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

Loretta J Nastoupil, MD
Associate Professor
Section Chief, Indolent Lymphoma
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Houston, Texas

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Commercial Support

This activity is supported by educational grants from ADC Therapeutics, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Genentech, a member of the Roche Group, Novartis and Seagen Inc.

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Dr Love — Disclosures

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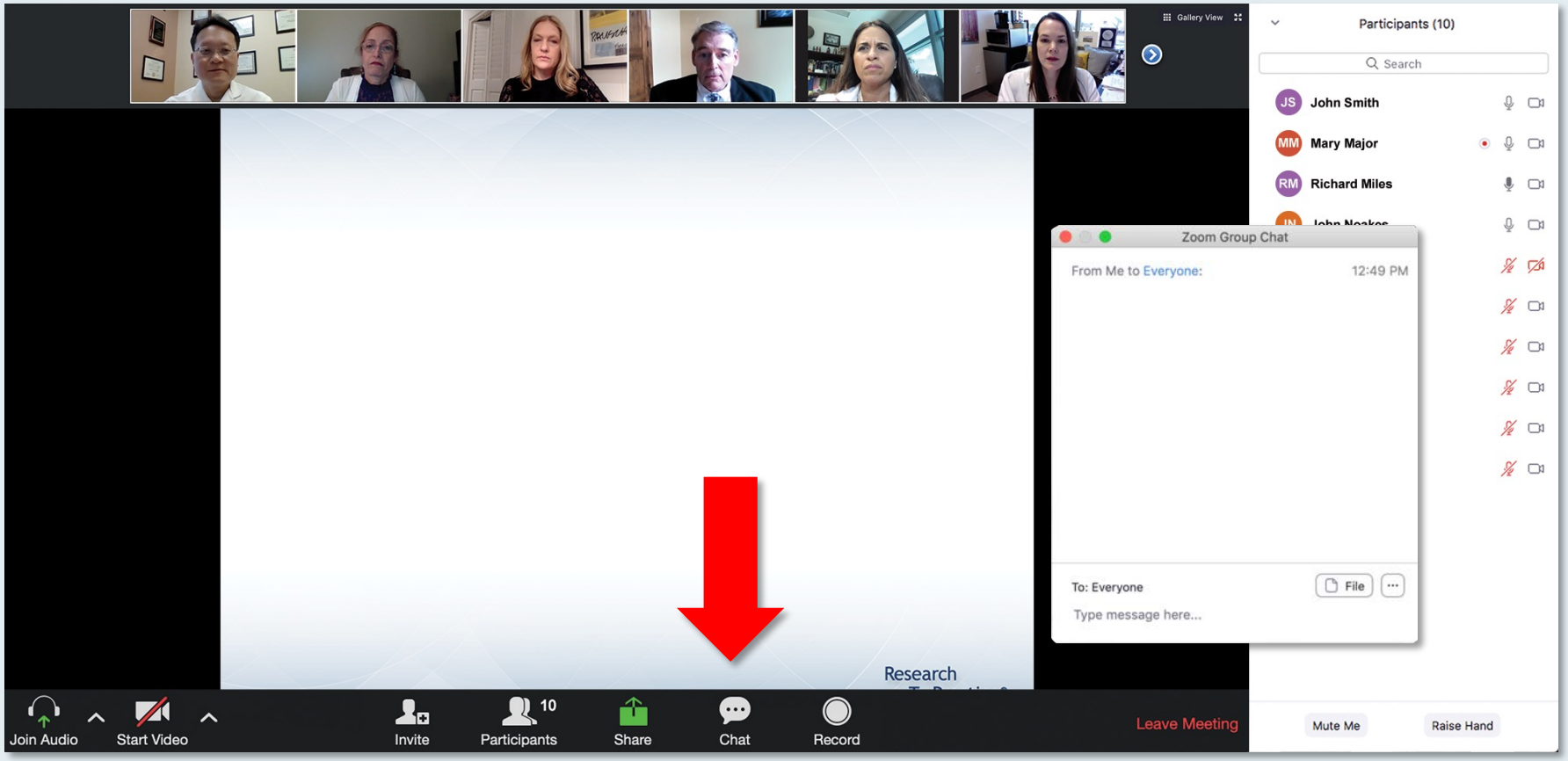
We Encourage Clinicians in Practice to Submit Questions



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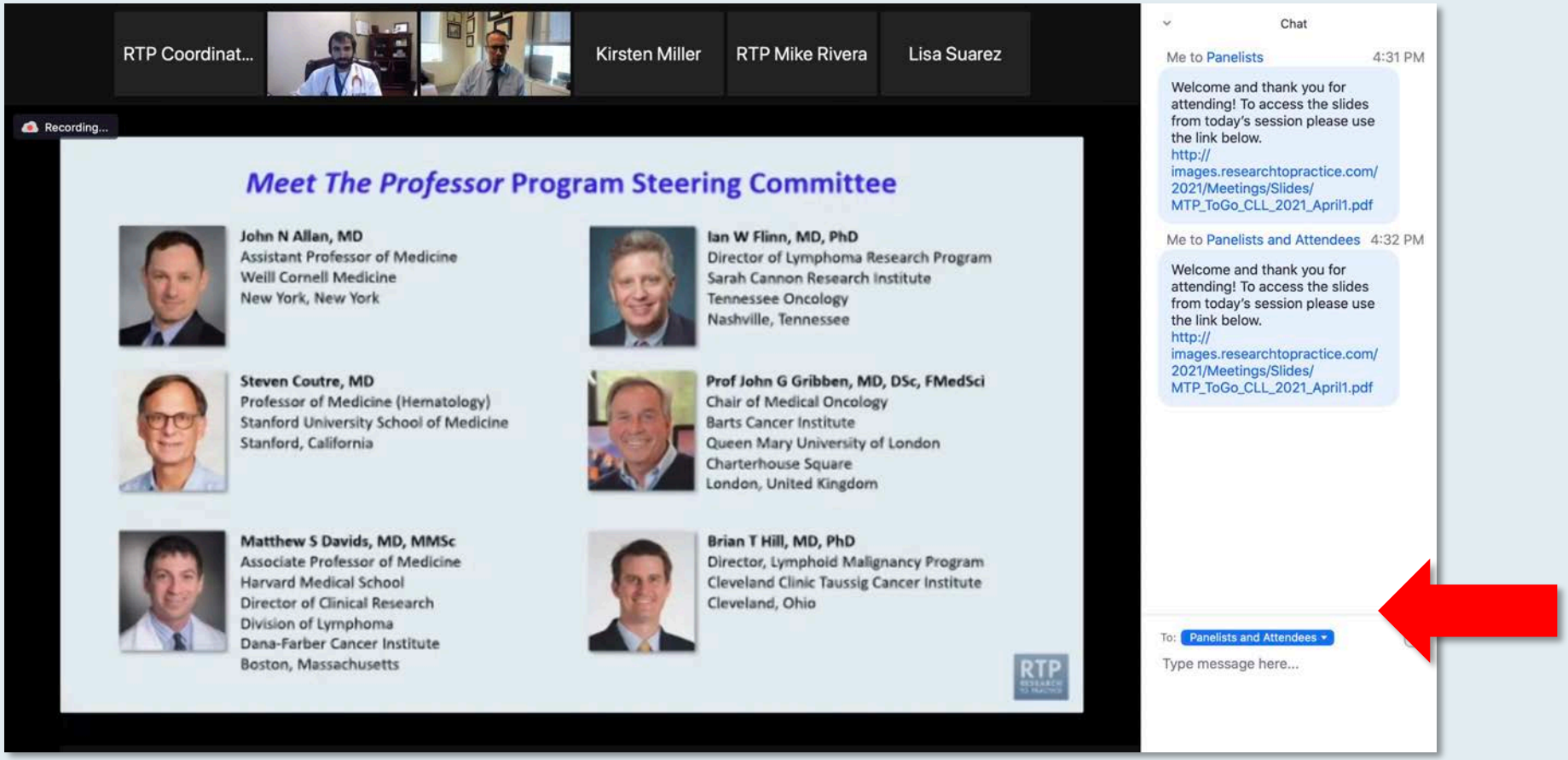

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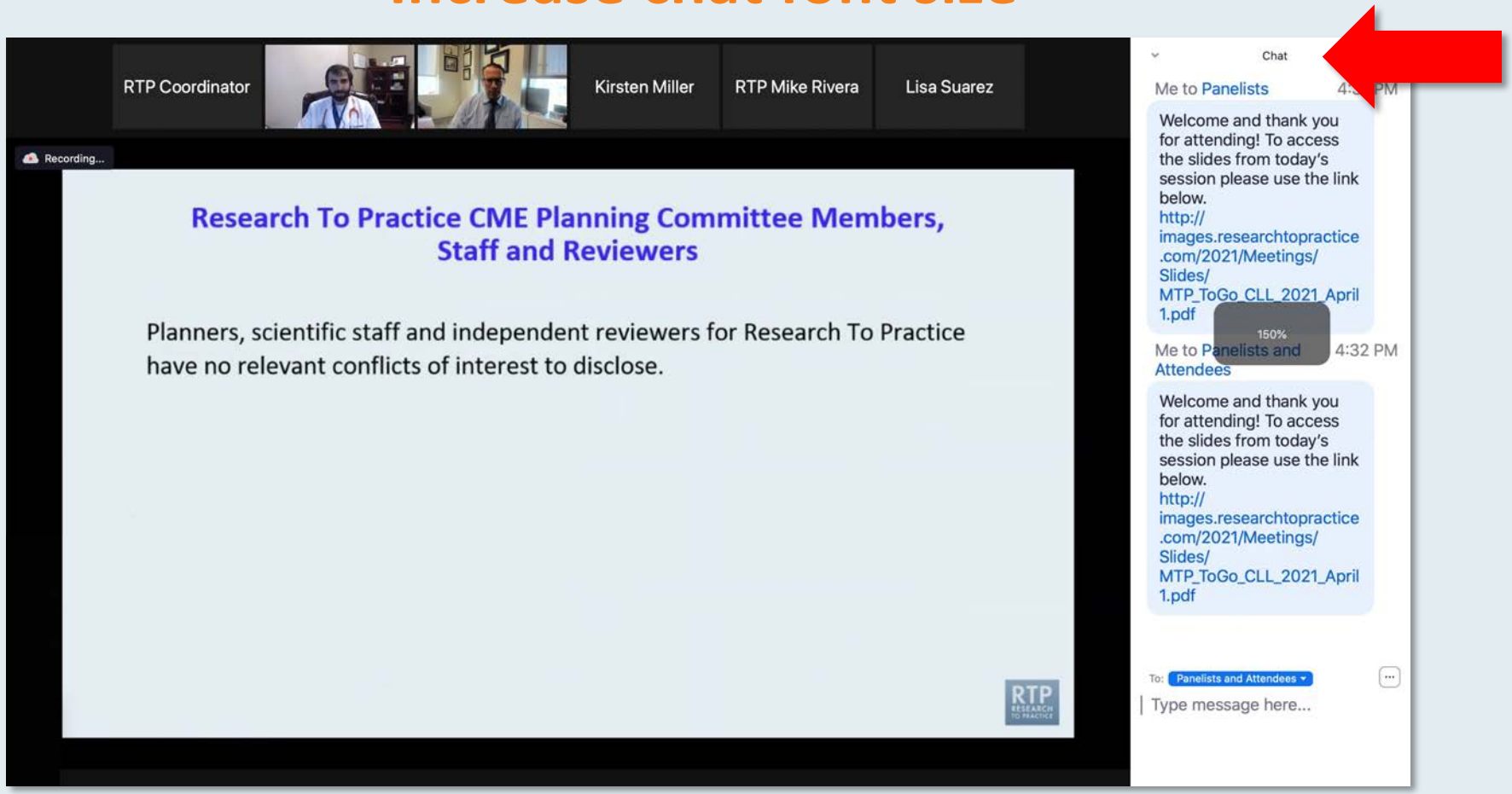

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WITH DR NEIL LOVE

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

Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Friday, September 17, 2021
12:00 PM – 1:00 PM ET

Faculty

Philip A Philip, MD, PhD, FRCP

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Urothelial Bladder Carcinoma

Tuesday, September 21, 2021
5:00 PM – 6:00 PM ET

Faculty

Jonathan E Rosenberg, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer

Wednesday, September 22, 2021
5:00 PM – 6:00 PM ET

Faculty

Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Monday, September 27, 2021
5:00 PM – 6:00 PM ET

Faculty

Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Triple-Negative Breast Cancer

Tuesday, September 28, 2021
5:00 PM – 6:00 PM ET

Faculty

Professor Peter Schmid, MD, PhD

Moderator

Neil Love, MD

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Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

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5:00 PM – 6:00 PM ET

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Brad S Kahl, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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Meet The Professor Program Participating Faculty

Nancy Bartlett, MD
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St Louis, Missouri

Carla Casulo, MD
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Division of Hematology/Oncology
Director, Hematology/Oncology Fellowship Program
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Wilmot Cancer Institute
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Brad S Kahl, MD
Professor of Medicine
Washington University School of Medicine
Director, Lymphoma Program
Siteman Cancer Center
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Michael E Williams, MD, ScM
Byrd S Leavell Professor of Medicine
Chief, Hematology/Oncology Division
Physician Lead, Cancer Service Line
University of Virginia School of Medicine
Charlottesville, Virginia

Loretta J Nastoupil, MD
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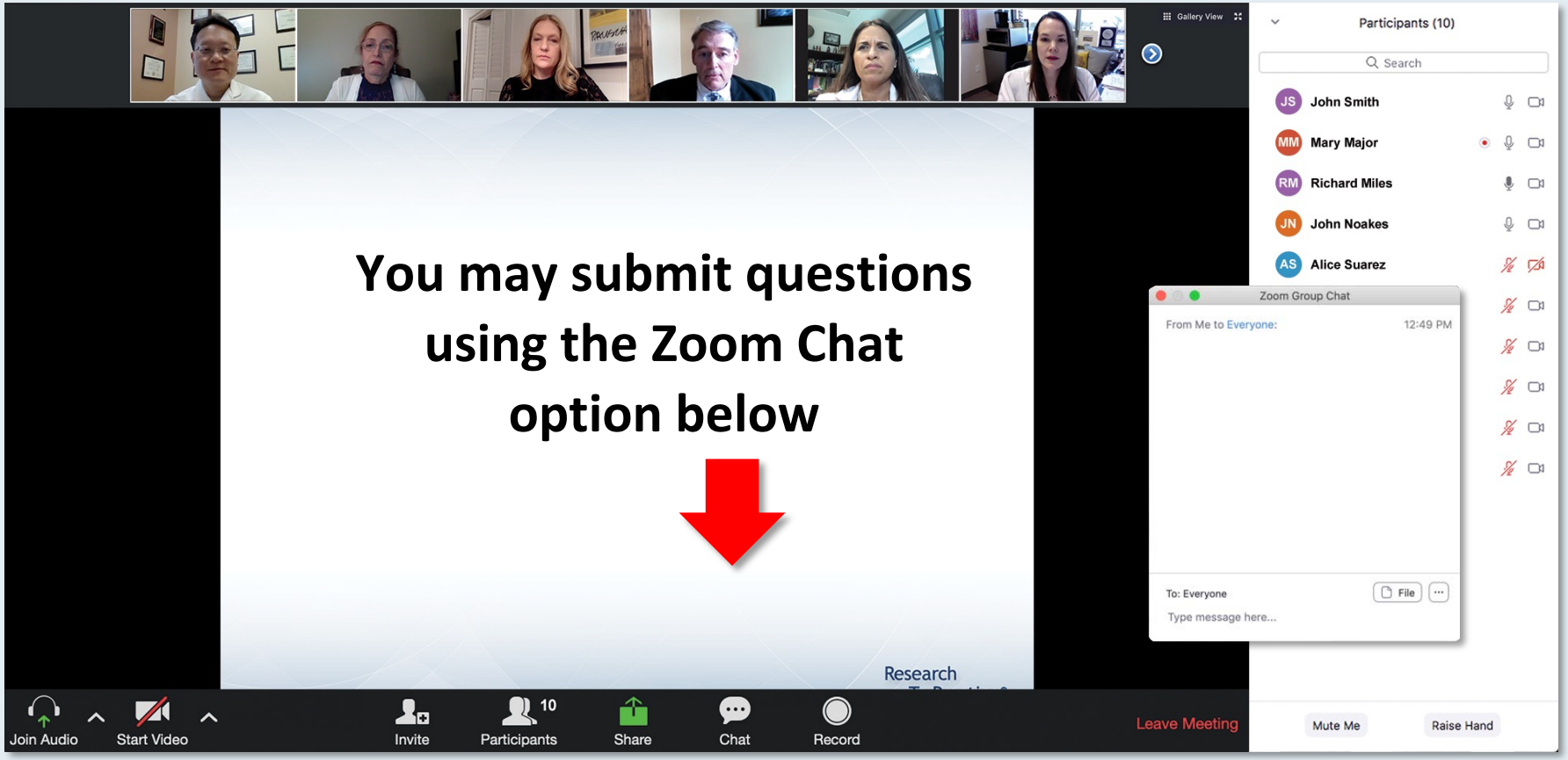

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Mitchell R Smith, MD, PhD
Clinical Professor of Medicine
George Washington University
Washington, DC

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Meet The Professor with Dr Nastoupil

Introduction: Is the management of diffuse large B-cell lymphoma (DLBCL) about to change dramatically?

MODULE 1: Case Presentations from Dr Smith

- A 69-year-old man with recurrent DLBCL and progression after ASCT
- A 33-year-old man with classic nodular sclerosing Hodgkin lymphoma
- A 72-year-old man with FL who experiences relapse 1 year after completing lenalidomide/rituximab
- A 58-year-old man with relapsed MCL after CAR T-cell therapy

MODULE 2: Journal Club with Dr Nastoupil

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets

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Agree or disagree? In 2022 the standard first-line treatment for DLBCL will be R-CHP/polatuzumab vedotin, with second-line therapy for fit patients being CAR T-cell therapy.

1. Agree with both
2. Agree with R-CHP/polatuzumab vedotin as first line
3. Agree with CAR T-cell therapy as second line
4. Disagree

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Phase III Study Shows Polatuzumab Vedotin with R-CHP Is the 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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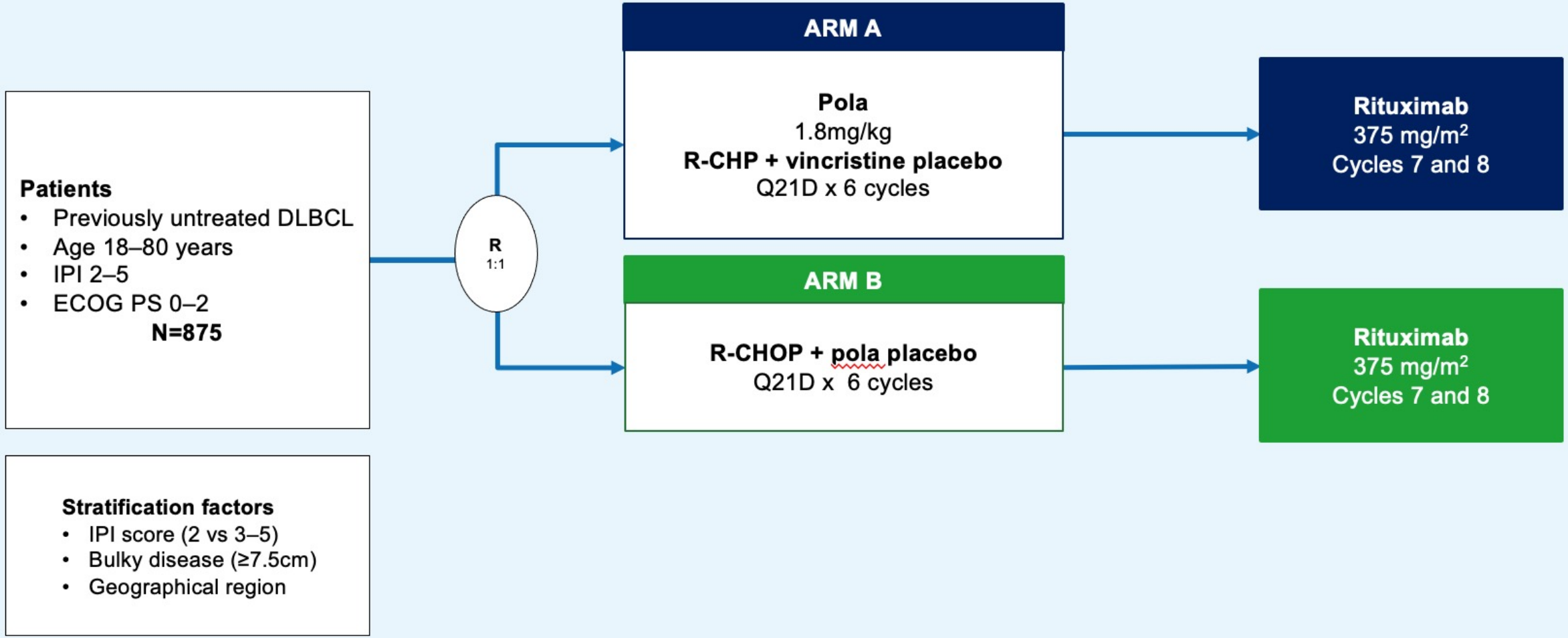
POLARIX Phase III Trial Design



Courtesy of Gilles Salles MD, PhD.

POLARIX

Trial has met its primary endpoint: improvement of PFS

<u>What to look for:</u>

- **Magnitude of the effect**
- **Safety of the 2 arms +++**
- **Response rates and DoR in the 2 arms**
- **Overall survival ?**

Courtesy of Gilles Salles MD, PhD.

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

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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

BELINDA Study Investigating Tisagenlecleucel as Second-Line Treatment in Aggressive B-Cell Non-Hodgkin Lymphoma Fails to Meet Primary Endpoint

Press Release – August 24, 2021

"The Phase III BELINDA study investigating tisagenlecleucel in aggressive B-cell non-Hodgkin lymphoma (NHL) after relapse or lack of response to first-line treatment did not meet its primary endpoint of event-free survival compared to treatment with the standard-of-care (SOC). SOC was salvage chemotherapy followed in responding patients by high-dose chemotherapy and stem cell transplant. The safety profile was consistent with the established safety profile of tisagenlecleucel."

https://www.novartis.com/news/media-releases/novartis-provides-update-belinda-study-investigating-kymriah-second-line-treatment-aggressive-b-cell-non-hodgkin-lymphoma

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CD19 CAR T versus ASCT for Patients with DLBCL at First Treatment Failure After R-CHOP (or Equivalent)

Axi-cel	ZUMA-7	+
Liso-cel	TRANSFORM	+
Tisa-cel	BELINDA	?

NCT03391466; NCT03575351; NCT03570892

Differences might exist:

- Inclusion criteria (histological subtypes, primary refractoriness definition…)
- **Bridging allowed before CAR T**
- Nb of chemo cycles in SOC arm
- **Product and time of manufacturing**
- **LD therapy**
- Timing of response/events assessment
- Precise definition of events (EFS)
- Cross over planned / optional & CAR T immediate availability in the SOC arm

Courtesy of Gilles Salles MD, PhD.

Meet The Professor with Dr Nastoupil

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Case Presentation – A 69-year-old man with recurrent DLBCL and progression after ASCT

Dr Mitchell Smith

- Presents with inguinal mass, diffuse LAN
- Biopsy: Stage IIIA DLBCL, non-GC subtype, double expressor for MYC/Bcl-2, IPI 2
- R-CHOP x 6 with EOT PET-negative
- 6 months later: Neck node biopsy-confirmed relapsed DLBCL, marrow negative
- R-ICE x 3 with PET CR → ASCT
- 1 year later: Relapsed with diffuse LAN but marrow still negative

Questions

- How do you select among the 4 treatments that have been approved in the past 2 years? If the patient can't get CAR T-cell therapy, or receives it and relapses, then how would you treat him?
- What's the experience in the real world of patients not getting adequate CAR T-cell development? Can you predict who will do poorly in terms of tolerability?

Case Presentation – A 69-year-old man with recurrent DLBCL and progression after ASCT (continued)

Dr Mitchell Smith

- Presents with inguinal mass, diffuse LAN
- Biopsy: Stage IIIA DLBCL, non-GC subtype, double expressor for MYC/Bcl-2, IPI 2
- R-CHOP x 6 with EOT PET-negative
- 6 months later: Neck node biopsy-confirmed relapsed DLBCL, marrow negative
- R-ICE x 3 with PET CR → ASCT
- 1 year later: Relapsed with diffuse LAN but marrow still negative
- ***Plan to enroll patient on a clinical trial of CAR T-cell therapy***

Questions

- ***How do you select patients for CAR T-cell therapy? Do you attempt to minimize disease burden before going to CAR T?***
- ***Do you think the apparent lesser toxicity with tiso-cel is due to our better understanding of the physiology in early intervention, or is it really due to a difference in the CAR T products?***

Case Presentation – A 33-year-old man with classic nodular sclerosing Hodgkin lymphoma

Dr Mitchell Smith

- Presents with fatigue, night sweats and large mass on the neck
- Biopsy: Stage IIBx Classic nodular sclerosing Hodgkin lymphoma, IPI 2
  - Albumin: 30, cardiac and pulmonary function unremarkable

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Case Presentation – A 33-year-old man with classic nodular sclerosing Hodgkin lymphoma (continued)

Dr Mitchell Smith

- Presents with fatigue, night sweats and large mass on the neck
- Biopsy: Stage IIBx Classic nodular sclerosing Hodgkin lymphoma, IPI 2
  - Albumin: 30, cardiac and pulmonary function unremarkable
- ***Patient desires to avoid the potential for peripheral neuropathy → ABVD x 2 → AVD x 2***
  - ***Bleomycin held due to pulmonary complaints***
  - ***PET2: Deauville 2 → AVD x 4 → EOT PET: Negative***

Case Presentation – A 72-year-old man with follicular lymphoma (FL) who experiences relapse 1 year after completing lenalidomide/rituximab

Dr Mitchell Smith

- Asymptomatic, with 2-3-cm neck, axillary and inguinal nodes
- Nodal biopsy: Low-grade FL (CD10+, CD20+, CD5-, IHC BCLL2+)
- Borderline anemia and renal function, matted retroperitoneal nodes, possible hydronephrosis
- BR x 6, with EOT PET-negative, with fever after 2nd or 3rd cycle

Questions

- Have you observed fever after the 2nd or 3rd cycle of bendamustine?
- How are you addressing maintenance rituximab, and has that been changed by COVID-19?

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Case Presentation – A 72-year-old man with FL who experiences relapse 1 year after completing lenalidomide/rituximab (continued)

Dr Mitchell Smith

- Asymptomatic, with 2-3-cm neck, axillary and inguinal nodes
- Nodal biopsy: Low-grade FL (CD10+, CD20+, CD5-, IHC BCLL2+)
- Borderline anemia and renal function, matted retroperitoneal nodes, possible hydronephrosis
- BR x 6, with EOT PET-negative, with fever after 2nd or 3rd cycle

Question

- ***During the COVID-19 era, what are your thoughts about using more lenalidomide/rituximab as opposed to chemoimmunotherapy regimens, such as bendamustine/rituximab, which can suppress immune functioning?***

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Case Presentation – A 72-year-old man with FL who experiences relapse 1 year after completing lenalidomide/rituximab (continued)

Dr Mitchell Smith

- Asymptomatic, with 2-3-cm neck, axillary and inguinal nodes
- Nodal biopsy: Low-grade FL (CD10+, CD20+, CD5-, IHC BCLL2+)
- Borderline anemia and renal function, matted retroperitoneal nodes, possible hydronephrosis
- BR x 6, with EOT PET-negative, with fever after 2nd or 3rd cycle
- ***1 year later: New axillary node, fatigue, 10-lbs weight loss***
- ***PET/CT: Diffuse increase in original nodes; Biopsy-confirmed low-grade FL, no transformation***

Question

- ***How do you manage a patient with FL who experiences relapse within 1 year of receiving bendamustine/rituximab?***

Case Presentation – A 72-year-old man with FL who experiences relapse 1 year after completing lenalidomide/rituximab (continued)

Dr Mitchell Smith

- Asymptomatic, with 2-3-cm neck, axillary and inguinal nodes
- Nodal biopsy: Low-grade FL (CD10+, CD20+, CD5-, IHC BCLL2+)
- Borderline anemia and renal function, matted retroperitoneal nodes, possible hydronephrosis
- BR x 6, with EOT PET-negative, with fever after 2nd or 3rd cycle
- 1 year later: New axillary node, fatigue, 10-lbs weight loss
- PET/CT: Diffuse increase in original nodes; Biopsy-confirmed low-grade FL, no transformation
- ***Lenalidomide/rituximab >1 year → PD***

Question

- ***How do you approach his next line of treatment – Transplant? CAR T-cell therapy? Tazemetostat? PI3 kinase inhibitor?***

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Case Presentation – A 58-year-old man with relapsed mantle cell lymphoma (MCL) after CAR T-cell therapy

Dr Mitchell Smith

- S/p VcR-CVAD x 6 on ECOG-1405 (declined ASCT, rituximab maintenance) for MCL (intermediate-risk MIPI) in 2009
- 2013: Recurrent disease → BR x 6 → Maintenance rituximab x 2 years, with CR
- 2016: New LAN, marked splenomegaly, cytopenias → Ibrutinib, with minor response → Splenectomy
- Axi-cel on the ZUMA-2 trial, with CR (Grade 2 CRS x 2 days, no ICANS)
- Two years later: Right pre-auricular squamous cell carcinoma → Mohs surgery
- Two months later: Recurrent masses near excision site → Re-excised
  - Positive for MCL → PET/CT: Negative for other disease → RT with remission
- Three months later: New retroperitoneal and inguinal LANs, biopsy-confirmed MCL

Question

- What do you do post CAR T in a guy who's had the disease for 12 years?

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Case Presentation – A 58-year-old man with relapsed MCL after CAR T-cell therapy (continued)

Dr Mitchell Smith

- S/p VcR-CVAD x 6 on ECOG-1405 (declined ASCT, rituximab maintenance) for MCL (intermediate-risk MIPI) in 2009
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  - Positive for MCL → PET/CT: Negative for other disease → RT with remission
- Three months later: New retroperitoneal and inguinal LANs, biopsy-confirmed MCL
- ***Lenalidomide/rituximab***

Question

- ***Is there a role for repeating CAR T-cell therapy 2 years later?***

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Journal Club with Dr Nastoupil

Diffuse Large B-Cell Lymphoma

- Fitzgerald L et al. **Real-world outcomes of elderly patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) treated with chimeric antigen receptor T-cell (CAR-T) therapy**. ASCO 2020;Abstract 8039.
- Spiegel JY et al. **Outcomes of patients with large B-cell lymphoma progressing after axicabtagene ciloleucel therapy.** *Blood* 2021;137(13):1832-5.
- Strati P et al. **Prognostic impact of corticosteroids on efficacy of chimeric antigen receptor T-cell therapy in large B-cell lymphoma.** *Blood* 2021;137(23):3272-6.
- Xie J et al. **Characteristics and treatment patterns of relapsed/refractory diffuse large B-cell lymphoma in patients receiving ≥3 therapy lines in post-CAR-T era.** *Curr Med Res Opin* 2021;1-10.

Mantle Cell Lymphoma

- Jain P et al. **Outcomes of relapsed mantle cell lymphoma patients after discontinuing acalabrutinib.** *Am J Hematol* 2021;96(5):E137-40.
- Jain P et al. **Outcomes and management of patients with mantle cell lymphoma after progression on brexucabtagene autoleucel therapy**. *Br J Haematol* 2021;192(2):e38-42.

RTP
RESEARCH
TO PRACTICE

Journal Club with Dr Nastoupil

Follicular Lymphoma

- Strati P et al. **Long-term follow-up of lenalidomide and rituximab as initial treatment of follicular lymphoma.** *Blood* 2021;137(8):1124-9.
- Nastoupil LJ. **When to use targeted therapy for the treatment of follicular lymphoma**. *Curr Hematol Malig Rep* 2021;16(1):45-51.
- Assouline SE et al. **Mosunetuzumab shows promising efficacy in patients with multiply relapsed follicular lymphoma: Updated clinical experience from a phase I dose-escalation trial.** ASH 2020; Abstract 702.
- Scholz CW et al. **A phase III trial (GO42909) evaluating mosunetuzumab in combination with lenalidomide (M-Len) versus rituximab-lenalidomide (R-Len) in patients with relapsed/refractory follicular lymphoma (FL).** EHA 2021;Abstract PB1565.
- Budde E et al. **Preliminary results of a Phase 1 dose escalation study of the first-in-class IgM based bispecific antibody Igm-2323 (anti-CD20 x anti-CD3) in patients with advanced B-cell malignancies.** ASH 2020;Abstract 1142.
- Munoz J et al. **Copanlisib for the treatment of malignant lymphoma: Clinical experience and future perspectives.** *Target Oncol* 2021;16(3):295-308.

RTP
RESEARCH
TO PRACTICE

Meet The Professor with Dr Nastoupil

Introduction: Is the management of diffuse large B-cell lymphoma (DLBCL) about to change dramatically?

MODULE 1: Case Presentations from Dr Smith

- A 69-year-old man with recurrent DLBCL and progression after ASCT
- A 33-year-old man with classic nodular sclerosing Hodgkin lymphoma
- A 72-year-old man with FL who experiences relapse 1 year after completing lenalidomide/rituximab
- A 58-year-old man with relapsed MCL after CAR T-cell therapy

MODULE 2: Journal Club with Dr Nastoupil

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets

RTP RESEARCH TO PRACTICE

Diffuse Large B-Cell Lymphoma

Which third- and fourth-line therapy would you generally recommend first for a 65-year-old patient with DLBCL who responds to R-CHOP and then R-DHAP followed by transplant on relapse but subsequently develops disease progression?

Dr Bartlett

CAR T-cell therapy → loncastuximab tesirine

Dr Flowers

CAR T-cell therapy → tafasitamab/ lenalidomide

Dr Friedberg

CAR T-cell therapy → polatuzumab vedotin/BR

Dr Hill

CAR T-cell therapy → tafasitamab/ lenalidomide

Dr Kahl

CAR T-cell therapy → tafasitamab/ lenalidomide

Dr Nastoupil

CAR T-cell therapy → polatuzumab vedotin/BR

Dr Williams

CAR T-cell therapy → tafasitamab/ lenalidomide

RTP RESEARCH TO PRACTICE

Which third- and fourth-line therapy would you generally recommend first for an 80-year-old patient with DLBCL who experiences disease progression on front-line R-CHOP and is not eligible for high-dose therapy?

Dr Bartlett

Loncastuximab tesirine → tafasitamab/ lenalidomide

Dr Flowers

CAR T-cell therapy → tafasitamab/ lenalidomide

Dr Friedberg

Tafasitamab/ lenalidomide → loncastuximab tesirine

Dr Hill

Tafasitamab/ lenalidomide → loncastuximab tesirine

Dr Kahl

Tafasitamab/ lenalidomide → loncastuximab tesirine

Dr Nastoupil

CAR T-cell therapy → polatuzumab vedotin/BR

Dr Williams

Tafasitamab/ lenalidomide → loncastuximab tesirine

RTP RESEARCH TO PRACTICE

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

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

RTP RESEARCH TO PRACTICE

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

 Dr Bartlett	At second relapse	 Dr Kahl	At second relapse
 Dr Flowers	At first relapse	 Dr Nastoupil	At first relapse
 Dr Friedberg	At first relapse	 Dr Williams	At second relapse
 Dr Hill	At first relapse		

RTP RESEARCH TO PRACTICE

Do you believe that CAR T-cell therapy is more efficacious than autologous stem cell transplantation for DLBCL as second-line treatment after R-CHOP?

 Dr Bartlett	Yes, but I'm still not sure	 Dr Kahl	Yes, but I'm still not sure
 Dr Flowers	Yes (but may vary by CAR T product)	 Dr Nastoupil	Yes
 Dr Friedberg	Yes	 Dr Williams	Yes, but I'm still not sure
 Dr Hill	Yes – for chemorefractory disease		

RTP RESEARCH TO PRACTICE

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

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

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RESEARCH
TO PRACTICE

Do you believe that CAR T-cell therapy is more tolerable for most patients than autologous stem cell transplantation?

 Dr Bartlett	Yes	 Dr Kahl	Yes
 Dr Flowers	Yes	 Dr Nastoupil	Yes
 Dr Friedberg	Yes	 Dr Williams	Yes
 Dr Hill	Yes – liso-cel and tisa-cel are likely more tolerable No – axi-cel is not more tolerable		

RTP RESEARCH TO PRACTICE

Hodgkin Lymphoma

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

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

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

RTP RESEARCH TO PRACTICE

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

Dr Bartlett

Brentuximab vedotin + nivolumab

Dr Flowers

Brentuximab vedotin/ dacarbazine

Dr Friedberg

Brentuximab vedotin + nivolumab

Dr Hill

Brentuximab vedotin

Dr Kahl

Pembrolizumab

Dr Nastoupil

Brentuximab vedotin + nivolumab

Dr Williams

Brentuximab vedotin

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in general, what is your preferred second-line therapy for a patient with HL who is experiencing disease relapse after up-front ABVD and is not considered a candidate for transplant?

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

Regulatory and reimbursement issues aside, what is your preferred next line of therapy for a patient with HL who is experiencing disease relapse after ABVD and autologous stem cell transplant?

 Dr Bartlett	Pembrolizumab
 Dr Flowers	Brentuximab vedotin + nivolumab
 Dr Friedberg	Nivolumab
 Dr Hill	Pembrolizumab
 Dr Kahl	Brentuximab vedotin + nivolumab
 Dr Nastoupil	Pembrolizumab
 Dr Williams	Brentuximab vedotin + nivolumab

RTP RESEARCH TO PRACTICE

Have you administered or would you administer brentuximab vedotin in combination with an immune checkpoint inhibitor to a patient with HL outside of a clinical trial setting?

 Dr Bartlett	I have	 Dr Kahl	I have
 Dr Flowers	I haven't but would for the right patient	 Dr Nastoupil	I have
 Dr Friedberg	I haven't but would for the right patient	 Dr Williams	I haven't but would for the right patient
 Dr Hill	I haven't but would for the right patient		

RTP RESEARCH TO PRACTICE

Follicular Lymphoma

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

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

RTP RESEARCH TO PRACTICE

What treatment do you generally recommend for a patient with symptomatic FL requiring treatment who refuses to receive cytoxic chemotherapy?

 Dr Bartlett	Rituximab alone	 Dr Kahl	Lenalidomide/ rituximab
 Dr Flowers	Lenalidomide/ rituximab	 Dr Nastoupil	Lenalidomide/ rituximab
 Dr Friedberg	Lenalidomide/ rituximab	 Dr Williams	Lenalidomide/ rituximab
 Dr Hill	Lenalidomide/ rituximab		

RTP RESEARCH TO PRACTICE

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

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

RTP RESEARCH TO PRACTICE

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

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

RTP RESEARCH TO PRACTICE

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

Dr Bartlett

Duvelisib → tazemetostat

Dr Flowers

Tazemetostat → umbralisib

Dr Friedberg

Tazemetostat → umbralisib

Dr Hill

Tazemetostat → umbralisib

Dr Kahl

Tazemetostat → umbralisib

Dr Nastoupil

Tazemetostat → axi-cel

Dr Williams

Tazemetostat → umbralisib

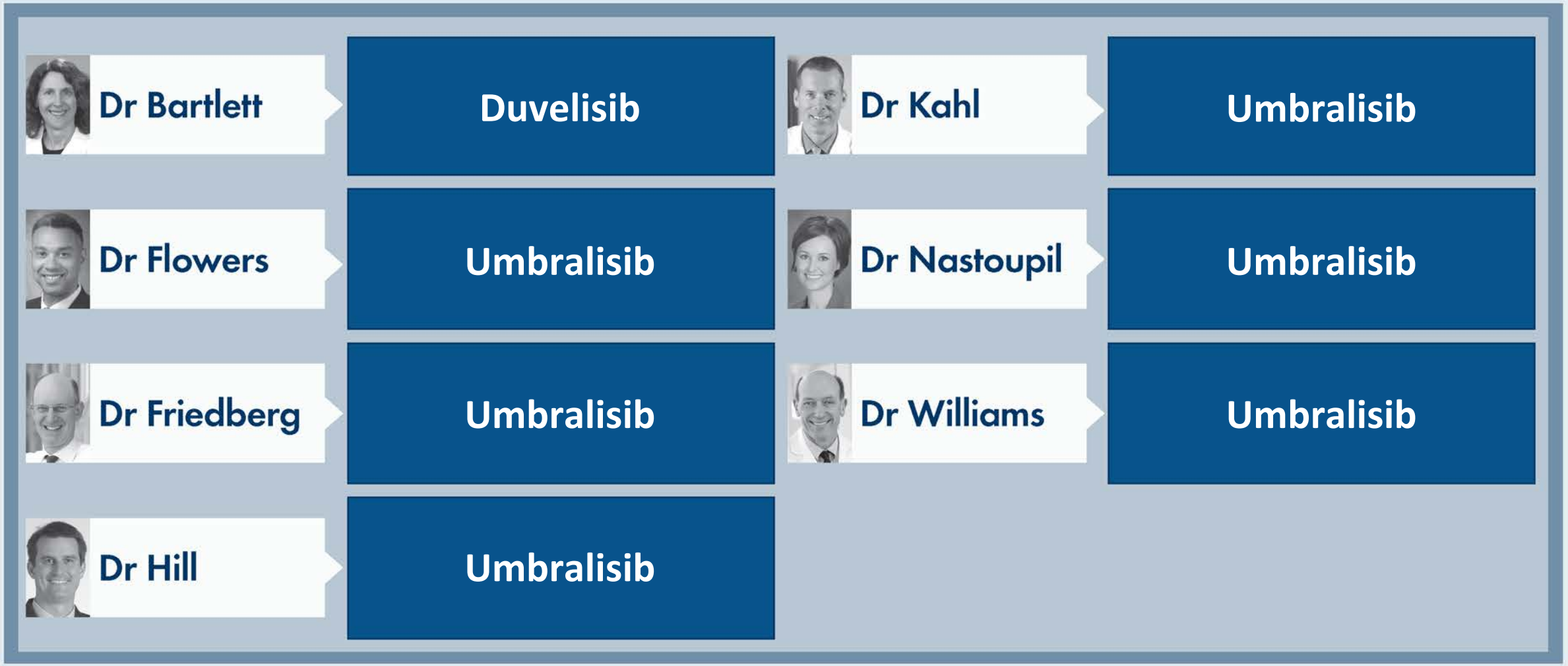
RTP RESEARCH TO PRACTICE

Are you typically assessing EZH2 mutation status for your patients with FL?

 Dr Bartlett	No
 Dr Flowers	Yes, for select patients: relapse after 2nd line
 Dr Friedberg	Yes, for all patients
 Dr Hill	Yes, for select patients: at relapse
 Dr Kahl	No
 Dr Nastoupil	Yes, for select patients: 3rd line
 Dr Williams	Yes, for select patients: 3rd line

RTP RESEARCH TO PRACTICE

Which PI3K inhibitor do you use most commonly?



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How would you generally sequence PI3K inhibitors and tazemetostat for a patient with relapsed FL who is eligible to receive both?

 Dr Bartlett	PI3K inhibitor → tazemetostat
 Dr Flowers	Tazemetostat → PI3K inhibitor
 Dr Friedberg	Tazemetostat → PI3K inhibitor
 Dr Hill	Tazemetostat → PI3K inhibitor
 Dr Kahl	Tazemetostat → PI3K inhibitor
 Dr Nastoupil	Tazemetostat → PI3K inhibitor
 Dr Williams	Tazemetostat → PI3K inhibitor

RTP RESEARCH TO PRACTICE

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

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

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TO PRACTICE

Mantle Cell Lymphoma

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

 Dr Bartlett	Brexucabtagene autoleucel
 Dr Flowers	Brexucabtagene autoleucel
 Dr Friedberg	Brexucabtagene autoleucel
 Dr Hill	Brexucabtagene autoleucel
 Dr Kahl	Brexucabtagene autoleucel
 Dr Nastoupil	Brexucabtagene autoleucel
 Dr Williams	Venetoclax + rituximab

RTP RESEARCH TO PRACTICE

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

 Dr Bartlett	At third relapse
 Dr Flowers	At first relapse
 Dr Friedberg	At second relapse after BTKi
 Dr Hill	At first relapse
 Dr Kahl	At second relapse
 Dr Nastoupil	At first relapse
 Dr Williams	At second relapse

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Nastoupil

Introduction: Is the management of diffuse large B-cell lymphoma (DLBCL) about to change dramatically?

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Diffuse Large B-Cell Lymphoma

original reports

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

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

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

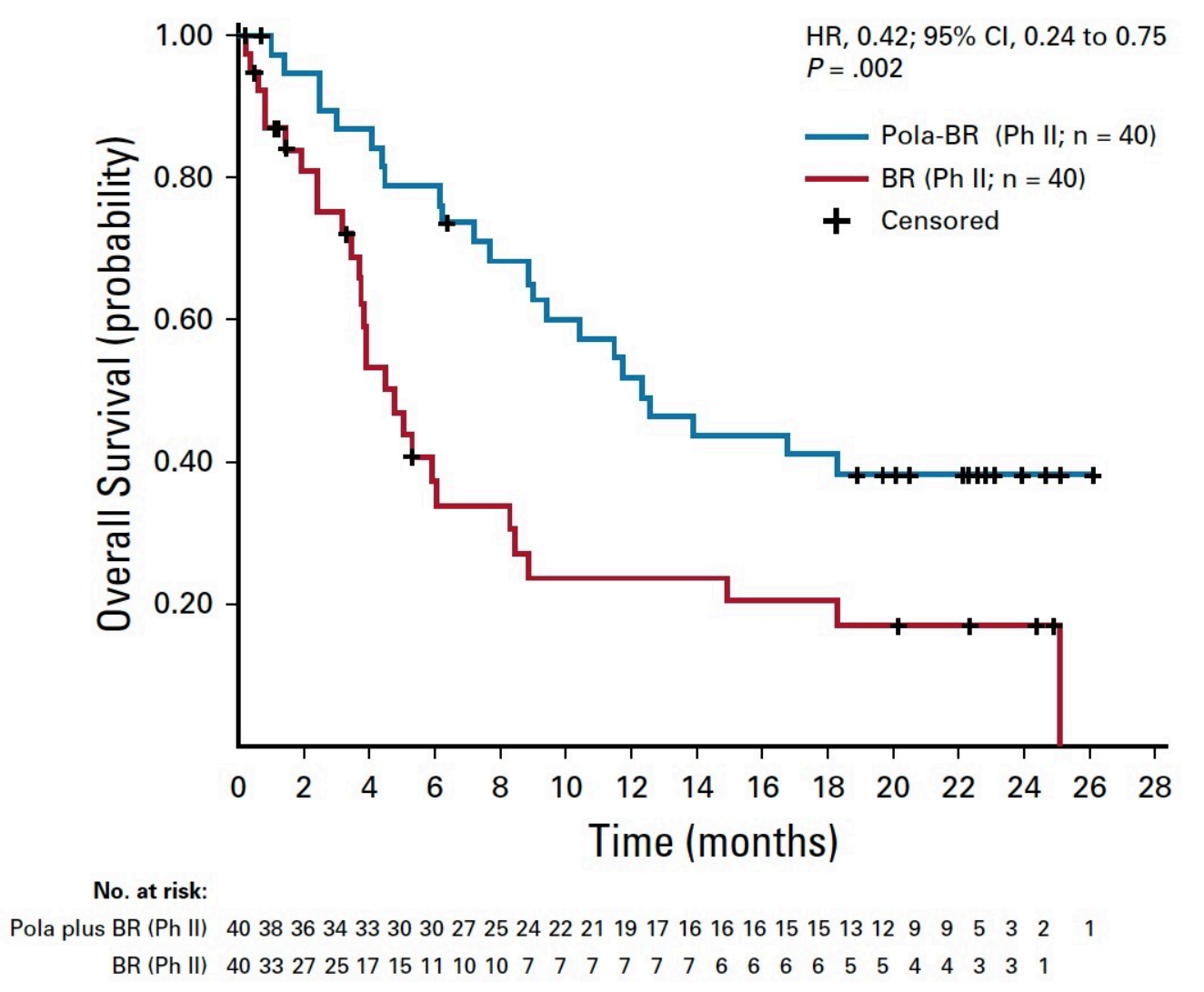
RTP RESEARCH TO PRACTICE

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.

FDA Approves Selinexor for R/R 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."

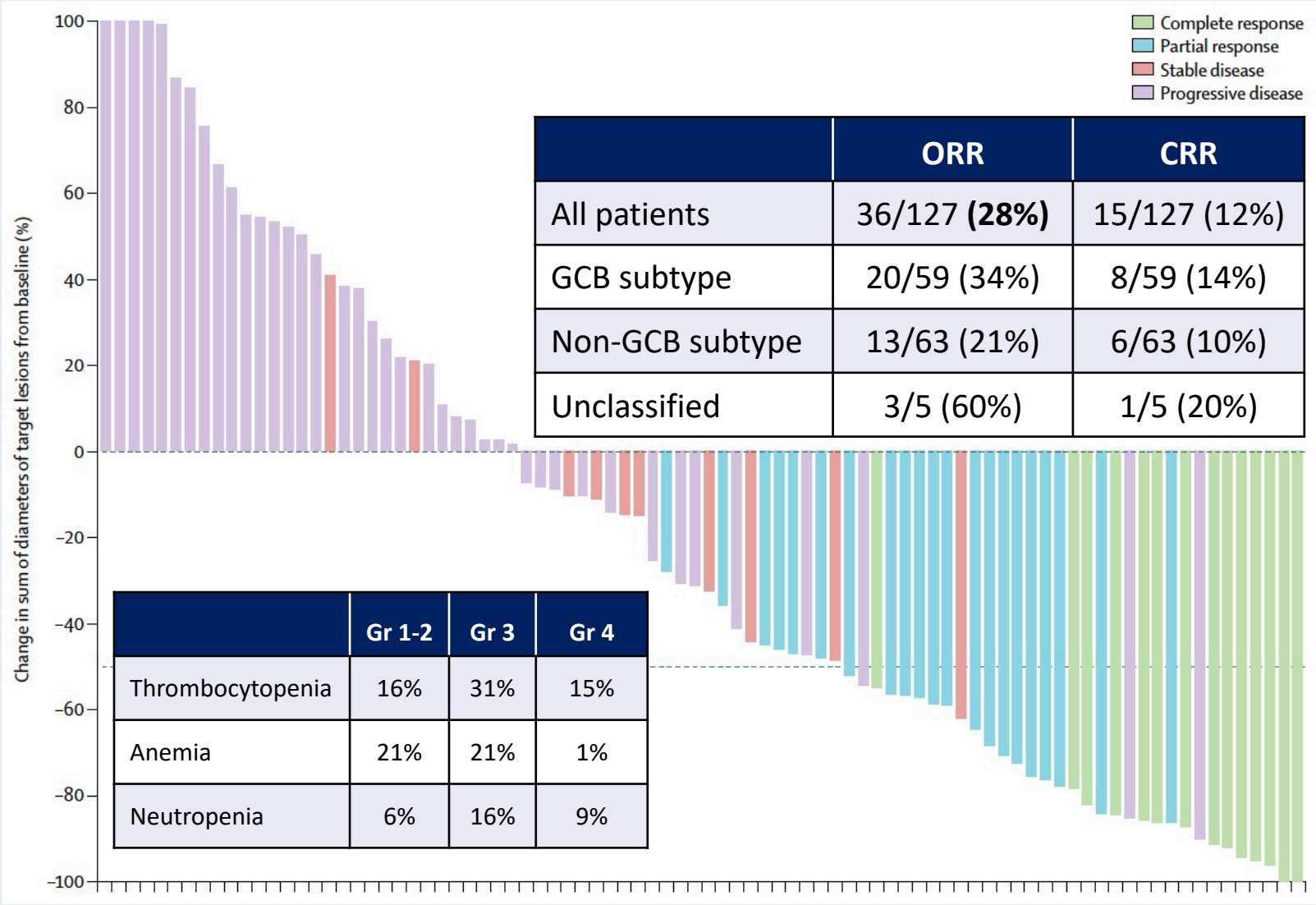
www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-selinexor-relapsedrefractory-diffuse-large-b-cell-lymphoma

Lancet Haematol 2020;7:e511-22.

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

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

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



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

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

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

FDA Grants Accelerated Approval to Tafasitamab-cxix for DLBCL

Press Release – July 31, 2020

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

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

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

Lancet Oncol 2020;21:978-88

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

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

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

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

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

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

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

Press Release – April 23, 2021

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

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

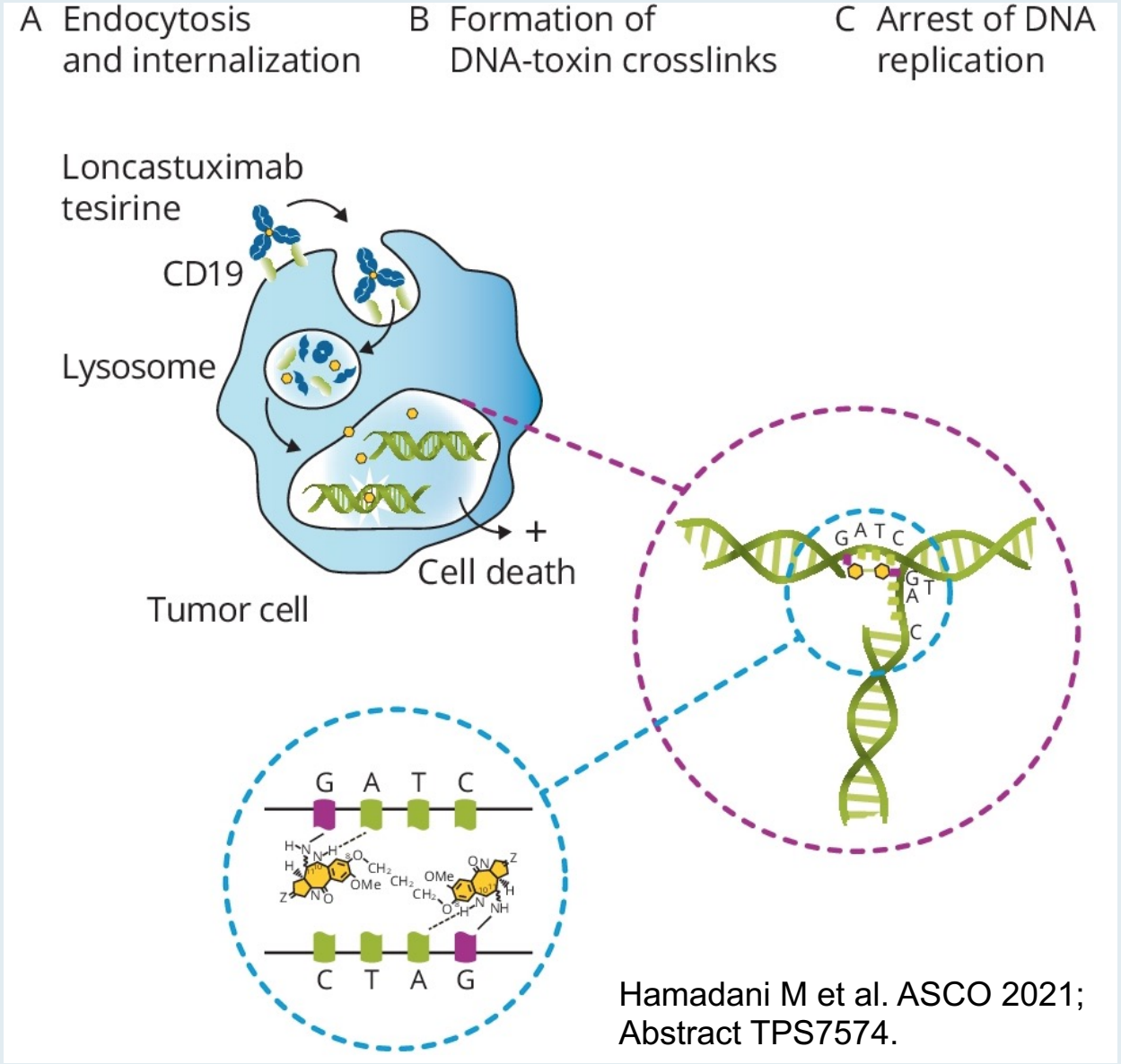
www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-loncastuximab-tesirine-lpyl-large-b-cell-lymphoma

Lancet Oncol 2021;22:790-800

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

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

Mechanism of Action of Loncastuximab Tesirine



Hamadani M et al. ASCO 2021; Abstract TPS7574.

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

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

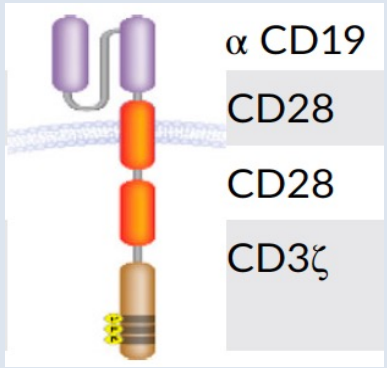
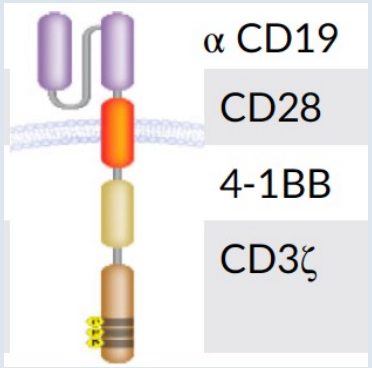
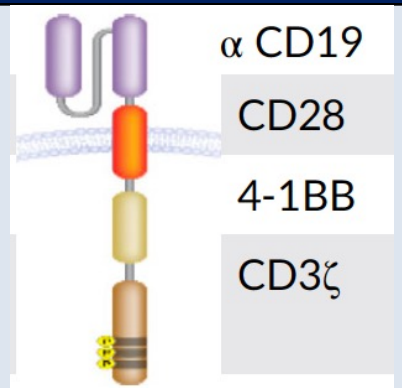
Caimi PF et al. *Lancet Oncol* 2021;22:790-800.

LOTIS-2: Common Treatment-Emergent Adverse Events

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

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

Summary of CAR T-Cell Pivotal Studies in DLBCL

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

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

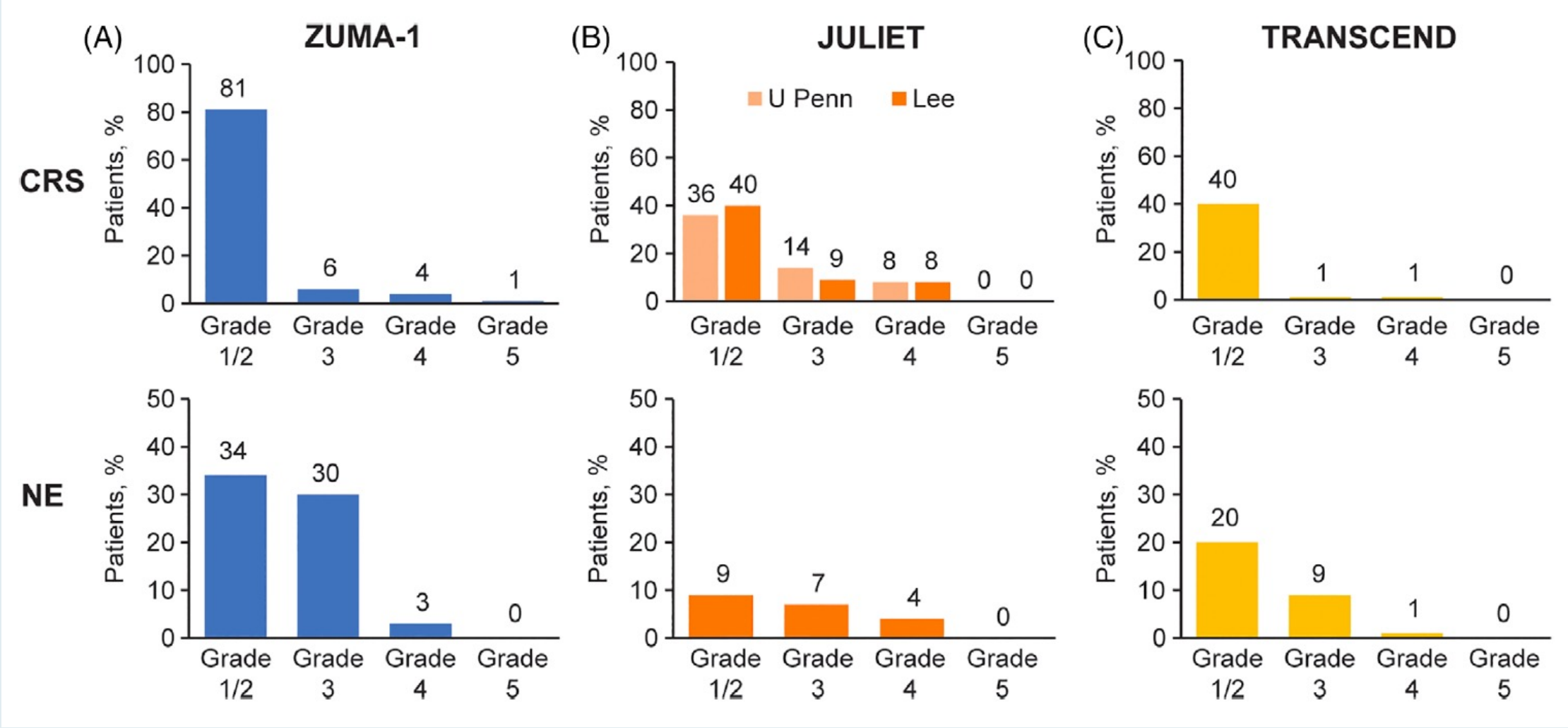
RTP RESEARCH TO PRACTICE

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

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

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

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



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

RTP RESEARCH TO PRACTICE

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

CRS — May be mild or life-threatening

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

Neurologic toxicity — May be mild or life-threatening

- Mechanism unclear, referred to as immune effector cell-associated neurotoxicity syndrome (ICANS)
- Encephalopathy
- Seizures
- Delirium, confusion, aphasia, agitation, sedation, coma

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

Hodgkin Lymphoma

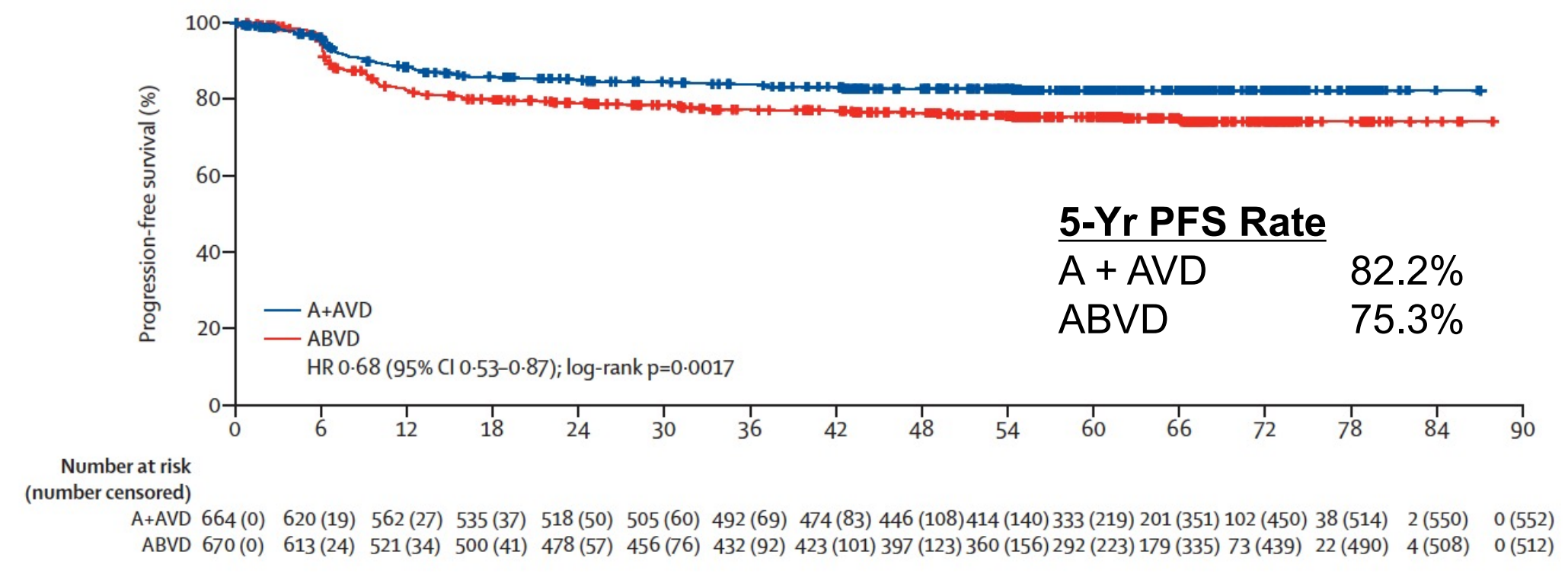
Lancet Haematol 2021;8(6):e410-21

Articles

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

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

ECHELON-1: Five-Year Update



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

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

RTP RESEARCH TO PRACTICE

original reports

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

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

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

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

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

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

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

Kumar A et al. *J Clin Oncol* 2021;[Online ahead of print].

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

Yasenchak CA et al.
ASH 2020;Abstract 471.

Best Responses per Investigator – Efficacy Evaluable Set

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

Patients who were not efficacy-evaluable included:

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

Yasenchak CA et al. ASH 2020;Abstract 471.

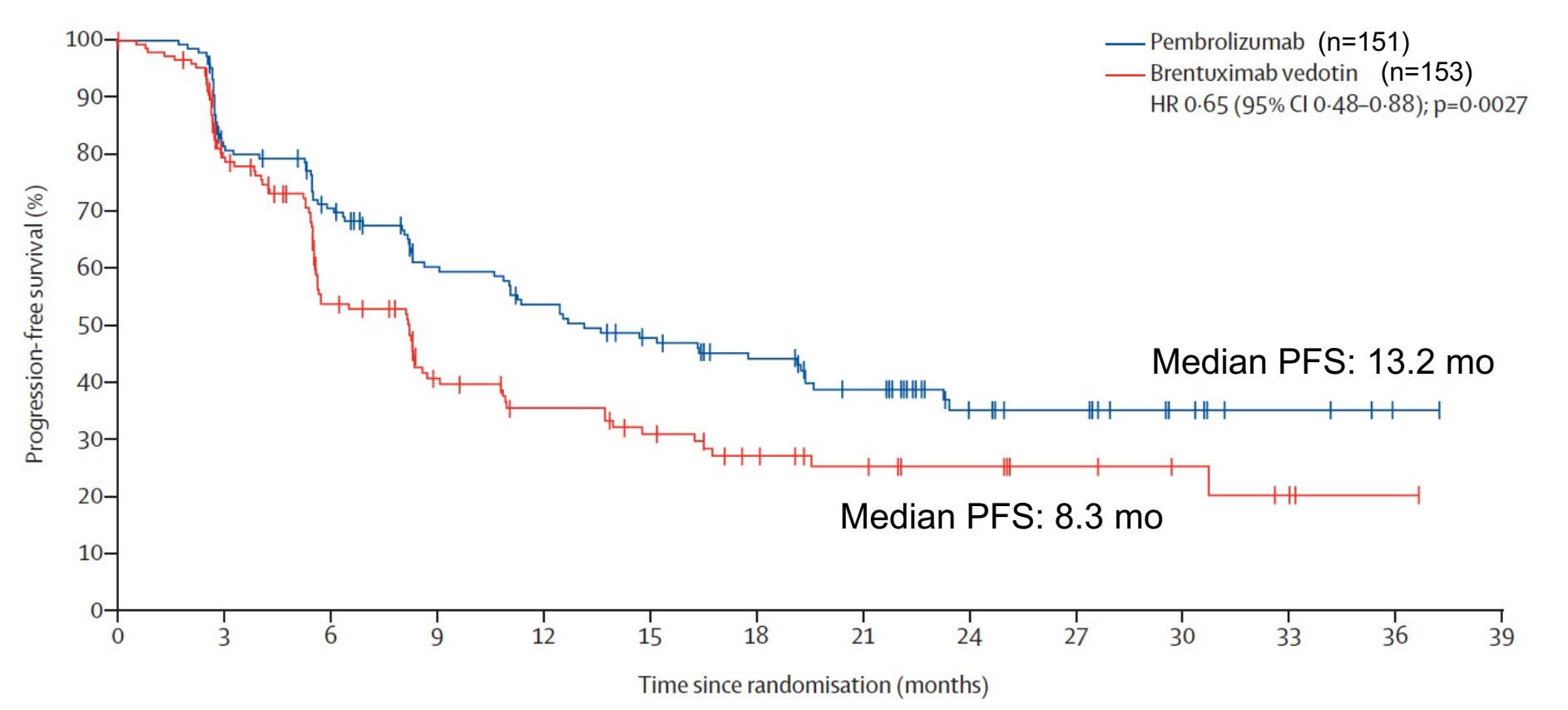
Articles

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

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

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

KEYNOTE-204: Interim Analysis



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

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

RTP RESEARCH TO PRACTICE

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

original reports

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

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

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

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

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

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

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

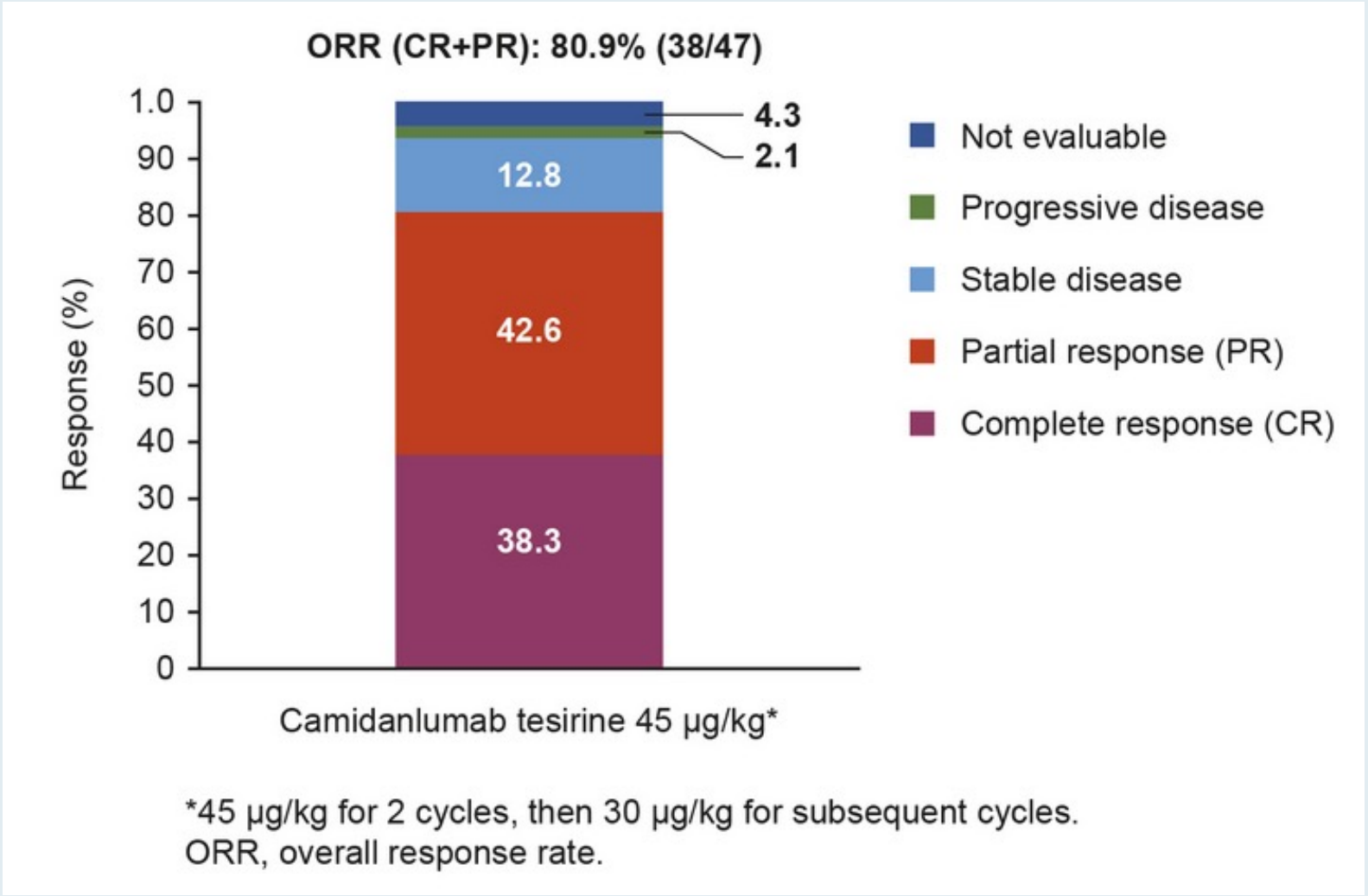
RTP RESEARCH TO PRACTICE

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

Herrera AF et al.

ASH 2020;Abstract 2020.

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



Herrera AF et al. ASH 2020;Abstract 2020.

Follicular Lymphoma

Approved PI3K Inhibitors for FL: Indication and Dosing

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

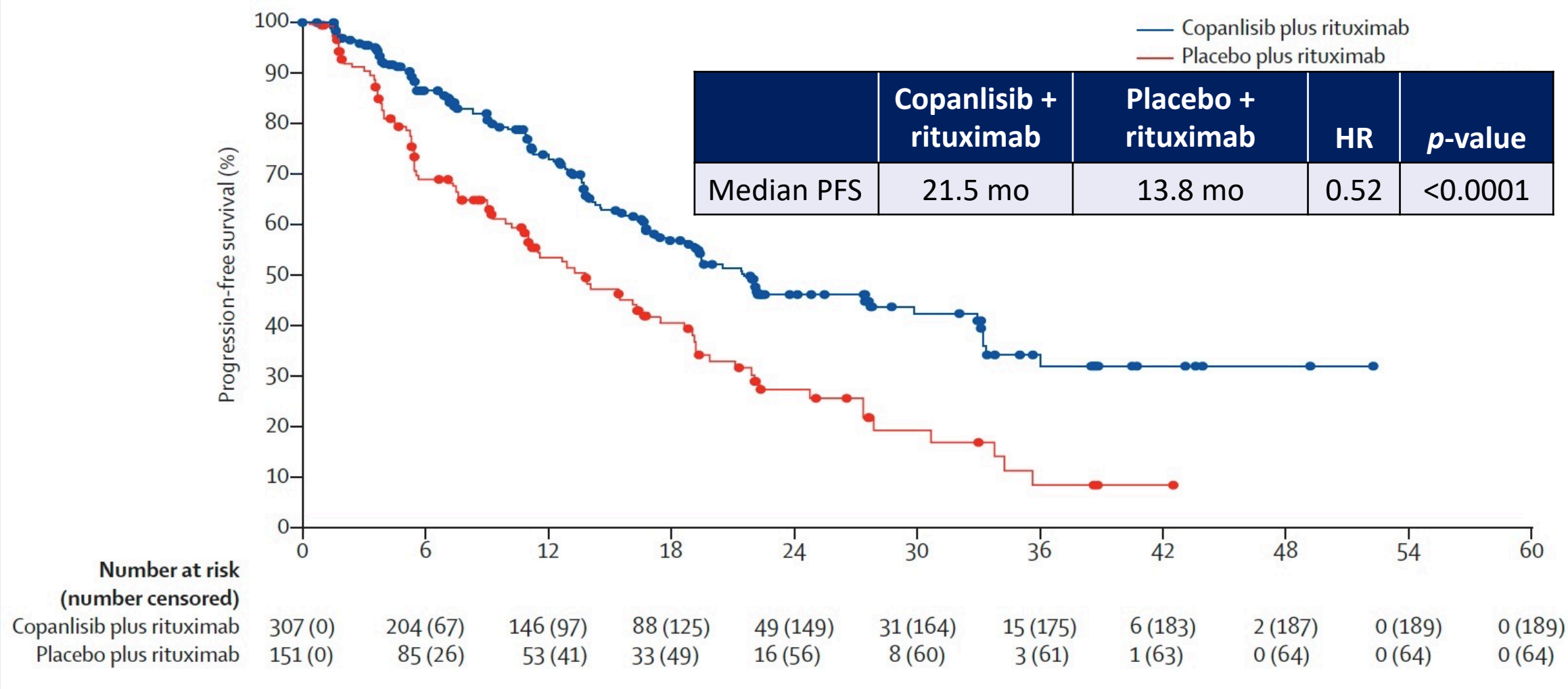
[1] Gopal AK et al. *N Engl J Med* 2014;370(11):1008-18; Idelalisib package insert, January 2018.
[2] Dreyling M et al. *J Clin Oncol* 2017;35(35):3898-905; Copanlisib package insert, September 2017.
[3] Flinn IW et al. *J Clin Oncol* 2019;[Epub ahead of print]; Zinzani PL et al. EHA 2017;Abstract S777;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

Lancet Oncol 2021;22:678-89

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

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

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



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

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

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

Press Release – February 5, 2021

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

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

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

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

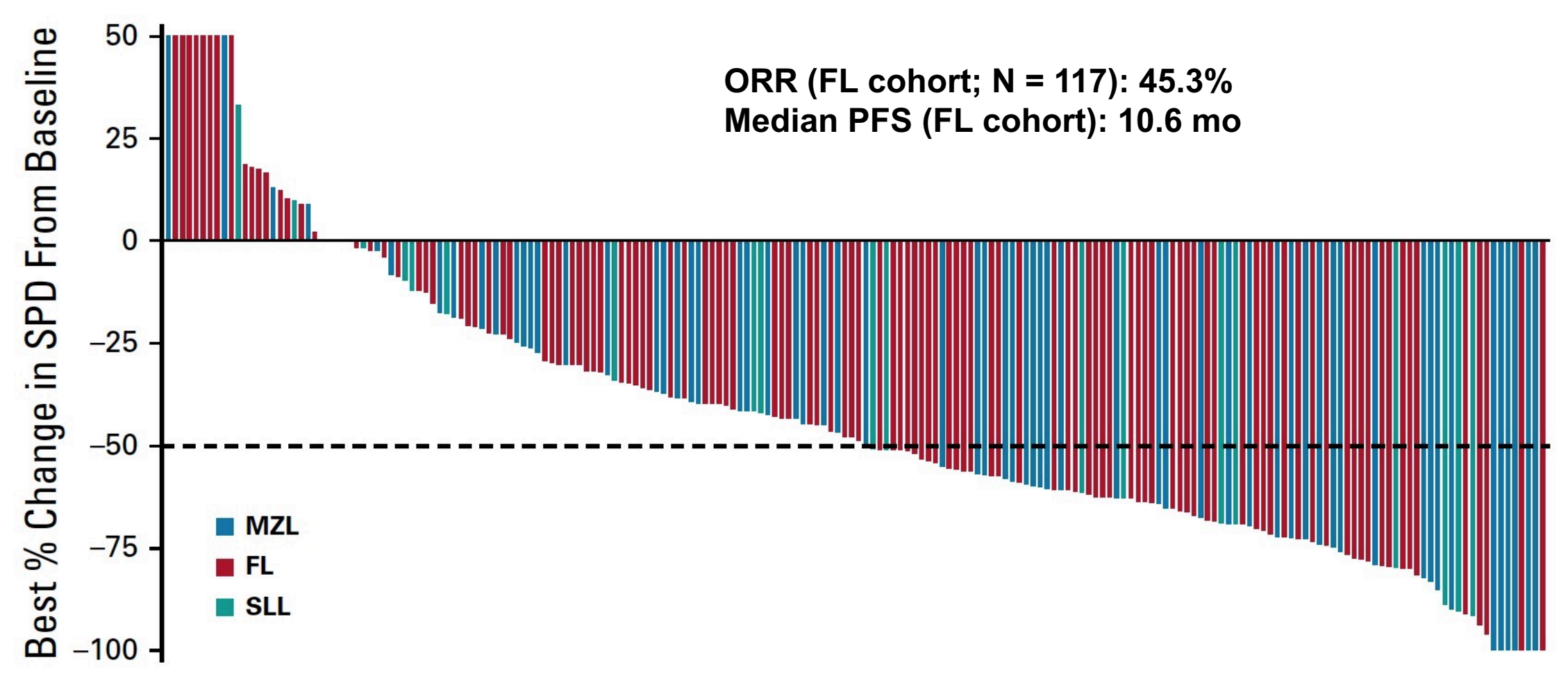
rapid communications

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

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

J Clin Oncol 2021;39:1609-18

Umbralisib for Heavily Pretreated R/R Indolent NHL



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

RTP RESEARCH TO PRACTICE

FDA Grants Accelerated Approval to Tazemetostat for Follicular Lymphoma

Press Release: June 18, 2020

"The Food and Drug Administration granted accelerated approval to tazemetostat, an EZH2 inhibitor, for adult patients with relapsed or refractory (R/R) follicular lymphoma (FL) whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least 2 prior systemic therapies, and for adult patients with R/R FL who have no satisfactory alternative treatment options.

Today, the FDA also approved the cobas®. EZH2 Mutation Test (Roche Molecular Systems, Inc) as a companion diagnostic for tazemetostat.

Approval was based on two open-label, single-arm cohorts (Cohort 4 - EZH2 mutated FL and Cohort 5 - EZH2 wild-type FL) of a multi-center trial (Study E7438-G000-101, NCT01897571) in patients with histologically confirmed FL after at least 2 prior systemic therapies. EZH2 mutations were identified prospectively using formalin-fixed, paraffin-embedded tumor samples, which were centrally tested using the cobas EZH2 Mutation Test. Patients received tazemetostat 800 mg orally twice daily until confirmed disease progression or unacceptable toxicity."

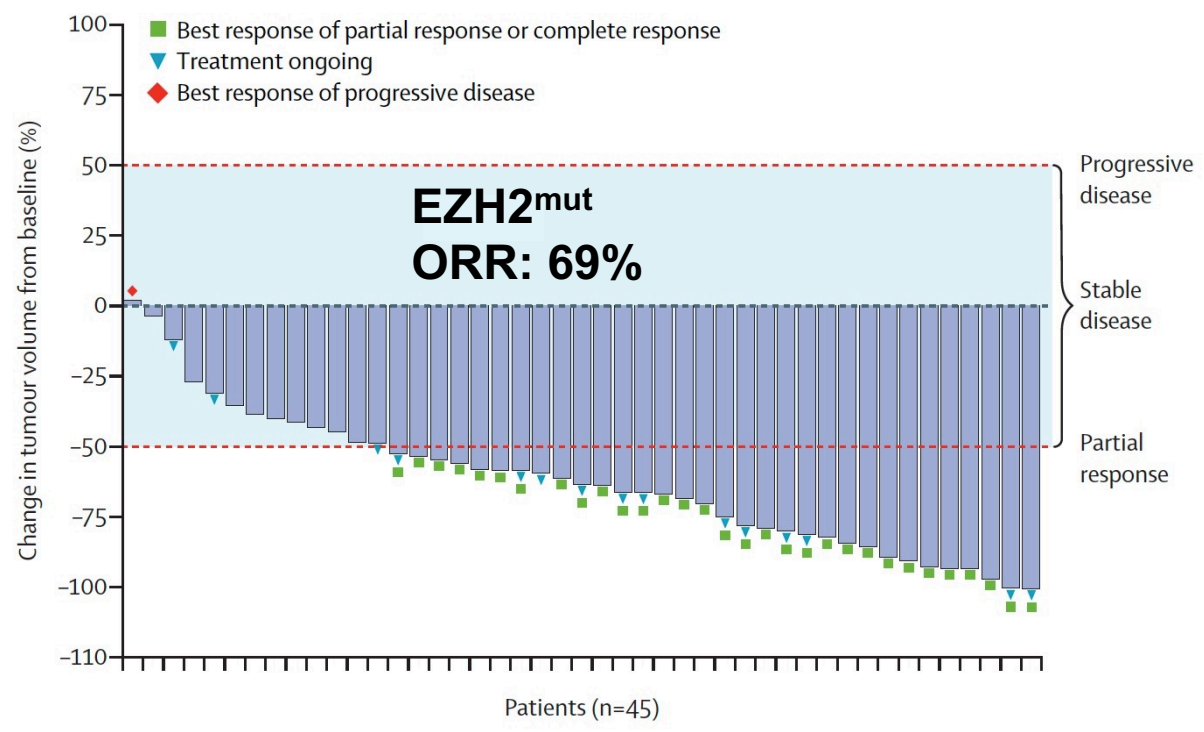
www.fda.gov/drugs/fda-granted-accelerated-approval-tazemetostat-follicular-lymphoma

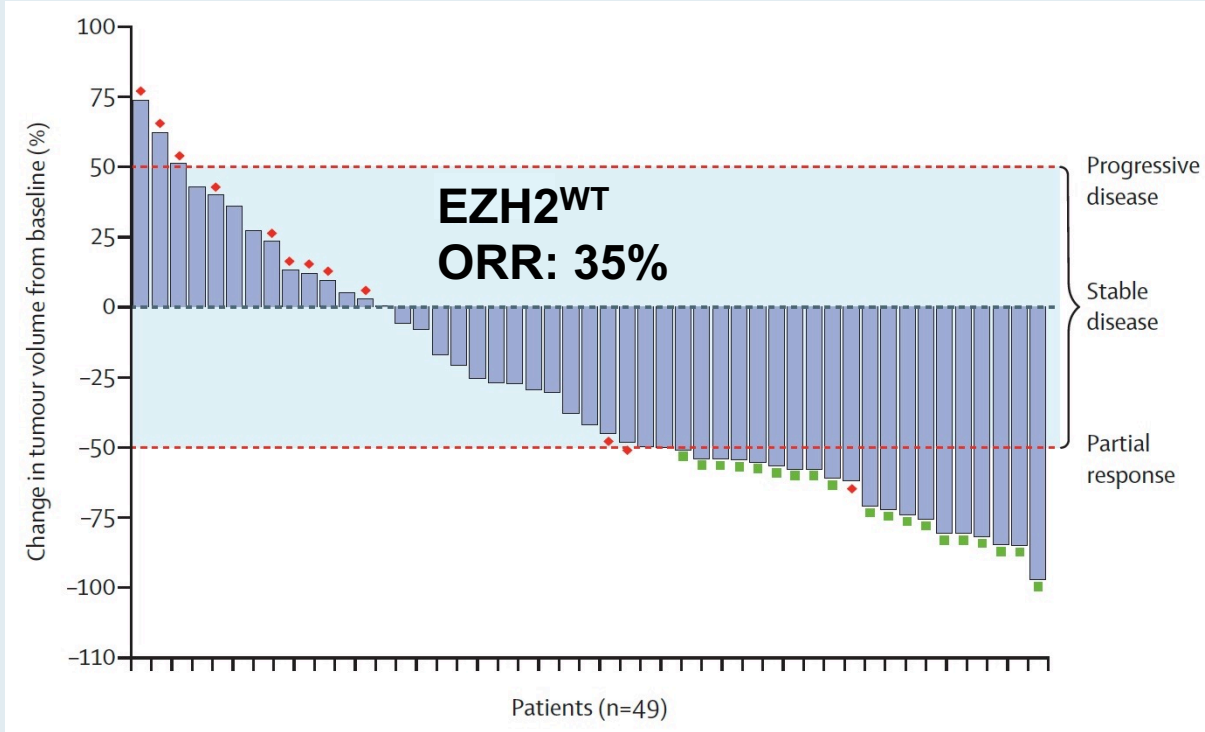
Lancet Oncol 2020;21:1433-42

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

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

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

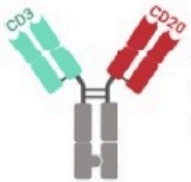
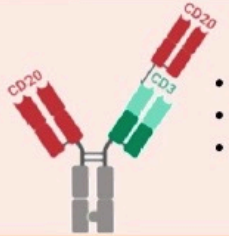
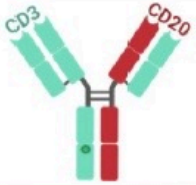




Morschhauser F et al. *Lancet Oncol* 2020;21:1433-42.

RTP RESEARCH TO PRACTICE

Structure of Selected Bispecific Antibodies

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

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

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

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

Press Release: July 14, 2020

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

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

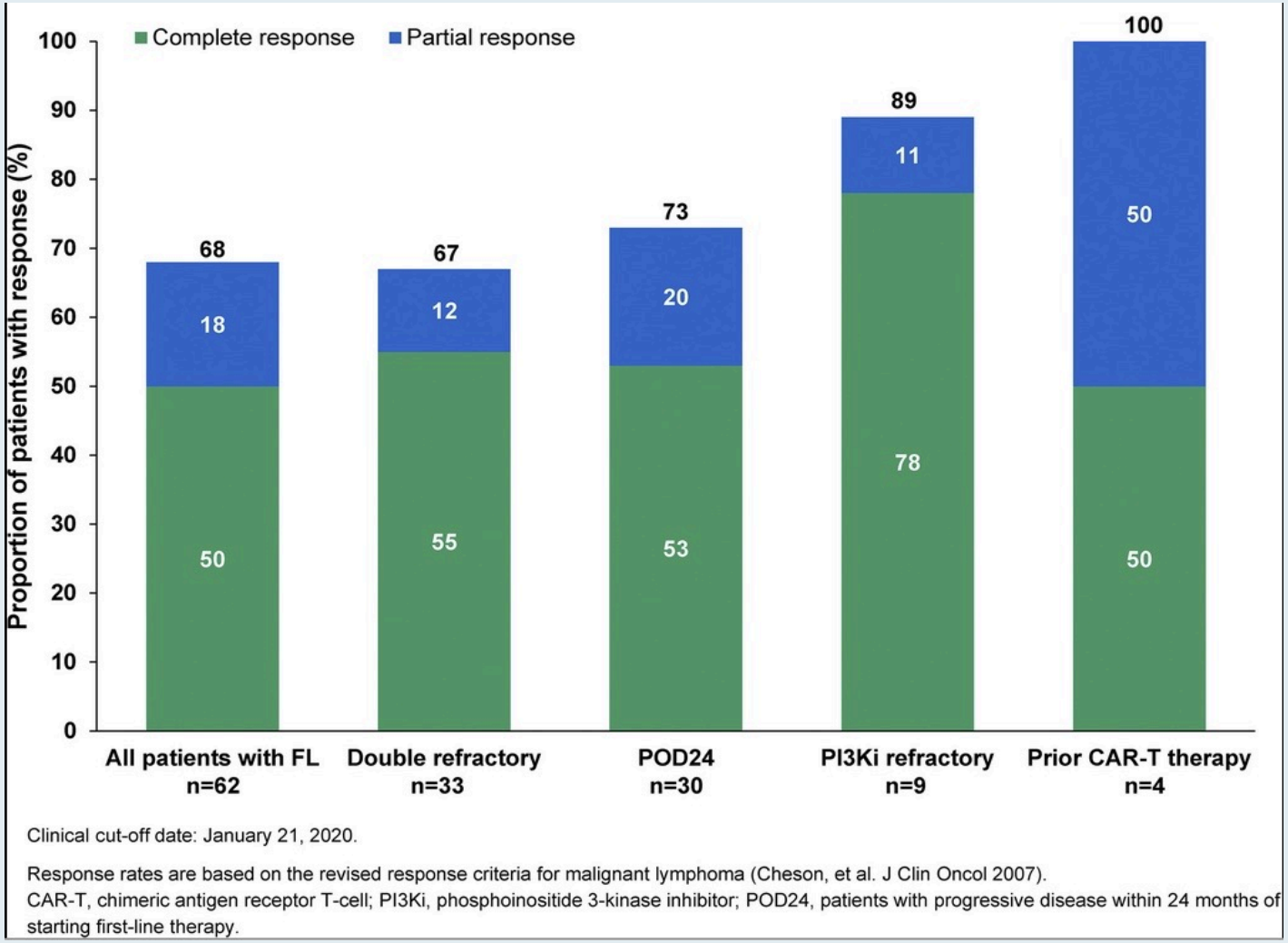
www.roche.com/investors/updates/inv-update-2020-07-14b.htm

Mosunetuzumab 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 to Mosunetuzumab in Patients with Follicular Lymphoma 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.

Cytokine release syndrome (CRS) rate: 35% (N = 22)

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

Neurologic adverse event rate: 45% (N = 28)

- All Grade 1/2

Assouline SE et al. ASH 2020;Abstract 702.

rapid communications

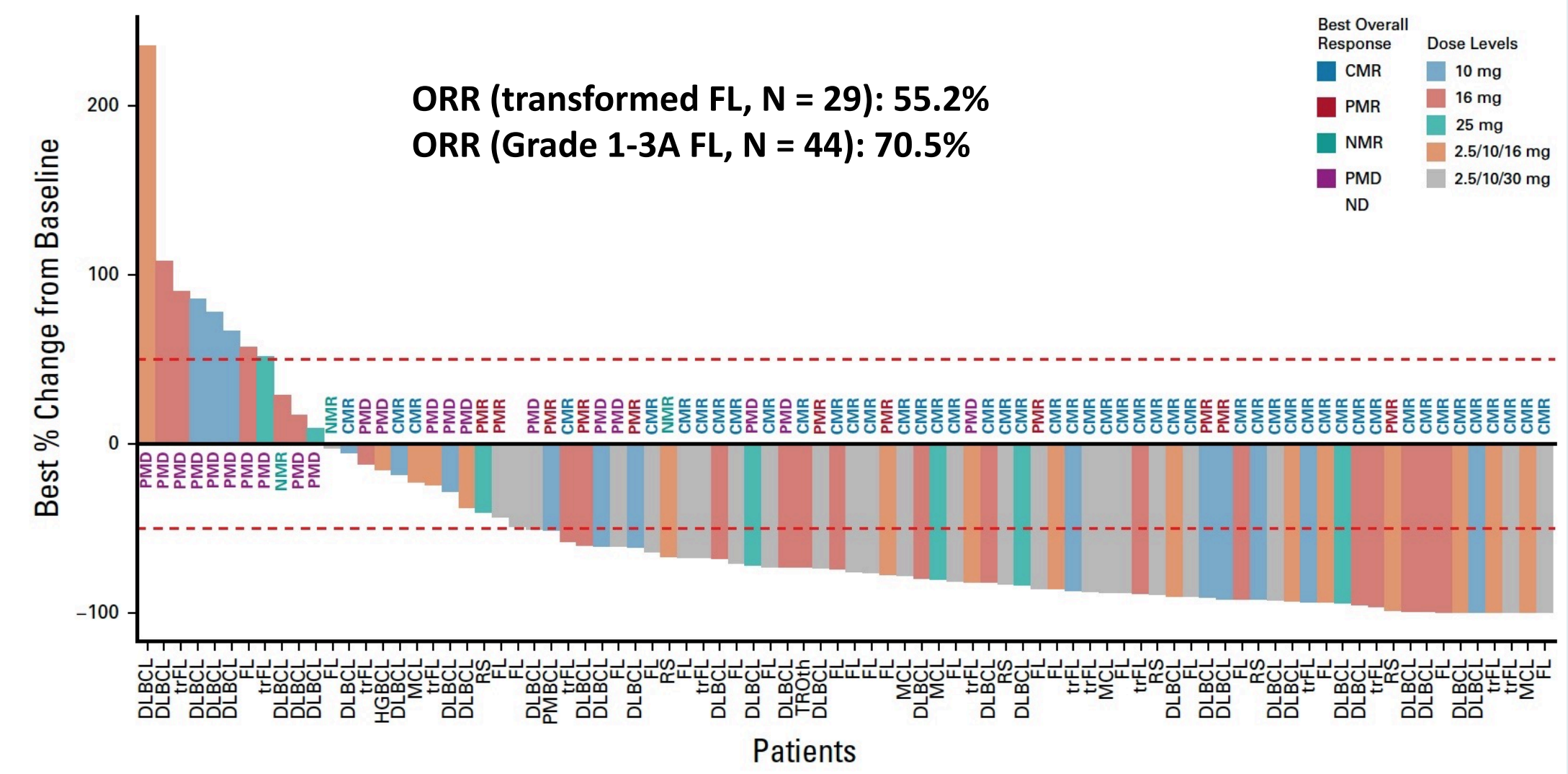
Glofitamab, a Novel, Bivalent CD20-Targeting T-Cell–Engaging Bispecific Antibody, Induces Durable Complete Remissions in Relapsed or Refractory B-Cell Lymphoma: A Phase I Trial

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.

RTP RESEARCH TO PRACTICE

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



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

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

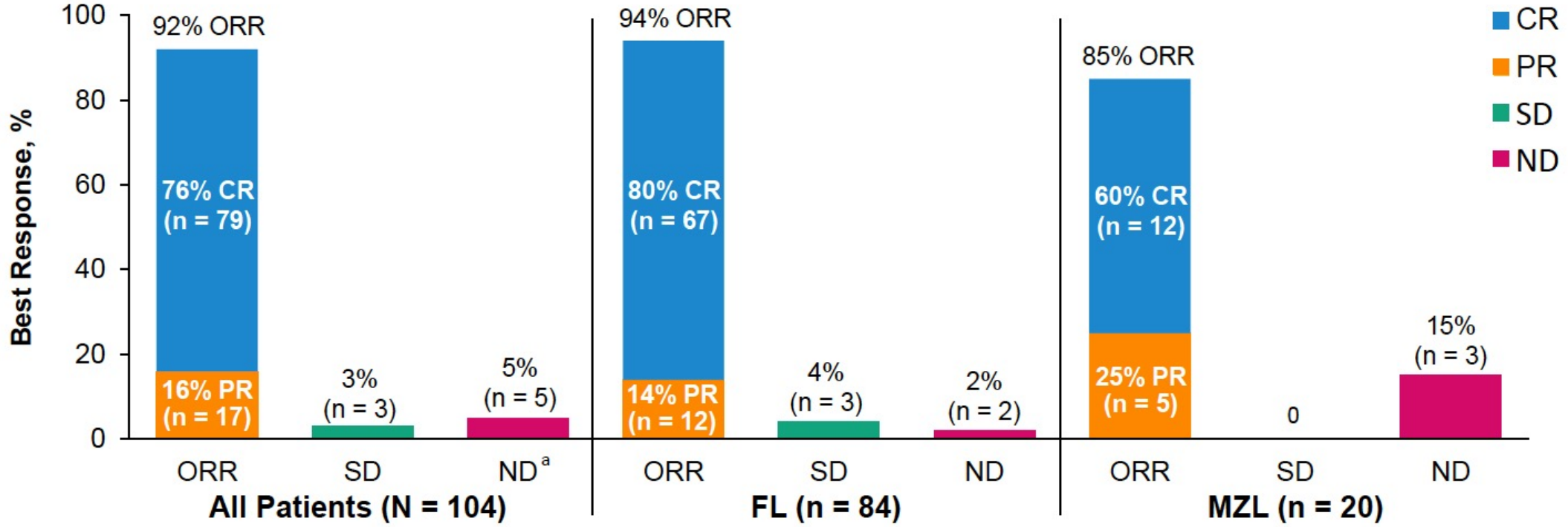
Primary Analysis of ZUMA-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

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.

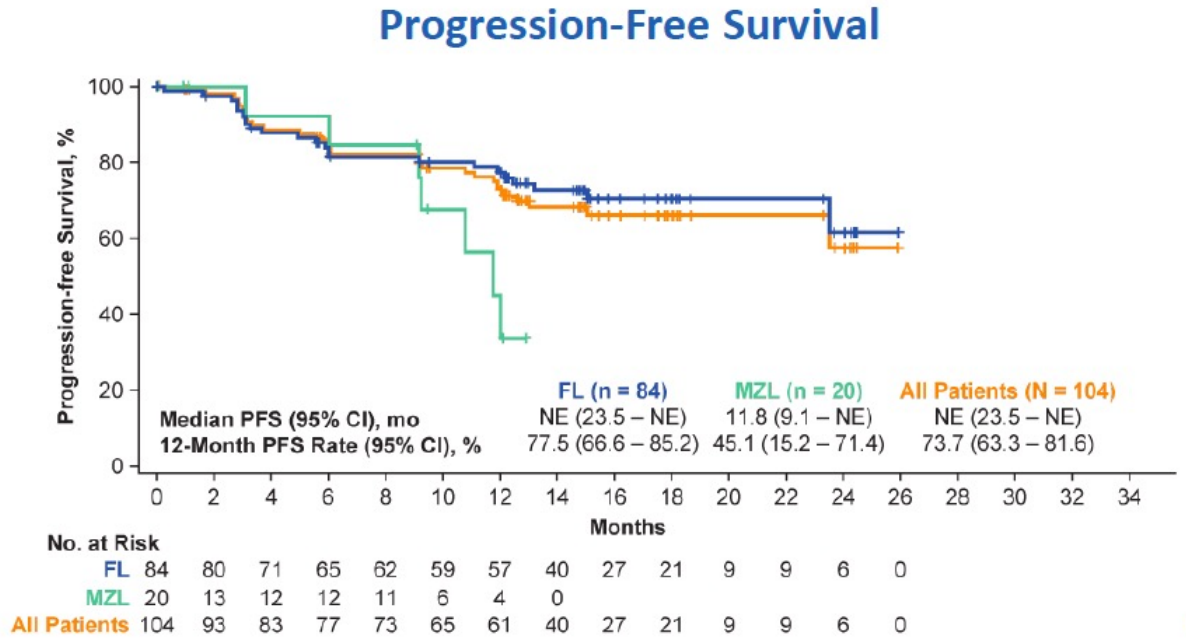
ZUMA-5: ORR by IRRC Assessment for Patients with Follicular Lymphoma Receiving Axicabtagene Ciloleucel

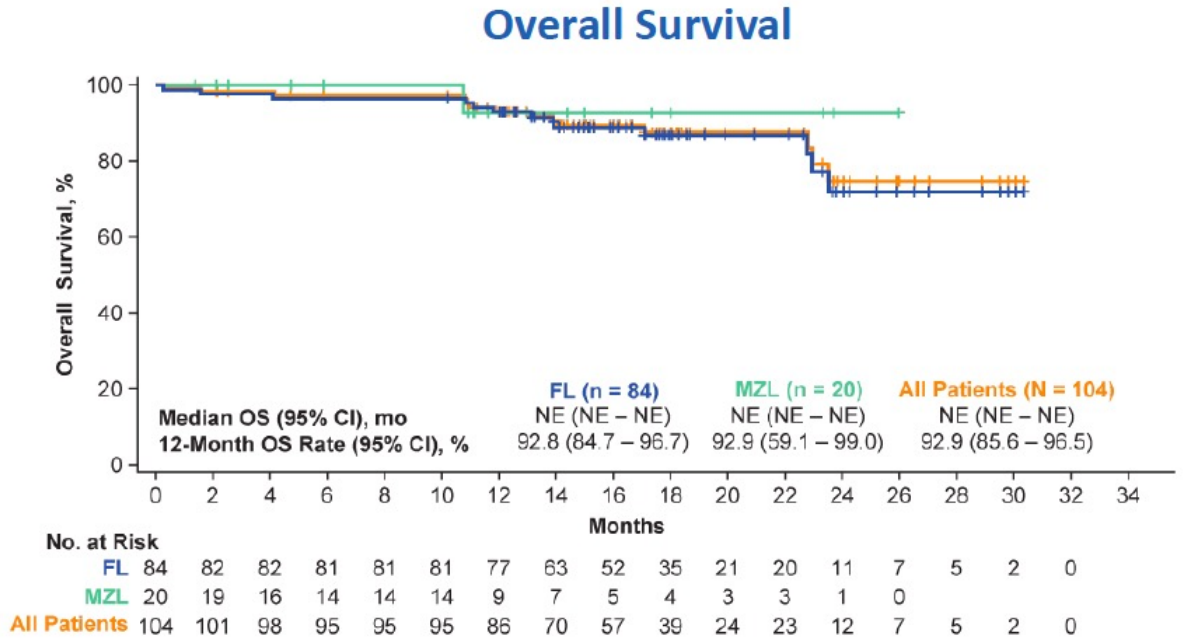


- The median time to first response was 1 month (range, 0.8 – 3.1)
- Among the 25 patients with FL who initially had a PR, 13 (52%) subsequently converted to a CR after a median of 2.2 months (range, 1.9 – 11.2)

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 (CRS)	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.

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2021 ASCO ANNUAL MEETING

Oral Presentation 7508

Efficacy and Safety of Tisagenlecleucel in Adult Patients With Relapsed/Refractory Follicular Lymphoma: Primary Analysis of the Phase 2 ELARA Trial

Stephen J. Schuster,[1] Michael Dickinson,[2] Martin Dreyling,[3] Joaquin Martinez-Lopez,[4] Arne Kolstad,[5] Jason Butler,[6] Monalisa Ghosh,[7] Leslie Popplewell,[8] Julio C. Chavez,[9] Emmanuel Bachy,[10] Koji Kato,[11] Hideo Harigae,[12] Marie José Kersten,[13] Charalambos Andreadis,[14] Peter A. Riedell,[15] Ahmed Abdelhady,[16a] Aiesha Zia,[17] Mony Chenda Morisse,[16] Nathan Hale Fowler,[18,19,*] Catherine Thieblemont[20,*]

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*Dr Fowler and Dr Thieblemont are co-senior authors. [a]Analysis completed while employed by Novartis Pharmaceuticals Corporation.

RTP RESEARCH TO PRACTICE

ELARA Primary Endpoint: Complete Response Rate by IRC

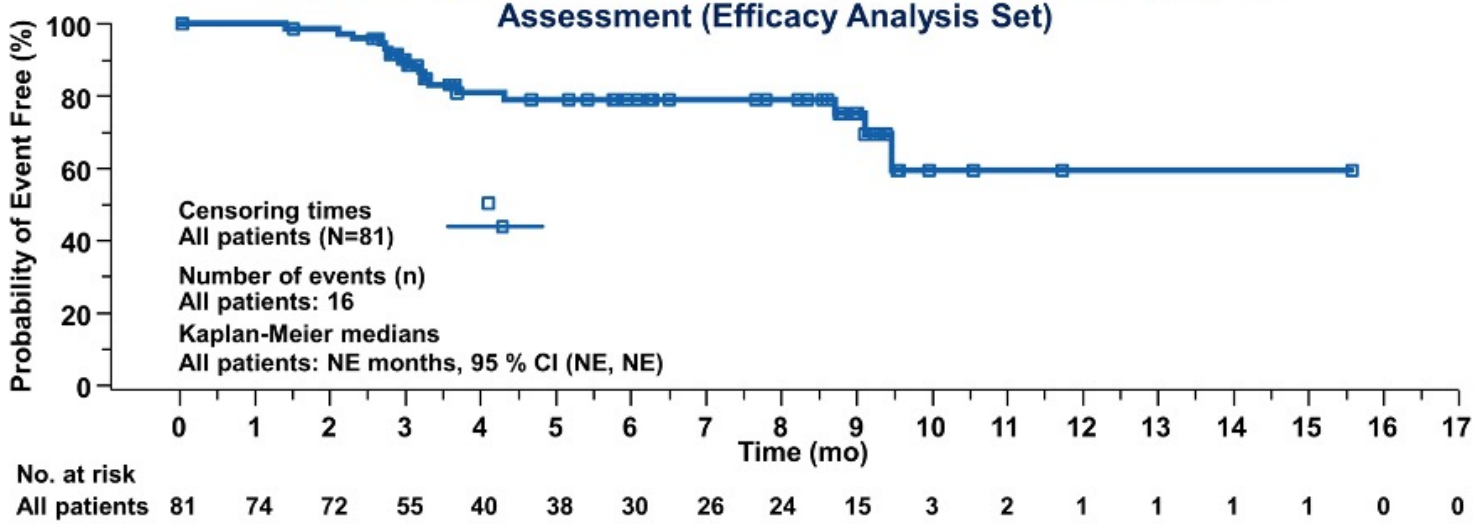
Best Overall Response Rate

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

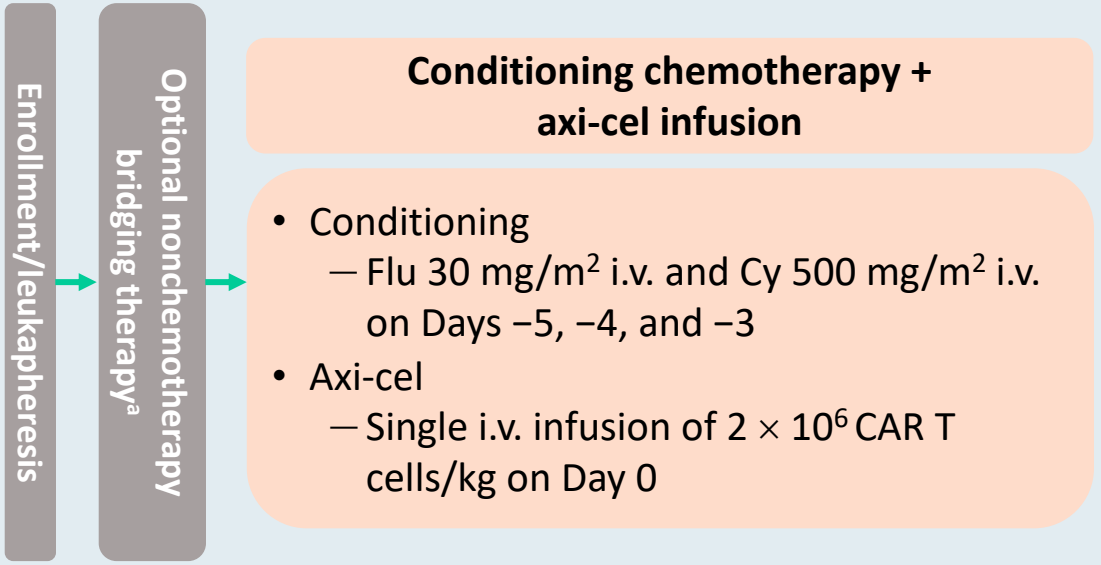
Schuster SJ et al. ASCO 2021;Abstract 7508.

Mantle Cell Lymphoma

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

Eligibility criteria

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



Primary endpoint

- CR[b]

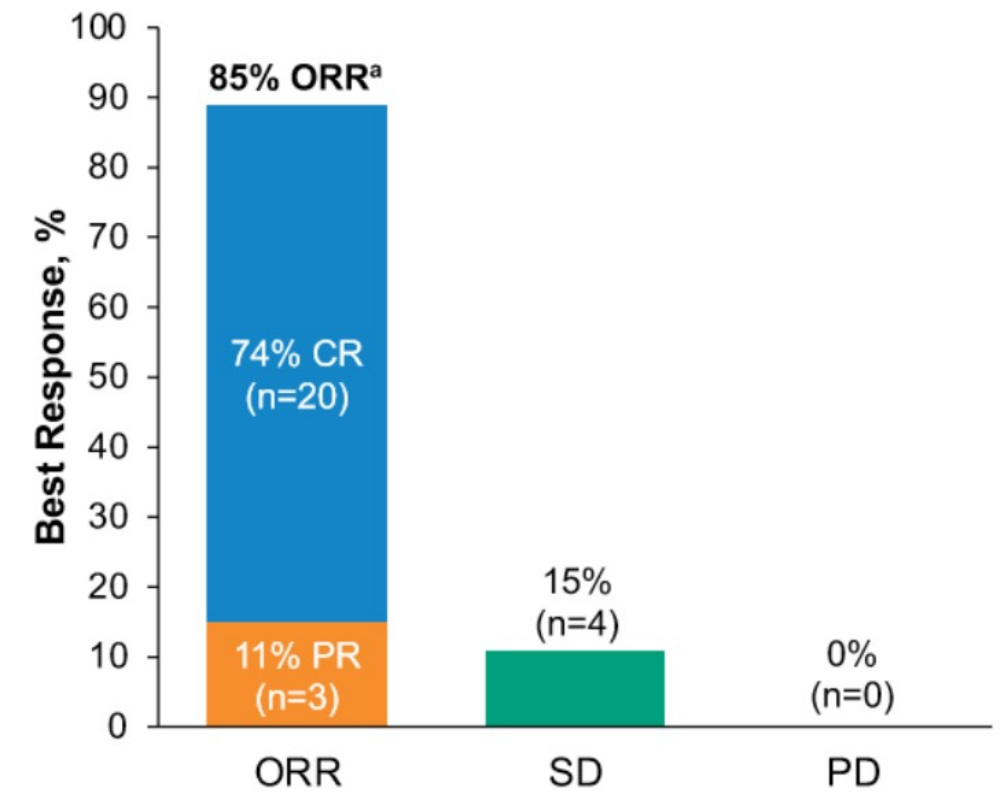
Key secondary endpoints

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

Neelapu SS et al. ASH 2020;Abstract 405.

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

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



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

Neelapu SS et al. ASH 2020;Abstract 405.

FDA Approves Brexucabtagene Autoleucel for Relapsed or Refractory Mantle Cell Lymphoma

Press Release – July 24, 2020

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

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

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

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

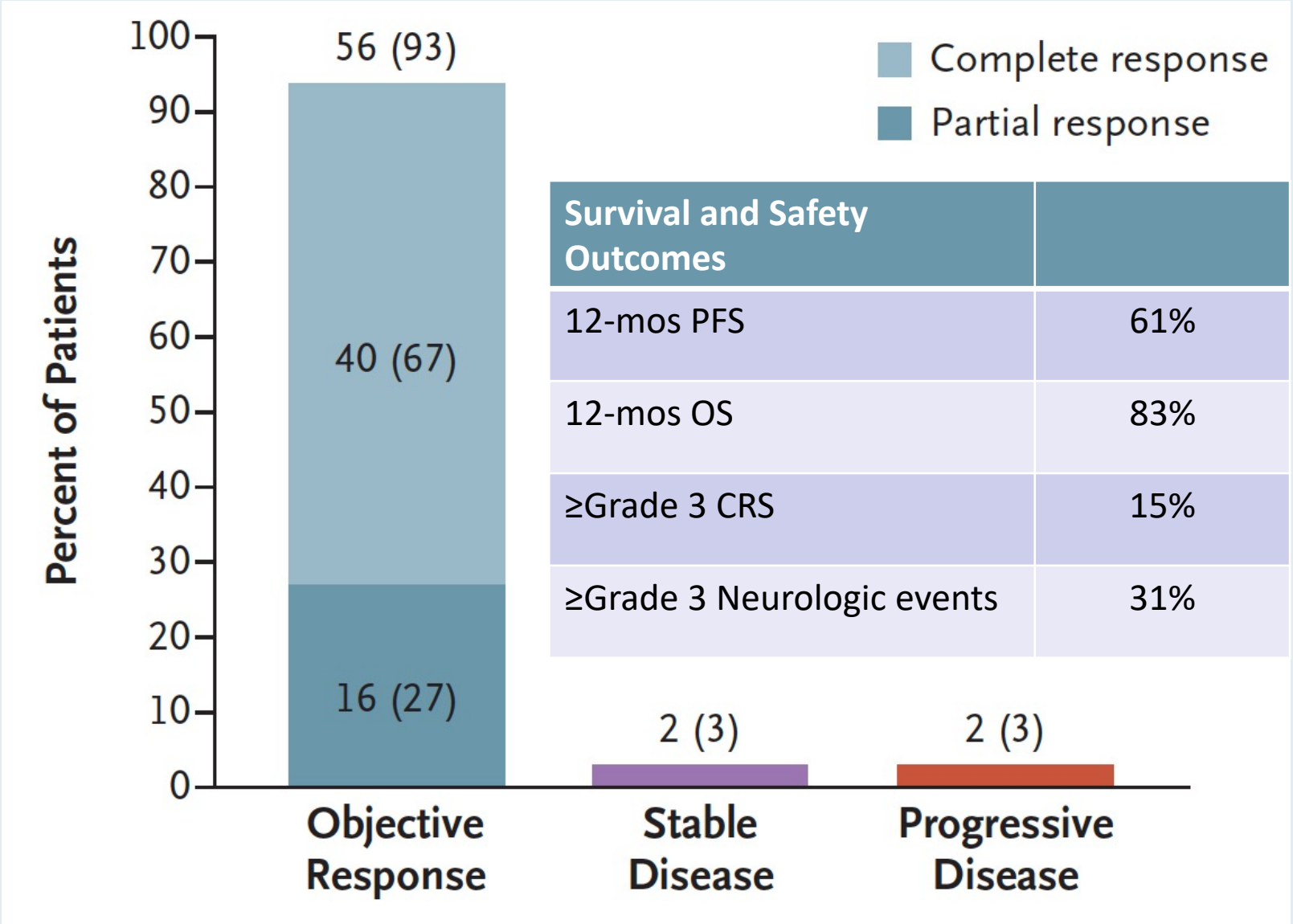
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

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

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



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

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

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Friday, September 17, 2021
12:00 PM – 1:00 PM ET

Faculty

Philip A Philip, MD, PhD, FRCP

Moderator

Neil Love, MD

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Thank you for joining us!

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

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