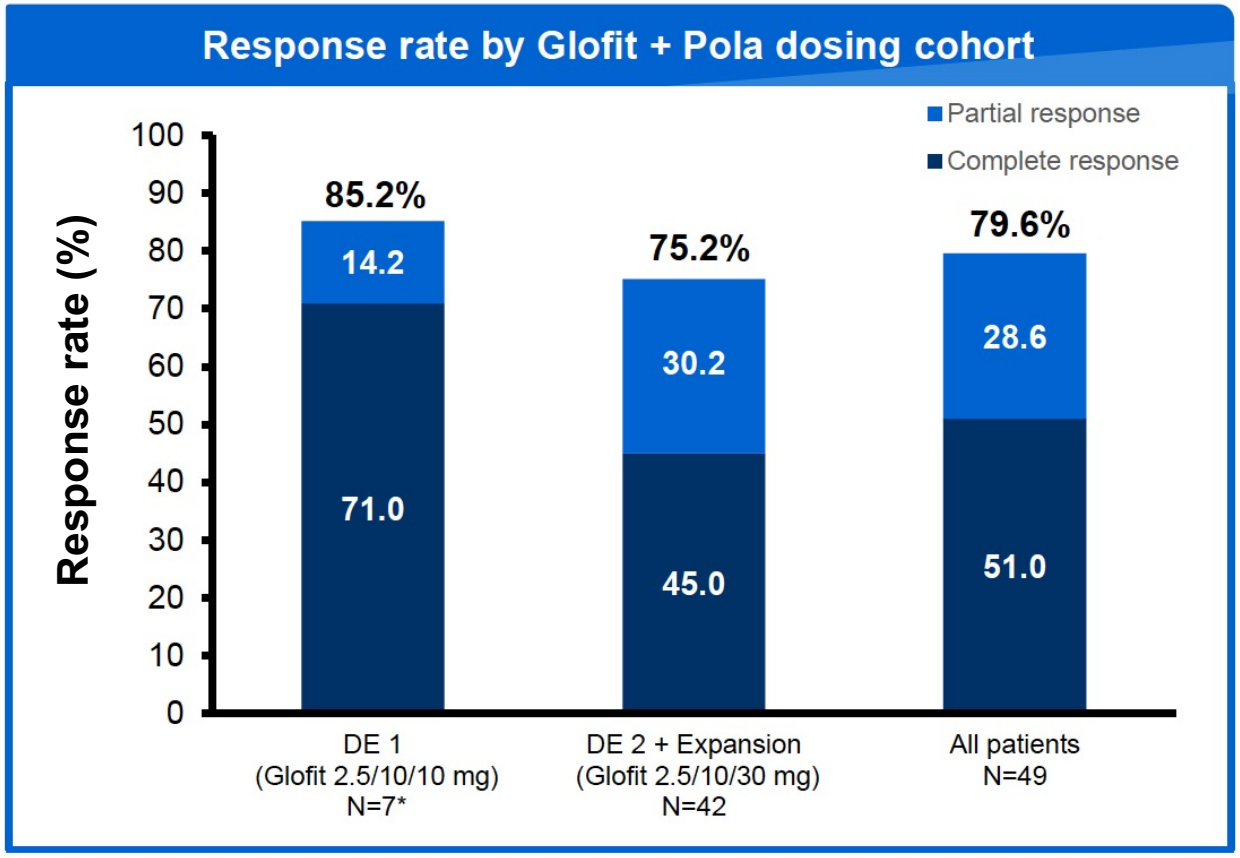
Martin Hutchings,[1] Anna Sureda,[2] Maria Jose Terol,[3] Francesc Bosch,[4] Paolo Corradini,[5] Thomas Stauffer Larsen,[6] Antonio Rueda Dominguez,[7] Anesh Panchal,[8] Alessia Bottos,[9] Yanjie Wang,[10] Audrey Filézac de L'Etang,[9] Maneesh Tandon,[8] Gila Sellam,[9] Giuseppe Gritti[11]

[1]Rigshospitalet, Copenhagen, Denmark; [2]Universitat de Barcelona, Barcelona, Spain; [3]Hospital Clínico Universitario INCLIVA, University of Valencia, Spain; [4]University Hospital Vall d'Hebron, Barcelona, Spain; [5]University of Milan and Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [6]Odense University Hospital, Odense, Denmark; [7]Regional and Virgen de la Victoria University Hospitals, Málaga, Spain; [8]Roche Products Ltd, Welwyn Garden City, United Kingdom; [9]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [10]F. Hoffmann-La Roche Ltd, Shanghai, China; [11]Ospedale Papa Giovanni XXIII, Bergamo, Italy.

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

ASH 2021;Abstract 525.

Phase Ib/II Study of Glofitamab Combined with Polatuzumab Vedotin for R/R DLBCL



- **49/59 patients were evaluable for interim response**
- **7/49 (14.3%) patients had PD as best response and discontinued study treatment**
- **Encouraging ORR and CR rates in patients with:**
  - trFL: ORR, 8/11 and CR, 7/11
  - HGBCL: ORR, 5/8 and CR, 4/8

- Safety profile of the combination was consistent with that of the individual drugs
- Majority of CRS events were Gr 1 and occurred after first dose of glofitamab (no Gr 3/4 cases)
- One Gr 1 ICANS AE was reported

Hutchings M et al. ASH 2021;Abstract 525.

RTP RESEARCH TO PRACTICE

Hodgkin Lymphoma

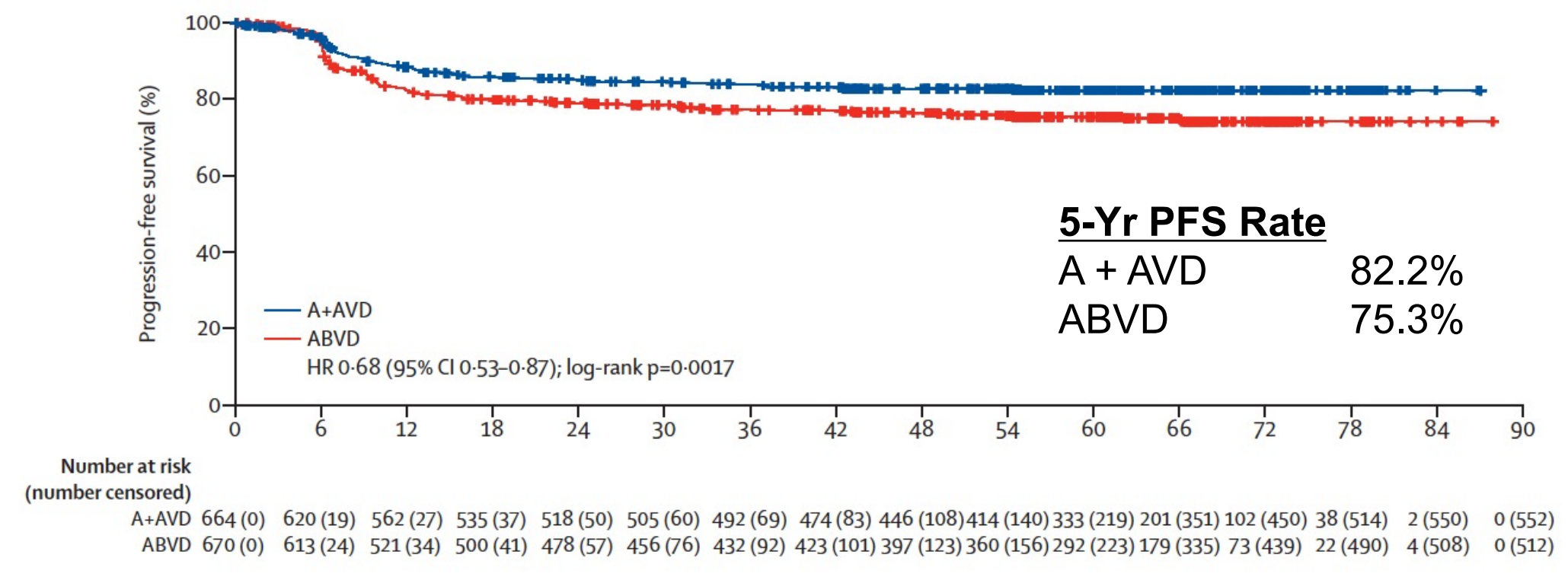
Lancet Haematol 2021;8(6):e410-21

Articles

Brentuximab vedotin with chemotherapy for stage III or IV classical Hodgkin lymphoma (ECHELON-1): 5-year update of an international, open-label, randomised, phase 3 trial

David J Straus, Monika Długosz-Danecka, Joseph M Connors, Sergey Alekseev, Árpád Illés, Marco Picardi, Ewa Lech-Maranda, Tatyana Feldman, Piotr Smolewski, Kerry J Savage, Nancy L Bartlett, Jan Walewski, Radhakrishnan Ramchandren, Pier Luigi Zinzani, Martin Hutchings, Javier Munoz, Hun Ju Lee, Won Seog Kim, Ranjana Advani, Stephen M Ansell, Anas Younes, Andrea Gallamini, Rachael Liu, Meredith Little, Keenan Fenton, Michelle Fanale, John Radford

ECHELON-1: Five-Year Update



- Five-year PFS was higher with A + AVD than with ABVD for both PET-2-negative and positive patients
- Peripheral neuropathy continued to improve or resolve over time with both A + AVD and ABVD; more patients had ongoing peripheral neuropathy in the A + AVD group than in the ABVD group (19% vs 9%).

Straus DJ et al. *Lancet Haematol* 2021;8(6):e410-21.

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;[Online ahead of print].

Multicenter Pilot Study of BV + 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;[Online ahead of print].

Frontline Brentuximab Vedotin as Monotherapy or in Combination for Older Hodgkin Lymphoma Patients

Yasenchak CA et al.
ASH 2020;Abstract 471.

Best Responses per Investigator – Efficacy Evaluable Set

Efficacy Evaluable Set	Part A BV mono N=25	Part B BV+DTIC N=19	Part C BV+benda N=17	Part D BV+nivo N=19
ORR, n (%)	**23 (92)**	**19 (100)**	**17 (100)**	**18 (95)**
Best overall response				
Complete response	18 (72)	13 (68)	15 (88)	15 (79)
Partial response	5 (20)	6 (32)	2 (12)	3 (16)
Stable disease	2 (8)	0	0	1 (5)
Progressive disease	0	0	0	0
Duration of response, n	23	19	17	18
Median (min, max)	9.1 (2.8, 81.4+)	45.4 (0.0+, 67.3)	39.0 (0.0+, 56.8+)	NR (1.4+, 27.5+)

Patients who were not efficacy-evaluable included:

- Patients with no post-baseline response assessment due to deaths (n=3) and patient withdrawal (non-AE related, n=2) on or before the first scheduled post-baseline scan at Cycle 2
- One patient lost to follow-up
- One patient who was not an eligible cHL subtype (nodular lymphocyte-predominant HL) but still achieved partial response after receiving BV

Yasenchak CA et al. ASH 2020;Abstract 471.

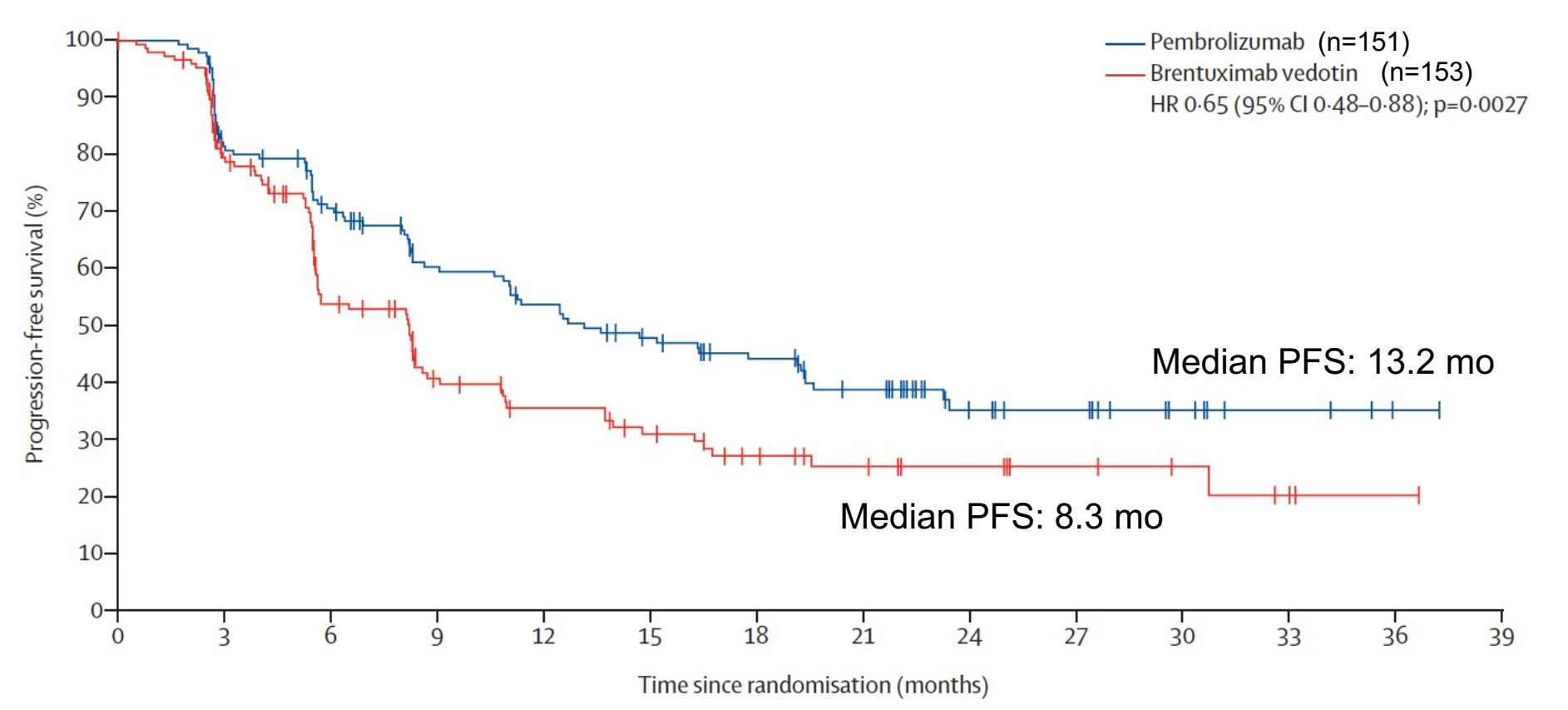
Articles

Lancet Oncol 2021;22(4):512-24.

Pembrolizumab versus brentuximab vedotin in relapsed or refractory classical Hodgkin lymphoma (KEYNOTE-204): an interim analysis of a multicentre, randomised, open-label, phase 3 study

*John Kuruvilla, Radhakrishnan Ramchandren, Armando Santoro, Ewa Paszkiewicz-Kozik, Robin Gasiorowski, Nathalie A Johnson, Laura Maria Fogliatto, Iara Goncalves, Jose S R de Oliveira, Valeria Buccheri, Guilherme F Perini, Neta Goldschmidt, Iryna Kriachok, Michael Dickinson, Mieczyslaw Komarnicki, Andrew McDonald, Muhit Ozcan, Naohiro Sekiguchi, Ying Zhu, Akash Nahar, Patricia Marinello, Pier Luigi Zinzani, on behalf of the KEYNOTE-204 investigators**

KEYNOTE-204: Interim Analysis



- The most common Grade 3-5 TRAEs in the pembrolizumab and brentuximab vedotin study arms included pneumonitis (4% vs 1%), neutropenia (2% vs 7%), and peripheral neuropathy (1% vs 3%).
- Serious TRAEs occurred in 16% of patients receiving pembrolizumab and 11% of patients receiving brentuximab vedotin.

Kuruvilla J et al. *Lancet Oncol* 2021;22(4):512-24.

RTP RESEARCH TO PRACTICE

J Clin Oncol 2020;38(32):3794-804.

original reports

Anti-CD30 CAR-T Cell Therapy in Relapsed and Refractory Hodgkin Lymphoma

Carlos A. Ramos, MD[1,2]; Natalie S. Grover, MD[3,4]; Anne W. Beaven, MD[3,4]; Premal D. Lulla, MD[1,2]; Meng-Fen Wu, MS[1,5]; Anastasia Ivanova, PhD[3,6]; Tao Wang, PhD[1,5]; Thomas C. Shea, MD[3,4]; Cliona M. Rooney, PhD[1,7,8]; Christopher Dittus, DO[3,4]; Steven I. Park, MD[3]; Adrian P. Gee, PhD[1,7]; Paul W. Eldridge, PhD[3]; Kathryn L. McKay, MS[3]; Birju Mehta, MS[1]; Catherine J. Cheng, MS[3]; Faith B. Buchanan, PA[3]; Bambi J. Grilley, RPh[1]; Kaitlin Morrison, PhD[3]; Malcolm K. Brenner, MD, PhD[1,2,7]; Jonathan S. Serody, MD[3,4,9]; Gianpietro Dotti, MD[3,9]; Helen E. Heslop, MD[1,2,7]; and Barbara Savoldo, MD, PhD[3,9,10]

Anti-CD30 CAR T-Cell Therapy After Lymphodepletion Regimens for R/R Hodgkin Lymphoma (HL)

- Two parallel Phase I/II studies (NCT02690545 and NCT02917083) at 2 independent centers involving patients with relapsed or refractory HL
- Anti-CD30 CAR T cells were administered after lymphodepletion with either bendamustine alone, bendamustine and fludarabine or cyclophosphamide and fludarabine

Response	All Patients (N = 37)	Benda (n = 5)	Benda-Flu (n = 15)	Cy-Flu (n = 17)
ORR				
CR + PR	23 (62)	0 (0)	12 (80)	11 (65)
Response rate				
CR	19 (51)	0 (0)	11 (73)	8 (47)
PR	4 (11)	0 (0)	1 (7)	3 (18)

- Cytokine release syndrome was observed in 10 patients, all of which were Grade 1. No neurologic toxicity was observed

Ramos CA et al. *J Clin Oncol* 2020;38(32):3794-804.

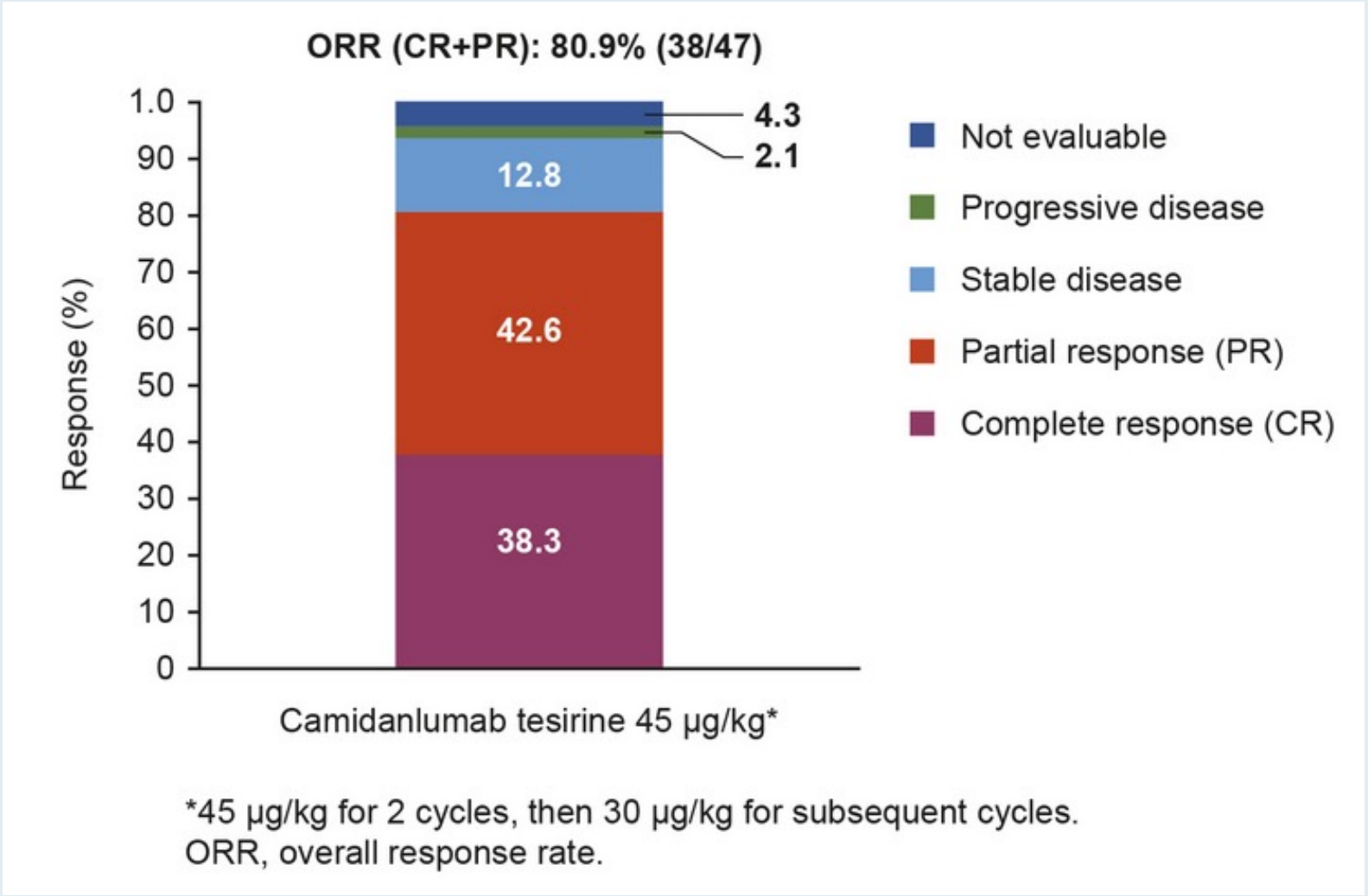
RTP RESEARCH TO PRACTICE

Preliminary Results of a Phase 2 Study of Camidanlumab Tesirine (Cami), a Novel Pyrrolobenzodiazepine-Based Antibody-Drug Conjugate, in Patients with Relapsed or Refractory Hodgkin Lymphoma

Herrera AF et al.

ASH 2020;Abstract 2020.

Response to Camidanlumab Tesirine in Patients with R/R Classical Hodgkin Lymphoma



Herrera AF et al. ASH 2020;Abstract 2020.

Follicular Lymphoma

Approved PI3K Inhibitors for FL: Indication and Dosing

	Idelalisib[1]	Copanlisib[2]	Duvelisib[3]	Umbralisib[4]
Mechanism of action	Selective PI3Kδ inhibitor	Dual inhibitor of PI3Kδ,α	Dual inhibitor of PI3Kδ,γ	Dual inhibitor of PI3Kδ and casein kinase CK1ε
Indication	Relapsed FL after at least 2 prior systemic therapies	Relapsed FL after at least 2 prior systemic therapies	R/R FL after at least 2 prior systemic therapies	R/R FL after at least 3 prior systemic therapies
Dosing	150 mg orally, twice daily	60 mg as a 1-hour IV infusion weekly (3 weeks on, 1 week off)	25 mg orally, twice daily	800 mg orally, once daily

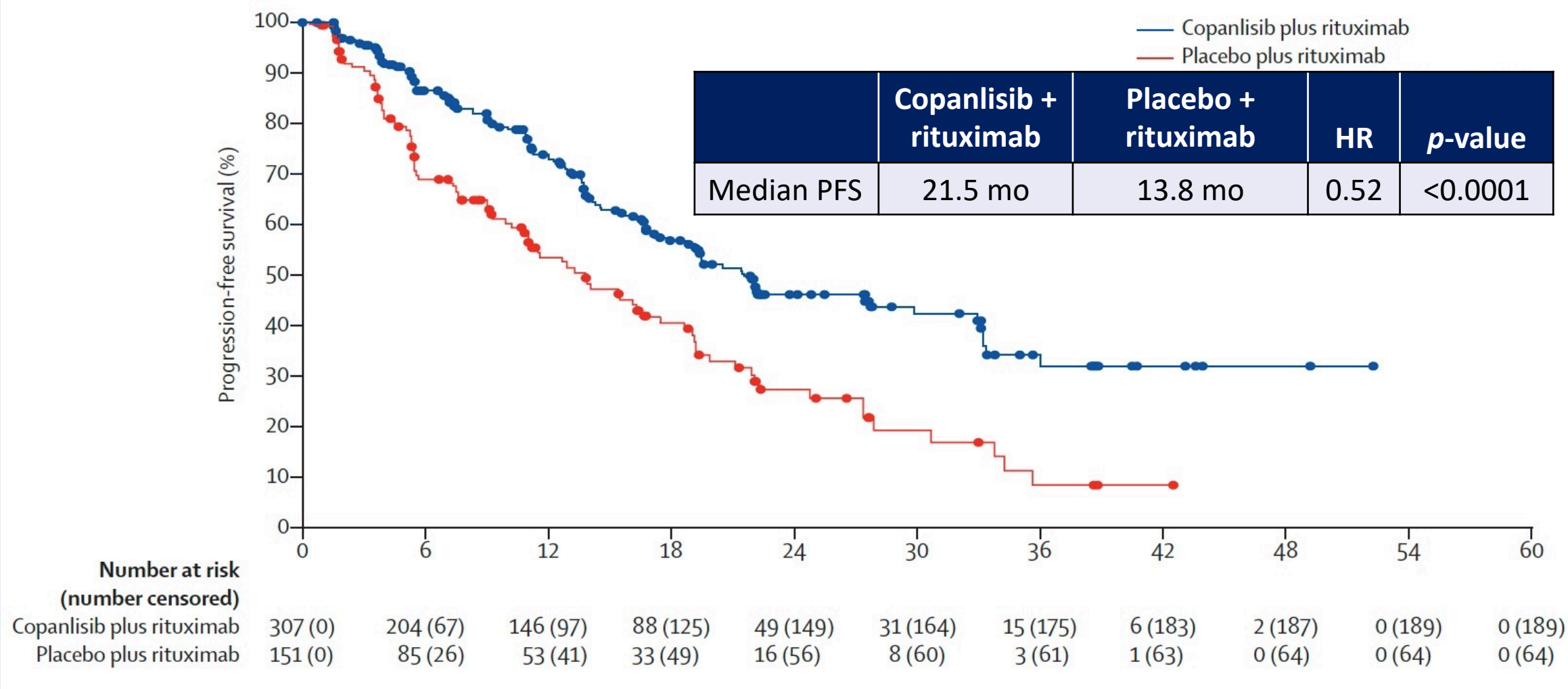
[1] Gopal AK et al. *N Engl J Med* 2014;370(11):1008-18; Idelalisib package insert, January 2018.
[2] Dreyling M et al. *J Clin Oncol* 2017;35(35):3898-905; Copanlisib package insert, September 2017.
[3] Flinn IW et al. *J Clin Oncol* 2019;[Epub ahead of print]; Zinzani PL et al. EHA 2017;Abstract S777; Duvelisib package insert, September 2018. [4] Umbralisib package insert, February 2021.

Lancet Oncol 2021;22:678-89

Copanlisib plus rituximab versus placebo plus rituximab in patients with relapsed indolent non-Hodgkin lymphoma (CHRONOS-3): a double-blind, randomised, placebo-controlled, phase 3 trial

Matthew J Matasar, Marcelo Capra, Muhit Özcan, Fangfang Lv, Wei Li, Eduardo Yañez, Katya Sapunarova, Tongyu Lin, Jie Jin, Wojciech Jurczak, Aryan Hamed, Ming-Chung Wang, Ross Baker, Igor Bondarenko, Qingyuan Zhang, Jifeng Feng, Klaus Geissler, Mihaela Lazaroiu, Guray Saydam, Árpád Szomor, Krimo Bouabdallah, Rinat Galiulin, Toshiki Uchida, Lidia Mongay Soler, Anjun Cao, Florian Hiemeyer, Aruna Mehra, Barrett H Childs, Yuankai Shi, Pier Luigi Zinzani

CHRONOS-3: Progression-Free Survival in R/R Indolent NHL



	Copanlisib + rituximab	Placebo + rituximab	HR	*p*-value
Median PFS	21.5 mo	13.8 mo	0.52	<0.0001

Matasar MJ et al. *Lancet Oncol* 2021;22:678-89.

FDA Grants Accelerated Approval to Umbralisib for Marginal Zone Lymphoma and Follicular Lymphoma

Press Release – February 5, 2021

"The Food and Drug Administration granted accelerated approval to umbralisib, a kinase inhibitor including PI3K-delta and casein kinase CK1-epsilon, for the following indications:

- Adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based regimen;
- Adult patients with relapsed or refractory follicular lymphoma (FL) who have received at least three prior lines of systemic therapy.

Approval was based on two single-arm cohorts of an open-label, multi-center, multi-cohort trial, UTX-TGR-205 (NCT02793583), in 69 patients with MZL who received at least one prior therapy, including an anti-CD20 containing regimen, and in 117 patients with FL after at least 2 prior systemic therapies. Patients received umbralisib 800 mg orally once daily until disease progression or unacceptable toxicity."

www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-umbralisib-marginal-zone-lymphoma-and-follicular-lymphoma

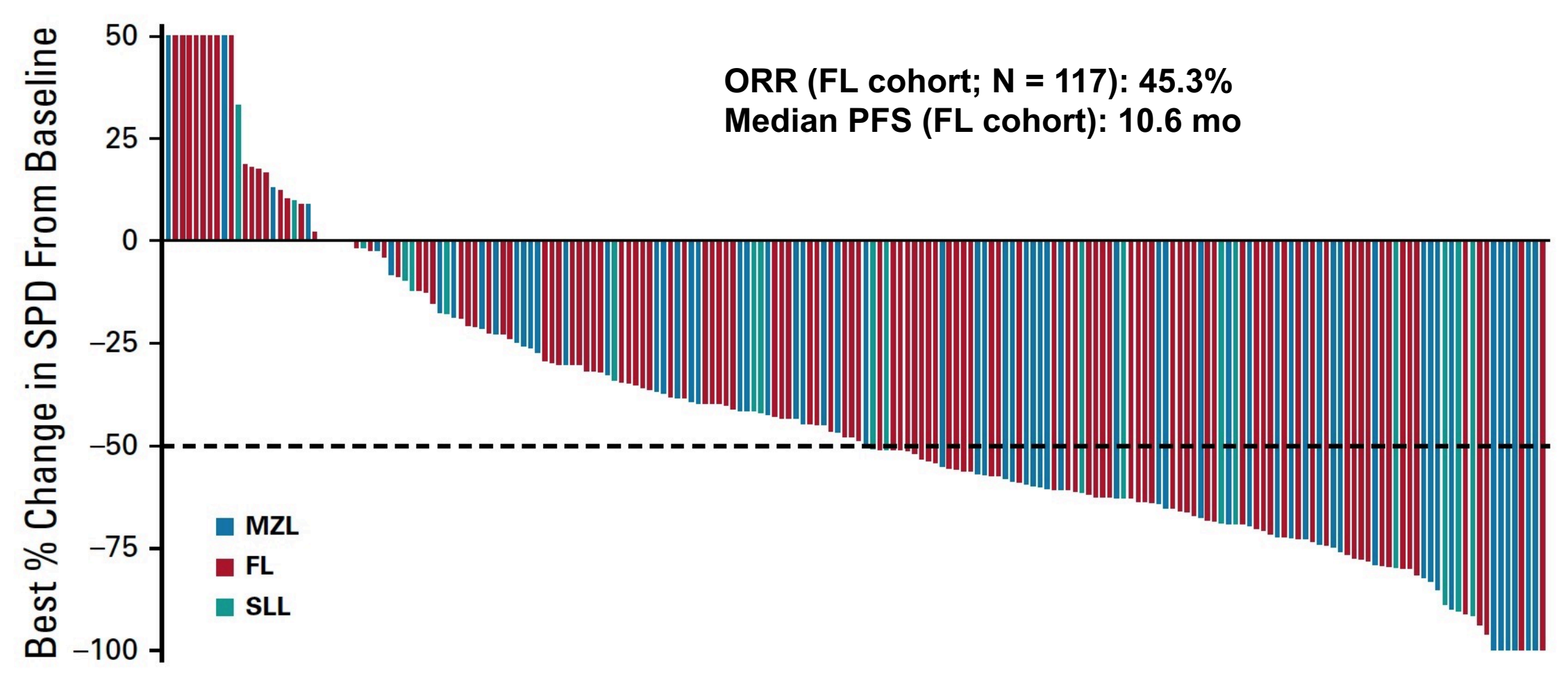
rapid communications

Umbralisib, a Dual PI3Kδ/CK1ε Inhibitor in Patients With Relapsed or Refractory Indolent Lymphoma

Nathan H. Fowler, MD[1]; Felipe Samaniego, MD[1]; Wojciech Jurczak, MD, PhD[2]; Nilanjan Ghosh, MD, PhD[3]; Enrico Derenzini, MD[4,5]; James A. Reeves, MD[6]; Wanda Knopińska-Posłuszny, MD[7]; Chan Y. Cheah, DMSc[8]; Tycel Phillips, MD[9]; Ewa Lech-Maranda, MD, PhD[10]; Bruce D. Cheson, MD[11]; Paolo F. Caimi, MD[12]; Sebastian Grosicki, MD, PhD[13]; Lori A. Leslie, MD[14]; Julio C. Chavez, MD[15]; Gustavo Fonseca, MD[16]; Sunil Babu, MD[17]; Daniel J. Hodson, MD[18]; Spencer H. Shao, MD[19]; John M. Burke, MD[20]; Jeff P. Sharman, MD[21]; Jennie Y. Law, MD[22]; John M. Pagel, MD, PhD[23]; Hari P. Miskin, MSc[24]; Peter Sportelli, BS[24]; Owen A. O'Connor, MD, PhD[24,25]; Michael S. Weiss, JD[24]; and Pier Luigi Zinzani, MD, PhD[26,27]

J Clin Oncol 2021;39:1609-18

Umbralisib for Heavily Pretreated R/R Indolent NHL



Fowler NH et al. *J Clin Oncol* 2021;39:1609-18.

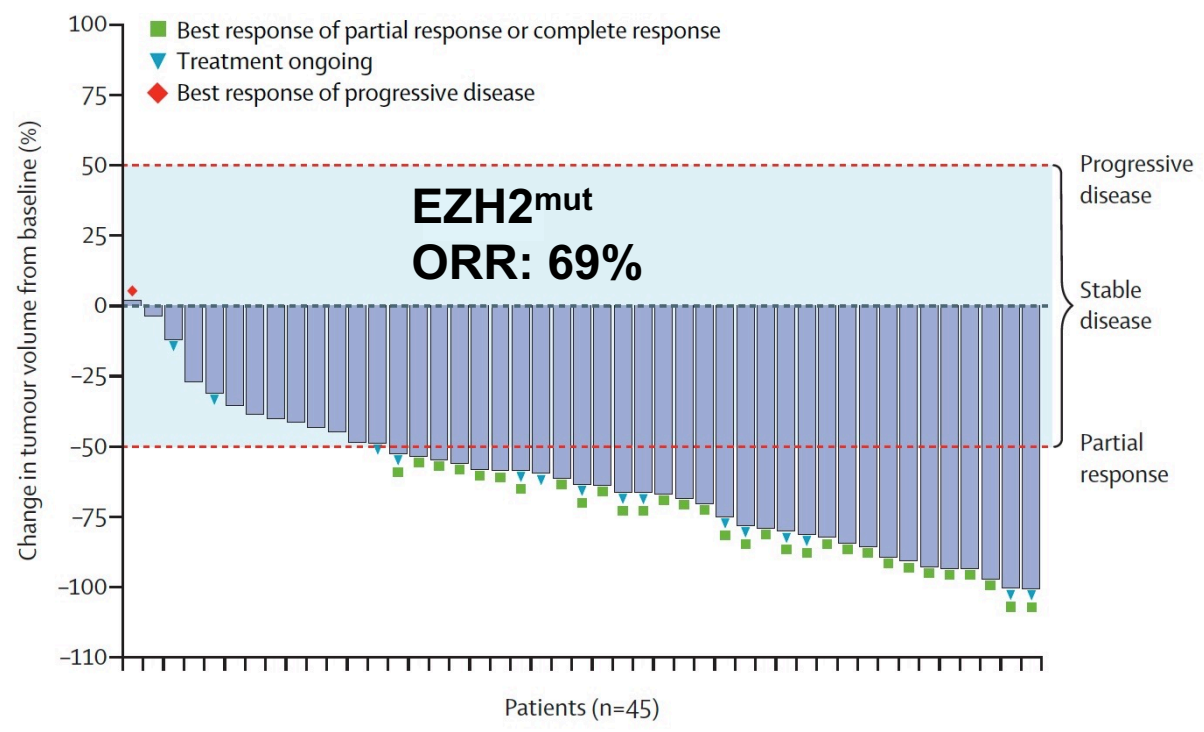
RTP RESEARCH TO PRACTICE

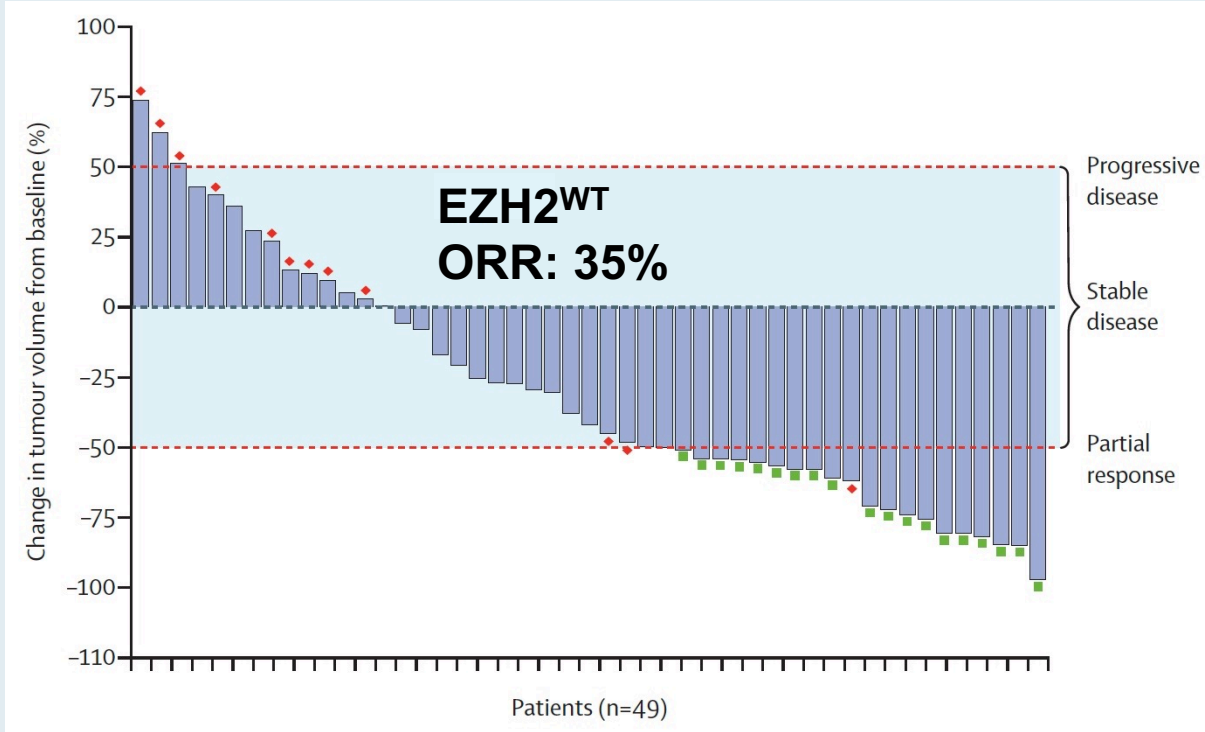
Lancet Oncol 2020;21:1433-42

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 EZH2-Mutated or EZH2 Wild-Type Tumors

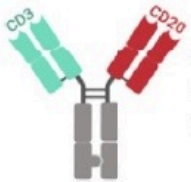
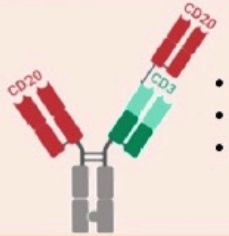
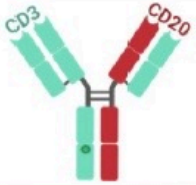




Morschhauser F et al. *Lancet Oncol* 2020;21:1433-42.

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.

FDA Grants Breakthrough Therapy Designation for the CD20 x CD3 Bispecific Cancer Immunotherapy Mosunetuzumab for Follicular Lymphoma

Press Release — July 14, 2020

"[The] investigational CD20xCD3 T-cell engaging bispecific mosunetuzumab has been granted Breakthrough Therapy Designation (BTD) by the US Food and Drug Administration (FDA) for the treatment of adult patients with relapsed or refractory (R/R) follicular lymphoma who have received at least two prior systemic therapies.

This designation was granted based on encouraging efficacy results observed in the phase I/Ib GO29781 study [NCT02500407] investigating mosunetuzumab in R/R non-Hodgkin lymphoma (NHL). The safety profile of this T-cell engaging bispecific was consistent with its mechanism of action."

www.roche.com/investors/updates/inv-update-2020-07-14b.htm

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]

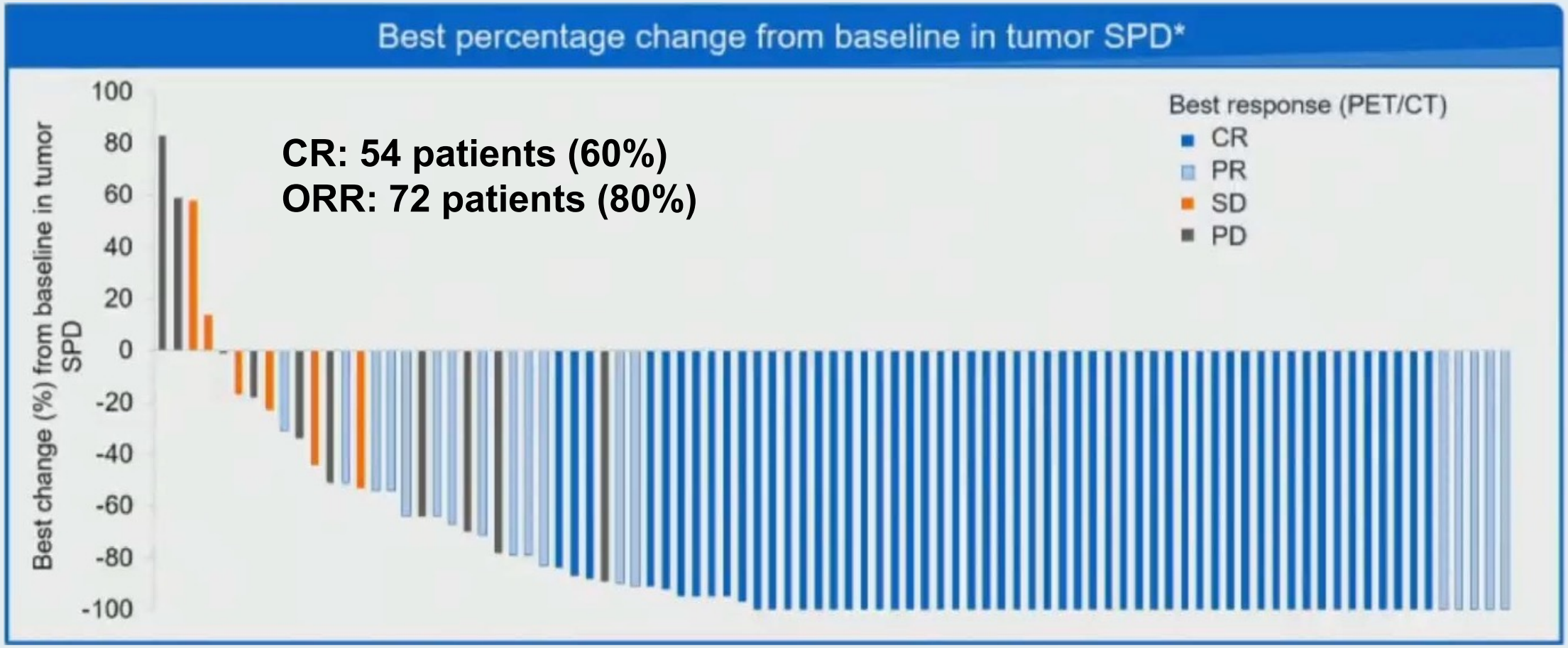
[1]*City of Hope, Duarte, CA, USA;* [2]*BC Cancer Centre for Lymphoid Cancer and University of British Columbia, Vancouver, BC, Canada;* [3]*Memorial Sloan Kettering Cancer Center, New York, NY, USA;* [4]*Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA;* [5]*Jewish 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.

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



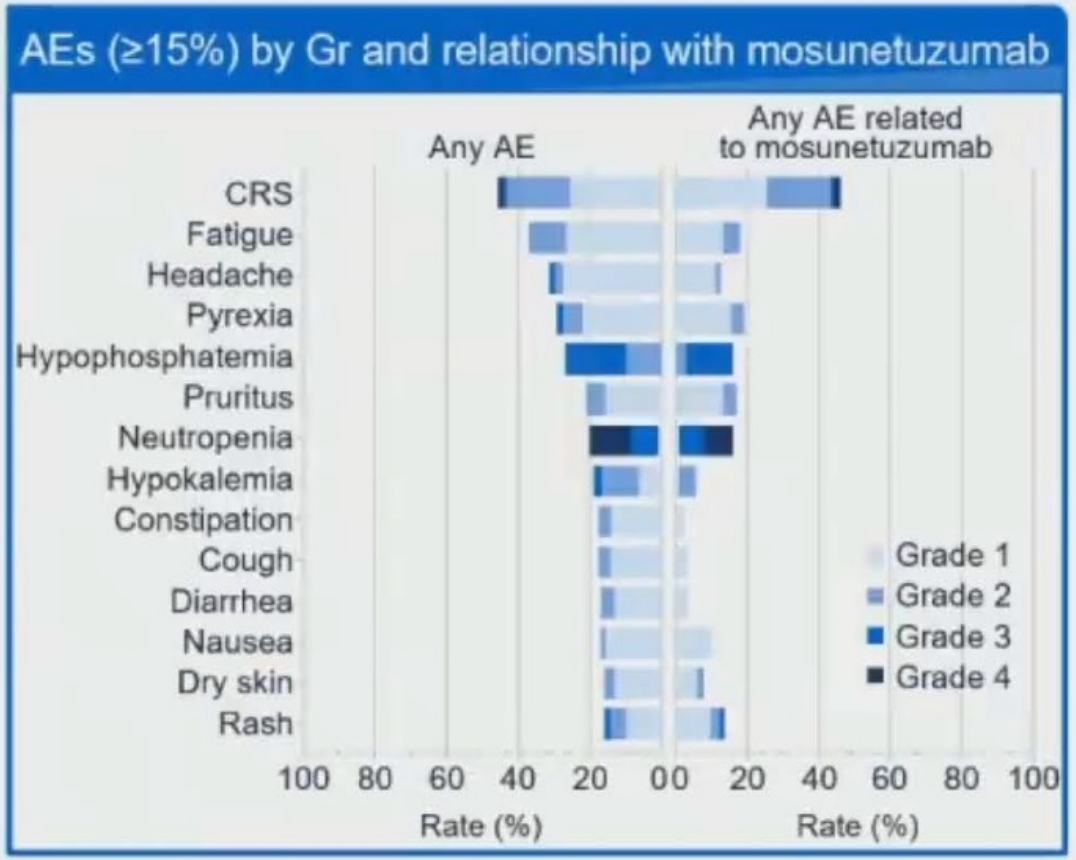
- Median DoR: 22.8 months
- Median PFS: 17.9 months

Budde EL et al. ASH 2021;Abstract 127.

RTP RESEARCH TO PRACTICE

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.

rapid communications

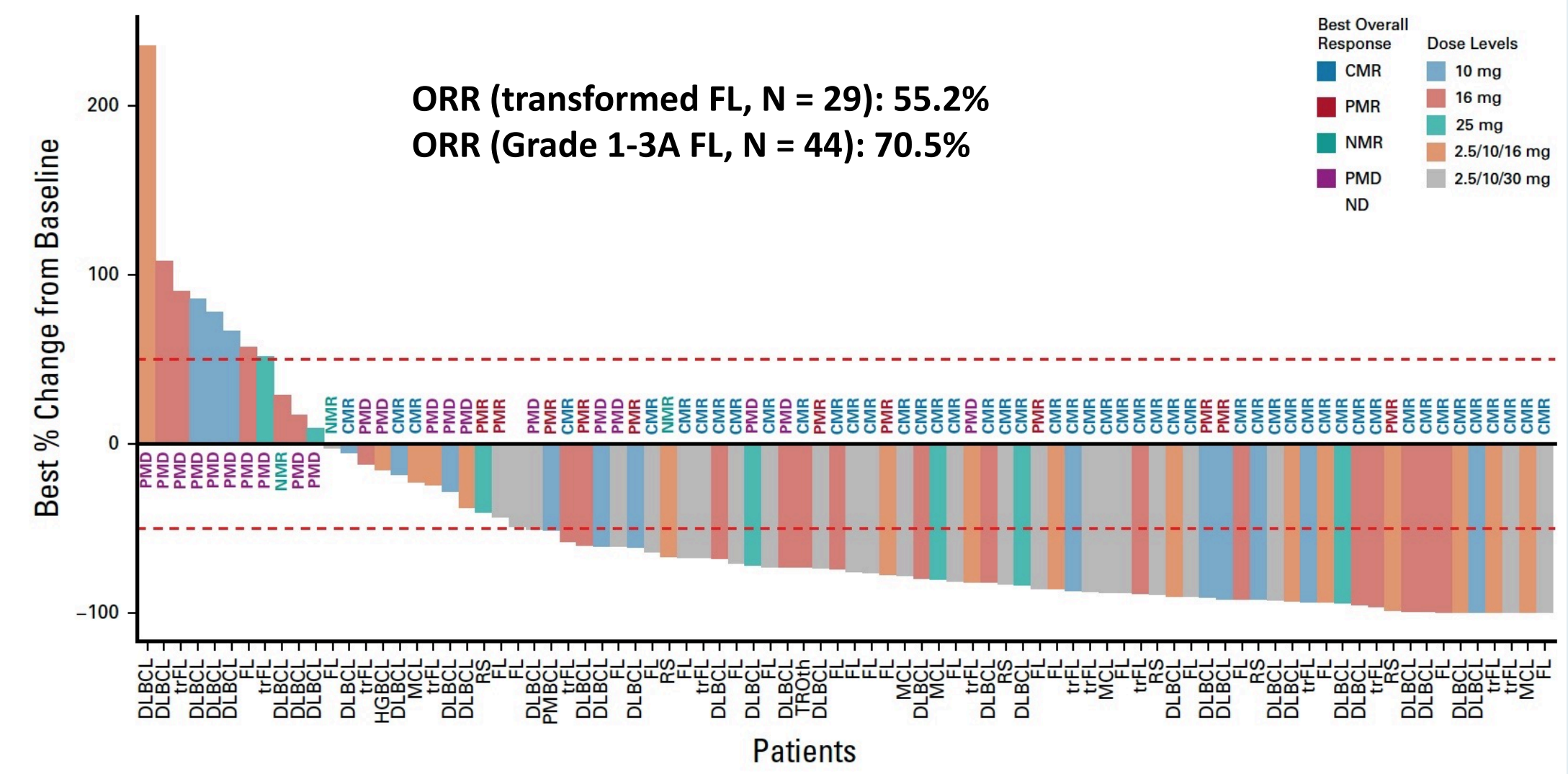
Glofitamab, a Novel, Bivalent CD20-Targeting T-Cell–Engaging Bispecific Antibody, Induces Durable Complete Remissions in Relapsed or Refractory B-Cell Lymphoma: A Phase I Trial

Martin Hutchings, PhD[1]; Franck Morschhauser, MD, PhD[2]; Gloria Iacoboni, MD[3,4]; Carmelo Carlo-Stella, MD[5]; Fritz C. Offner, MD, PhD[6]; Anna Sureda, MD, PhD[7]; Gilles Salles, MD[8]; Joaquín Martínez-Lopez, MD, PhD, MBA[9]; Michael Crump, MD[10]; Denise N. Thomas, MSc[11]; Peter N. Morcos, PharmD[11]; Cristiano Ferlini, MD[11]; Ann-Marie E. Bröske, PhD[12]; Anton Belousov, PhD[13]; Marina Bacac, PhD[13]; Natalie Dimier, PhD[14]; David J. Carlile, PhD[14]; Linda Lundberg, PhD[15]; David Perez-Callejo, MD, PhD[15]; Pablo Umaña, PhD[13]; Tom Moore, MD[12]; Martin Weisser, MD[12]; and Michael J. Dickinson, MBBS, DMedSci[16]

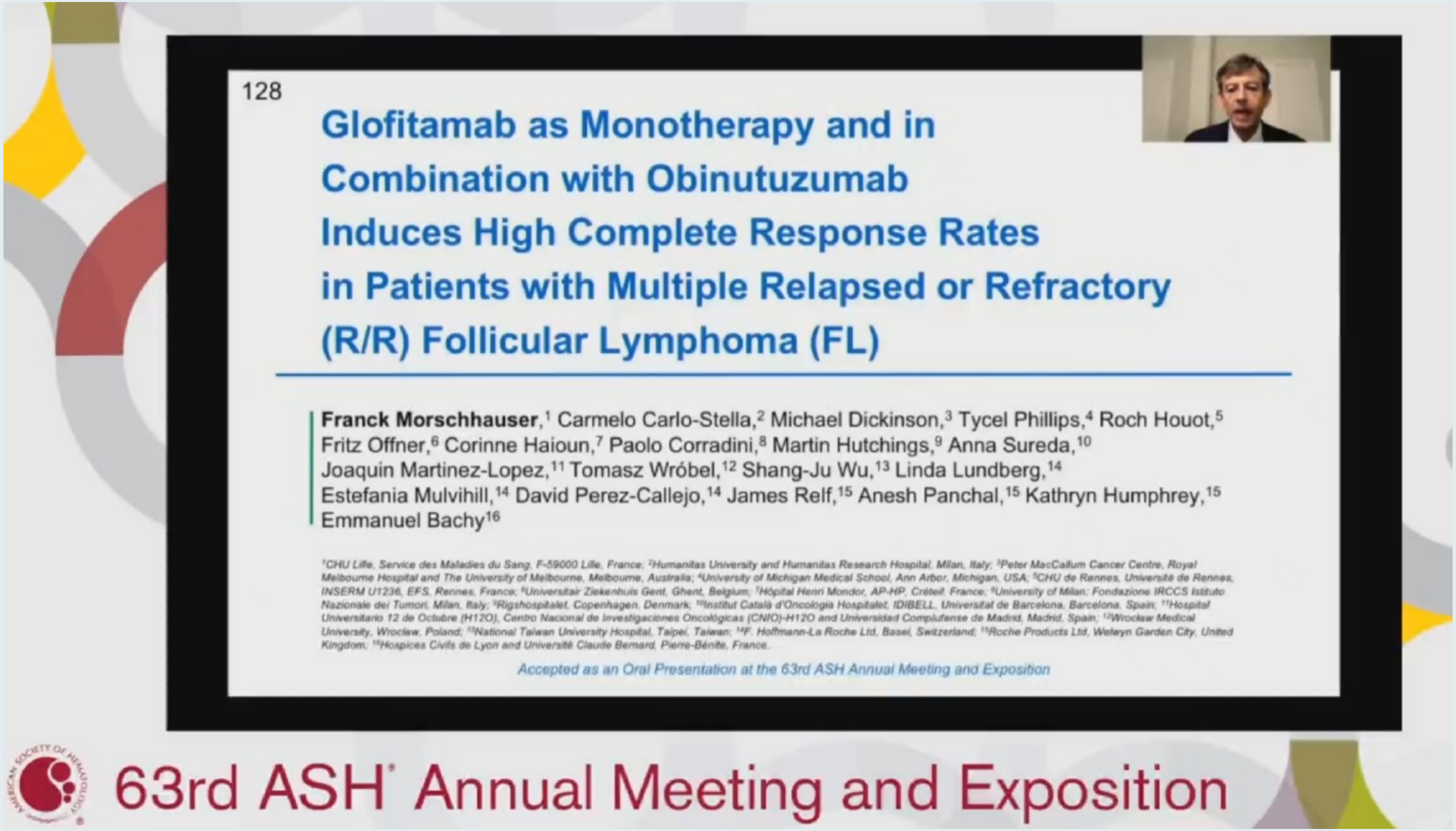
J Clin Oncol 2021;39:1959-70.

RTP RESEARCH TO PRACTICE

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

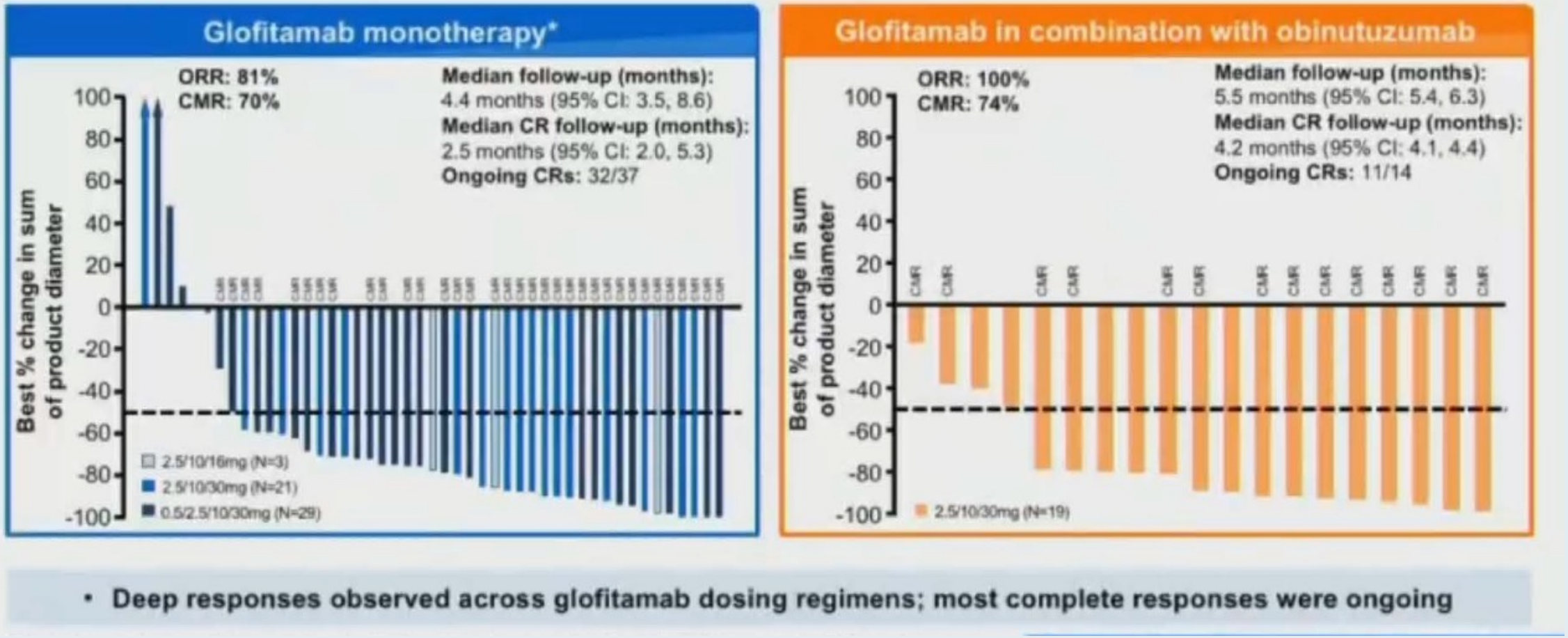


Hutchings M et al. *J Clin Oncol* 2021;39:1959-70.



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
- CRS rates were high and comparable, and cases were mainly low grade

Morschhauser F et al. ASH 2021;Abstract 128.

RTP RESEARCH TO PRACTICE

FDA Grants Accelerated Approval to Axicabtagene Ciloleucel for Relapsed or Refractory Follicular Lymphoma

Press Release – March 5, 2021

"The Food and Drug Administration granted accelerated approval to axicabtagene ciloleucel for adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

Approval in FL was based on a single-arm, open-label, multicenter trial (ZUMA-5; NCT03105336) that evaluated axicabtagene ciloleucel, a CD19-directed chimeric antigen receptor (CAR) T cell therapy, in adult patients with relapsed or refractory FL after two or more lines of systemic therapy, including the combination of an anti-CD20 monoclonal antibody and an alkylating agent. Following lymphodepleting chemotherapy, axicabtagene ciloleucel was administered as a single intravenous infusion."

www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-axicabtagene-ciloleucel-relapsed-or-refractory-follicular-lymphoma

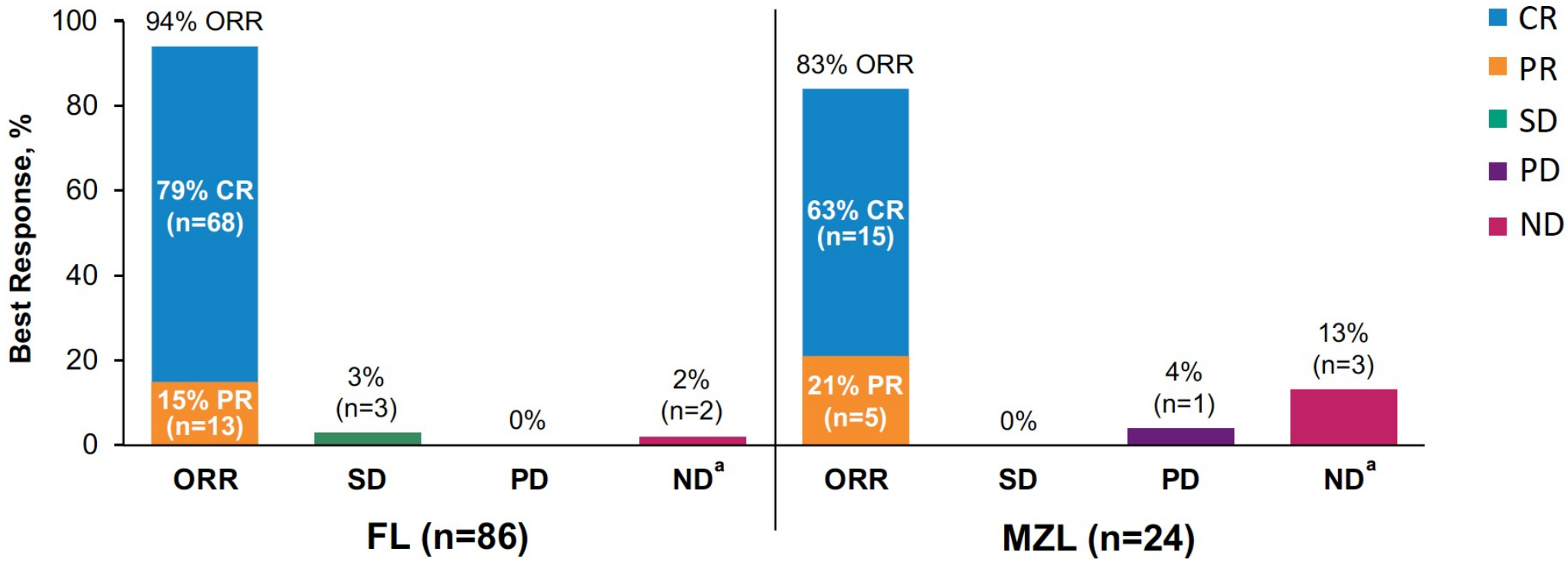
Long-Term Follow-Up Analysis of ZUMA-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

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.

ZUMA-5: ORR by Central Review

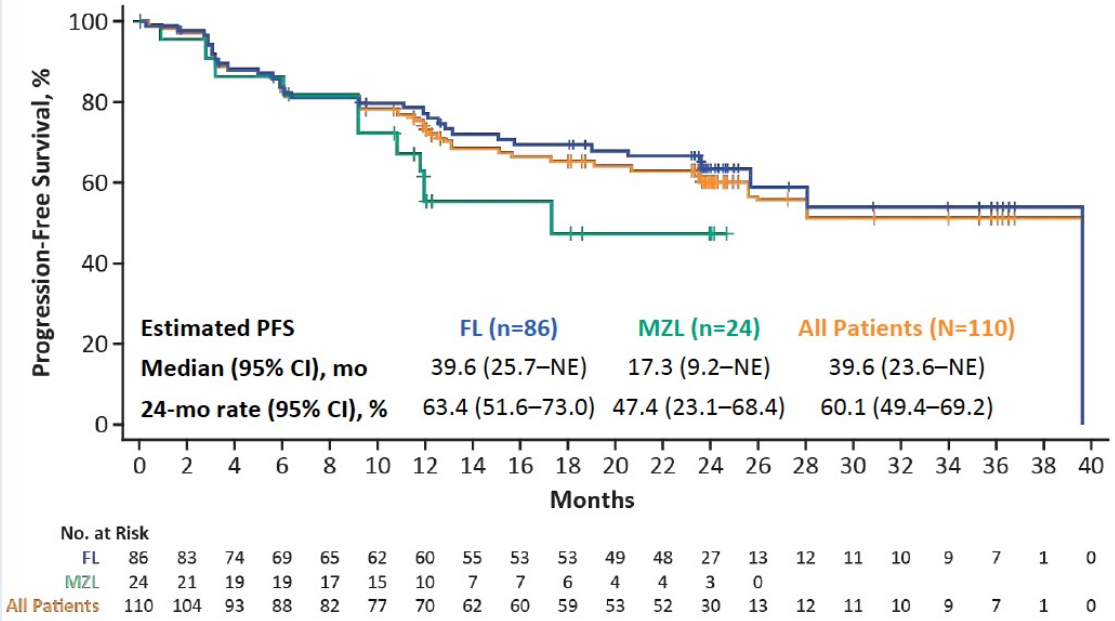


- Among efficacy-eligible patients with iNHL (n=110), the ORR was 92% (95% CI, 85–96), with a 75% CR rate
- Among all treated patients with iNHL (n=149), the ORR was 92% (95% CI, 86–96), with a 77% CR rate

Neelapu SS et al. ASH 2021;Abstract 93.

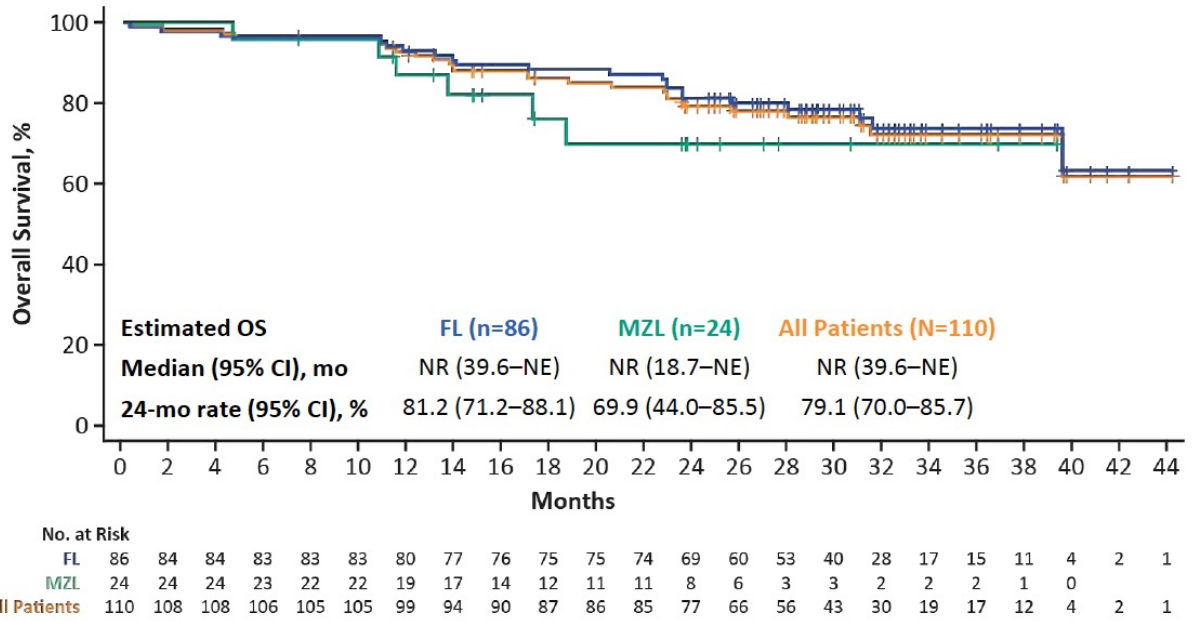
ZUMA-5: Progression-Free and Overall Survival

Progression-Free Survival



No. at Risk																					
FL	86	83	74	69	65	62	60	55	53	53	49	48	27	13	12	11	10	9	7	1	0
MZL	24	21	19	19	17	15	10	7	7	6	4	4	3	0							
All Patients	110	104	93	88	82	77	70	62	60	59	53	52	30	13	12	11	10	9	7	1	0

Overall Survival



No. at Risk																									
FL	86	84	84	83	83	83	80	77	76	75	75	74	69	60	53	40	28	17	15	11	4	2	1
MZL	24	24	24	23	22	22	19	17	14	12	11	11	8	6	3	3	2	2	2	1	0		
All Patients	110	108	108	106	105	105	99	94	90	87	86	85	77	66	56	43	30	19	17	12	4	2	1

- 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.

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.

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

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Thieblemont C et al. ASH 2021;Abstract 131.

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%).

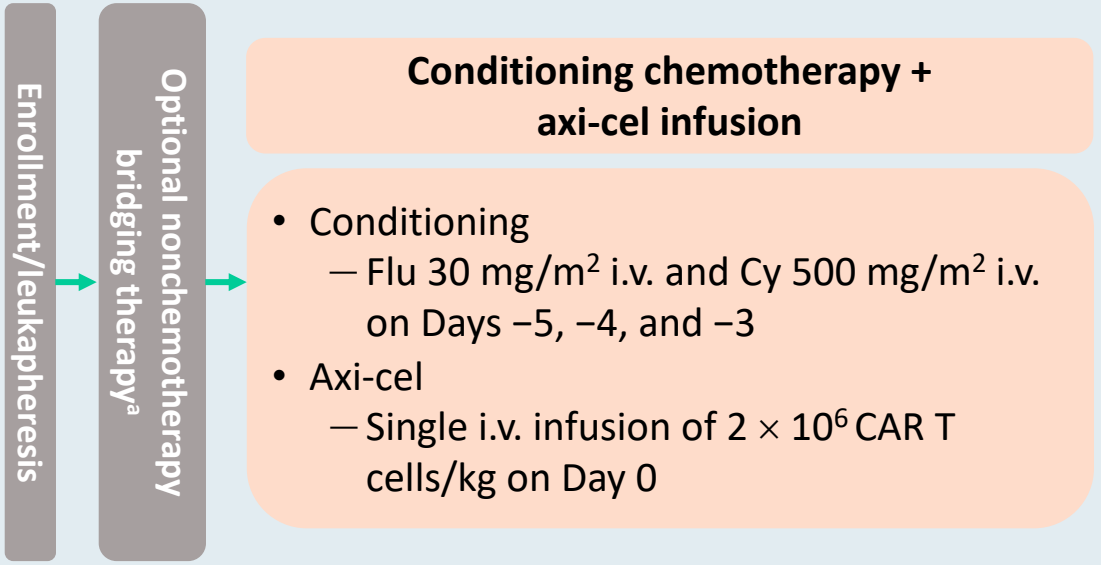
Thieblemont C et al. ASH 2021;Abstract 131.

Mantle Cell Lymphoma

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[b]

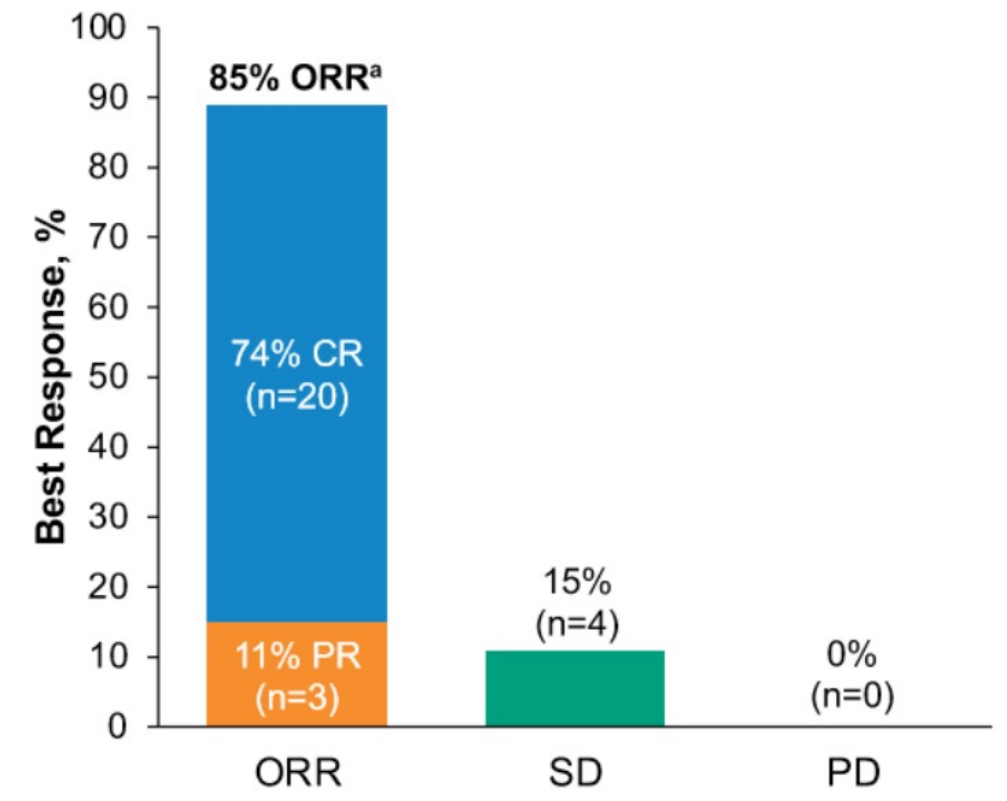
Key secondary endpoints

- ORR
- DOR
- EFS
- PFS
- OS
- Safety
- CAR T cells in blood and cytokine levels in serum

Neelapu SS et al. ASH 2020;Abstract 405.

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

ORR and CR in response-evaluable cohort (N = 27)



Safety	CRS (N = 32)	Neurologic events (N = 32)
Any grade, n (%)	32 (100%)	22 (69%)
Grade ≥3, n (%)	3 (9%)	8 (25%)
Grade 4, n (%)	0	2 (6%)
Grade 5, n (%)	0	0
Most common any-grade symptoms, n (%)	Pyrexia: 32 (100%) Chills: 8 (25%) Hypotension: 8 (25%)	Encephalopathy: 10 (31%) Confusional state: 9 (28%)

Neelapu SS et al. ASH 2020;Abstract 405.

FDA Approves Brexucabtagene Autoleucel for Relapsed or Refractory Mantle Cell Lymphoma

Press Release – July 24, 2020

"The Food and Drug Administration granted accelerated approval to brexucabtagene autoleucel, a CD19-directed genetically modified autologous T cell immunotherapy, for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).

Approval was based on ZUMA-2 (NCT02601313), an open-label, multicenter, single-arm trial of 74 patients with relapsed or refractory MCL who had previously received anthracycline- or bendamustine-containing chemotherapy, an anti-CD20 antibody, and a Bruton tyrosine kinase inhibitor. Patients received a single infusion of brexucabtagene autoleucel following completion of lymphodepleting chemotherapy. The primary efficacy outcome measure was objective response rate (ORR) per Lugano [2014] criteria as assessed by an independent review committee."

www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-brexucabtagene-autoleucel-relapsed-or-refractory-mantle-cell-lymphoma

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

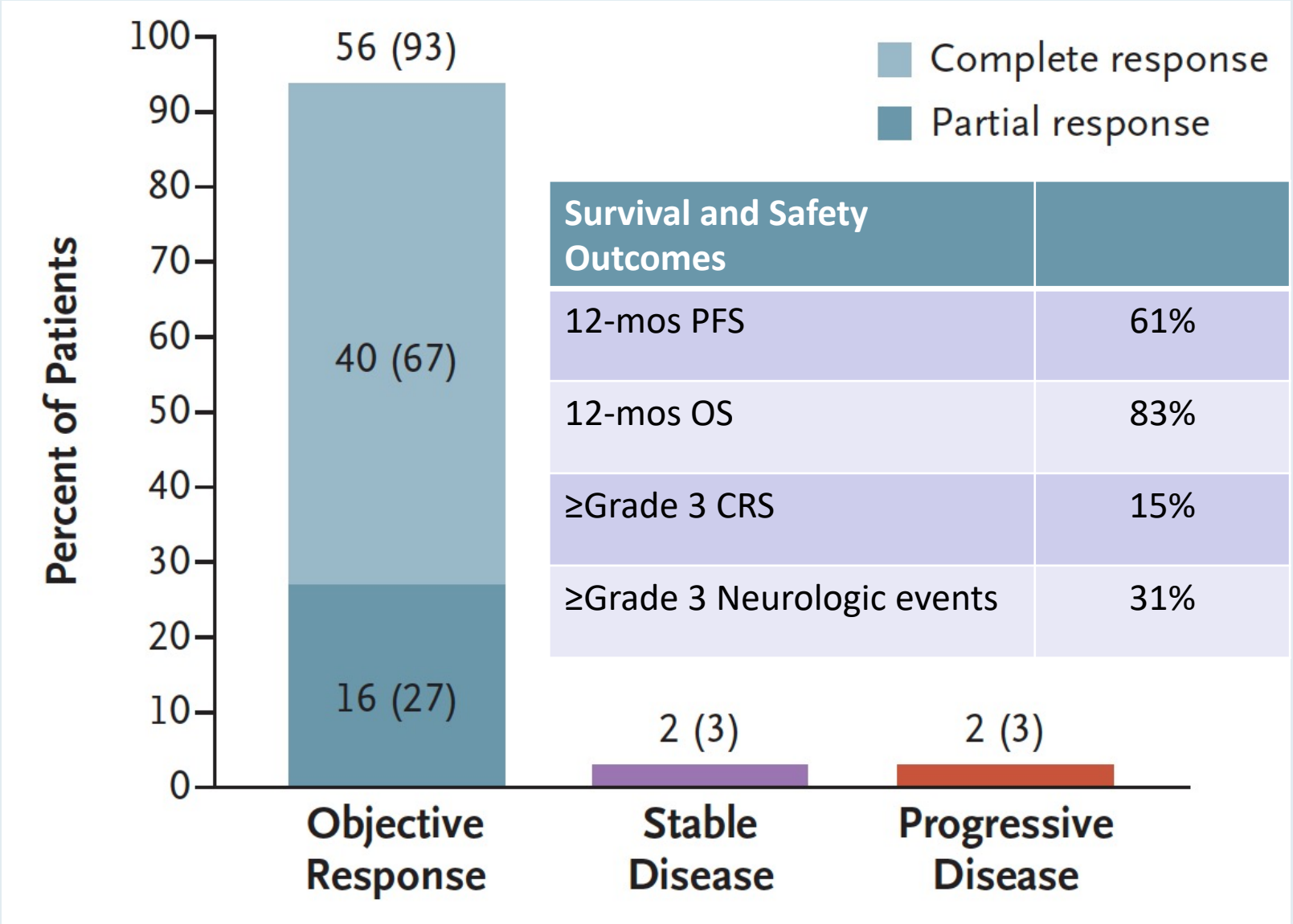
The NEW ENGLAND JOURNAL of MEDICINE

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

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.

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with ER-Positive Breast Cancer

Thursday, December 16, 2021
5:00 PM – 6:00 PM ET

Faculty

Ruth O'Regan, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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