Data + Perspectives: Clinical Investigators Discuss the Current and Future Management of Non-Hodgkin Lymphoma

A Virtual CME Satellite Symposium Series in Conjunction with the Society of Hematologic Oncology 2021 Annual Meeting

Tuesday, August 31, 2021
7:00 PM – 8:00 PM ET

Faculty

Andrew M Evens, DO, MSc
Ian W Flinn, MD, PhD
Gilles Salles, MD, PhD

Moderator

Neil Love, MD

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Faculty

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Associate Vice Chancellor, Clinical Innovation and Data Analytics
Rutgers Biomedical and Health Sciences, Rutgers University
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Nashville, Tennessee

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Commercial Support

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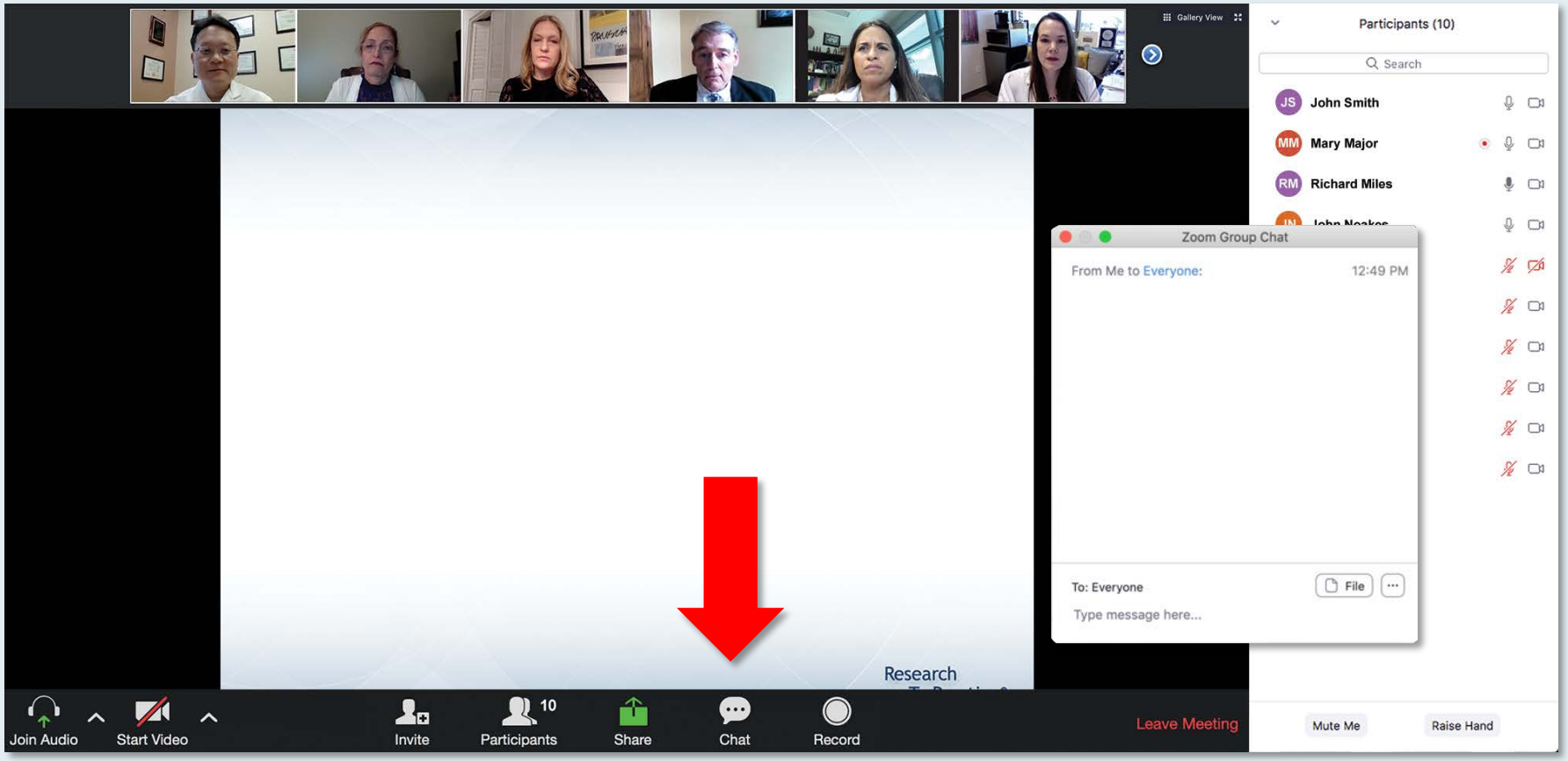
We Encourage Clinicians in Practice to Submit Questions



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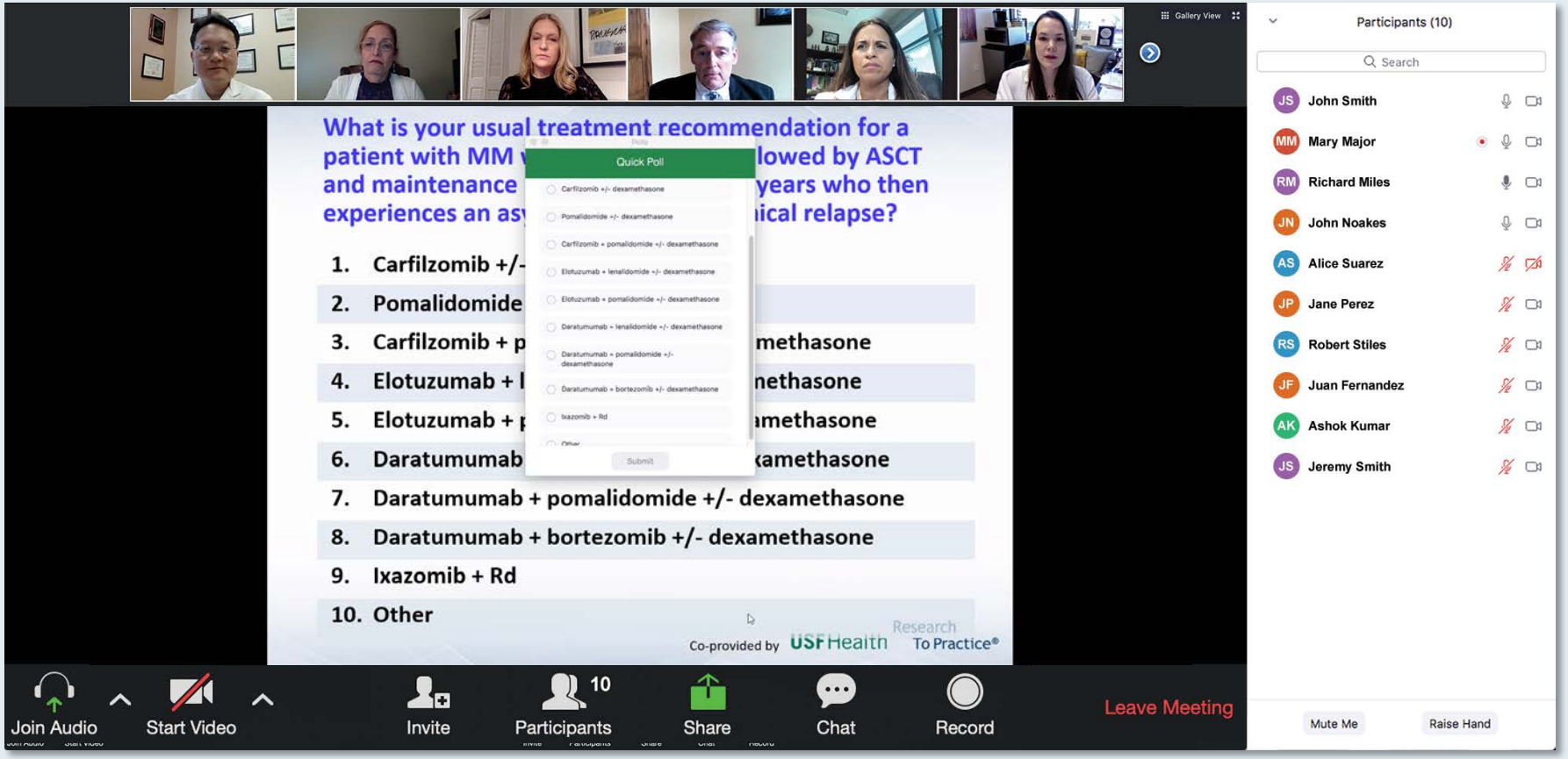

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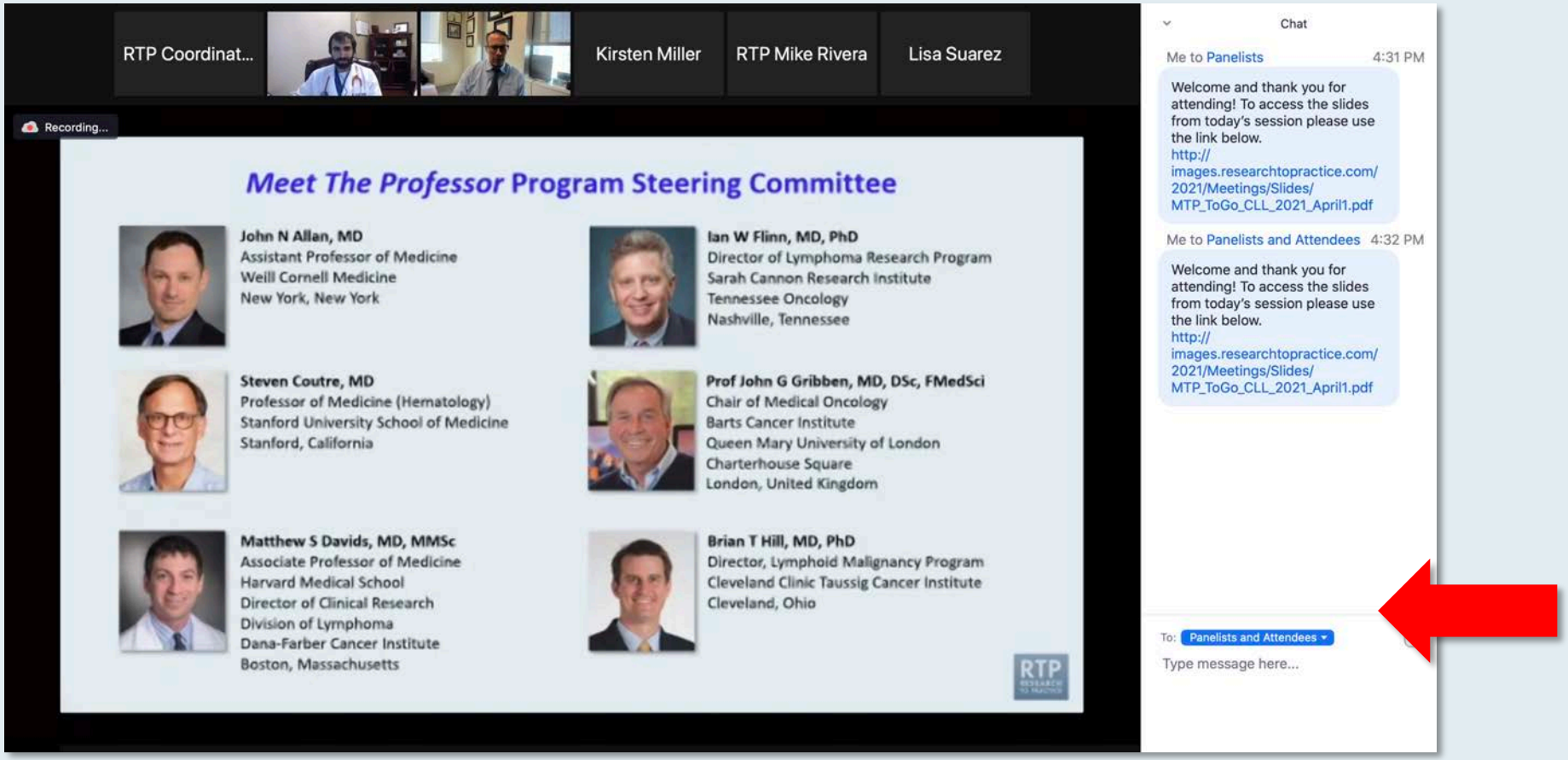

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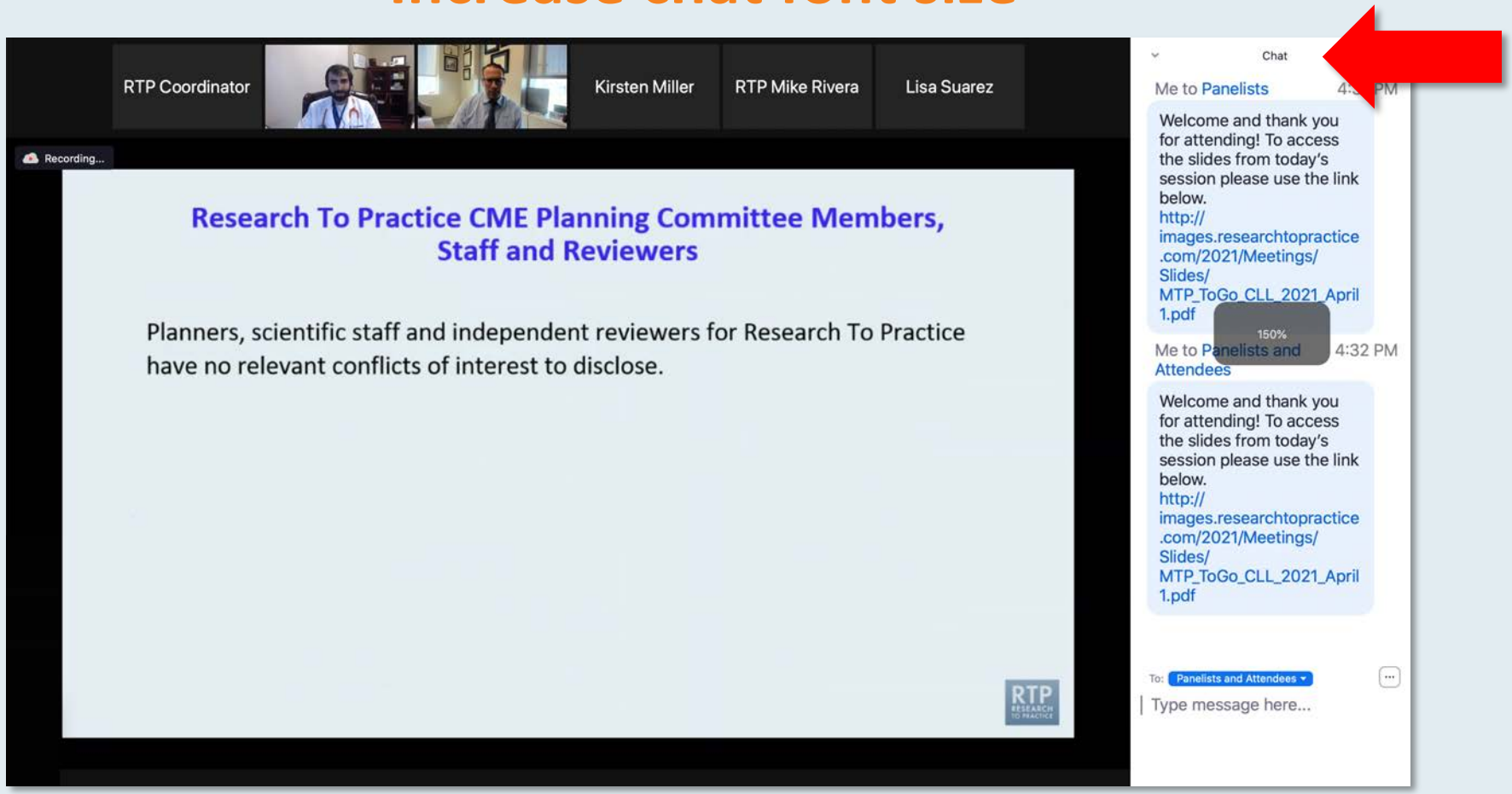

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You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Key Presentations on Non-Hodgkin and Hodgkin Lymphomas from the 2020 ASH Annual Meeting

DR LAURIE SEHN

BC CANCER CENTRE FOR LYMPHOID CANCER

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Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Wednesday, September 1, 2021
5:00 PM – 6:00 PM ET

Faculty

Joyce F Liu, MD, MPH

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Data + Perspectives: Clinical Investigators Discuss the Current and Future Management of Acute Myeloid Leukemia and Myelodysplastic Syndromes

A Virtual CME Satellite Symposium During the Society of Hematologic Oncology 2021 Annual Meeting

Wednesday, September 8, 2021
7:30 PM – 9:00 PM Central Time

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Courtney D DiNardo, MD, MSCE
Daniel A Pollyea, MD, MS
David Sallman, MD
Eunice S Wang, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Exploring Key Issues Affecting the Care of Patients with Metastatic Colorectal Cancer with BRAF Mutations

A CME/MOC-Accredited Virtual Event

Thursday, September 9, 2021
5:00 PM – 6:00 PM ET

Faculty
Scott Kopetz, MD, PhD

Consulting Clinical Investigator
Wells A Messersmith, MD

Moderator
Neil Love, MD

RTP RESEARCH TO PRACTICE

Expert Second Opinion: Investigators Discuss Available Clinical Research in the Care of Patients with Early-Stage Non-Small Cell Lung Cancer

A Live Webinar Held as a Satellite CME/MOC Symposium During the IASLC 2021 World Conference on Lung Cancer Worldwide Virtual Event

Sunday, September 12, 2021
9:15 PM – 10:15 PM MDT / 11:15 PM – 12:15 AM ET

Faculty

Edward B Garon, MD, MS
Harvey I Pass, MD
Heather Wakelee, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Addressing Current Questions and Controversies in the Management of Prostate Cancer

A Virtual CME Satellite Symposium During the the American Urological Association (AUA) 2021 Annual Meeting

Monday, September 13, 2021
5:30 PM – 7:00 PM ET / 2:30 PM – 4:00 PM PT

Faculty

Maha Hussain, MD, FACP, FASCO
A Oliver Sartor, MD
Neal D Shore, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

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

Faculty

Loretta Nastoupil, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.

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Associate Vice Chancellor, Clinical Innovation and Data Analytics
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Associate Director (Clinical Services), Rutgers Cancer Institute of New Jersey
Professor of Medicine, Rutgers Robert Wood Johnson Medical School
System Director of Medical Oncology, and Oncology Lead for the Combined Medical Group
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Service Chief, Lymphoma Service
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Sarah Cannon Research Institute
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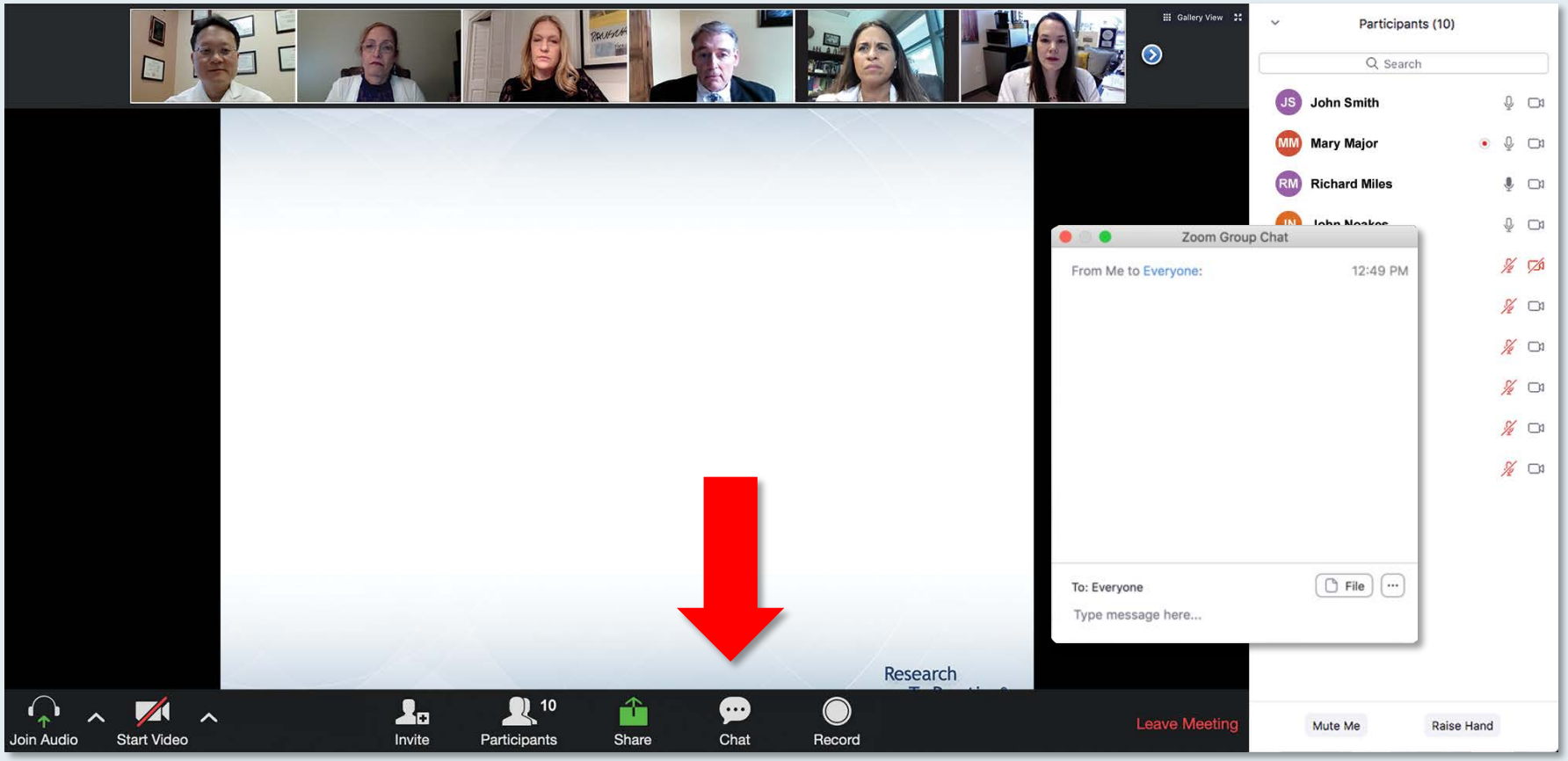

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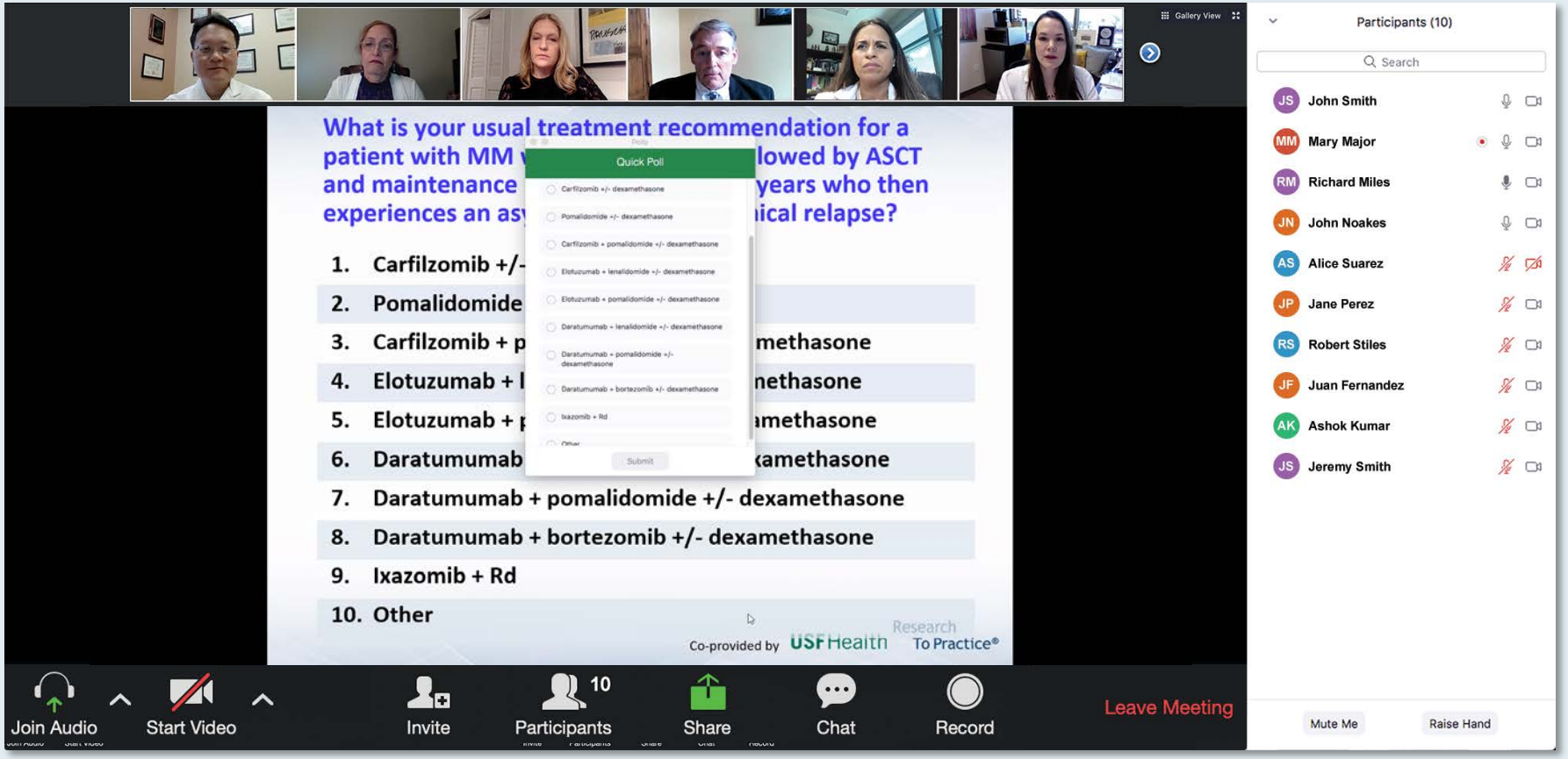

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Agenda
Top 13 Questions in Non-Hodgkin Lymphoma

Module 1: Follicular Lymphoma (FL)

- What is the optimal line of treatment to use R-squared, and when using it up front what dose and duration of rituximab and lenalidomide do you use?
- When should a PI3K inhibitor be used in FL and how do you select the best agent?
- What is the optimal role of tazemetostat and how do you select and use EZH2 assays? What are the key tolerability issues with this agent?
- What is known about the efficacy and tolerability of anti-CD20xCD3 T-cell engaging bispecific agents, including mosunetuzumab, in FL?

Module 2: Mantle Cell Lymphoma (MCL)

- When should a BTK inhibitor be introduced into treatment of MCL and how do you select a specific agent? What is known about pirtobrutinib?
- In what situations do you use venetoclax for MCL and how do you use it (alone or in combination)? What type of ramp-up schedule do you utilize?
- In what situations do you generally refer patients with MCL to receive CAR-T? What outcomes have you observed?

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Agenda
Top 13 Questions in Non-Hodgkin Lymphoma

Module 3: Diffuse Large B-Cell Lymphoma (DLBCL)

- What is your current use of polatuzumab vedotin and do you expect to be using it in the first-line setting in DLBCL? What are the key tolerability issues with this agent?
- What is the role of lenalidomide/tafasitamab in DLBCL and how does it compare to R-squared?
- What is the optimal role of loncastuximab tesirine in DLBCL? What are the key tolerability issues with this agent?

Module 4: CAR T-Cell Therapy in Lymphoma

- What are some of the key functional issues, including age, in determining eligibility for CAR-T?
- What is the current optimal clinical situation (ie, line of treatment) in which to use CAR-T in DLBCL and do you expect it to replace ASCT in the near future?
- Which specific features differentiate the approved CAR-T products and are there specific clinical situations where you favor one over another?

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Agenda

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Module 2: Mantle Cell Lymphoma (MCL)

Module 3: Diffuse Large B-Cell Lymphoma (DLBCL)

Module 4: CAR T-Cell Therapy in Lymphoma

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What is the optimal line of treatment to use R-squared, and when using it up front what dose and duration of rituximab and lenalidomide do you use?

When should a PI3K inhibitor be used in FL and how do you select the best agent?

Regulatory and reimbursement issues aside, what would be your most likely initial treatment choice for a 78-year-old patient with Stage III, Grade I or II FL with fatigue and symptomatic bulky adenopathy who requires treatment?

1. Rituximab
2. BR
3. R-CHOP
4. R-CVP
5. Obinutuzumab/bendamustine
6. Obinutuzumab/CHOP
7. Rituximab/lenalidomide
8. Other

If you were going to administer a PI3 kinase inhibitor to a patient with relapsed/refractory FL, which do you generally prefer?

1. Idelalisib
2. Copanlisib
3. Duvelisib
4. Umbralisib

Case Presentation – Dr Evens: A 71-year-old man with relapsed/refractory (R/R) FL

- A 71-year-old man on routine physical noted to have an inguinal hernia with an associated adjacent enlarged lymph node. CT imaging in August 2018 showed a left inguinal node measuring 2.7cm, a second inguinal node 1.4cm, a left external iliac node 1.8cm, and a right inguinal node 1.8cm. The patient then had hernia repair along with excisional node biopsy in 9/18, the latter showing pathology diagnosis of follicular lymphoma grade 1/2 of 3.
- Staging PET in 10/18 showed multiple hypermetabolic lesions including extensive foci throughout the neck including parotid and submandibular glands all <1.0 with SUV up to 8.9 and also in the left mediastinum with SUV 6.0 and right posteromedial pleural-based 1.4 x 0.5 cm with SUV 2.8, right inguinal 2 x 2.2 cm with SUV 8.7, left inguinal 1.8 x 1.3 cm with SUV 8.7, and right external iliac 2.1 x 1.4 cm.
- After a long discussion, the patient strongly preferred therapy. The patient received 4 induction weekly doses of single-agent rituximab December 2018 into a partial remission (PR) and initiated single-agent rituximab maintenance therapy in February 2019 being given q 8 weeks through December 2020 in a metabolic CR. The patient then had a PET/CT (3/9/21) that showed multiple hypermetabolic subcutaneous nodules including on the right upper back, the left back, a left inguinal node, a right inguinal node, the subcutaneous tissues of left lateral thigh.

What is the optimal role of tazemetostat and how do you select and use EZH2 assays? What are the key tolerability issues with this agent?

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 BR but then experiences disease relapse 4 years later?

1. Re-treatment with BR
2. Obinutuzumab/bendamustine
3. R-CHOP
4. Rituximab/lenalidomide
5. A PI3K inhibitor
6. Tazemetostat
7. Other

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

1. Idelalisib
2. Copanlisib
3. Duvelisib
4. Umbralisib
5. Tazemetostat
6. R-CHOP
7. Obinutuzumab +/- chemotherapy
8. Other

Case Presentation – Dr Flinn: A 67-year-old woman with R/R FL and a EZH2 mutation

67-year-old woman was diagnosed with follicular lymphoma 7 years ago wen she presented with asymptomatic inguinal adenopathy. Biopsy reveals FCC grade 2 disease. CT and PET scans reveal bilateral axillary, right inguinal, l retroperitoneal, and mesenteric adenopathy. Largest mass is 2.5 CM in mesentery with SUV of 6.

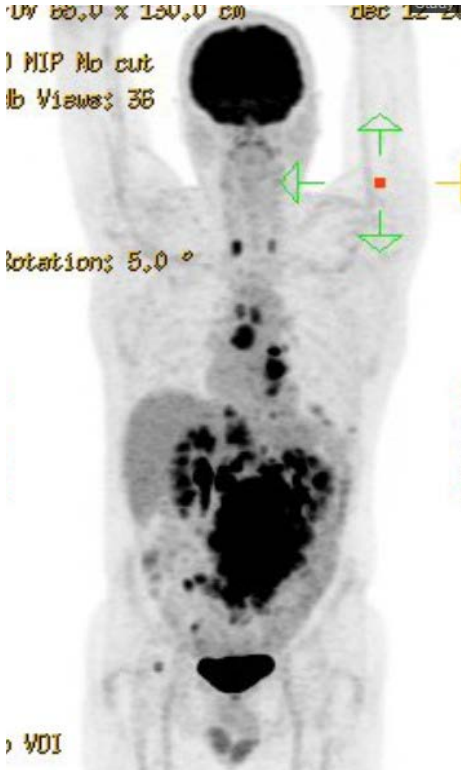
The patient is asymptomatic and is observed for 2 years until she progresses and develops symptoms in right inguinal mass. She is treated with BR for 6 cycles and achieves a CR. Three years later she again has symptomatic progression. PET scan reveals max SUV of 7.

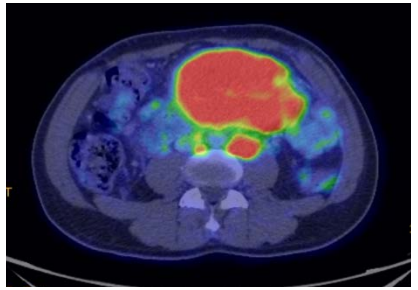
Biopsy of a mesenteric mass which has the highest SUV reveals continued grade 2 disease She denies B symptoms but once again has pain in right inguinal area and develops edema in right leg.

She is started on lenalidomide and rituximab (R^2). She tolerates therapy well except for rash and diarrhea. She achieves PR and does well for 2 years until she again has symptomatic progression. Testing of her original biopsy reveals an EZH2 mutation. At this time, she is started on tazemetostat.

Case Presentation – Dr Salles: A 61-year-old man with R/R FL

- 61 year old man
- Previous medical history: high blood pressure, hypothyroidism
- In 2017
  - grade 1 follicular lymphoma. Ann Arbor stage IV (marrow involvement)
  - Treated with 6 cycles of R-benda – achieved a CR
  - No maintenance
- In 2019
  - Inguinal recurrence. Biopsy confirmed FL grade 1-2 – disseminated - mode bulk
  - Treated with Lenalidomide – Rituximab according to the Augment schema
  - Reached a PET-CR (bone marrow not controlled
- Today (65 years)
  - Disease recurrence in the abdomen
  - LDH = 1.5 times UNL
  - Blood counts normal; ECOG performance status = 1
  - Biopsy in the abdominal mass : FL without transformation
  - Sequencing panel shows mutations in CREBBP, KMT2D, and EZH2





Case Presentation – Dr Salles: A 61-year-old man with R/R FL (continued)

Treatment options

1. R-CHOP followed by ASCT
2. Copanlisib + rituximab
3. Axicabtagene ciloleucel
4. Repeat R-Benda
5. Tazemetostat

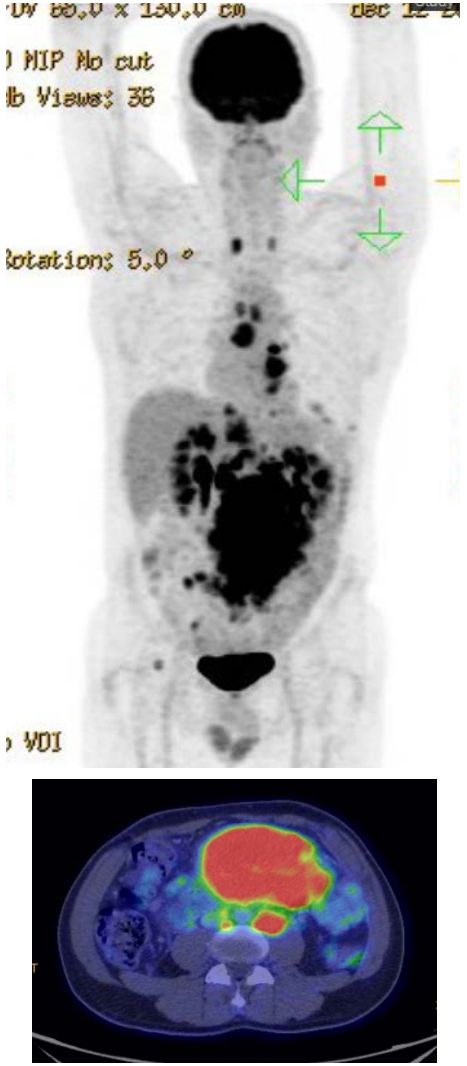
65 years old

Case Presentation – Dr Salles: A 61-year-old man with R/R FL (continued)

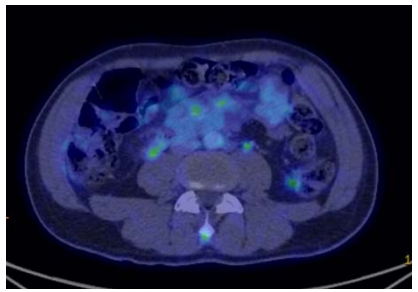
Treatment chosen

1. Axicabtagene ciloleucel

Pre CAR T cell



3 months post CAR T cell



What is known about the efficacy and tolerability of anti-CD20xCD3 T-cell engaging bispecific agents, including mosunetuzumab, in FL?

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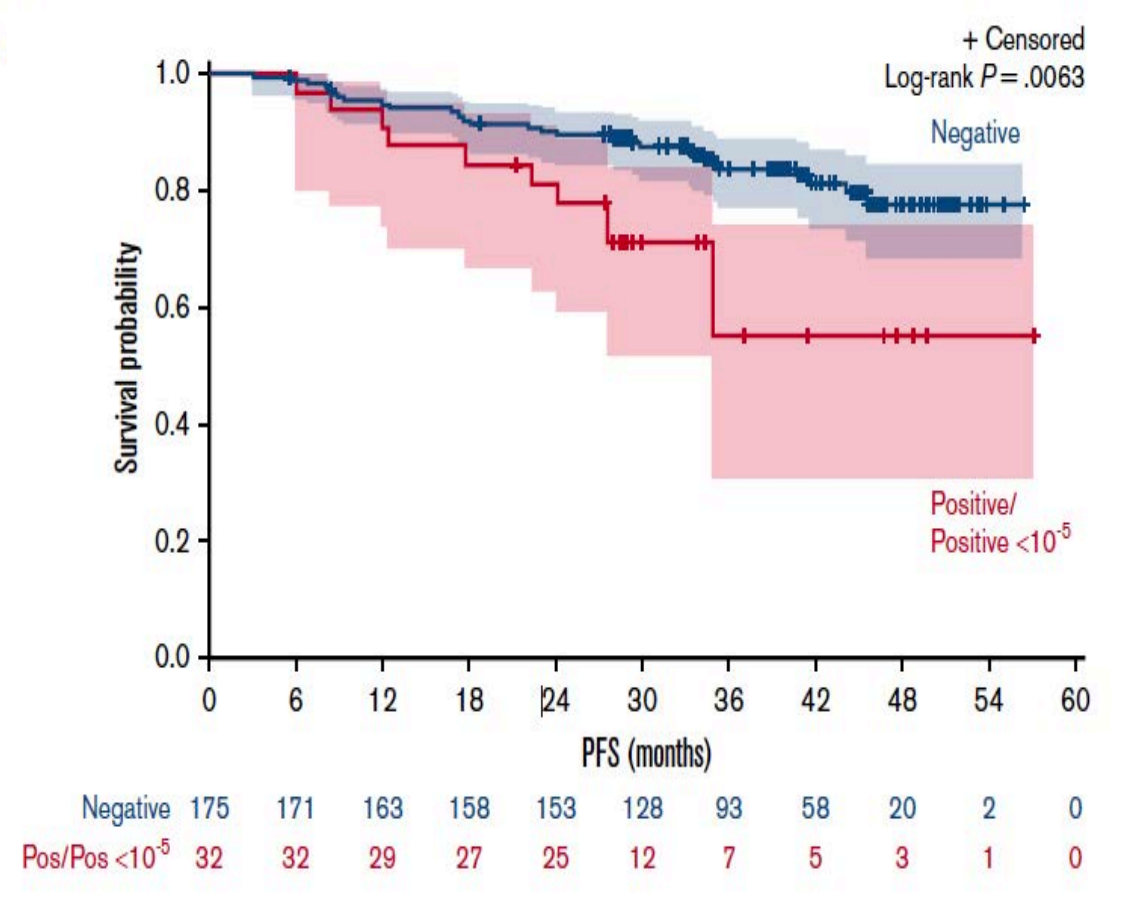
Key Recent Data Sets

LYSA Ancillary RELEVANCE Study: Rates of Molecular Response with Lenalidomide/Rituximab (R^2) in untreated FL

Impact of positive MRD at week 24 on PFS in PB and/or BM



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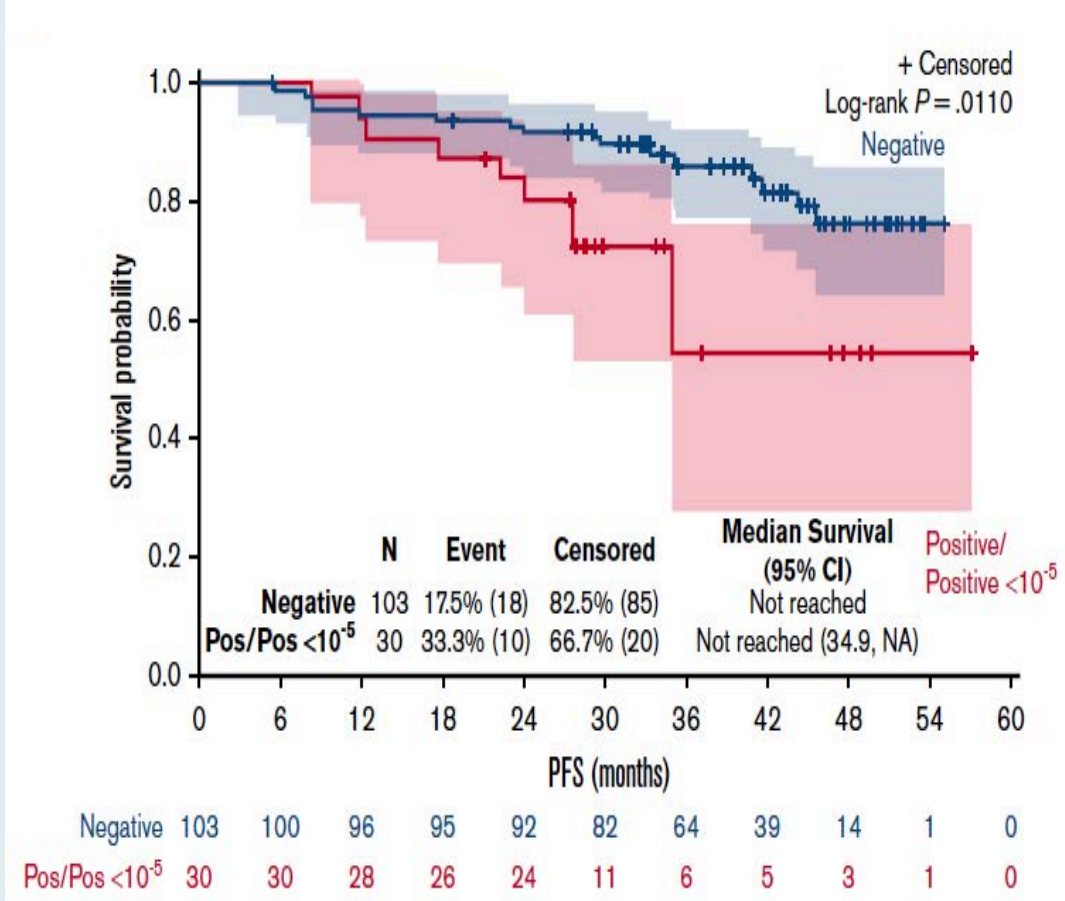

Delfau-Larue MH et al. *Blood Adv* 2020;4(14):3217-23.

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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

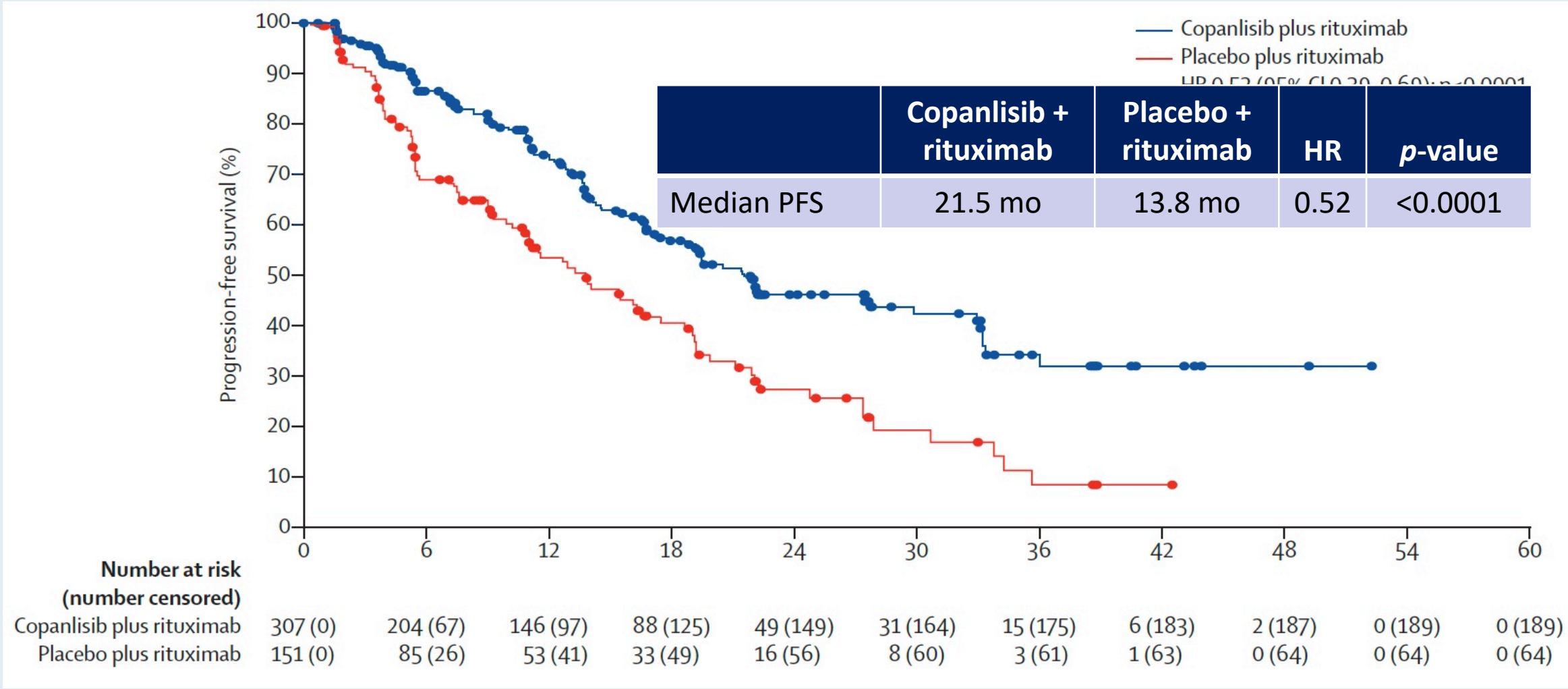
[1] Gopal AK et al. *N Engl J Med* 2014;370(11):1008-18; Idelalisib package insert, January 2018.
[2] Dreyling M et al. *J Clin Oncol* 2017;35(35):3898-905; Copanlisib package insert, September 2017.
[3] Flinn IW et al. *J Clin Oncol* 2019;[Epub ahead of print]; Zinzani PL et al. EHA 2017;Abstract S777;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

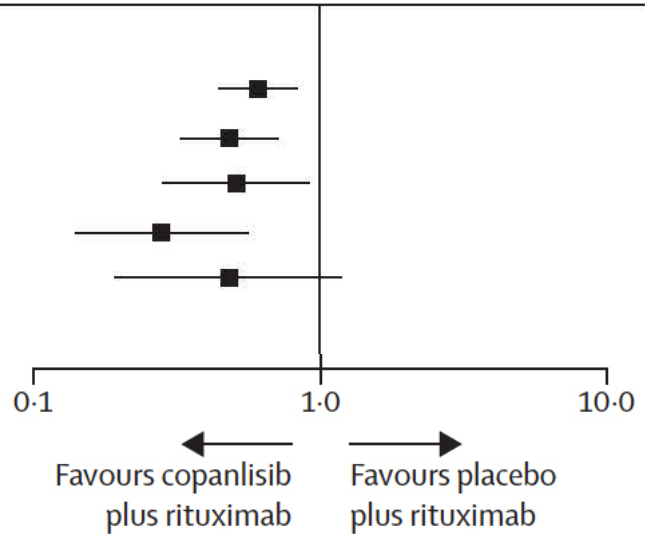


	Copanlisib + rituximab	Placebo + rituximab	HR	*p*-value
Median PFS	21.5 mo	13.8 mo	0.52	<0.0001

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

CHRONOS-3: Progression-Free Survival by Subgroup

	Copanlisib plus rituximab group		Placebo plus rituximab group		HR (95% CI)	One-sided p value
	Number of events/N	Median, months (95% CI)	Number of events/N	Median, months (95% CI)		
Indolent non-Hodgkin lymphoma histology						
Follicular lymphoma	69/184	22·2 (17·8–33·1)	52/91	18·7 (10·2–21·1)	0·58 (0·40–0·83)	0·0014
Other indolent non-Hodgkin lymphoma	49/123	21·5 (14·6–33·4)	35/60	11·0 (5·7–15·4)	0·44 (0·29–0·69)	<0·0001
Marginal zone lymphoma	22/66	22·1 (13·8–NE)	15/29	11·5 (5·6–16·3)	0·48 (0·25–0·92)	0·012
Small lymphocytic lymphoma	20/35	14·2 (10·9–20·5)	12/15	5·7 (3·5–11·0)	0·24 (0·11–0·53)	<0·0001
Lymphoplasmacytic lymphoma–Waldenström macroglobulinaemia	7/22	33·4 (15·5–NE)	8/16	16·6 (4·4–27·4)	0·44 (0·16–1·23)	0·054



Matasar MJ et al. *Lancet Oncol* 2021;22(5):678-89.

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

Press Release – February 5, 2021

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

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

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

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

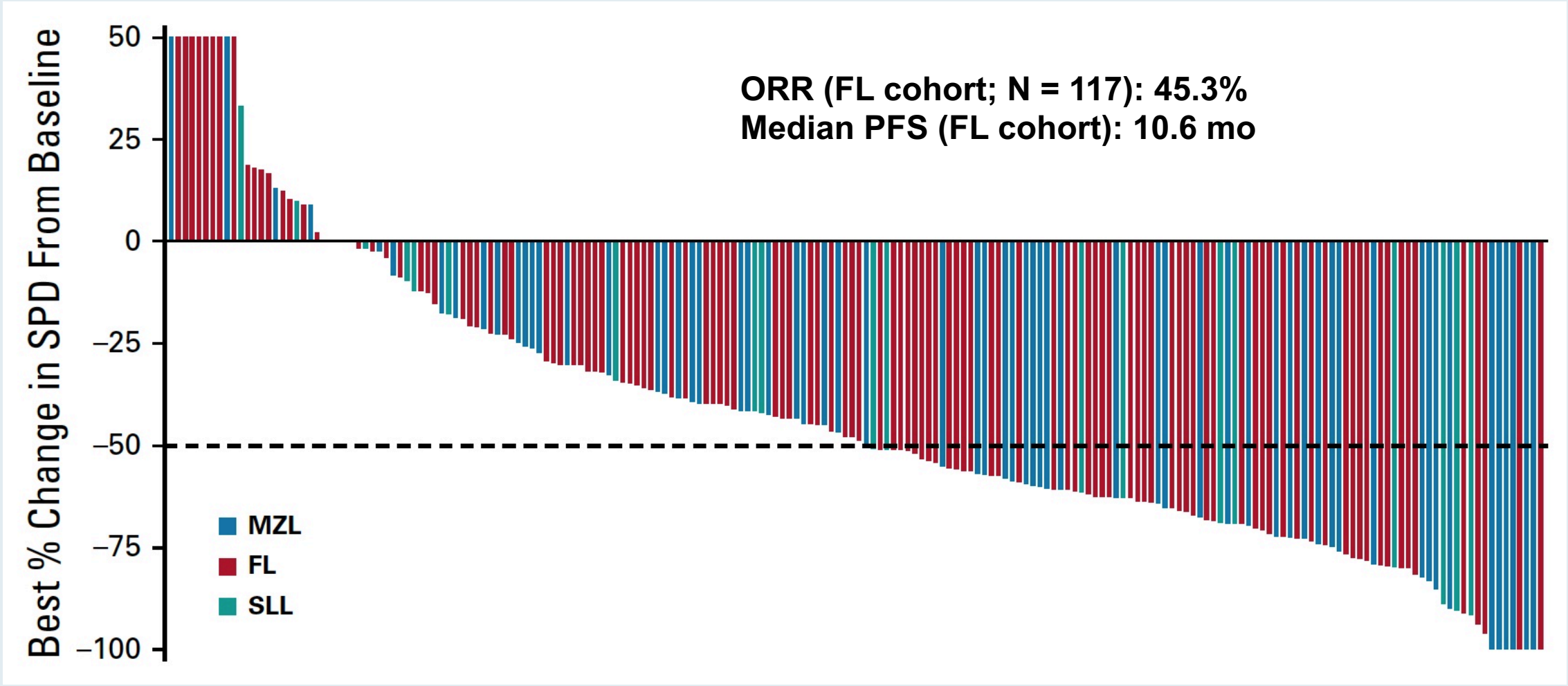
rapid communications

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

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

J Clin Oncol 2021;39:1609-18.

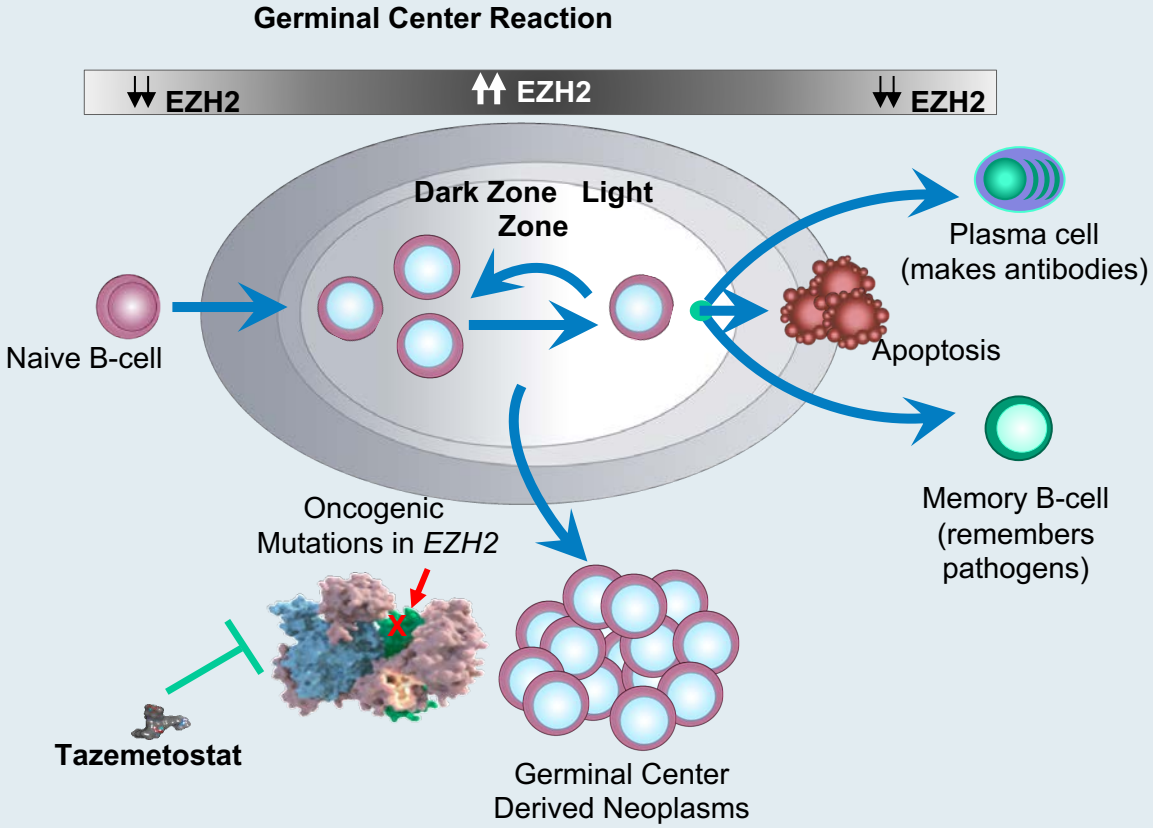
Umbralisib for Heavily Pretreated R/R Indolent NHL



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

Follicular Lymphoma and EZH2

- *EZH2* an epigenetic regulator of gene expression and cell fate decisions[1]
- *EZH2* is required for normal B-cell biology and germinal center formation[2]
  - Oncogenic mutations in *EZH2* suppress exit from germinal state and "lock" B cells in this state thereby transforming into a cancer[2]
- *EZH2* biology relevant in both mutant (MT) and wild-type (WT) *EZH2* FL
  - ~20% of patients with FL also have *EZH2* gain of function mutations[3]



Tazemetostat, a selective, oral inhibitor of EZH2 has shown antitumor activity in non-Hodgkin's lymphoma patients with either MT or WT EZH2[4,5]

1. Gan L, et al. *Biomark Res*. 2018;6(1):10; 2. Béguelin W, et al. *Cancer Cell*. 2013;23(5)677-692.
3. Bödör C, et al. *Blood*. 2013;122:3165-3168. 4. Italiano A, et al. *Lancet Oncol*. 2018;19(5):649-59;
5. Morschhauser F, et al. *Hematol Oncol*. 2017 Jun;35:24-5.

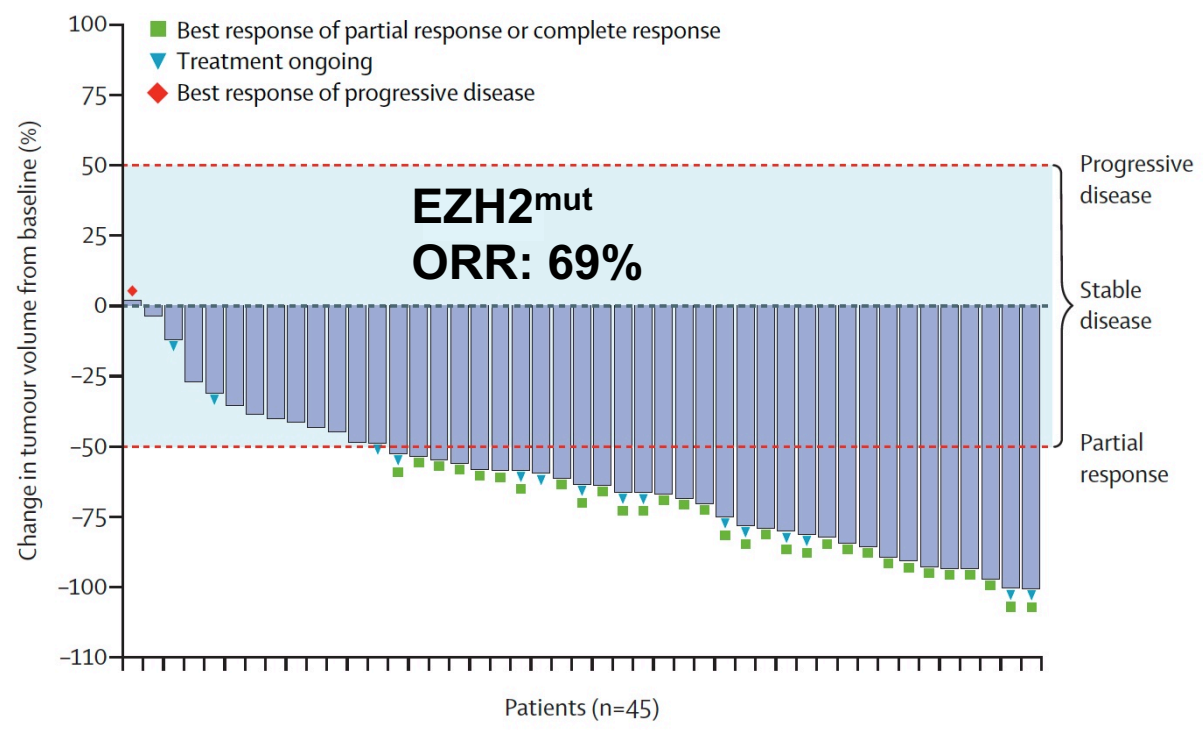
Courtesy of John P Leonard, MD

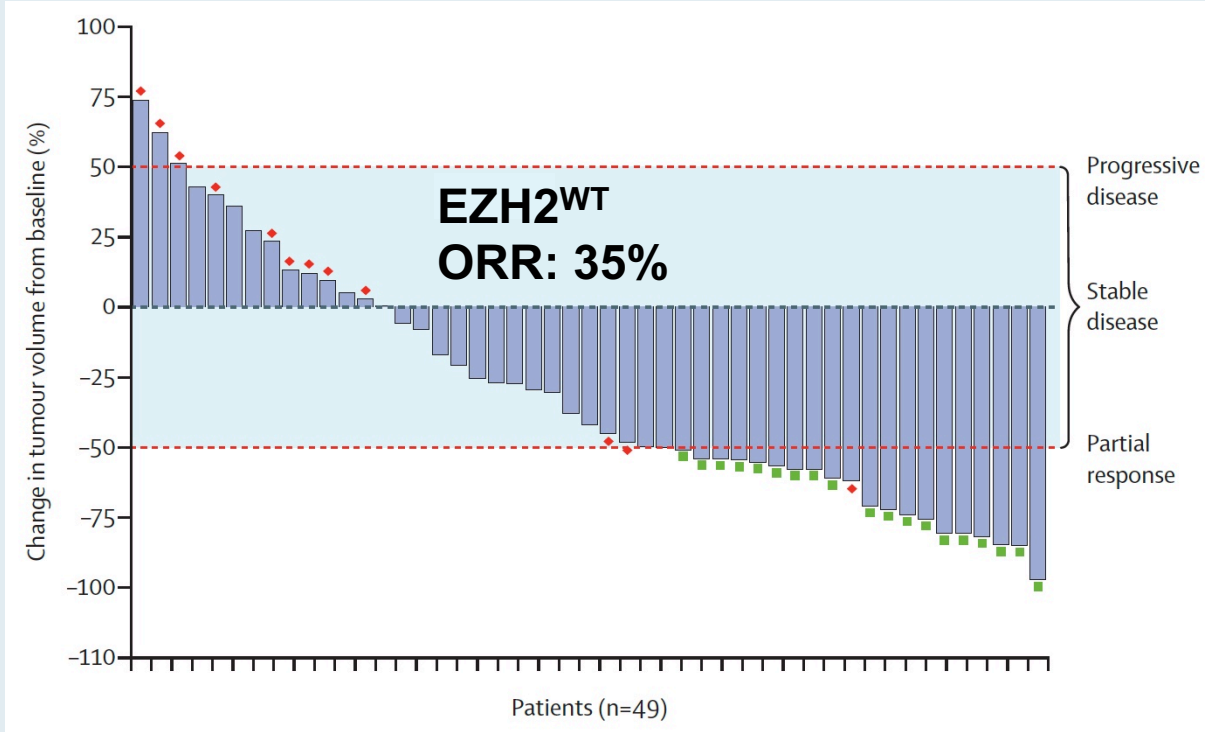
Lancet Oncol 2020;21:1433-42.

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

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

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





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

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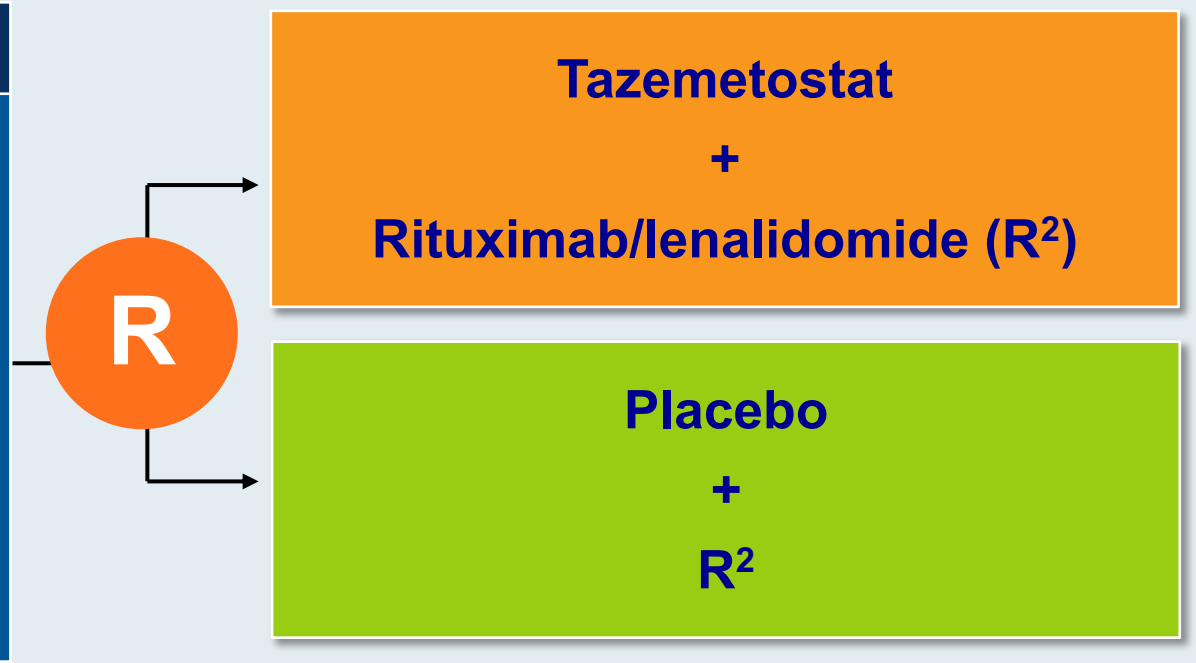
EZH-302: Ongoing Phase Ib/III Trial of Tazemetostat + R^2 for R/R FL

Target accrual (N = 518)

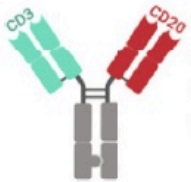
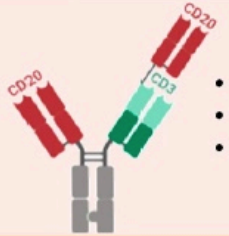
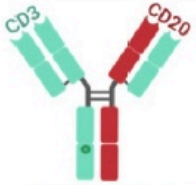
- Grade I to IIIA FL
- At least 1 prior line of therapy
- No prior EZH2 inhibitor
- No prior lenalidomide for FL



- **Primary endpoint:**
  - **Stage 1: RP3D of tazemetostat in combination with R^2**
  - **Stage 2: PFS**

Batlevi CL et al. ASH 2020;Abstract 2052; www.clinicaltrials.gov. NCT04224493. Accessed August 2021.

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):113-6.

FDA Grants Breakthrough Therapy Designation to the CD20 x CD3 Bispecific Cancer Immunotherapy Mosunetuzumab for FL

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."

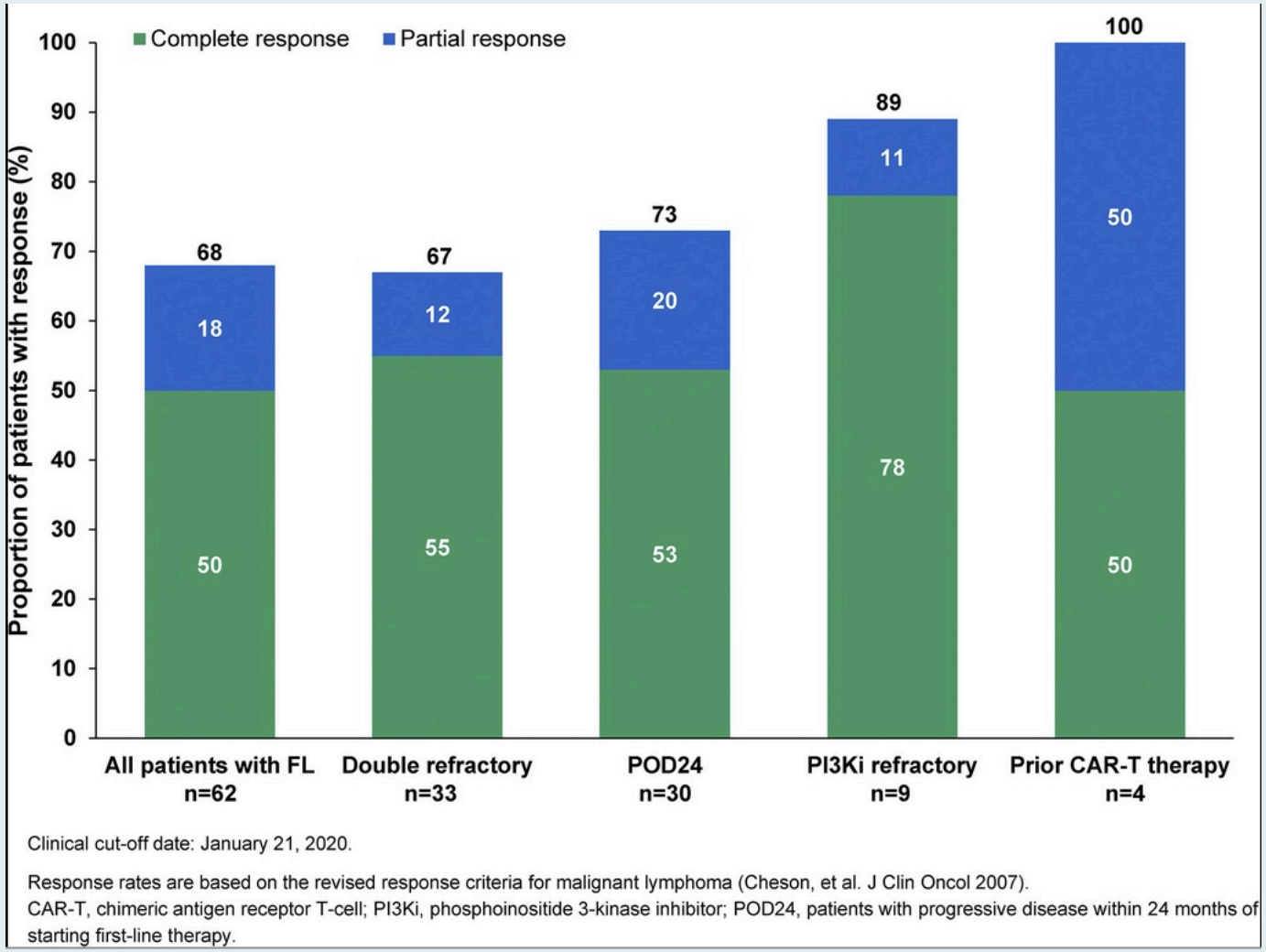
www.roche.com/investors/updates/inv-update-2020-07-14b.htm

Mosunetuzumab Shows Promising Efficacy in Patients with Multiply Relapsed Follicular Lymphoma: Updated Clinical Experience from a Phase I Dose-Escalation Trial

Assouline SE et al.

ASH 2020;Abstract 702.

Investigator-Assessed Best Response in Patients with FL Who Have Received at Least 2 Prior Systemic Therapies



Clinical cut-off date: January 21, 2020.

Response rates are based on the revised response criteria for malignant lymphoma (Cheson, et al. J Clin Oncol 2007).

CAR-T, chimeric antigen receptor T-cell; PI3Ki, phosphoinositide 3-kinase inhibitor; POD24, patients with progressive disease within 24 months of starting first-line therapy.

CRS rate: 35% (N = 22)

- Classified as SAE in N = 4
- No patient required tocilizumab, intensive care unit admission or use of vasopressors for CRS management

Neurologic AE rate: 45% (N = 28)

- All Grade 1/2

Assouline SE et al. ASH 2020;Abstract 702.

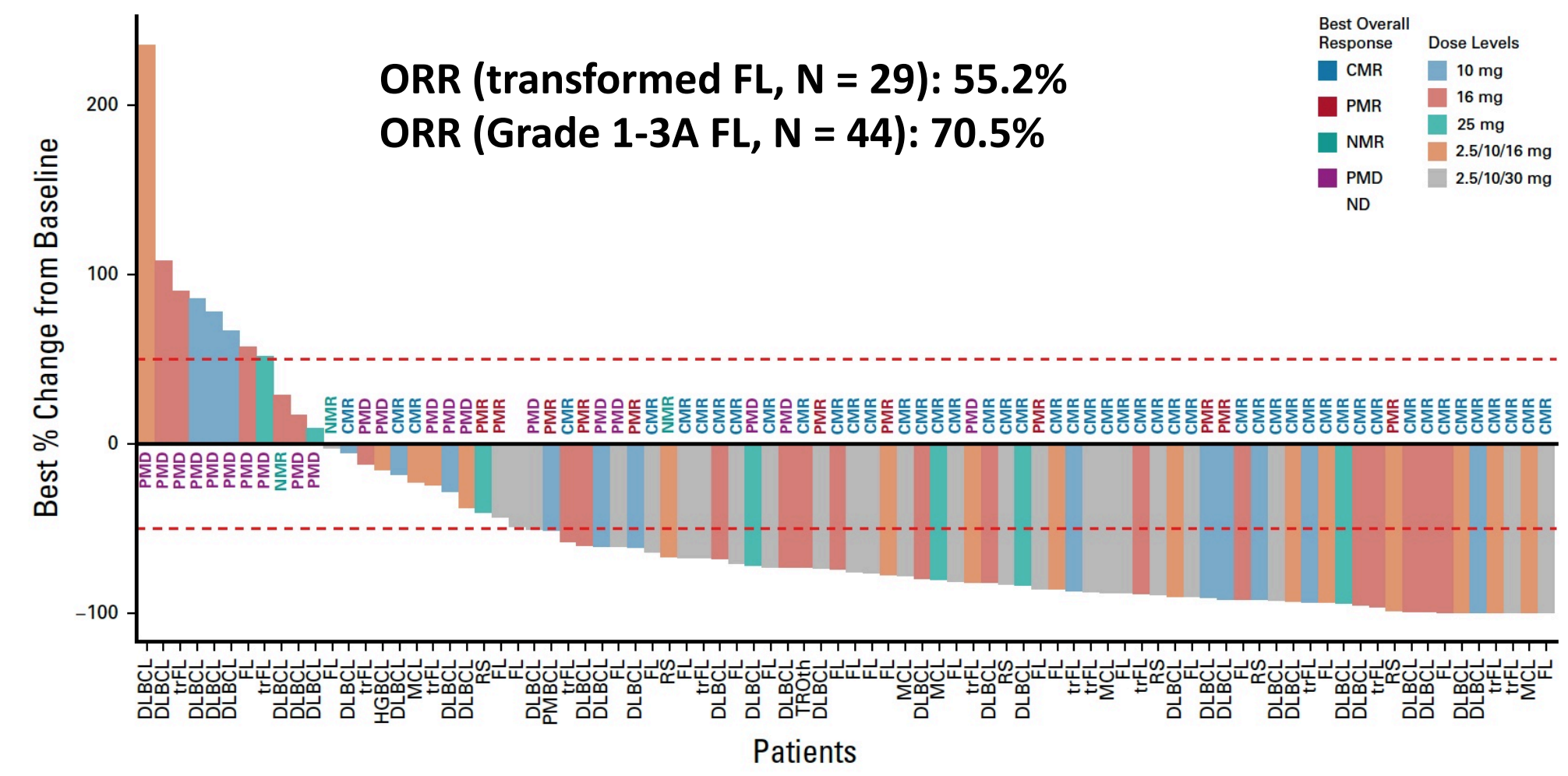
rapid communications

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 R/R B-Cell Lymphomas



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

Agenda

Module 1: Follicular Lymphoma (FL)

Module 2: Mantle Cell Lymphoma (MCL)

- When should a BTK inhibitor be introduced into treatment of MCL and how do you select a specific agent? What is known about pirtobrutinib?
- In what situations do you use venetoclax for MCL and how do you use it (alone or in combination)? What type of ramp-up schedule do you utilize?
- In what situations do you generally refer patients with MCL to receive CAR-T? What outcomes have you observed?

Module 3: Diffuse Large B-Cell Lymphoma (DLBCL)

Module 4: CAR T-Cell Therapy in Lymphoma

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When should a BTK inhibitor be introduced into treatment of MCL and how do you select a specific agent? What is known about pirtobrutinib?

Have you administered or would you administer a Bruton tyrosine kinase (BTK) inhibitor as front-line treatment to a patient with MCL who is too frail to receive chemotherapy?

1. I haven’t and would not
2. I haven’t but would for the right patient
3. I have

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A 78-year-old patient with MCL initially treated with BR followed by 2 years of maintenance rituximab experiences disease relapse 3 years later. The patient is otherwise healthy. What would you recommend?

1. Ibrutinib
2. Acalabrutinib
3. Zanubrutinib
4. Lenalidomide
5. Lenalidomide + rituximab
6. Venetoclax
7. Venetoclax + rituximab
8. Other

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Case Presentation – Dr Flinn: A 73-year-old man with MCL

- A 73-year-old man with PMH significant for HTN and DM was diagnosed with mantle cell lymphoma 3 years ago when he presented with abdominal pain. CT and PET scan reveal adenopathy above and below diaphragm with largest mass that was 7 cm in retroperitoneum. Biopsy reveals CD 5+, CD 20+, CD 23 -, FMC7 + B malignancy. FISH reveal 11:14 translocation. Ki-67 is 30%. TP53 mutations are negative. Bone marrow is positive for lymphoma in 5% of cells.
- The patient receives 6 cycles of BR and tolerates well with exception of mild neutropenia and thrombocytopenia occurring after completion of BR that took 3 months to resolve. Post treatment PET scan reveals Deauville score of 1.
- The patient was observed until 3 months ago when he developed progressive adenopathy in bilateral axilla and retroperioneum. Biopsy of axillary mass is unchanged from initial biopsy at diagnosis.
- The patient is mostly asymptomatic but does report some low grade back pain. The patient is started on zanubrutinib 160 mg bid and notices rapid decrease in palpable axillary lymph nodes as well as resolution of his back pain.

In what situations do you use venetoclax for MCL and how do you use it (alone or in combination)? What type of ramp-up schedule do you utilize?

Regulatory and reimbursement issues aside, would you attempt to access venetoclax for select patients with relapsed/refractory MCL?

1. Yes, as up-front treatment
2. Yes, after a BTK inhibitor
3. Yes, after a BTK inhibitor → lenalidomide
4. Yes, in other situations
5. No

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

1. Lenalidomide
2. Lenalidomide + rituximab
3. Bortezomib
4. Bortezomib + rituximab
5. Venetoclax
6. Acalabrutinib
7. Zanubrutinib
8. Brexucabtagene autoleucel
9. Other

In what situations do you generally refer patients with MCL to receive CAR-T? What outcomes have you observed?

Case Presentation – Dr Evens: A 69-year-old woman with MCL who received a BTK inhibitor and was treated with CAR T-cell therapy

A 69-year-old female who originally presented in 2008 with stage IV mantle cell lymphoma, treated with the following regimens over time: 2008 R–hyper CVAD, with CR by 6 cycles though significant dose reductions, intolerant of further therapy, unable to go for a SCT. Then, in 2011 pt received R+bortezomib, with CR after 4 cycles but with significant neuropathy. In 2014: ibrutinib, PR with rapid response but requiring dose reduction for toxicity and then only intermittently compliant, relapsed when off therapy for prolonged time, responded to retreatment, but ultimately intolerant of even low-dose dosing and stopped, then with recurrent disease.

Then, in 2016: bendamustine/rituximab x2 cycles with rapid response, but intolerant and discontinued therapy. Then in 2018: single-agent lenalidomide at progressively lower and lower doses ultimately discontinuing for side effects, with stable partial response. Then, in April 2019: progressive bulky disease, hydronephrosis, requiring stents. June 2019: single agent venetoclax, rapid response within 1 week of initial 50 mg, titrated up to 400 mg, ultimately intolerant decreasing to 200 mg alternating with 150 mg; discontinued in early December 2019 due to progressive symptoms, pancytopenia experienced secondary to venetoclax.

January 2020: Pt was found to have diffuse marrow involvement of spine with ventral epidural disease on the entire spine without cord compression and evidence of HLH. The patient had a good clinically response to RICE x 2 with IT MTX with initial response but with progression. She had re-initiation of BTK inhibitor (acalabrutinib) obtaining PR for approximately a year. However, with tolerance and ultimate progression. Patient referred for anti-CD19 CART therapy.

Case Presentation – Dr Flinn: A 63-year-old man with R/R MCL

- A 63-year-old man with unremarkable PMH is diagnosed with blastoid variant mantle cell lymphoma after he presents with cervical adenopathy. In addition to t(11;14), the biopsy reveals Ki-67 of 60% and mutation in TP53.
- Staging CTs reveal adenopathy on neck, chest, abdomen, and pelvis. Largest mass is 5 cm. Bone marrow biopsy reveal lymphoma in 10% of cells. The patient is started on the Nordic regimen and after 2 cycles achieves PR but progresses after 4 cycles.
- He enters a clinical trial of ibrutinib and venetoclax. He once again initially responds but within 6 months he begins to progress. The decision is made to treat him with brexucabtagene autoleucel. The ibrutinib and venetoclax is discontinued 2 days prior to apheresis.
- Within a few days of the apheresis the patient develops night sweats, fever, abdominal pain, and obvious progression of the palpable lymph nodes. Steroids are used to help with symptom control and bridge the patient until 3 weeks after the apheresis and the CAR T cells are available.

Case Presentation – Dr Flinn: A 63-year-old man with R/R MCL

- He receives lymphodepleting chemotherapy and subsequent infusion of brexucabtagene autoleucel.
- Thirty-six hours after infusion the patient develops first CRS followed by ICANS requiring tociluzimab, steroids, pressors, and ultimately intubation for severe obtundation. Five days later he is able to be extubated.
- His course is further complicated by steroid myopathy from the slow taper of steroids as well as persistent cytopenias with platelets 20K and ANC 600. However, the patient achieves a CR.
- One year later, the patient is still in CR. His cytopenias have resolved.

Key Recent Data Sets

Pooled Analysis of Ibrutinib for R/R MCL: Median 41 Months Follow-Up

(Phase II PCYC-1104 and SPARK and Phase III RAY Studies)

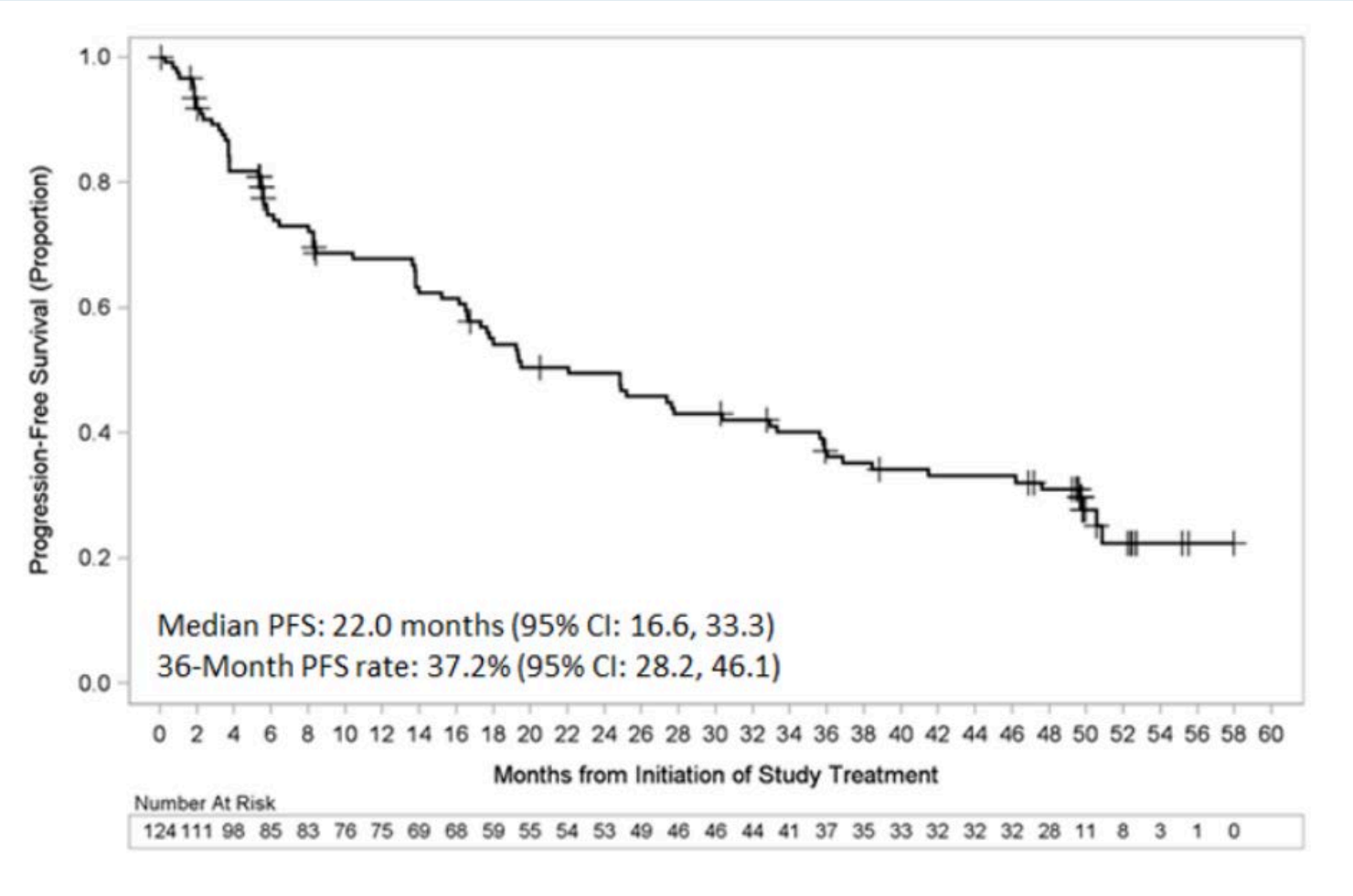
Endpoint	Overall (N = 370)	Prior lines of therapy	
		1 (n = 99)	>1 (n = 271)
Median PFS	**12.5 mo**	**25.4 mo**	**10.3 mo**
Median PFS by best response CR (n = 102) PR (n = 156)	 67.7 mo 12.6 mo	 68.5 mo 24.2 mo	 67.7 mo 10.5 mo
Median OS	**26.7 mo**	**61.6 mo**	**22.5 mo**
Median OS by best response CR (n = 102) PR (n = 156)	 Not reached 23.6 mo	 Not reached 36.0 mo	 Not reached 22.6 mo
ORR, CR	**70%, 28%**	**78%, 37%**	**67%, 24%**

Rule S et al. ASH 2019;Abstract 1538.

Acalabrutinib Monotherapy in Patients with Relapsed/Refractory Mantle Cell Lymphoma: Long-Term Efficacy and Safety Results from a Phase 2 Study

Wang M et al.
ASH 2020;Abstract 2040.

ACE-LY-004 Long-Term Follow-Up: Progression-Free Survival



The adverse event profile was largely unchanged with an additional year of follow-up.

Wang M et al. ASH 2020;Abstract 2040.

RTP RESEARCH TO PRACTICE

Efficacy of Zanubrutinib for MCL

Study	Evaluable patients	ORR, CR	Median DoR	Median PFS
Phase I/II (NCT02343120)	N = 48 R/R = 37 TN = 11	87%, 31% 87%, 30% 88%, 38%	16.2 mo (all) 14.7 mo 14.7 mo	15.4 mo
Phase II (NCT03206970)	N = 86 R/R	84%, 69%	19.5 mo	22.1 mo

Song Y et al. ICML 2019;Abstract 015; Tam CS et al. ICML 2019;Abstract 191;
Tam CS. *Clin Advances in Hem Oncol* 2019;17(1):32-34; Song Y et al. *Clin Cancer Res* 2020;26(16):4216-24.

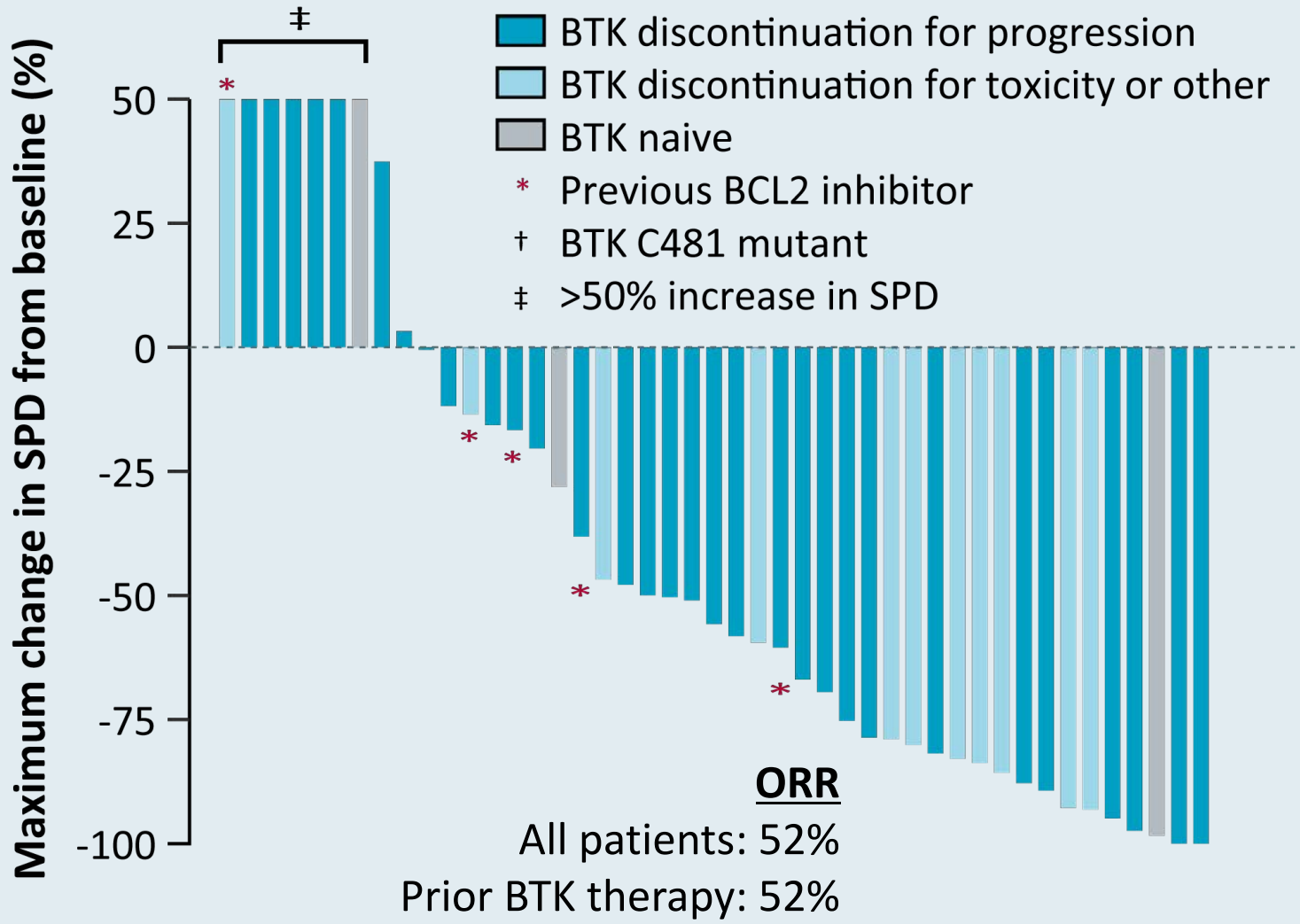
Articles

Pirtobrutinib in relapsed or refractory B-cell malignancies (BRUIN): a phase 1/2 study

Anthony R Mato, Nirav N Shah, Wojciech Jurczak, Chan Y Cheah, John M Pagel, Jennifer A Woyach, Bita Fakhri, Toby A Eyre, Nicole Lamanna, Manish R Patel, Alvaro Alencar, Ewa Lech-Maranda, William G Wierda, Catherine C Coombs, James N Gerson, Paolo Ghia, Steven Le Gouill, David John Lewis, Suchitra Sundaram, Jonathon B Cohen, Ian W Flinn, Constantine S Tam, Minal A Barve, Bryone Kuss, Justin Taylor, Omar Abdel-Wahab, Stephen J Schuster, M Lia Palomba, Katharine L Lewis, Lindsey E Roeker, Matthew S Davids, Xuan Ni Tan, Timothy S Fenske, Johan Wallin, Donald E Tsai, Nora C Ku, Edward Zhu, Jessica Chen, Ming Yin, Binoj Nair, Kevin Ebata, Narasimha Marella, Jennifer R Brown, Michael Wang

Lancet 2021;397(10277):892-901.

BRUIN: Change in Tumor Burden from Baseline with Pirtobrutinib (LOXO-305) in Evaluable Patients with MCL



Mato AR et al. *Lancet* 2021;397(10277):892-901.

Venetoclax Monotherapy for BTK Inhibitor-Resistant MCL: Results Summary

Clinical endpoint	Venetoclax (N = 20)
Overall response rate (ORR) Complete response rate	60% 20%
ORR (prior response to BTKi) ORR (primary resistance to BTKi)	72.7% 44.4%
Median PFS	2.6 mo
Median OS	4.3 mo

No cases of clinical TLS were observed.

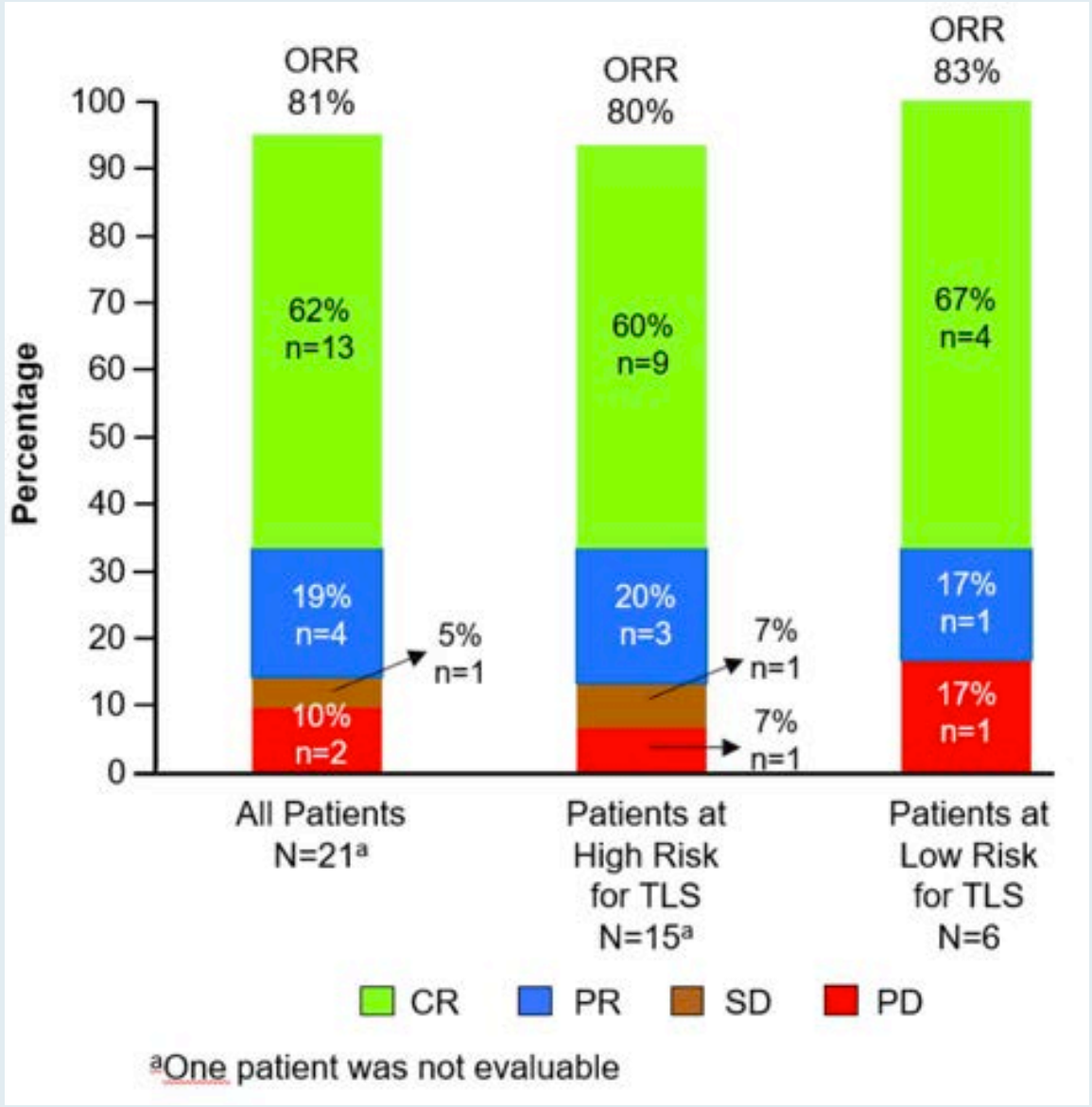
Eyre T et al. EHA 2018;Abstract S855.

Ibrutinib plus Venetoclax in Patients with Relapsed/Refractory Mantle Cell Lymphoma: Results from the Safety Run-In Period of the Phase 3 SYMPATICO Study

Tam CS et al.

ASH 2020;Abstract 2938.

SYMPATICO: Response in Patients at High and Low Risk for TLS



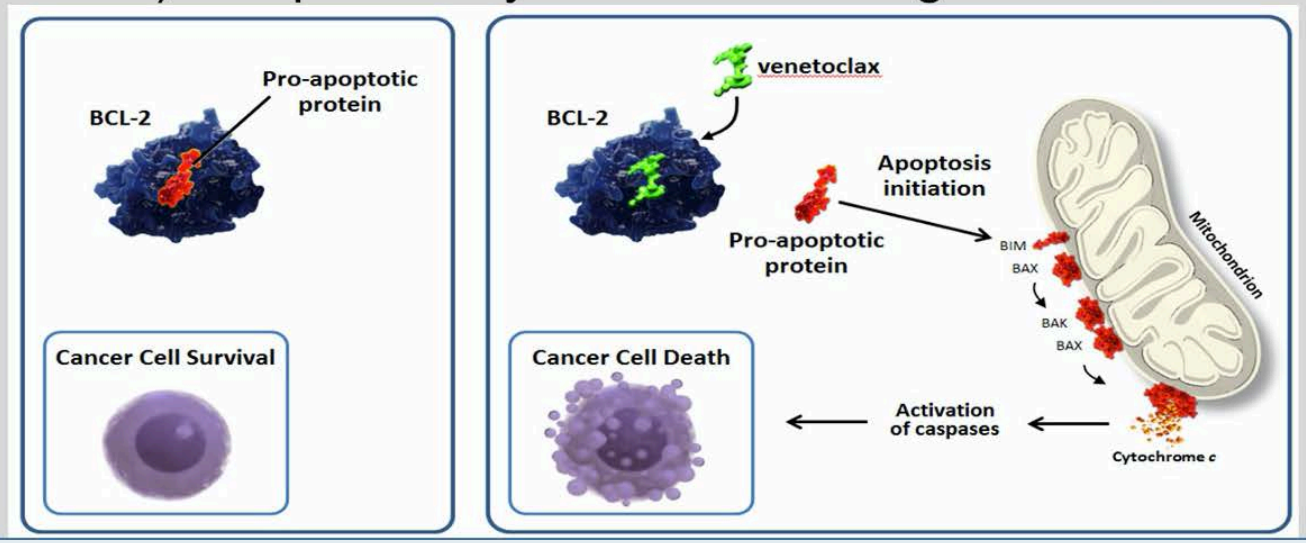
Tam CS et al. ASH 2020;Abstract 2938.

The Combination of Venetoclax, Lenalidomide, and Rituximab in Patients with Newly Diagnosed Mantle Cell Lymphoma Induces High Response Rates and MRD Undetectability

Phillips TJ et al.
ASCO 2021;Abstract 7505.

Biologic Rationale for Combining Venetoclax with R^2

- Venetoclax is oral BCL-2 inhibitor with a current FDA approval in CLL and R/R AML.
- Study by Davids et al. demonstrated efficacy in R/R MCL[1].
- Pre-clinical data suggested synergy with lenalidomide[2].
- We hypothesized that the combination of venetoclax, lenalidomide and rituximab would be safe with the potential to improve ORR, time to best response (as compared to what was reported for R2) and potentially induce MRD negative disease.



Phillips TJ et al. ASCO 2021;Abstract 7505.

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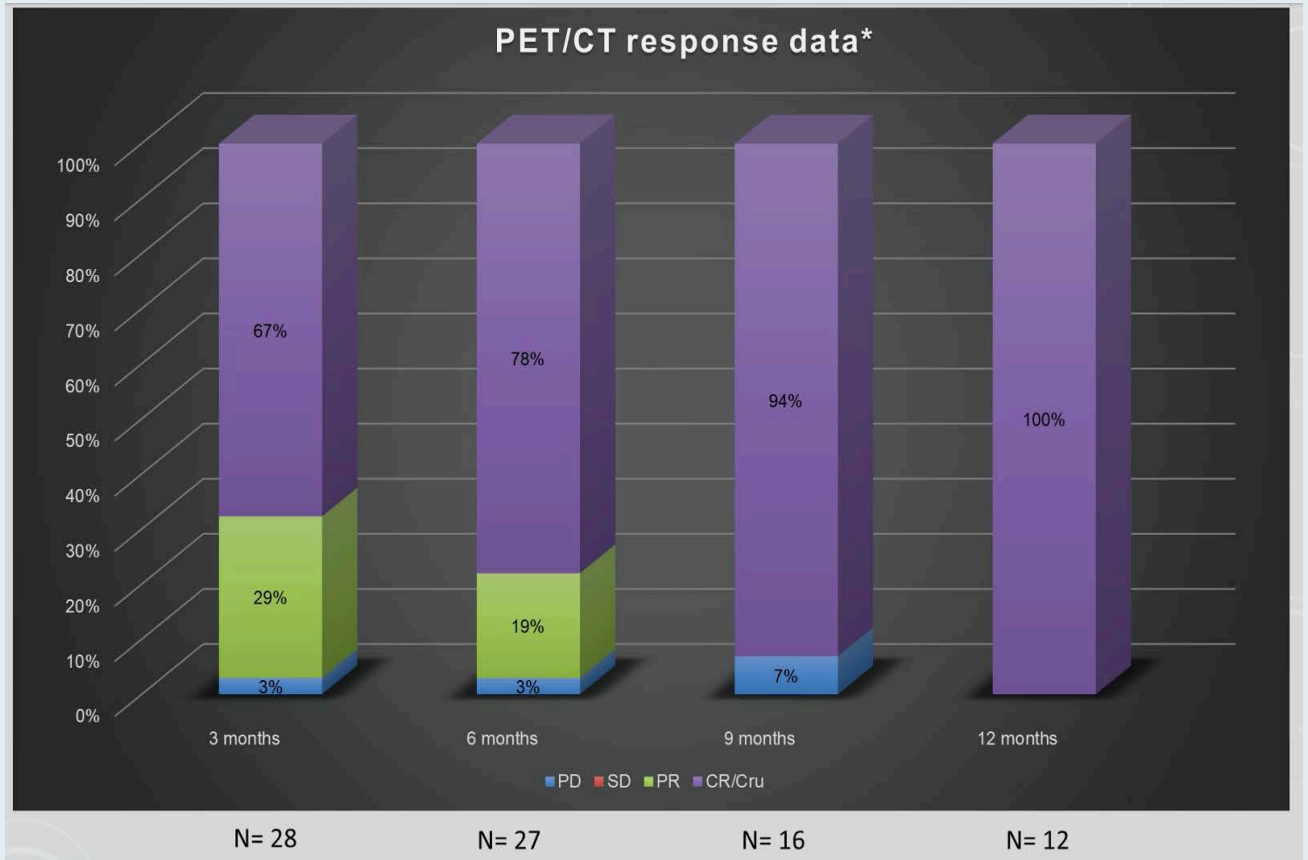
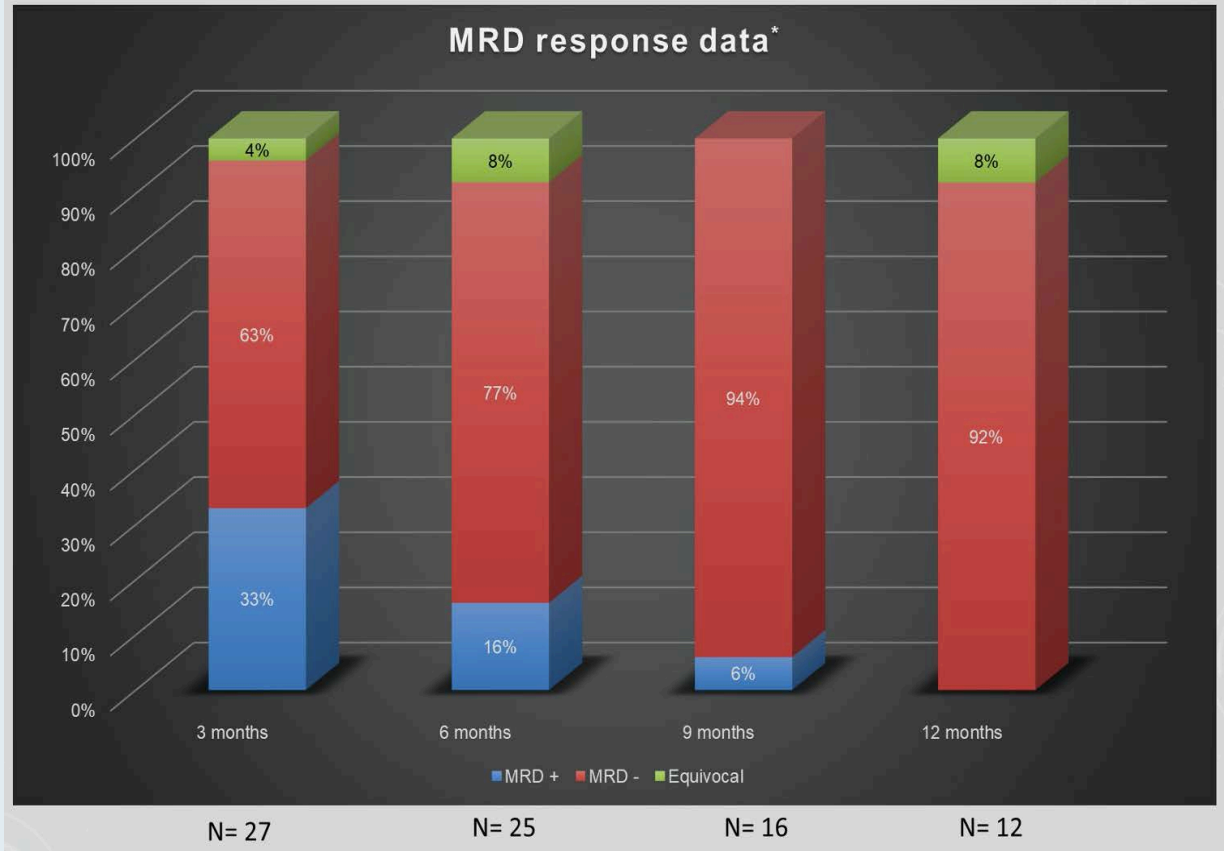
Response and MRD Rates with Venetoclax and R^2

Radiographic Response



MRD Results (negative if <10^{-6})



Phillips TJ et al. ASCO 2021;Abstract 7505.

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Agenda

Module 1: Follicular Lymphoma (FL)

Module 2: Mantle Cell Lymphoma (MCL)

Module 3: Diffuse Large B-Cell Lymphoma (DLBCL)

- **What is your current use of polatuzumab vedotin and do you expect to be using it in the first-line setting in DLBCL? What are the key tolerability issues with this agent?**
- **What is the role of lenalidomide/tafasitamab in DLBCL and how does it compare to R-squared?**
- **What is the optimal role of loncastuximab tesirine in DLBCL? What are the key tolerability issues with this agent?**

Module 4: CAR T-Cell Therapy in Lymphoma

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What is your current use of polatuzumab vedotin and do you expect to be using it in the first-line setting in DLBCL? What are the key tolerability issues with this agent?

Which treatment 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?

1. Polatuzumab vedotin/BR
2. Tafasitamab/lenalidomide
3. Lenalidomide
4. Lenalidomide/rituximab
5. Selinexor
6. CAR T-cell therapy
7. Loncastuximab tesirine
8. I'm not sure

Case Presentation – Dr Flinn: A 81-year-old man with R/R DLBCL

- An 81-year-old man with PMH significant for CAD,HTN,DM was diagnosed with Stage 3 DLBCL 18 months ago.
- Pathology reveals the lymphoma is non-Germinal center by Hans criteria. He is treated with RCHOP (25% dose reduced) and achieves a CR.
- Unfortunately he develops recurrent adenopathy firs presenting in neck, although CT scans reveal progression in nodes in abdomen and pelvis as well.
- The patient is not interested in intensive therapy. He instead receives BR polatuzumab for 5 cycles. The bendamustine was decreased by 50%.
- Despite this reduction, he still requires some treatment delays. He achieves a CR and the decision is made not to give a 6^{th} cycle.

What is the role of lenalidomide/tafasitamab in DLBCL and how does it compare to R-squared?

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Case Presentation – Dr Salles: A 77-year-old woman with DLBCL

- 77-year-old woman
- PMH: thyroidectomy, hypertension, diabetes, STEMI 2 years ago with 2 stents (current LVEF = 55%)
- Large abdominal mass
  - Biopsy: DLBCL, GCB (CD10 and BCL6)
  - Stage IV (bone marrow positive)
  - 2 extra-nodal sites of disease (bone involvement)
  - LDH x 2 normal
  - Performance status of 1

Case Presentation – Dr Salles: A 77-year-old woman with DLBCL (continued)

Because high CNS-IPI risk, MRI and LP performed, both negative,
FISH for MYC and BCL2 negative

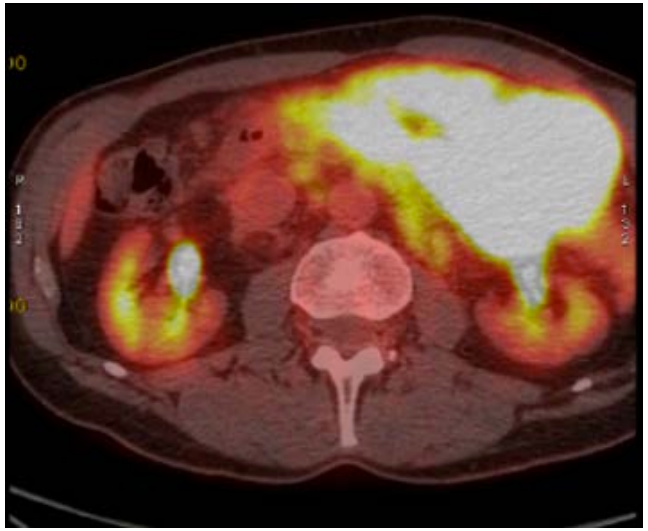
R-CHOP x 6 was chosen as therapy

Achieved a complete response

Disease recurrence 10 months later

- Treated with R-GEMOX – partial response after 4 cycles
- ECOG of 1, disease related symptoms

- Discussion of treatment plan
  - Pola BR ?
  - tisagenlecleucel ?
  - Tafa–len ?



SUV max 28

What is the optimal role of loncastuximab tesirine in DLBCL? What are the key tolerability issues with this agent?

Key Recent Data Sets

FDA Grants Accelerated Approval to Tafasitamab-cxix for DLBCL

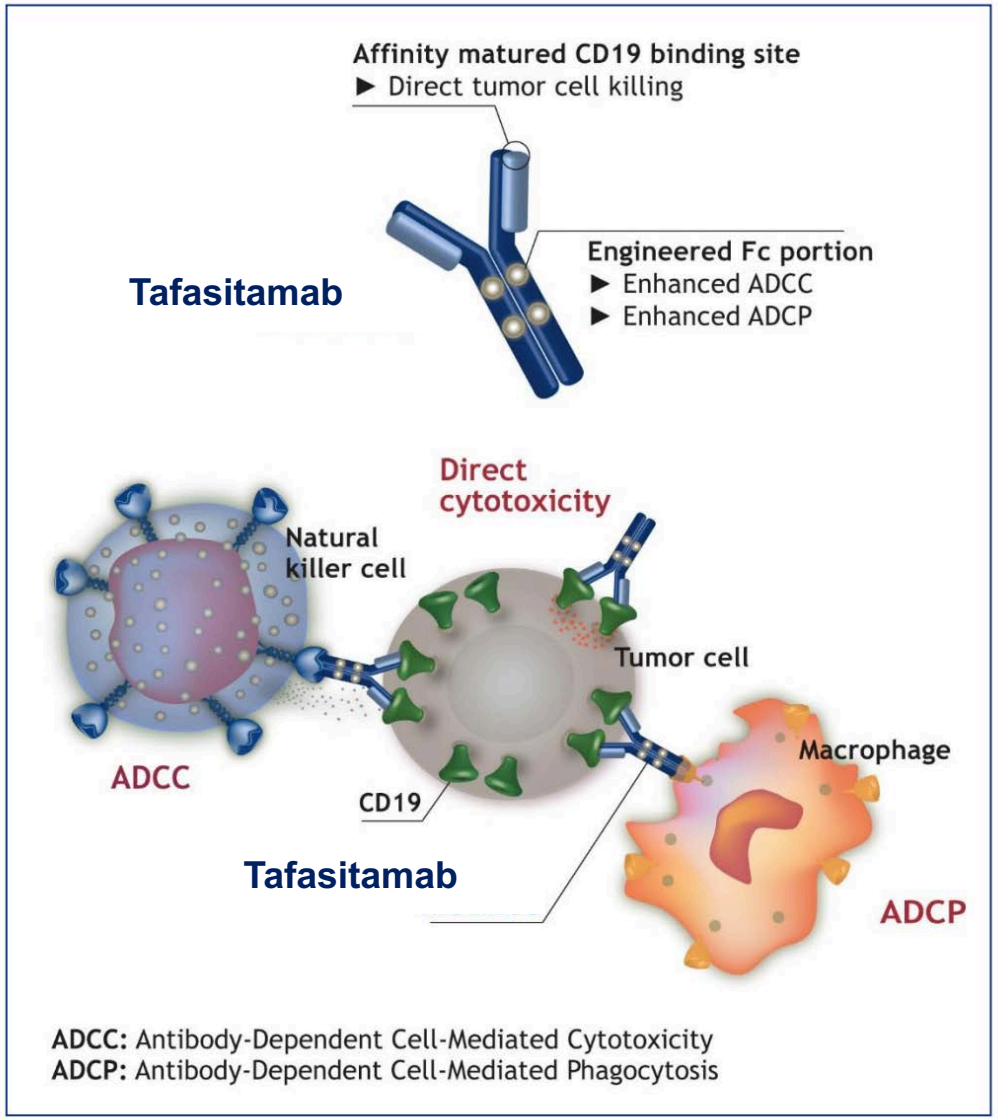
Press Release – July 31, 2020

"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

Tafasitamab (MOR208)



Lenalidomide enhances NK function with enhanced ADCC in vitro

Salles et al. *Lancet Onc* 2020.

Courtesy of Ann S LaCasce, MD, MMSc

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Lancet Oncol 2020;21:978-88

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

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

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

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

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

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

FDA Approves Selinexor for Relapsed/Refractory DLBCL

Press Release – June 22, 2020

"The Food and Drug Administration granted accelerated approval to selinexor for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy.

Approval was based on SADAL (KCP-330-009; NCT02227251), a multicenter, single-arm, open-label trial in patients with DLBCL after 2 to 5 systemic regimens. Patients received selinexor 60 mg orally on days 1 and 3 of each week."

www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-selinexor-relapsedrefractory-diffuse-large-b-cell-lymphoma

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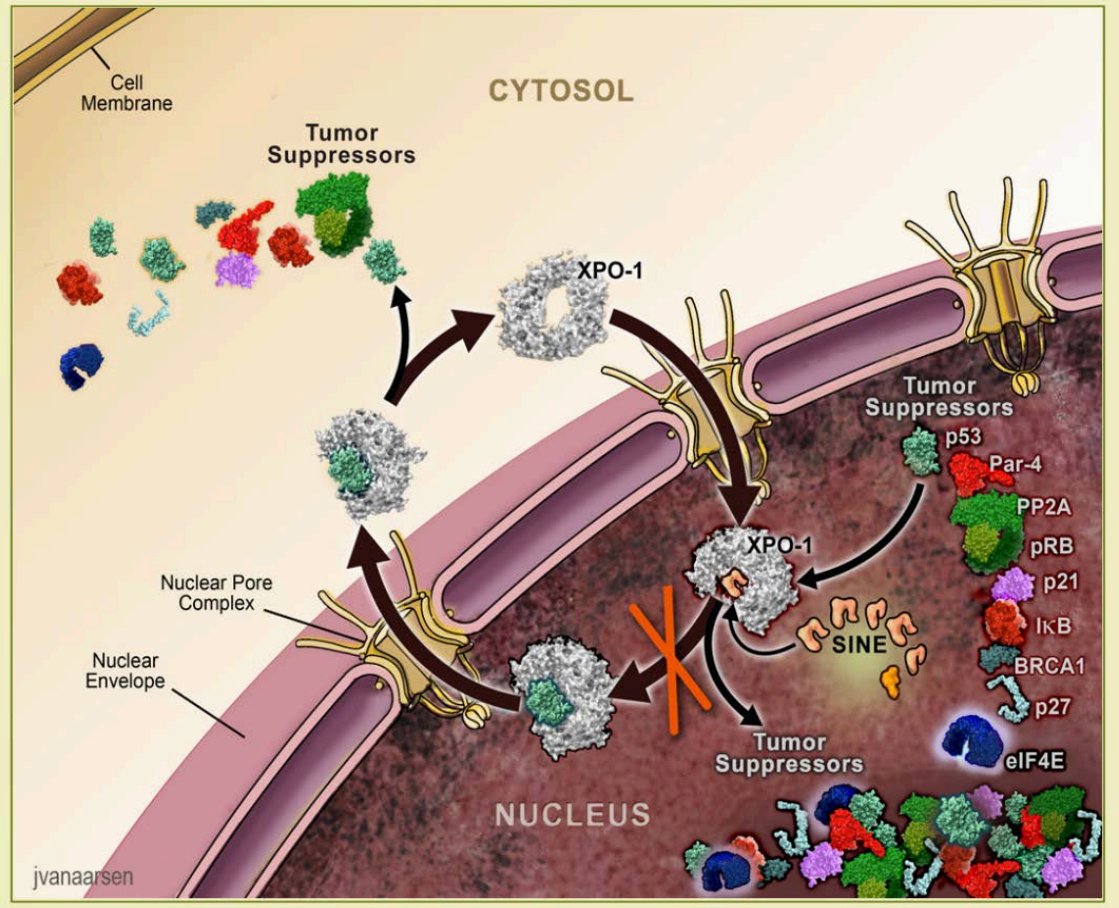
Selinexor has a novel mechanism of action: XPO-1 inhibitor



XPO1 over-expressed in DLBCL and correlates with poor prognosis

Induces nuclear accumulation of tumor suppressors including p53, p73, IkBk and FOXO

Decreases production of oncoproteins including c-MYC, BCL2, BCL6 and BCL-XL

Kalakonda. *Lancet Heme* 2020.

Courtesy of Ann S LaCasce, MD, MMSc

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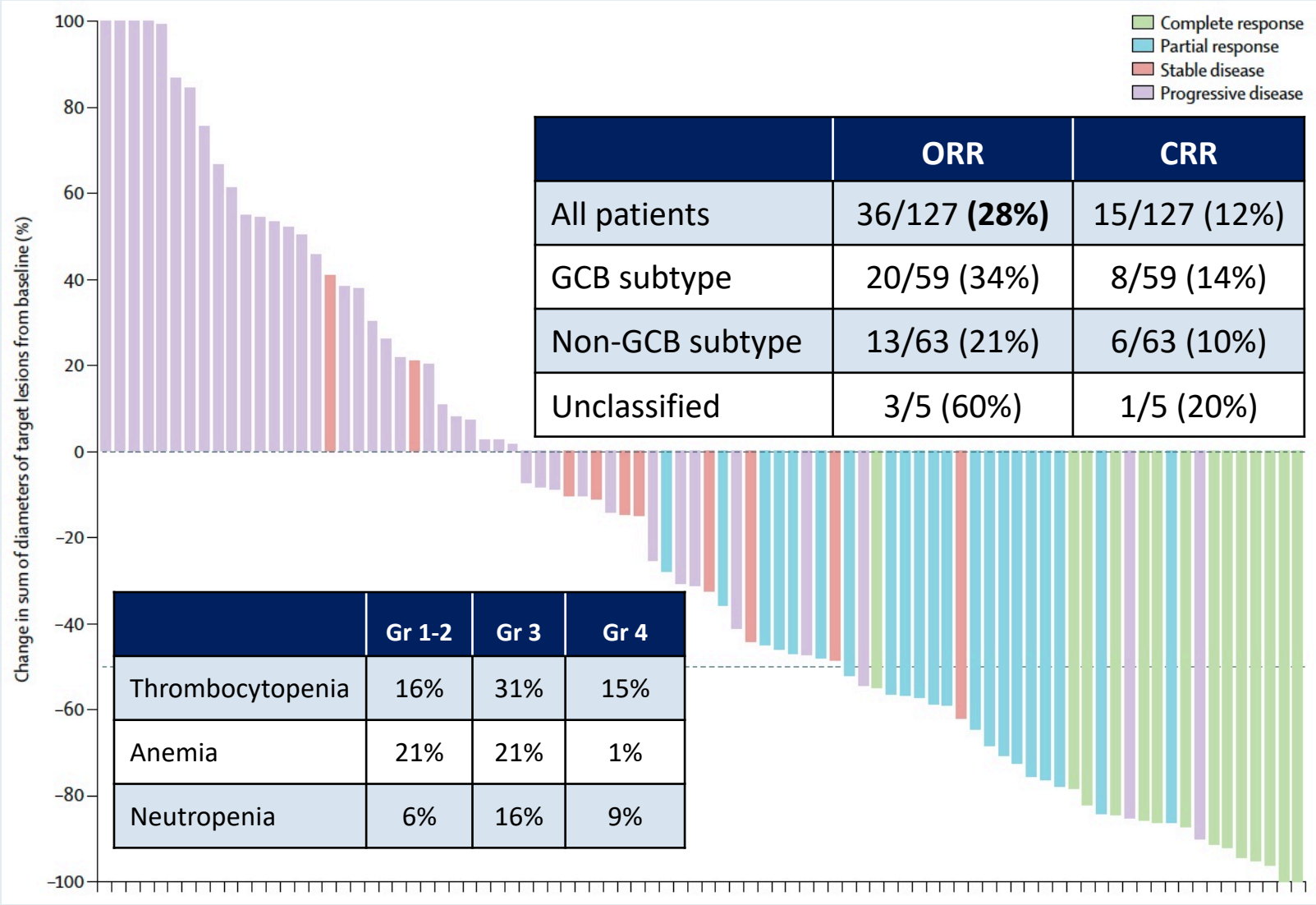
Lancet Haematol 2020;7:e511-22

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 in Patients with 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.

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Phase III Study Shows Polatuzumab Vedotin with R-CHP to Be First Regimen in 20 Years to Significantly Improve Outcomes in Previously Untreated Aggressive Form of Lymphoma

Press Release – August 9, 2021

"Pivotal Phase III POLARIX trial comparing polatuzumab vedotin in combination with chemotherapy regimen R-CHP versus the standard of care R-CHOP in treatment of first-line diffuse large B-cell lymphoma (DLBCL) met its primary endpoint of investigator assessed progression-free survival.

Prolonging survival without disease advancement could be transformative for newly diagnosed DLBCL patients, as currently 40% of patients relapse after disease progression.

Data will be submitted to health authorities globally as soon as possible and presented at an upcoming medical meeting."

https://finance.yahoo.com/news/phase-iii-study-shows-genentechs-050000152.html

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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]

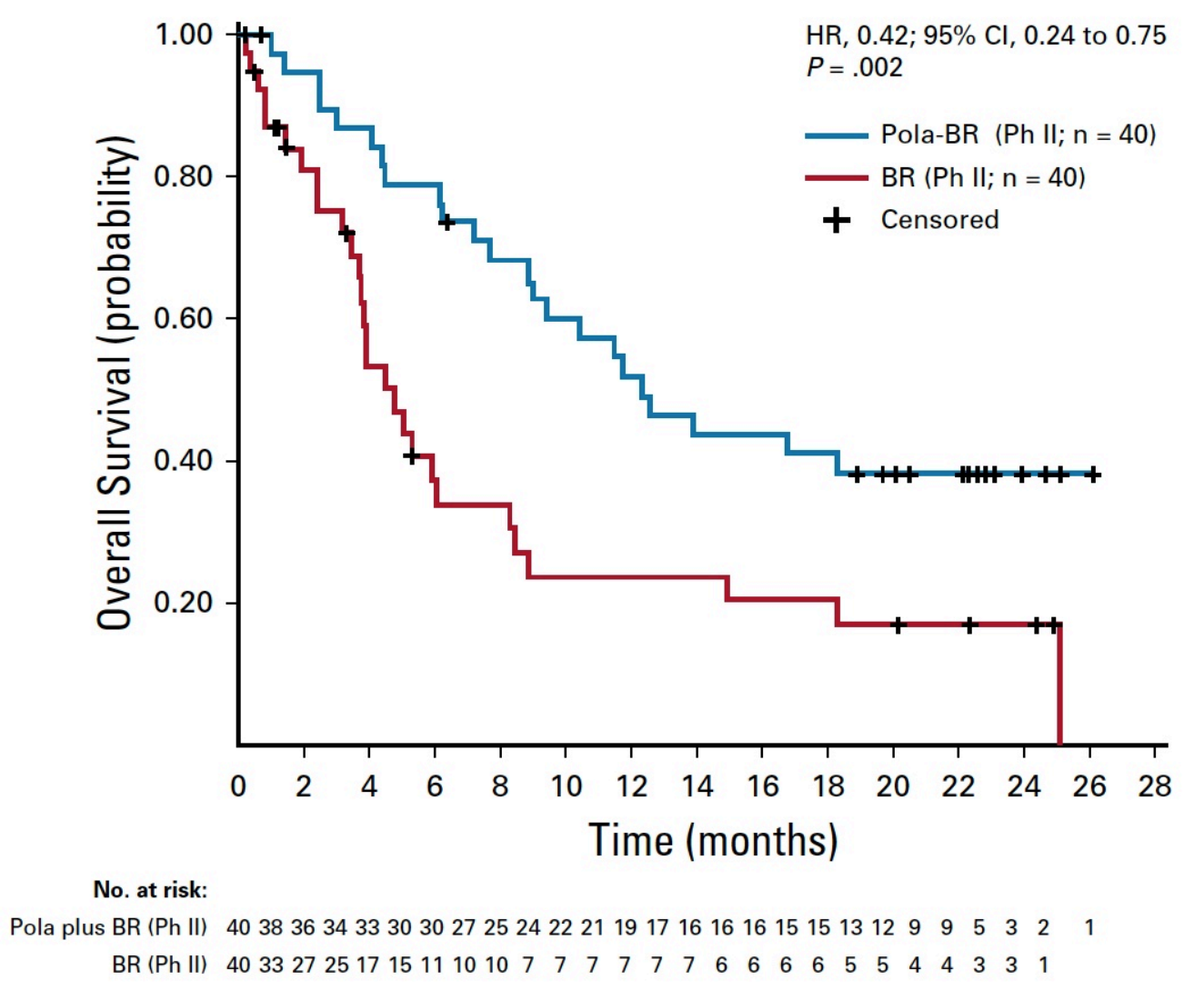
J Clin Oncol 2020;38(2):155-65

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

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

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

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



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

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

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.

Agenda

Module 1: Follicular Lymphoma (FL)

Module 2: Mantle Cell Lymphoma (MCL)

Module 3: Diffuse Large B-Cell Lymphoma (DLBCL)

Module 4: CAR T-Cell Therapy in Lymphoma

- **What are some of the key functional issues, including age, in determining eligibility for CAR-T?**
- **What is the current optimal clinical situation (ie, line of treatment) in which to use CAR-T in DLBCL and do you expect it to replace ASCT in the near future?**
- **Which specific features differentiate the approved CAR-T products and are there specific clinical situations where you favor one over another?**

What are some of the key functional issues, including age, in determining eligibility for CAR-T?

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A patient with DLBCL should be in adequate physical condition to undergo ASCT to be a suitable candidate for CAR T-cell therapy.

1. Agree
2. Disagree
3. I’m not sure

What is the current optimal clinical situation (ie, line of treatment) in which to use CAR-T in DLBCL and do you expect it to replace ASCT in the near future?

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

1. At first relapse
2. At second relapse
3. At third relapse
4. I am not referring patients for CAR T-cell therapy
5. Other

Management of cytokine release syndrome after administration of CAR T-cell therapy would involve the use of which of the following?

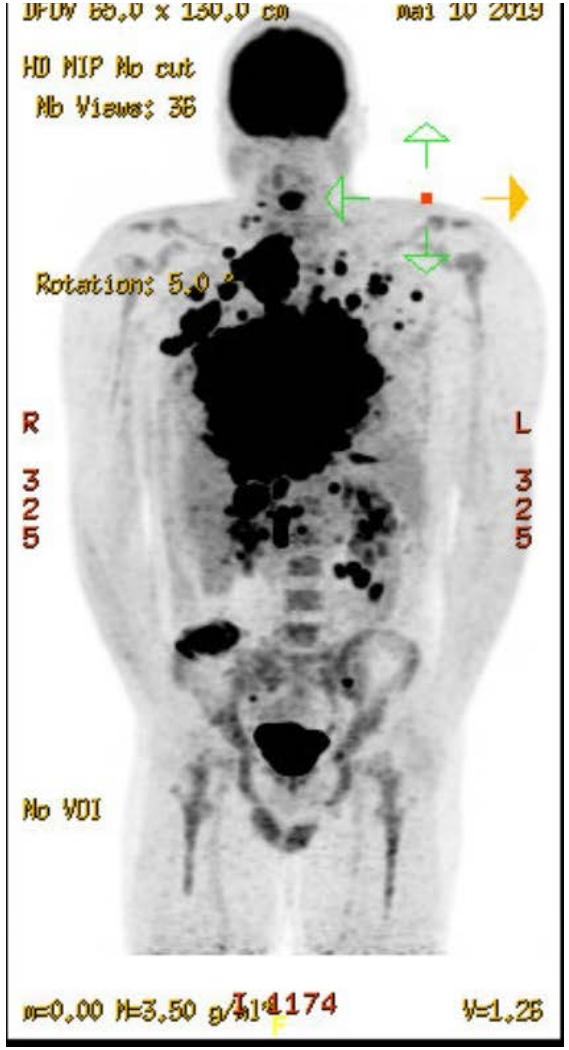
1. Tocilizumab only
2. Corticosteroids only
3. Tafasitamab/lenalidomide
4. Both tocilizumab and corticosteroids
5. Neither tocilizumab nor corticosteroids
6. I’m not sure

Case Presentation – Dr Salles: A 28-year-old man with R/R DLBCL treated with CAR T-cell therapy

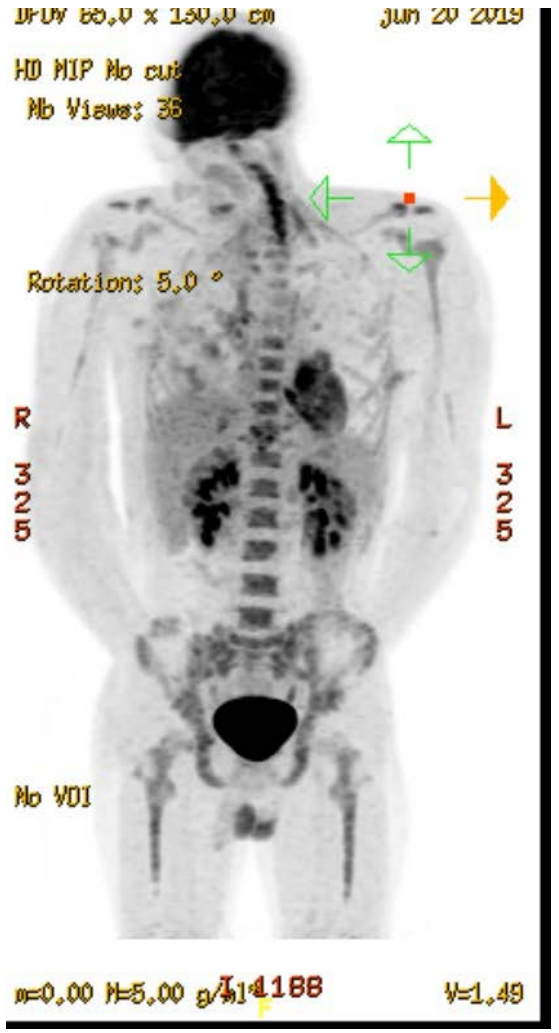
- 28 years old man, very good physical condition
- Diagnosed in 2019 with Primary Mediastinal B cell Lymphoma
- Received 6 cycles of R-EPOCH
  - PET-CT end of treatment: some residual SUV update at the end of the 6 cycles
  - PET-CT 2 months later: disease progression
- Moved to another center
  - Biopsy: active disease
- Treatment plan
  - R-ICE x 3 followed by ASCT
- After 2 cycles of R-ICE, disease progression +++
  - Patient had an ECOG PS of 2
  - Oxygen dependent
  - LDH ~ 3 times normal
- Decision was to move to CAR T
  - Was apheresed, received 1 infusion of pembrolizumab
  - Underwent CAR T

Case Presentation – Dr Salles: A 28-year-old man with R/R DLBCL treated with CAR T-cell therapy (continued)

Mediastinal lymphoma treated with CAR-T
(Axi cel on May 2020)



10 May 2020



20 June 2020

Case Presentation – Dr Flinn: A 57-year-old woman with Stage III non-GCB DLBCL

- A 57-year-old woman with Stage 3 non GCB DLBCL receives 6 cycles of R-CHOP. Mid treatment PET is improved but still with Deauville of 4.
- Post treatment PET CT reveals progressive disease with enlarging lymph nodes in mesentery and retroperitoneum. Deauville score is 5. Repeat biopsy confirms the diagnosis. The patient is given 3 cycles of RICE but does not respond.
- She is then considred for CAR T cells. Four weeks later, after significant logistical delays, the patient undergoes apheresis for axi-cel.
- At this time she has significant symptoms requiring 1 cycle of bridging therapy with BR polatuzumab. She has mild improvement in symptoms and 4 weeks after apheresis she receives LD chemo and axi-cel.
- Her post infusion course is complicated by grade 2 CRS and grade 1 ICANS which responds rapidly to fluids, tocilizumab, and steroids. Three months post treatment the patient is in CR with Deauville of 1.

Which specific features differentiate the approved CAR-T products and are there specific clinical situations where you favor one over another?

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Do you view the 3 available CD19-directed CAR T-cell therapies as equivalent therapeutic options for patients with DLBCL?

1. Yes
2. No
3. I’m not sure

Case Presentation – Dr Evens: A 47-year-old woman with relapsed DLBCL who received CD19-directed CAR T-cell therapy

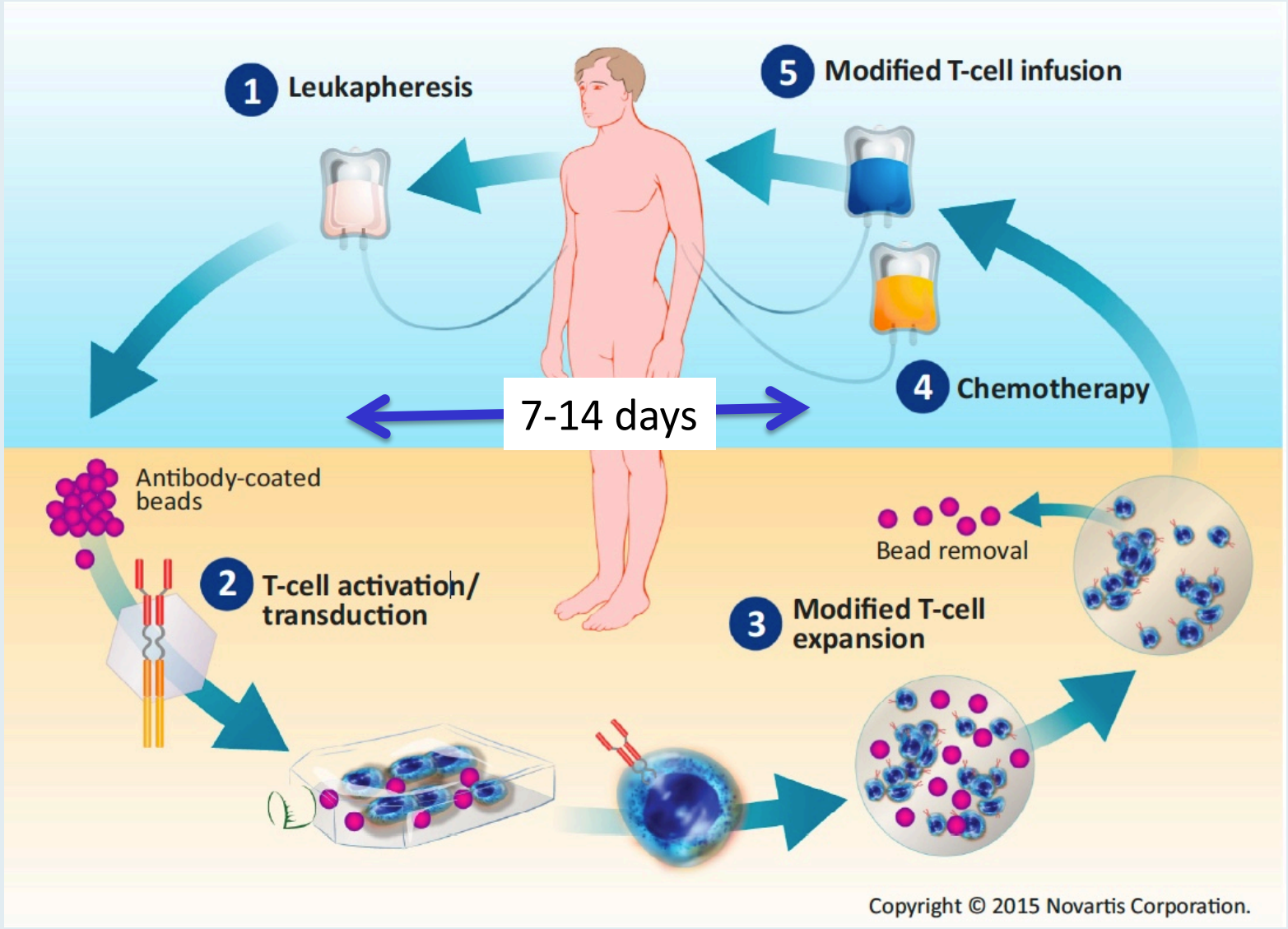
A 47-year-old woman who was in her usual state of health in 2/2020 when she developed progressive post-prandial abdominal pain and fatigue. By 3/2020, symptoms progressed to the point where she had nausea and vomiting with nearly every meal. She saw GI specialist for evaluation and underwent EGD end of 4/2020 which showed *H. pylori* per patient, and she was treated with a course of antibiotics without symptomatic improvement.

She had imaging concerning for liver mass and underwent 2 liver biopsies that were nondiagnostic as was biopsy of a mesenteric mass. She ultimately underwent ex-lap with distal duodenal resection, gastrojejunostomy in June 2020 with pathology consistent with DLBCL, high Ki-67 approximately 80%. Activated B-cell type, negative for BCL2/C-myc rearrangements, positive for BCL6 rearrangement.

She was treated with R-CHOP. She had initial PR (disease decreased by 70% with Deauville 4) but post-therapy re-staging PET/CT after 6 cycles with concern for refractory/progressive disease and presents today for consultation regarding next line of therapy. She was treated with R-ICE and had no response s/p 2 cycles of therapy with continued significant gastrointestinal symptomatology. Patient was referred for salvage therapy.

Key Recent Data Sets

Overview of CAR T-Cell Therapy



Modification, Courtesy, David Porter, MD

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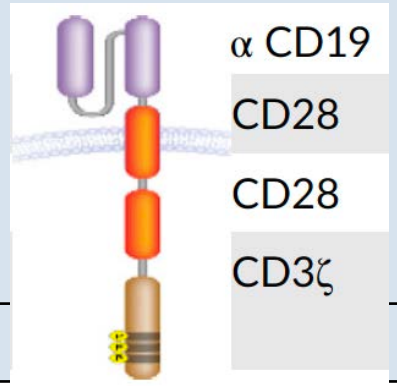
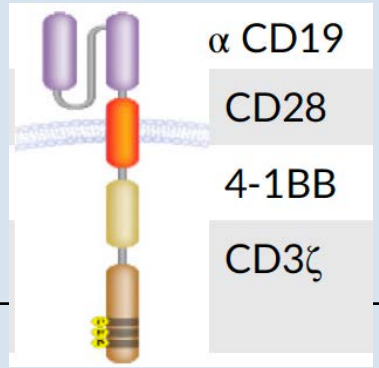
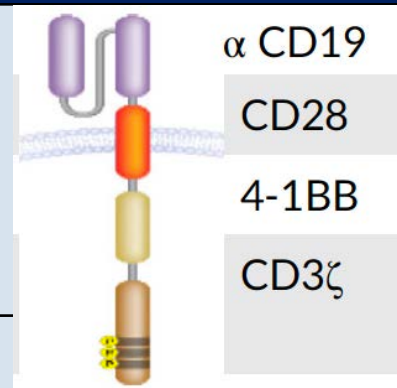
Summary of CAR T-Cell Pivotal Studies in DLBCL

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

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

RTP RESEARCH TO PRACTICE

Summary of Efficacy Outcomes in CAR T-Cell Pivotal Studies 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].

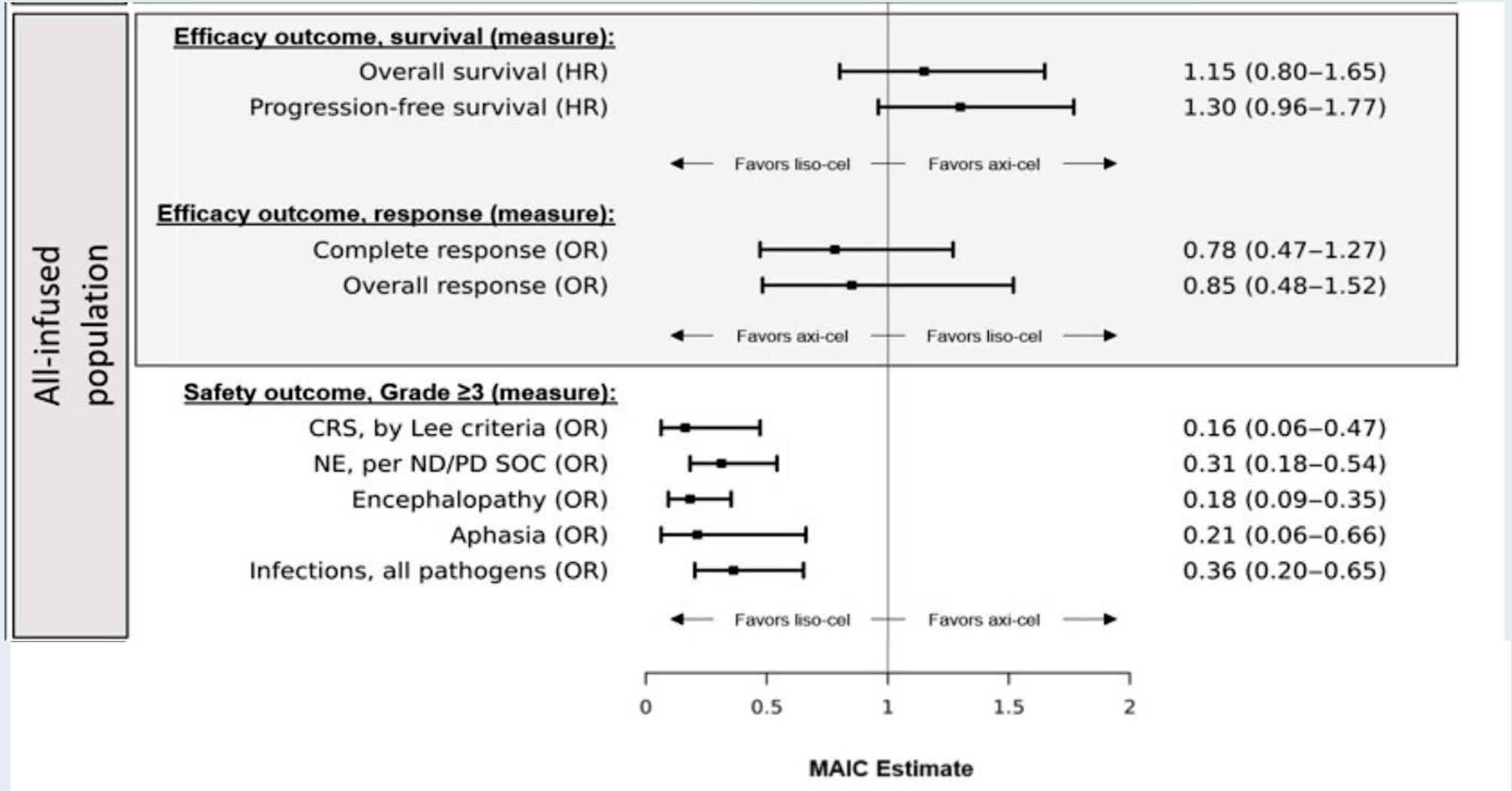
RTP RESEARCH TO PRACTICE

Matching-Adjusted Indirect Comparison (MAIC) of Lisocabtagene Maraleucel (Liso-cel) vs Axicabtagene Ciloleucel (Axi-cel) and Tisagenlecleucel in Relapsed/Refractory (R/R) Large B-Cell Lymphoma (LBCL)

Maloney DG et al.

ASH 2020;Abstract 2116.

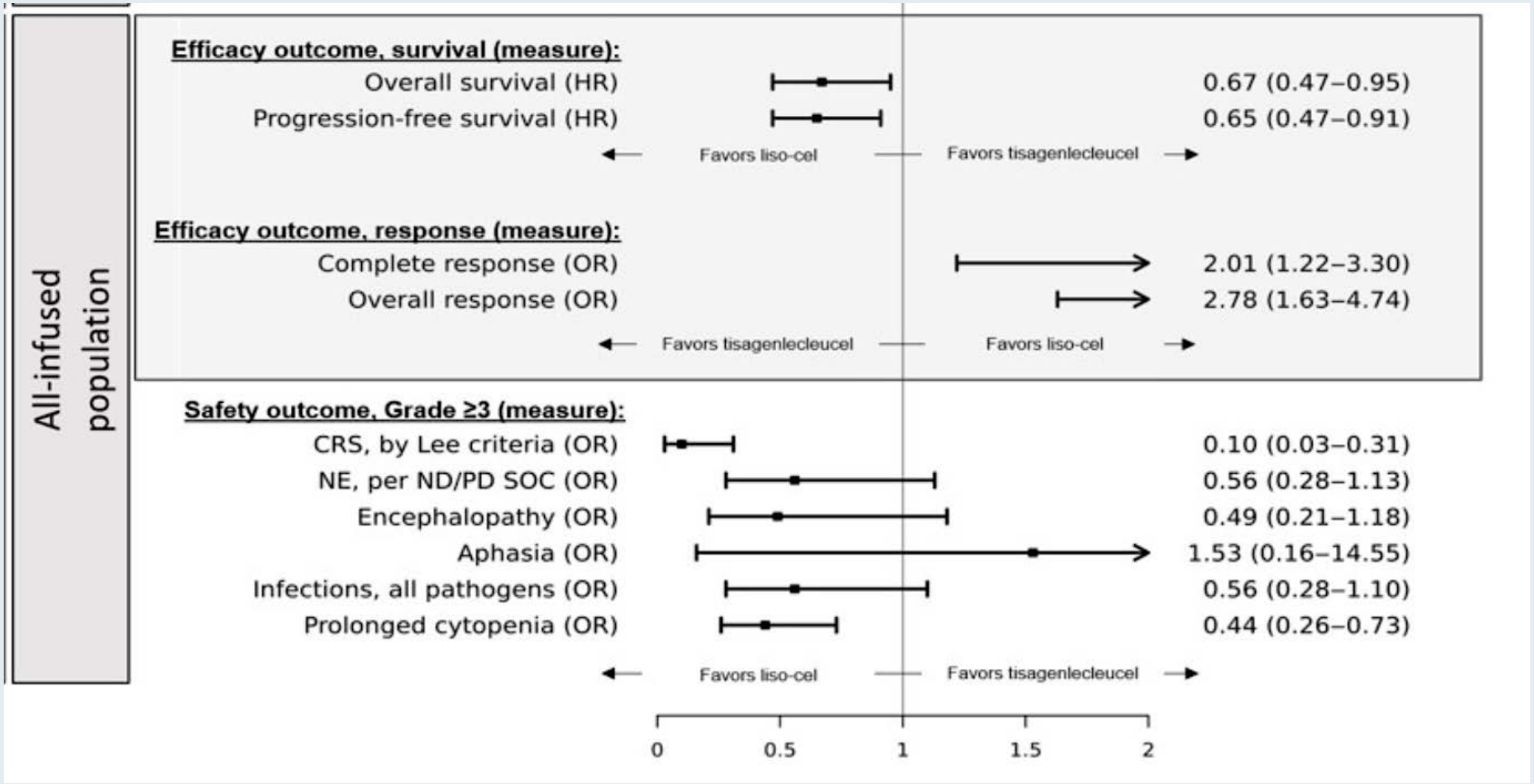
Matching-Adjusted Indirect Comparison of Liso-cel versus Axi-cel



Maloney DG et al. ASH 2020;Abstract 2116.

RTP RESEARCH TO PRACTICE

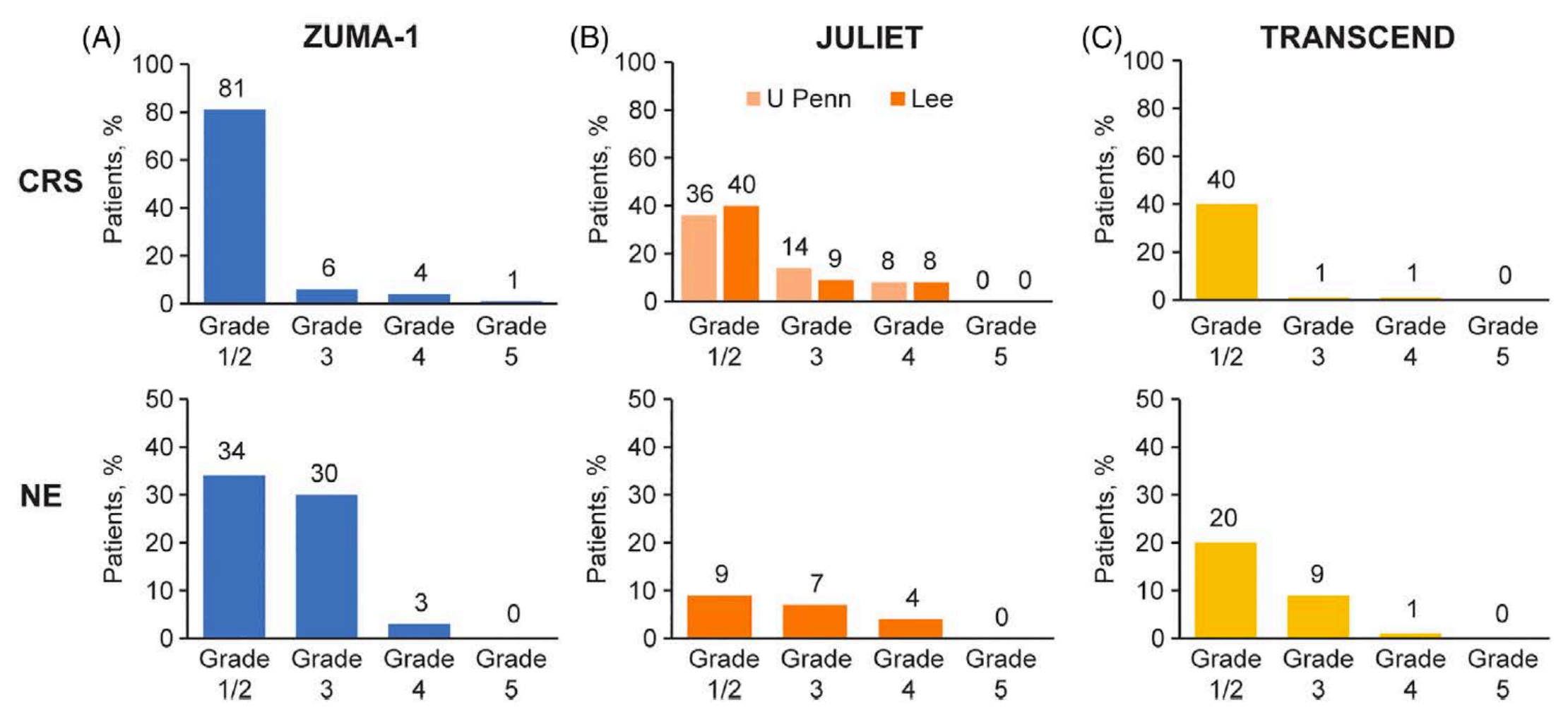
Matching-Adjusted Indirect Comparison of Liso-cel versus Tisagenlecleucel



Maloney DG et al. ASH 2020;Abstract 2116.

RTP RESEARCH TO PRACTICE

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



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

RTP RESEARCH TO PRACTICE

CAR-T Therapy-Associated 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.

FDA Approves Lisocabtagene Maraleucel for Relapsed or Refractory Large B-Cell Lymphoma

Press Release – February 5, 2021

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

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

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-lisocabtagene-maraleucel-relapsed-or-refractory-large-b-cell-lymphoma

Phase III TRANSFORM Trial of Liso-Cel Meets Primary Endpoint

Press Release – June 10, 2021

"Data from the Phase 3 TRANSFORM trial (NCT03575351) of the chimeric antigen receptor (CAR) T-cell therapy lisocabtagene maraleucel (liso-cel) as second-line therapy for patients with relapsed/refractory large B-cell lymphoma (LBCL) resulted in a statistically significant improvement in the primary end point of event-free survival versus therapy with the standard-of-care comparator arm, according to the company responsible for developing the agent.

Additionally, the toxicity profile observed with liso-cel was consistent with the safety data reported in the TRANSCEND NHL 001 trial (NCT02631044) which led to the FDA approving the CD19-directed therapy for patients with certain types of non-Hodgkin lymphoma, including diffuse large B-cell lymphoma (DLBCL), following 2 or more prior therapies. These data represent the first time a treatment for relapsed/refractory LBCL has demonstrated benefit over high-dose chemotherapy and hematopoietic stem cell transplant (HSCT).

Results regarding the primary end point will be evaluated and shared at an upcoming medical conference as well as with regulatory authorities."

https://www.cancernetwork.com/view/liso-cel-meets-primary-end-point-of-event-free-survival-improvement-in-phase-3-trial

RTP RESEARCH TO PRACTICE

Phase III ZUMA-7 Trial of Axi-Cel Meets Primary Endpoint

Press Release – June 30, 2021

"The ZUMA-7 trial (NCT03391466) demonstrated superiority of axicabtagene ciloleucel (axi-cel) compared with standard of care (SOC) autologous stem cell transplant (ASCT) after meeting the primary end point of event-free survival (EFS) improvement for patients with relapsed or refractory large B-cell lymphoma (LBCL), according to a press release from the company responsible for manufacturing the chimeric antigen receptor (CAR) T-cell therapy. A statistically significant EFS benefit (HR, 0.398; P <0.0001) was observed as well as improvement in the secondary end point of objective response rate (ORR).

The top-line results of the randomized ZUMA-7 trial paint the picture of a potential paradigm shift in the treatment of large B-cell lymphoma, Frederick L Locke, MD, ZUMA-7 lead principal investigator and co-leader of the Immuno-Oncology Program at Moffitt Cancer Center in Tampa, Florida, said in the press release. Investigators mentioned that these data are still immature and further analyses are planned for the future. The trial was conducted under a Special Protocol Agreement from the FDA where the trial design, end points, and statistical analysis were agreed in advance."

https://www.cancernetwork.com/view/zuma-7-trial-meets-event-free-survival-end-point-in-large-b-cell-lymphoma

RTP RESEARCH TO PRACTICE

Multicenter Phase II ZUMA-12 Schema: First-Line Therapy for High-Risk LBCL

Eligibility criteria

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

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]

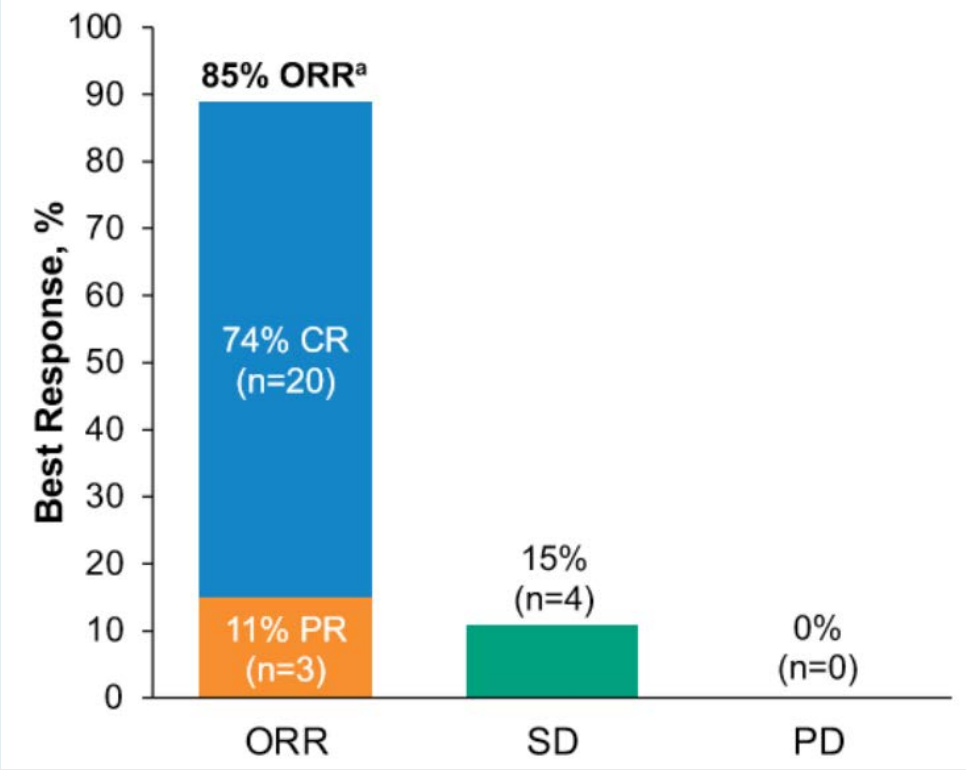
Key secondary endpoints

- 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 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

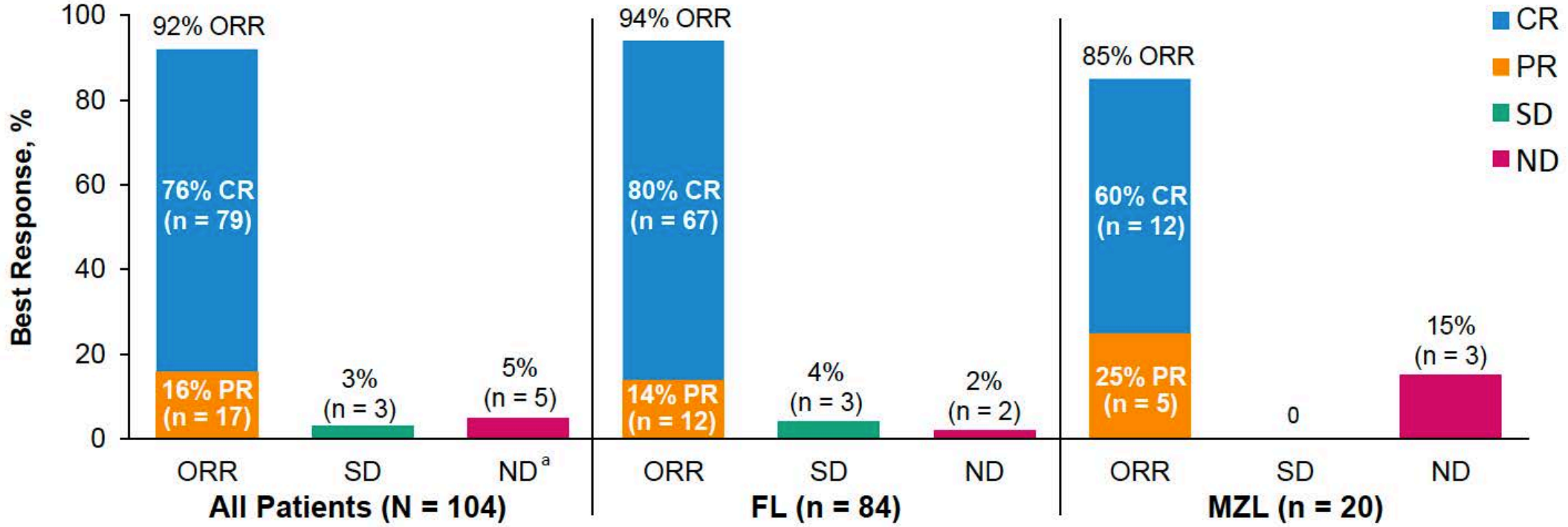
Primary Analysis of ZUMA-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

Caron Jacobson, MD[1]; Julio C. Chavez, MD[2]; Alison Sehgal, MD[3]; Basem William, MD[4]; Javier Munoz, MD, MS, FACP[5]; Gilles Salles, MD, PhD[6]; Pashna Munshi, MD[7]; Carla Casulo, MD[8]; David Maloney, MD, PhD[9]; Sven de Vos, MD, PhD[10]; Ran Reshef, MD[11]; Lori Leslie, MD[12]; Ibrahim Yakoub-Agha, MD, PhD[13]; Olalekan Oluwole, MD, MPH, MBBS[14]; Henry Chi Hang Fung, MD[15]; Joseph Rosenblatt, MD[16]; John Rossi, MS[17]; Lovely Goyal, PhD[17]; Vicki Plaks, LLB, PhD[17]; Yin Yang, MS[17]; Jennifer Lee, BS[17]; Wayne Godfrey, MS, MD[17]; Remus Vezan, MD, PhD[17]; Mauro Avanzi, MD, PhD[17]; and Sattva S. Neelapu, MD[18]

[1]Dana-Farber Cancer Institute, Boston, MA, 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, NY, USA; [12]John Theurer Cancer Center, Hackensack, NJ, USA; [13]CHU de Lille, Univ Lille, INSERM U1286, Infinite, 59000 Lille, France; [14]Vanderbilt University Medical Center, Nashville, TN, USA; [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]The University of Texas MD Anderson Cancer Center, Houston, TX, USA

ASH 2020;Abstract 700

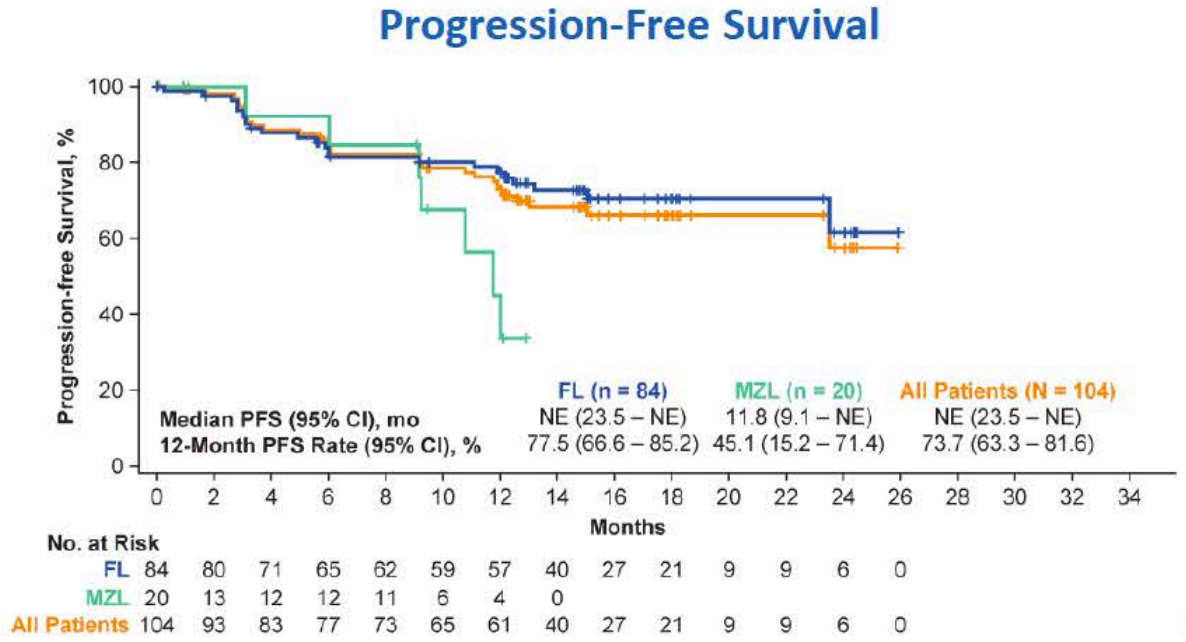
ZUMA-5: ORR by IRRC Assessment for Patients with FL Receiving Axicabtagene Ciloleucel

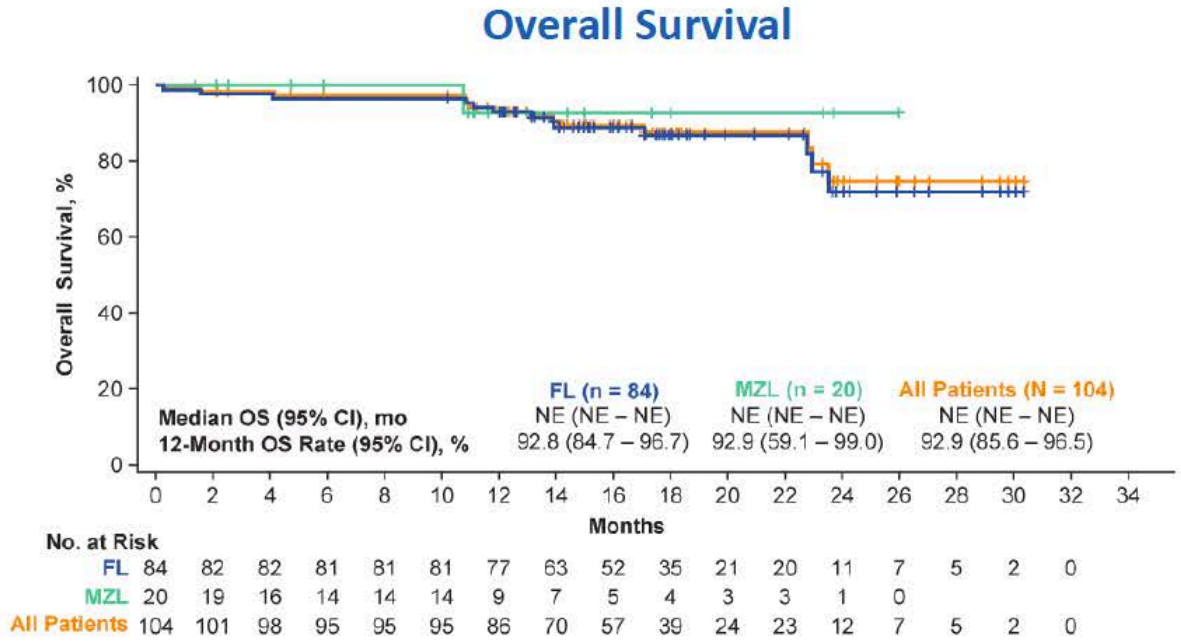


- The median time to first response was 1 month (range, 0.8 – 3.1)
- Among the 25 patients with FL who initially had a PR, 13 (52%) subsequently converted to a CR after a median of 2.2 months (range, 1.9 – 11.2)

Jacobson C et al. ASH 2020;Abstract 700.

ZUMA-5: Progression-Free and Overall Survival





- With a median follow-up of 17.5 months, median PFS and median OS were not reached
  - The 12-month PFS rate was 73.7% (95% CI, 63.3 – 81.6) for all patients
  - The 12-month OS rate was 92.9% (95% CI, 85.6 – 96.5) for all patients

Jacobson C et al. ASH 2020;Abstract 700.

ZUMA-5: Cytokine Release Syndrome and Neurologic Events

Cytokine release syndrome	FL (n = 124)	MZL (n = 22)
Any grade	78%	100%
Grade ≥3	6%	9%
Median time to onset (range)	4 (1-15) days	4 (1-9) days
Median duration of events (range)	6 (1-27) days	6 (2-14) days
Patients with resolved events	99%	100%
Neurologic events		
Any grade	56%	77%
Grade ≥3	15%	41%
Median time to onset (range)	7 (1-177) days	7 (3-19) days
Median duration of events (range)	14 (1-452) days	10 (2-81) days
Patients with resolved events	96%	82%

Jacobson C et al. ASH 2020;Abstract 700.

Efficacy and Safety of Tisagenlecleucel (Tisa-cel) in Adult Patients (Pts) with Relapsed/Refractory Follicular Lymphoma (R/R FL): Primary Analysis of the Phase 2 Elara Trial

Schuster SJ et al.

ASCO 2021;Abstract 7508.

ELARA Primary Analysis: Primary CR Endpoint

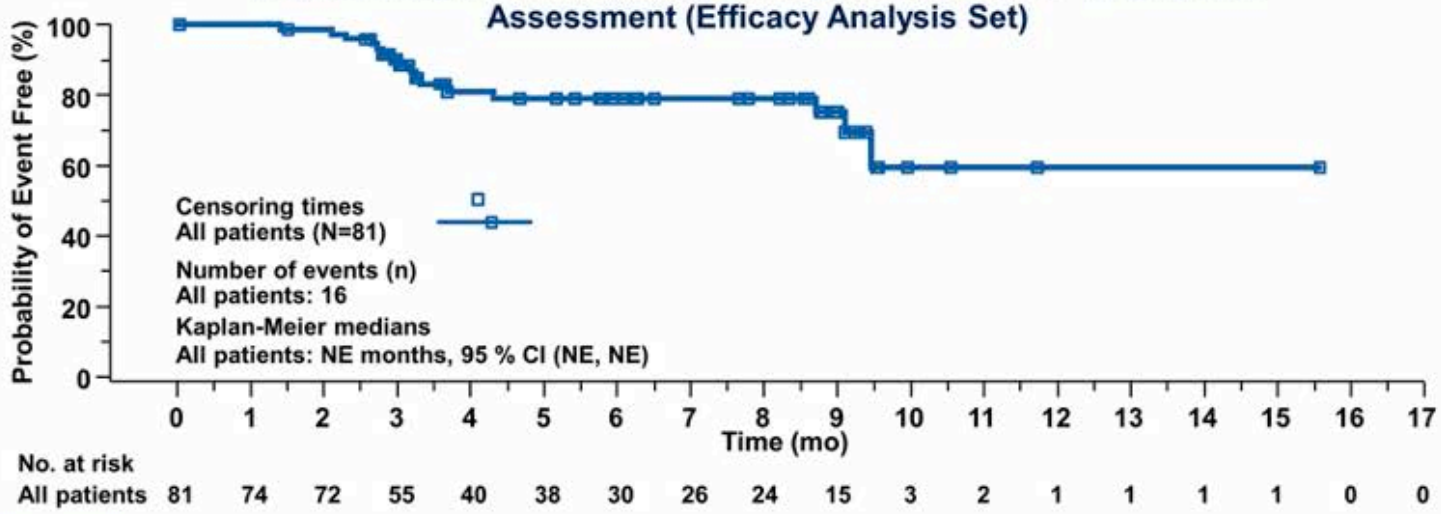
Best Overall Response Rate

Response Rate, %	Patients Evaluable for Efficacy[b] (n=94)
CR	66.0[b]
PR	20.2
ORR (CR+PR)	86.2

- Investigator-assessed CRR was 69.1%[c] (ORR 90.4%)
- CRRs/ORRs were comparable among key high-risk subgroups

Median DOR Was Not Reached at 11 Months Median Follow-Up

Kaplan-Meier Plot of Duration of Response (DOR, CR+PR), by IRC Assessment (Efficacy Analysis Set)



- Median follow-up for efficacy (n=94): 10.9 (4.3-19.7) months
- Probability for a responding patient to remain in response ≥6 months was 79% (95% CI, 66-87)
- 12 of 31 PRs (38.7%) converted to CRs; all but 1 occurred between Month 3 and Month 6
- Median time to next antilymphoma treatment was not reached

Schuster SJ et al. ASCO 2021;Abstract 7508.

ELARA: Adverse Events

Overall Safety Profile

Adverse Events, n (%)	Treated Patients N=97
Any AE (all grade)	96 (99.0)
AEs suspected to be drug-related	75 (77.3)
Any SAE	40 (41.2)
Suspected to be drug-related	28 (28.9)
Any grade 3/4 AE	74 (76.3)
Suspected to be drug-related	44 (45.4)
Death	3 (3.1)
Deaths due to study indication	3 (3.1)
Deaths within 30 days post infusion	0
AE management, n (%)	
Tocilizumab[a]	16 (34)
Corticosteroids[a]	3 (6.4)

Adverse Events of Special Interest (AESI)

	Treated Patients N=97	
AESI (within 8 weeks of infusion)	**All grades, %**	**Grade ≥3, %**
Cytokine release syndrome[a,1]	48.5	**0**
Neurological adverse reactions	9.3	**1.0**
Infections	18.6	5.2
Tumor lysis syndrome	1.0	1.0
Prolonged depletion of B cells and/or agammaglobulinemia[b]	10.3	0
Hematologic disorders including cytopenias		
Neutropenia[c,d]	30.9	27.8
Anemia[c]	24.7	13.4
Thrombocytopenia[c]	16.5	9.3

All neurological and CRS events resolved with appropriate management

Schuster SJ et al. ASCO 2021;Abstract 7508.

RTP RESEARCH TO PRACTICE

FDA Approves Brexucabtagene Autoleucel for Relapsed or Refractory Mantle Cell Lymphoma

Press Release – July 24, 2020

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

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

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

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

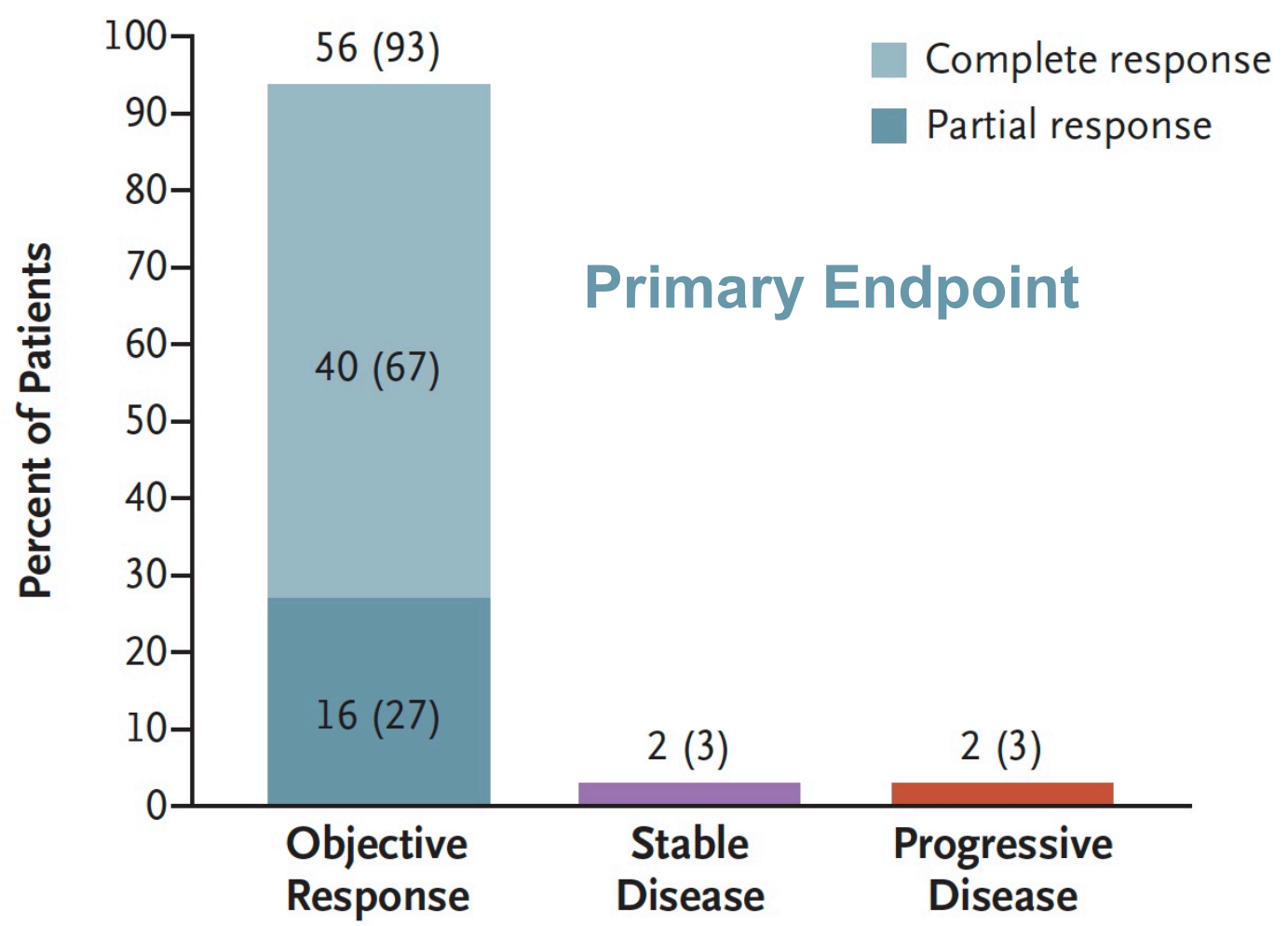
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

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

ZUMA-2: Objective Response (IRR), Survival and Key Toxicities



Estimated 12-month survival rate	
Median PFS	61%
Median OS	83%

Key toxicities		
	Grade 1-2	Grade 3-4
Cytokine release syndrome	76%	15%
Neurologic events	32%	31%
Cytopenias	—	94%
Infections	23%	32%

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

Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Wednesday, September 1, 2021
5:00 PM – 6:00 PM ET

Faculty

Joyce F Liu, MD, MPH

Moderator

Neil Love, MD

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Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.