Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

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

RTP RESEARCH TO PRACTICE

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.

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, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences, 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, 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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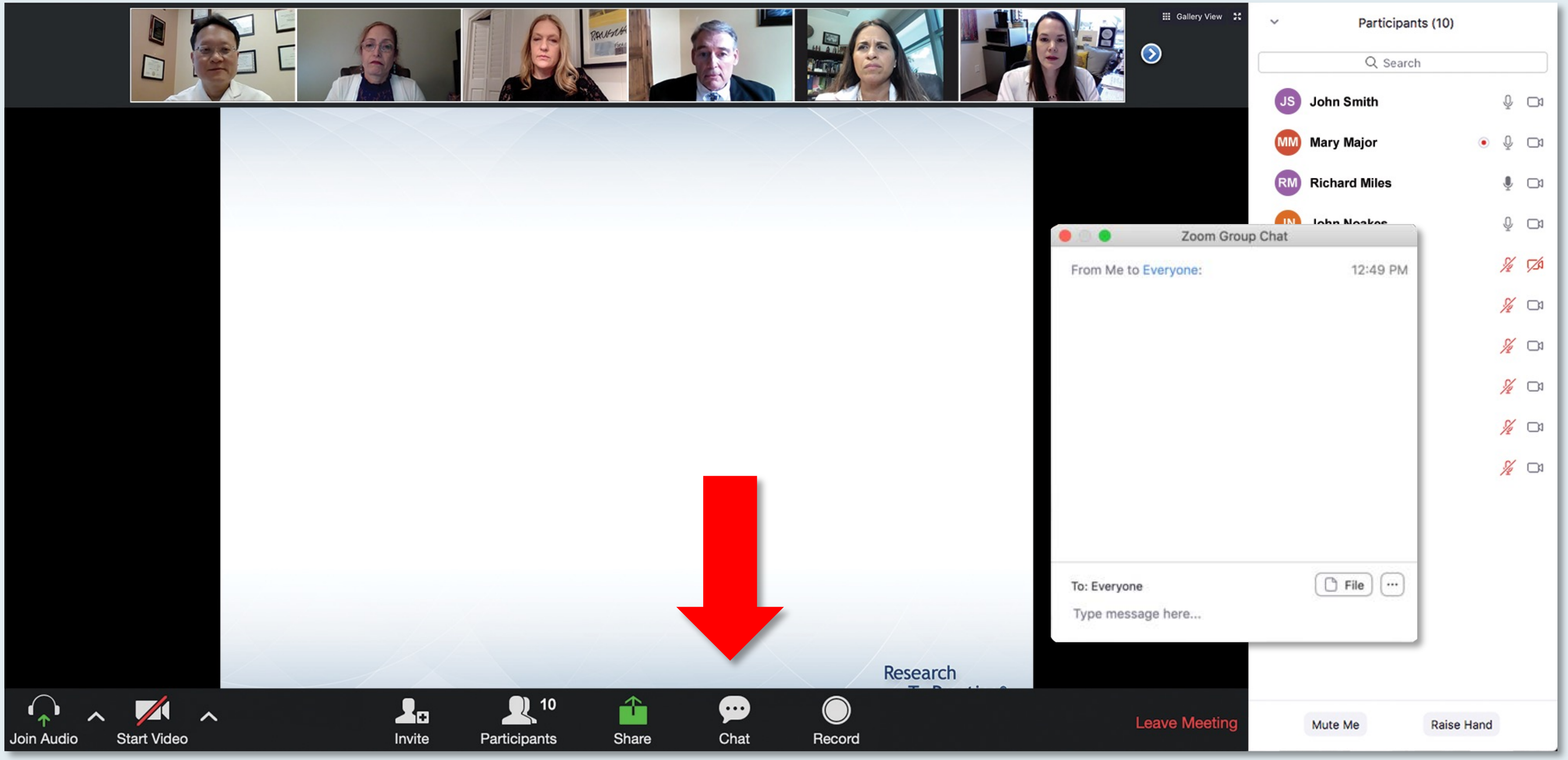
Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Williams — Disclosures

Advisory Committee	AbbVie Inc, Celgene Corporation, Janssen Biotech Inc, Kite, A Gilead Company, Kymera Therapeutics, TG Therapeutics Inc
Contracted Research	Celgene Corporation, Janssen Biotech Inc, Pharmacyclics LLC, an AbbVie Company, TG Therapeutics Inc

We Encourage Clinicians in Practice to Submit Questions



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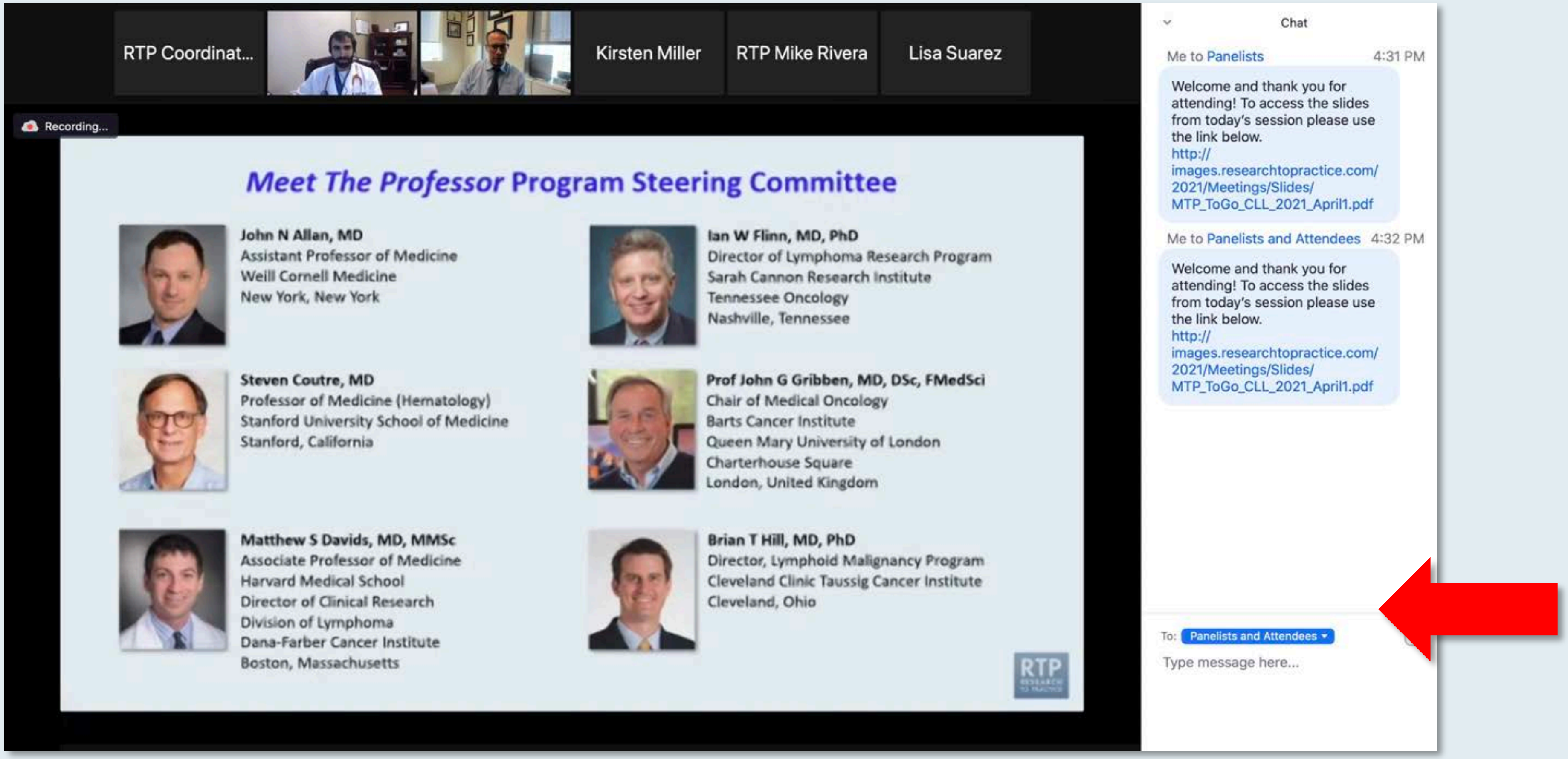
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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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Meet The Professor

Optimizing the Management of Metastatic Castration-Resistant Prostate Cancer

Wednesday, March 2, 2022
5:00 PM – 6:00 PM ET

Faculty

Andrew J Armstrong, MD, ScM

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor

Current and Future Management of Chronic Lymphocytic Leukemia

Thursday, March 3, 2022
5:00 PM – 6:00 PM ET

Faculty

William G Wierda, MD, PhD

Moderator

Neil Love, MD

Meet The Professor

Current and Future Role of Immunotherapy in the Management of Lung Cancer

Monday, March 7, 2022
5:00 PM – 6:00 PM ET

Faculty

Charu Aggarwal, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Year in Review:
Kidney and Bladder Cancer

Tuesday, March 8, 2022
5:00 PM – 6:00 PM ET

Faculty

Elizabeth R Plimack, MD, MS
Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

Meet The Professor
Optimizing the Management of Acute Myeloid Leukemia

Wednesday, March 9, 2022
5:00 PM – 6:00 PM ET

Faculty
Rebecca L Olin, MD, MSCE

Moderator
Neil Love, MD

Meet The Professor

Current and Future Management of Myelofibrosis

Thursday, March 10, 2022
5:00 PM – 6:00 PM ET

Faculty

Srdan Verstovsek, MD, PhD

Moderator

Neil Love, MD

Thank you for joining us!

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

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University of Virginia School of Medicine
Charlottesville, Virginia

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

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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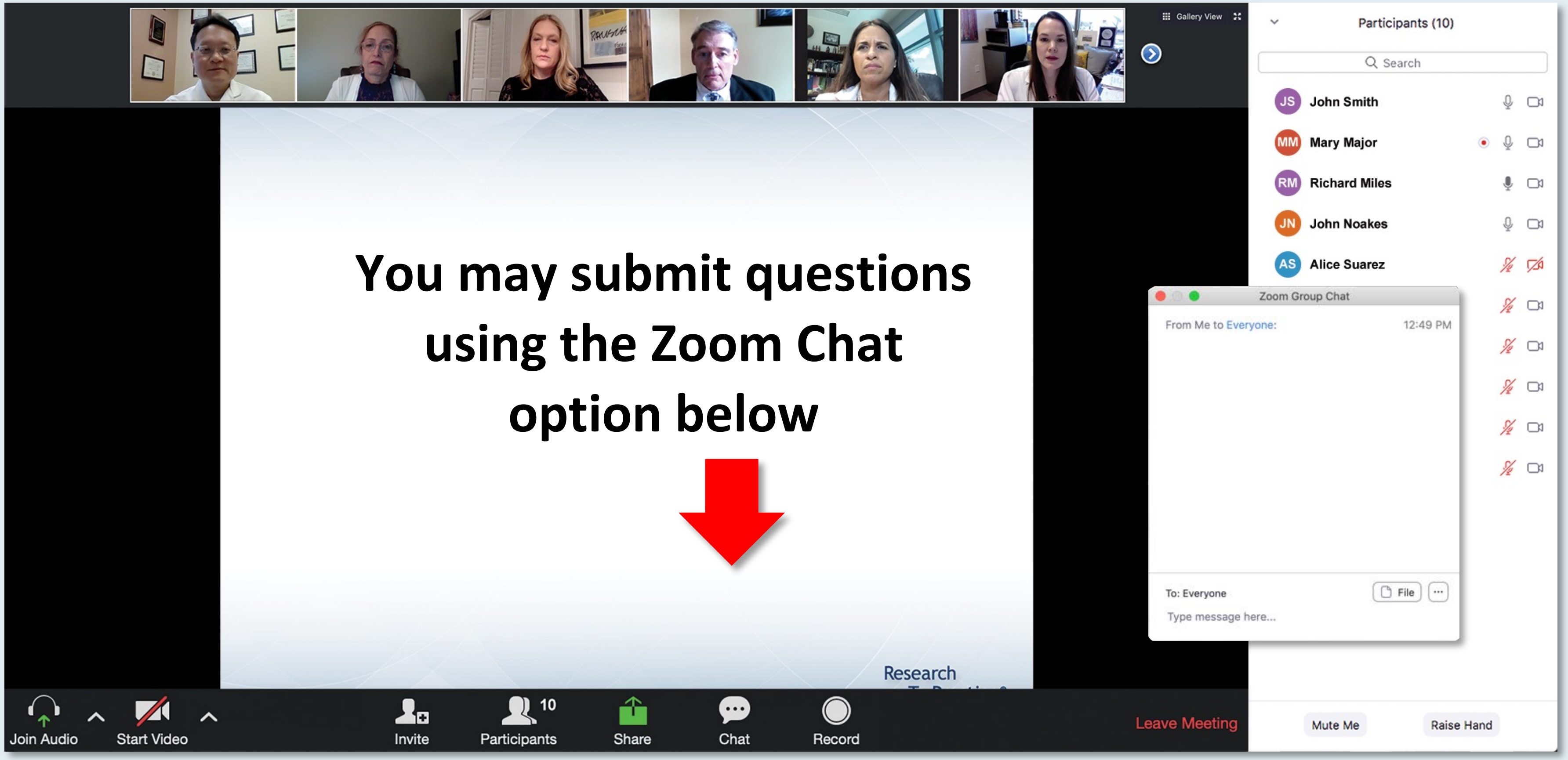

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Dr Williams — Disclosures

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Contracted Research	Celgene Corporation, Janssen Biotech Inc, Pharmacyclics LLC, an AbbVie Company, TG Therapeutics Inc

Laurie Matt-Amaral, MD, MPH
Cleveland Clinic Akron General
Akron, Ohio

Anthony Nguyen, MD
Loma Linda University Health
Loma Linda, California

Neil Morganstein, MD
Atlantic Health System
Summit, New Jersey

Priya Rudolph, MD, PhD
Georgia Cancer Specialists
Athens, Georgia

Meet The Professor with Dr Williams

MODULE 1: Case Presentations – Mantle Cell Lymphoma, Diffuse Large B-Cell Lymphoma (DLBCL)

- Dr Rudolph: A 56-year-old woman with Stage IV mantle cell lymphoma
- Dr Morganstein: A 52-year-old woman with nongerminal-center DLBCL with renal, adrenal and cardiac involvement
- Dr Nguyen: A 65-year-old man with bulky DLBCL and gastric outlet obstruction
- Dr Rudolph: A 78-year-old woman with germinal-center DLBCL and Child-Pugh A cirrhosis
- Dr Morganstein: A 54-year-old man with DLBCL transformed from follicular lymphoma (FL)

MODULE 2: Case Presentations – Follicular Lymphoma, Hodgkin Lymphoma

- Dr Matt-Amaral: An otherwise healthy 89-year-old man with Grade III FL
- Dr Rudolph: A 77-year-old woman with nonbulky Grade I FL (FLIPI 4)
- Dr Morganstein: A 34-year-old woman with nodular sclerosing Hodgkin lymphoma
- Dr Morganstein: A 42-year-old woman with Stage IIB Hodgkin lymphoma in remission who develops triple-negative breast cancer with a BRCA2 germline mutation

MODULE 3: Faculty Survey Results

MODULE 4: Appendix of Key Data Sets

Meet The Professor with Dr Williams

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MODULE 4: Appendix of Key Data Sets

Antibody and T-Cell Responses to Covid-19 mRNA Vaccines in Patients with B-Cell Lymphomas and Chronic Lymphocytic Leukemia (CLL)

Ayers EC et al.

ASH 2021;Abstract 1335.

Case Presentation: A 56-year-old woman with Stage IV mantle cell lymphoma

Dr Priya Rudolph (Athens, Georgia)

Current Oncology Reports (2021) 23: 102
https://doi.org/10.1007/s11912-021-01094-y

LEUKEMIA (A AGUAYO, SECTION EDITOR)

Leukemic Variant of Mantle Cell Lymphoma: Clinical Presentation and Management

Krista M. Isaac[1] · Craig A. Portell[1] · Michael E. Williams[1]

American Society of Hematology
2021 L Street NW, Suite 900,
Washington, DC 20036
Phone: 202-776-0544 | Fax 202-776-0545
bloodadvances@hematology.org

Blood Adv 2021;[Online ahead of print].

Dose Finding Study of Ibrutinib and Venetoclax in Relapsed or Refractory Mantle Cell Lymphoma

Tracking no: ADV-2021-005357R1

Craig Portell (University of Virginia, United States) Nolan Wages (University of Virginia, United States) Brad Kahl (Washington University in St. Louis, United States) Lihua Budde (City of Hope National Medical Center, United States) Robert Chen (City of Hope National Medical Center, United States) Jonathon Cohen (Emory University, United States) Nikole Varhegyi (University of Virginia, United States) Gina Petroni (University of Virginia, United States) Michael Williams (University of Virginia School of Medicine, United States)

Case Presentation: A 52-year-old woman with nongerminal-center DLBCL with renal, adrenal and cardiac involvement

Dr Neil Morganstein (Summit, New Jersey)

Case Presentation: A 65-year-old man with bulky DLBCL and gastric outlet obstruction

Dr Anthony Nguyen (Loma Linda, California)

Case Presentation: A 78-year-old woman with germinal-center DLBCL and Child-Pugh A cirrhosis

Dr Priya Rudolph (Athens, Georgia)

Case Presentation: A 78-year-old woman with germinal-center DLBCL and Child-Pugh A cirrhosis (continued)

Dr Priya Rudolph (Athens, Georgia)

Case Presentation: A 54-year-old man with DLBCL transformed from FL

Dr Neil Morganstein (Summit, New Jersey)

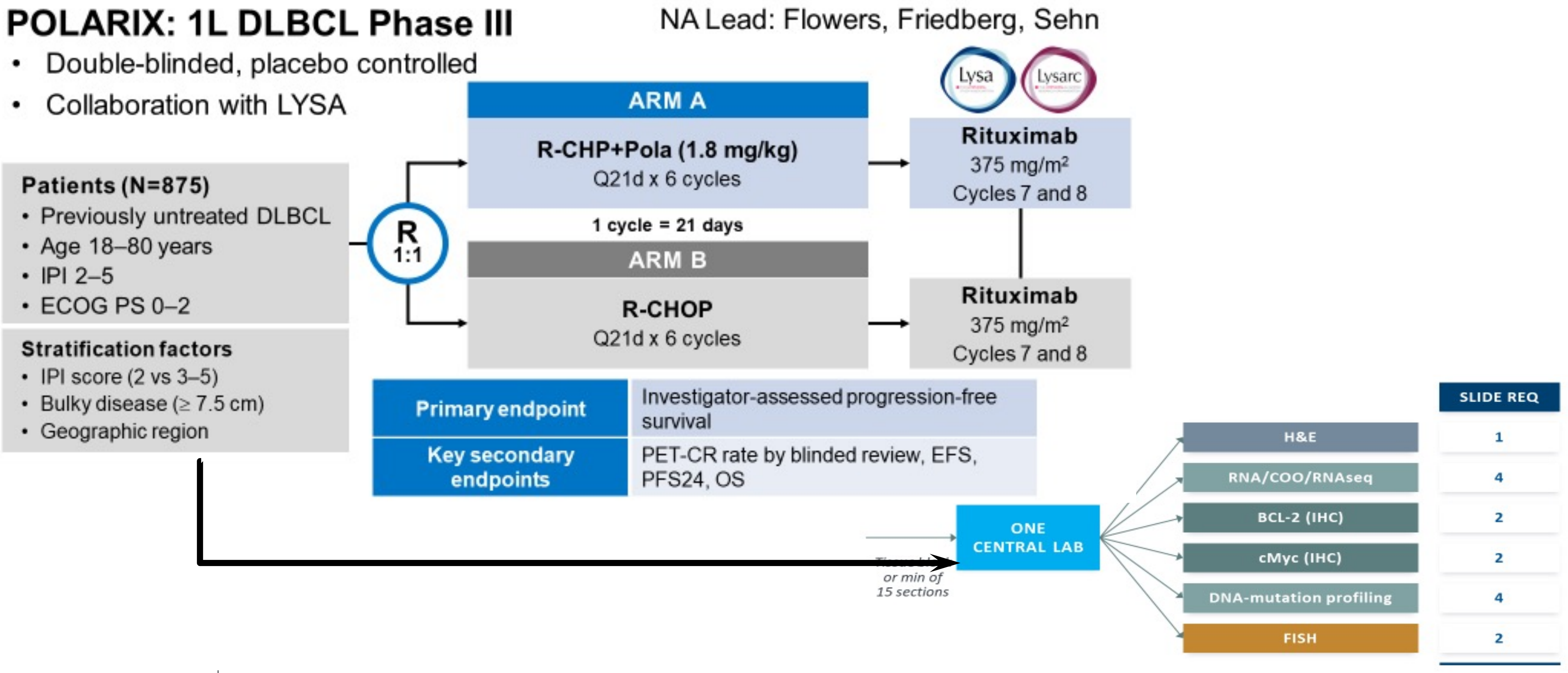
RTP RESEARCH TO PRACTICE

POLARIX Study: Polatuzumab Vedotin with Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone (Pola-R-CHP) Versus Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (R-CHOP) Therapy in Patients with Previously Untreated Diffuse Large B-Cell Lymphoma

Hervé Tilly, Franck Morschhauser, Laurie H. Sehn, Jonathan W. Friedberg, Marek Trněný, Jeff P. Sharman, Charles Herbaux, John M. Burke, Matthew Matasar, Shinya Rai, Koji Izutsu, Neha Mehta-Shah, Lucie Oberic, Adrien Chauchet, Wojciech Jurczak, Yuqin Song, Richard Greil, Larysa Mykhalska, Juan Miguel Bergua Burgués, Matthew C. Cheung, Antonio Pinto, Ho-Jin Shin, Greg Hapgood, Eduardo Munhoz, Pau Abrisqueta, Jyh-Pyng Gau, Jamie Hirata, Yanwen Jiang, Mark Yan, Calvin Lee, Christopher Flowers, Gilles Salles

Courtesy of Christopher R Flowers, MD, MS

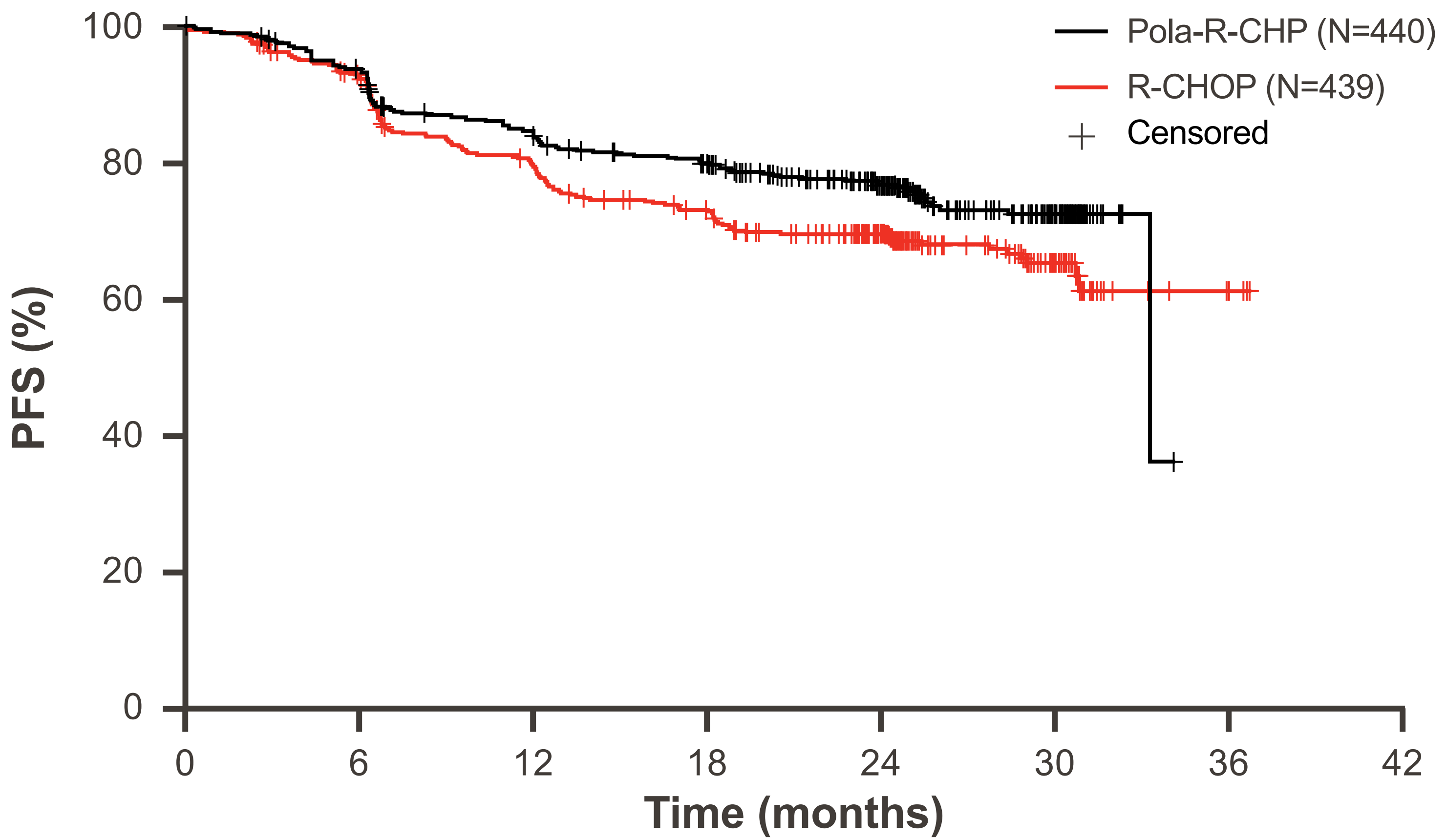
POLARIX: A randomized double-blinded study



Courtesy of Christopher R Flowers, MD, MS

POLARIX: Primary endpoint: Progression-free survival

Pola-R-CHP significantly improved PFS versus R-CHOP



No. of patients at risk								
Pola-R-CHP	440	404	353	327	246	78	NE	NE
R-CHOP	439	389	330	296	220	78	3	NE

HR 0.73 (P<0.02)

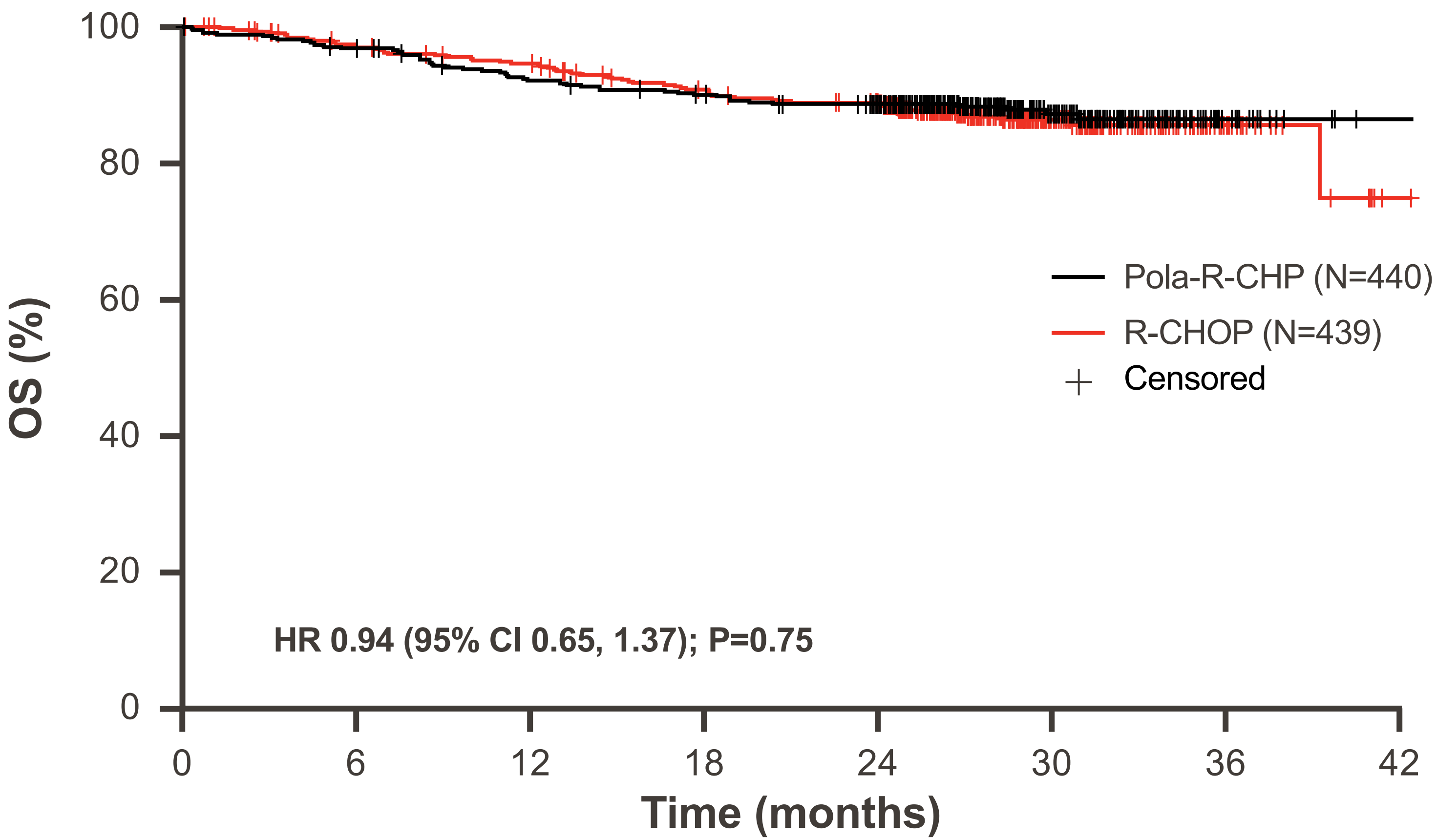
95% CI: 0.57, 0.95

- Pola-R-CHP demonstrated a **27% reduction in the relative risk of disease progression, relapse, or death** versus R-CHOP
- **24-month PFS:** 76.7% with Pola-R-CHP versus 70.2% with R-CHOP (Δ=**6.5%**)

Tilly H et al. *N Engl J Med* 2022;386(4):351-63; *ASH* 2021;Abstract LBA1.

Courtesy of Christopher R Flowers, MD, MS

POLARIX: Overall survival

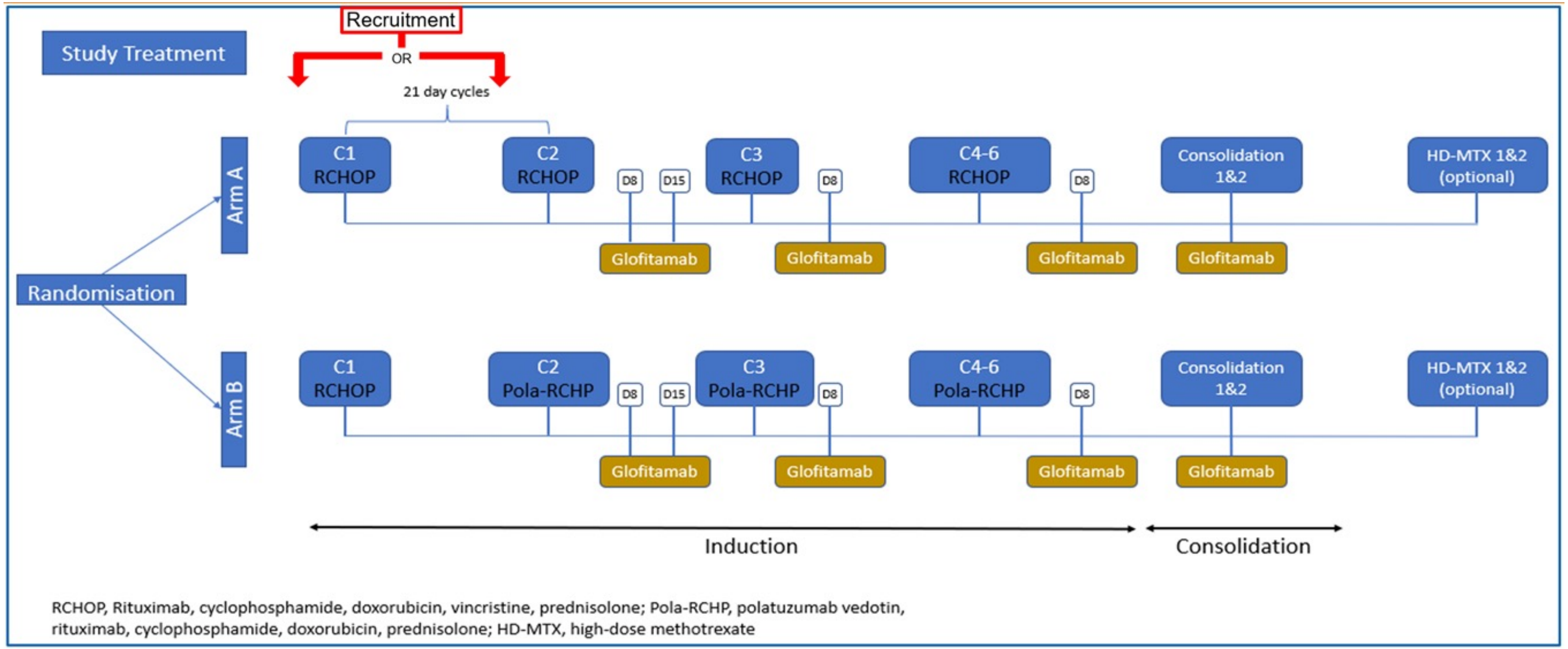


No. of patients at risk								
Pola-R-CHP	440	423	397	384	362	140	15	1
R-CHOP	439	414	401	376	355	132	20	1

Tilly H et al. *N Engl J Med* 2022;386(4):351-63; *ASH* 2021;Abstract LBA1.

Courtesy of Christopher R Flowers, MD, MS

Trial in Progress: A Multicentre, Parallel Arm, Open-Label Trial of Frontline R-CHOP/Polatuzumab Vedotin-RCHP and Glofitamab in Younger Patients with Higher Risk Diffuse Large B Cell Lymphoma (COALITION)



Minson A et Al, ASH 2021

Courtesy of Grzegorz Nowakowski, MD

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

The NEW ENGLAND JOURNAL of MEDICINE

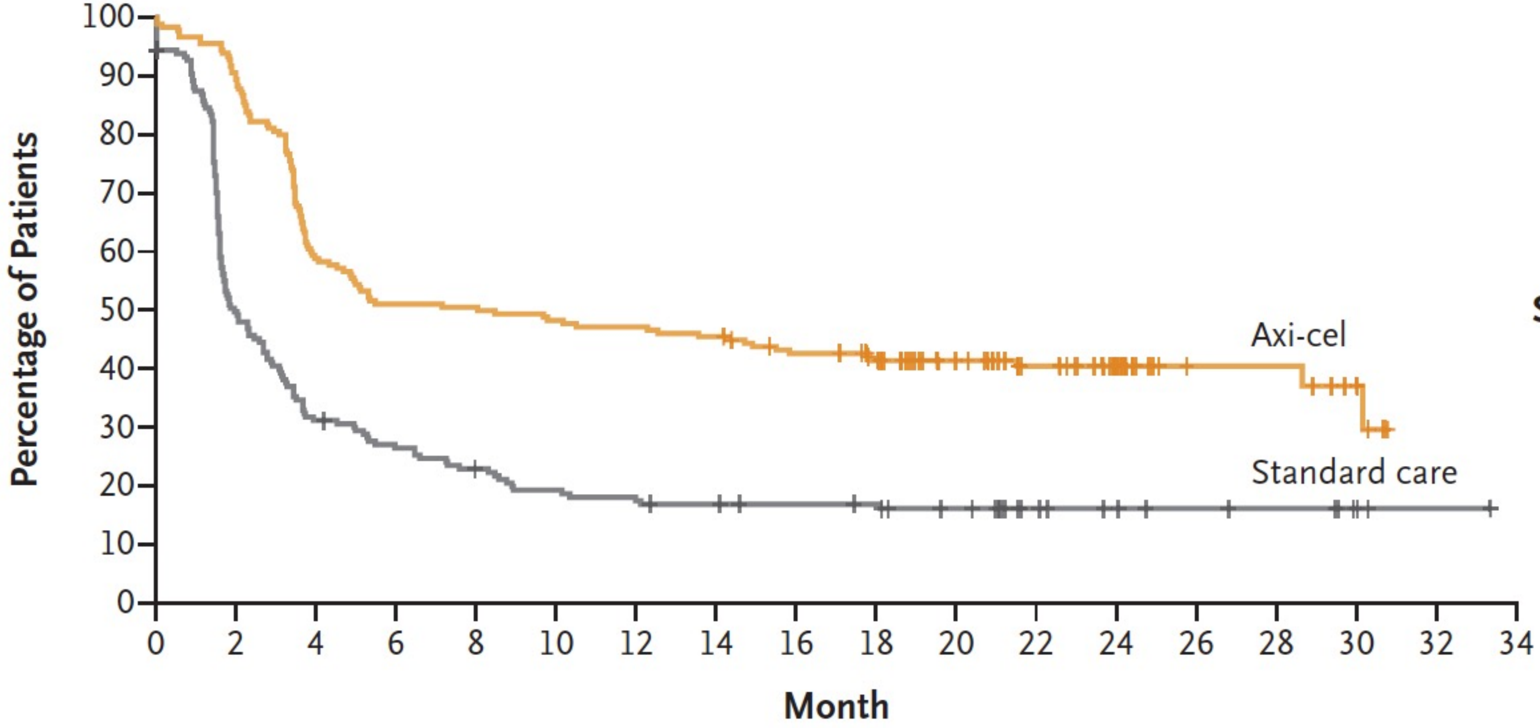
ORIGINAL ARTICLE

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].

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

The NEW ENGLAND JOURNAL of MEDICINE

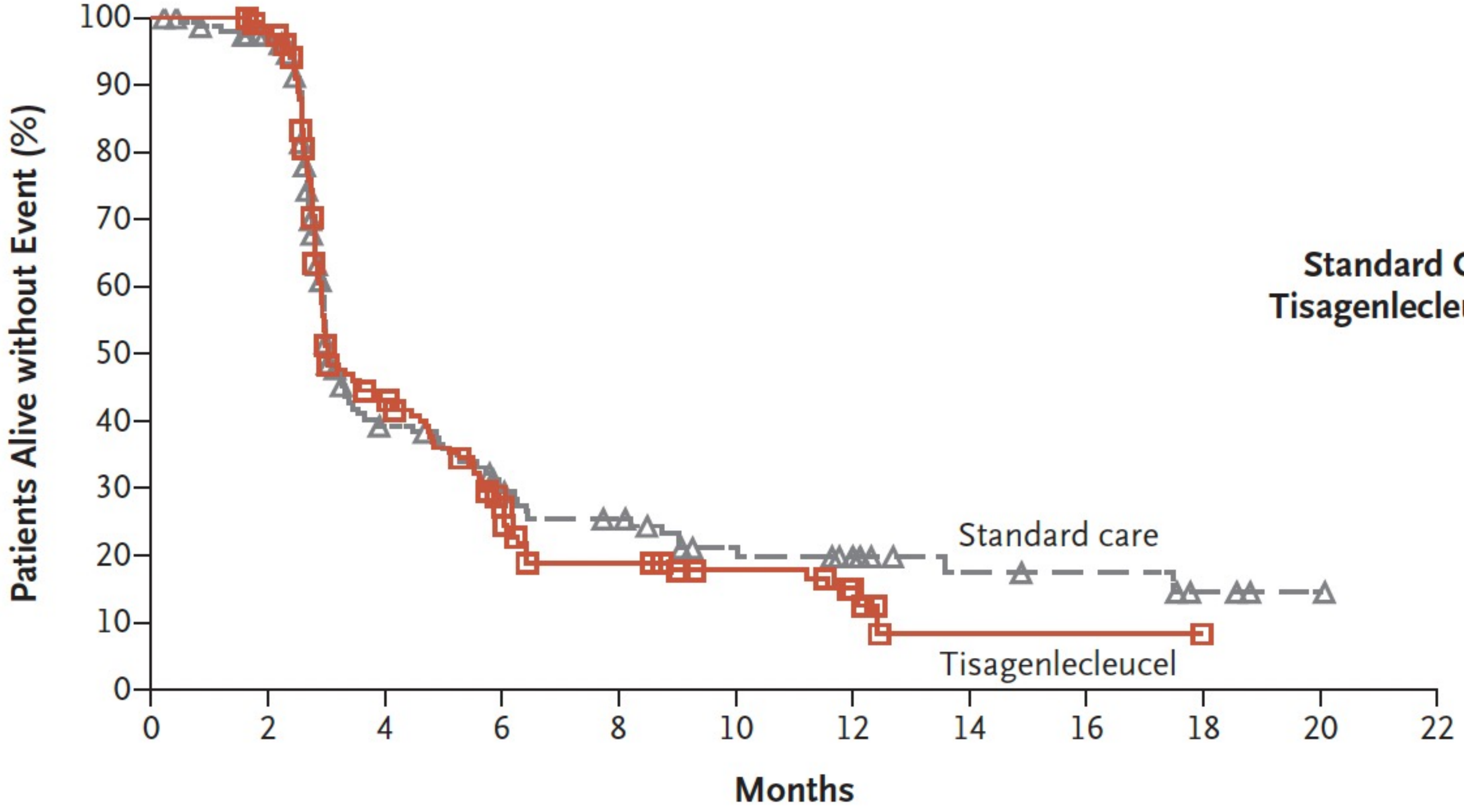
ORIGINAL ARTICLE

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

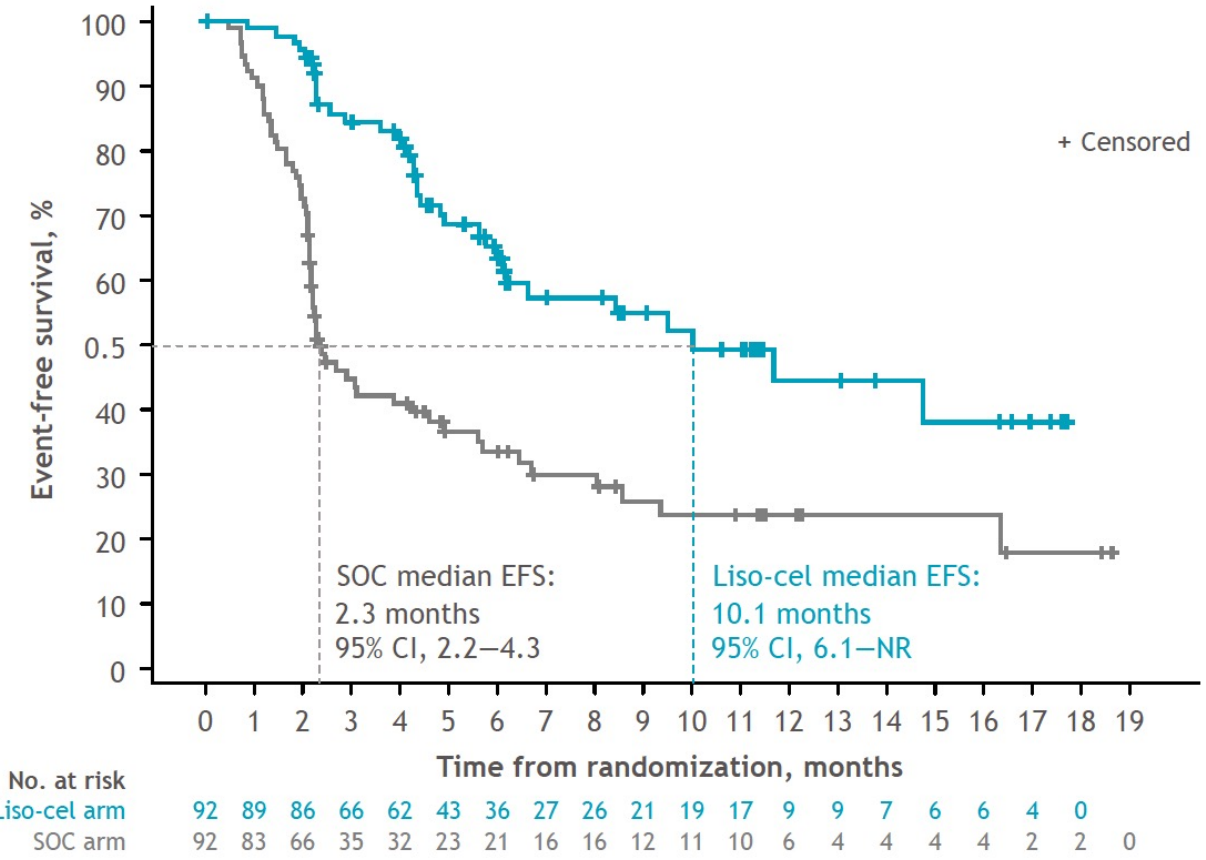
Manali Kamdar,[1] Scott R. Solomon,[2] Jon Arnason,[3] Patrick B. Johnston,[4] Bertram Glass,[5] Veronika Bachanova,[6] Sami Ibrahimi,[7] Stephan Mielke,[8] Pim Mutsaers,[9] Francisco Hernandez-Ilizaliturri,[10] Koji Izutsu,[11] Franck Morschhauser,[12] Matthew Lunning,[13] David G. Maloney,[14] Alessandro 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)

Median follow-up in both arms: 6.2 months



	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

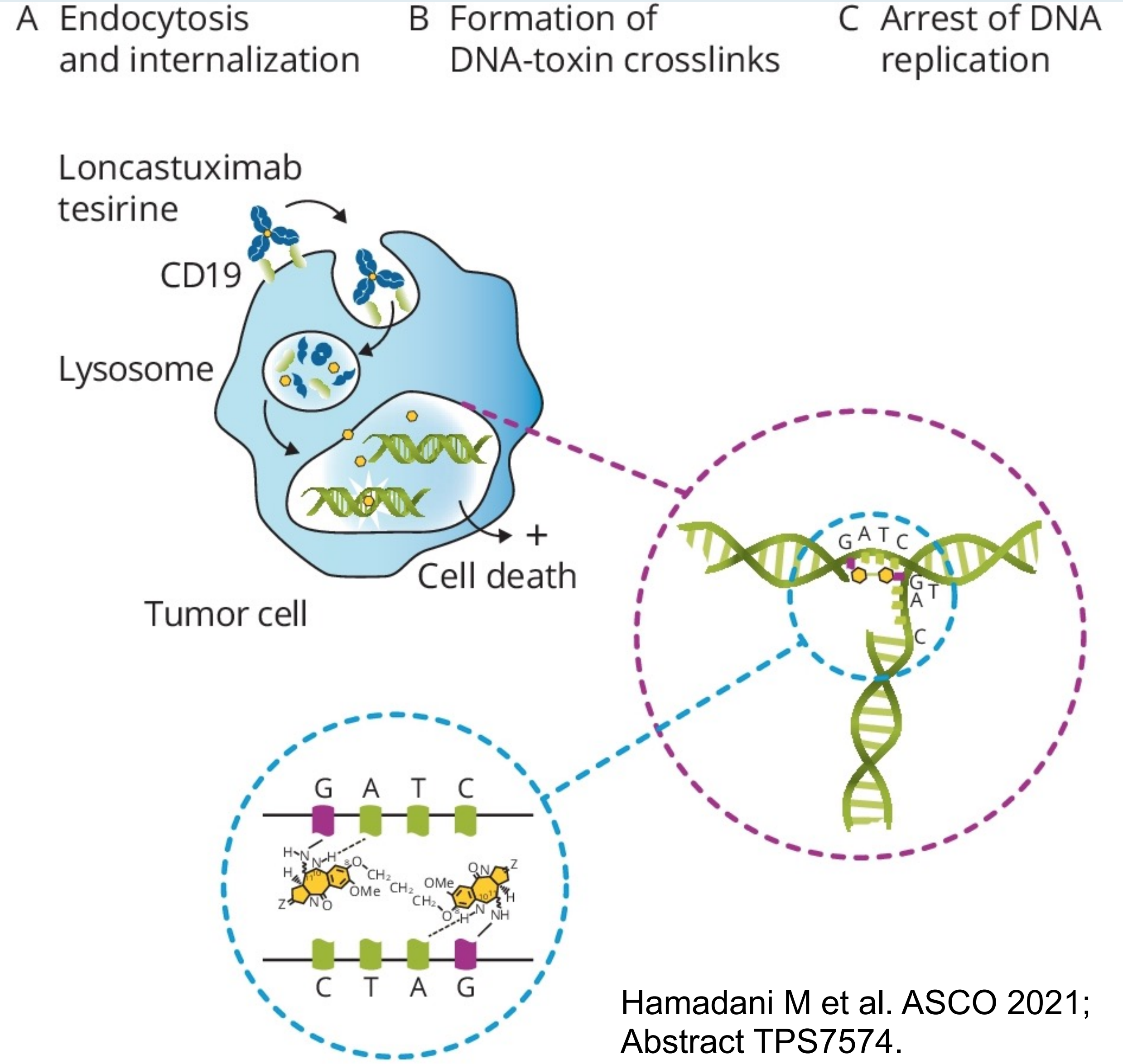
Kamdar M et al. ASH 2021;Abstract 91.

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

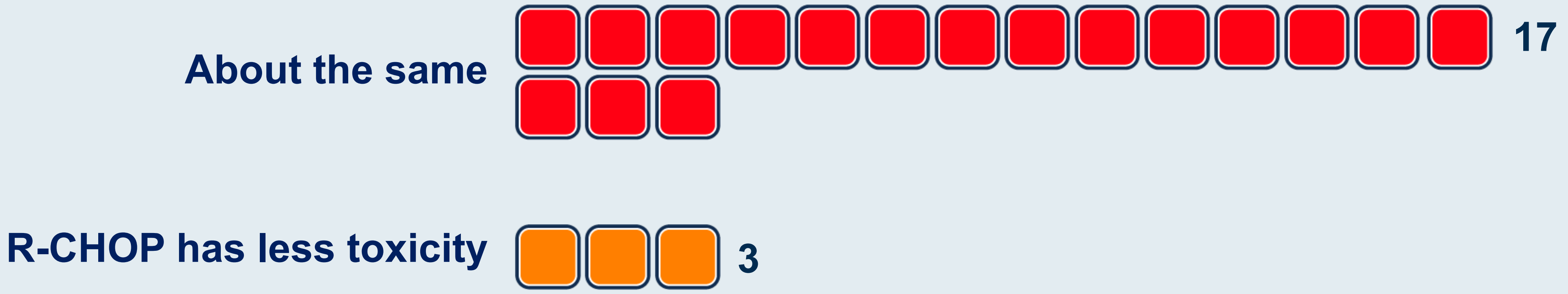
Response	As-treated population (N = 145)
Overall response rate	70/145 (48.3%)
Complete response rate	35/145 (24.1%)
Complete response	35 (24%)
Partial response	35 (24%)
Stable disease	22 (15%)
Progressive disease	30 (21%)
Not evaluable	23 (16%)
Survival	**As-treated population (N = 145)**
Median progression-free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

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

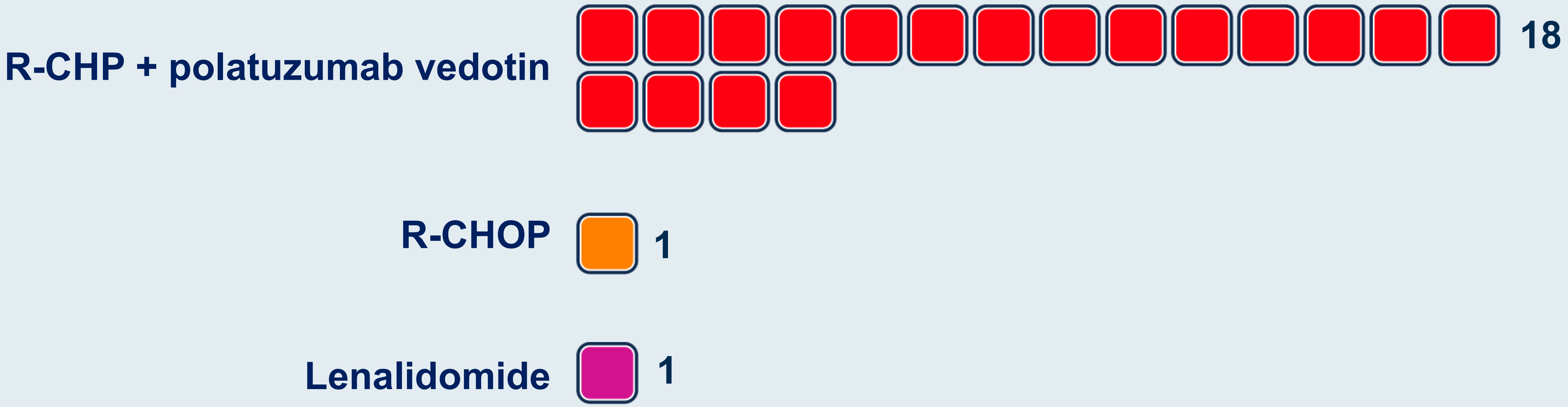
If future data continue not to demonstrate an overall survival advantage with polatuzumab vedotin in combination with R-CHP over R-CHOP when used as up-front therapy for DLBCL, do you think the clinical benefit with this regimen is greater than the risk?

Survey of Lymphoma Clinical Investigators

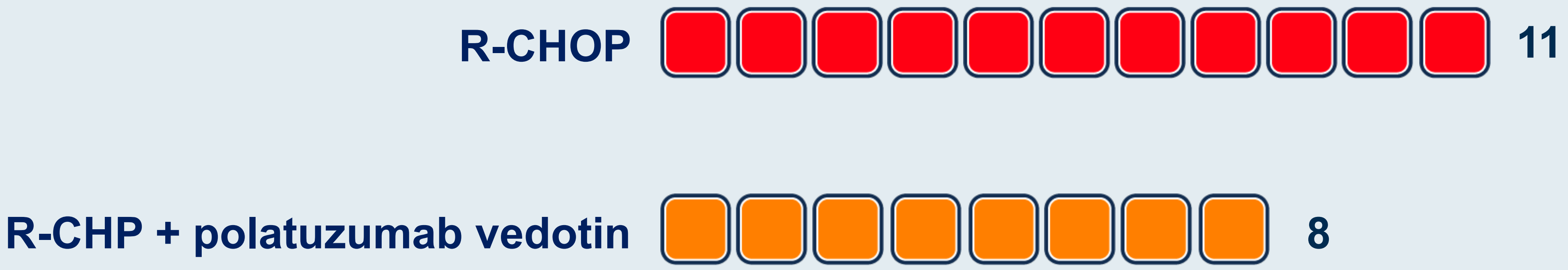
Based on available evidence and your own experience, how would you compare the global tolerability/toxicity of polatuzumab vedotin in combination with R-CHP to that of R-CHOP when used as up-front therapy for DLBCL?



Regulatory and reimbursement issues aside, which first-line therapy would you generally recommend for an otherwise healthy 65-year-old patient with Stage IV activated B-cell (ABC)-type DLBCL?

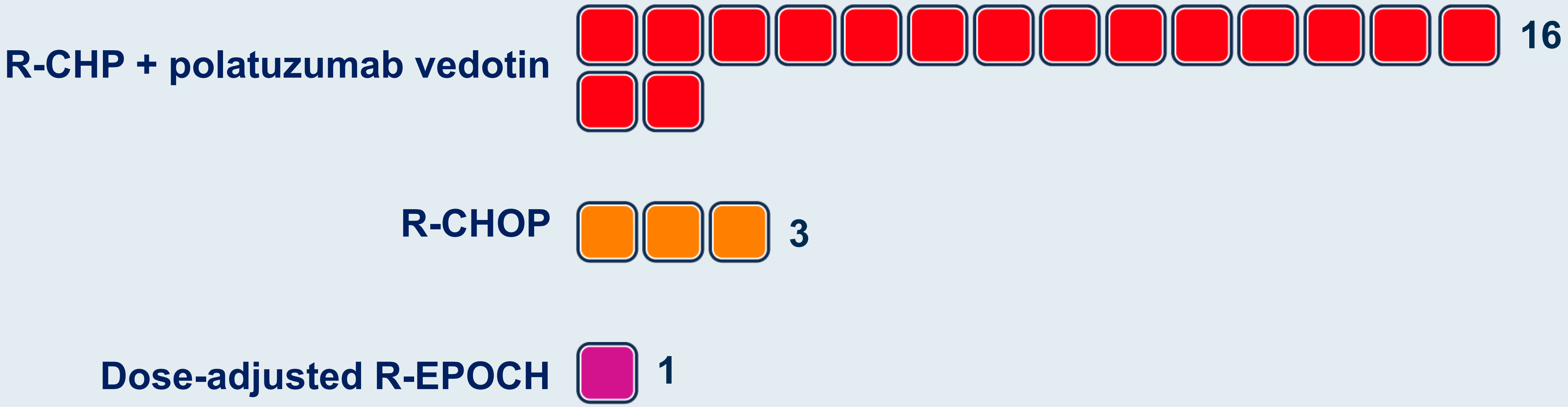


Regulatory and reimbursement issues aside, which first-line therapy would you generally recommend for an otherwise healthy 65-year-old patient with Stage IV germinal center B-cell (GCB)-type DLBCL?



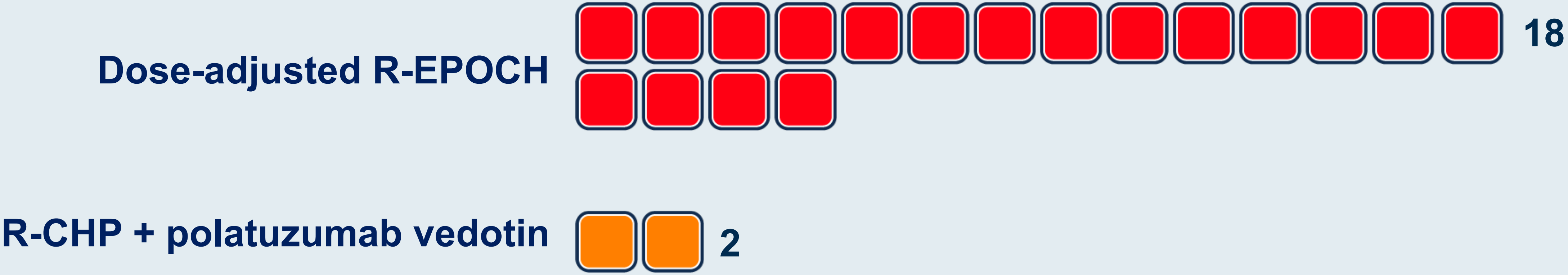
Survey of Lymphoma Clinical Investigators

Regulatory and reimbursement issues aside, which first-line therapy would you generally recommend for an otherwise healthy 65-year-old patient with Stage IV double-expressor DLBCL?



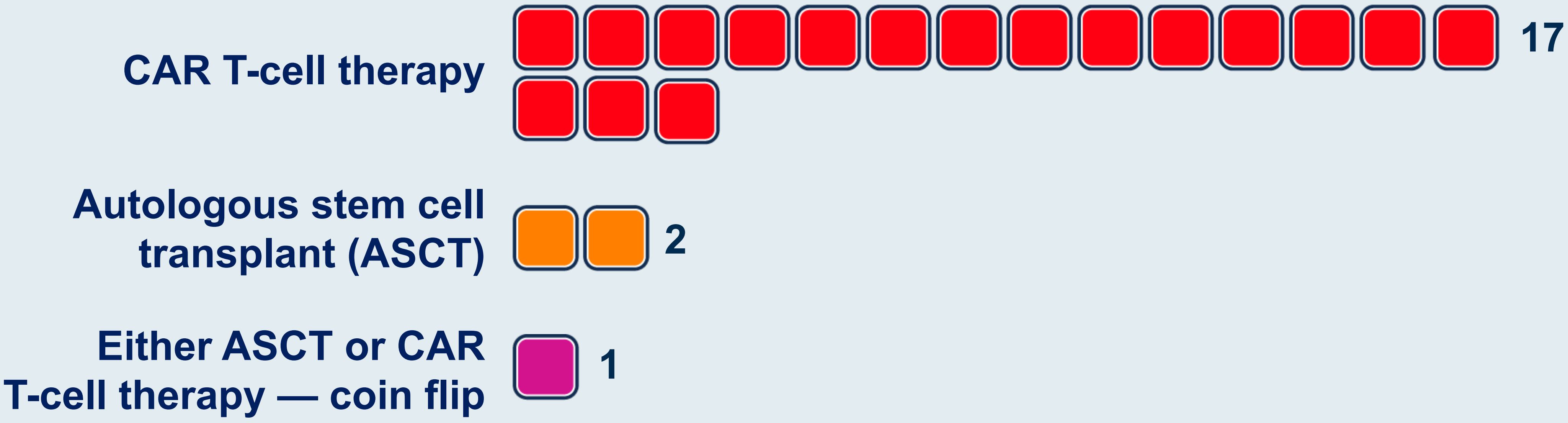
Survey of Lymphoma Clinical Investigators

Regulatory and reimbursement issues aside, which first-line therapy would you generally recommend for an otherwise healthy 65-year-old patient with Stage IV double-hit DLBCL?



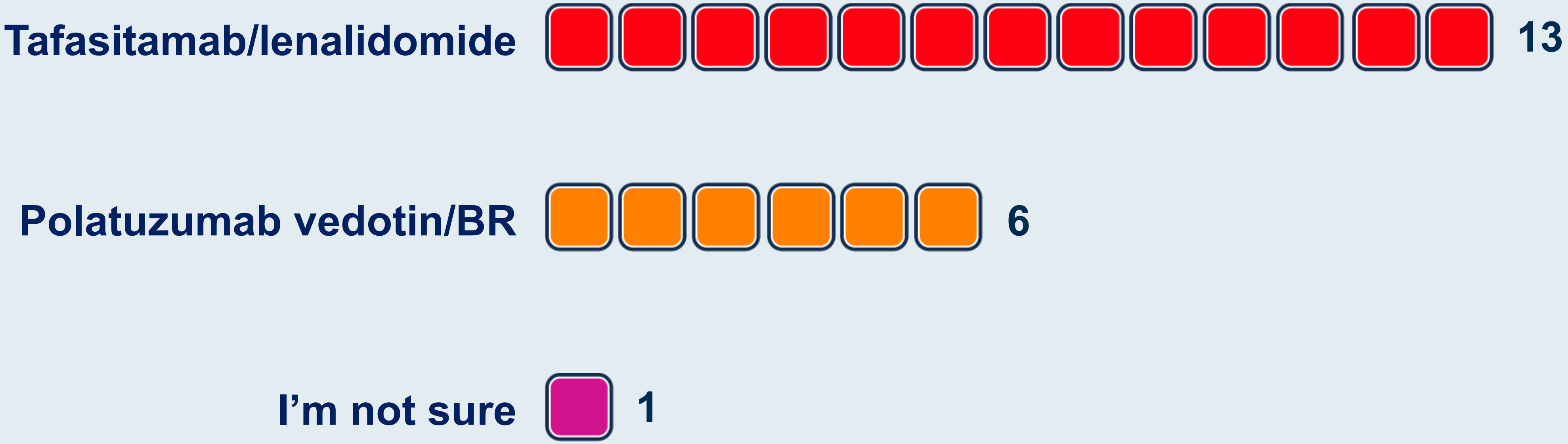
Survey of Lymphoma Clinical Investigators

Regulatory and reimbursement issues aside, which second-line therapy would you recommend for a younger, transplant-eligible patient with DLBCL who experiences disease relapse 12 months after R-CHOP?



Survey of Lymphoma Clinical Investigators

Which therapy would you generally recommend first for a patient with DLBCL who experiences disease progression on front-line R-CHOP and is <u>not eligible for high-dose therapy or CAR T-cell therapy</u>?



Survey of Lymphoma Clinical Investigators

Meet The Professor with Dr Williams

MODULE 1: Case Presentations – Mantle Cell Lymphoma, Diffuse Large B-Cell Lymphoma (DLBCL)

- Dr Rudolph: A 56-year-old woman with Stage IV mantle cell lymphoma
- Dr Morganstein: A 52-year-old woman with nongerminal-center DLBCL with renal, adrenal and cardiac involvement
- Dr Nguyen: A 65-year-old man with bulky DLBCL and gastric outlet obstruction
- Dr Rudolph: A 78-year-old woman with germinal-center DLBCL and Child-Pugh A cirrhosis
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MODULE 2: Case Presentations – Follicular Lymphoma, Hodgkin Lymphoma

- Dr Matt-Amaral: An otherwise healthy 89-year-old man with Grade III FL
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- Dr Morganstein: A 42-year-old woman with Stage IIB Hodgkin lymphoma in remission who develops triple-negative breast cancer with a BRCA2 germline mutation

MODULE 3: Faculty Survey Results

MODULE 4: Appendix of Key Data Sets

Case Presentation: An otherwise healthy 89-year-old man with Grade III FL

Dr Laurie Matt-Amaral (Akron, Ohio)

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

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.

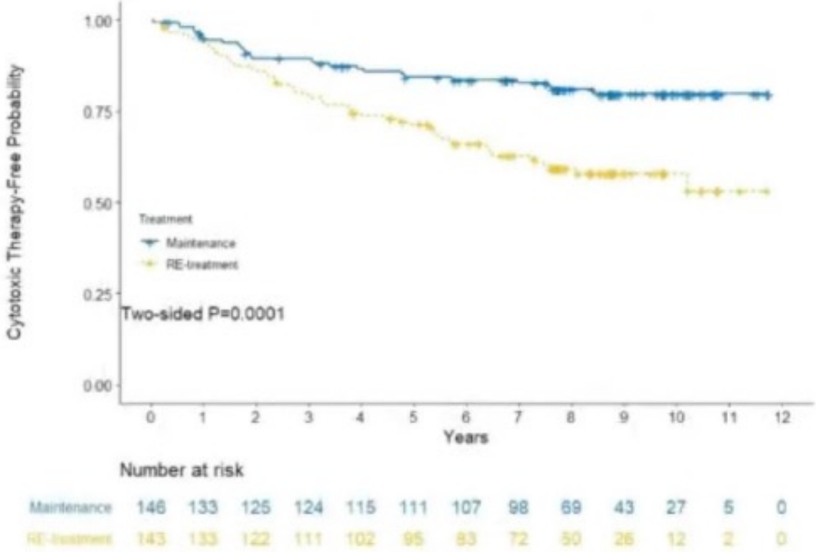
JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Freedom from First Cytotoxic Therapy

	3 years	5 years	7 years
MR	89%	84%	83%
RR	79%	71%	63%

HR 2.37 (1.5-3.76)

Median Follow up – 8.7 years



American Society of Hematology

63rd ASH® Annual Meeting and Exposition

Kahl B et al. ASH 2021;Abstract 815.

JC JOURNAL CLUB 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 patient 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.

JC JOURNAL CLUB

RTP RESEARCH TO PRACTICE

Case Presentation: A 77-year-old woman with nonbulky Grade I FL (FLIPI 4)

Dr Priya Rudolph (Athens, Georgia)

Case Presentation: A 34-year-old woman with nodular sclerosing Hodgkin lymphoma

Dr Neil Morganstein (Summit, New Jersey)

Case Presentation: A 42-year-old woman with Stage IIB Hodgkin lymphoma in remission who develops triple-negative breast cancer with a BRCA2 germline mutation

Dr Neil Morganstein (Summit, New Jersey)

Meet The Professor with Dr Williams

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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

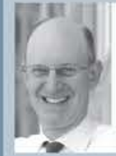
Regulatory and reimbursement issues aside, what is your usual second-line therapy for a 65-year-old patient with FL who achieves a complete response to 6 cycles of bendamustine/rituximab (BR) but then experiences disease relapse 4 years later?

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

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

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 Kahl	Tazemetostat → umbralisib
	Dr Flowers	Tazemetostat → umbralisib		Dr Nastoupil	Tazemetostat → axi-cel
	Dr Friedberg	Tazemetostat → umbralisib		Dr Williams	Tazemetostat → umbralisib
	Dr Hill	Tazemetostat → umbralisib			

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

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

RTP RESEARCH TO PRACTICE

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

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

Meet The Professor with Dr Williams

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Diffuse Large B-Cell Lymphoma

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

Patients
- Previously untreated DLBCL
- Age 18–80 years
- IPI 2–5
- ECOG PS 0–2

N=875

R
1:1

ARM A

Pola
1.8mg/kg
R-CHP + vincristine placebo
Q21D x 6 cycles

Rituximab
375 mg/m^2
Cycles 7 and 8

ARM B

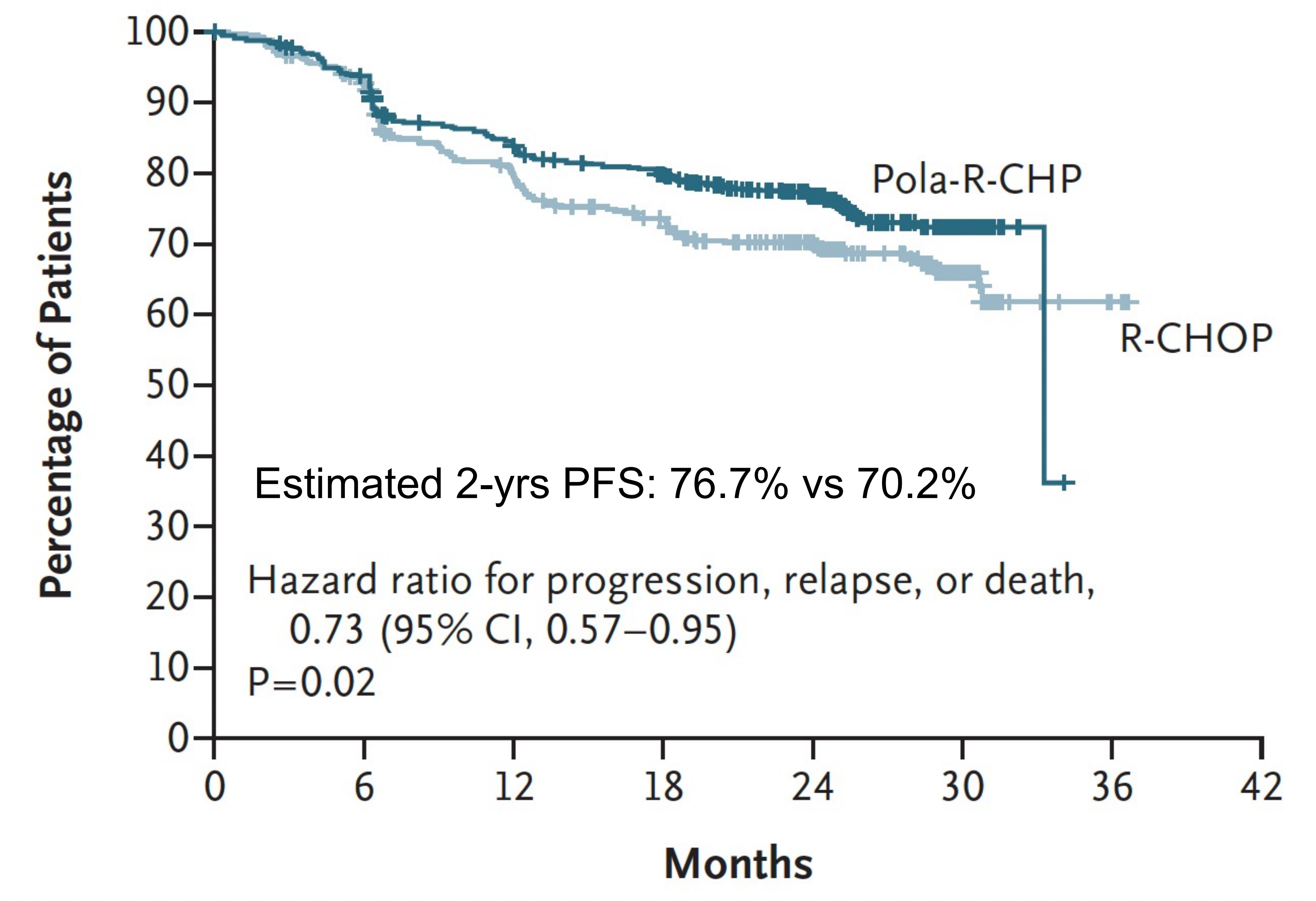
R-CHOP + pola placebo
Q21D x 6 cycles

Rituximab
375 mg/m^2
Cycles 7 and 8

Stratification factors
- IPI score (2 vs 3–5)
- Bulky disease (≥7.5cm)
- Geographical region

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].

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.

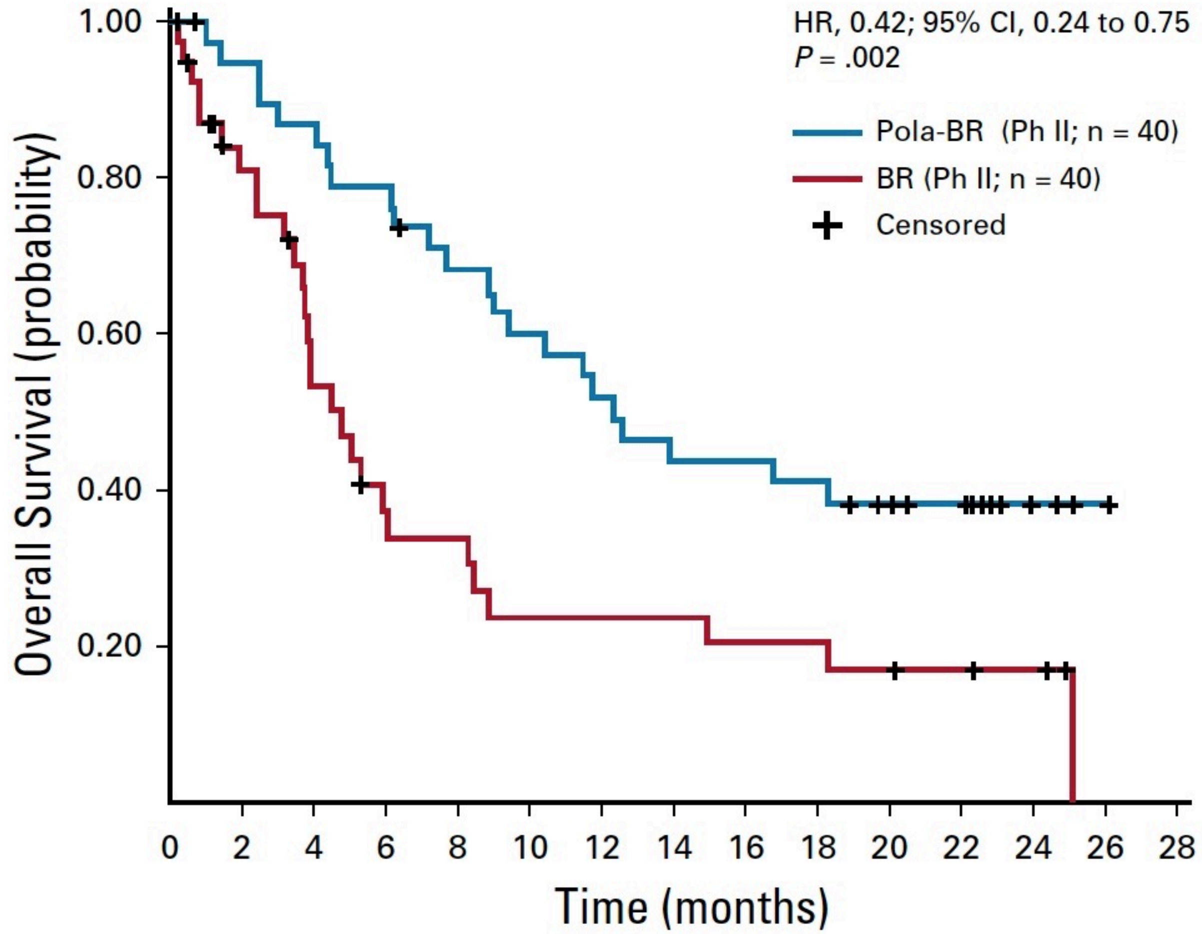
Polatuzumab Vedotin with Bendamustine/Rituximab for Transplant-Ineligible R/R DLBCL: End-of-Treatment CR Rate

Outcome	Phase II Randomized Pola-BR (n = 40)	Phase II Randomized 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.

RTP RESEARCH TO PRACTICE

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



No. at risk:

Pola plus BR (Ph II)	40	38	36	34	33	30	30	27	25	24	22	21	19	17	16	16	16	15	15	13	12	9	9	5	3	2	1
BR (Ph II)	40	33	27	25	17	15	11	10	10	7	7	7	7	7	7	6	6	6	6	5	5	4	4	3	3	1	

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

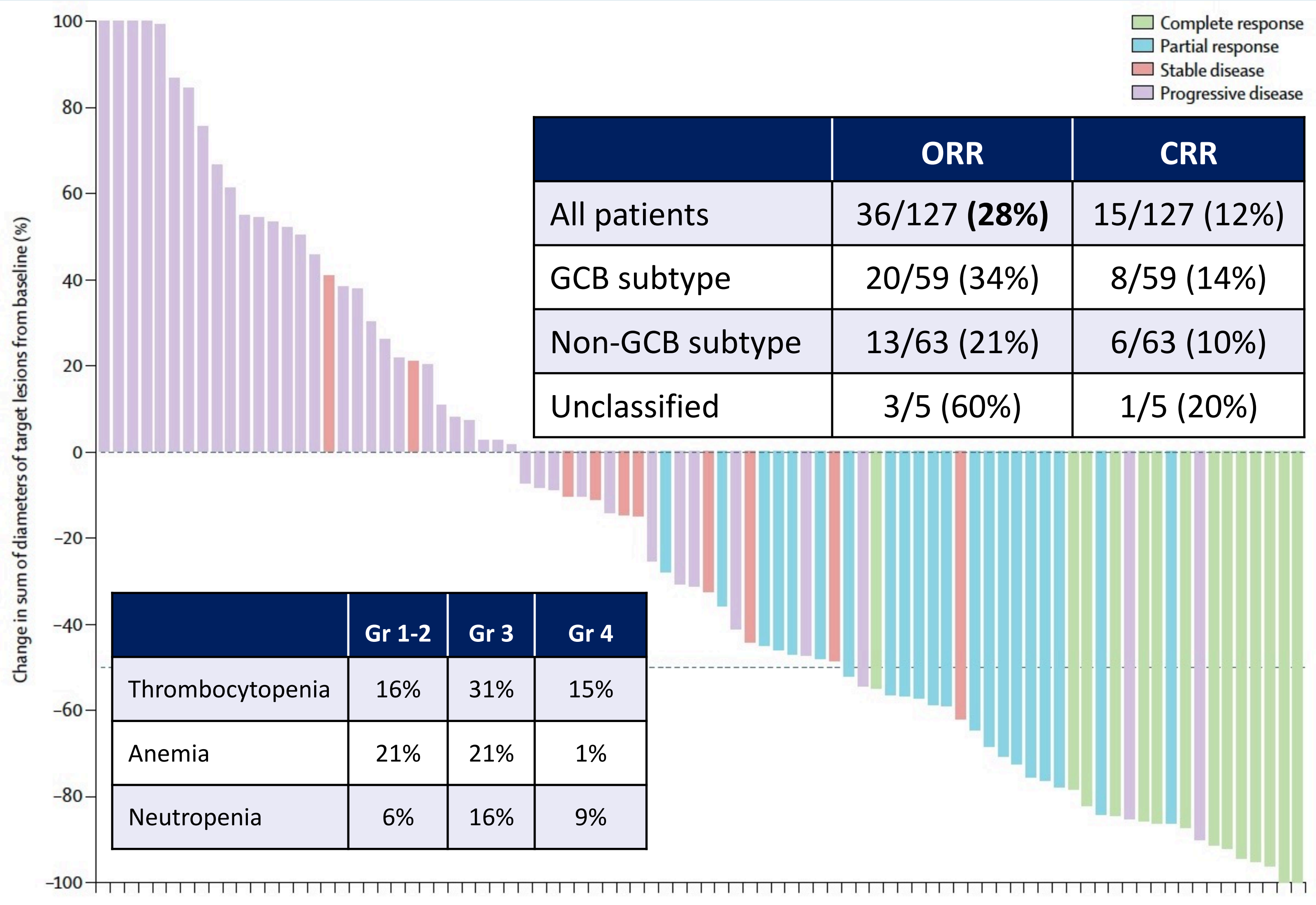
Lancet Haematol 2020;7:e511-22.

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

RTP
RESEARCH TO PRACTICE

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.

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

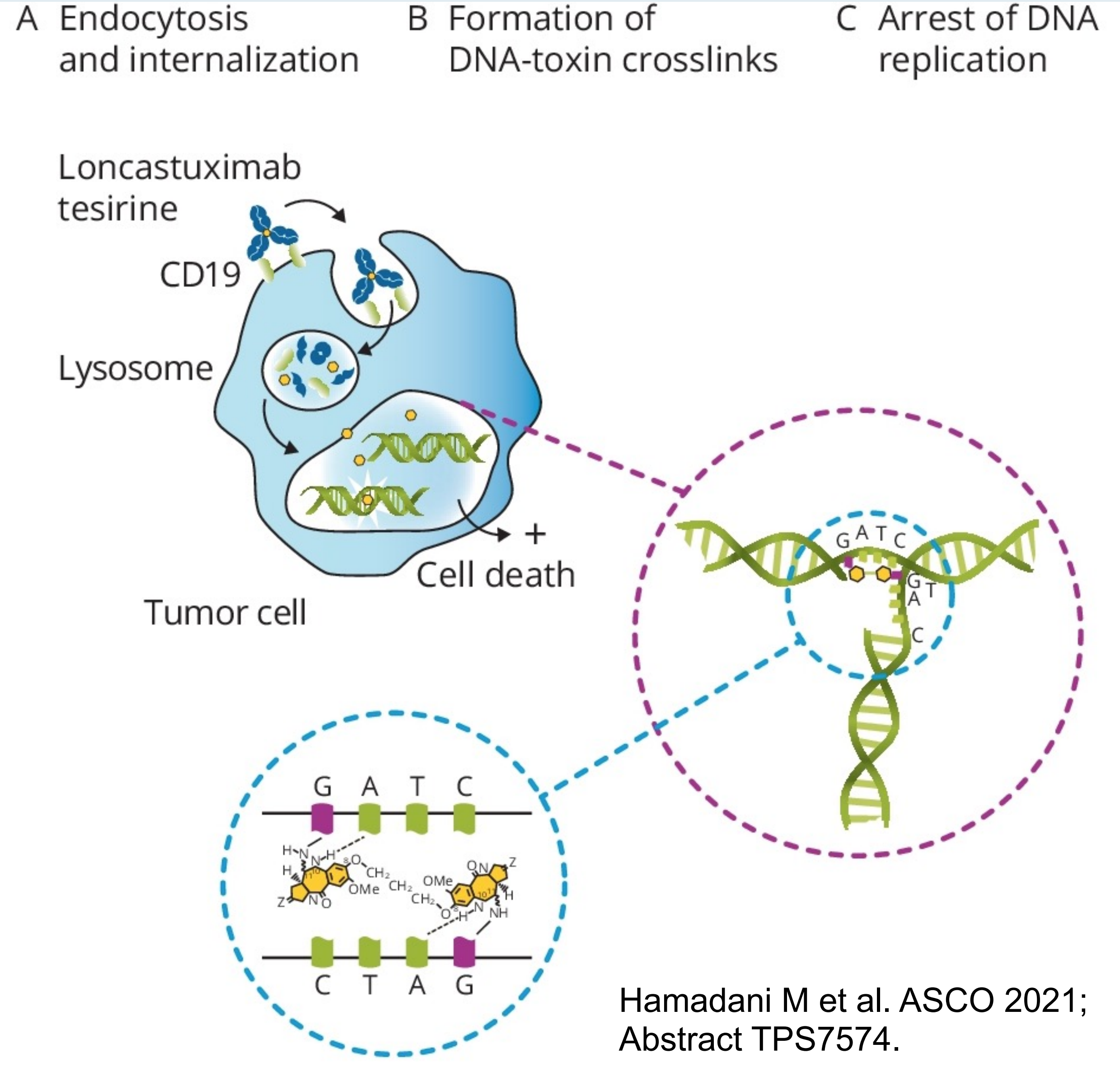
Lancet Oncol 2021;22:790-800

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

RTP RESEARCH TO PRACTICE

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

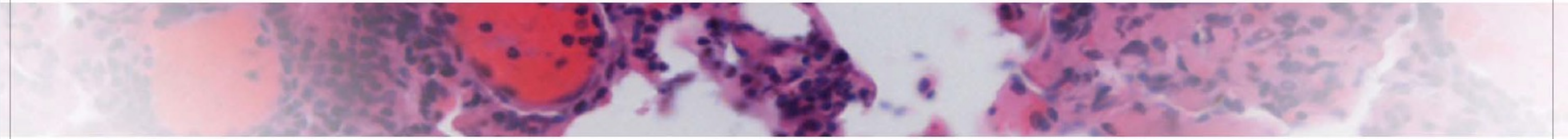
Response	As-treated population (N = 145)
Overall response rate	70/145 (48.3%)
Complete response rate	35/145 (24.1%)
Complete response	35 (24%)
Partial response	35 (24%)
Stable disease	22 (15%)
Progressive disease	30 (21%)
Not evaluable	23 (16%)
Survival	**As-treated population (N = 145)**
Median progression-free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

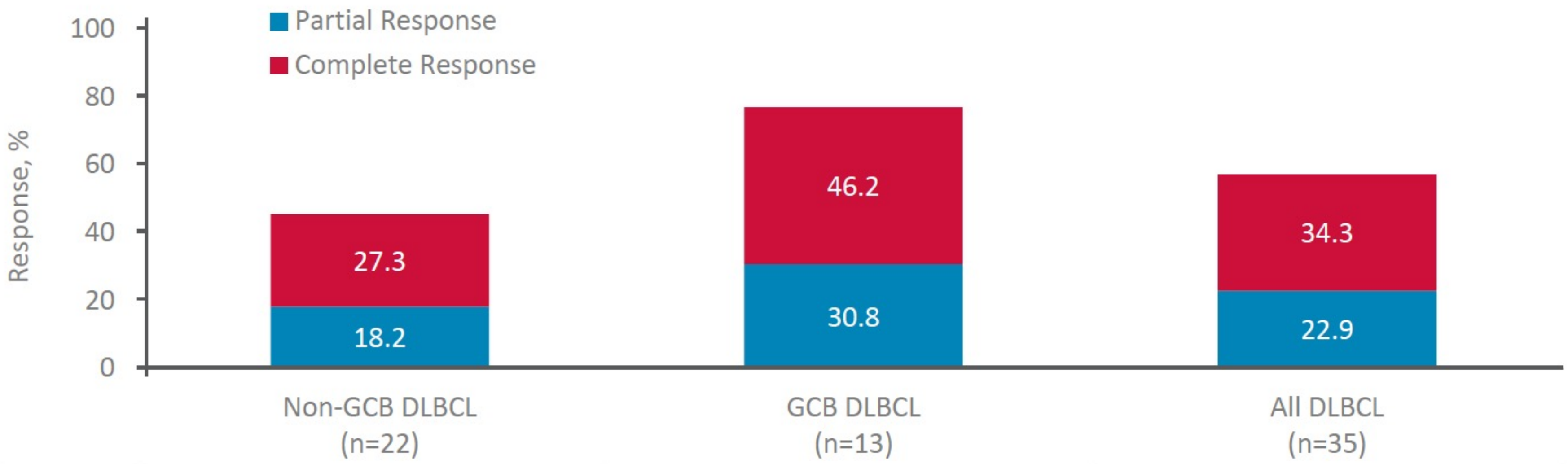
Oral Presentation, 63rd ASH Annual Meeting and Exposition, December 11–14, 2021

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

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

Efficacy: Response Rates[a]



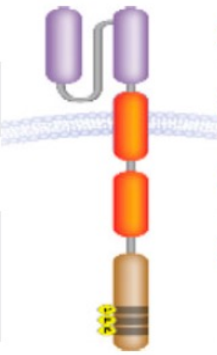
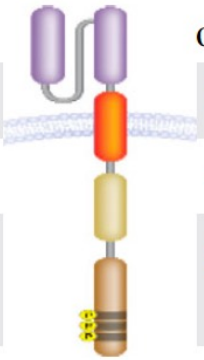
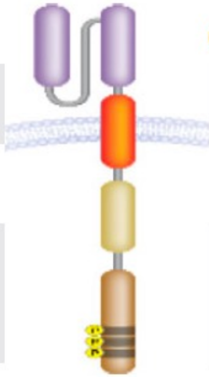
ORR (n/N) (95% CI)[b]	45.5% (10/22) (24.4, 67.8)	76.9% (10/13) (46.2, 95.0)	57.1% (20/35) (39.4, 73.7)

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.

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	α CD19	α CD19	α CD19
Transmembrane domain	CD28	CD28	CD28
Co-stimulatory doman	CD28	4-1BB	4-1BB
T-cell activation domain	CD3ζ	CD3ζ	CD3ζ
			
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

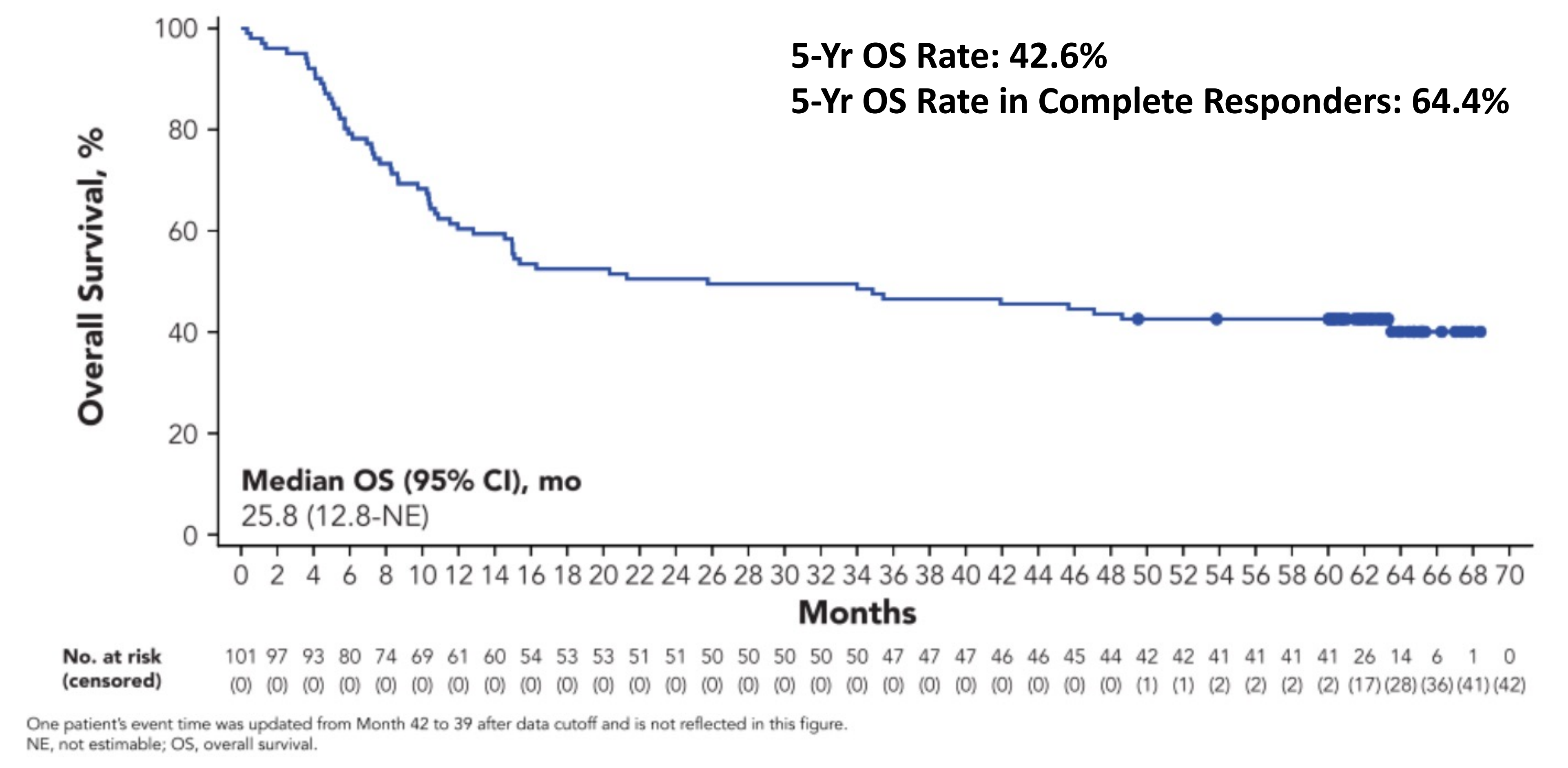
Westin JR et al. *Am J Hematol* 2021;[Online ahead of print].

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



- 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.

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

The NEW ENGLAND JOURNAL of MEDICINE

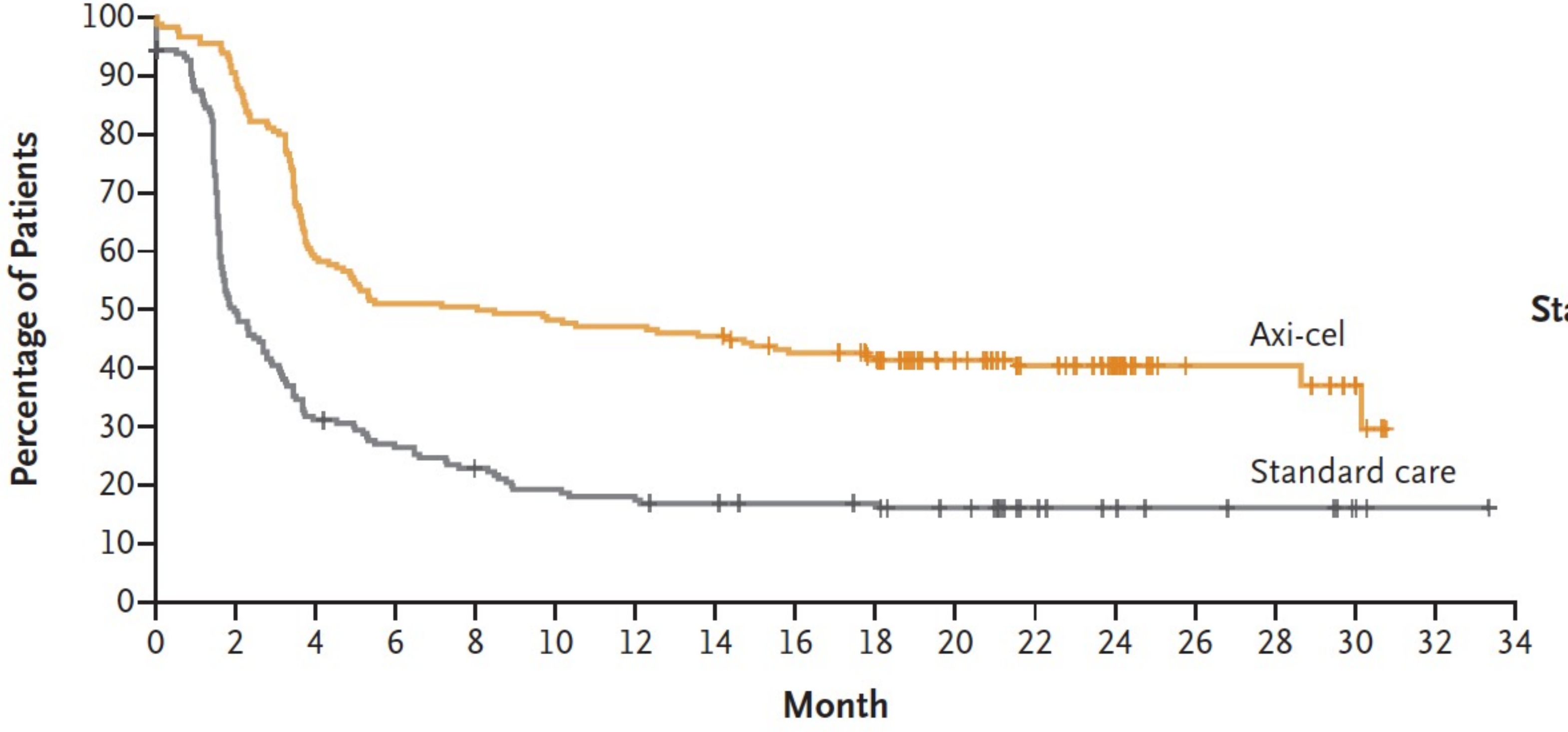
ORIGINAL ARTICLE

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



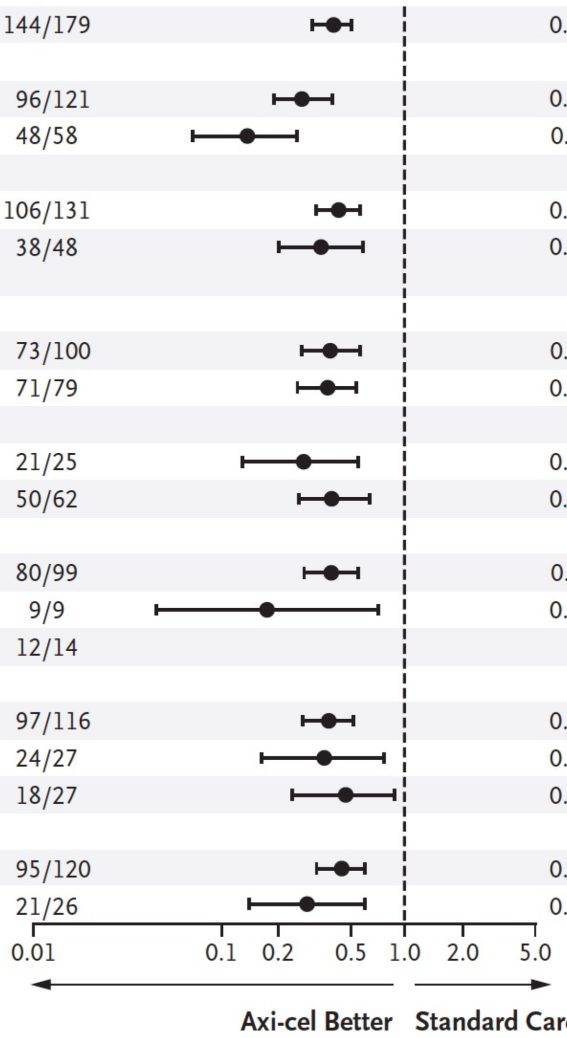
	No. of Patients	Median Event-free Survival (95% CI)
		mo
Axi-cel	180	8.3 (4.5–15.8)
Standard Care	179	2.0 (1.6–2.8)

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].

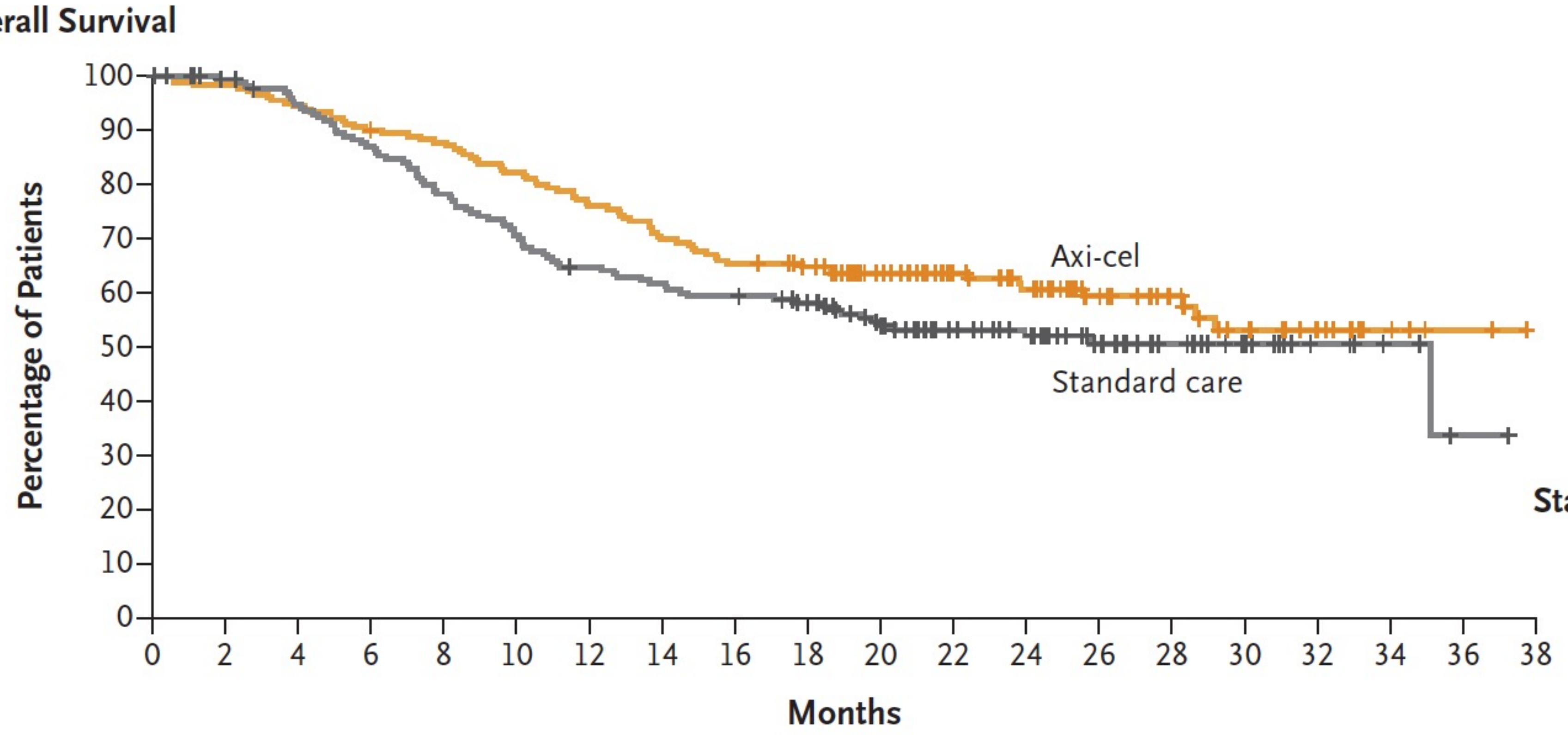
ZUMA-7: Event-Free Survival Subgroup Analysis

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



	No. of Patients	Median Overall Survival (95% CI)
		mo
Axi-cel	180	NR (28.3–NE)
Standard Care	179	35.1 (18.5–NE)

Stratified hazard ratio for death, 0.73 (95% CI, 0.53–1.01)

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

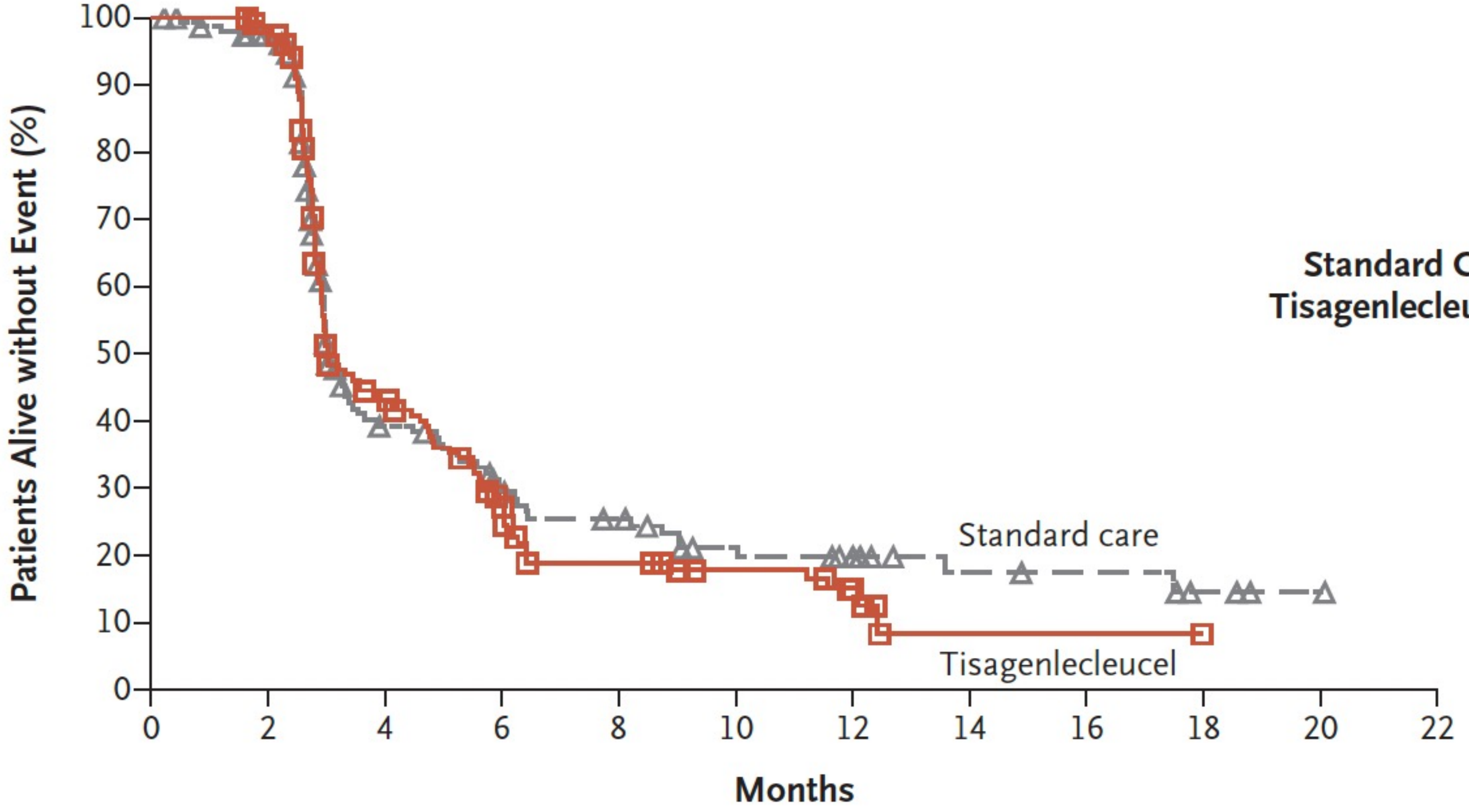
ORIGINAL ARTICLE

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].

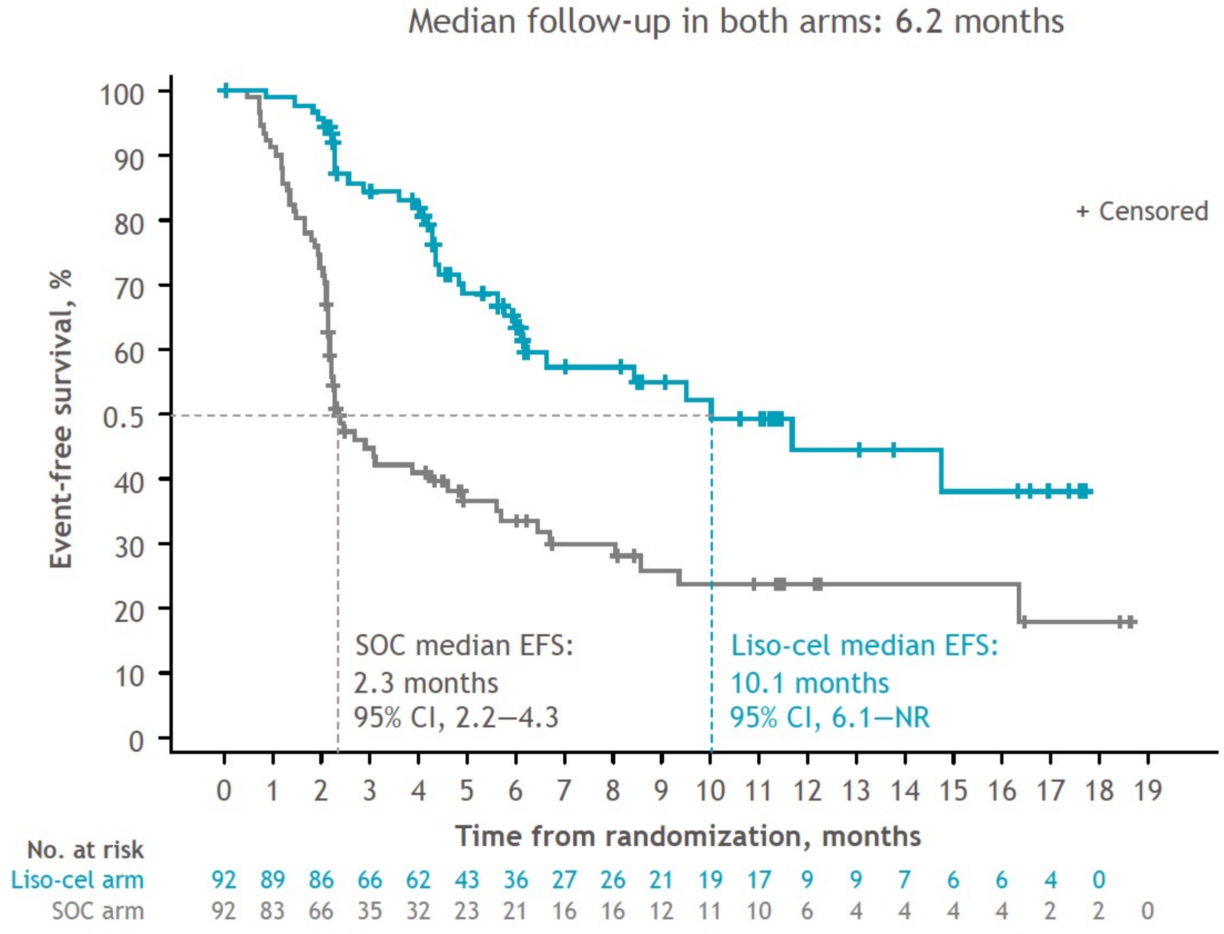
Lisocabtagene Maraleucel, a CD19-Directed Chimeric Antigen Receptor T Cell Therapy, Versus Standard of Care with Salvage Chemotherapy Followed by Autologous Stem Cell Transplantation as Second-Line Treatment in Patients with Relapsed or Refractory Large B-Cell Lymphoma: Results from the Randomized Phase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

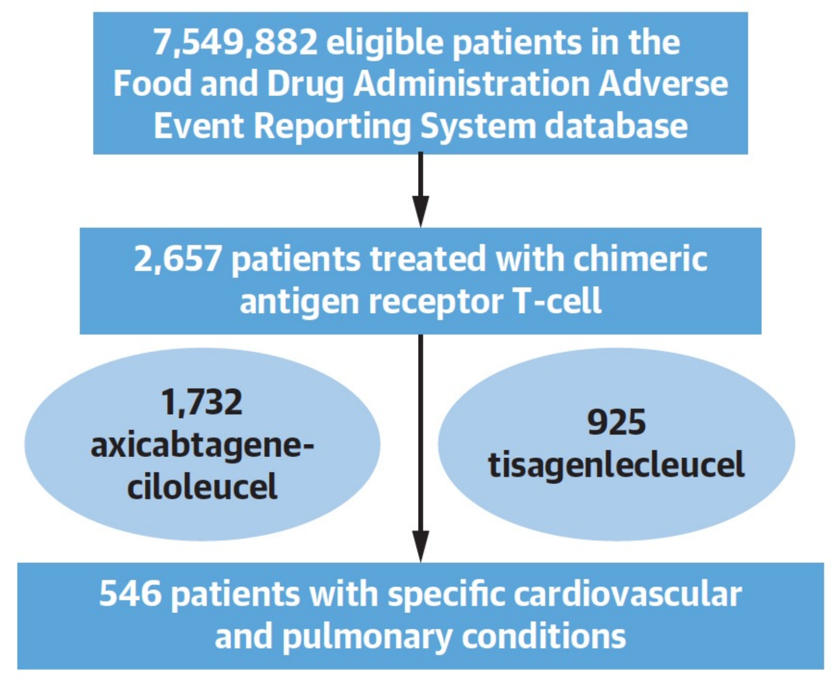
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 78, NO. 18, 2021

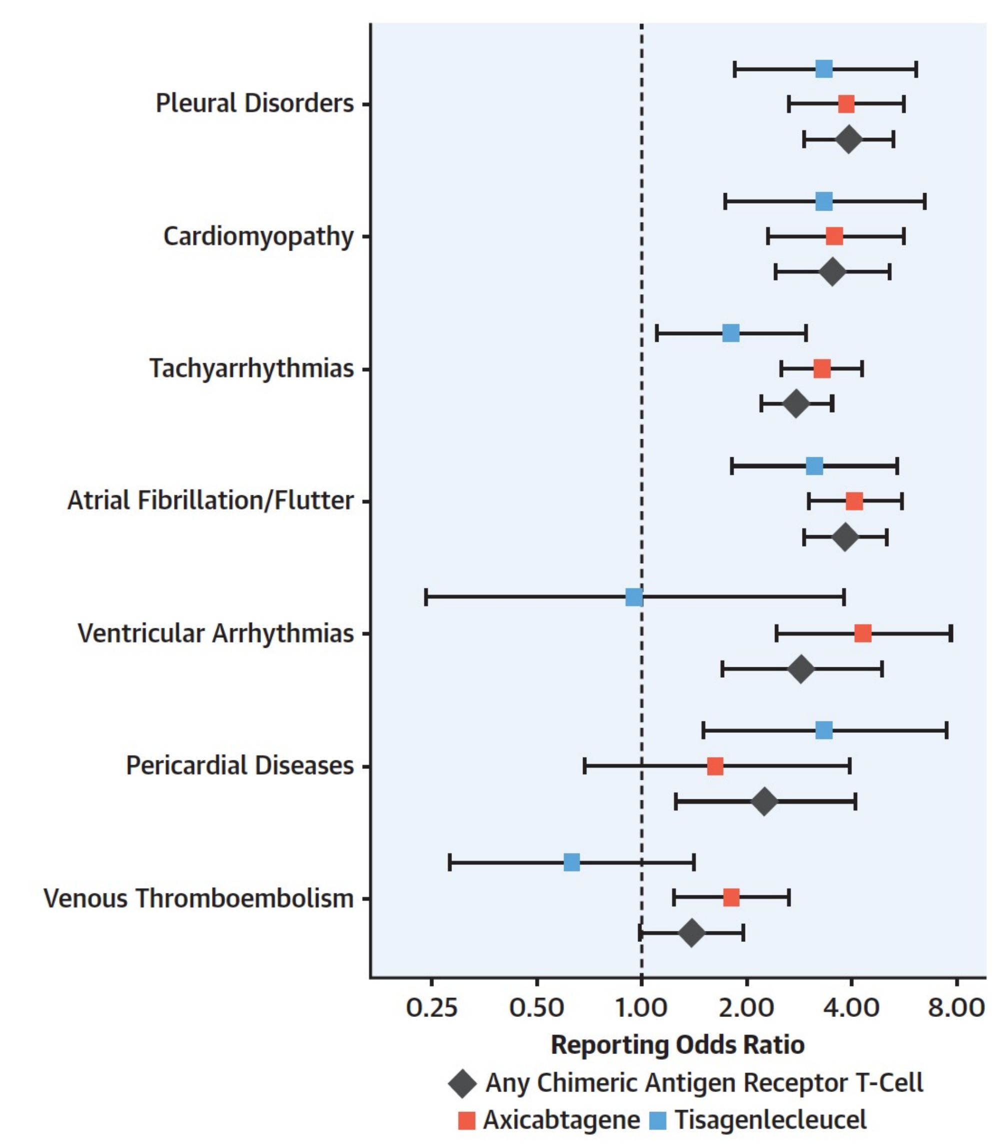
PUBLISHED BY ELSEVIER

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.

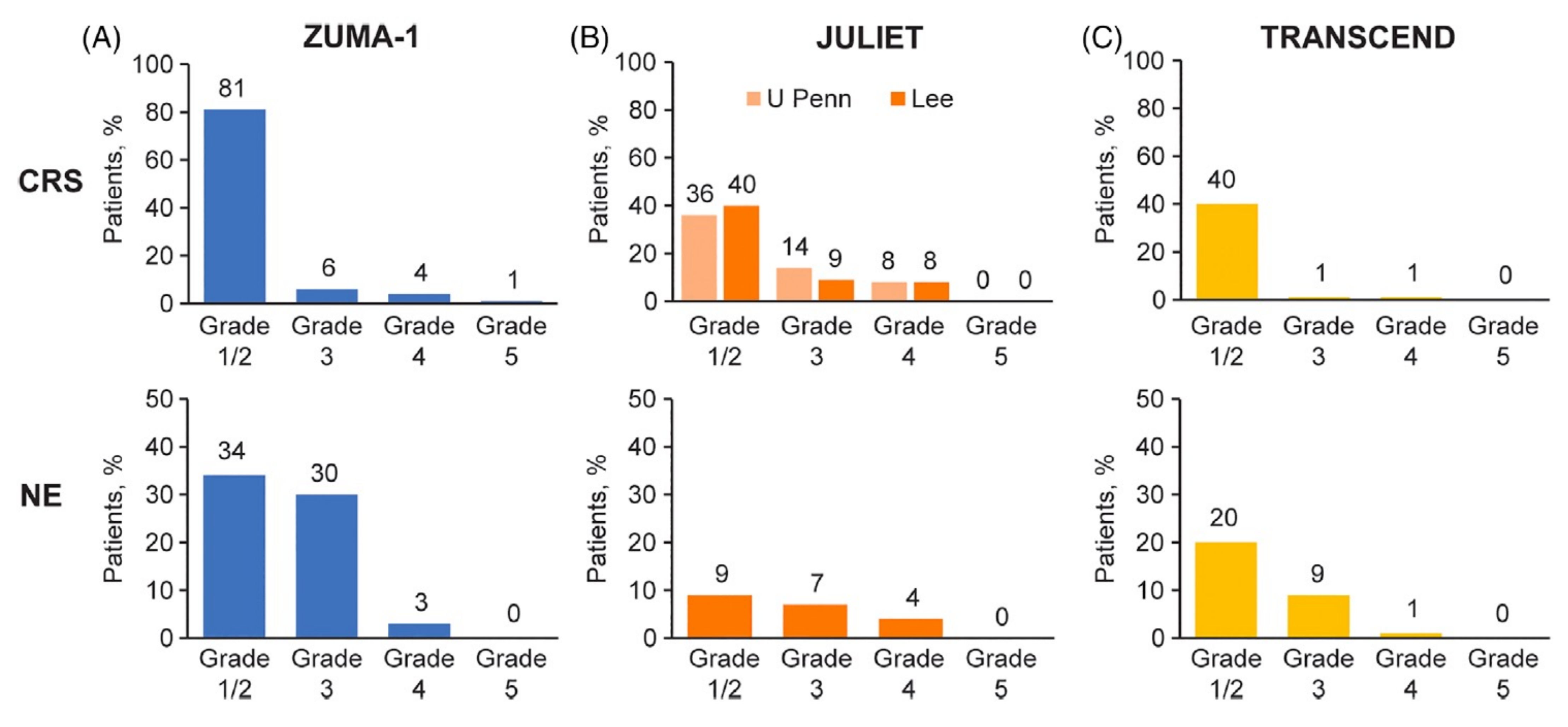
Summary of Efficacy Outcomes in Pivotal Studies of CAR T-Cell Therapy for DLBCL

	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].

RTP RESEARCH TO PRACTICE

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].

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)

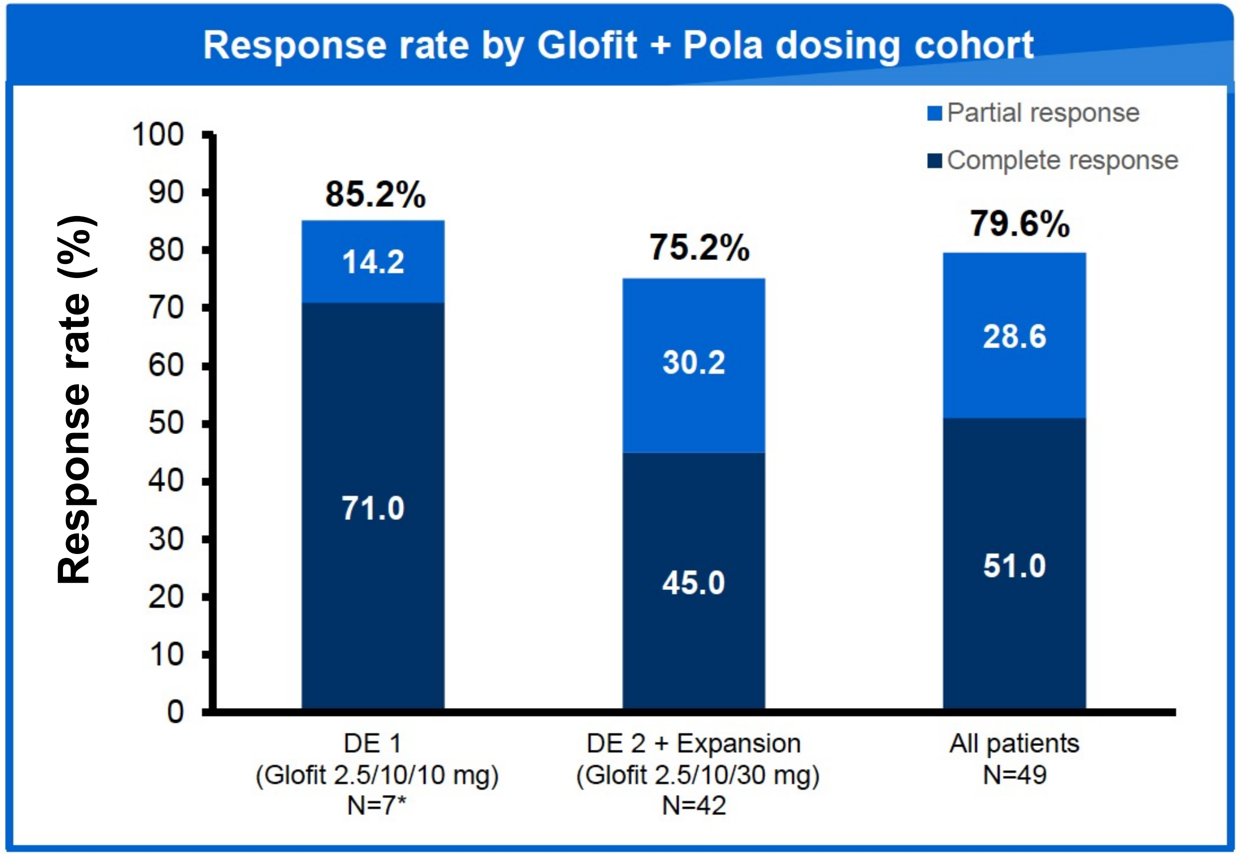
Martin Hutchings,[1] Anna Sureda,[2] Maria Jose Terol,[3] Francesc Bosch,[4] Paolo Corradini,[5] Thomas Stauffer Larsen,[6] Antonio Rueda Dominguez,[7] Anesh Panchal,[8] Alessia Bottos,[9] Yanjie Wang,[10] Audrey Filézac de L'Etang,[9] Maneesh Tandon,[8] Gila Sellam,[9] Giuseppe Gritti[11]

[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.

Hodgkin Lymphoma

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

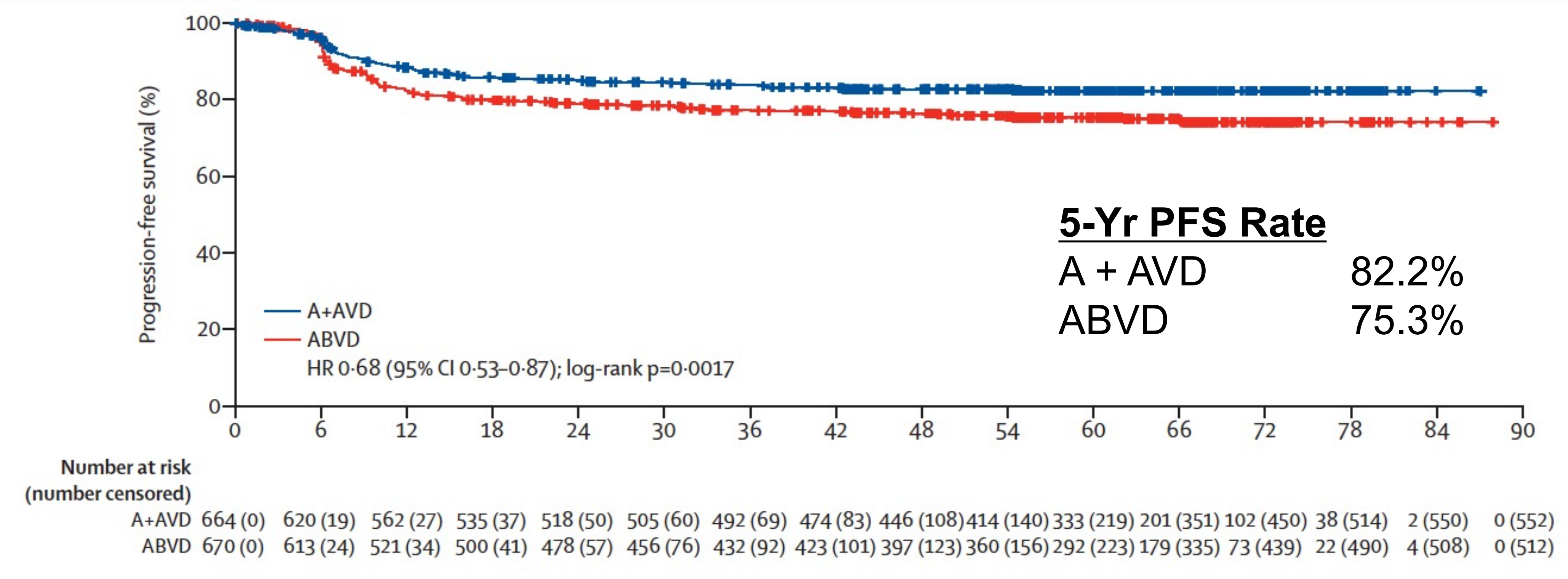
Articles

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

RTP
RESEARCH TO PRACTICE

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.

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].

RTP RESEARCH TO PRACTICE

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.

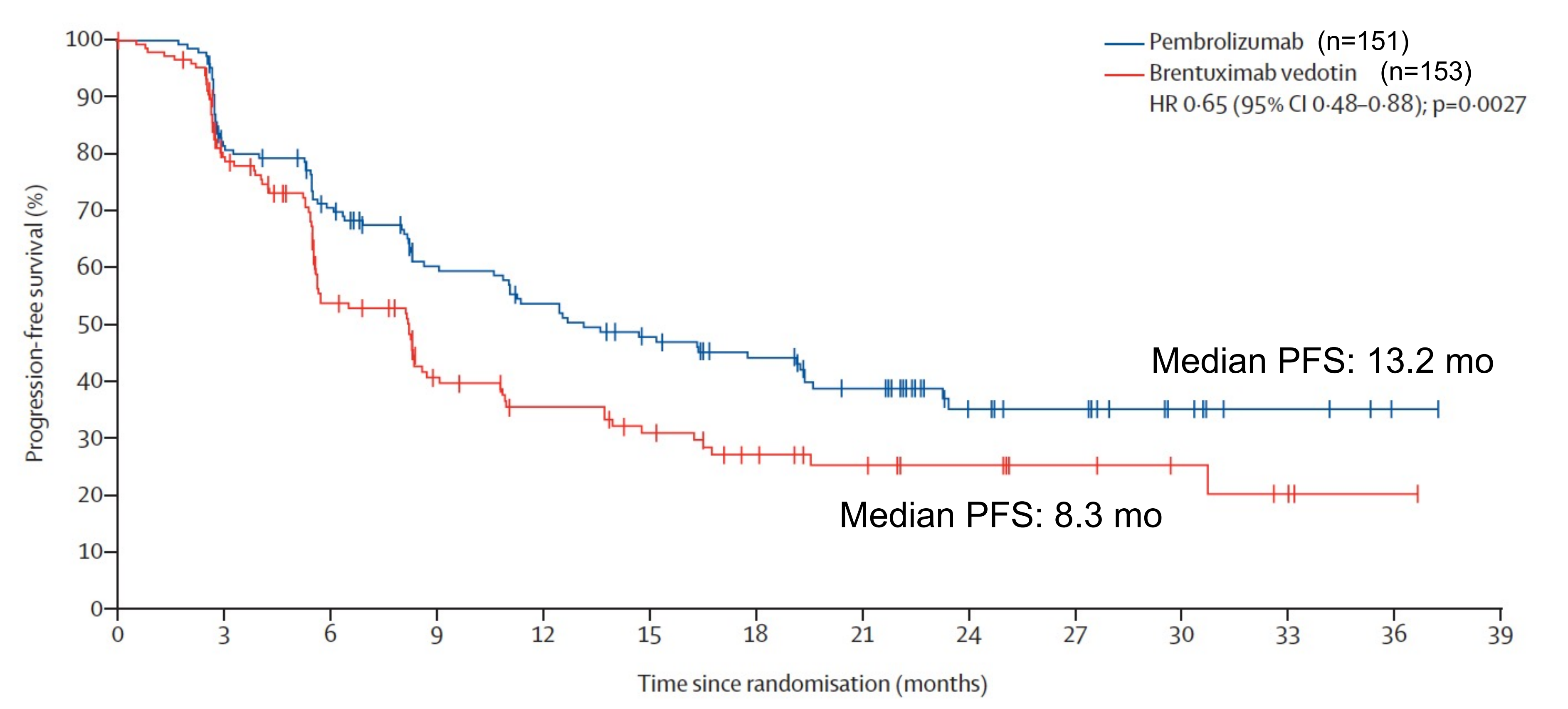
CrossMark

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**

RTP RESEARCH TO PRACTICE

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.

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

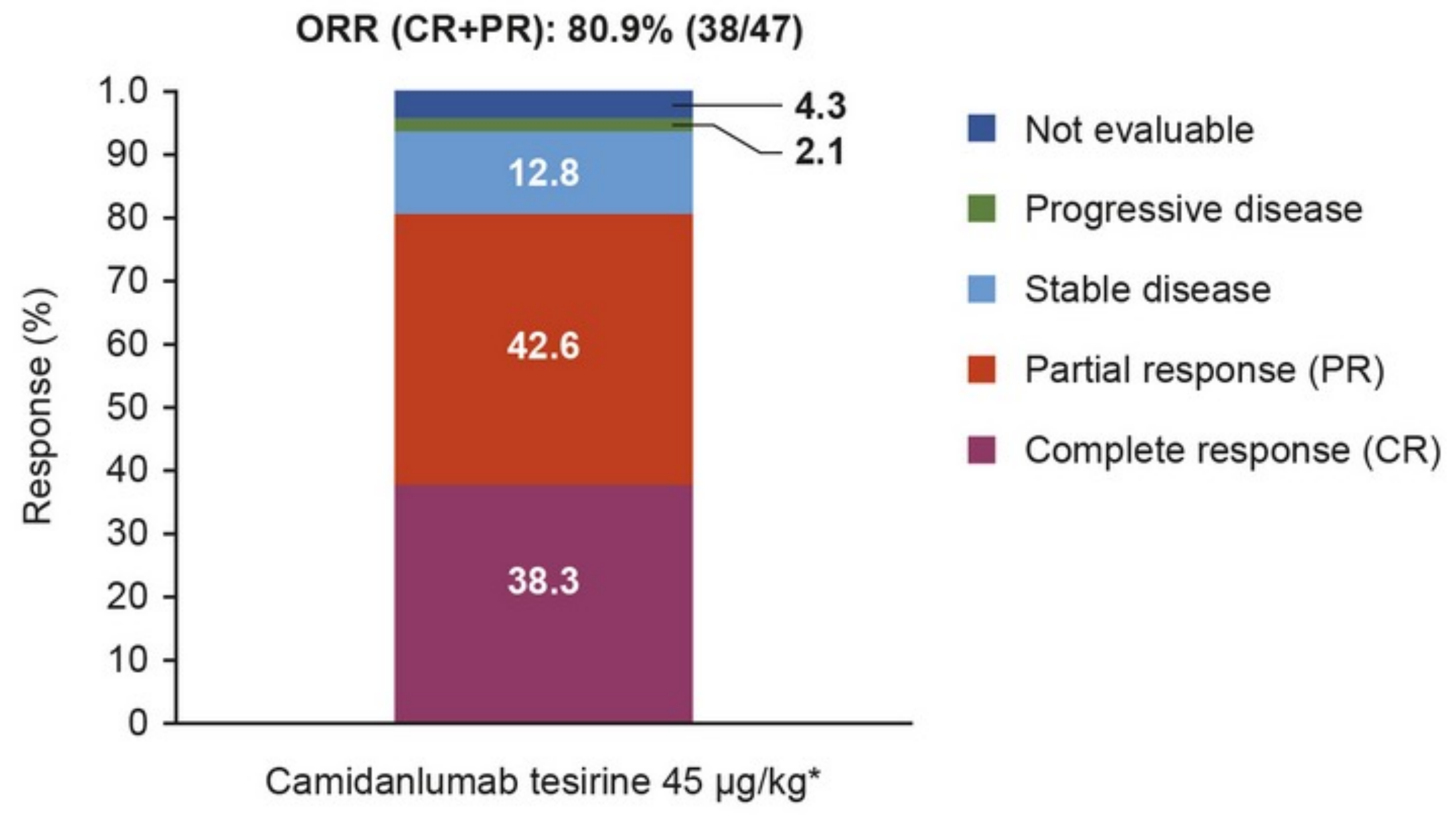
Ramos CA et al. *J Clin Oncol* 2020;38(32):3794-804.

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



*45 µg/kg for 2 cycles, then 30 µg/kg for subsequent cycles.
ORR, overall response rate.

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

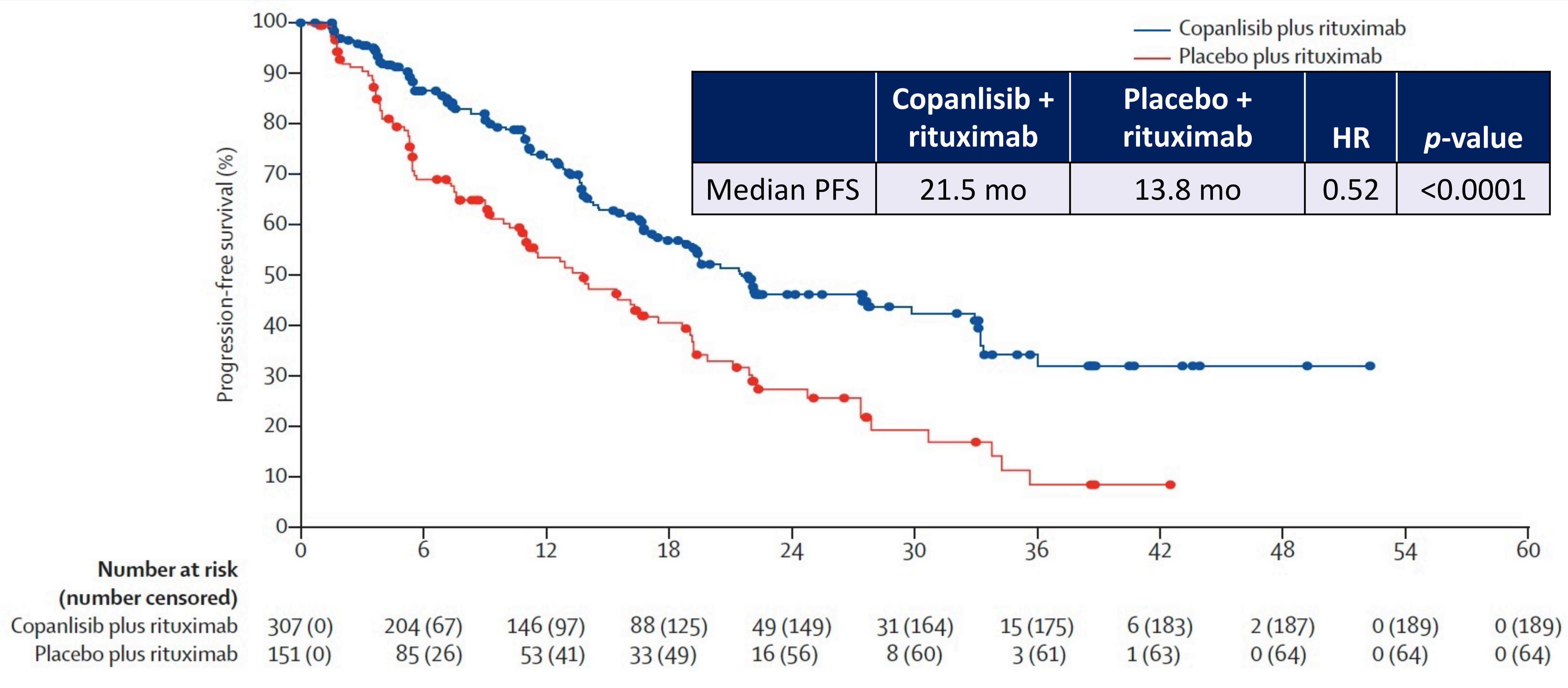
[1] Gopal AK et al. *N Engl J Med* 2014;370(11):1008-18; Idelalisib package insert, January 2018.
[2] Dreyling M et al. *J Clin Oncol* 2017;35(35):3898-905; Copanlisib package insert, September 2017.
[3] Flinn IW et al. *J Clin Oncol* 2019;[Epub ahead of print]; Zinzani PL et al. EHA 2017;Abstract S777;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

RTP
RESEARCH
TO PRACTICE

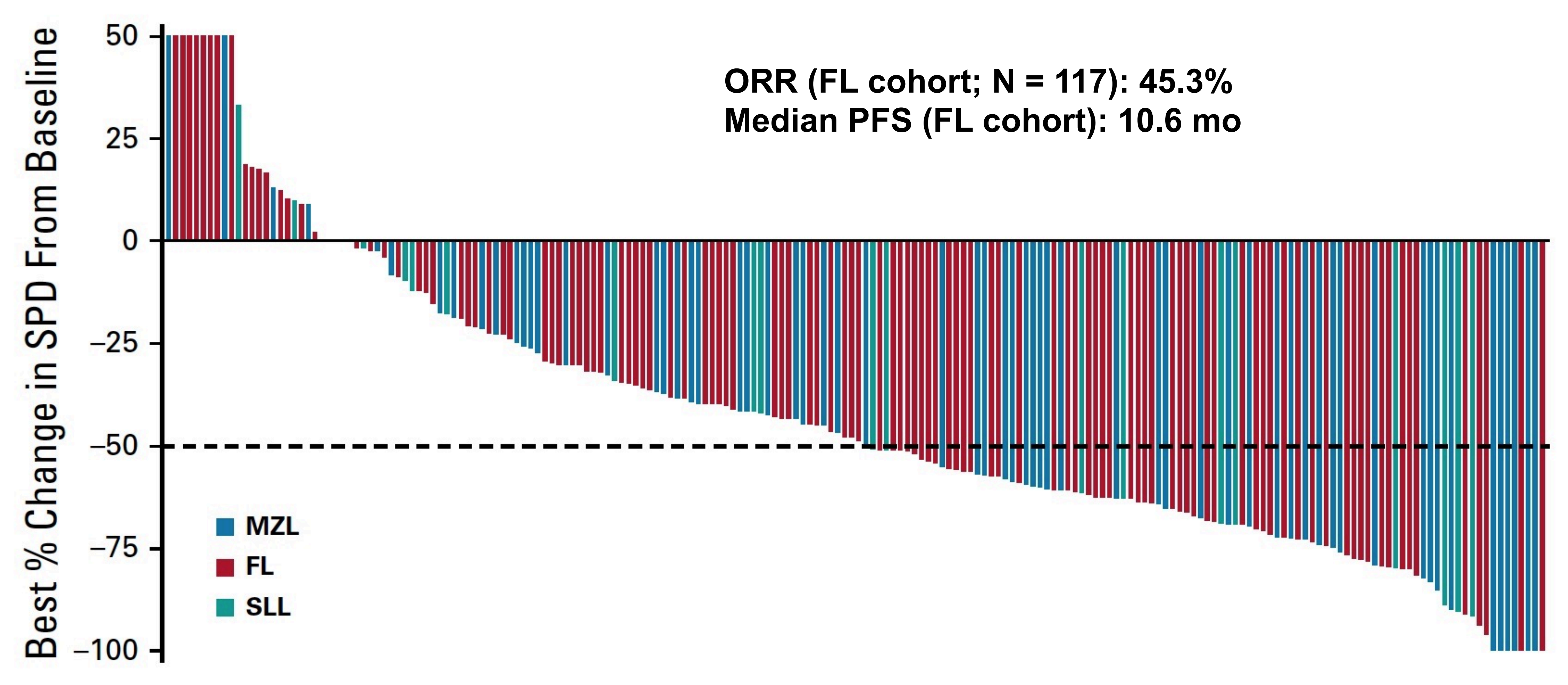
rapid communications

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.

Lancet Oncol 2020;21:1433-42

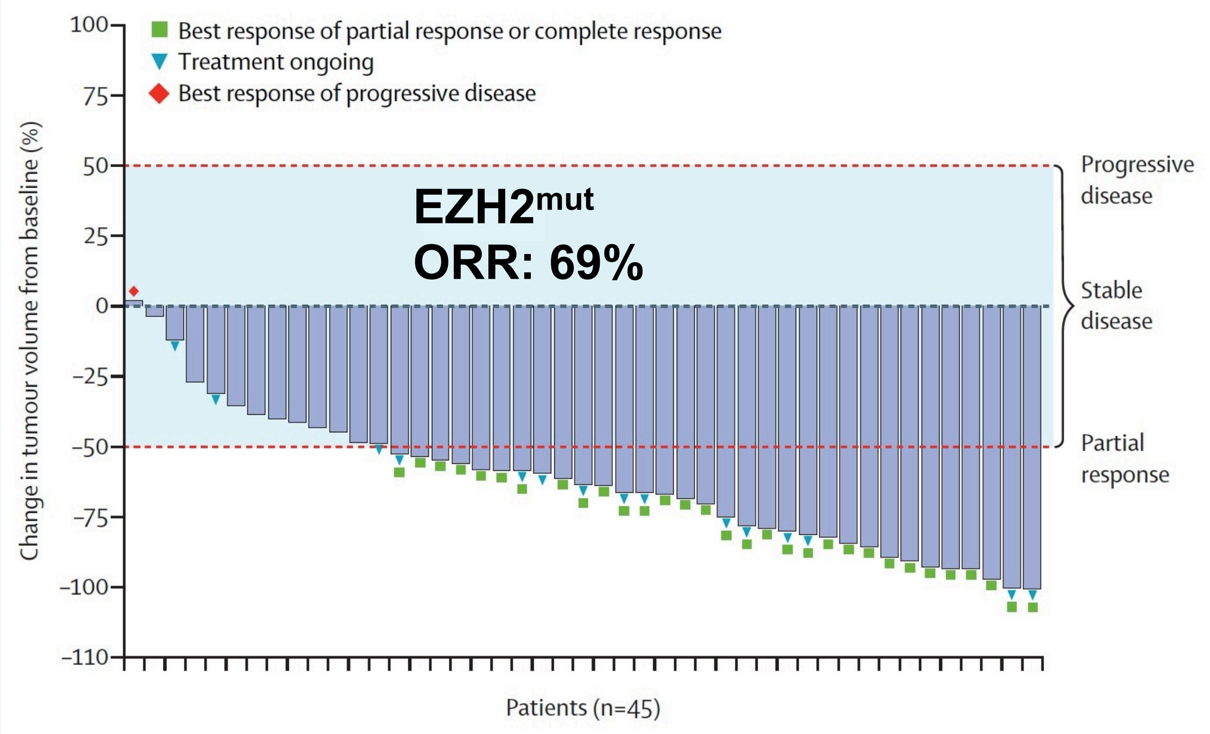
Tazemetostat for patients with relapsed or refractory follicular lymphoma: an open-label, single-arm, multicentre, phase 2 trial

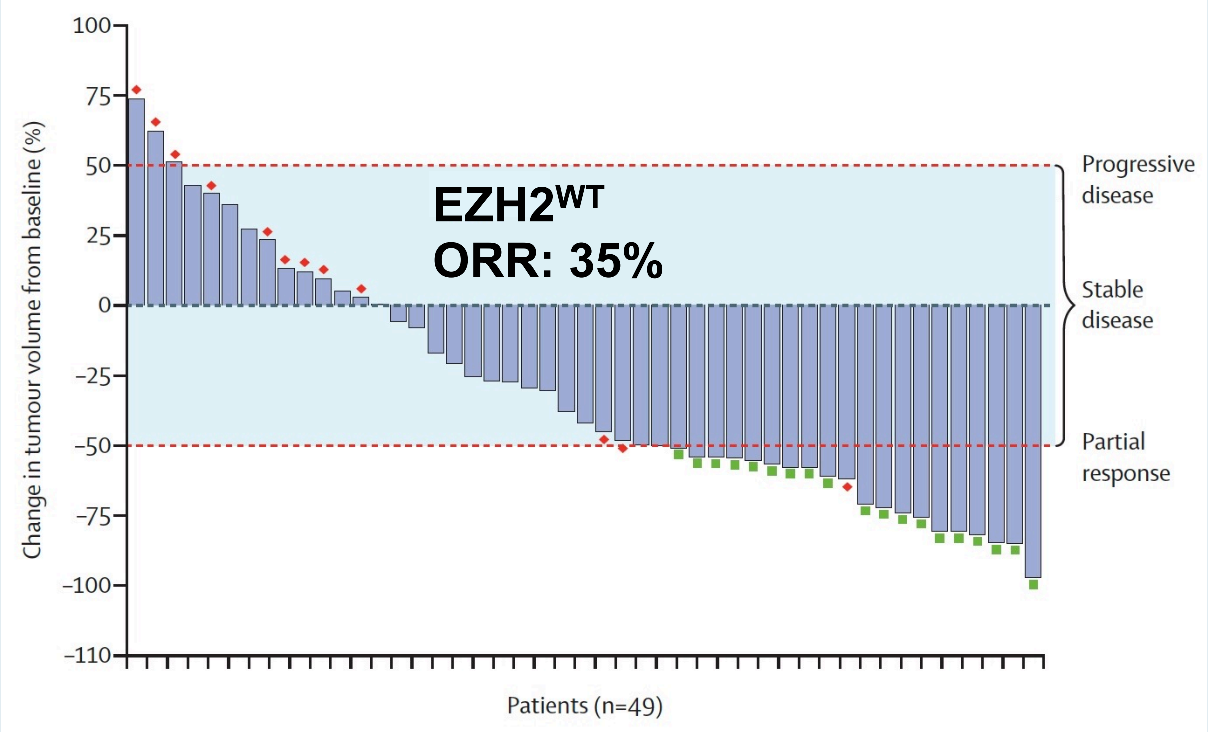
Franck Morschhauser, Hervé Tilly, Aristeidis Chaidos, Pamela McKay, Tycel Phillips, Sarit Assouline, Connie Lee Batlevi, Phillip Campbell, Vincent Ribrag, Gandhi Laurent Damaj, Michael Dickinson, Wojciech Jurczak, Maciej Kazmierczak, Stephen Opat, John Radford, Anna Schmitt, Jay Yang, Jennifer Whalen,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

CrossMark

RTP RESEARCH TO PRACTICE

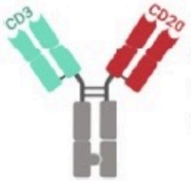
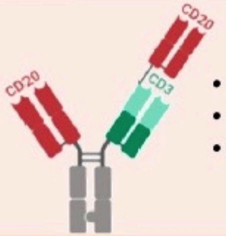
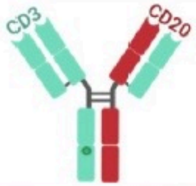
Response to Tazemetostat in Patients with R/R FL and EZH2-Mutated or EZH2 Wild-Type Tumors





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

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

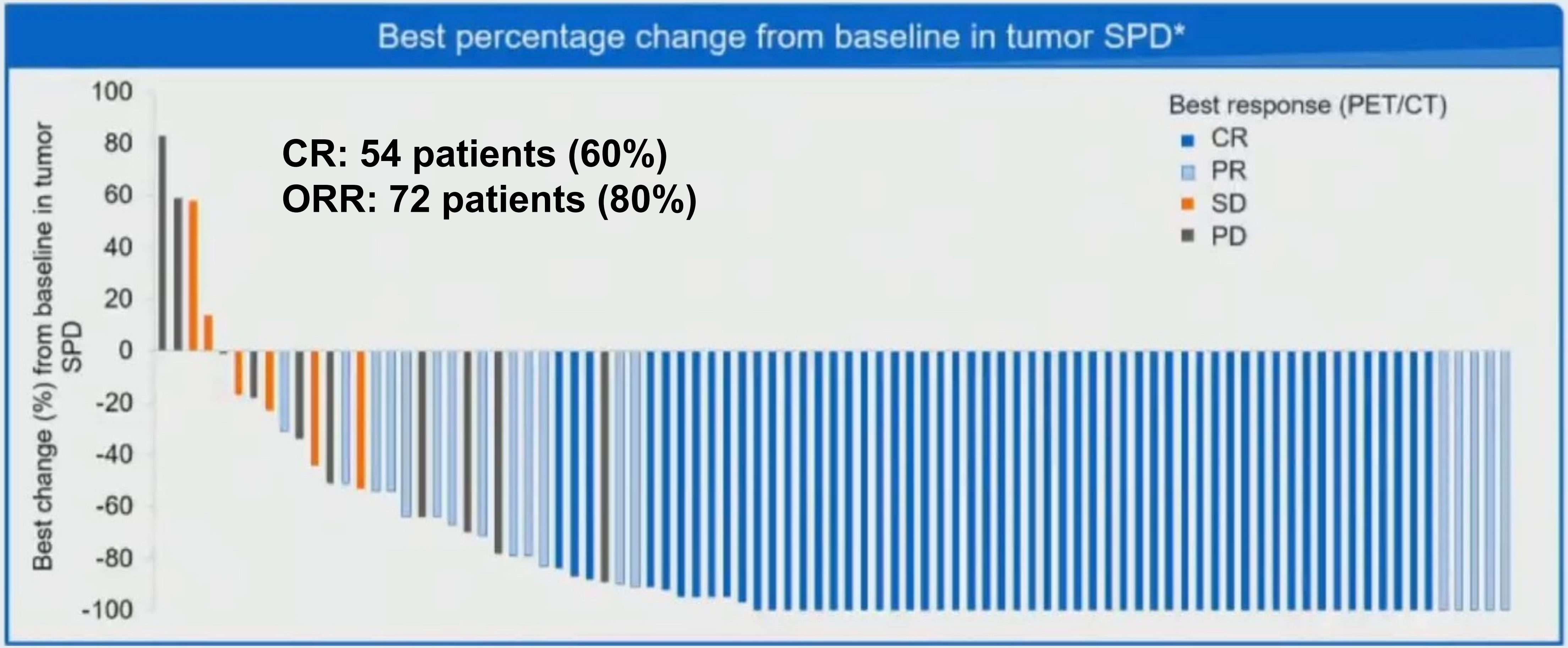
Accepted as an Oral Presentation at the 63rd ASH Annual Meeting and Exposition

63rd ASH® Annual Meeting and Exposition

ASH 2021;Abstract 127.

RTP RESEARCH TO PRACTICE

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



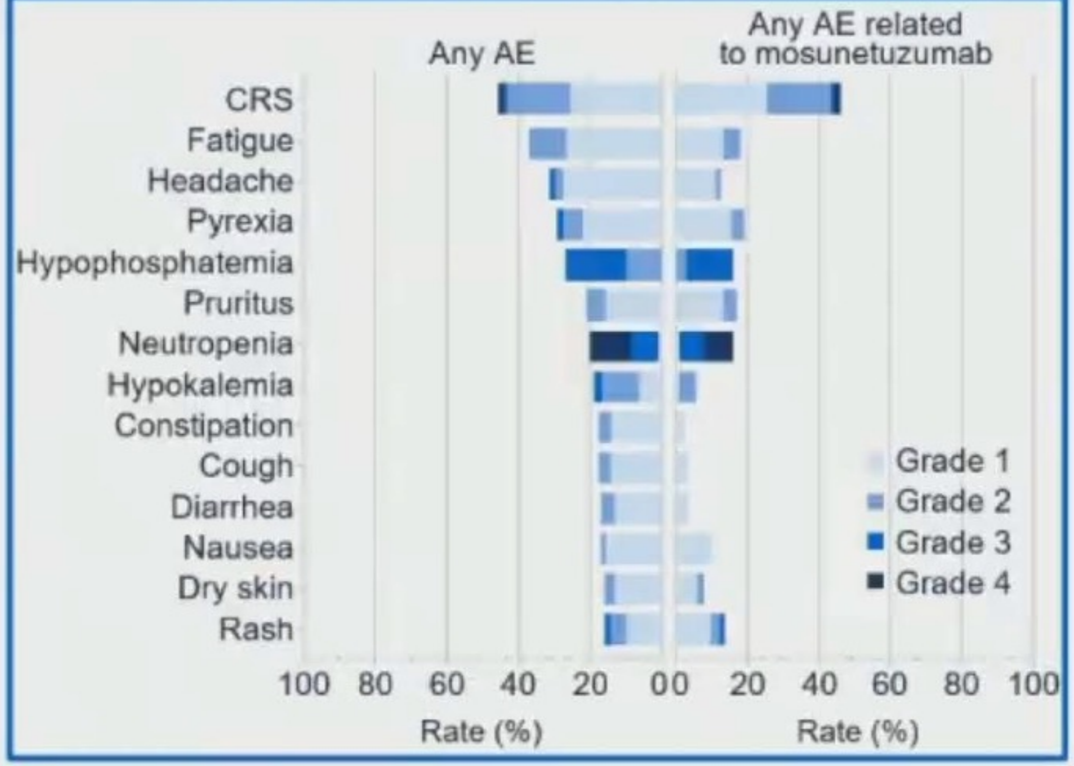
- Median DoR: 22.8 months
- Median PFS: 17.9 months

Budde EL et al. ASH 2021;Abstract 127.

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%)‡

AEs (≥15%) by Gr and relationship with mosunetuzumab



*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.

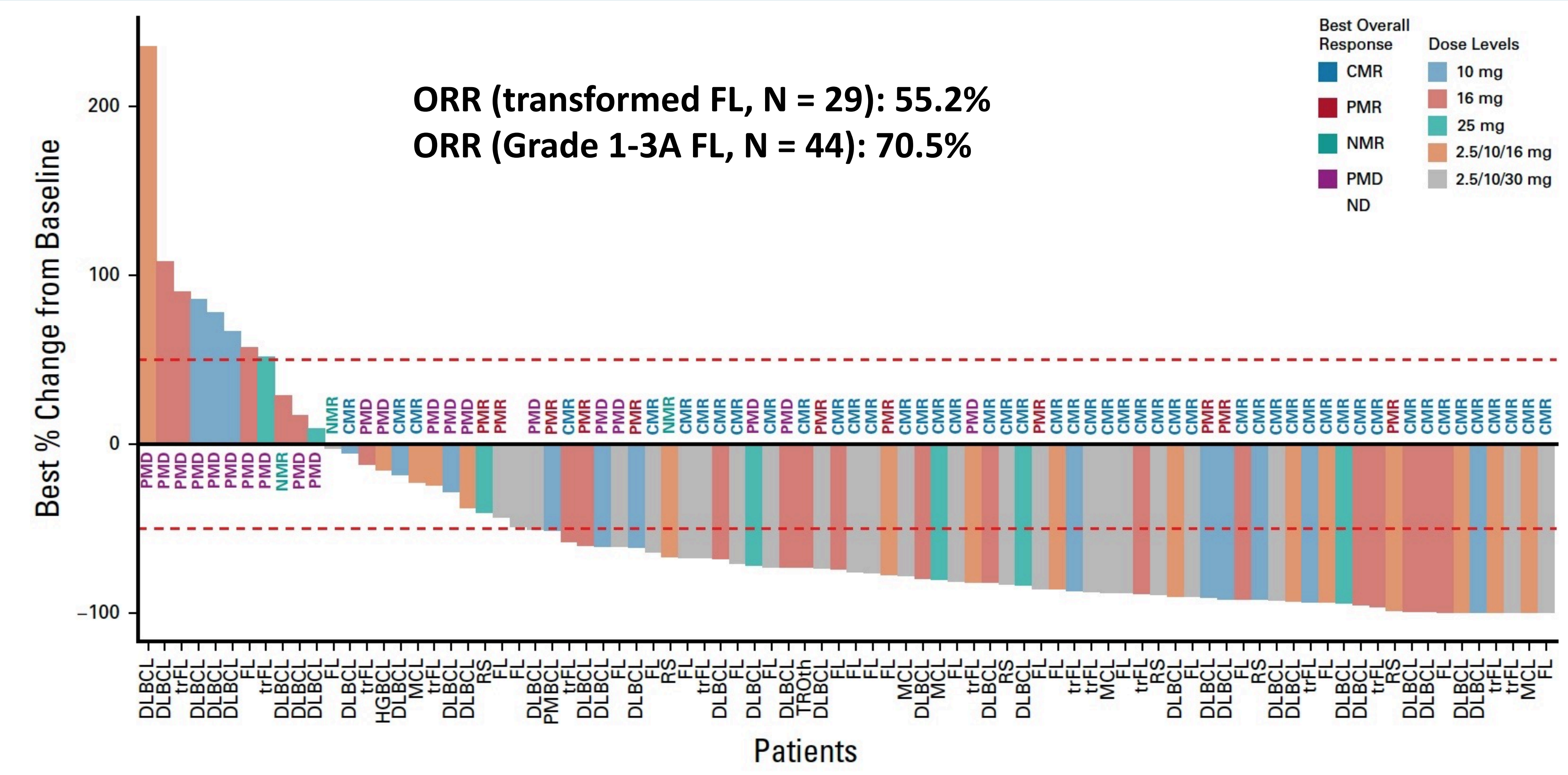
rapid communications

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.

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



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

128

Glofitamab as Monotherapy and in Combination with Obinutuzumab Induces High Complete Response Rates in Patients with Multiple Relapsed or Refractory (R/R) Follicular Lymphoma (FL)

Franck Morschhauser,[1] Carmelo Carlo-Stella,[2] Michael Dickinson,[3] Tycel Phillips,[4] Roch Houot,[5] Fritz Offner,[6] Corinne Haioun,[7] Paolo Corradini,[8] Martin Hutchings,[9] Anna Sureda,[10] Joaquin Martinez-Lopez,[11] Tomasz Wróbel,[12] Shang-Ju Wu,[13] Linda Lundberg,[14] Estefania Mulvihill,[14] David Perez-Callejo,[14] James Relf,[15] Anesh Panchal,[15] Kathryn Humphrey,[15] Emmanuel Bachy[16]

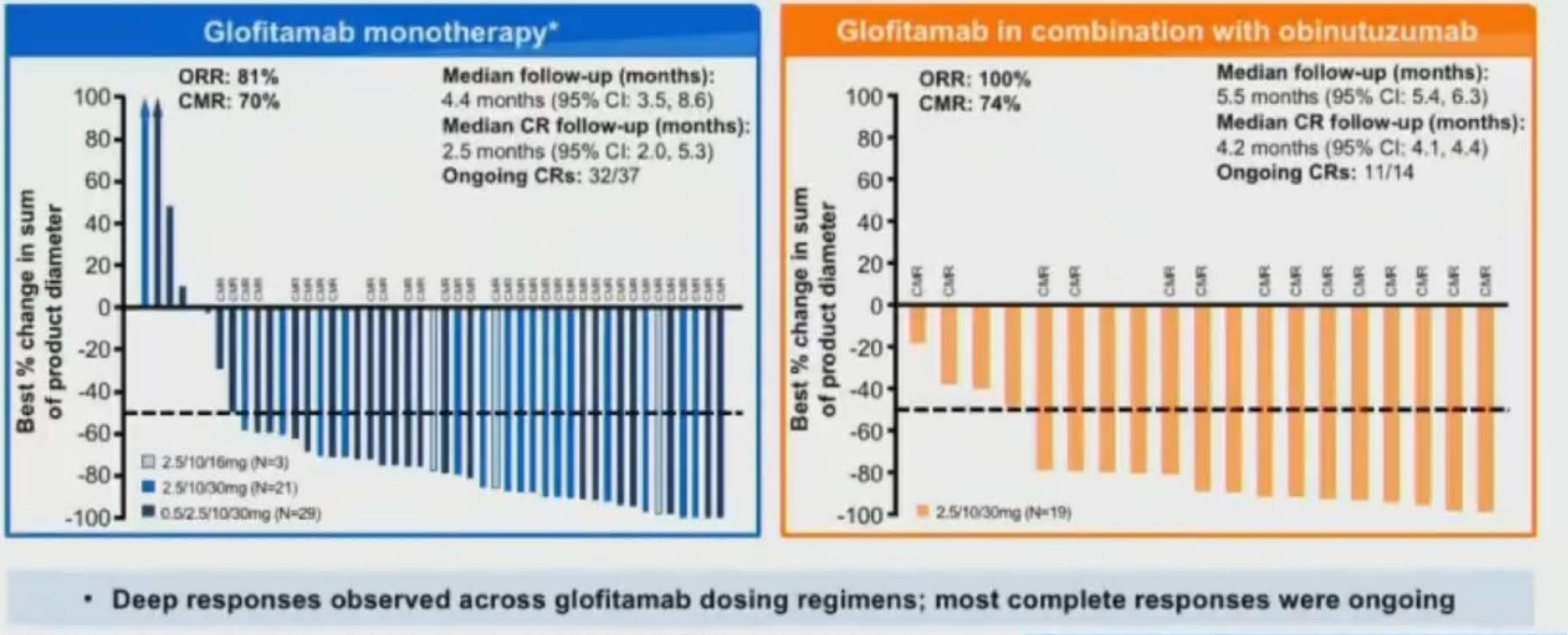
[1]CHU Lille, Service des Maladies du Sang, F-59000 Lille, France; [2]Humanitas University and Humanitas Research Hospital, Milan, Italy; [3]Peter MacCallum Cancer Centre, Royal Melbourne Hospital and The University of Melbourne, Melbourne, Australia; [4]University of Michigan Medical School, Ann Arbor, Michigan, USA; [5]CHU de Rennes, Université de Rennes, INSERM U1236, EFS, Rennes, France; [6]Universitair Ziekenhuis Gent, Ghent, Belgium; [7]Hôpital Henri Mondor, AP-HP, Créteil, France; [8]University of Milan; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [9]Rigshospitalet, Copenhagen, Denmark; [10]Institut Català d'Oncologia Hospitalet, IDIBELL, Universitat de Barcelona, Barcelona, Spain; [11]Hospital Universitario 12 de Octubre (H12O), Centro Nacional de Investigaciones Oncológicas (CNIO)-H12O and Universidad Complutense de Madrid, Madrid, Spain; [12]Wroclaw Medical University, Wroclaw, Poland; [13]National Taiwan University Hospital, Taipei, Taiwan; [14]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [15]Roche Products Ltd, Welwyn Garden City, United Kingdom; [16]Hospices Civils de Lyon and Université Claude Bernard, Pierre-Bénite, France.

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

63rd ASH® Annual Meeting and Exposition

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.

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

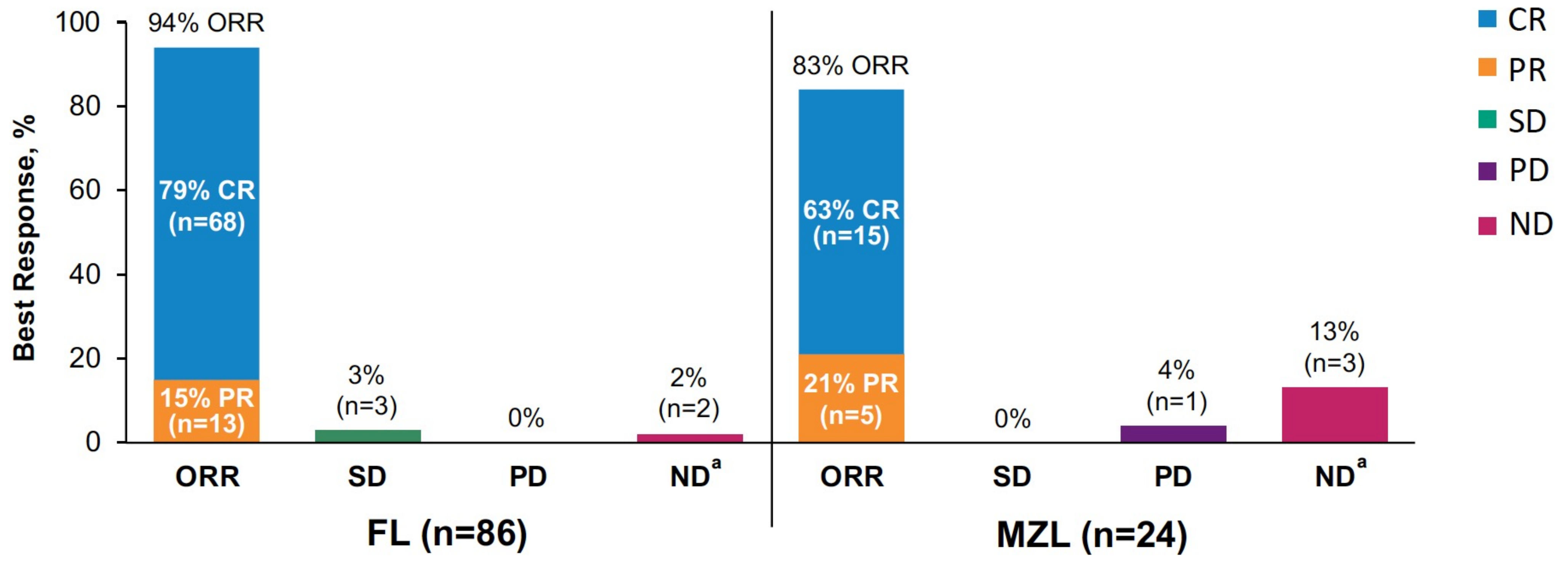
Sattva S. Neelapu, MD[1]*; Julio C. Chavez, MD[2]*; Alison R. Sehgal, MD[3]; Narendranath Epperla, MD, MS[4]; Matthew Ulrickson, MD[5]; Emmanuel Bachy, MD, PhD[6]; Pashna N. Munshi, MD[7]; Carla Casulo, MD[8]; David G. Maloney, MD, PhD[9]; Sven de Vos, MD, PhD[10]; Ran Reshef, MD[11]; Lori A. Leslie, 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.

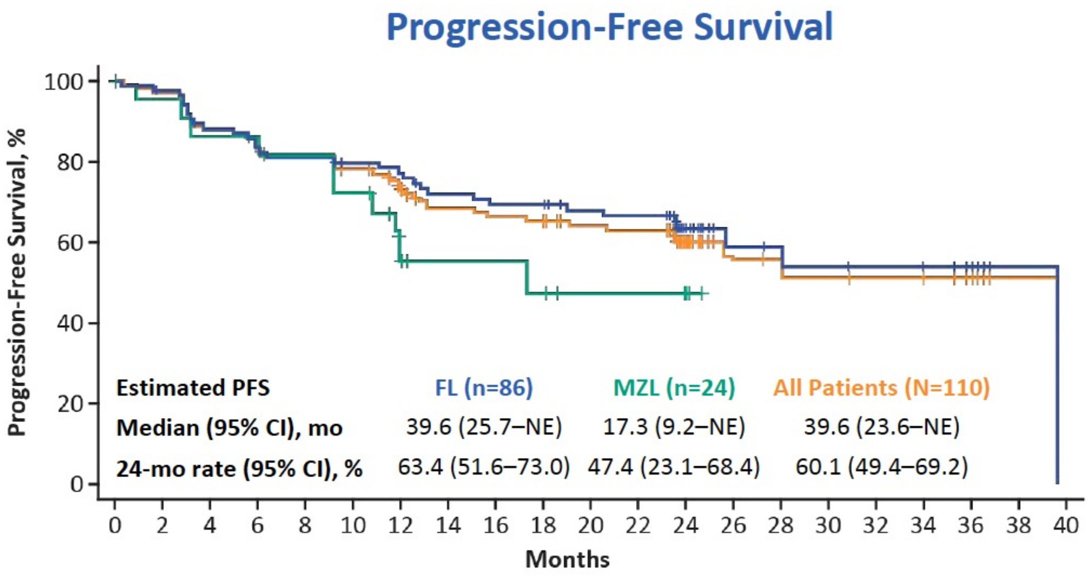
ZUMA-5: ORR by Central Review



- 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

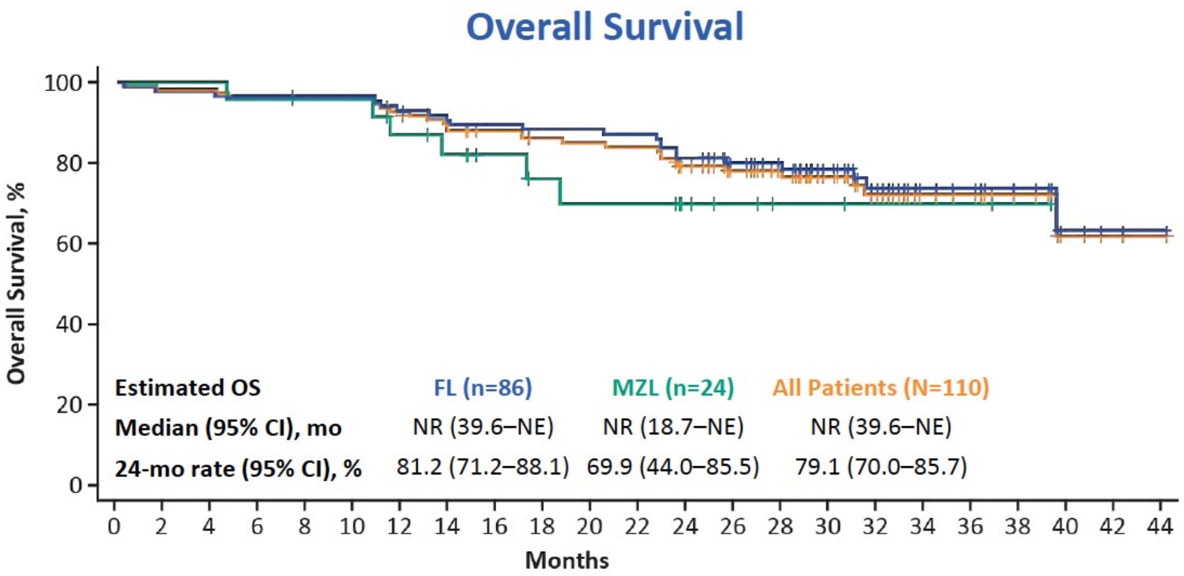
Neelapu SS et al. ASH 2021;Abstract 93.

ZUMA-5: Progression-Free and Overall Survival



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



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

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]

[1]Department of Hemato-Oncology, Saint Louis Hospital, Paris, France; [2]Department of Clinical Haematology, Peter MacCallum Cancer Centre and The Royal Melbourne Hospital, Melbourne, Australia; [3]Centro de Investigación Biomédica en Red Cáncer (CIBERONC), Hospital Universitario 12 de Octubre, Complutense University, CNIO, Madrid, Spain; [4]Oslo University Hospital Radiumhospitalet, Oslo, Norway; [5]Royal Brisbane and Women's Hospital, Brisbane, Australia; [6]Michigan Medicine University of Michigan, Ann Arbor, MI, USA; [7]Department of Hematology/HCT, City of Hope National Medical Centre, Duarte, CA, USA; [8]Division of Malignant Hematology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [9]Hospices Civils de Lyon and Université Claude Bernard, Pierre-Bénite, France; [10]Kyushu University Hospital, Fukuoka, Japan; [11]Tohoku University Hospital, Sendai, Japan; [12]Amsterdam UMC, Department of Hematology, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands; [13]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, San Francisco, CA, USA; [14]The University of Chicago Medical Center, Chicago, IL, USA; [15]Royal Prince Alfred Hospital and Department of Medicine, The University of Sydney, Sydney, Australia; [16]Department of Hematology, Hospital Universitario Virgen del Rocio, Instituto de Biomedicina de Sevilla (IBIS)/CSIC/Universidad de Sevilla, Spain, Sevilla, Spain; [17]Oregon Health and Science University, Portland, OR, USA; [18]Department of Lymphoma and Myeloma, The University of Texas, MD Anderson Cancer Center, Houston, TX, USA; [19]University of Cologne, Cologne, Germany; [20]Lymphoma Unit, Department of Onco-Haematology, IRCCS San Raffaele Scientific Institute, Milano, Italy; [21]Department of Hematology, Hokkaido University Hospital, Sapporo, Japan; [22]Department of Haematological Medicine, King's College Hospital, London, UK; [23]Division of Hematologic Malignancies & Cellular Therapeutics, University of Kansas Medical Center, Kansas City, KS, USA; [24]Internal Medicine I, Ordensklinikum Linz GmbH Elisabethinen, Linz, Austria; [25]University Hospital Ghent, Gent, Belgium; [26]Department of Internal Medicine III, University Hospital of Ulm, Ulm, Germany; [27]Institute of Hematology "L. e A. Seràgnoli", University of Bologna, Bologna, Italy; [28]Cambridge University Hospitals NHS Foundation Trust, Cambridge, CA, UK; [29]Novartis Pharma AG, Basel, Switzerland; [30]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [31]Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; [32]Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [33]Klinikum Der Universität München-Grosshadern, Medizinische Klinik und Poliklinik III, München, Germany

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 *BLCL2* 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

Enrollment/leukapheresis → Optional nonchemotherapy bridging therapy[a] →

Conditioning chemotherapy + axi-cel infusion

- Conditioning
  - Flu 30 mg/m^2 i.v. and Cy 500 mg/m^2 i.v. on Days −5, −4, and −3
- Axi-cel
  - Single i.v. infusion of 2×10^6 CAR T cells/kg on Day 0

Primary endpoint

- CR[b]

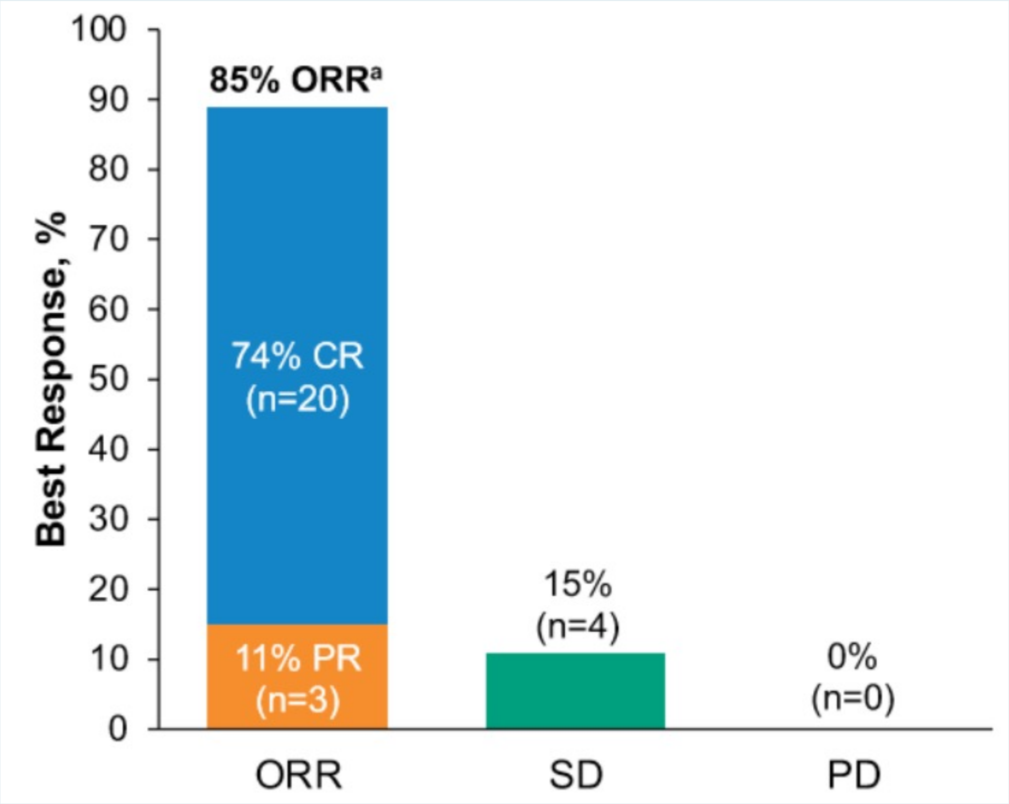
Key secondary endpoints

- 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

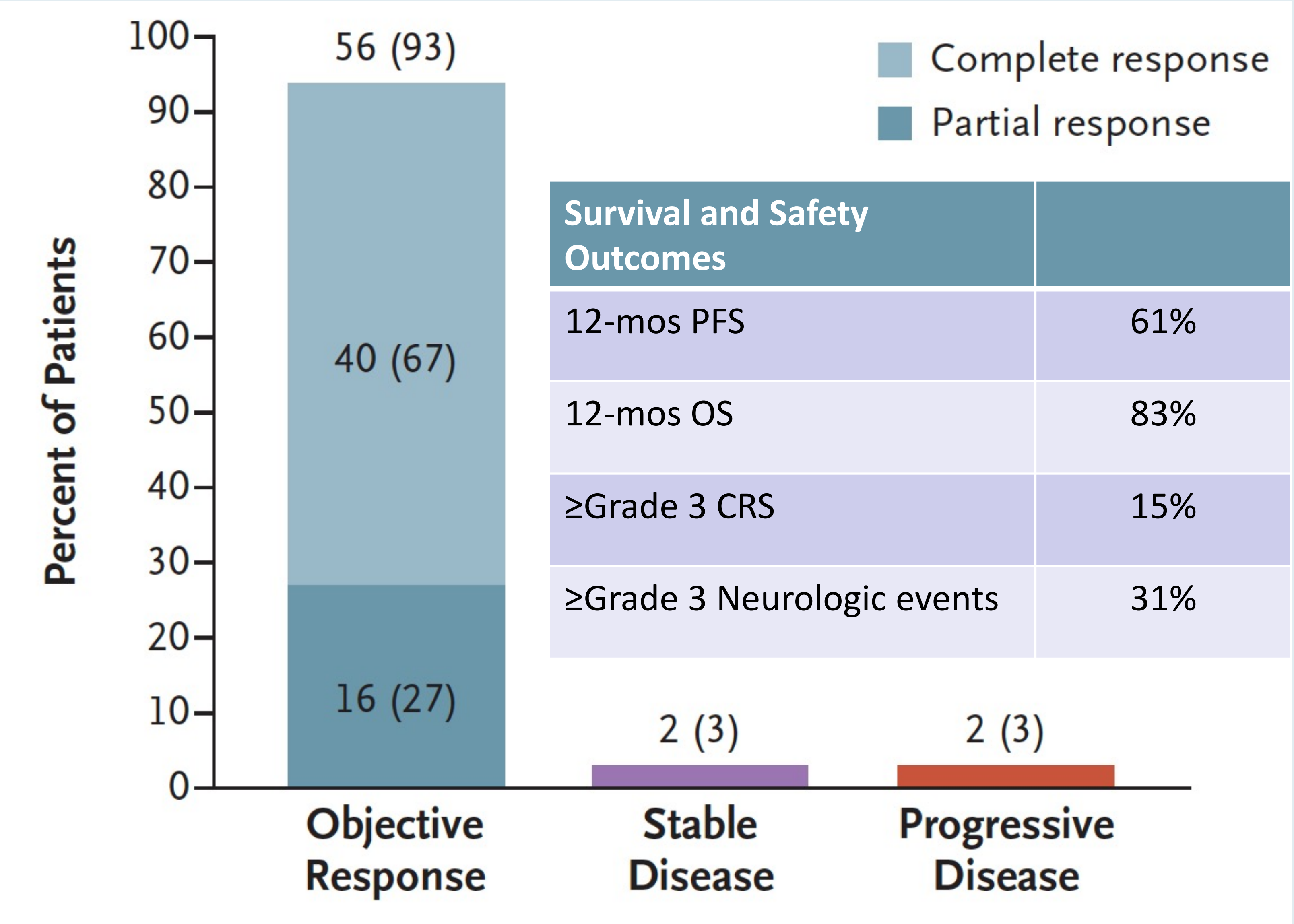
ORIGINAL ARTICLE

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

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.

Meet The Professor

Optimizing the Management of Metastatic Castration-Resistant Prostate Cancer

Wednesday, March 2, 2022
5:00 PM – 6:00 PM ET

Faculty

Andrew J Armstrong, MD, ScM

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

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