# Meet The Professor Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Sonali M Smith, MD
Elwood V Jensen Professor of Medicine
Chief, Section of Hematology/Oncology
Co-Leader, Cancer Service Line
Co-Director, Lymphoma Program
The University of Chicago
Chicago, Illinois



### **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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Contracted Research	Acerta Pharma — A member of the AstraZeneca Group, Bristol-Myers Squibb Company, Celgene Corporation, Epizyme Inc, Forty Seven Inc, Genentech, a member of the Roche Group, Karyopharm Therapeutics, Pharmacyclics LLC, an AbbVie Company, Portola Pharmaceuticals Inc, TG Therapeutics Inc
Speaking Engagement	ADC Therapeutics ICML



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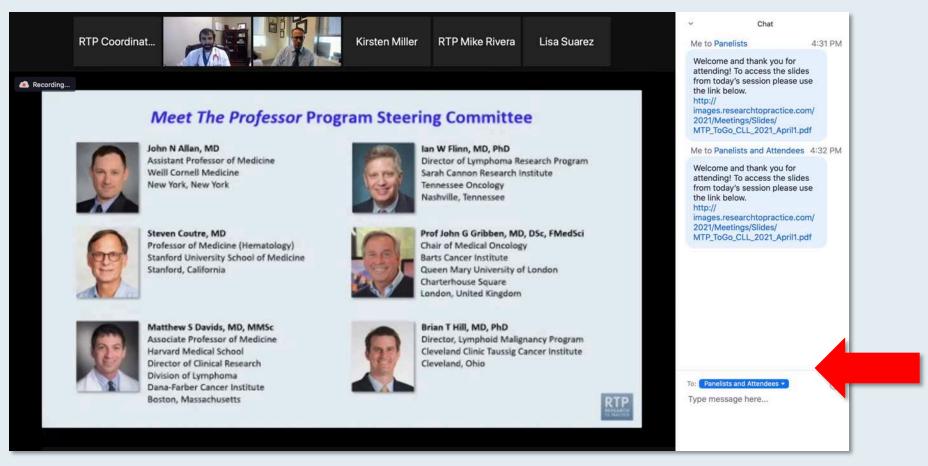


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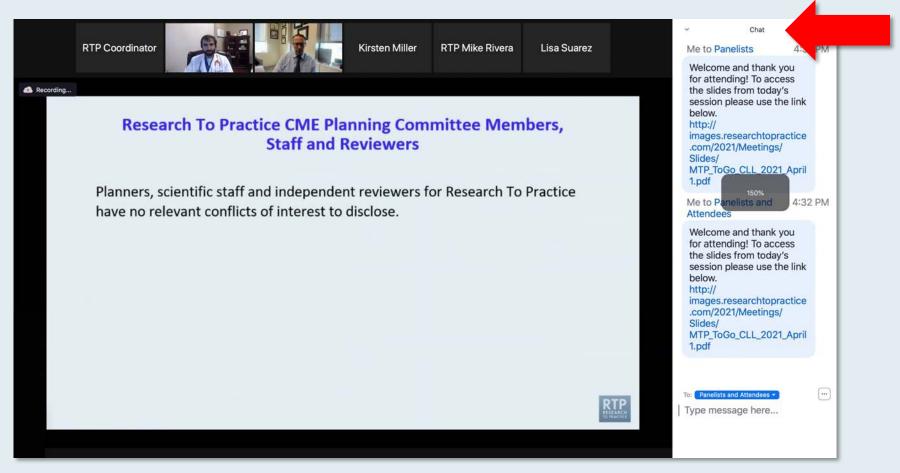


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### ONCOLOGY TODAY

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









# Meet The Professor Current and Future Management of Chronic Lymphocytic Leukemia

Thursday, March 17, 2022 5:00 PM – 6:00 PM ET

**Faculty** 

Peter Hillmen, MB ChB, PhD



## Data + Perspectives: Clinical Investigators Discuss the Current and Future Management of Ovarian Cancer

Saturday, March 19, 2022 2:30 PM – 4:00 PM ET

**Faculty** 

Mansoor Raza Mirza, MD Kathleen N Moore, MD, MS David M O'Malley, MD

**Moderator Robert L Coleman, MD** 



### Meet The Professor

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

Wednesday, March 30, 2022 5:00 PM - 6:00 PM ET

Faculty
Sarah B Goldberg, MD, MPH



# Meet The Professor Current and Future Management of Chronic Lymphocytic Leukemia

Thursday, March 31, 2022 5:00 PM - 6:00 PM ET

**Faculty** 

Kerry Rogers, MD



# Meet The Professor Optimizing the Management of Myelodysplastic Syndromes

Tuesday, April 5, 2022 5:00 PM - 6:00 PM ET

Faculty Rami Komrokji, MD



# Meet The Professor Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Wednesday, April 6, 2022 5:00 PM - 6:00 PM ET

**Faculty** 

Andrew M Evens, DO, MSc



## "What I Tell My Patients" 16<sup>th</sup> Annual RTP/ONS CE Seminar Series ONS Congress, Anaheim, California — April 27 - May 1, 2022

**Prostate Cancer** 6:00 AM - 7:30 AM PT (9:00 AM - 10:30 AM ET) **Ovarian Cancer** Thursday 12:15 PM - 1:45 PM PT (3:15 PM - 4:45 PM ET) April 28 Non-Small Cell Lung Cancer 6:00 PM - 7:30 PM PT (9:00 PM - 10:30 PM ET) **Small Cell Lung Cancer** 6:00 AM - 7:30 AM PT (9:00 AM - 10:30 AM ET) Chronic Lymphocytic Leukemia Friday 12:15 PM - 1:45 PM PT (3:15 PM - 4:45 PM ET) April 29 **Breast Cancer** 6:00 PM - 8:00 PM PT (9:00 PM - 11:00 PM ET) **Cervical and Endometrial Cancer** 6:00 AM - 7:30 AM PT (9:00 AM - 10:30 AM ET) Saturday April 30 **Bladder Cancer** 12:15 PM - 1:45 PM PT (3:15 PM - 4:45 PM ET)



### Thank you for joining us!

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



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Chicago, Illinois



### **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



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



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



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



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



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

### **Meet The Professor Program Participating Faculty**



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



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



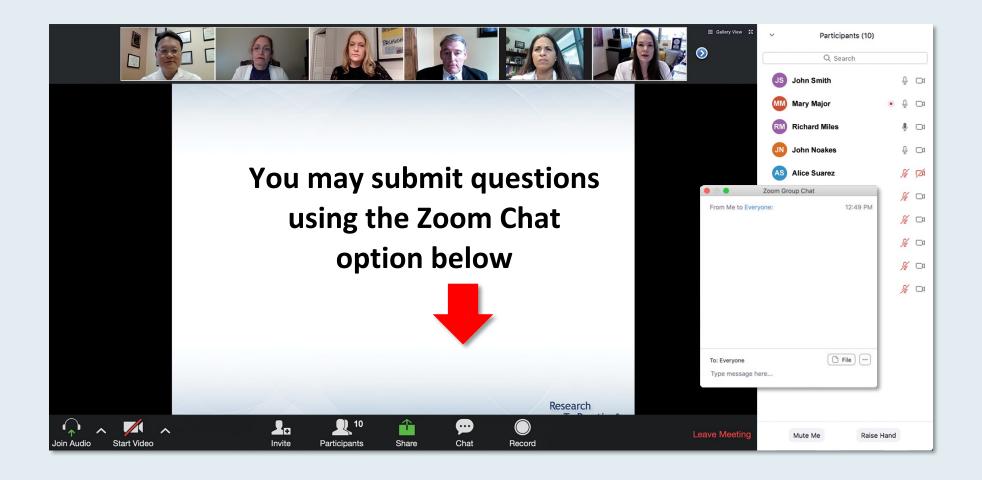
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Research To Practice
Miami, Florida



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Speaking Engagement	ADC Therapeutics ICML





Justin Peter Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina



**Neil Morganstein, MD** Atlantic Health System Summit, New Jersey



Khuda Dad Khan, MD, PhD Norton Cancer Institute Prospect, Kentucky



**Benjamin Parsons, DO**Gundersen Health System
Madison, Wisconsin



Pavel A Levin, MD, PhD
Texas Oncology-Pearland
Houston, Texas



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



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



Raman Sood, MD
Brooks Memorial Hospital
Dunkirk, New York



#### **Meet The Professor with Dr Smith**

#### Introduction

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

- Dr Rudolph: A 78-year-old woman with DLBCL receiving tafasitamab/lenalidomide
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**MODULE 3: Faculty Survey Results** 

**MODULE 4: Journal Club with Dr Smith** 

**MODULE 5: Appendix of Key Data Sets** 



## Phase II AMEERA Study of the Oral SERD Amcenestrant in ER-Positive, HER2-Negative Advanced or Metastatic Breast Cancer Fails to Meet PFS Endpoint

Press Release – March 14, 2022

"The Phase 2 AMEERA-3 clinical trial evaluating amcenestrant, an investigational optimized oral selective estrogen receptor degrader (SERD), did not meet its primary endpoint of improving progression-free survival (PFS) as assessed by an independent central review. The trial evaluated amcenestrant as monotherapy compared to endocrine treatment of physician's choice in patients with locally advanced or metastatic estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2-) breast cancer who progressed on or after hormonal therapies. No new safety signals were identified and the safety profile of amcenestrant in AMEERA-3 was consistent with earlier studies."





**Elwood V Jensen** 



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Contents lists available at ScienceDirect

#### Journal of Geriatric Oncology



#### Clinical Trial Protocol

SWOG 1918: A phase II/III randomized study of R-miniCHOP with or without oral azacitidine (CC-486) in participants age 75 years or older with newly diagnosed aggressive non-Hodgkin lymphomas – Aiming to improve therapy, outcomes, and validate a prospective frailty tool

Elizabeth A. Brem <sup>a,\*</sup>, Hongli Li <sup>b,c</sup>, Anne W. Beaven <sup>d</sup>, Paolo F. Caimi <sup>e</sup>, Leandro Cerchietti <sup>f</sup>, Ash A. Alizadeh <sup>g</sup>, Rebecca Olin <sup>h</sup>, N. Lynn Henry <sup>i</sup>, Hildy Dillon <sup>j</sup>, Richard F. Little <sup>k</sup>, Cara Laubach <sup>l</sup>, Michael LeBlanc <sup>b,c</sup>, Jonathan W. Friedberg <sup>m</sup>, Sonali M. Smith <sup>n</sup>



S1918: A Phase II/III Randomized Study of R-Minichop with or without Oral Azacitidine (CC-486) in Participants Age 75 Years or Older with Newly Diagnosed Diffuse Large B Cell Lymphoma, Grade IIIb Follicular Lymphoma, Transformed Lymphoma, and High-Grade B-Cell Lymphomas with MYC and BCL2 and/or BCL6 Rearrangements

Brem EA et al.

ASH 2021; Abstract 3565.



# Improving Survival and Predicting Toxicity in Older Patients With DLBCL: A Delicate Balance Sonali M. Smith, MD<sup>1</sup>

Sonali M. Smith, MD1

Journal of Clinical Oncology 2021;39(11):1193-5.



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## Case Presentation: A 78-year-old woman with DLBCL receiving tafasitamab/lenalidomide



Dr Priya Rudolph (Athens, Georgia)



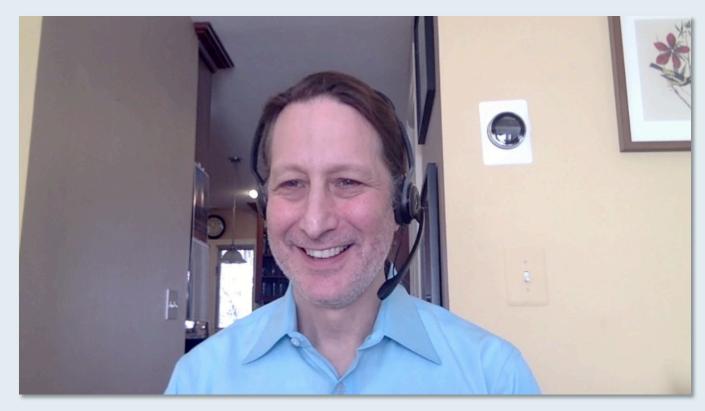
## Case Presentation: A 78-year-old woman with DLBCL receiving tafasitamab/lenalidomide (continued)



Dr Priya Rudolph (Athens, Georgia)



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



**Dr Neil Morganstein (Summit, New Jersey)** 



## Case Presentation: A 51-year-old man with intense abdominal pain is diagnosed with DLBCL

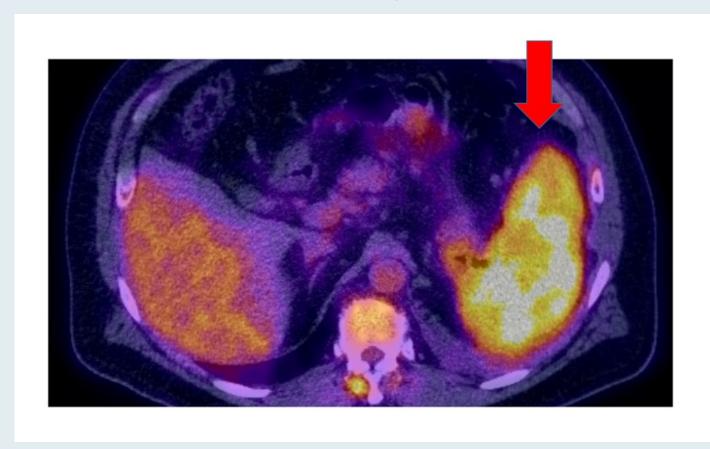


**Dr Laurie Matt-Amaral (Akron, Ohio)** 



## Case Presentation: A 51-year-old man with intense abdominal pain is diagnosed with DLBCL (continued)

**PET at Diagnosis** 





#### Case Presentation: An 83-year-old woman with relapsed MCL



Dr Benjamin Parsons (Madison, Wisconsin)



#### Case Presentation: A 53-year-old man with MCL, blastoid variant



**Dr Justin Favaro (Charlotte, North Carolina)** 



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#### Case Presentation: A 75-year-old man with newly diagnosed FL



Dr Khuda Dad Khan (Prospect, Kentucky)



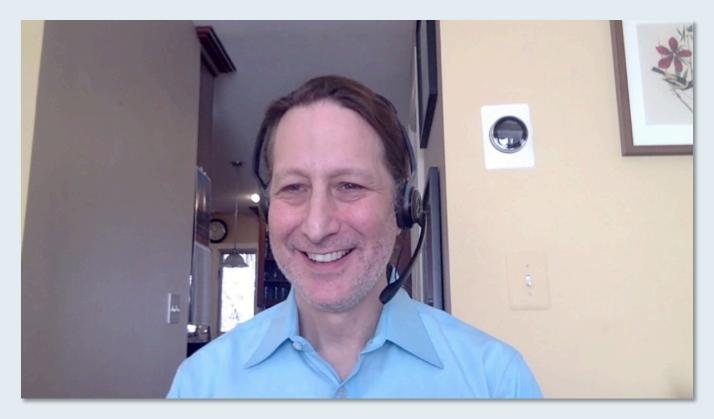
## Case Presentation: A 36-year-old man with newly diagnosed Grade I FL with a high proliferative index



**Dr Pavel Levin (Houston, Texas)** 



## Case Presentation: A 38-year-old woman with Stage II lymphocyte-predominant HL



**Dr Neil Morganstein (Summit, New Jersey)** 



#### Case Presentation: A 60-year-old woman with recurrent HL



**Dr Raman Sood (Dunkirk, New York)** 



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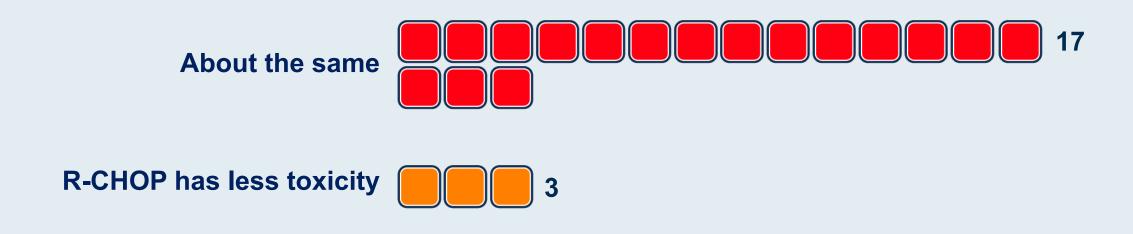
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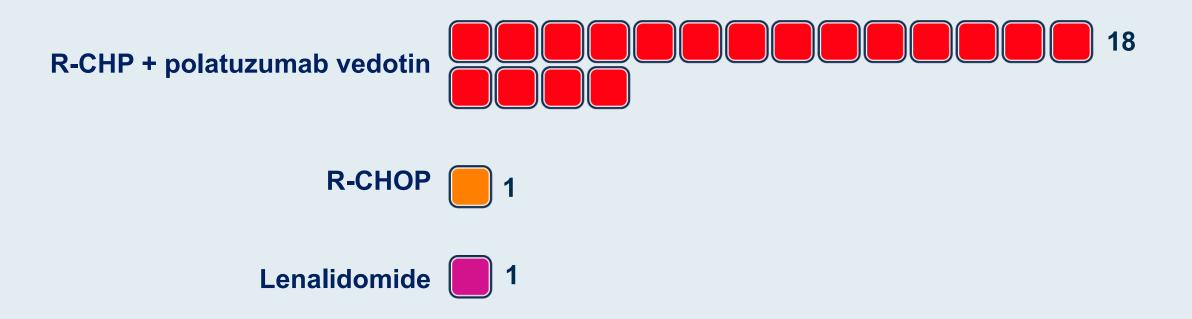
If future data continue not to demonstrate an overall survival advantage with polatuzumab vedotin in combination with R-CHP over R-CHOP when used as up-front therapy for DLBCL, do you think the clinical benefit with this regimen is greater than the risk?



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?



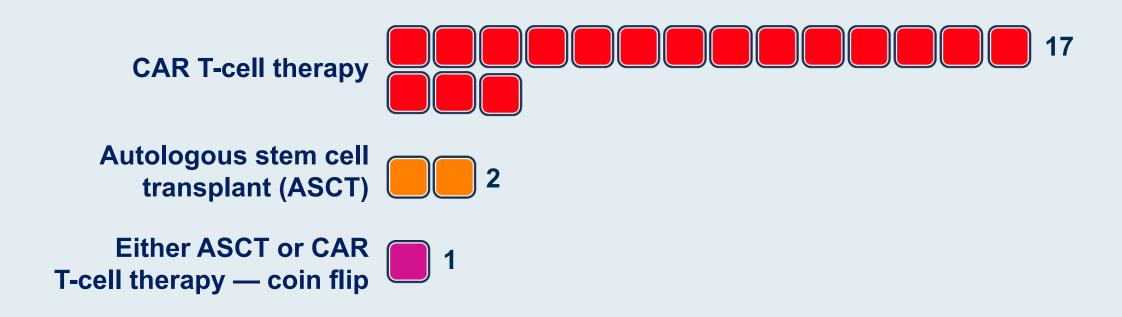
Regulatory and reimbursement issues aside, which first-line therapy would you generally recommend for an otherwise healthy <u>65-year-old</u> patient with Stage IV <u>activated B-cell</u> (ABC)-type DLBCL?



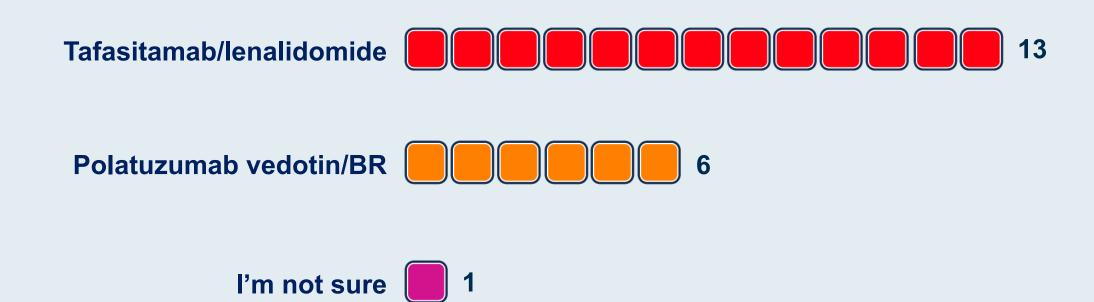
Regulatory and reimbursement issues aside, which first-line therapy would you generally recommend for an otherwise healthy <u>65-year-old</u> patient with Stage IV germinal center B-cell (GCB)-type DLBCL?



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?



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



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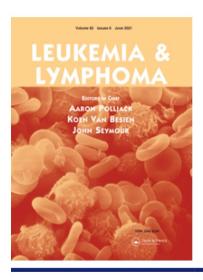
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#### Leukemia & Lymphoma

Leukemia & Lymphoma 2021;62(6):1497-501.

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ilal20

## Bloodless chimeric antigen receptor (CAR) T-cell therapy in Jehovah's Witnesses

Peter A. Riedell, Meng Wu, Jennifer M. Collins, Jacklyn M. Gideon, Andrzej J. Jakubowiak, Justin P. Kline, Satyajit Kosuri, Hongtao Liu, Sonali M. Smith & Michael R. Bishop



#### REVIEW

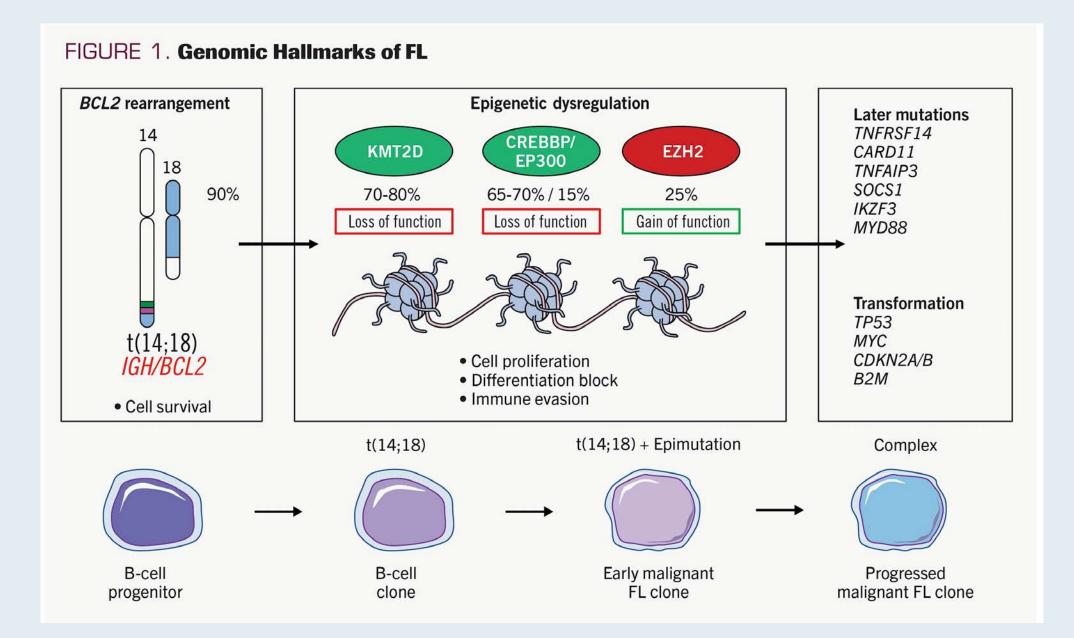
ONCOLOGY® ANNUAL REVIEW OF TREATMENTS IN HEMATOLOGIC MALIGNANCIES

2022;36(2):97-106

### Follicular Lymphoma: a Focus on Current and Emerging Therapies

Kirk E. Cahill, MD1; and Sonali M. Smith, MD1





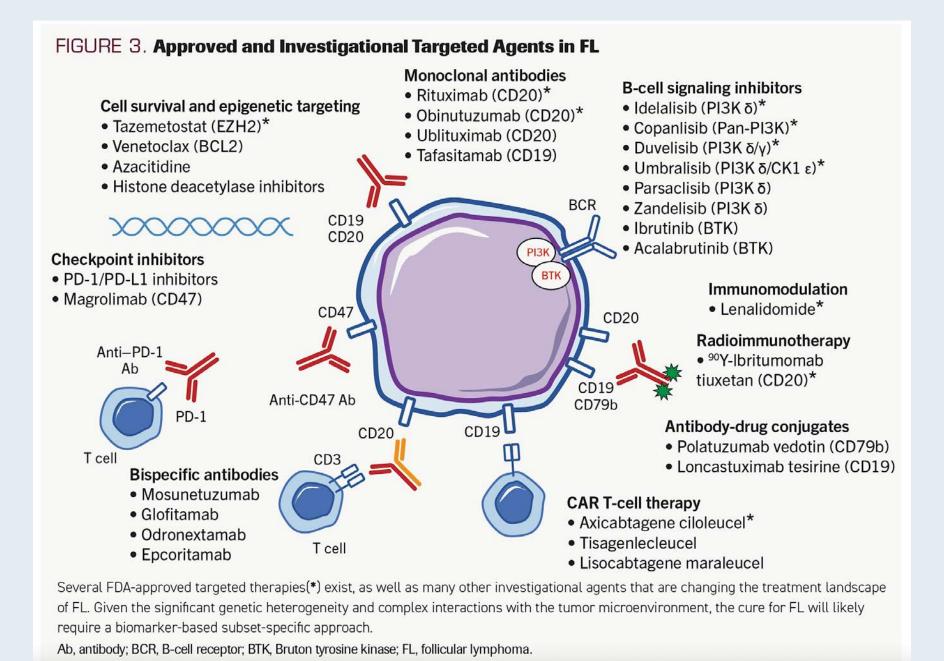






TABLE 3. Bispecific Antibodies Under Investigation in FL

		A STATE OF THE PARTY OF THE PAR			
Bispecific Antibody	Mosunetuzumab	Mosunetuzumab + Lenalidomide	Epcoritamab	Glofitamab	Odronextamab
Phase	1/2	1	1/2	1/2	1
Trial	NCT02500407	NCT04246086	NCT03625037	NCT03075696	NCT02290951
Patients (FL)	90 (90)	29 (29)	68 (12)	53 (mono) 19 (+obin)	127 (28)
Median prior therapies (range)	3 (2-10)	1 (1-6)	5 (3-8)	3 (1-12) (mono) 2 (1-5) (+obin)	3 (1-11)
ORR % (CR%)	80 (60)	90 (66)	90 (50)	81 (70) (mono) 100 (74) (+obin)	93 (75)
Median DOR (months)	22.8	NR	NR	NR	8.1
Median PFS (months)	17.9	NR	NR	NR	12.8
Grade ≥3 CRS (%)	2	0	0	4 (mono) 0 (+obin)	6
Grade ≥3 neurotoxicity (%)	0	0	3	0 (mono) 0 (+obin)	4
Median follow-up (months)	18.3	5.4	13.6	4.4 (mono) 5.5 (+obin)	3.9

FL, follicular lymphoma; CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; mono, monotherapy; NR, not reported; obin, obinutuzumab; ORR, overall response rate; PFS, progression-free survival; RP2D, recommended phase 2 dose.



#### **EDITORIALS**

#### Too much and not enough: revisiting maintenance rituximab in indolent lymphomas

Sonali M. Smith

Section of Hematology/Oncology, University of Chicago, Chicago, IL, USA

E-mail: SONALI M. SMITH - smsmith@medicine.bsd.uchicago.edu

doi:10.3324/haematol.2021.279101

"Since maintenance rituximab has yet to offer cure or improved overall survival after chemoimmunotherapy induction, it seems more appropriate to identify the minimum number of doses rather than trying to expand or extend treatment."





Efficacy and safety assessment of prolonged maintenance with subcutaneous rituximab in patients with relapsed or refractory indolent non-Hodgkin lymphoma: results of the phase III MabCute study

**Haematologica** 2022 Volume 107(2):500-509 Simon Rule,<sup>1</sup> Wolney Gois Barreto,<sup>2</sup> Javier Briones,<sup>3</sup> Angelo M. Carella,<sup>4</sup> Olivier Casasnovas,<sup>5</sup> Chris Pocock,<sup>6</sup> Clemens-Martin Wendtner,<sup>7</sup> Francesco Zaja,<sup>8</sup> Susan Robson,<sup>9</sup> Lachlan MacGregor,<sup>9</sup> Roger R. Tschopp,<sup>9</sup> Sonja Nick<sup>9</sup> and Martin Dreyling<sup>10</sup>



Clin Adv Hematol Oncol 2021;19(11):698-709.

## DA-R-EPOCH vs R-CHOP in DLBCL: How Do We Choose?

Ajay Major, MD, MBA, and Sonali M. Smith, MD Section of Hematology/Oncology, The University of Chicago





#### **ARTICLE**

## ASTCT, CIBMTR, and EBMT clinical practice recommendations for transplant and cellular therapies in mantle cell lymphoma

Pashna N. Munshi 1 · Mehdi Hamadani 2 · Ambuj Kumar 3 · Peter Dreger 4 · Jonathan W. Friedberg · Martin Dreyling · Brad Kahl · Mats Jerkeman 8 · Mohamed A. Kharfan-Dabaja 9 · Frederick L. Locke 10 · Mazyar Shadman · Brian T. Hill · Sairah Ahmed 11 · Alex F. Herrera · Craig S. Sauter · Veronika Bachanova 16 · Nilanjan Ghosh · Matthew Lunning · Vaishalee P. Kenkre · Mahmoud Aljurf · Michael Wang 16 · Kami J. Maddocks · John P. Leonard · Manali Kamdar · Tycel Phillips · Amanda F. Cashen · David J. Inwards · Anna Sureda · Jonathon B. Cohen · Sonali M. Smith · Carmello Carlo-Stella 13 · Bipin Savani · Stephen P. Robinson · Timothy S. Fenske ·



## ASTCT, CIBMTR, and EBMT Clinical Practice Recommendations for Transplant and Cellular Therapies in Mantle Cell Lymphoma

# Estimated number of newly diagnosed lymphoma patients seen by individual member annually

>75	23 (69.7%)
51-75	6 (18.2%)
26-50	3 (9.1%)
≤25	1 (3.0%)

## Estimated number of mantle cell lymphoma patients seen by individual member annually

>40	6 (18.2%)
31-40	3 (9.1%)
21-30	14 (42.4%)
≤20	10 (30.3%)

# Estimated annual CAR T-cell therapies performed at respective centers for lymphoma (on or off clinical trial)

>20	21 (63.6%)
16-20	3 (9.1%)
11-15	5 (15.2%)
≤10	4 (12.1%)





## Regular Article

#### LYMPHOID NEOPLASIA

#### Single-route CNS prophylaxis for aggressive non-Hodgkin lymphomas: real-world outcomes from 21 US academic institutions

Victor Manuel Orellana-Noia, 1,2 Daniel R. Reed, 2,3 Ashley Alesia McCook, 4 Jeremy Michael Sen, 5 Christian M. Barlow, 2 Mary-Kate Malecek, Marcus Watkins, Brad S. Kahl, Michael A. Spinner, Ranjana Advani, Timothy J. Voorhees, 9,9 Anson Snow, 8 Natalie Sophia Grover, Amy Ayers, Jason Romancik, Yuxin Liu, Scott F. Huntington, Julio C. Chavez, Hayder Saeed, Landington, Amy Ayers, Amy Ayers, Landington, Scott F. Huntington, Union C. Chavez, Hayder Saeed, Landington, Aleksandr Lazaryan, 11 Vikram Raghunathan, 12,13 Stephen E. Spurgeon, 12 Thomas A. Ollila, 14 Christopher Del Prete, 14 Adam Olszewski, <sup>14</sup> Emily C. Ayers, <sup>2,15</sup> Daniel J. Landsburg, <sup>15</sup> Benjamin Echalier, <sup>16</sup> Jun Lee, <sup>16</sup> Manali Kamdar, <sup>16</sup> Paolo F. Caimi, <sup>17,18</sup> Timothy Fu, 19 Jiegi Liu, 19 Kevin A. David, 19 Hanan Alharthy, 20 Jennie Law, 21 Reem Karmali, 22 Harsh Shah, 23 Deborah M. Stephens, 23 Ajay Major,<sup>24</sup> Alexandra E. Rojek,<sup>24</sup> Sonali M. Smith,<sup>24</sup> Amulya Yellala,<sup>25</sup> Avyakta Kallam,<sup>25</sup> Shazi Nakhoda,<sup>26</sup> Nadia Khan,<sup>26</sup> Mohammad Ahsan Sohail, 18 Brian T. Hill, 18 Odeth Barrett-Campbell, 27 Frederick Lansigan, 27 Jeffrey Switchenko, 4 Jonathon Cohen, 1 and Craig A. Portell<sup>2</sup> Blood 2022;139(3):413-23.





#### **Blood Cancer Journal**

www.nature.com/bcj

# Evolution of therapy for limited stage diffuse large B-cell lymphoma

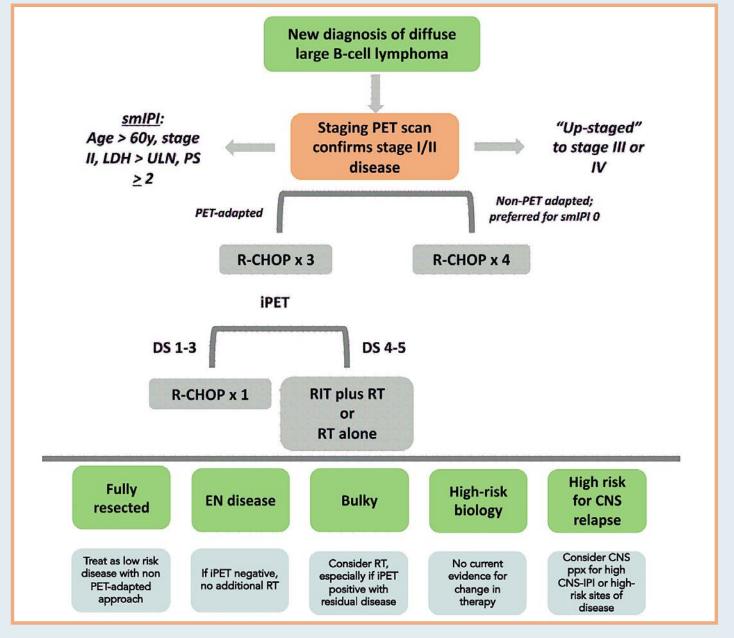
Alexandra E. Rojek¹ and Sonali M. Smith (□)<sup>2</sup>

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Blood Cancer J 2022;12(2):33.



### Management of Limited-Stage Diffuse Large B-Cell Lymphoma (DLBCL)





### Efficacy Comparison of Tisagenlecleucel versus Standard of Care in Patients with Relapsed or Refractory Follicular Lymphoma

Salles G et al.

ASH 2021; Abstract 3528.



### ADVANCES IN LLM

Current Developments in the Management of Leukemia, Lymphoma, and Myeloma

Section Editor: Susan O'Brien, MD

Clin Adv Hematol Oncol 2021;19(10):624-6.

### Evolving Strategies for the Management of Transformed Lymphoma



Sonali M. Smith, MD Elwood V. Jensen Professor in Medicine Chief, Section of Hematology/Oncology UChicago Medicine Chicago, Illinois



# A Multicenter, Single-Arm, Phase I/II Dose Finding and Efficacy Study of Venetoclax, CC-486, and Obinutuzumab in Minimally-Pretreated Follicular Lymphoma

Cahill KE et al. ASH 2021; Abstract 2420.



#### **Meet The Professor with Dr Smith**

#### Introduction

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

- Dr Rudolph: A 78-year-old woman with DLBCL receiving tafasitamab/lenalidomide
- Dr Morganstein: A 54-year-old man with DLBCL transformed from follicular lymphoma
- Dr Matt-Amaral: A 51-year-old man with intense abdominal pain is diagnosed with DLBCL
- Dr Parsons: An 83-year-old woman with relapsed MCL
- Dr Favaro: A 53-year-old man with MCL, blastoid variant

#### **MODULE 2: Case Presentations – Follicular Lymphoma (FL), Hodgkin Lymphoma (HL)**

- Dr Khan: A 75-year-old man with newly diagnosed FL
- Dr Levin: A 36-year-old man with newly diagnosed Grade I FL with a high proliferative index
- Dr Morganstein: A 38-year-old woman with Stage II lymphocyte-predominant HL
- Dr Sood: A 60-year-old woman with recurrent HL

**MODULE 3: Faculty Survey Results** 

**MODULE 4: Journal Club with Dr Smith** 



### **Diffuse Large B-Cell Lymphoma**



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

The NEW ENGLAND JOURNAL of MEDICINE

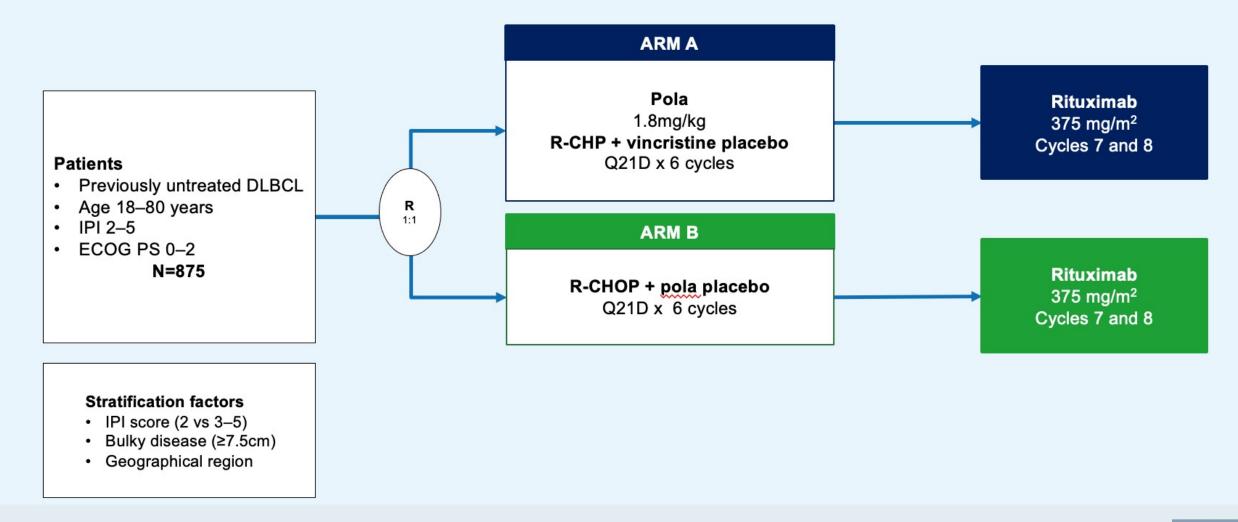
#### ORIGINAL ARTICLE

### 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

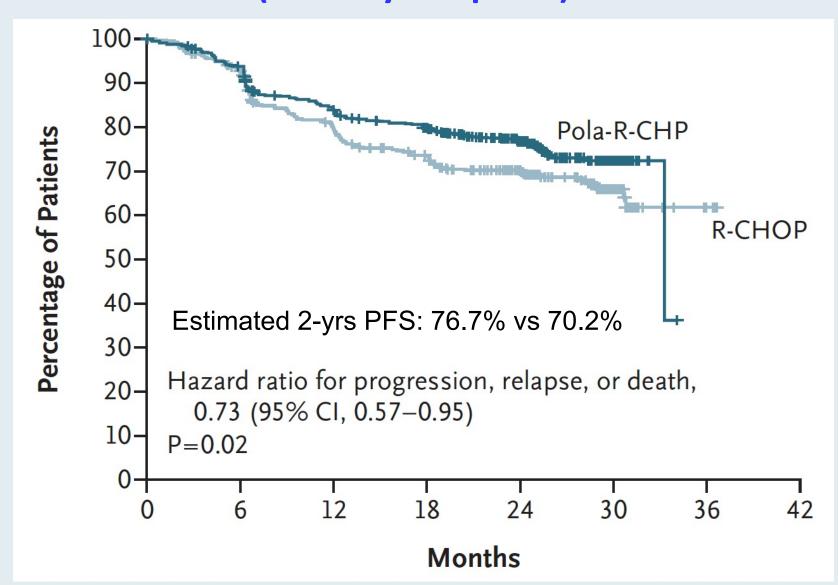


### **POLARIX Phase III Trial Design**





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





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

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

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

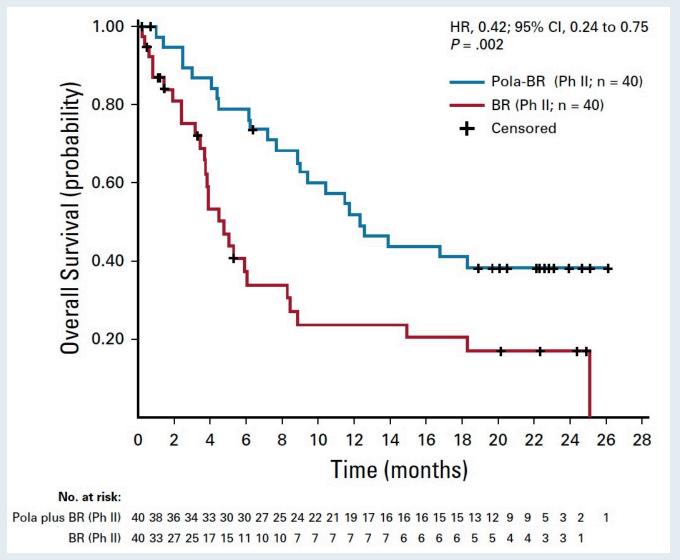


### Polatuzumab Vedotin with Bendamustine/Rituximab for Transplant-Ineligible R/R DLBCL: End-of-Treatment CR Rate

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

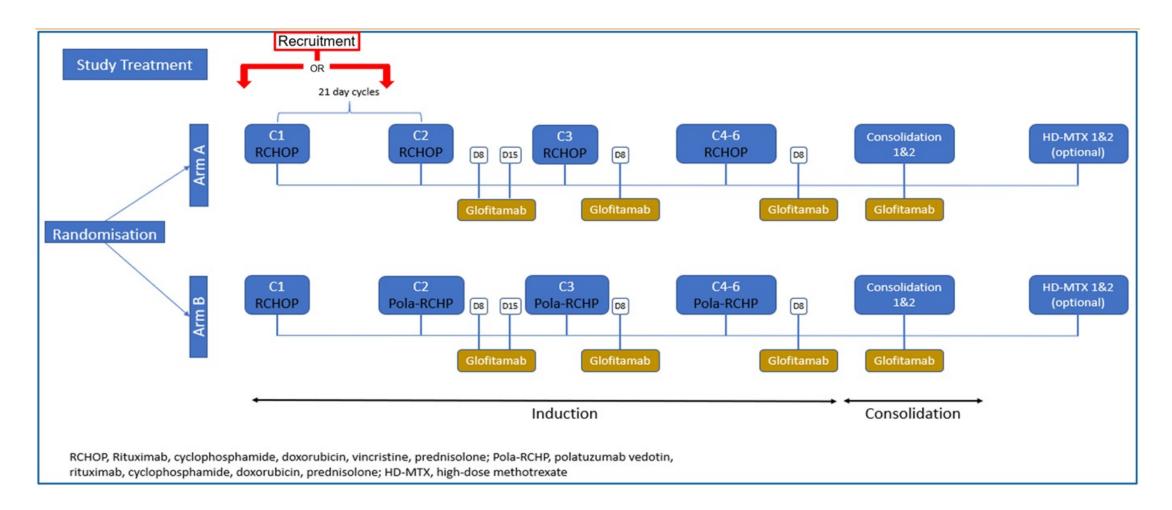


### Polatuzumab Vedotin with Bendamustine/Rituximab for Transplant-Ineligible R/R DLBCL: Overall Survival





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)



Lancet Haematol 2020;7:e511-22.

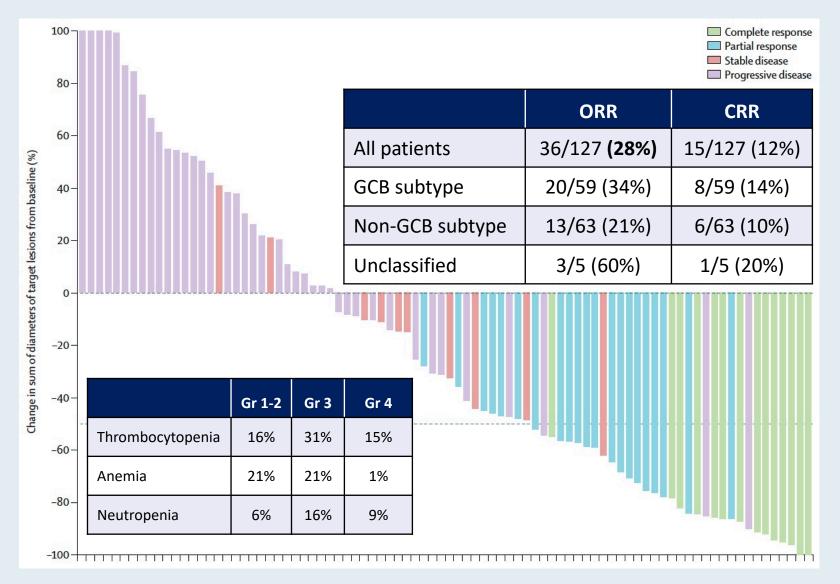
# Selinexor in patients with relapsed or refractory diffuse large B-cell lymphoma (SADAL): a single-arm, multinational, multicentre, open-label, phase 2 trial



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



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





### 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."



#### 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 tafasitamal 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.



### FDA Grants Accelerated Approval to Loncastuximab Tesirine-Ipyl 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."



#### Lancet Oncol 2021;22:790-800

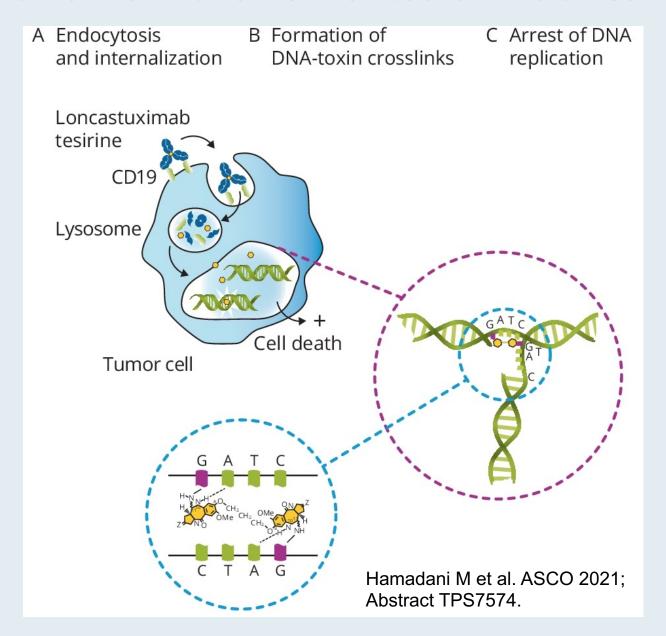


### Loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma (LOTIS-2): a multicentre, open-label, single-arm, phase 2 trial

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**





### 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		



### **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%





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

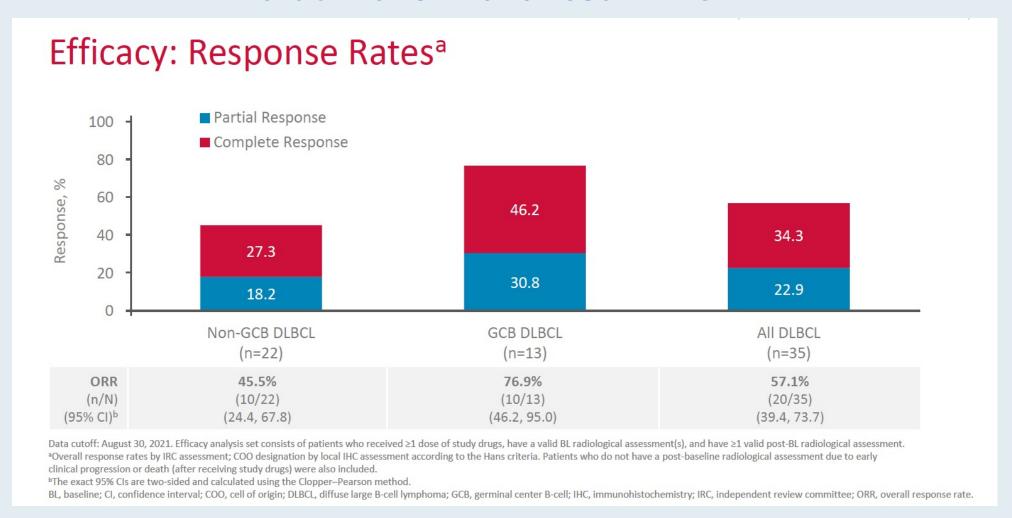
Oral Presentation, 63rd ASH Annual Meeting and Exposition, December 11–14, 2021

Carmelo Carlo-Stella, MD¹, Pier Luigi Zinzani, MD², Murali Janakiram, MD, MS³, Vivian Dai, MD⁴, Xiaomin He, PhD⁴, Annette Ervin-Haynes, DO, MPA⁴, Julien Depaus, MD⁵

<sup>1</sup>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; <sup>2</sup>IRCCS Azienda Ospedaliero-Universitaria di Bologna Istituto di Ematologia "Seràgnoli," and Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale Università di Bologna, Bologna, Bologna, Italy; <sup>3</sup>Division of Hematology, Oncology and Transplantation, University of Minnesota, Minneapolis, MN, USA; <sup>4</sup>Clinical Development, ADC Therapeutics America, Inc., Murray Hill, NJ, USA; <sup>5</sup>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



Safety data were consistent with those reported previously



### **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
	<b>*</b>		
Leukapheresis	Fresh product	Cryopreserved product	Fresh product
Outpatient administration	Not allowed	Allowed	Allowed
Bridging therapy, %	Not allowed	92%	59%
Lymphodepletion chemotherapy	Cy/Flu <mark>500/30</mark> mg/m <sup>2</sup> × 3d	Cy/Flu <mark>250/25</mark> mg/m <sup>2</sup> x 3d Bendamustine 90 mg/m <sup>2</sup> x 2d	Cy/Flu <mark>300/30</mark> mg/m² x 3d



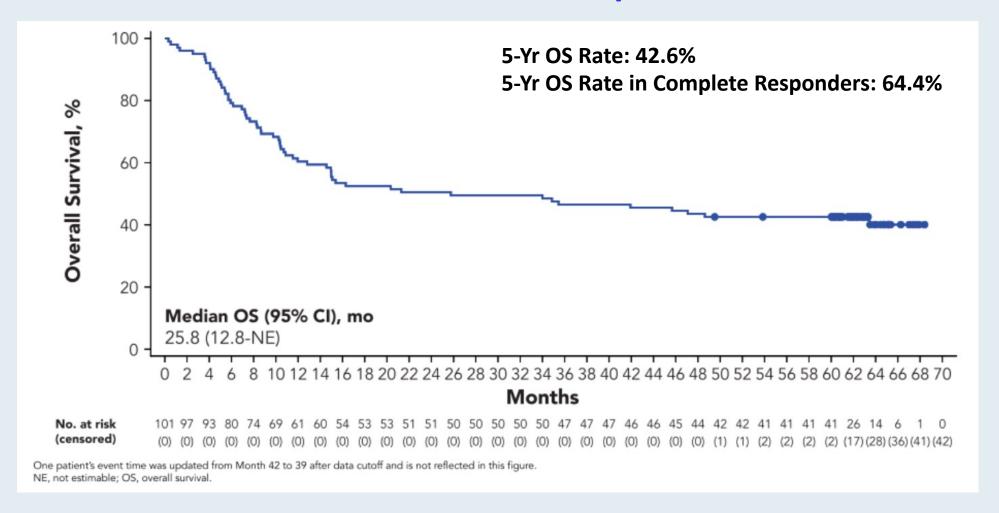
Long-Term (4- and 5-Year) Overall Survival in ZUMA-1, the Pivotal Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients with Refractory Large B-Cell Lymphoma (LBCL)

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



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

The NEW ENGLAND JOURNAL of MEDICINE

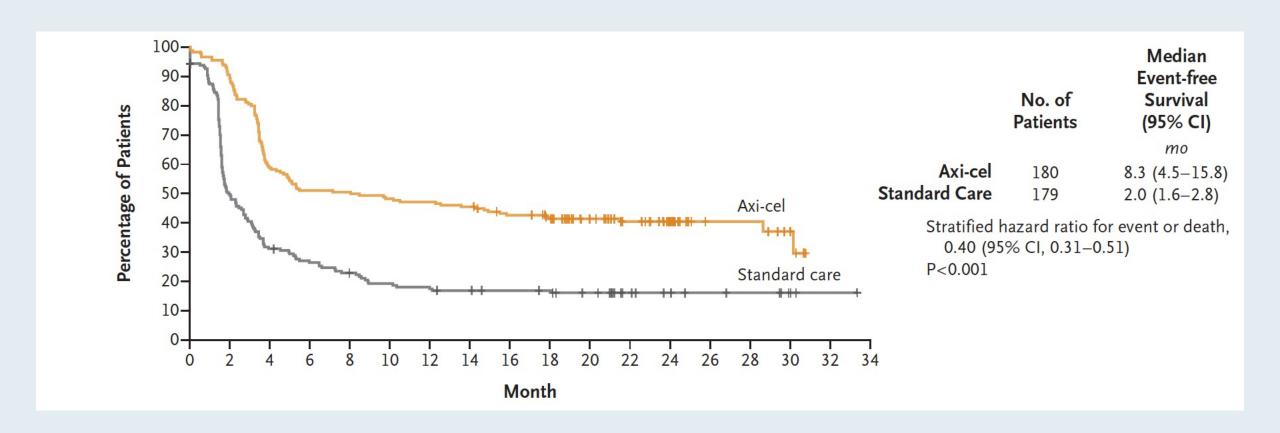
#### ORIGINAL ARTICLE

### 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\*



#### **ZUMA-7: Event-Free Survival**



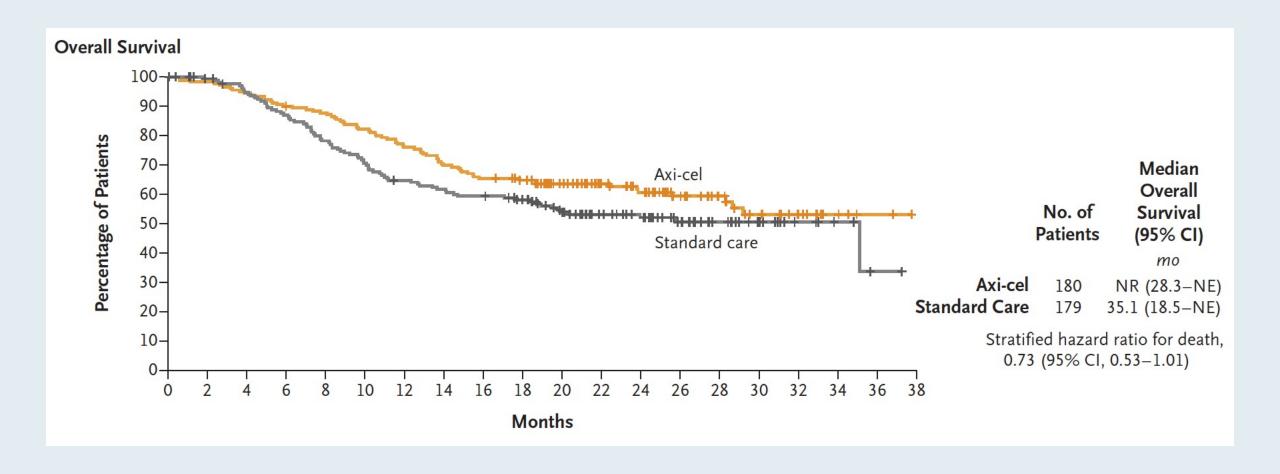


### **ZUMA-7: Event-Free Survival Subgroup Analysis**

		5. 1.16	Hazard Ratio for Event or Death	
Subgroup no	<b>Axi-cel</b> o. of patients	<b>Standard Care</b> with event/total no.	(95% CI)	
Overall	108/180	144/179	H <del>O</del> H	0.40 (0.31-0.51)
Age				
<65 yr	81/129	96/121	<b>→</b>	0.49 (0.36-0.67)
≥65 yr	27/51	48/58	<b>-</b> →	0.28 (0.16-0.46)
Response to first-line therapy at randomization				
Primary refractory disease	85/133	106/131	<b>⊢</b>	0.43 (0.32-0.57)
Relapse ≤12 mo after initiation or completion of first-line therapy	23/47	38/48	<b>⊢</b>	0.34 (0.20-0.58)
Second-line age-adjusted IPI				
0 or 1	54/98	73/100	<b>⊢</b>	0.41 (0.28-0.58)
2 or 3	54/82	71/79	<b>⊢</b>	0.39 (0.27-0.56)
Prognostic marker according to central laboratory				
HGBL, double- or triple-hit	15/31	21/25	<b>⊢</b>	0.28 (0.14-0.59)
Double-expressor lymphoma	35/57	50/62	<b>⊢</b>	0.42 (0.27-0.67)
Molecular subgroup according to central laboratory				
Germinal center B-cell–like	64/109	80/99	<b>⊢●</b> ⊢	0.41 (0.29-0.57)
Activated B-cell–like	11/16	9/9	<del></del>	0.18 (0.05-0.72)
Unclassified	8/17	12/14		_
Disease type according to investigator			i	
DLBCL, not otherwise specified	68/110	97/116	₩ .	0.37 (0.27-0.52)
Large-cell transformation from follicular lymphoma	10/19	24/27	<b>├</b>	0.35 (0.16-0.77)
HGBL, including rearrangement of MYC with BCL2 or BCL6 or both	23/43	18/27	<b></b>	0.47 (0.24-0.90)
Disease type according to central laboratory				
DLBCL	79/126	95/120	H <b>4</b> H	0.44 (0.32-0.60)
HGBL, including rearrangement of MYC with BCL2 or BCL6 or both	15/31	21/26	<b>——</b>	0.28 (0.14–0.59)
		0.01	0.1 0.2 0.5 1.0 2.	0 5.0
			Axi-cel Better Stan	dard Care Better



#### **ZUMA-7: Overall Survival**





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

The NEW ENGLAND JOURNAL of MEDICINE

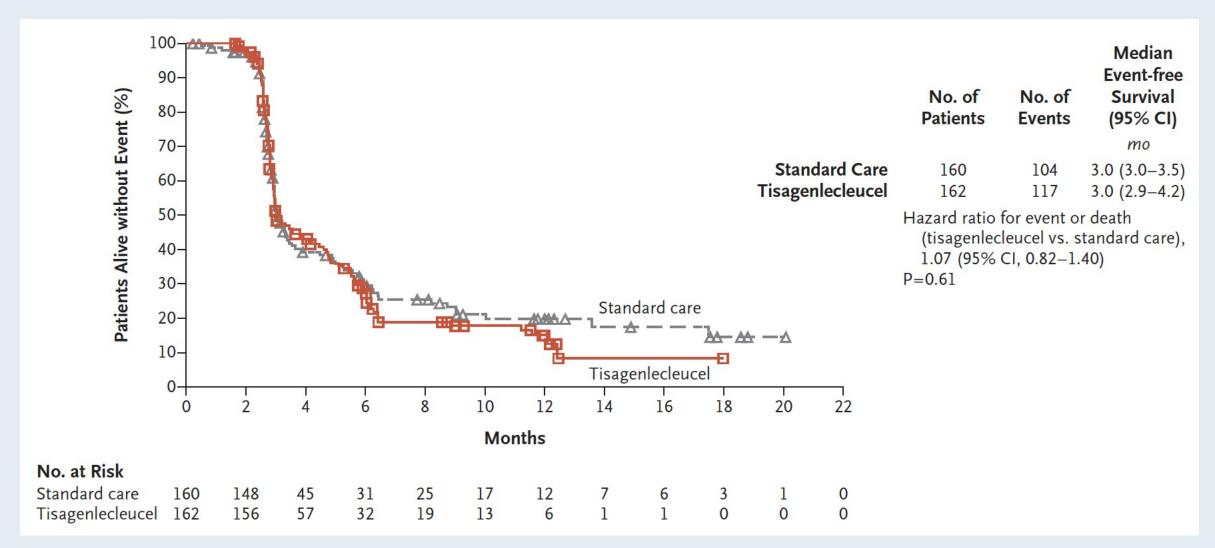
#### ORIGINAL ARTICLE

### 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



### **BELINDA: Event-Free Survival (Primary Endpoint)**





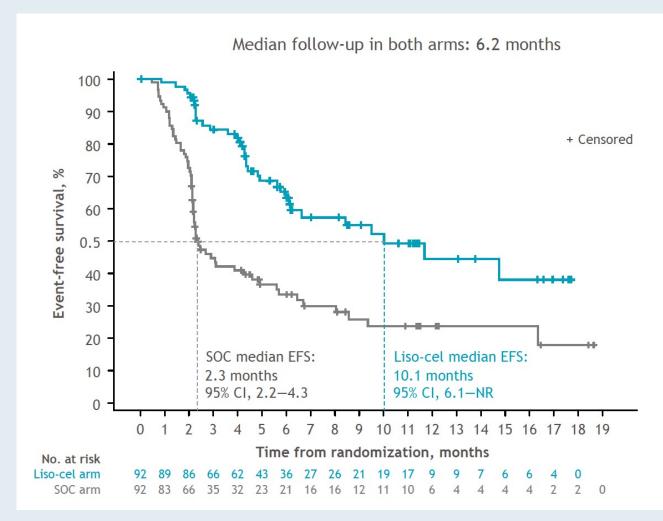
Lisocabtagene Maraleucel, a CD19-Directed Chimeric Antigen Receptor T Cell Therapy, Versus Standard of Care with Salvage Chemotherapy Followed by Autologous Stem Cell Transplantation as Second-Line Treatment in Patients with Relapsed or Refractory Large B-Cell Lymphoma: Results from the Randomized Phase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

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

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



### 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



#### 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

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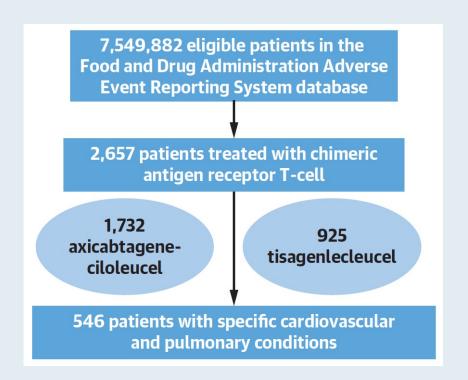
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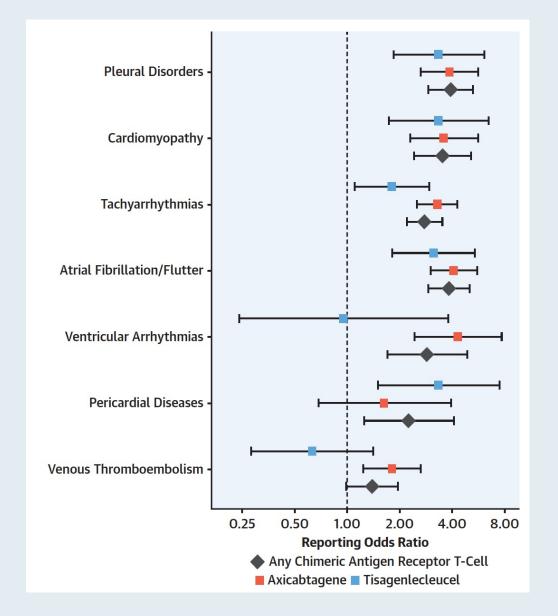
### Adverse Cardiovascular and Pulmonary Events Associated With Chimeric Antigen Receptor T-Cell Therapy

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, Joshua Fein, MD, Richard M. Steingart, MD, c,d Syed S. Mahmood, MD, MPH, Wendy L. Schaffer, MD, PhD, d,d Miguel-Angel Perales, MD, d,h Roni Shouval, MD, PhD, PhD, d,h



#### **Cardiovascular and Pulmonary Toxicities of CAR T-Cell Therapy**





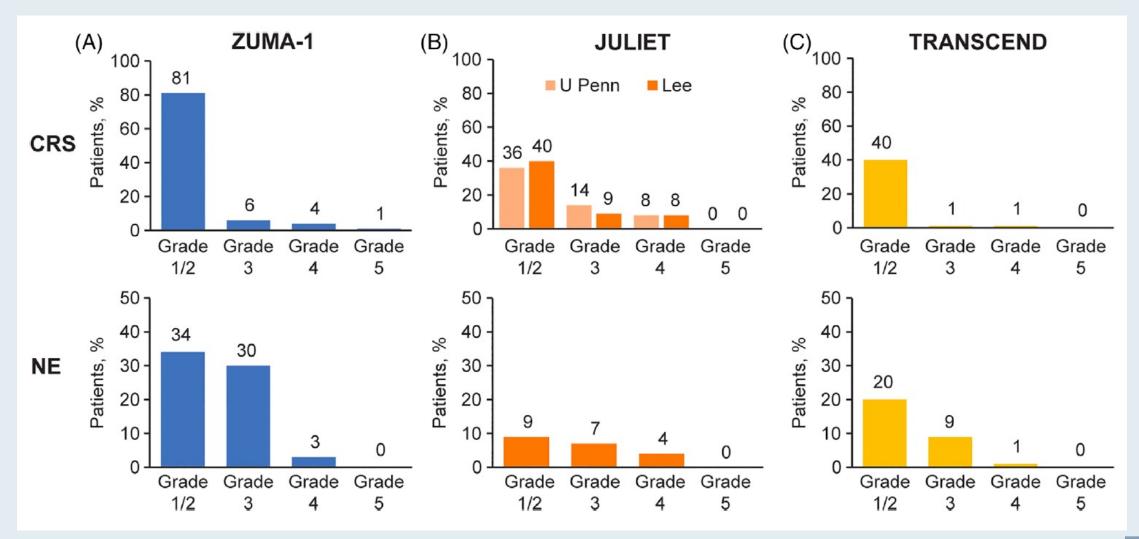


### Summary of Efficacy Outcomes in Pivotal Studies of CAR T-Cell Therapy for DLBCL

	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



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





### 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, IFNy, 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



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

Bianca D. Santomasso, MD, PhD¹; Loretta J. Nastoupil, MD²; Sherry Adkins, RN, MS²; Christina Lacchetti, MHSc³; Bryan J. Schneider, MD⁴; Milan Anadkat, MD⁵; Michael B. Atkins, MD⁶; Kelly J. Brassil, PhD, RN²; Jeffrey M. Caterino, MD, MPH⁻; Ian Chau, MD⁶; Marianne J. Davies, DNP⁶; Marc S. Ernstoff, MD¹⁰; Leslie Fecher, MD⁴; Pauline Funchain, MD¹¹; Ishmael Jaiyesimi, DO, MS¹²; Jennifer S. Mammen, MD, PhD¹³; Jarushka Naidoo, MD¹⁴; Aung Naing, MD²; Tanyanika Phillips, MD¹⁵; Laura D. Porter, MD¹⁶; Cristina A. Reichner, MD¹⁷; Carole Seigel, MBA¹⁶; Jung-Min Song, MSN, RN, CNS¹¹; Alexander Spira, MD, PhD¹⁶; Maria Suarez-Almazor, MD²; Umang Swami, MD²⁰; John A. Thompson, MD²¹; Praveen Vikas, MD²²; Yinghong Wang, MD²; Jeffrey S. Weber, MD, PhD²³; Kathryn Bollin, MD²⁴; and Monalisa Ghosh, MD²⁵

J Clin Oncol 2021;39:3978-92



# 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)

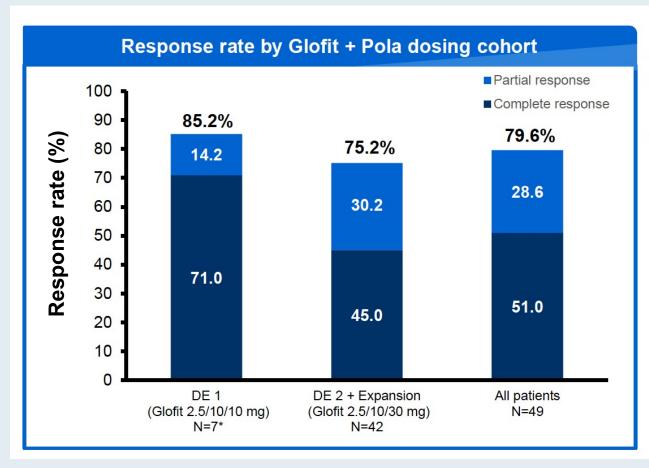
Martin Hutchings,<sup>1</sup> Anna Sureda,<sup>2</sup> Maria Jose Terol,<sup>3</sup> Francesc Bosch,<sup>4</sup> Paolo Corradini,<sup>5</sup> Thomas Stauffer Larsen,<sup>6</sup> Antonio Rueda Dominguez,<sup>7</sup> Anesh Panchal,<sup>8</sup> Alessia Bottos,<sup>9</sup> Yanjie Wang,<sup>10</sup> Audrey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

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

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



### 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

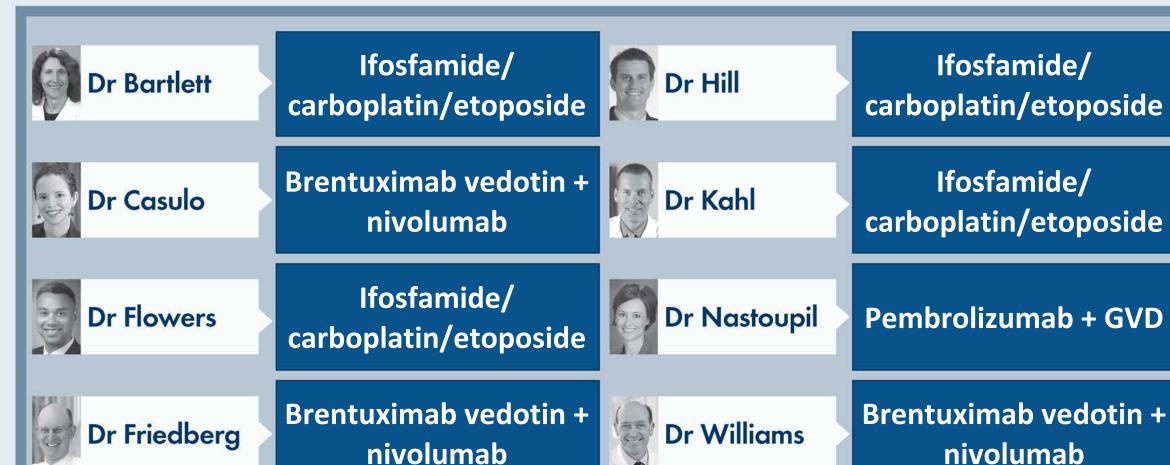
- Safety profile of the combination was consistent with that of the individual drugs
- Majority of CRS events were Gr 1 and occurred after first dose of glofitamab (no Gr 3/4 cases)
- One Gr 1 ICANS AE was reported



### **Hodgkin Lymphoma**

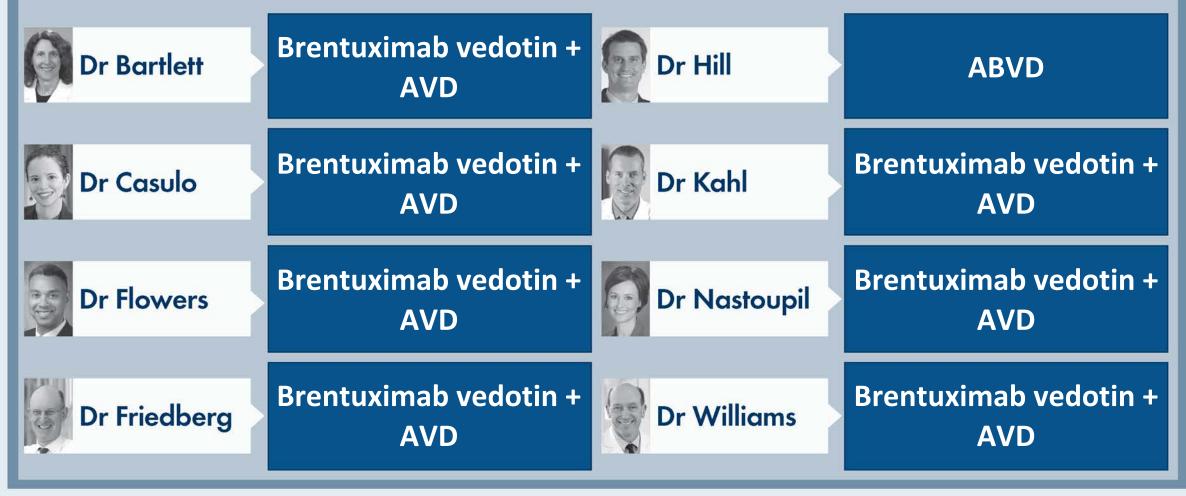


# Regulatory and reimbursement issues aside, in general, what would be your preferred bridge to transplant for a patient with HL who is experiencing disease relapse after up-front ABVD?



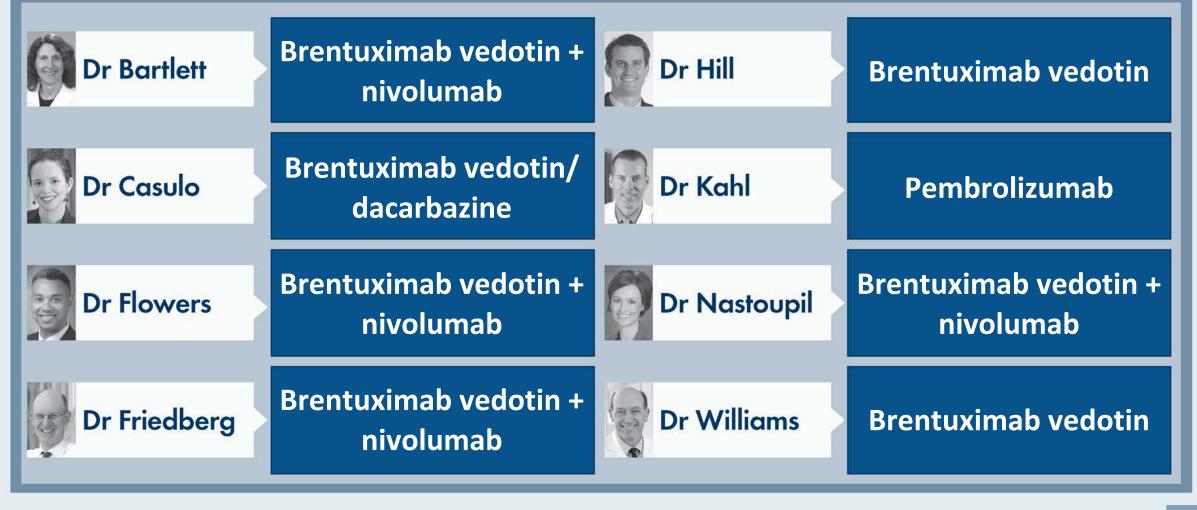


What initial treatment would you recommend for a 26-year-old patient with classical Hodgkin lymphoma (HL) with anemia, diffuse adenopathy, hepatosplenomegaly and diffuse bone marrow involvement?





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?





#### Articles

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

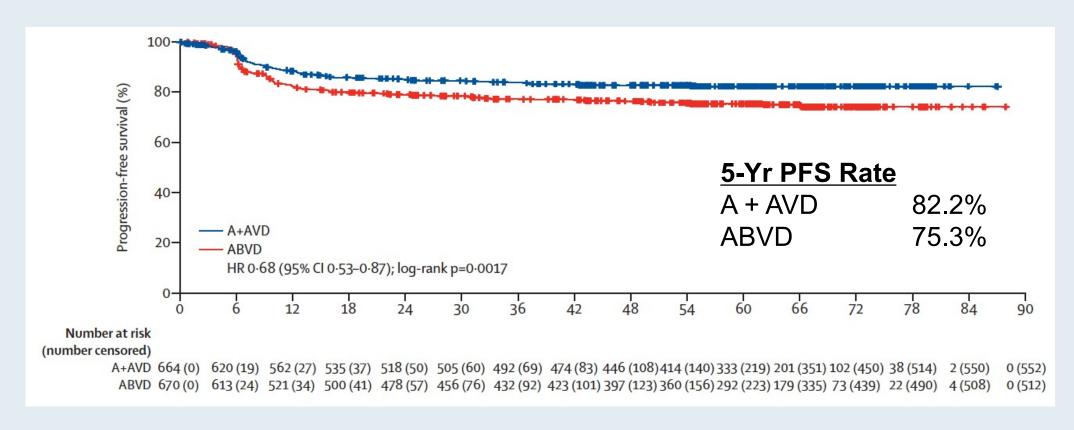


# Brentuximab vedotin with chemotherapy for stage III or IV classical Hodgkin lymphoma (ECHELON-1): 5-year update of an international, open-label, randomised, phase 3 trial

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



### **ECHELON-1: Five-Year Update**



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



original reports

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

Anita Kumar, MD¹; Carla Casulo, MD²; Ranjana H. Advani, MD³; Elizabeth Budde, MD⁴; Paul M. Barr, MD²; Connie L. Batlevi, MD, PhD¹; Philip Caron, MD¹; Louis S. Constine, MD²; Savita V. Dandapani, MD⁴; Esther Drill, MD¹; Pamela Drullinsky, MD¹; Jonathan W. Friedberg, MD²; Clare Grieve, BA¹; Audrey Hamilton, MD¹; Paul A. Hamlin, MD¹; Richard T. Hoppe, MD³; Steven M. Horwitz, MD¹; Ashlee Joseph, BA¹; Niloufer Khan, MD¹; Leana Laraque, BA¹; Matthew J. Matasar, MD¹; Alison J. Moskowitz, MD¹; Ariela Noy, MD¹; Maria Lia Palomba, MD¹; Heiko Schöder, MD¹; David J. Straus, MD¹; Shreya Vemuri, BA¹; Joanna Yang, MD⁵; Anas Younes, MD⁶; Andrew D. Zelenetz, MD, PhD¹; Joachim Yahalom, MD¹; and Craig H. Moskowitz, MD⁵

J Clin Oncol 2021;[Online ahead of print].



### Multicenter Pilot Study of BV + AVD with or without Consolidative Radiation Therapy for Early-Stage, Unfavorable-Risk Hodgkin Lymphoma

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

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

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



### 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



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

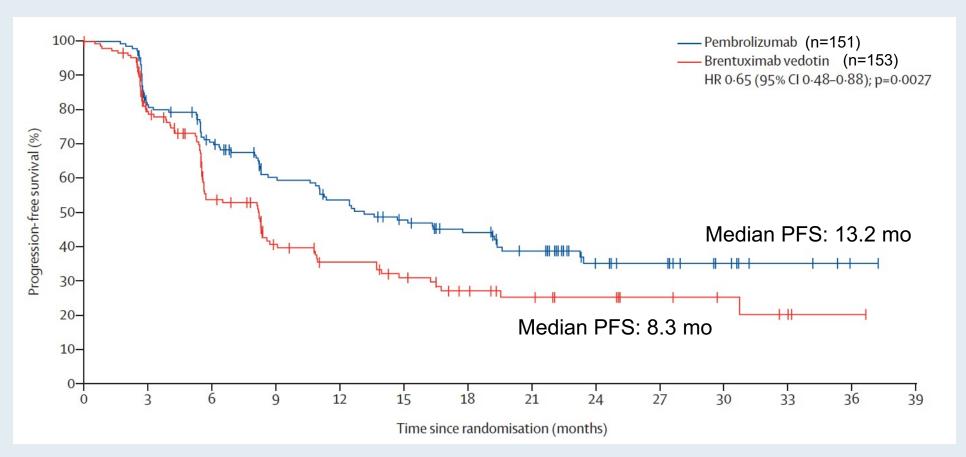


Pembrolizumab versus brentuximab vedotin in relapsed or refractory classical Hodgkin lymphoma (KEYNOTE-204): an interim analysis of a multicentre, randomised, open-label, phase 3 study

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



#### **KEYNOTE-204: Interim Analysis**



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



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

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

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



### 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



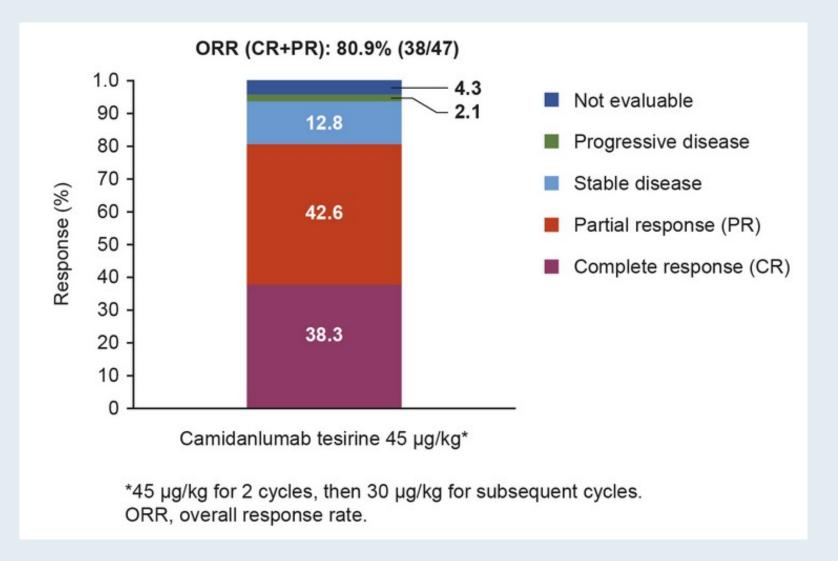
Preliminary Results of a Phase 2 Study of Camidanlumab Tesirine (Cami), a Novel Pyrrolobenzodiazepine-Based Antibody-Drug Conjugate, in Patients with Relapsed or Refractory Hodgkin Lymphoma

Herrera AF et al.

ASH 2020; Abstract 2020.



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





### **Follicular Lymphoma**

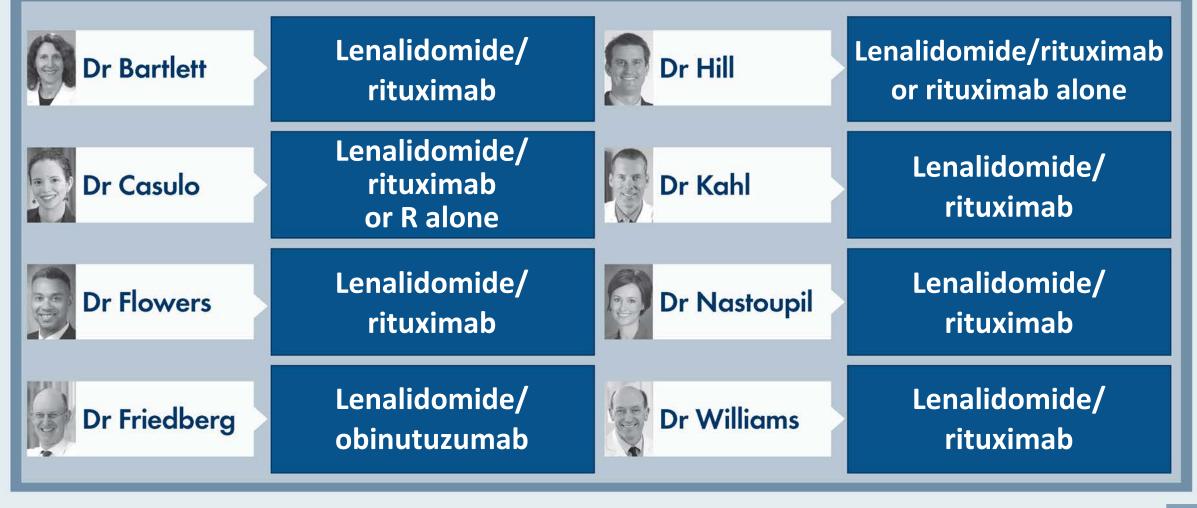


# What treatment do you generally recommend for an <u>otherwise</u> <u>healthy 65-year-old</u> patient with symptomatic FL requiring treatment?

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

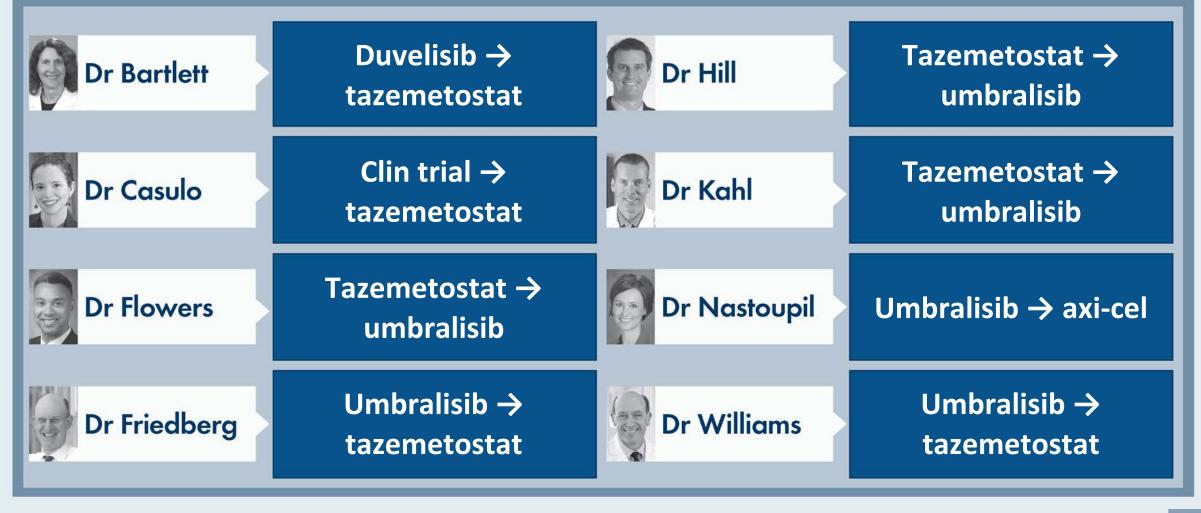


Regulatory and reimbursement issues aside, what is your usual second-line therapy for a 65-year-old patient with FL who achieves a complete response to 6 cycles of bendamustine/rituximab (BR) but then experiences disease <u>relapse 4 years later?</u>





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?





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?





### **Approved PI3K Inhibitors for FL: Indication and Dosing**

	Idelalisib <sup>1</sup>	Copanlisib <sup>2</sup>	Duvelisib <sup>3</sup>	Umbralisib <sup>4</sup>
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



<sup>&</sup>lt;sup>1</sup>Gopal AK et al. N Engl J Med 2014;370(11):1008-18; Idelalisib package insert, January 2018.

<sup>&</sup>lt;sup>2</sup> Dreyling M et al. *J Clin Oncol* 2017;35(35):3898-905; Copanlisib package insert, September 2017.

<sup>&</sup>lt;sup>3</sup> 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. <sup>4</sup> Umbralisib package insert, February 2021.

#### Lancet Oncol 2021;22:678-89

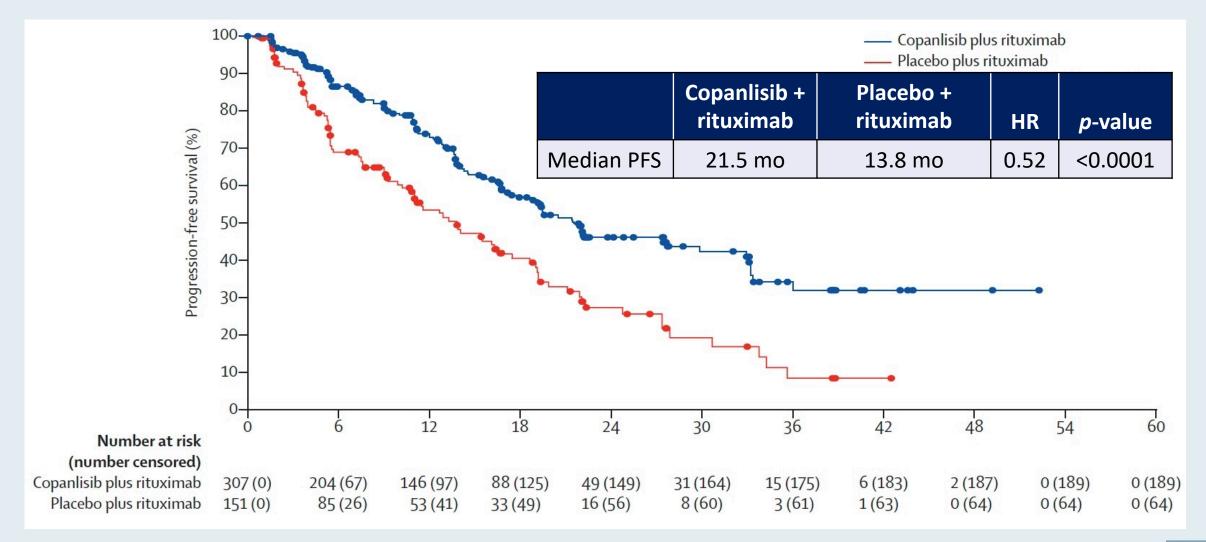


Copanlisib plus rituximab versus placebo plus rituximab in patients with relapsed indolent non-Hodgkin lymphoma (CHRONOS-3): a double-blind, randomised, placebo-controlled, phase 3 trial

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





### 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."



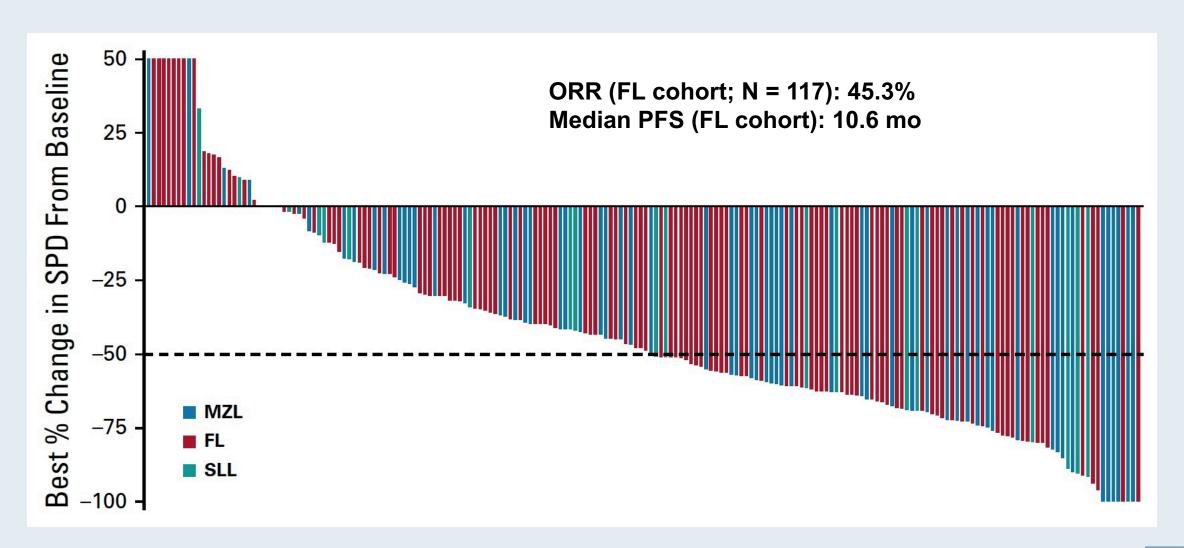
# <sup>®</sup> Umbralisib, a Dual PI3Kδ/CK1ε Inhibitor in Patients With Relapsed or Refractory Indolent Lymphoma Nathan H. Fowler, MD¹; Felipe Samaniego, MD¹; Wojciech Jurczak, MD, PhD²; Nilanjan Ghosh, MD, Ph James A. Reeves, MD6; Wanda Knopińska-Posłuszny, MD7; Chan Y. Cheah, DMSc8; Tycel Phillips, MD9; Ew Bruce D. Cheson, MD¹¹; Paolo F. Caimi, MD¹²; Sebastian Grosicki, MD, PhD¹³; Lori A. Leslie, MD¹⁴; Jul Gustavo Fonseca, MD¹6; Sunil Babu, MD¹7; Daniel J. Hodson, MD¹8; Spencer H. Shao, MD¹9; John M. Ey Jeff P. Sharman, MD²¹; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Hari P. Miskin, MSc²⁴; Peter Starman, MD²¹; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Hari P. Miskin, MSc²⁴; Peter Starman, MD²¹; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Hari P. Miskin, MSc²⁴; Peter Starman, MD²¹; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Hari P. Miskin, MSc²⁴; Peter Starman, MD²¹; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Hari P. Miskin, MSc²⁴; Peter Starman, MD²¹; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Hari P. Miskin, MSc²⁴; Peter Starman, MD²²; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Hari P. Miskin, MSc²⁴; Peter Starman, MD²²; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Jennie Y. Law, MD²²; John M. Pagel, MD²²; Jennie Y. Law, MD²²; Jennie Y. Law, MD²²; John M. Pagel, MD²²; Jennie Y. Law, MD²²; Jennie

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

J Clin Oncol 2021;39:1609-18



### **Umbralisib for Heavily Pretreated R/R Indolent NHL**





#### Lancet Oncol 2020;21:1433-42

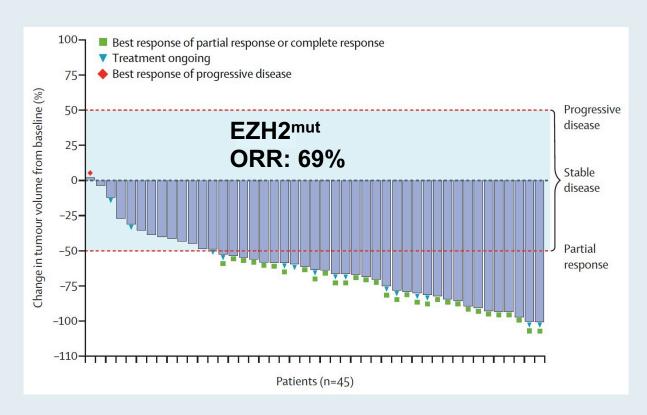
## Tazemetostat for patients with relapsed or refractory follicular lymphoma: an open-label, single-arm, multicentre, phase 2 trial

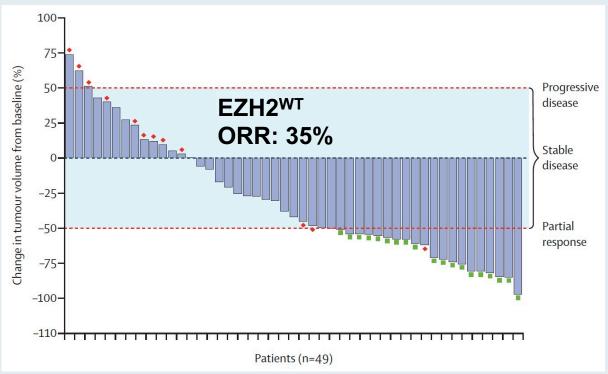


Franck Morschhauser, Hervé Tilly, Aristeidis Chaidos, Pamela McKay, Tycel Phillips, Sarit Assouline, Connie Lee Batlevi, Phillip Campbell, Vincent Ribrag, Gandhi Laurent Damaj, Michael Dickinson, Wojciech Jurczak, Maciej Kazmierczak, Stephen Opat, John Radford, Anna Schmitt, Jay Yang, Jennifer Whalen,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



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







#### **Structure of Selected Bispecific Antibodies**

Bi-Specific Antibody	Targets	Design	lg Fragment Formats
blinatumomab	CD19 x CD3	CONT.	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		<ul> <li>humanized mouse heterodimeric IgG1-based antibody</li> <li>monovalent CD20 and monovalent CD3 binding</li> <li>modified Fc devoid of FcyR and complement binding</li> </ul>
glofitamab	(CD20) <sub>2</sub> x CD3		<ul> <li>humanized mouse IgG1-based antibody</li> <li>bivalent CD20 and monovalent CD3c binding</li> <li>modified Fc devoid of FcyR and complement binding</li> </ul>
odronextamab	CD20 x CD3	H	<ul> <li>fully human IgG4-based heterodimeric antibody</li> <li>monovalent CD20 and monovalent CD3ε binding</li> <li>Fc-dependent effector function-minimized antibody with Fc of the anti-CD3ε heavy chain modified to reduce Protein A binding</li> <li>common κ light chain from anti-CD3ε mAb</li> </ul>
epcoritamab	CD20 x CD3		<ul> <li>humanized mouse IgG1-based heterodimeric antibody</li> <li>monovalent CD20 and monovalent CD3 binding</li> <li>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</li> </ul>
Ig, immunoglobulin; scFv, sir	ngle-chain variable frag	ment; mAb, monoclor	nal antibody; Fc, fragment crystallizable; FcγR, Fc gamma receptor



## 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."



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

"City of Hope, Duarte, CA, USA; "BC Cancer Centre for Lymphoid Cancer and University of British Columbia, Vancouver, BC, Canada; "Memorial Sloan Kettering Cancer Center, New York, NY, USA; "Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; "Jewish General Hospital, Montreal, OC, Canada; "Royal Adelaide Hospital, Australia; "Princess Margaret Cancer Centre, Toronto, ON, Canada; "Hospital University of Le Paz, Medirid, Spain; "Universital Heidelberg, Heidelberg, Germany; "St Vincent's Hospital and Royal North Shore Hospital, Sydney, Australia; "St Vincent's Hospital, University of Melbourne, Melbourne, Australia; "MO Anderson Cancer Center, Houston, TX, USA; "Generatech, Inc., South San Francisco, CA, USA; "Froffmann-La Roche Ltd, Mississauga, ON, Canada; "Roche Products Ltd, Welvyn Garden City, United Kingdom;" "Siteman Center, Weshington University School of Medicine, St. Louis, MO, USA

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

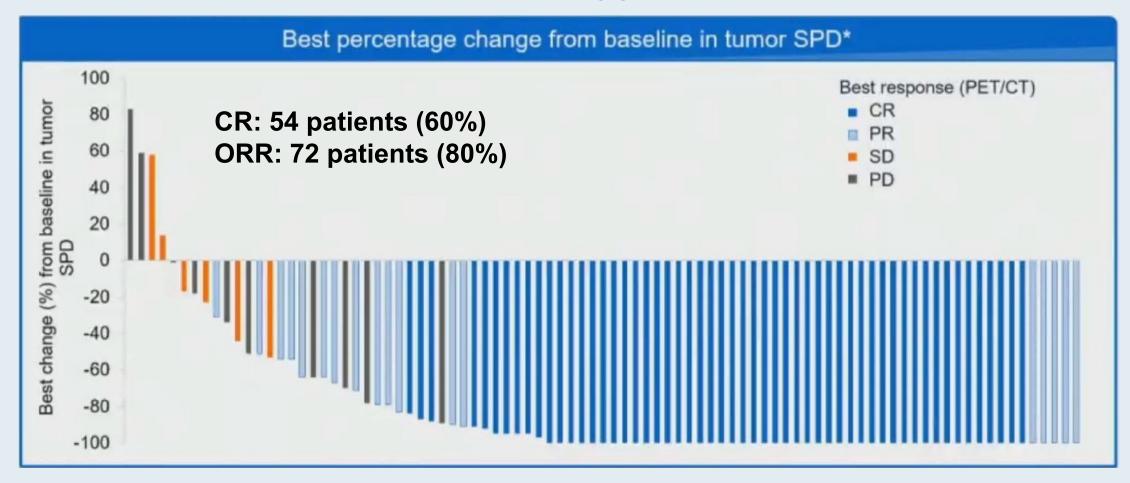


63rd ASH Annual Meeting and Exposition





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



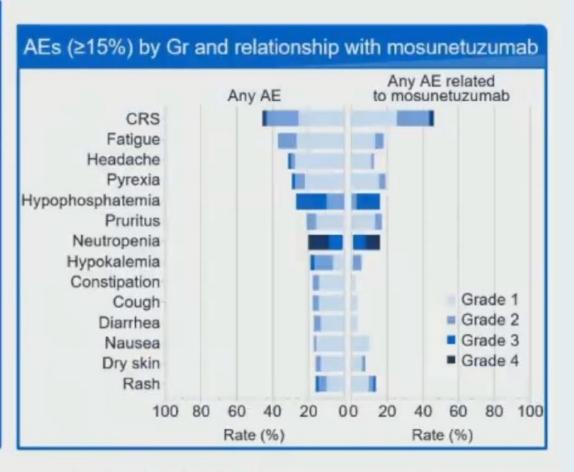
Median DoR: 22.8 months

Median PFS: 17.9 months



## 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%)‡



<sup>\*</sup>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



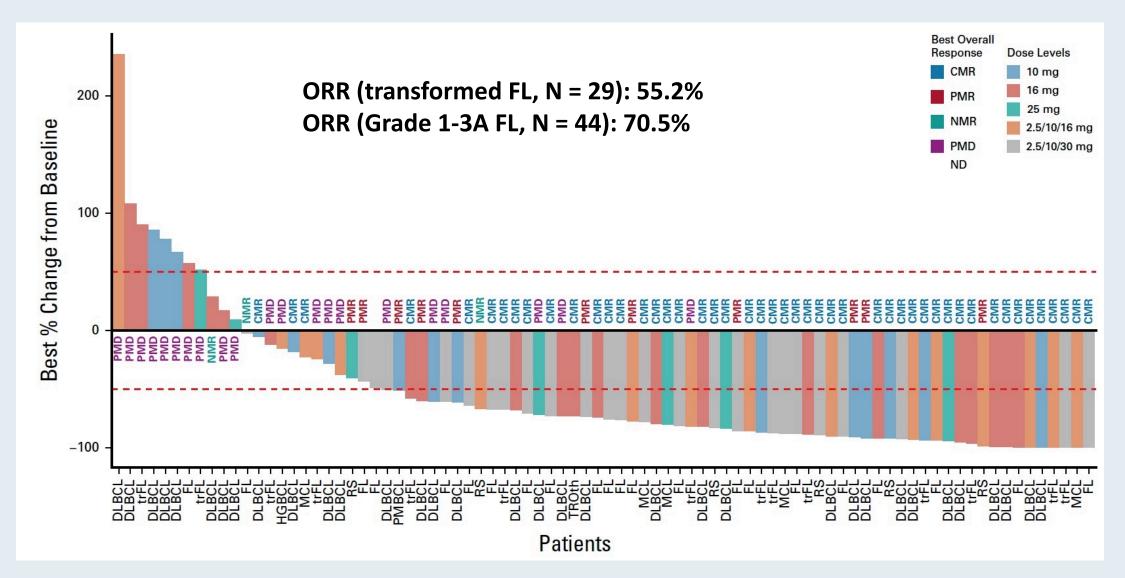
# Glofitamab, a Novel, Bivalent CD20-Targeting T-Cell-Engaging Bispecific Antibody, Induces Durable Complete Remissions in Relapsed or Refractory B-Cell Lymphoma: A Phase I Trial

Martin Hutchings, PhD¹; Franck Morschhauser, MD, PhD²; Gloria Iacoboni, MD³,⁴; Carmelo Carlo-Stella, MD⁵; Fritz C. Offner, MD, PhD⁶; Anna Sureda, MD, PhDˀ; Gilles Salles, MD˚; Joaquín Martínez-Lopez, MD, PhD, MBAց; Michael Crump, MD¹o; Denise N. Thomas, MSc¹¹; Peter N. Morcos, PharmD¹¹; Cristiano Ferlini, MD¹¹; Ann-Marie E. Bröske, PhD¹²; Anton Belousov, PhD¹³; Marina Bacac, PhD¹³; Natalie Dimier, PhD¹⁴; David J. Carlile, PhD¹⁴; Linda Lundberg, PhD¹⁵; David Perez-Callejo, MD, PhD¹⁵; Pablo Umaña, PhD¹³; Tom Moore, MD¹²; Martin Weisser, MD¹²; and Michael J. Dickinson, MBBS, DMedSci¹⁶

J Clin Oncol 2021;39:1959-70.



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





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

CHU Lille, Service des Maladies du Sang, F-59000 Lille, France; <sup>3</sup>Humanitas University and Humanitas Research Hospital, Milan, Italy; <sup>3</sup>Peter MacCallum Cancer Centre, Royal Melibourne Hospital and The University of Melibourne, Australia; <sup>3</sup>University of Milchigan Madicial School, Ann Arbor, Michigan, USA; <sup>3</sup>CHU de Rennes, Université of Milan, Italy; <sup>3</sup>Rigsherines Gente, University of Milan, Italy; <sup>3</sup>Rigshespitalet, Copenhagen, Denmark; <sup>3</sup>Institut Catala d'Oncologia Hospitalet, IDIBELL, Universitat de Barcelona, Barcelona, Spain; <sup>3</sup>Hospital Universitat de Octubre (H12O), Centro Nacional de Investigaciones Oncològicas (CNIO)-H12O and Universidad Complutense de Madrid, Madrid, Spain; <sup>13</sup>Wroclaw Medical University, Wroclaw, Poland; <sup>13</sup>National Taiwan Université Claude Bernerd, Pierre-Bénite, France.

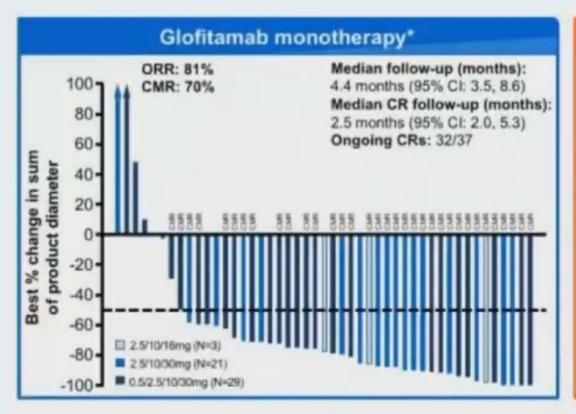
Accepted as an Oral Presentation at the 63rd ASH Annual Meeting and Exposition

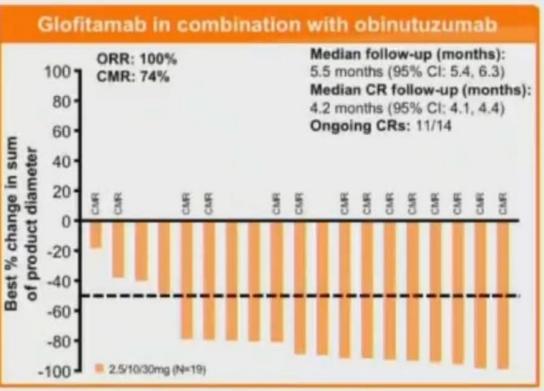


63rd ASH' Annual Meeting and Exposition



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





- · Deep responses observed across glofitamab dosing regimens; most complete responses were ongoing
- Myelosuppression was more common with the combination
- CRS rates were high and comparable, and cases were mainly low grade



## 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."



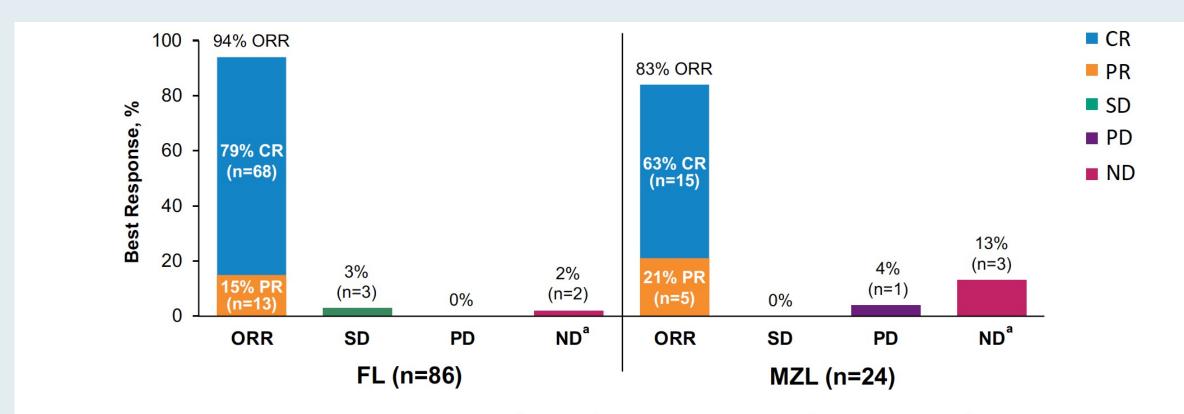
## Long-Term Follow-Up Analysis of ZUMA-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

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

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



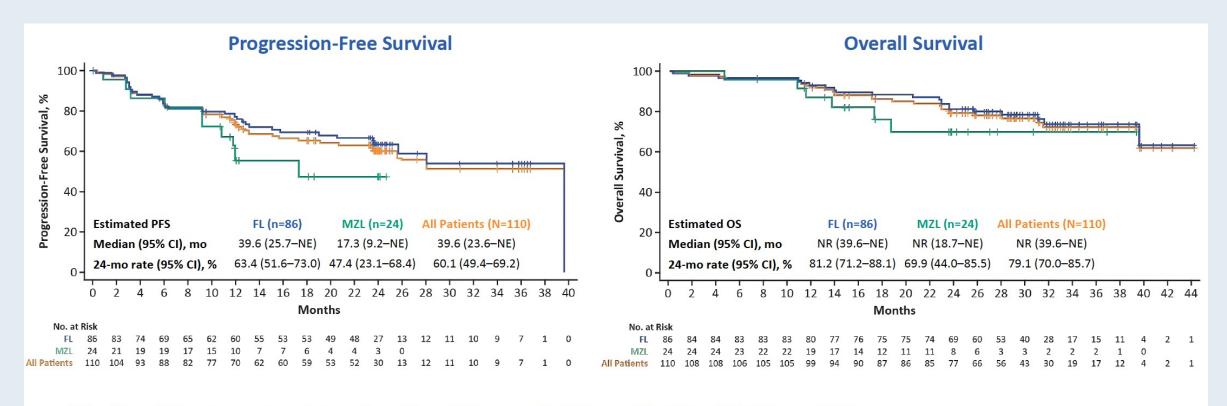
#### **ZUMA-5: ORR by Central Review**



- 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



#### **ZUMA-5: Progression-Free and Overall Survival**



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



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

	Follicular L (N=1	'	Marginal Zon (N=		All Pat (N=1	
AE, n (%)	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<sup>b</sup>
  - 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<sup>c</sup> (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)



<sup>&</sup>lt;sup>a</sup> 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). <sup>b</sup> No Grade 5 AEs were due to progressive disease.

<sup>&</sup>lt;sup>c</sup> The Grade 5 PML event occurred after axi-cel retreatment.

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

**Catherine Thieblemont,** Michael Dickinson, Joaquin Martinez-Lopez, Arne Kolstad, Jason P. Butler, Monalisa Ghosh, Leslie L. Popplewell, Julio C. Chavez, Emmanuel Bachy, Koji Kato, Hideo Harigae, Marie José Kersten, Charalambos Andreadis, Arne Kolstad, Arne Kolstad, Jason P. Butler, Monalisa Ghosh, Leslie L. Popplewell, Julio C. Chavez, Arnori C. Chavez, Andreadis, Arnori C. Chavez, Arno

Department of Hemato-Oncology, Saint Louis Hospital, Paris, France; <sup>2</sup>Department of Clinical Haematology, Peter MacCallum Cancer Centre and The Royal Melbourne Hospital, Robourne, Australia; <sup>2</sup>Ocentro de Investigación Biomédica en Red Cáncer (CIBERONC), Hospital University Complutense University, CNIO, Madnd, Spain; <sup>4</sup>Oslo University Hospital Radiumhospitalet, Oslo, Norway, <sup>5</sup>Royal Brisbane and Women's Hospital, Brisbane, Australia; <sup>8</sup>Michigan Medicine University of Michigan, Ann Arbor, MI, USA; <sup>5</sup>Division of Malignant Hematology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; <sup>5</sup>Hospital, Brisbane Augustian, Paris Paris Center and Research Institute, Tampa, FL, USA; <sup>5</sup>Hospital, Brisbane Augustian, Paris Paris Center and Research Institute, Tampa, FL, USA; <sup>5</sup>Hospital, Sendai, Japan, <sup>11</sup>Tohoku University Hospital, Sendai, Japan, <sup>12</sup>Amsterdam UMC, Department of Hematology, Amsterdam UMC, University of Amsterdam, A



#### **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)	
ORRa	<b>86.2</b> (77.5-92.4)	
CRR <sup>a</sup>	<b>69.1</b> (58.8-78.3)	
12-mo PFS	<b>67.0</b> (56.0-75.8)	
9-mo DOR	<b>76.0</b> (64.6-84.2)	

<sup>a</sup>ORR and CRR were comparable with the primary efficacy analysis (ORR 86.2% and CRR 66.0%).



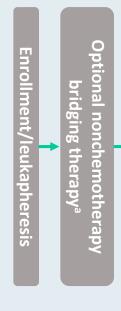
#### **Mantle Cell Lymphoma**



#### 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



#### Conditioning chemotherapy + axi-cel infusion

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

#### **Primary endpoint**

• CRb

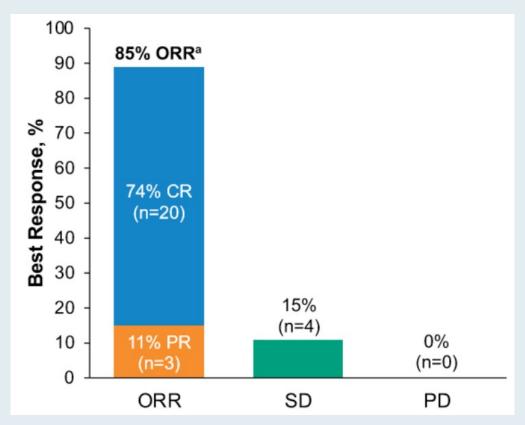
#### **Key secondary endpoints**

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



### **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%)



## 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."



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

The NEW ENGLAND JOURNAL of MEDICINE

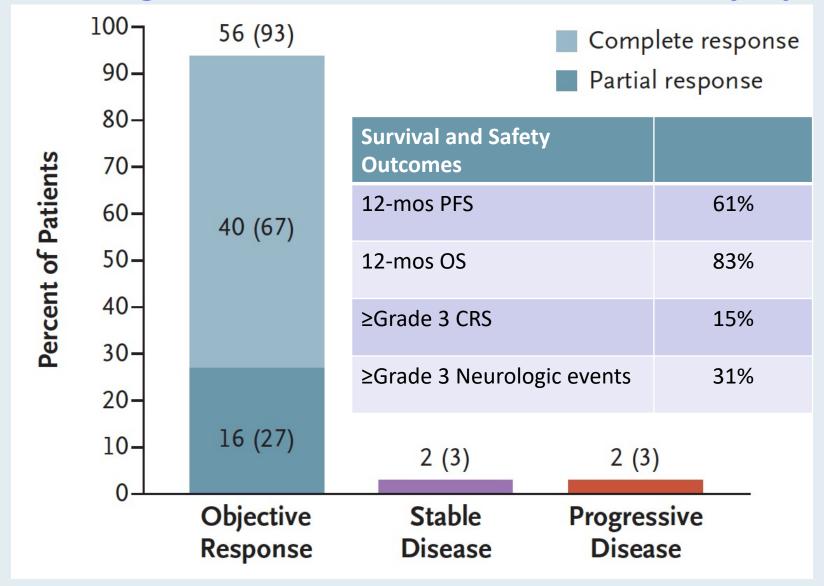
#### ORIGINAL ARTICLE

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

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



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





# Meet The Professor Current and Future Management of Chronic Lymphocytic Leukemia

Thursday, March 17, 2022 5:00 PM – 6:00 PM ET

**Faculty** 

Peter Hillmen, MB ChB, 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.

