# Fall Oncology Nursing Series

*A Complimentary NCPD-Accredited Virtual Curriculum*

# Hodgkin and Non-Hodgkin Lymphomas

**Thursday, October 7, 2021**
**5:00 PM – 6:00 PM ET**

## Faculty

**Stephen M Ansell, MD, PhD**
**Robin Klebig, APRN, CNP, AOCNP**

## Moderator

**Neil Love, MD**

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# Faculty

**Stephen M Ansell, MD, PhD**
Professor of Medicine
Chair, Lymphoma Group
Mayo Clinic
Rochester, Minnesota

**Moderator**
**Neil Love, MD**
Research To Practice
Miami, Florida

**Robin Klebig, APRN, CNP, AOCNP**
Nurse Practitioner
Assistant Professor of Medicine
Division of Hematology
Mayo Clinic
Rochester, Minnesota

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# Commercial Support

This activity is supported by educational grants from Bristol-Myers Squibb Company, Epizyme Inc, Incyte Corporation, Novartis and Seagen Inc.

# Dr Love — Disclosures

**Dr Love** is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, Daiichi Sankyo Inc, Eisai Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.

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

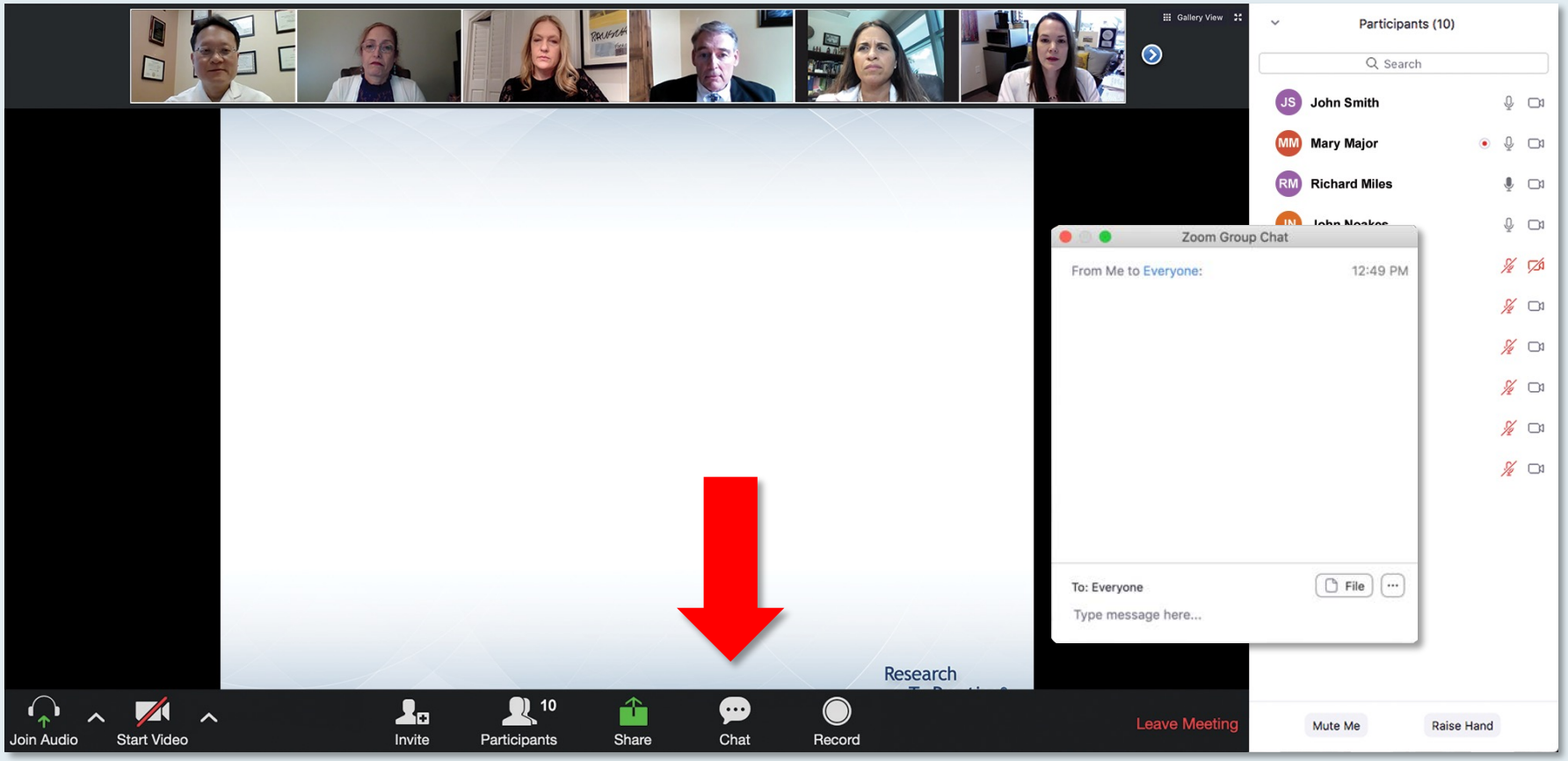
# Dr Ansell — Disclosures

| | |
|---|---|
| **Contracted Research (to Institution)** | ADC Therapeutics, Affimed, Bristol-Myers Squibb Company, Regeneron Pharmaceuticals Inc, Seagen Inc, Takeda Pharmaceuticals USA Inc, Trillium Therapeutics Inc |

# Ms Klebig — Disclosures

No relevant conflicts of interest to disclose.

# We Encourage Clinicians in Practice to Submit Questions




**Feel free to submit questions now before the program begins and throughout the program.**

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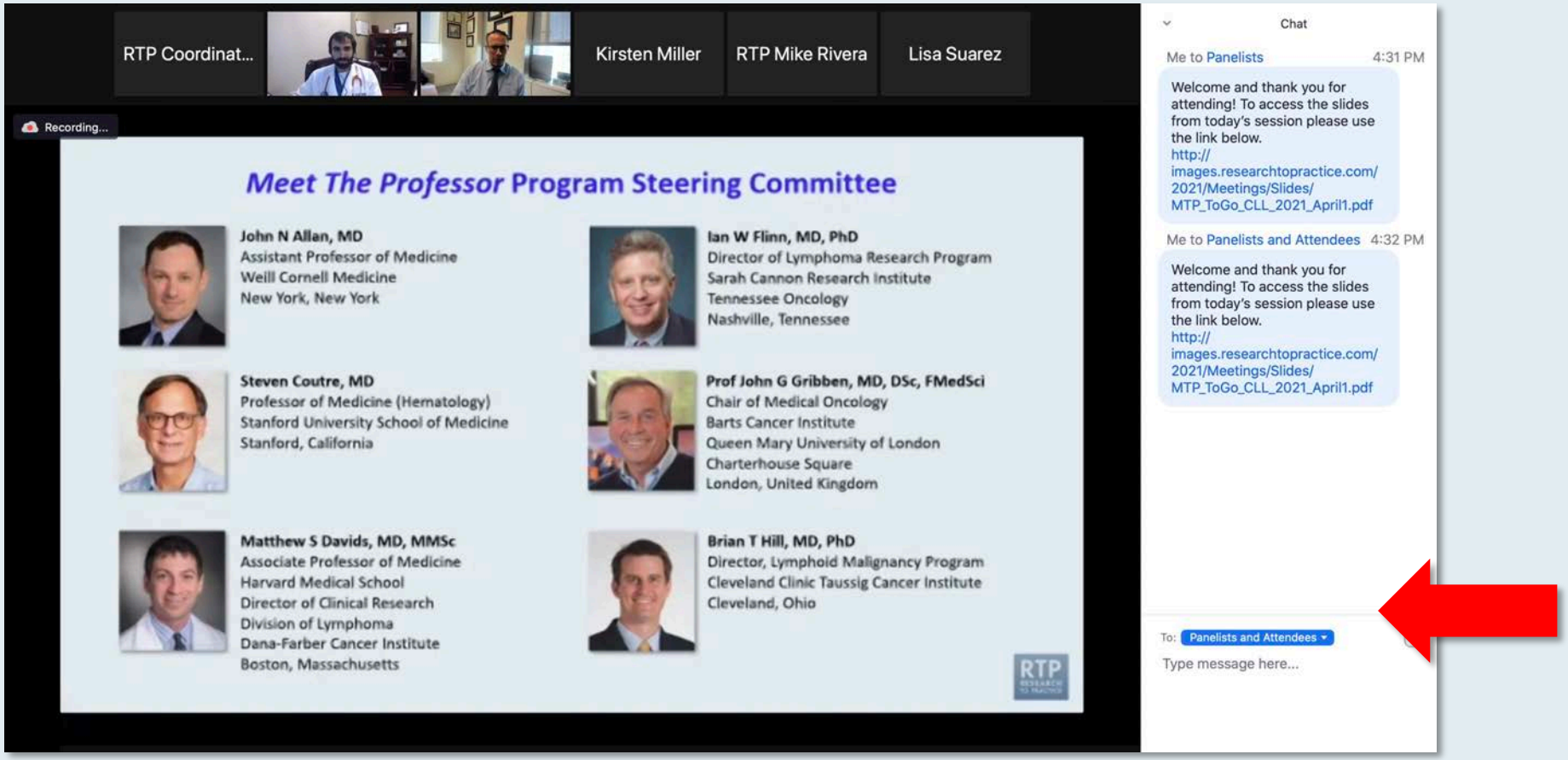
# Familiarizing Yourself with the Zoom Interface

## Expand chat submission box




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

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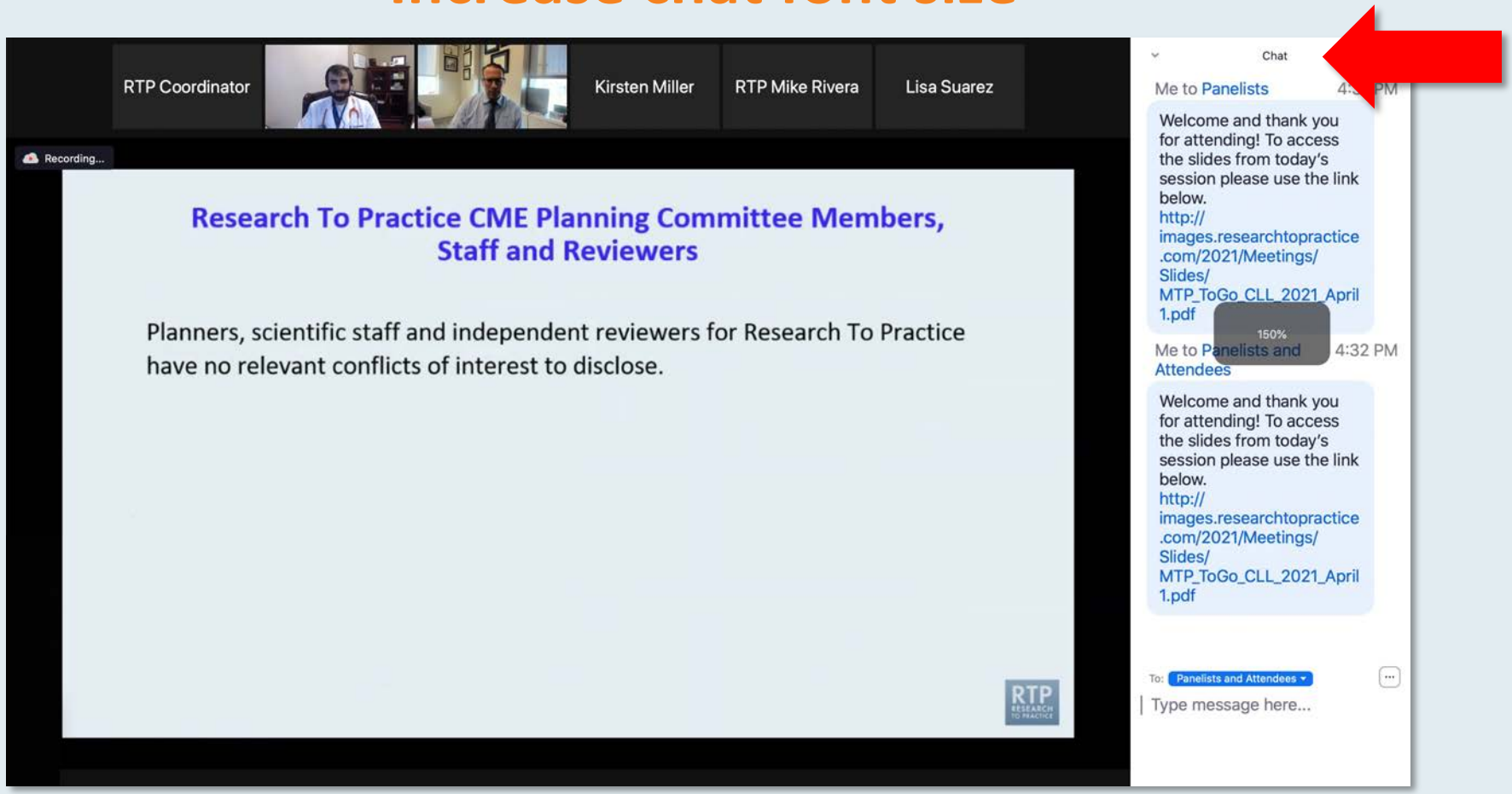
# Familiarizing Yourself with the Zoom Interface

## Increase chat font size




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

# ONCOLOGY TODAY

WITH DR NEIL LOVE

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


DR LAURIE SEHN

BC CANCER CENTRE FOR LYMPHOID CANCER


Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

# *Meet The Professor*

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

**Friday, October 8, 2021**
**12:00 PM – 1:00 PM ET**

## Faculty

**Eileen M O'Reilly, MD**

## Moderator

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# Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

**Monday, October 11, 2021**
**5:00 PM – 6:00 PM ET**

## Faculty

**Elizabeth R Plimack, MD, MS**

## Moderator

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# *Meet The Professor*

# Immunotherapy and Novel Agents in Gynecologic Cancers

**Tuesday, October 12, 2021**
**5:00 PM – 6:00 PM ET**

## Faculty

**Shannon N Westin, MD, MPH**

## 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, October 13, 2021**
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**Erika Hamilton, MD**

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# Chronic Lymphocytic Leukemia

**Thursday, October 14, 2021**
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**Corinne Hoffman, MS, APRN-CNP, AOCNP**

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# Chimeric Antigen Receptor T-Cell Therapy in Chronic Lymphocytic Leukemia and Lymphomas

**Monday, October 18, 2021**
**5:00 PM – 6:00 PM ET**

## Faculty

**Jeremy Abramson, MD**
**Elizabeth Zerante, MS, AGACNP-BC**

## 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

**Wednesday, October 20, 2021**
**5:00 PM – 6:00 PM ET**

## Faculty

**Aditya Bardia, MD, MPH**

## Moderator

**Neil Love, MD**

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# Recent Advances and Future Directions in Oncology: A Daylong Multitumor Educational Webinar in Partnership with Florida Cancer Specialists

*A CME-MOC/NCPD Accredited Virtual Event*

**Saturday, October 23, 2021**
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**Tanios Bekaii-Saab, MD**
**Kristen K Ciombor, MD, MSCI**
**Brad S Kahl, MD**
**Mark Levis, MD, PhD**
**Mark D Pegram, MD**
**Daniel P Petrylak, MD**
**Noopur Raje, MD**
**David Sallman, MD**
**Lecia V Sequist, MD, MPH**
**David R Spigel, MD**
**Saad Zafar Usmani, MD, MBA**
**Andrew D Zelenetz, MD, PhD**
*Additional faculty to be announced.*

## Moderator

**Neil Love, MD**

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*Thank you for joining us!*

*NCPD credit information will be emailed to each participant shortly.*

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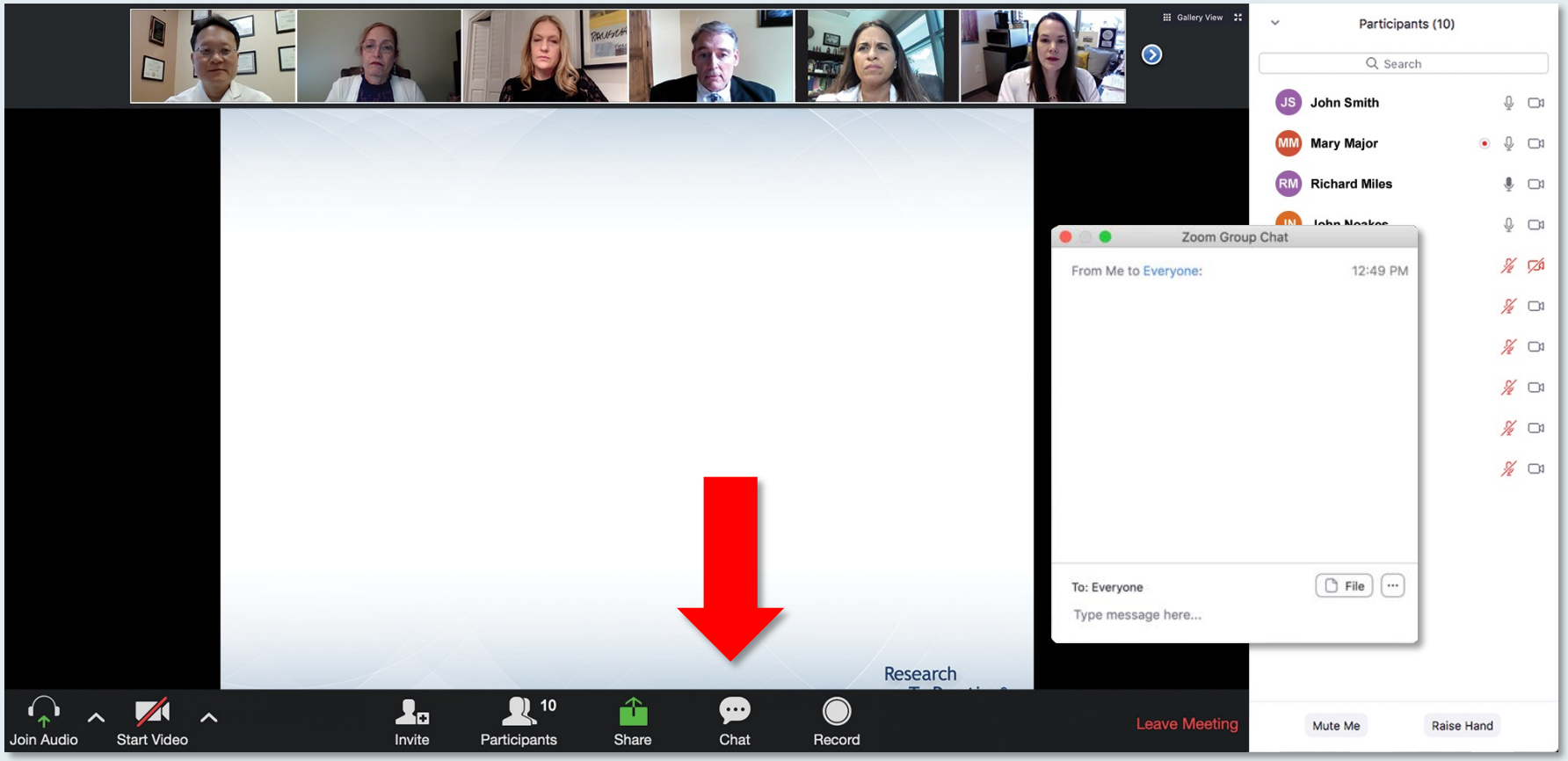


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**Module 1:** Breast Cancer – 9:30 AM – 10:20 AM

**Module 2:** Lung Cancer – 10:30 AM – 11:20 AM

**Module 3:** Gastrointestinal Cancers – 11:30 AM – 12:20 PM

**Module 4:** Genitourinary Cancers – 12:30 PM – 1:20 PM

**Module 5:** CLL and Lymphomas – 1:30 PM – 2:20 PM

**Module 6:** Multiple Myeloma – 2:30 PM – 3:20 PM

**Module 7:** AML and MDS – 3:30 PM – 4:20 PM

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# Research To Practice Education Platform

**Oncology Nurse Practitioners**

***Case Presentations***

- Key patient-education issues
- Biopsychosocial considerations:
  - Family/loved ones
  - The bond that heals

**Clinical Investigators**

***Oncology Strategy***

- New agents and regimens
- Predictive biomarkers
- Ongoing research and implications

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# Agenda

## Module 1: Diffuse Large B-Cell Lymphoma (DLBCL)

- Case: An 83-year-old woman with relapsed DLBCL

## Module 2: Hodgkin Lymphoma

- Case: A 77-year-old man with newly diagnosed Hodgkin lymphoma

## Module 3: Follicular Lymphoma

- Case: A 76-year-old man with newly diagnosed follicular lymphoma

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- Case: A 61-year-old woman with R/R mantle cell lymphoma

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# Key Recent FDA Approvals for Diffuse Large B-Cell Lymphoma

- Polatuzumab vedotin – August 1, 2019
- Selinexor – June 22, 2020
- Tafasitamab – July 31, 2020
- Loncastuximab tesirine – April 23, 2021

# 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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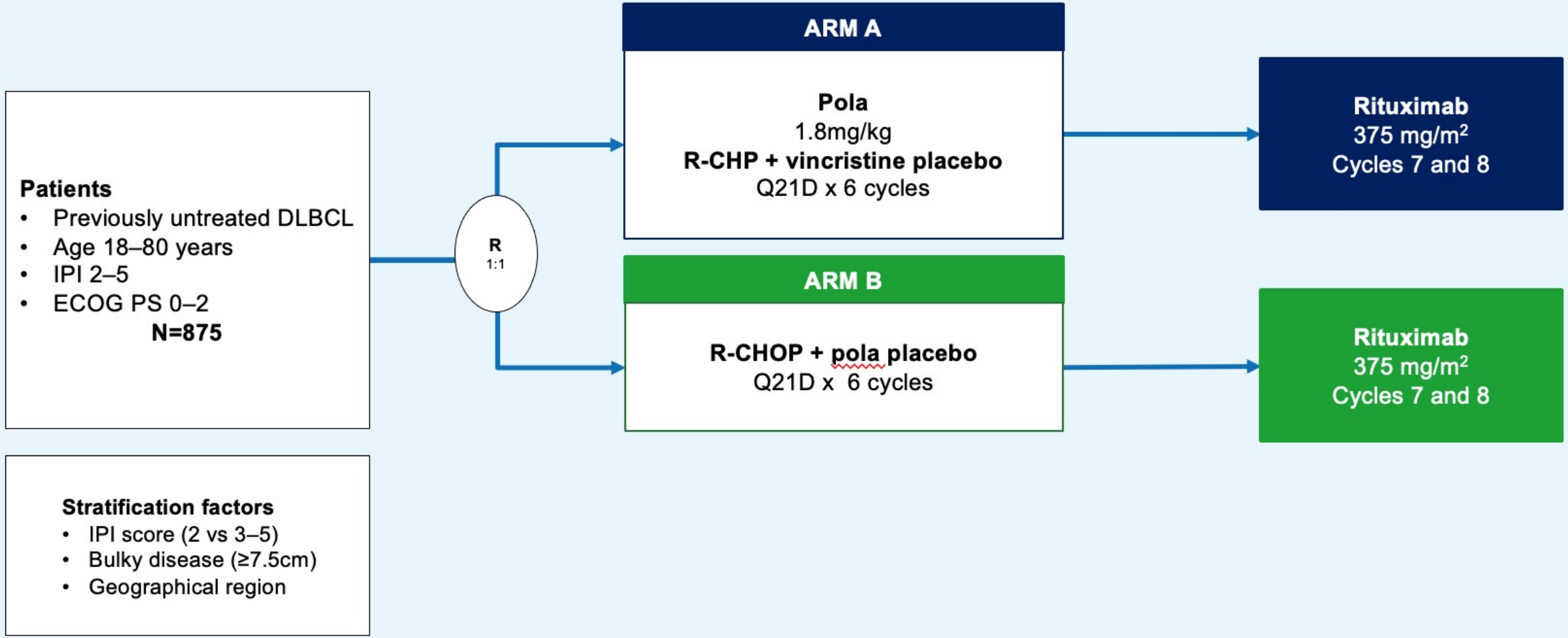
# POLARIX Phase III Trial Design




Courtesy of Gilles Salles MD, PhD.

# 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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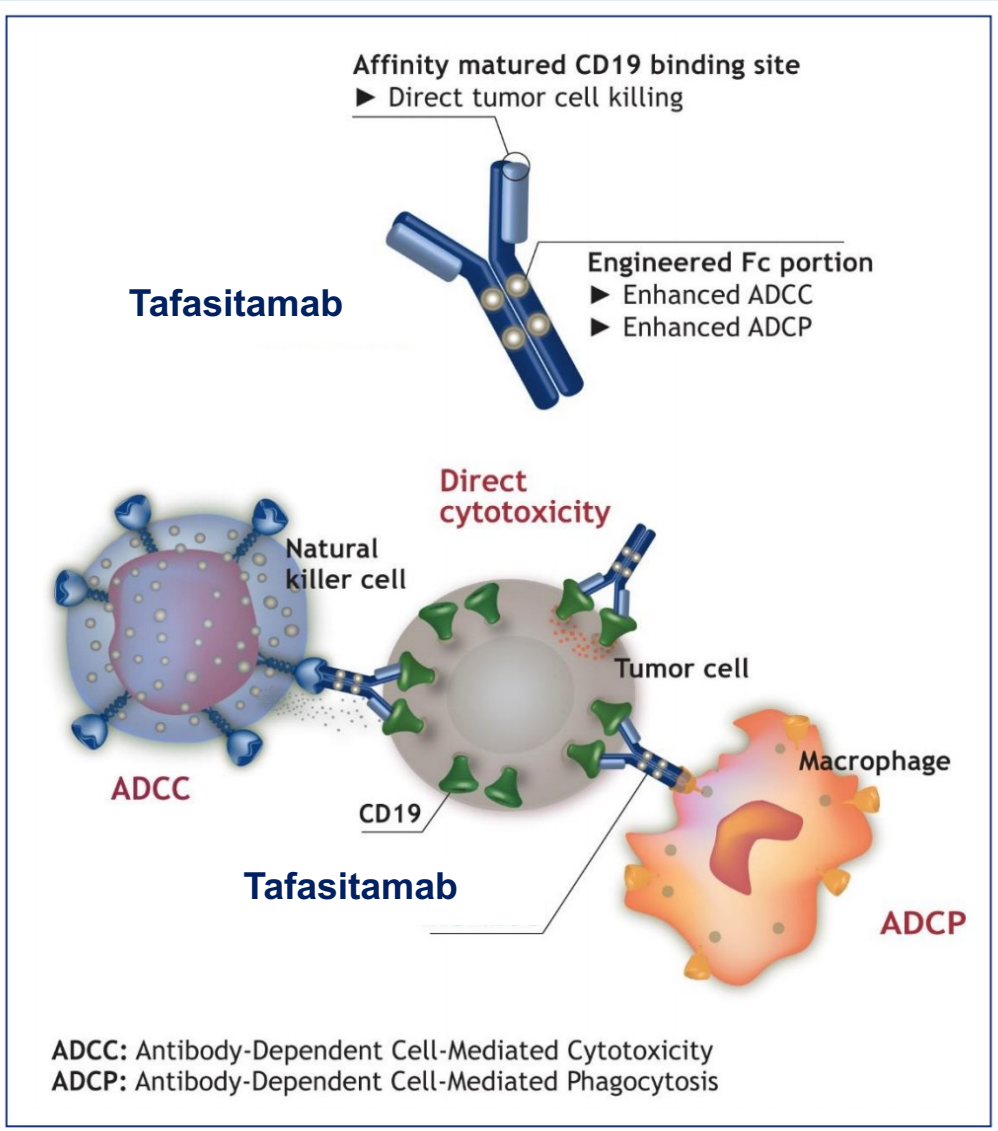
# Case Presentation – An 83-year-old woman with relapsed DLBCL

- 2018: Diagnosed with DLBCL, s/p R-CHOP x 6
- 2019: Relapsed disease → Rituximab x 4 → PD 2 months later
- 8/2019: Tafasitamab/bendamustine on clinical trial MOR208C204
  - Treatment every 2 weeks until PD or intolerability
- 9/2021: Imaging confirms sustained remission for over 24 months
  - Continues to tolerate treatment well, remains on therapy

# 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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# Long-Term Subgroup Analyses from L-Mind, a Phase II Study of Tafasitamab (MOR208) Combined with Lenalidomide in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Maddocks KJ et al.

ASH 2020;Abstract 3021.

# L-MIND: Summary

| Clinical endpoint | N = 80 |
|---|---|
| ORR | 57.5% |
| CR | 40.0% |
| Median DOR | 34.6 mo |
| 24 mo DOR rate | 71.3% |
| 24 mo OS rate | 57.2% |

In the subgroup analysis, patients with CR as best objective response had better outcomes than those with PR:

- Median DOR: NR vs 5.6
- 24-month DOR rate: 86.4% vs 38.5%
- 24-month OS rate: 90.6% vs 42.7%

Maddocks KJ et al. ASH 2020;Abstract 3021.

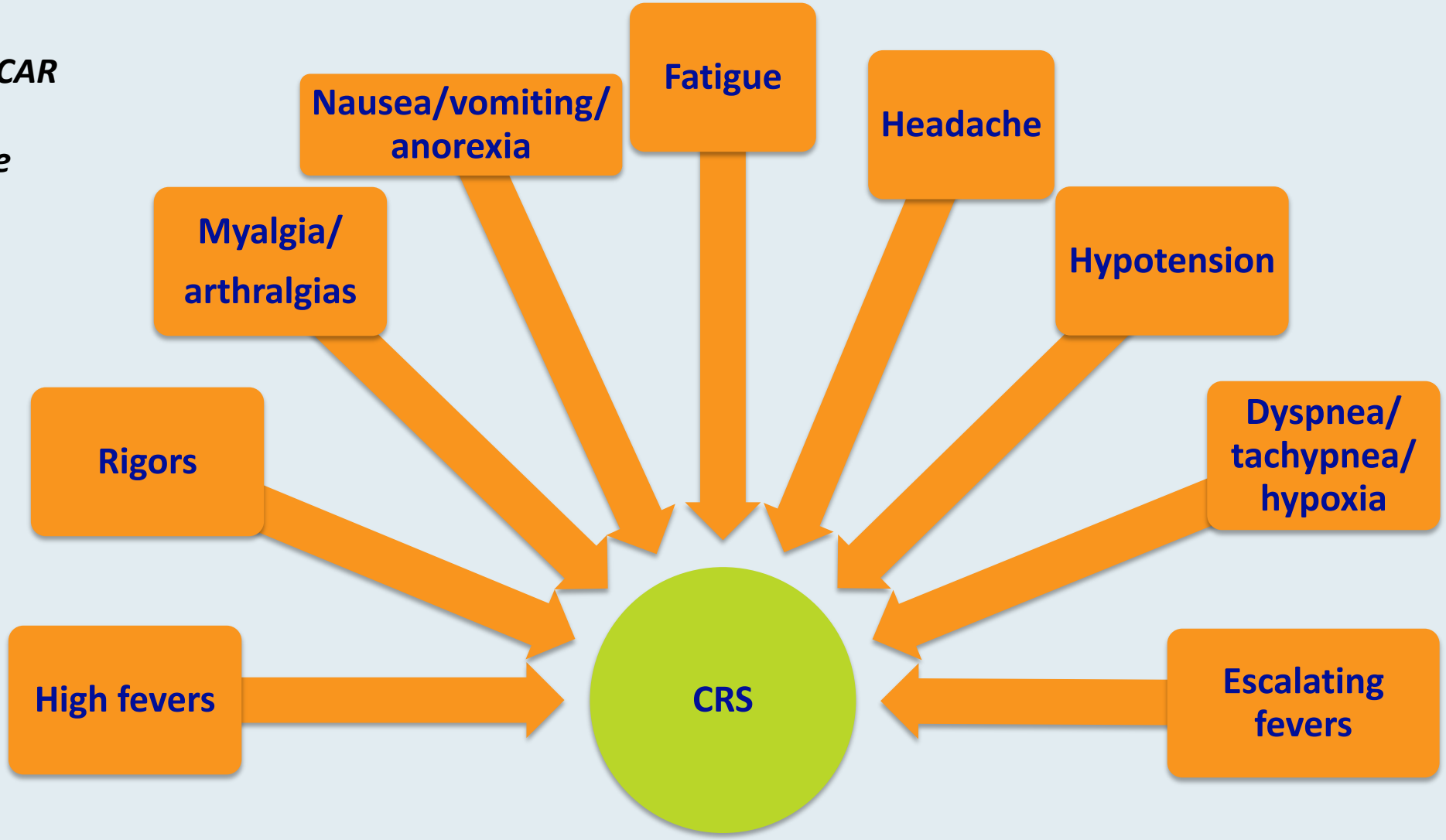
# Pivotal CAR-T Studies in DLBCL: Summary of Efficacy

| | ZUMA-1 Axicabtagene ciloleucel | JULIET Tisagenlecleucel | TRANSCEND NHL 001 Lisocabtagene maraleucel |
|---|---|---|---|
| Evaluable patients | 101 | 93 | 102 (core: 73) |
| Median follow-up | 15.4 mo | 19.3 mo | 12 mo |
| Best ORR | 83% | 52% | 75% |
| CR | 58% | 40% | 55% |
| 6-mo ORR | 41% | 33% | 47% |
| 12-mo OS | 59% | 49% | 63% |

Locke F et al; ZUMA-1 Investigators. *Lancet Oncol* 2019;20(1):31-42.
Schuster SJ et al; JULIET Investigators. *N Engl J Med* 2019;380(1):45-56.
Abramson JS et al; TRANSCEND NHL 001 Investigators. *Proc ASCO* 2018;Abstract 7505.

# Cytokine Release Syndrome (CRS): Common Symptoms

***Based on CAR T-cell experience***




**Diagnosis based on <u>clinical</u> symptoms and events**

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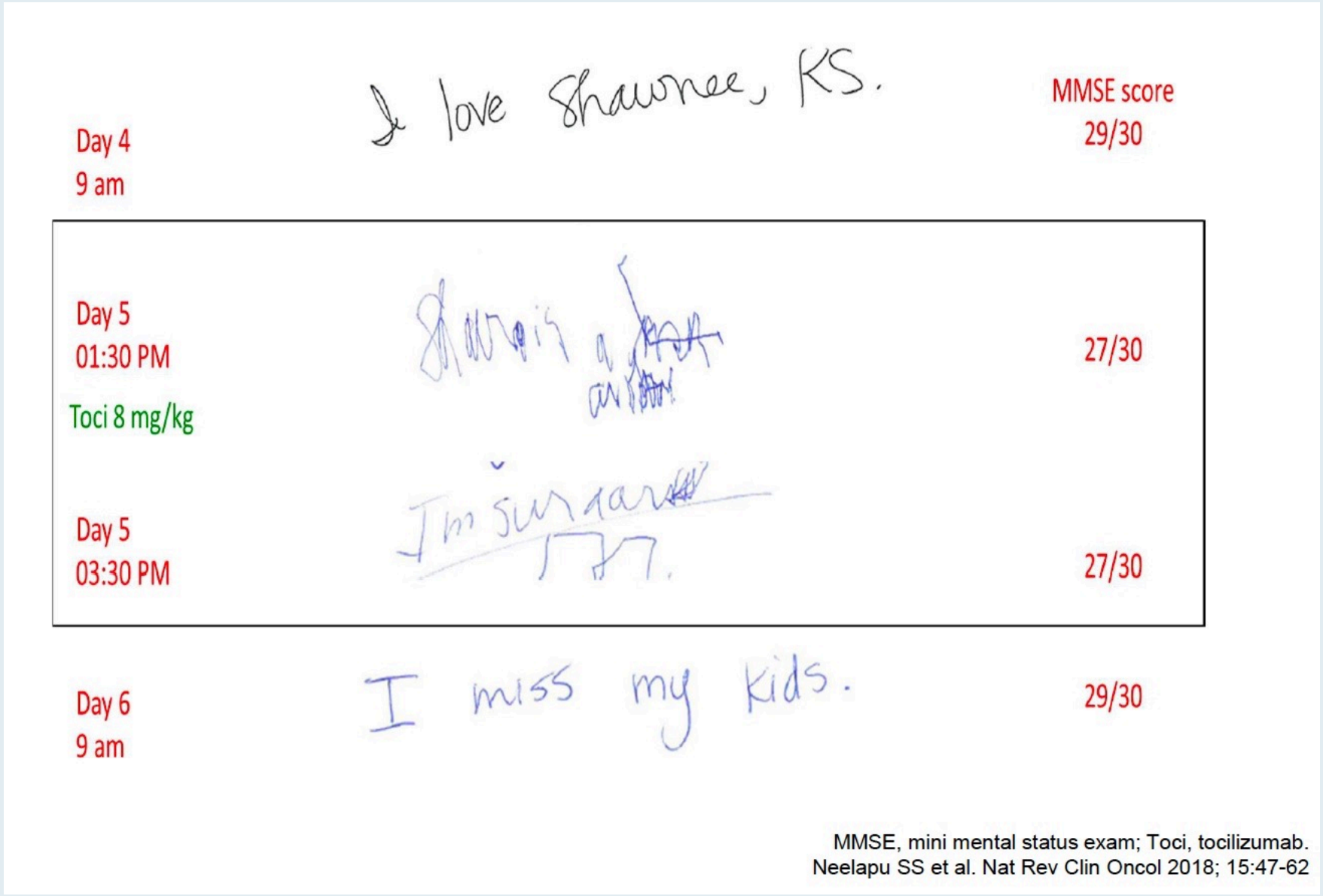
# CAR T-Cell Therapy-Associated Neurologic Toxicity

## 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.

# Example of Handwriting Deterioration Associated with Neurotoxicity from CAR T-Cell Therapy




MMSE, mini mental status exam; Toci, tocilizumab.
Neelapu SS et al. Nat Rev Clin Oncol 2018; 15:47-62

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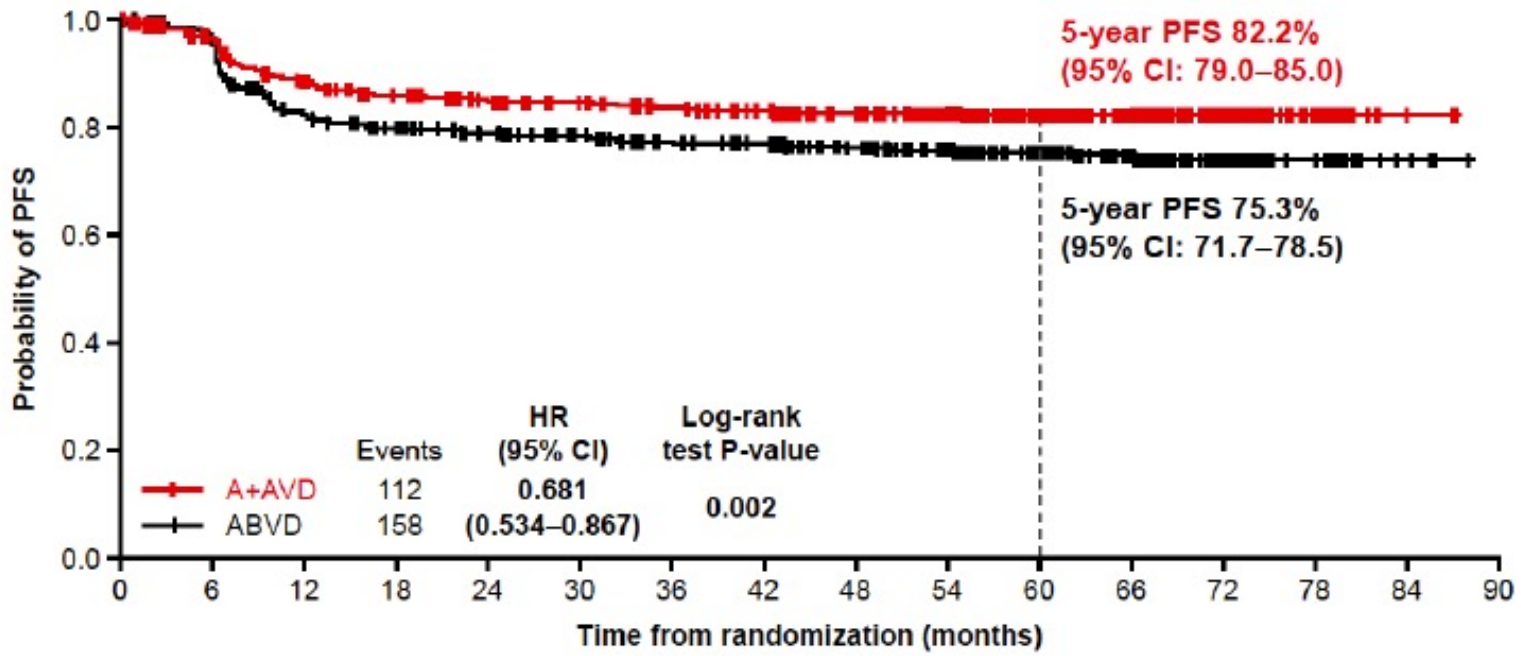
# ECHELON-1: PFS per investigator at 5 years' follow-up*




**Number of patients at risk**

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A+AVD | 664 | 620 | 562 | 535 | 518 | 505 | 492 | 474 | 446 | 414 | 333 | 201 | 102 | 38 | 2 | 0 |
| ABVD | 670 | 613 | 521 | 500 | 478 | 456 | 432 | 423 | 397 | 360 | 292 | 179 | 73 | 22 | 4 | 0 |

- As of the 5-year follow-up, the prespecified number of events required to trigger an OS analysis have not been reached.
- OS was a prespecified key secondary endpoint.

*September 14, 2020 data cut-off.

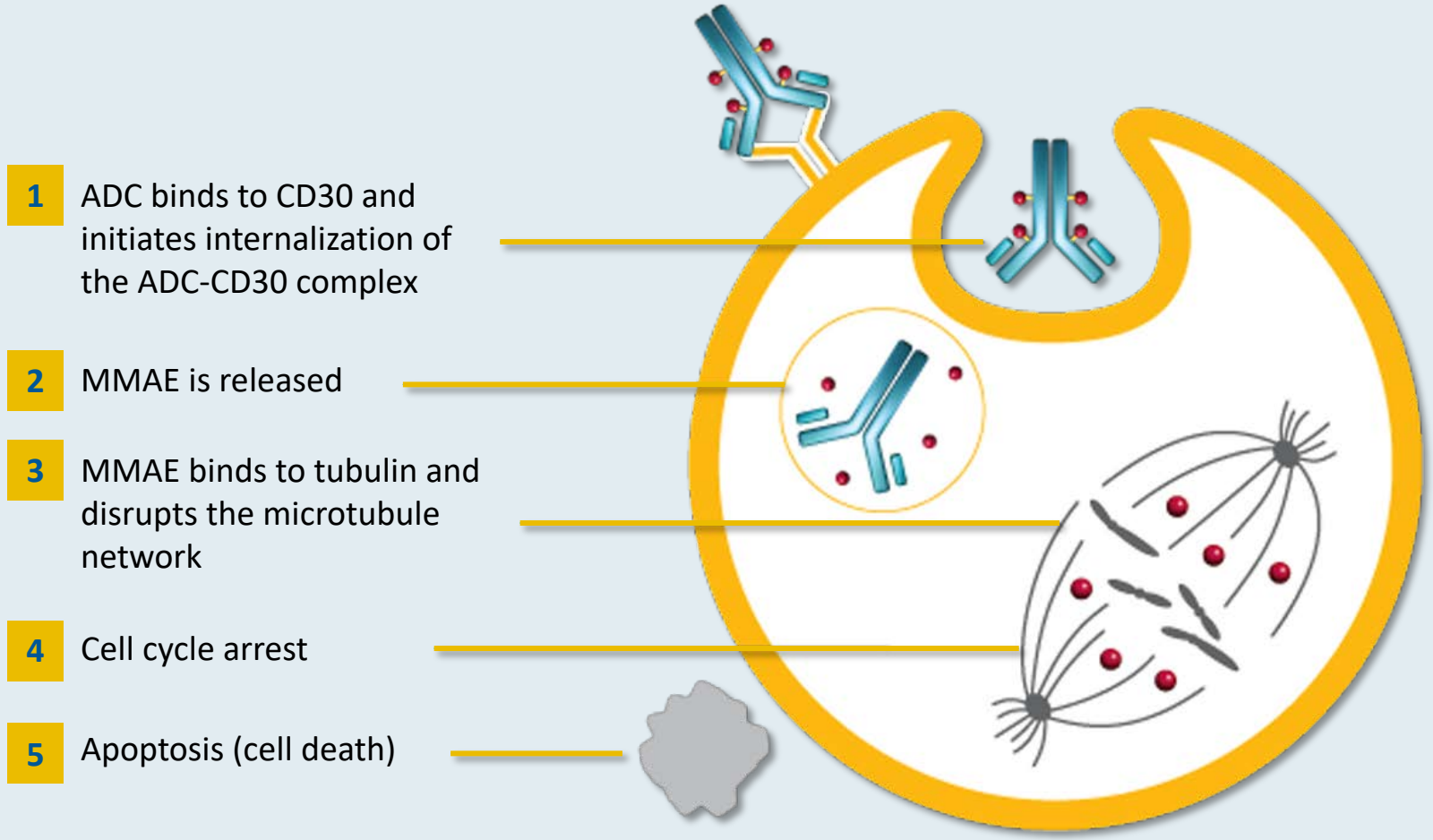
Straus DJ et al. ASH 2020;Abstract 2973.

# Case Presentation – A 77-year-old man with newly diagnosed Hodgkin lymphoma

- Original plan: 2 doses brentuximab vedotin (BV) – 6 cycles AVD – 4 cycles BV
  - AVD was poorly tolerated (neuropathy, weakness)
- Patient required dose reductions of BV due to neuropathy
- Completed therapy ultimately
- Remains in remission

# Mechanism of Action of Brentuximab Vedotin

**Brentuximab vedotin is an antibody-drug conjugate (ADC) targeted to cells expressing CD30 on their surface**




Courtesy of Julie M Vose, MD, MBA.

# Brentuximab Vedotin with Chemotherapy for Patients with Previously Untreated, Stage III/IV Classical Hodgkin Lymphoma: 5-Year Update of the ECHELON-1 Study

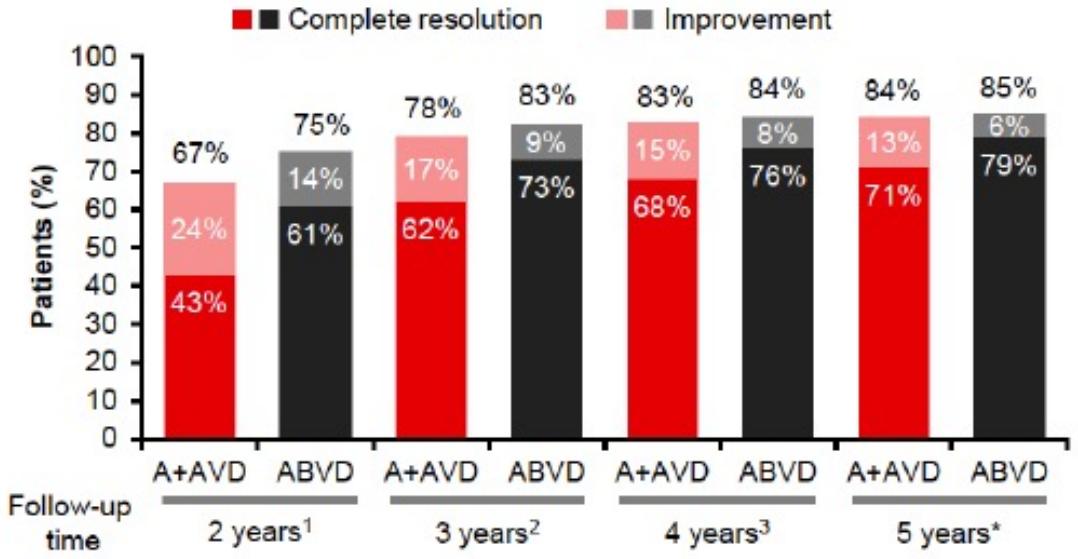
Straus DJ et al.

ASH 2020;Abstract 2973.

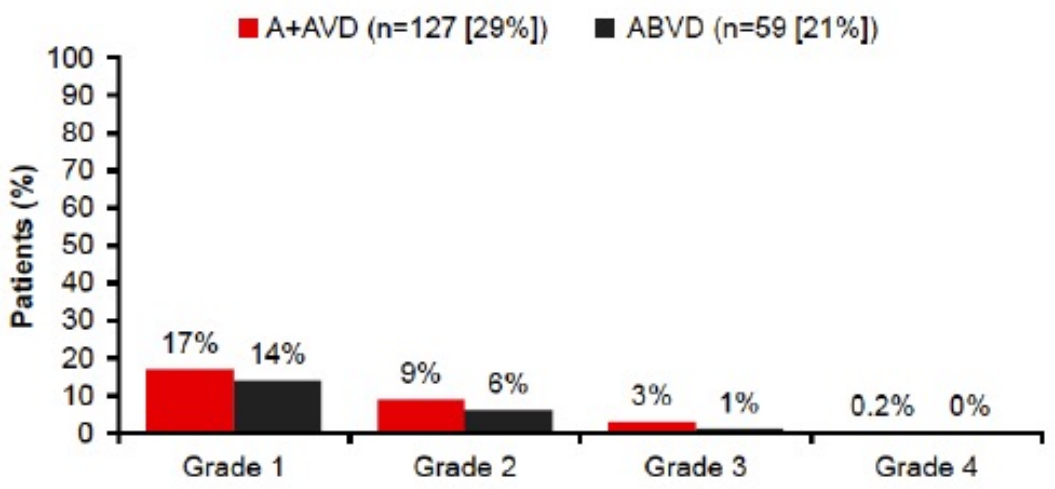
# ECHELON-1: PN resolution and improvement

- At the primary analysis, 442 and 286 patients in A+AVD and ABVD arms, respectively, had experienced PN.

**Patients with complete resolution or improvement of PN over time (%)***




**Patients with ongoing PN by grade at last follow-up†**

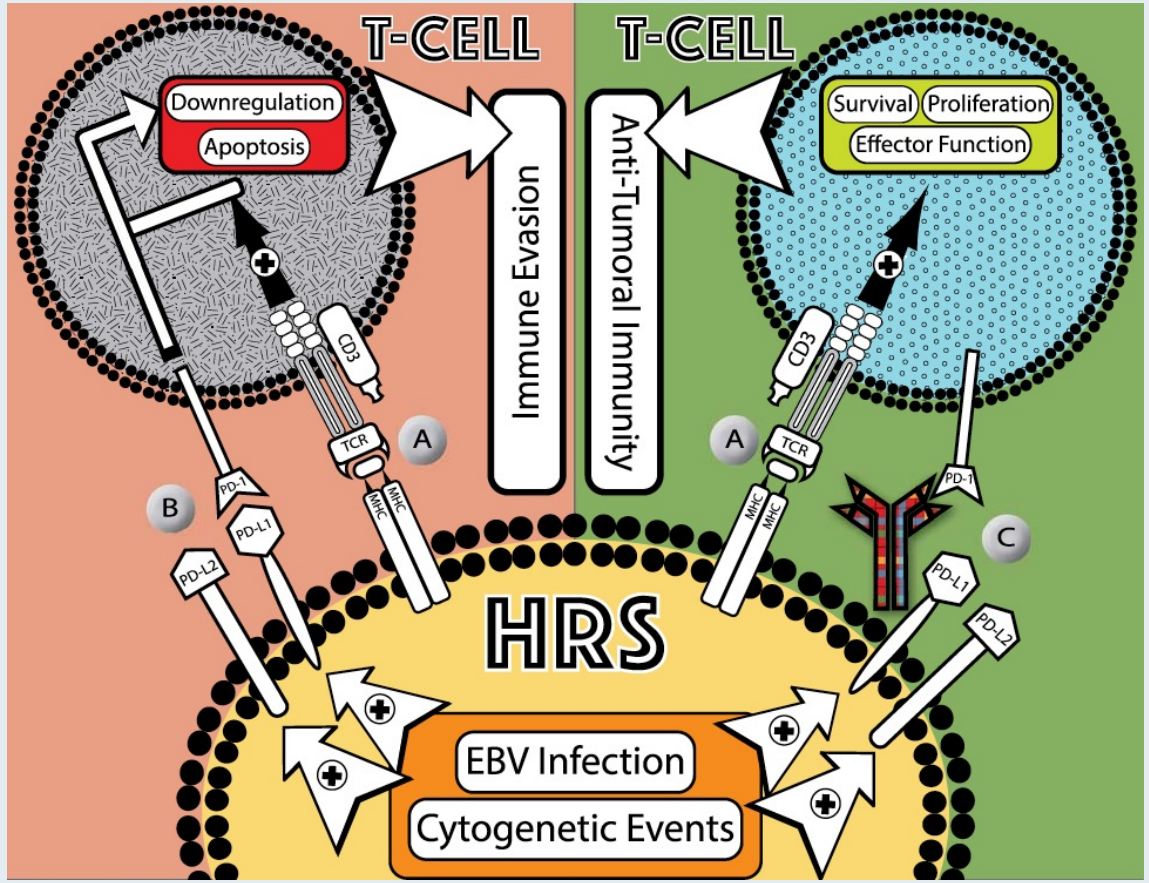



Resolution was defined as event outcome of "resolved" or "resolved with sequelae"; Improvement was defined as "improved by ≥1 grade from worst grade as of the latest assessment"; *Percentages rounded to nearest integer; †Median follow-up 236.9 weeks (range: 0–344); Assessment of ongoing PN with maximum severity of grade 3/4 was confounded in 12 of the 15 A+AVD patients by death prior to resolution (n=3), loss to follow-up (n=4), and withdrawal from study (n=5); Among the ABVD patients with grade 3 PN, two were lost to follow-up and two died prior to resolution of PN.


1. Connors JM, et al. N Engl J Med 2018;378:331–44;
2. Straus DJ, et al. Blood 2020;135:735–42;
3. Bartlett NL, et al. Blood 2019;134 (Suppl. 1):4026.


Straus DJ et al. ASH 2020;Abstract 2973.

# Targeting the PD-1/PD-L1 Axis in HL




- **HL characterized by small number of malignant Hodgkin Reed-Sternberg cells (HRS) surrounded by normal immune cells**
- 9p24.1 chromosomal abnormalities frequently observed in HRS
- **More than 90% of HRS have alterations in PD-L1 and PD-L2 loci**
- Malignant Hodgkin and RS cells overexpress PD-L1/L2 ligands (due to cytogenetic events, infection with EBV)

Villasboas JC, Ansell SA. *Cancer J* 2016;22(1):17-22; Roemer MGM et al. *J Clin Oncol* 2016;34(23):2690-7.

# Agenda

## Module 1: Diffuse Large B-Cell Lymphoma (DLBCL)

- Case: An 83-year-old woman with relapsed DLBCL

## Module 2: Hodgkin Lymphoma

- Case: A 77-year-old man with newly diagnosed Hodgkin lymphoma

## Module 3: Follicular Lymphoma

- Case: A 76-year-old man with newly diagnosed follicular lymphoma

## Module 4: Mantle Cell Lymphoma

- Case: A 61-year-old woman with R/R mantle cell lymphoma

# Key Recent Pivotal Data Sets/FDA Approvals in Follicular Lymphoma

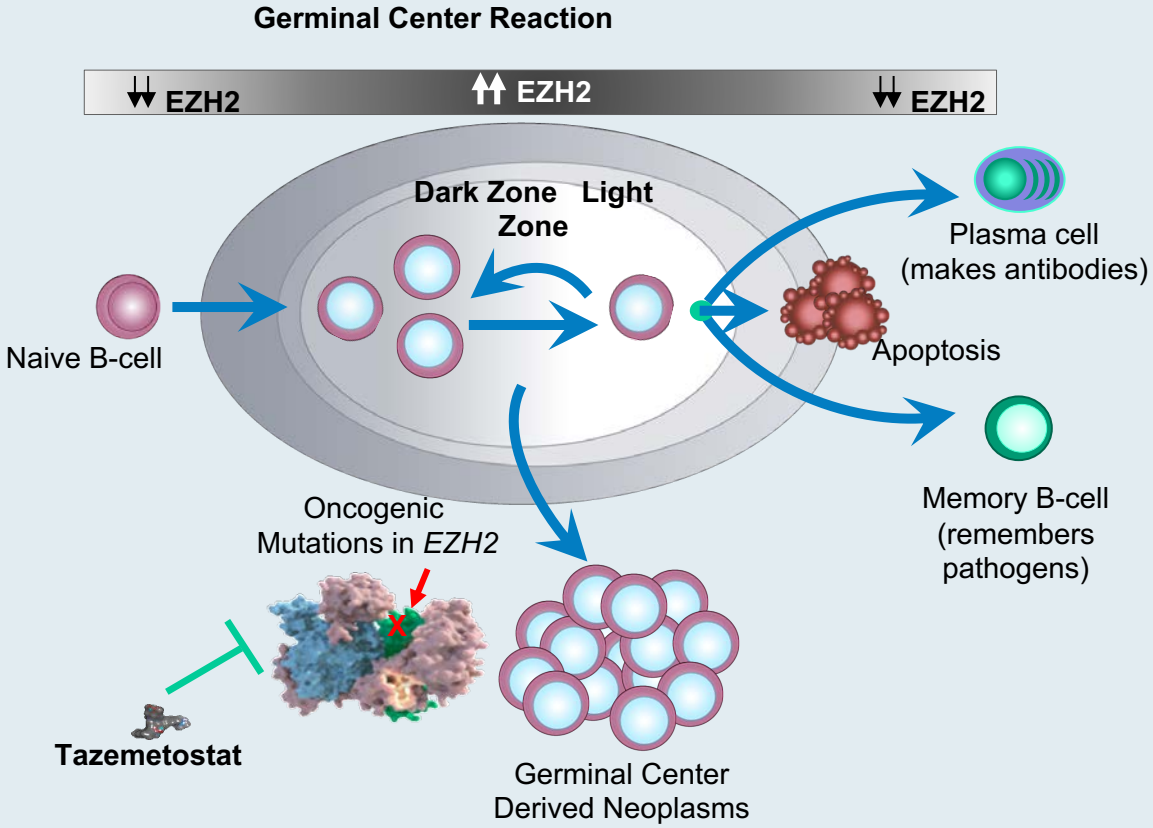
- RELEVANCE – Lenalidomide/rituximab – ASCO 2018
- Study E7438-G000-101 – Tazemetostat – June 18, 2020
- ELARA – Tisagenlecleucel – ASCO 2021
- ZUMA-5 – Axicabtagene ciloleucel – March 5, 2021

# Case Presentation – A 76-year-old man with newly diagnosed follicular lymphoma

- PMH: Progressive aphasia, short-term memory loss likely due to Alzheimer's disease
- Patient is a farmer, wife is healthcare surrogate
- 9/2019: Diagnosed with Grade 1-2, Stage IV follicular lymphoma
- Lenalidomide/rituximab ($R^2$), with rash and neutropenia requiring dose adjustments
  - After 5 months: Complete remission (CR)
- 8/12/2021: Most recent CT imaging: Remains in CR
- Continues to require 24/7 care at home due to progressive Alzheimer's dementia
- Becoming more difficult to come to appointments; agreed to d/c treatment and observe

# 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

# Analyzing Efficacy Outcomes from the Phase 2 Study of Single-Agent Tazemetostat as Third-Line Therapy in Patients with Relapsed or Refractory Follicular Lymphoma to Identify Predictors of Response

Salles G et al.

ASH 2020;Abstract 2047.

# Phase 2 Efficacy Outcomes

| Efficacy Outcome[a] | Combined WT and MT *EZH2* (N=99) | WT *EZH2* (n=54)[1] | MT *EZH2* (n=45)[1] |
|---|---|---|---|
| ORR, % (95% CI) | 51 (40–61) | 35 (23-49) | 69 (53-82) |
| Median DOR, months (95% CI) | 11 (7–19) | 13 (6-NE) | 11 (7-NE) |
| Median PFS, months (95% CI) | 12 (8–15) | 11 (4-15) | 14 (11-22) |
| Median OS, months (95% CI) | NR (38–NE) | NR | NR |

- The DOR was consistent between WT and MT *EZH2* groups[1]
- Consistent ORRs were also observed across high-risk subgroups, such as patients with POD24, double-refractory disease, and refractoriness to rituximab therapy, regardless of mutation status[1]

[a]ORR, DOR, and PFS are based on IRC assessments.

**1.** Morschhauser F, et al. *Lancet Oncology*; 2020;21(11):1433-42.

CI, confidence interval; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; EZH2, enhancer of zeste homolog 2; IRC, independent radiology committee; MT, mutant; NE, not estimable; NR, not reached; ORR, objective response rate; OS, overall survival; MT, mutant; NE, not evaluable; NR, not reached; PFS, progression-free survival; WT, wild type.



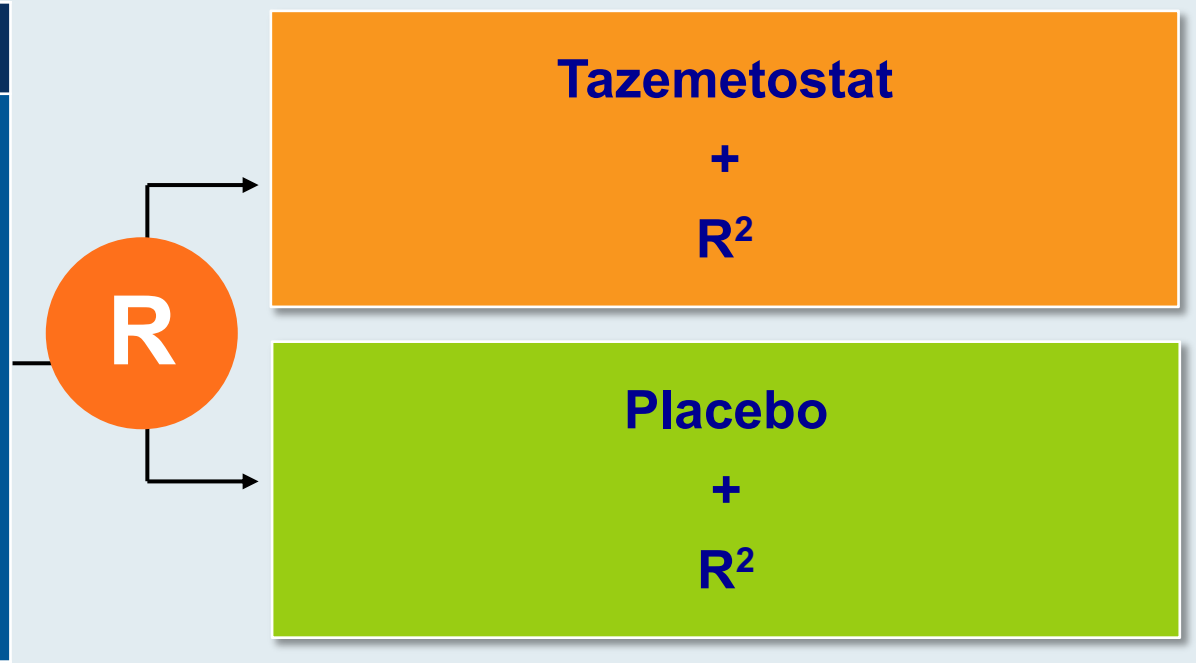


Salles G et al. ASH 2020;Abstract 2047.

# Ongoing Phase Ib/III Trial of Tazemetostat + Lenalidomide/Rituximab ($R^2$) for R/R FL

**Target accrual (N = 518)**

- Must have 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: Recommended Phase III dose of tazemetostat in combination with $R^2$
  - Stage 2: Progression-free survival

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

Stephen J. Schuster, MD
Stephen.Schuster@pennmedicine.upenn.edu

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,*]

[1]University of Pennsylvania, Philadelphia, PA; [2]Peter MacCallum Cancer Centre and Royal Melbourne Hospital, Melbourne, Australia; [3]Medizinische Klinik III, LMU Klinikum, Munich, Germany; [4]Hospital 12 De Octubre, Complutense University, CNIO, Madrid, Spain; [5]Oslo University Hospital, Oslo, Norway; [6]Royal Brisbane Hospital, Herston, Australia; [7]Michigan Medicine University of Michigan, Ann Arbor, MI; [8]City of Hope National Medical Center, Duarte, CA; [9]Moffitt Cancer Center, Tampa, FL; [10]Hospices Civils de Lyon and Université Claude Bernard Lyon 1, Lyon, France; [11]Kyushu University Hospital, Fukuoka, Japan; [12]Tohoku University Hospital, Sendai, Japan; [13]Amsterdam UMC, University of Amsterdam, Cancer Center Amsterdam, Amsterdam, Netherlands, on behalf of HOVON/LLPC; [14]Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA; [15]University of Chicago, Chicago, IL; [16]Novartis Pharmaceuticals Corporation, East Hanover, NJ; [17]Novartis Pharma AG, Basel, Switzerland; [18]The University of Texas MD Anderson Cancer Center, Houston, TX; [19]BostonGene, Waltham, MA; [20]APHP, Hôpital Saint-Louis-Université de Paris, Paris, France

*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

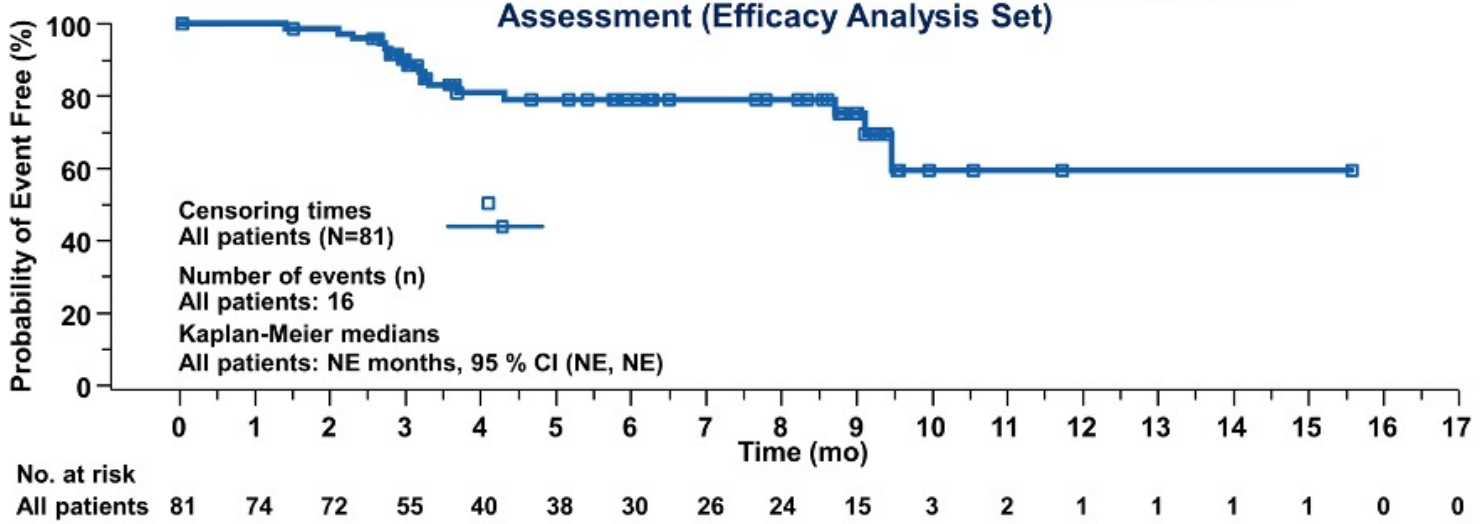
## Best Overall Response Rate

| 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.

# FDA Grants Accelerated Approval to Axicabtagene Ciloleucel for R/R 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.

The main efficacy measures were objective response rate (ORR) and duration of response (DOR) as determined by an independent review committee. Among 81 patients in the primary efficacy analysis, the ORR was 91% with a complete remission (CR) rate of 60% and a median time-to-response of 1 month. The median DOR was not reached, and the 1-year rate of continued remission was 76.2%. For all leukapheresed patients in this trial (n=123), the ORR was 89% with a CR rate of 62%."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-axicabtagene-ciloleucel-relapsed-or-refractory-follicular-lymphoma

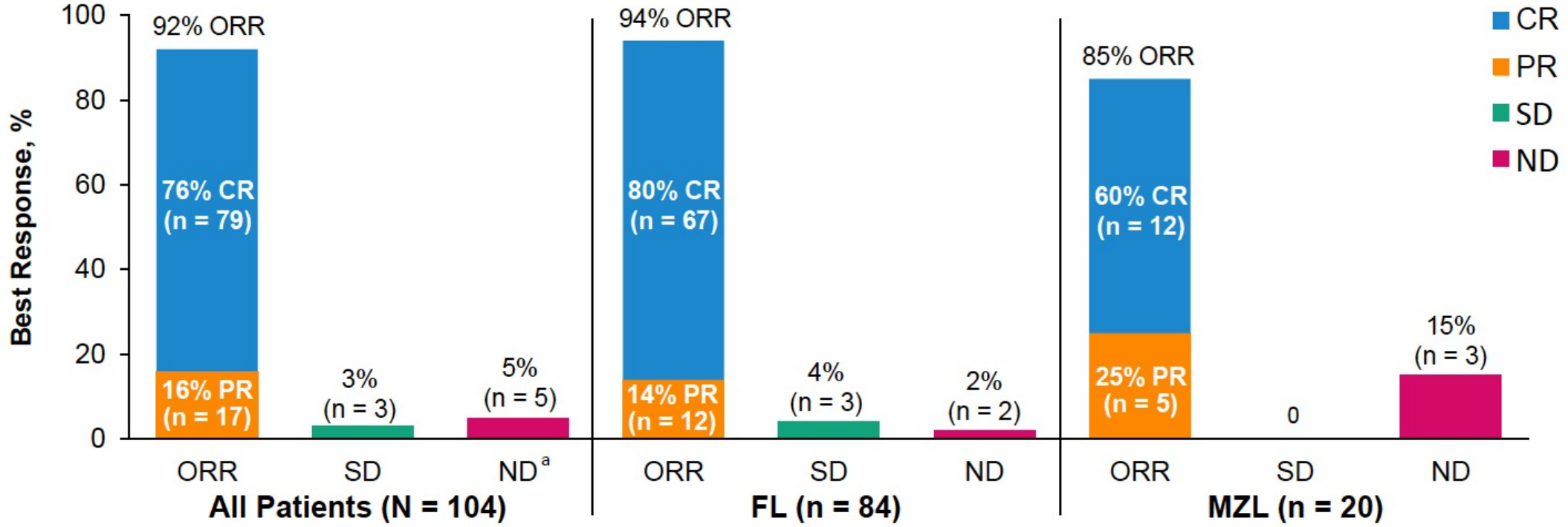
# Primary Analysis of ZUMA-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

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.**

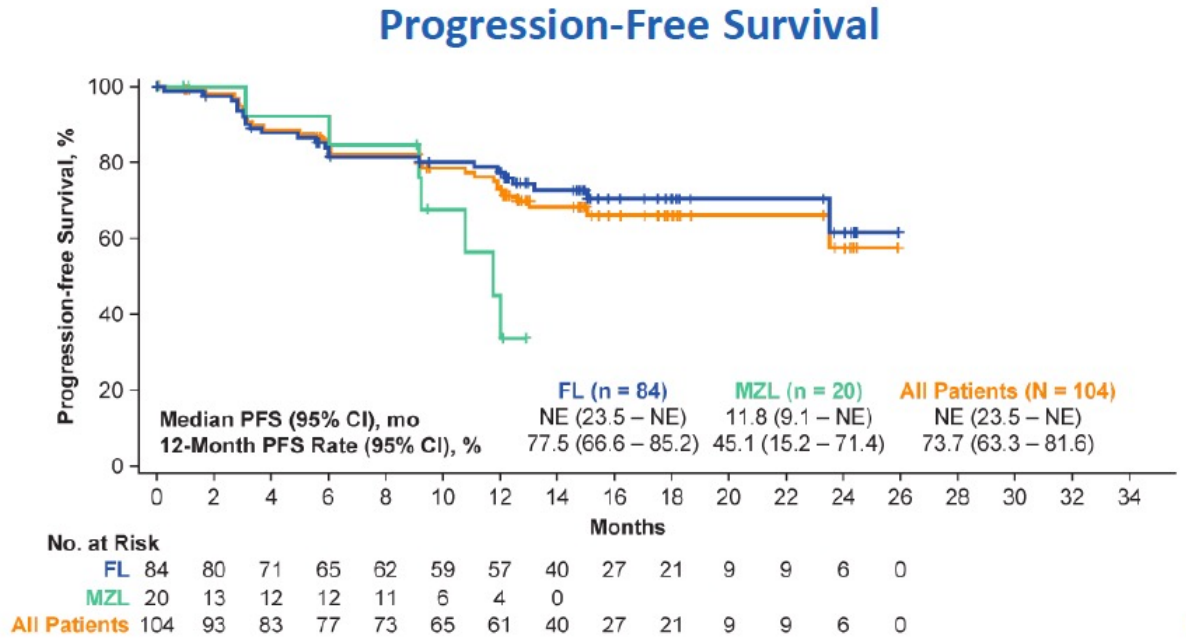
# ZUMA-5: ORR by IRRC Assessment for Patients with Follicular Lymphoma Receiving Axicabtagene Ciloleucel

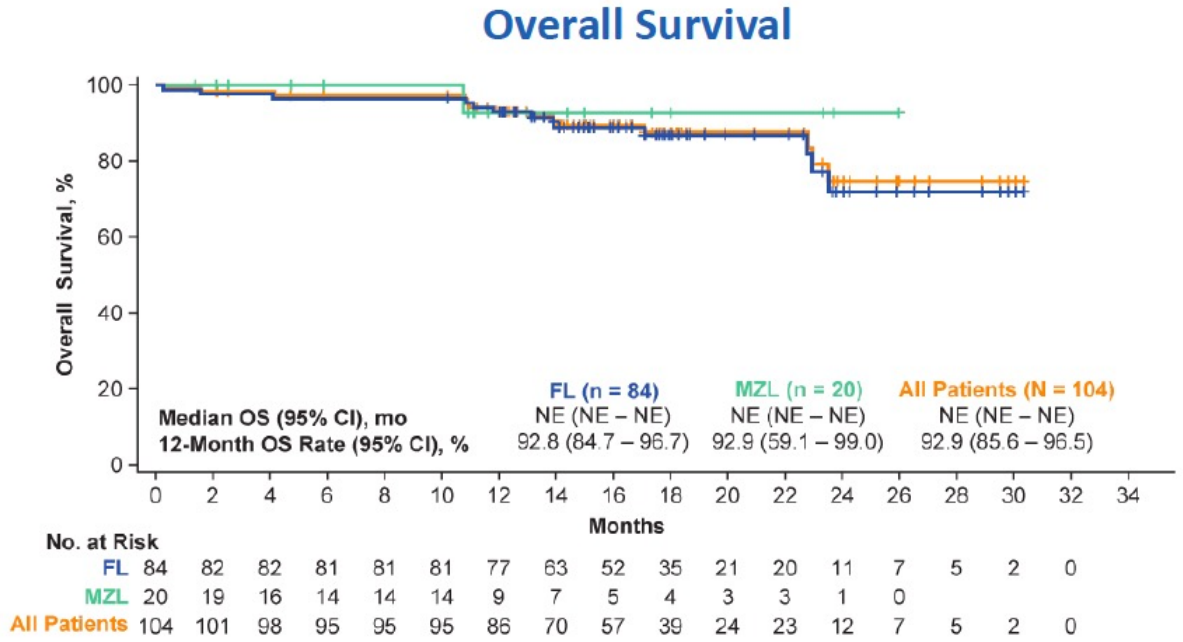



- The median time to first response was 1 month (range, 0.8 – 3.1)
- Among the 25 patients with FL who initially had a PR, 13 (52%) subsequently converted to a CR after a median of 2.2 months (range, 1.9 – 11.2)

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 | 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.

# Agenda

## Module 1: Diffuse Large B-Cell Lymphoma (DLBCL)

- Case: An 83-year-old woman with relapsed DLBCL

## Module 2: Hodgkin Lymphoma

- Case: A 77-year-old man with newly diagnosed Hodgkin lymphoma

## Module 3: Follicular Lymphoma

- Case: A 76-year-old man with newly diagnosed follicular lymphoma

## Module 4: Mantle Cell Lymphoma

- Case: A 61-year-old woman with R/R mantle cell lymphoma

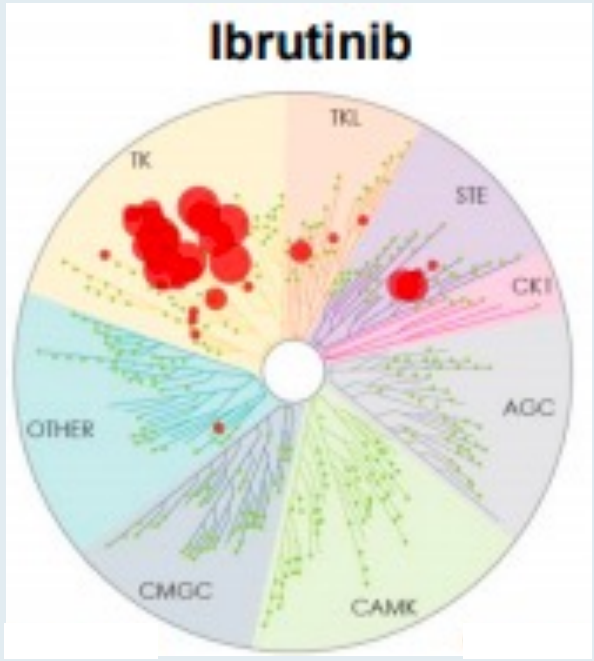
# Key Recent Developments in Mantle Cell Lymphoma

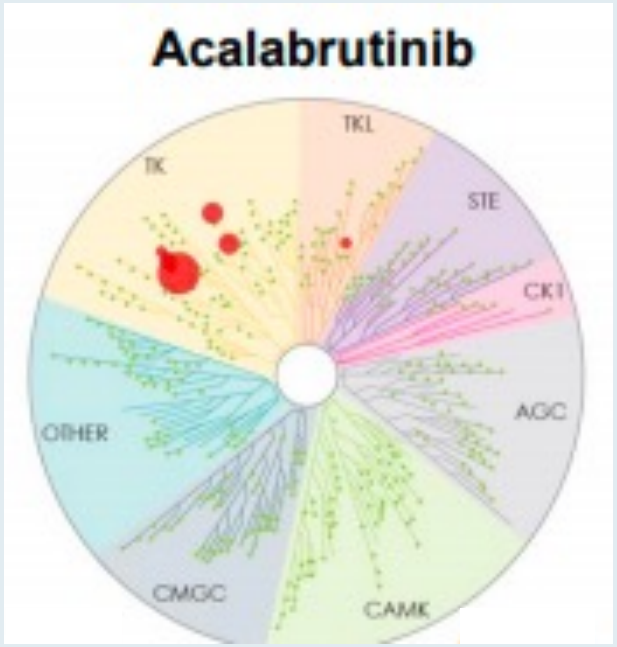
- BTK inhibitors (ibrutinib, acalabrutinib, zanubrutinib)
- CAR T-cell therapy (brexucabtagene autoleucel)

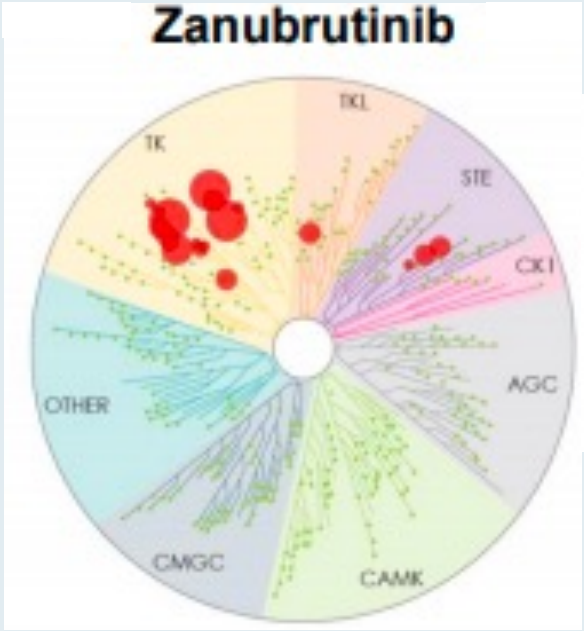
# Case Presentation – A 61-year-old woman with R/R mantle cell lymphoma

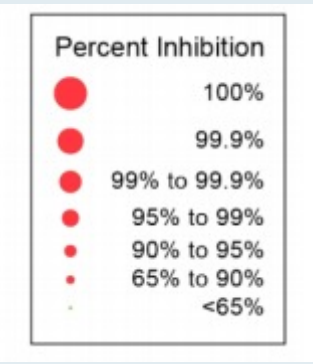
- Now 61 yo female diagnosed with MCL in 2011
- Delightful person and gift shop owner
- 2013: CNS relapse treated with high dose MTX and rituximab
  - Lenalidomide added and continued lenalidomide/rituximab maintenance 2013-2017
- 9/2020: Disease recurrence treated with methotrexate/rituximab/venetoclax
  - Near CR after 1 month of addition of venetoclax
- Initiation of CAR-T planned, unfortunately MRI documented progressive leptomeningeal disease

# FDA-Approved BTK Inhibitors for Relapsed MCL




**Second-generation BTKi were designed to maximize BTK occupancy and minimize off-target inhibition of TEC- and EGFR-family kinases**

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# FDA Approves Brexucabtagene Autoleucel for R/R 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

The NEW ENGLAND JOURNAL of MEDICINE

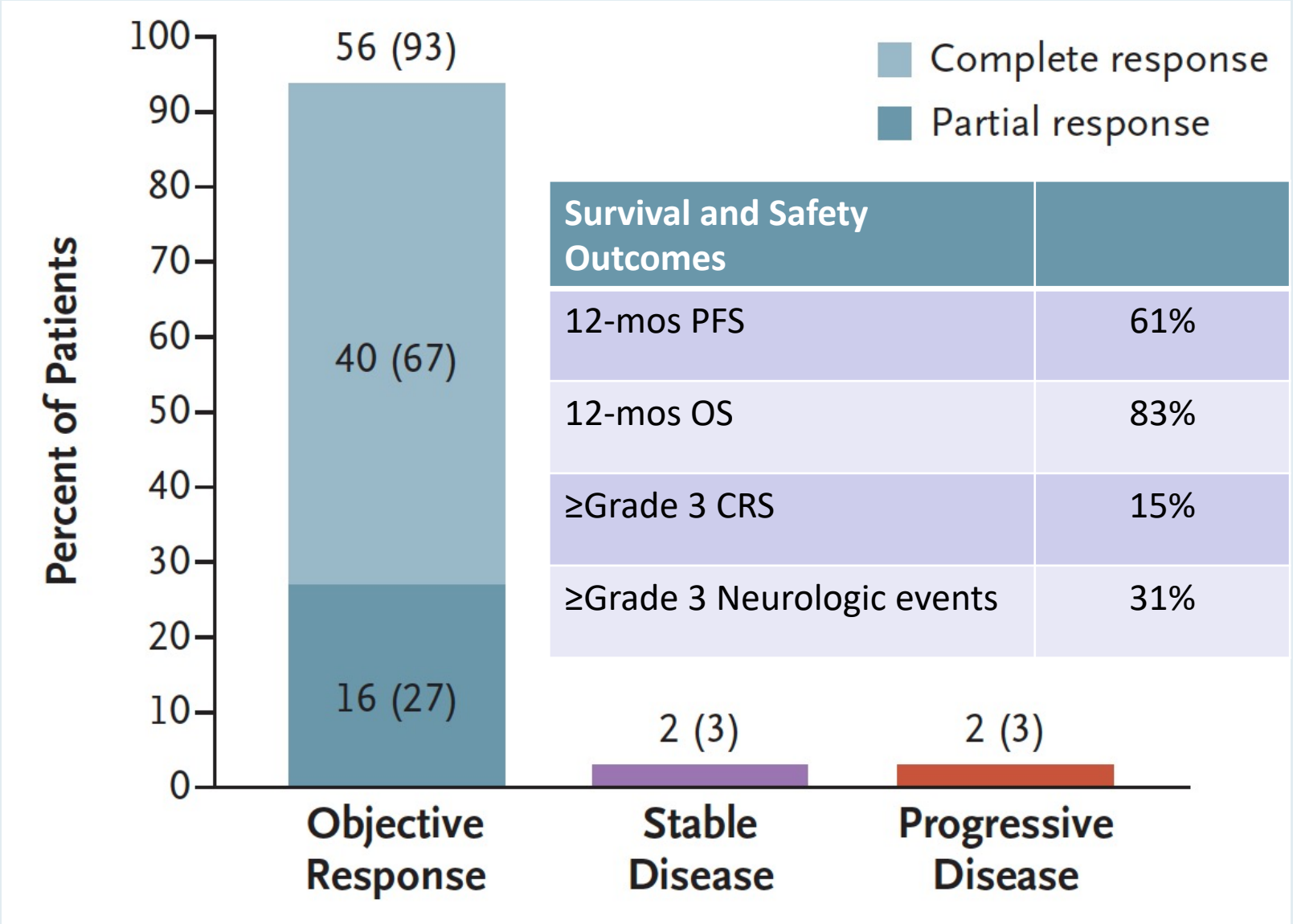
ORIGINAL ARTICLE

# 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

*N Engl J Med* 2020;382:1331-42

# 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, October 8, 2021**
**12:00 PM – 1:00 PM ET**

## Faculty

**Eileen M O'Reilly, MD**

## Moderator

**Neil Love, MD**

RTP
RESEARCH TO PRACTICE

*Thank you for joining us!*

*NCPD credit information will be emailed to each participant shortly.*

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