Fall Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Hodgkin and Non-Hodgkin Lymphomas

Thursday, September 23, 2021
5:00 PM – 6:00 PM ET

Faculty

John P Leonard, MD
Amy Goodrich, CRNP

Moderator

Neil Love, MD

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Faculty

John P Leonard, MD
Richard T Silver Distinguished Professor of
Hematology and Medical Oncology
Senior Associate Dean for Innovation and Initiatives
Executive Vice Chair, Joan and Sanford I Weill
Department of Medicine
Weill Cornell Medicine
New York, New York

Amy Goodrich, CRNP
Nurse Practitioner
The Sidney Kimmel Comprehensive Cancer Center
Johns Hopkins Medicine
Baltimore, Maryland

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

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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, Genentech, a member of the Roche Group, 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, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.

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Research To Practice CME Planning Committee Members, Staff and Reviewers

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

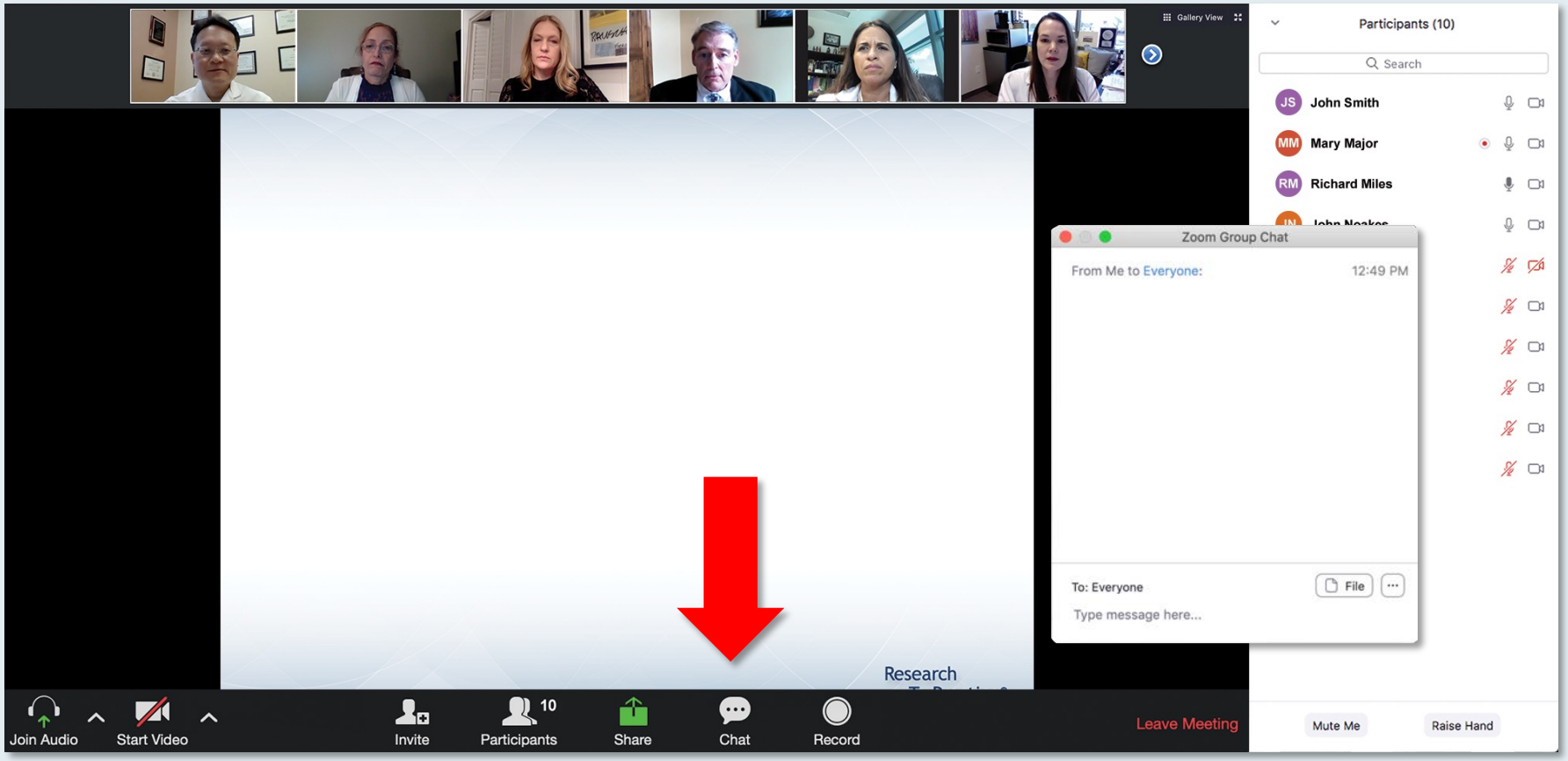
Dr Leonard — Disclosures

Consulting Agreements	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Celgene Corporation, Epizyme Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, Incyte Corporation, Janssen Biotech Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Miltenyi Biotec, Regeneron Pharmaceuticals Inc, Sutro Biopharma
Contracted Research	Epizyme Inc, Genentech Foundation, Janssen Biotech Inc
Data and Safety Monitoring Board/Committee	Genentech, a member of the Roche Group

Ms Goodrich — 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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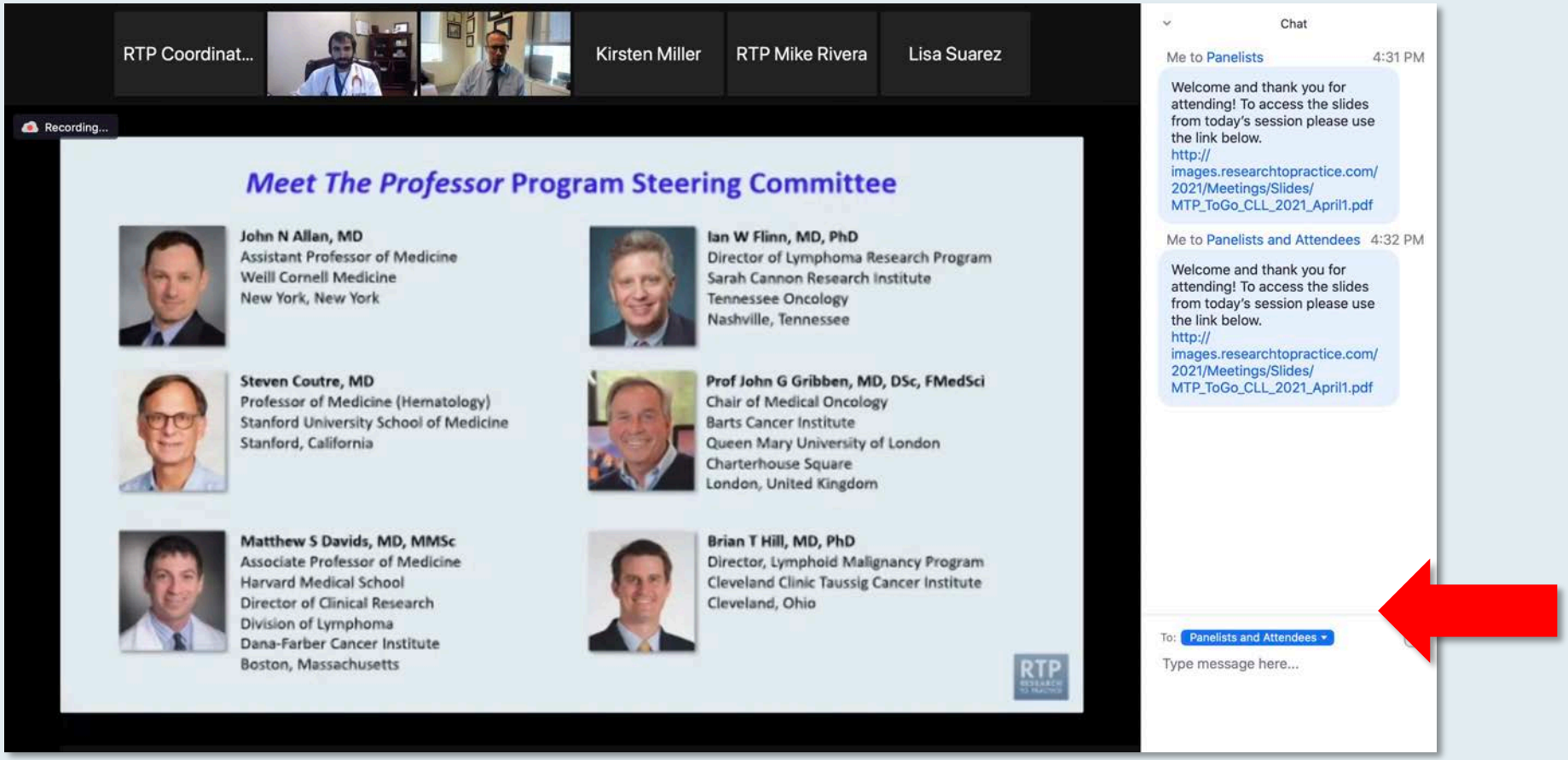
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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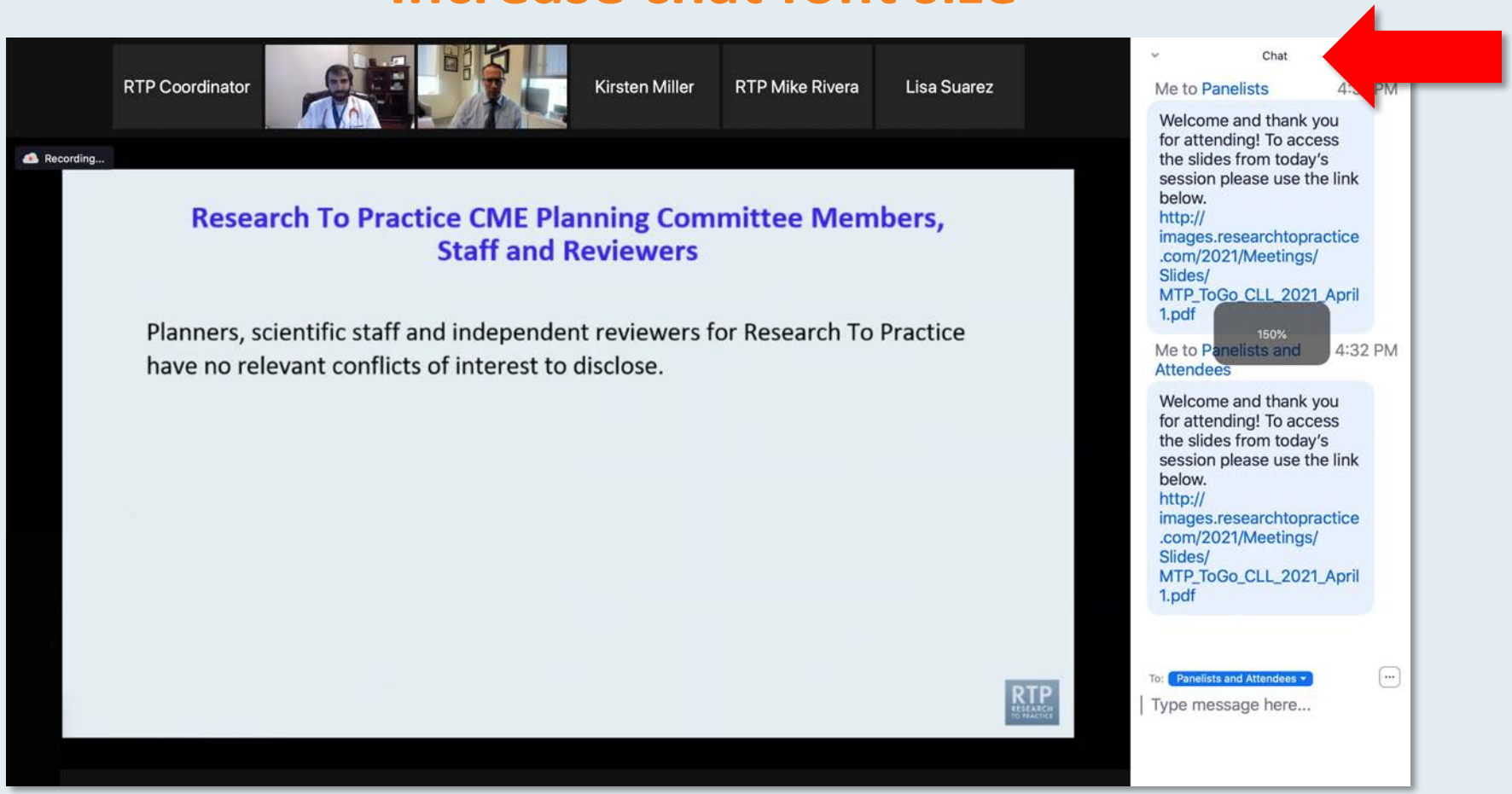
Familiarizing Yourself with the Zoom Interface

Increase chat font size



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

ONCOLOGY TODAY

WITH DR NEIL LOVE

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

DR LAURIE SEHN

BC CANCER CENTRE FOR LYMPHOID CANCER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Friday, September 24, 2021
12:00 PM – 1:00 PM ET

Faculty

Martee L Hensley, MD, MSc

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

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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RESEARCH TO PRACTICE

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

RTP
RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Wednesday, September 29, 2021
5:00 PM – 6:00 PM ET

Faculty

Brad S Kahl, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

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

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

Faculty

Hans Hammers, MD, PhD

Moderator

Neil Love, MD

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RESEARCH
TO PRACTICE

Identifying, Managing and Mitigating Therapy-Related Adverse Events in Patients with Chronic Lymphocytic Leukemia and Mantle Cell Lymphoma

A CME/MOC-Accredited Virtual Event

Monday, October 4, 2021
5:00 PM – 6:00 PM ET

Faculty

Richard R Furman, MD
Lindsey Roeker, MD

Consulting Cardiologist

Daniel J Lenihan, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Meet The Professor

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

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

Faculty

Virginia Kaklamani, MD, DSc

Moderator

Neil Love, MD

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RESEARCH
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Hodgkin and Non-Hodgkin Lymphomas

Thursday, October 7, 2021
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Stephen M Ansell, MD, PhD
Robin Klebig, APRN, CNP, AOCNP

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

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
9:30 AM – 4:30 PM ET

Faculty

Tanios Bekaii-Saab, MD
Brad S Kahl, MD
Mark Levis, MD, PhD
Mark D Pegram, MD
David Sallman, MD
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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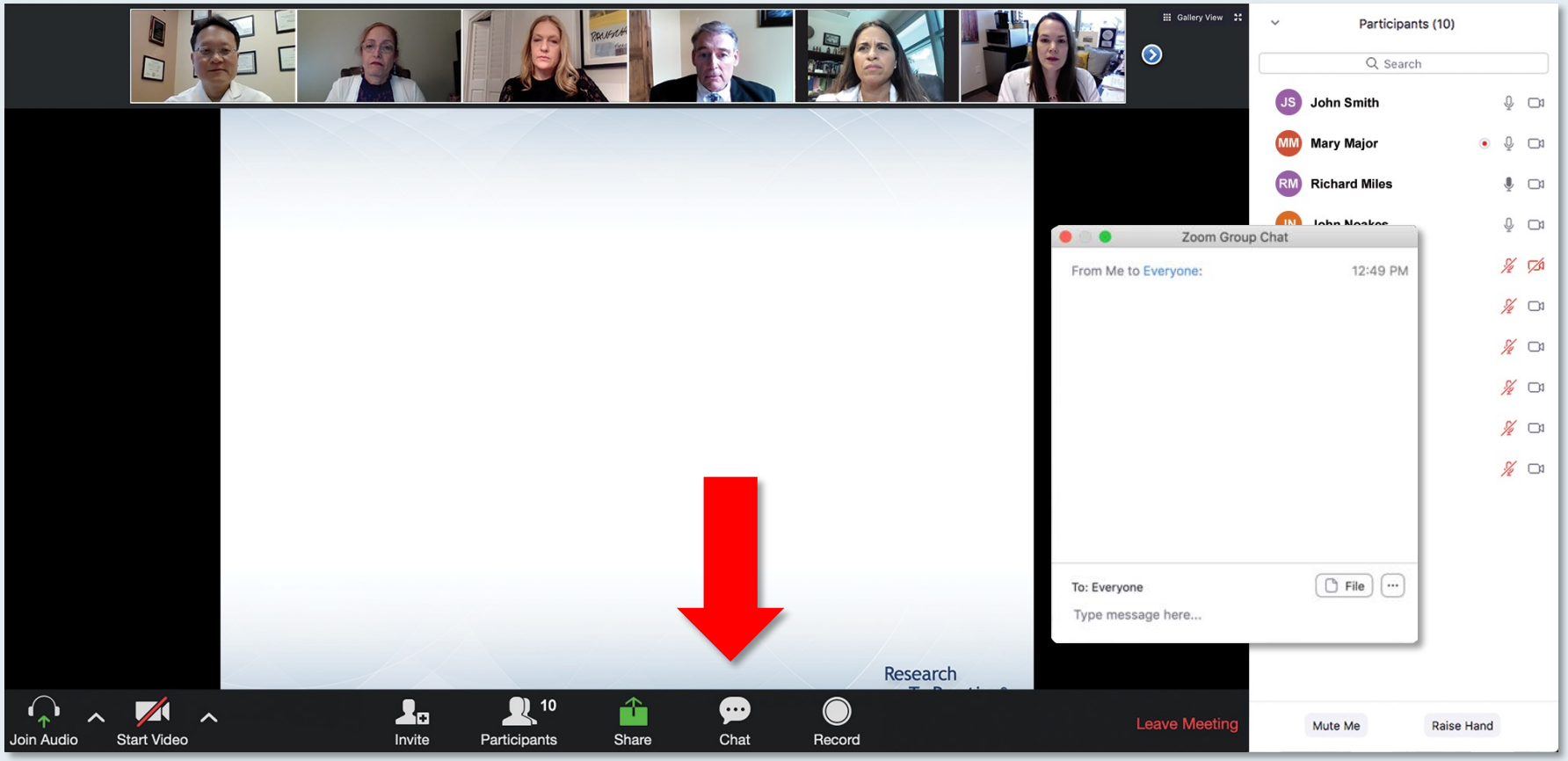

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Kristen K Ciombor, MD, MSCI
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Mark Levis, MD, PhD
Mark D Pegram, MD
David Sallman, MD

Additional faculty to be announced.

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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

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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TO PRACTICE

Oncology Grand Rounds Nursing Webinar Series

April 2021

Monday	Tuesday	Wednesday	Thursday	Friday
19	20 Breast Ca 8:30 AM Lung Ca 5:00 PM	21 AML 12:00 PM CRC and GE Ca 4:45 PM	22 Prostate Ca 8:30 AM Lymphomas 5:00 PM	23
26	27 Multiple Myeloma 8:30 AM GYN 5:00 PM	28 Bladder Ca 12:00 PM	29 CLL 8:30 AM CAR-T 5:00 PM	30

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13th Annual Oncology Grand Rounds

A Complimentary NCPD Live Webinar Series
Held During the 46th Annual ONS Congress

Hodgkin and Non-Hodgkin Lymphomas

Thursday, April 22, 2021
5:00 PM – 6:30 PM ET

Medical Oncologists

Stephen M Ansell, MD, PhD
Carla Casulo, MD
John P Leonard, MD

Oncology Nurse Practitioners

Jacklyn Gideon, MSN, AGPCNP-BC
Robin Klebig, APRN, CNP, AOCNP
Mollie Moran, APRN-CNP, AOCNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE


Jacklyn Gideon, MSN, AGPCNP-BC


Robin Klebig, APRN, CNP, AOCNP


Mollie Moran, APRN-CNP, AOCNP

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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 1: A 35-year-old woman with Stage IV DLBCL

Module 2: Hodgkin Lymphoma

- Case 2: A 27-year-old man with newly diagnosed Hodgkin lymphoma

Module 3: Follicular Lymphoma

- Case 3: A 51-year-old woman with Stage IVB follicular lymphoma

Module 4: Mantle Cell Lymphoma

- Case 4: A 59-year-old man with Stage IVB mantle cell lymphoma

How do you determine eligibility for CD19-directed CAR-T therapy, including age and performance status? Any specific comorbidities that concern you? How do these compare to ASCT? Is outpatient CAR T feasible? How do you deal with COVID-19 vaccination and timing of CAR T? Do you use anti-CD19-based therapies before or after CAR T? What is the role, if any, of repeat CAR T?

Agenda

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

- Case 1: A 35-year-old woman with Stage IV DLBCL

Module 2: Hodgkin Lymphoma

- Case 2: A 27-year-old man with newly diagnosed Hodgkin lymphoma

Module 3: Follicular Lymphoma

- Case 3: A 51-year-old woman with Stage IVB follicular lymphoma

Module 4: Mantle Cell Lymphoma

- Case 4: A 59-year-old man with Stage IVB mantle cell lymphoma

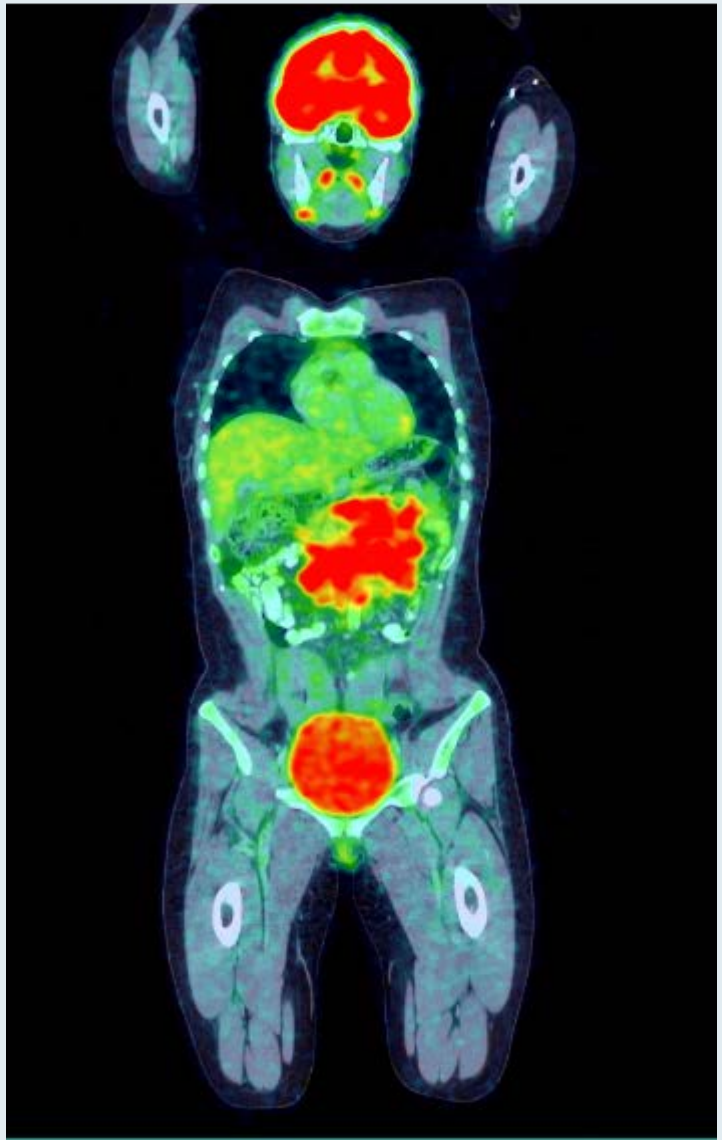
How do you currently approach first-line treatment of DLBCL, and what will you be looking for in the upcoming presentation of the pivotal Phase III POLARIX trial?

For patients with DLBCL not eligible for CAR-T therapy or who experience disease progression after it, how do you sequence the 4 approved strategies and others?

How do you currently approach second-line treatment of DLBCL, and what will you be looking for in the forthcoming presentations of these Phase III trials evaluating CAR T vs ASCT (ZUMA-7, TRANSFORM, BELINDA)?

Case Presentation – A 35-year-old woman with Stage IV DLBCL

- Now 35 yo healthy female diagnosed with Stage IV DLBCL in Eastern Europe in 6/2018
- Was in the process of relocating to the U.S.
- Presented in 11/2018 in our ED with significant back pain
- Noted to have extensive adenopathy, including paraspinal mass



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Case Presentation – A 35-year-old woman with Stage IV DLBCL (continued)

- Married, 6 year old son
- Living with mother, who had been in the U.S.
- Works remotely as an accountant

Case Presentation – A 35-year-old woman with Stage IV DLBCL (continued)

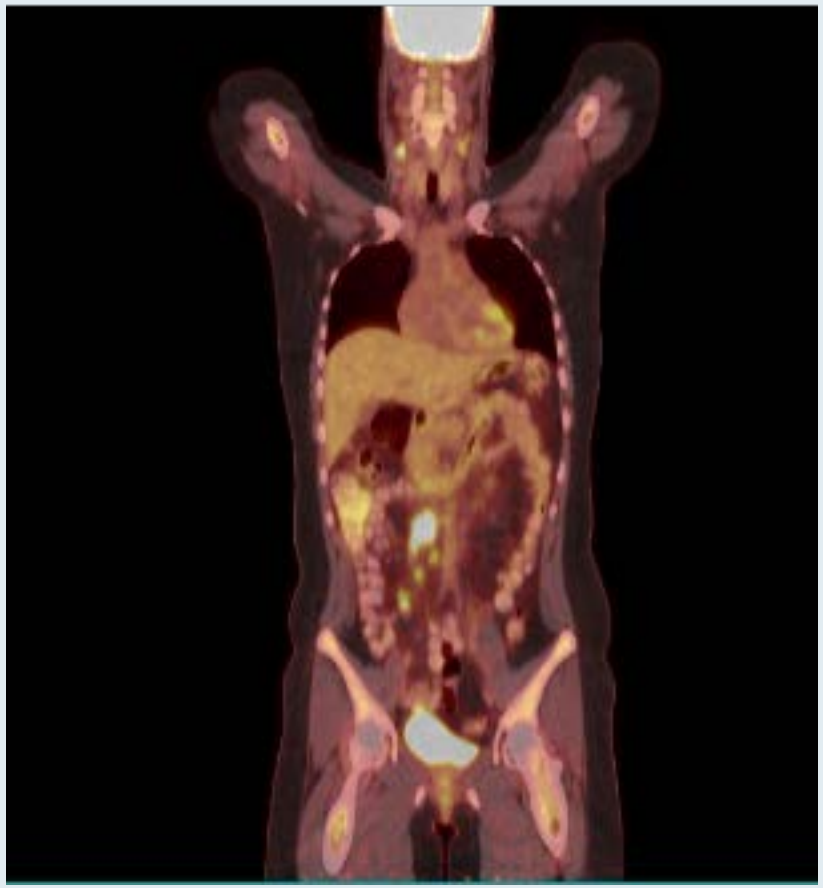
- Admitted for steroids and initiation of R-CHOP
- CR after 6 cycles R-CHOP
- 7/2020 Routine CT showed new retroperitoneal adenopathy
- Biopsy revealed Grade 3A FL (likely original diagnosis was transformed FL)
- Having mild flank pain
- By this time, is divorced and ex-husband is back in Europe
- Is sole income and source of medical insurance
- Started remote counseling with European counselor for ease of language

Case Presentation – A 35-year-old woman with Stage IV DLBCL (continued)

- Wants to avoid chemotherapy
- Focused on maintaining work schedule and stable home for son
- Opts for lenalidomide + R, starts 9/2020
- During Cycle 1, develops COVID-19 infection
- Treatment held, patient recovers
- Develops rapid progression and increasing pain, LDH over 1,000
- Biopsy reveals DLBCL, GCB subtype

Case Presentation – A 35-year-old woman with Stage IV DLBCL (continued)

- Receives R-ICE x 4
- Plan is to consolidate with non-myeloablative allogeneic transplant
- Post-chemo PET continues to be positive

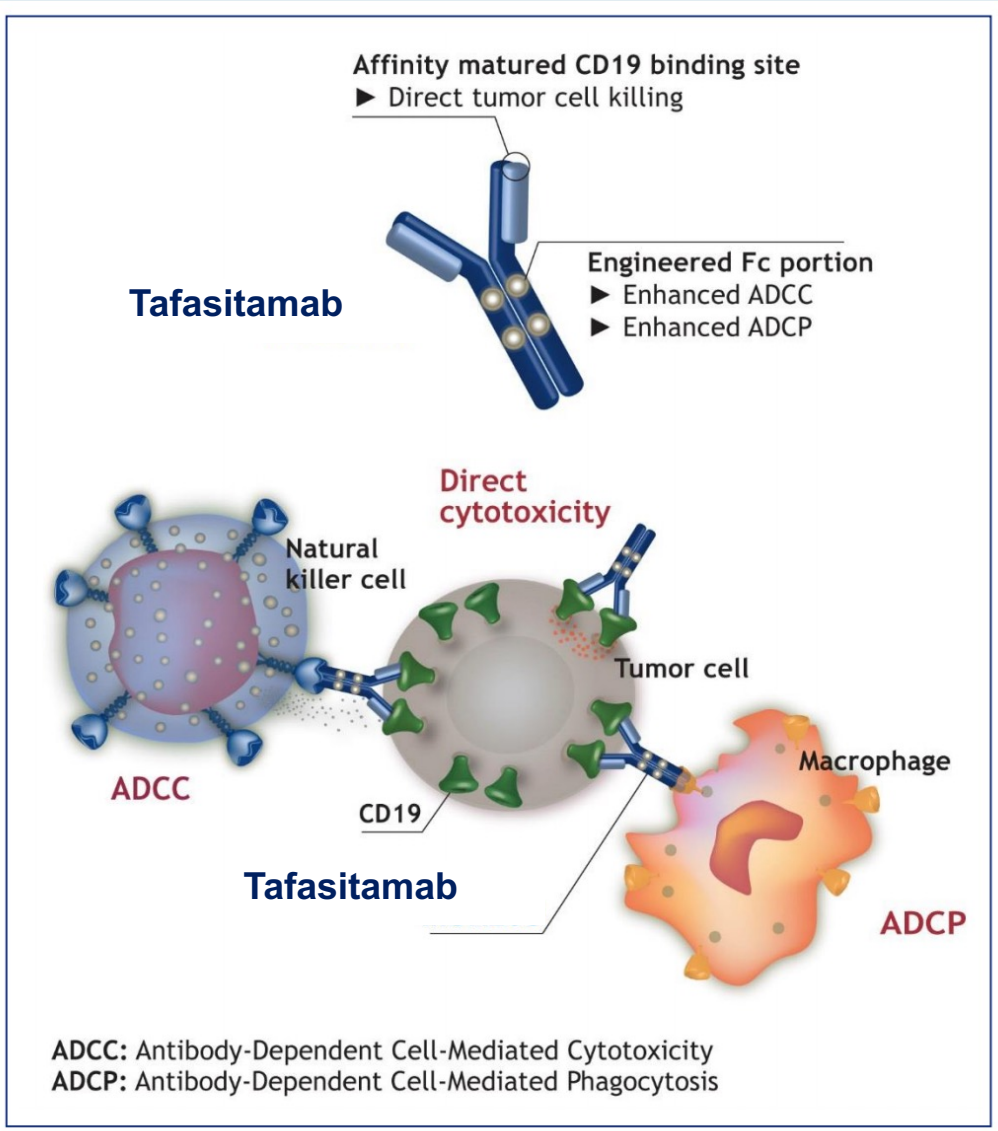


Case Presentation – A 35-year-old woman with Stage IV DLBCL (continued)

- Undergoes axicabtagene ciloleucel in 5/21
- Developed fevers (CRS Grade 1), nausea, anorexia, diarrhea, fatigue, headaches and cytopenias requiring transfusion support
- Recovers quickly
- By Day 37, mild fatigue and low but transfusion-independent counts
- CT shows improving adenopathy
- Doing well, in observation

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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.

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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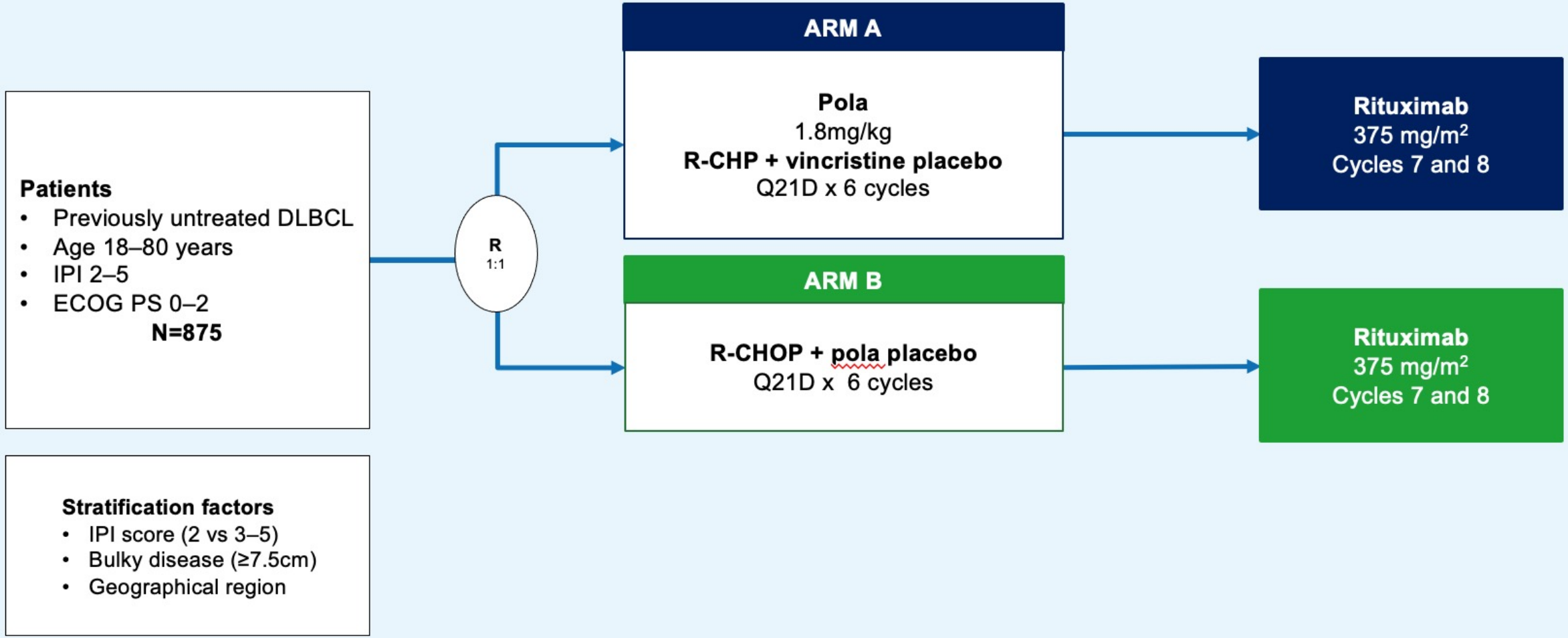
POLARIX Phase III Trial Design



Courtesy of Gilles Salles MD, PhD.

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.

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

RTP RESEARCH TO PRACTICE

CAR T-Cell Therapy-Associated Cytokine Release Syndrome (CRS)

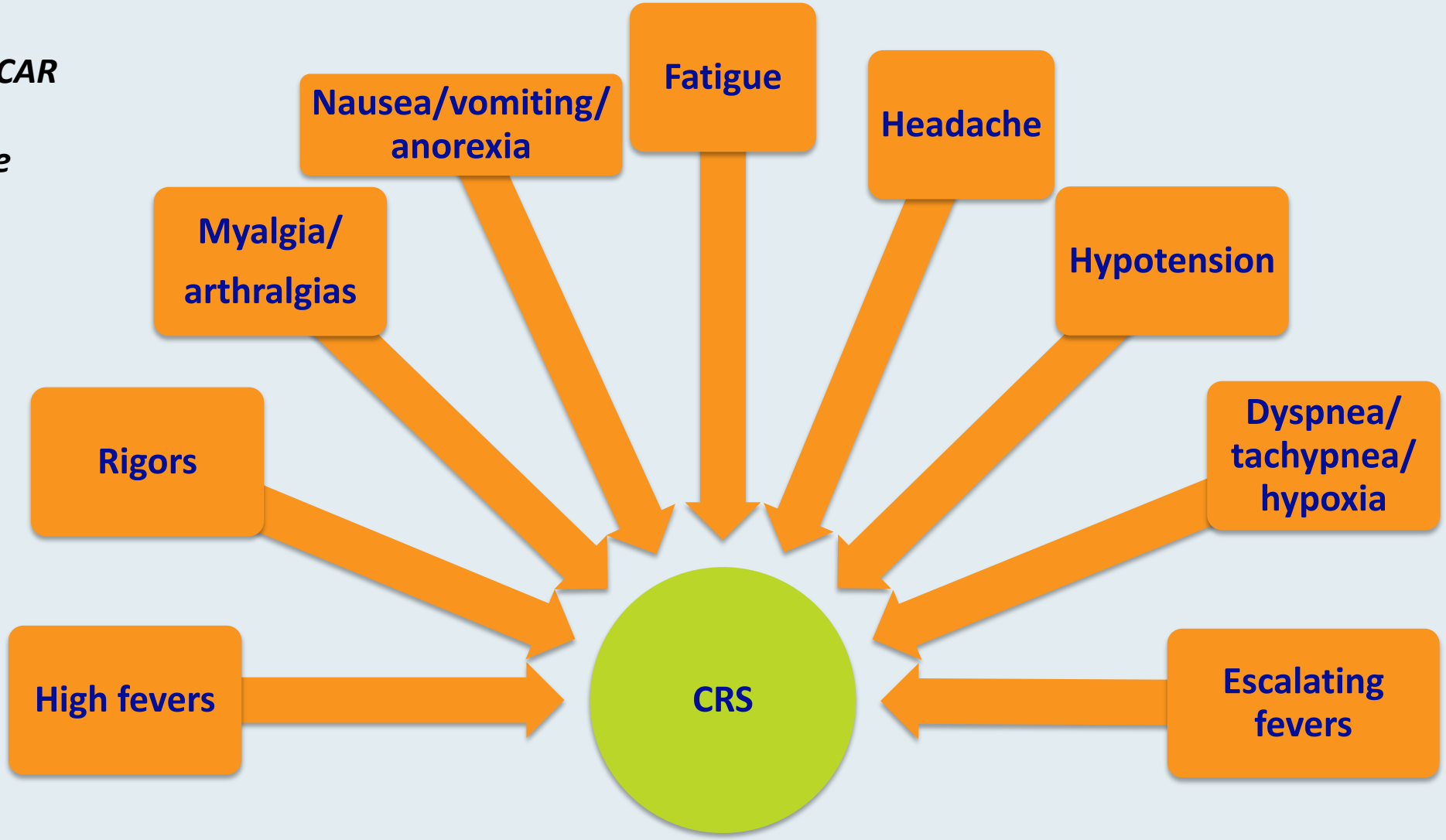
CRS — May be mild or life-threatening

- 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%

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

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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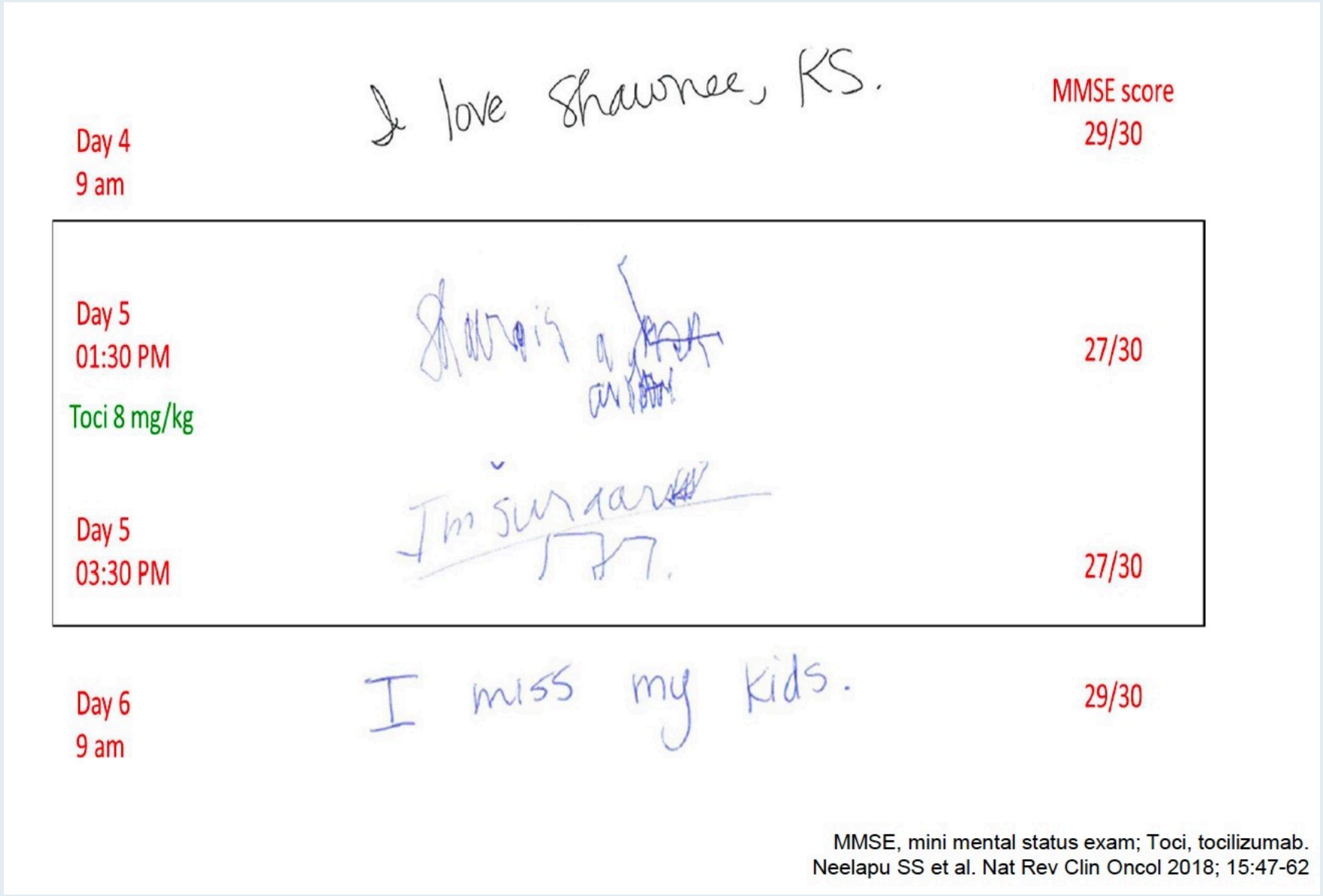
CAR T-Cell Therapy-Associated Neurologic Toxicity

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

Agenda

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

- Case 1: A 35-year-old woman with Stage IV DLBCL

Module 2: Hodgkin Lymphoma

- Case 2: A 27-year-old man with newly diagnosed Hodgkin lymphoma

Module 3: Follicular Lymphoma

- Case 3: A 51-year-old woman with Stage IVB follicular lymphoma

Module 4: Mantle Cell Lymphoma

- Case 4: A 59-year-old man with Stage IVB mantle cell lymphoma

How do you approach first-line treatment of extensive-stage and localized HL, and where does brentuximab vedotin (BV) fit in? If you use BV up front, do you use it as part of a bridge to transplant or post-transplant consolidation?

Case Presentation – A 27-year-old man with newly diagnosed Hodgkin lymphoma

- 27 yo healthy male presented with 2 month persistent cough and 20 lb weight loss in 4-6 months
- CXR revealed 13 x 9 cm mediastinal mass
- Biopsy revealed classical HL
- Outside PET: Enlarged nodes in mediastinum, hilar region, paratracheal and upper abdomen
- BV-AVD recommended
- Was going to be treated locally, opted to come to JH

Case Presentation – A 27-year-old man with newly diagnosed Hodgkin lymphoma (continued)

- Works remotely in finance
- Lives with girlfriend
- Supportive family
- No PMH
- Problematic insurance coverage (imaging locally only, growth factor - $10K copay)

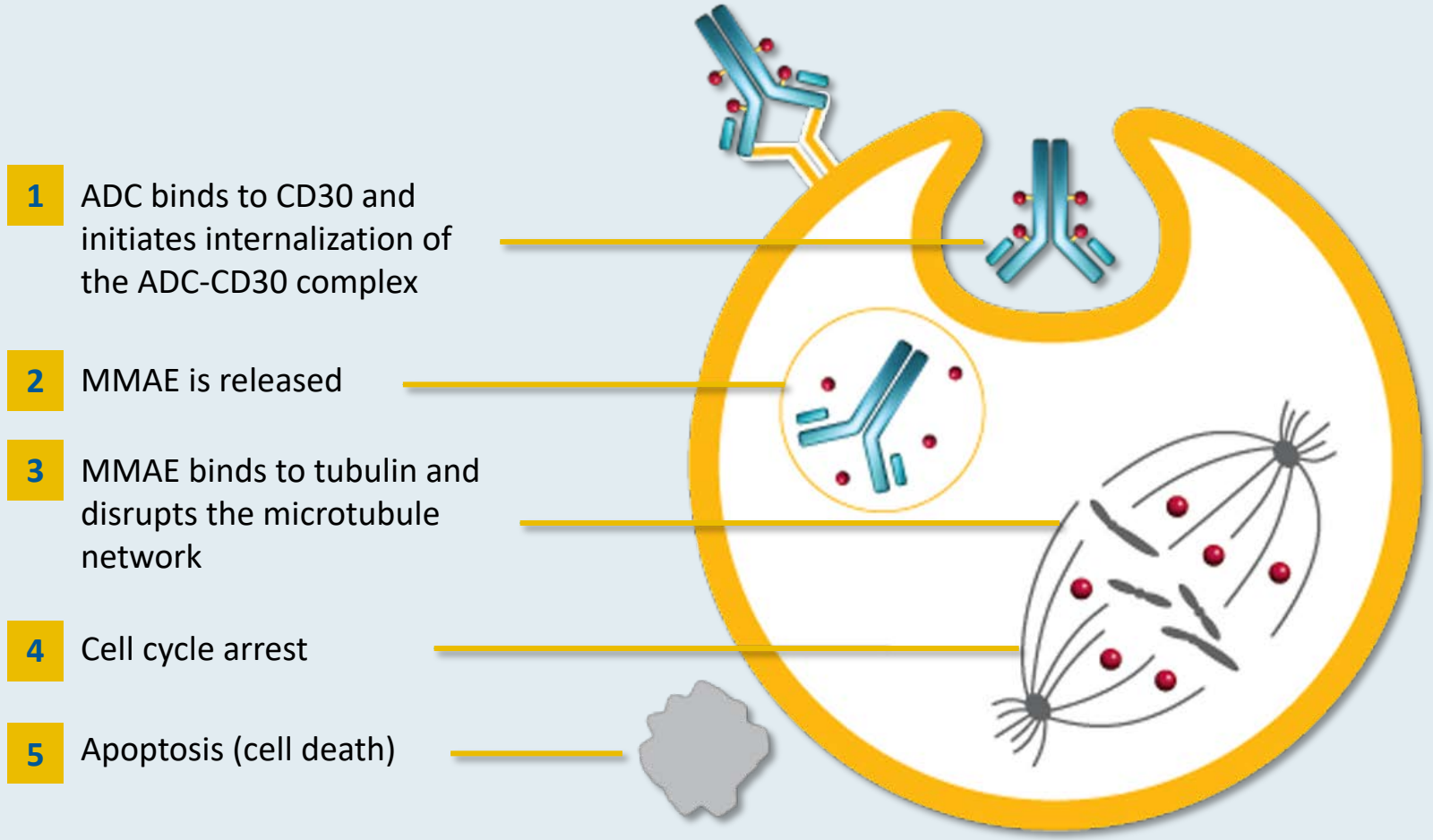
Case Presentation – A 27-year-old man with newly diagnosed Hodgkin lymphoma (continued)

- Currently receiving BV-AVD
- Experiences 2-3 days of nausea and constipation post chemo, controls well with antiemetics and OTC bowel regimen
- No peripheral neuropathy thus far
- No significant cytopenias
- Continues working full time
- Tolerating well

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

Mechanism of Action of Brentuximab Vedotin

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



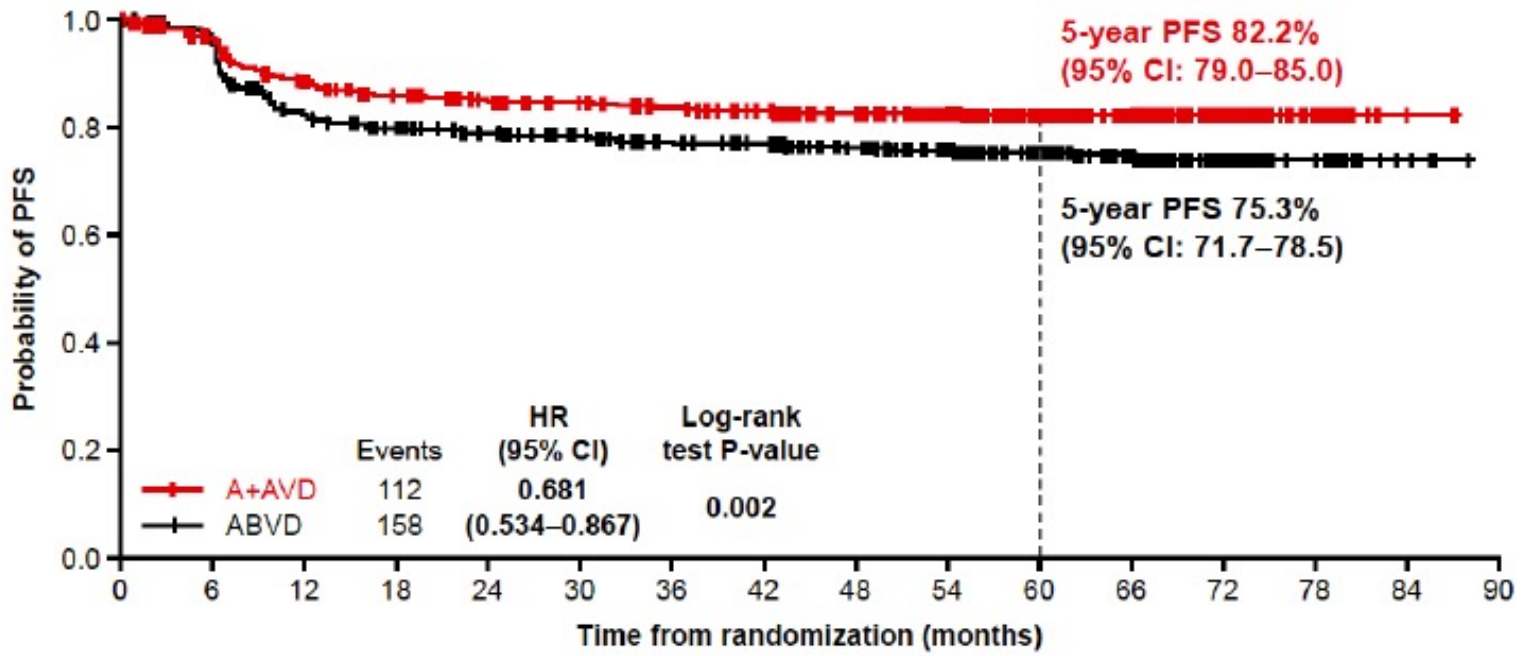
Courtesy of Julie M Vose, MD, MBA.

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: 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.

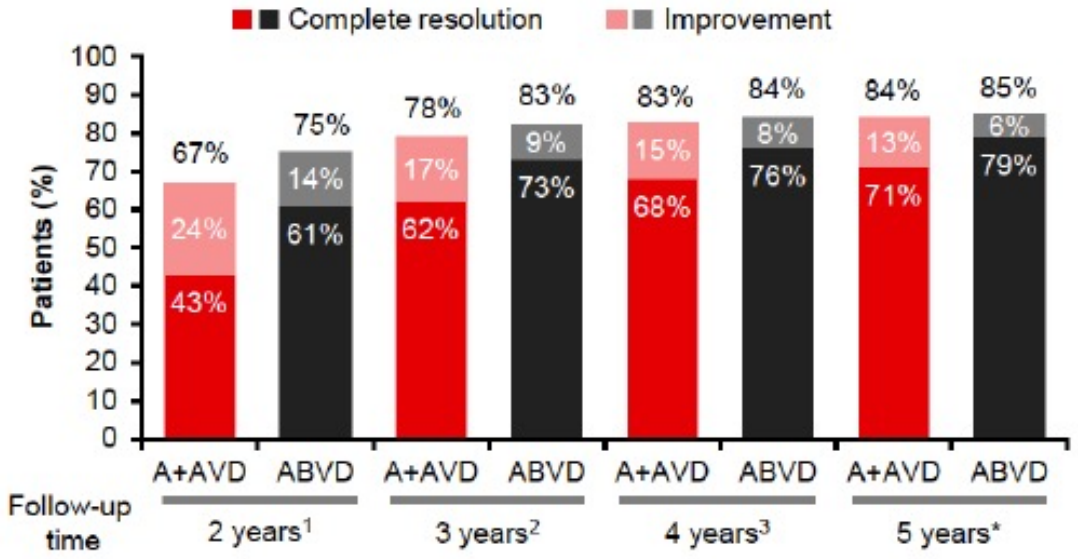
*September 14, 2020 data cut-off.

Straus DJ et al. ASH 2020;Abstract 2973.

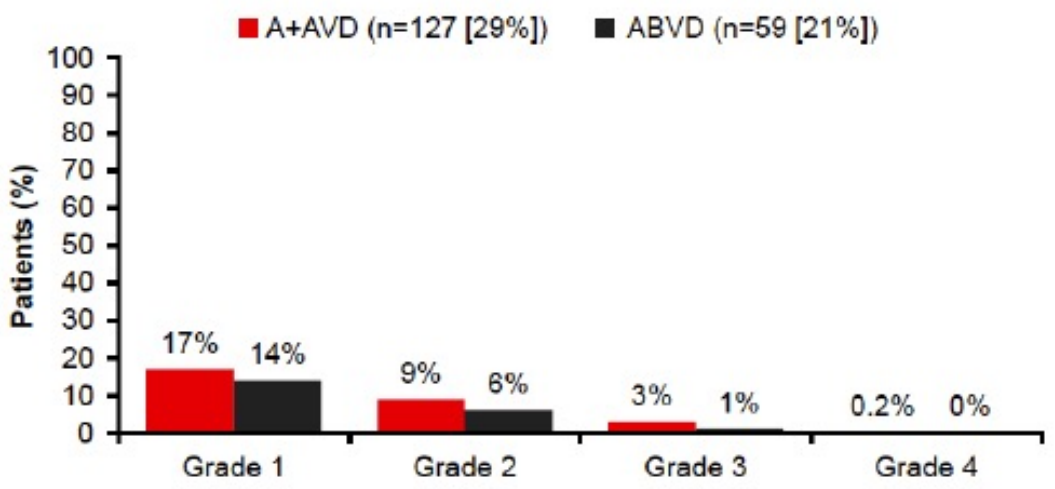
ECHELON-1: PN resolution and improvement

- 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.

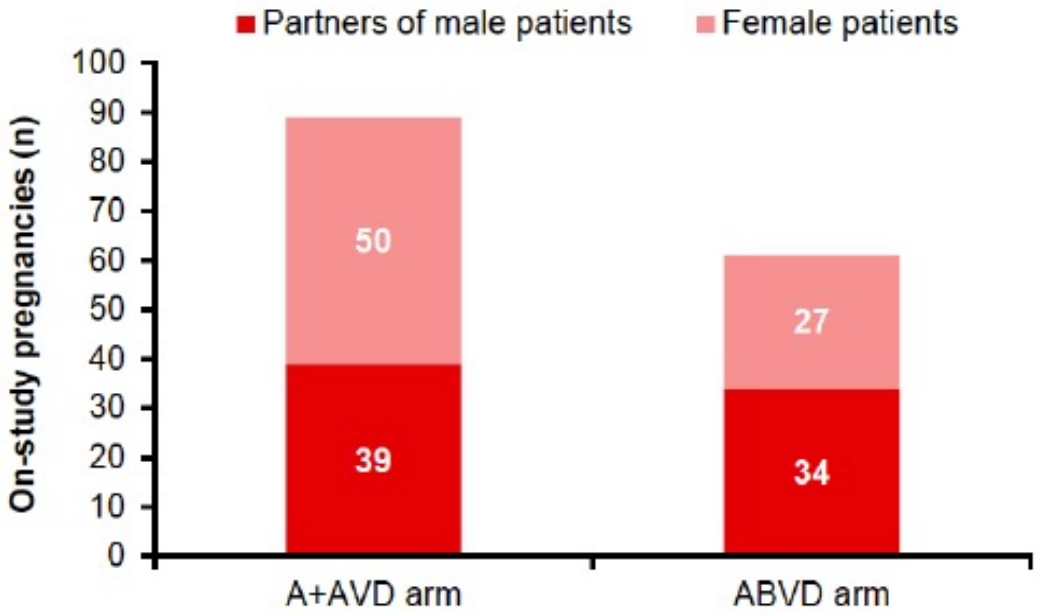
1. Connors JM, et al. N Engl J Med 2018;378:331–44;
2. Straus DJ, et al. Blood 2020;135:735–42;
3. Bartlett NL, et al. Blood 2019;134 (Suppl. 1):4026.

Straus DJ et al. ASH 2020;Abstract 2973.

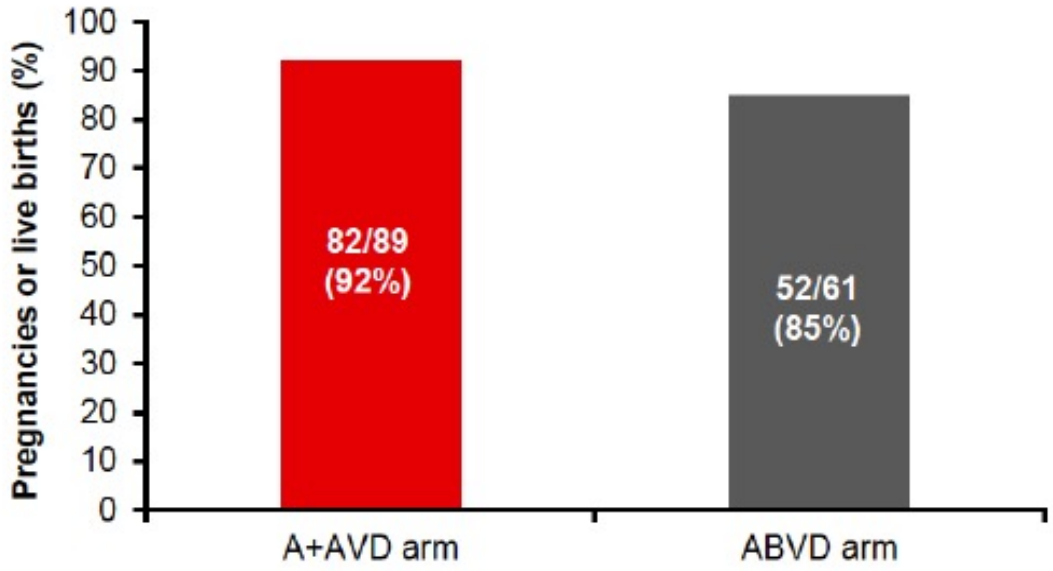
ECHELON-1: Pregnancies

- A total of 150 pregnancies were reported among study participants and their partners.

On-study pregnancies in patients or their partners

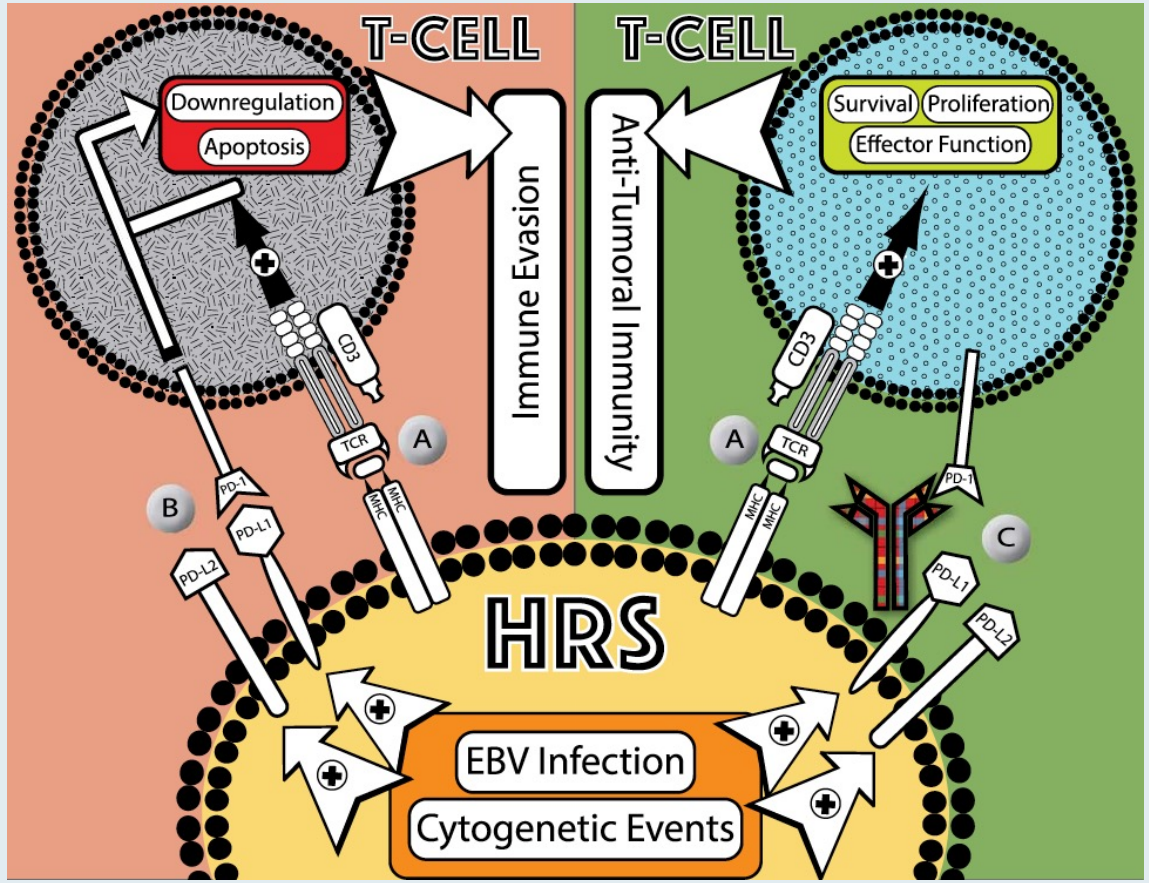


Ongoing pregnancies or live births



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.

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- Case 4: A 59-year-old man with Stage IVB mantle cell lymphoma

How would you compare the clinical risks and benefits of BR to R^2 as first-line treatment of FL? What schedule of R^2 would you use for a patient who preferred this approach?

What are your usual second- and third-line treatments for patients with FL? Do you use EZH2 assays? Which PI3K inhibitor do you prefer?

Case Presentation – A 51-year-old woman with Stage IVB follicular lymphoma

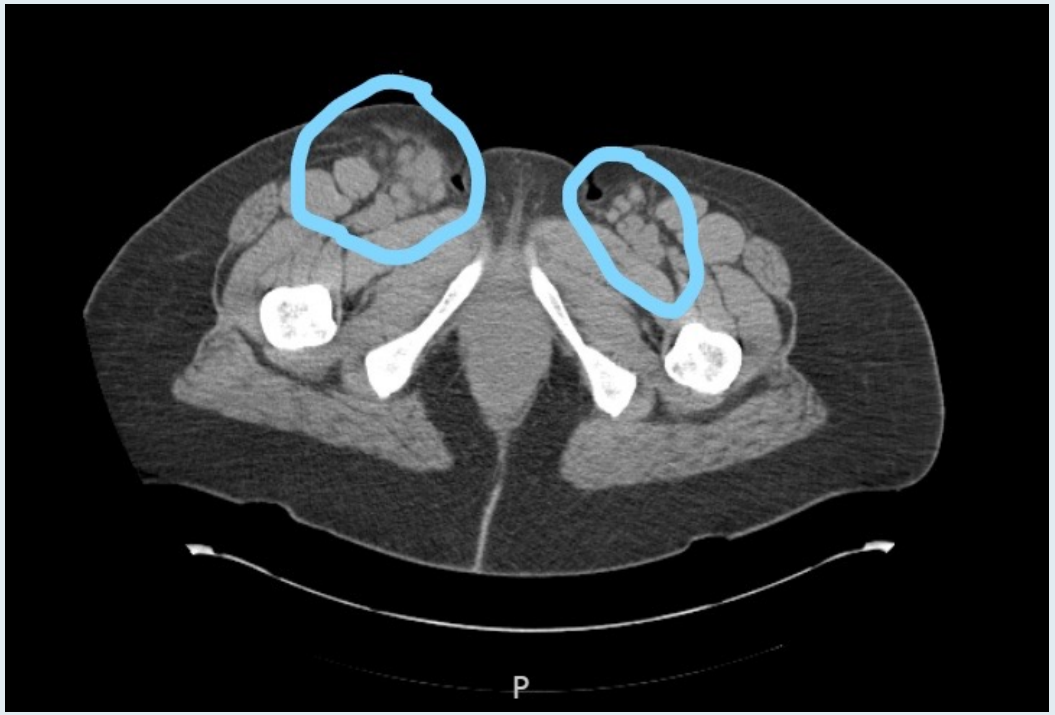
- Now 51 yo female
- Diagnosed with Stage IVB FL in 2004 at age 34
- No notable PMH
- Married, 3 daughters
- Husband with poorly controlled diabetes, s/p stroke with significant mobility issues, patient is primary caregiver
- One daughter opposed to clinical trials, patient has declined participation in all trials offered
- Patient has declined all transplant options

Case Presentation – A 51-year-old woman with Stage IVB follicular lymphoma (continued)

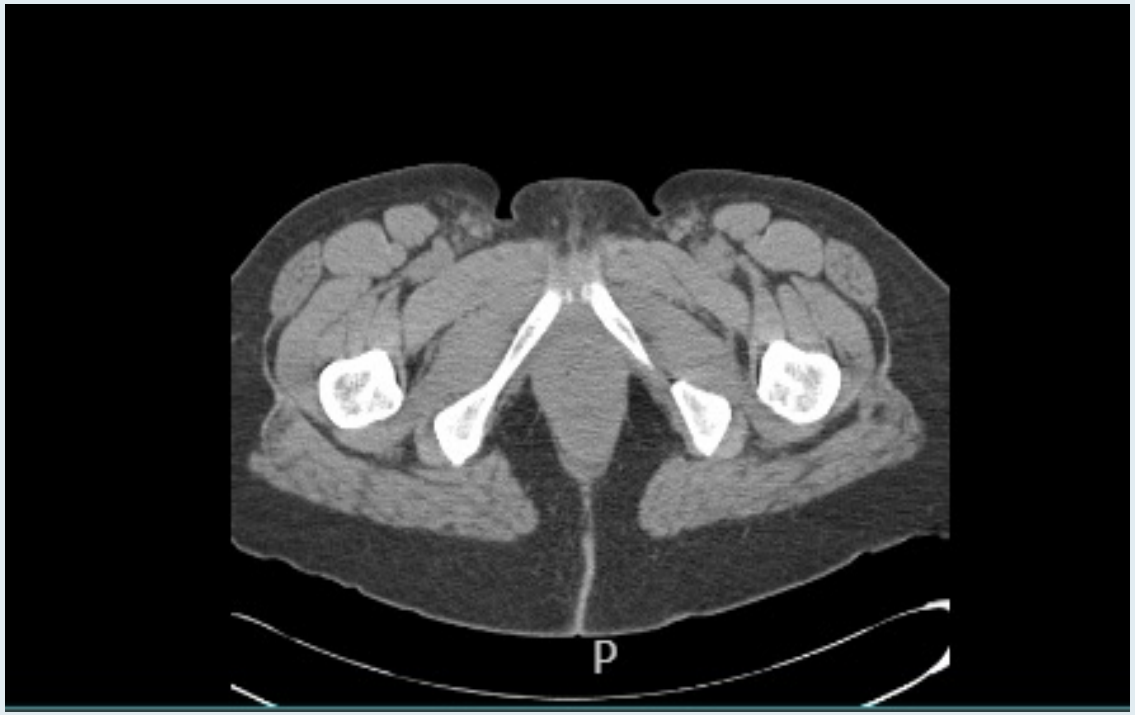
- Treated with:
  - 2004 Rituximab monotherapy
  - 2005 R-CHOP x 6
  - 2007 R-ICE x 3 pre-transplant, lost to follow up
  - Husband died, returned when became symptomatic
  - 2009 Rituximab monotherapy with maintenance x 2 years
  - 2012 BR x 5, stopped due to significant rash
  - 2015 Lenalidomide + rituximab

Case Presentation – A 51-year-old woman with Stage IVB follicular lymphoma (continued)

Pre Len + R



After Cycle 4 Len + R



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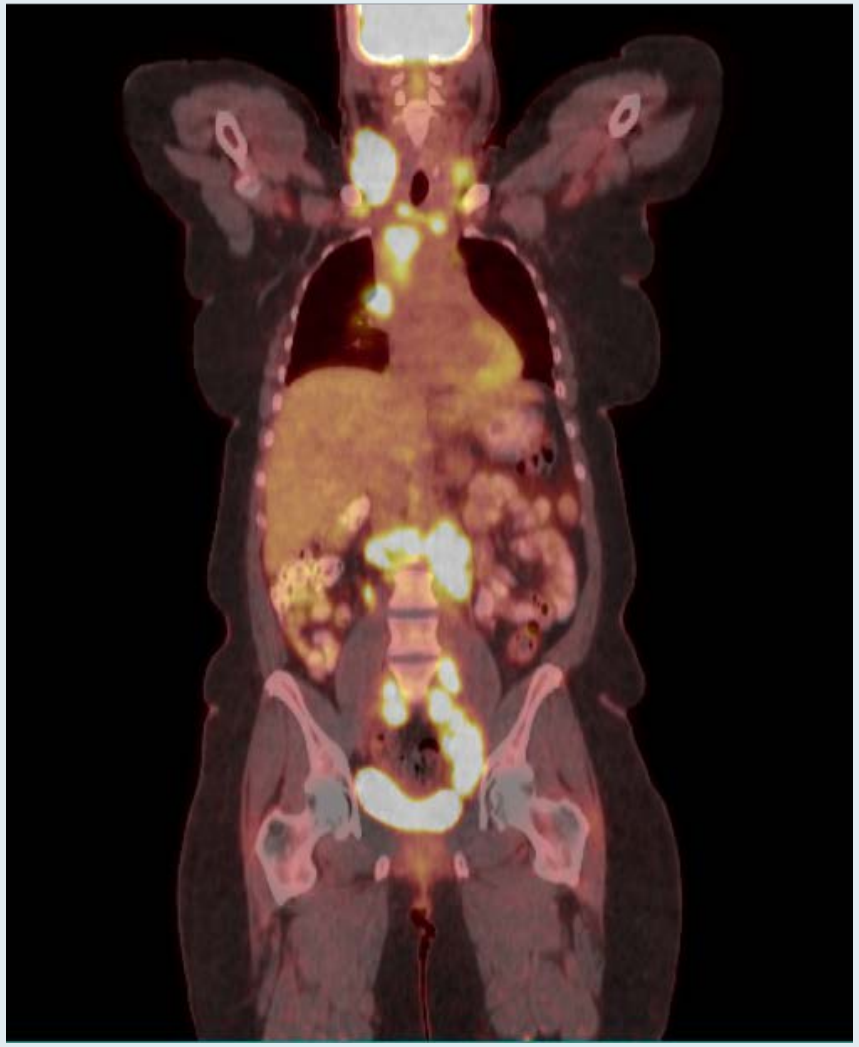
Case Presentation – A 51-year-old woman with Stage IVB follicular lymphoma (continued)

- Tolerates Len + R with minimal fatigue and mild fluid retention
- Aspirin prophylaxis recommended in 2015 for high risk patients only
- Today, prophylaxis is recommended for all patients
- During Cycle 8:
  - Syncopal episode
  - Right sided weakness and blindness
  - Brain MRI revealed ischemic stroke
  - Heparin drip started
  - Symptoms quickly resolved
  - Lenalidomide stopped
  - In good PR

Case Presentation – A 51-year-old woman with Stage IVB follicular lymphoma (continued)

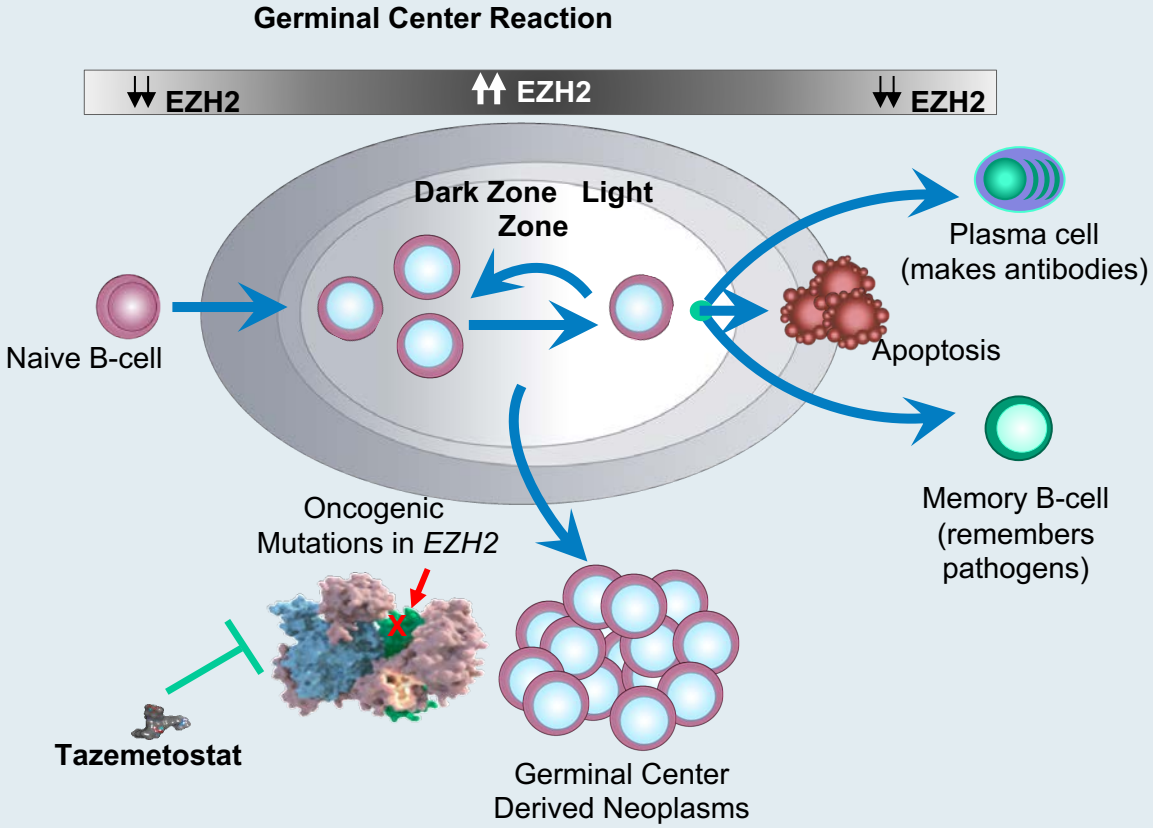
- Observed until 2021
- Increasing adenopathy
- Cervical node biopsy reveals ongoing low grade FL
- EZH2 mutated
- Starts tazemetostat
- In cycle 2, minimal nausea
- Thinking about CAR T



How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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.

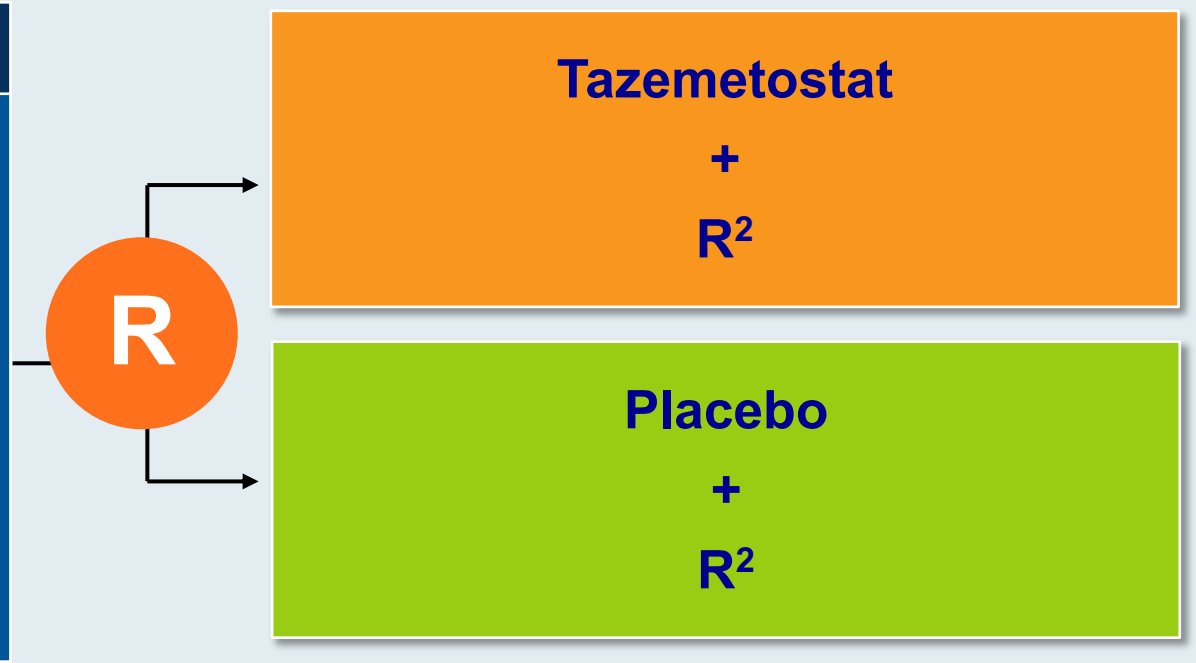
CI, confidence interval; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; EZH2, enhancer of zeste homolog 2; IRC, independent radiology committee; MT, mutant; NE, not estimable; NR, not reached; ORR, objective response rate; OS, overall survival; MT, mutant; NE, not evaluable; NR,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

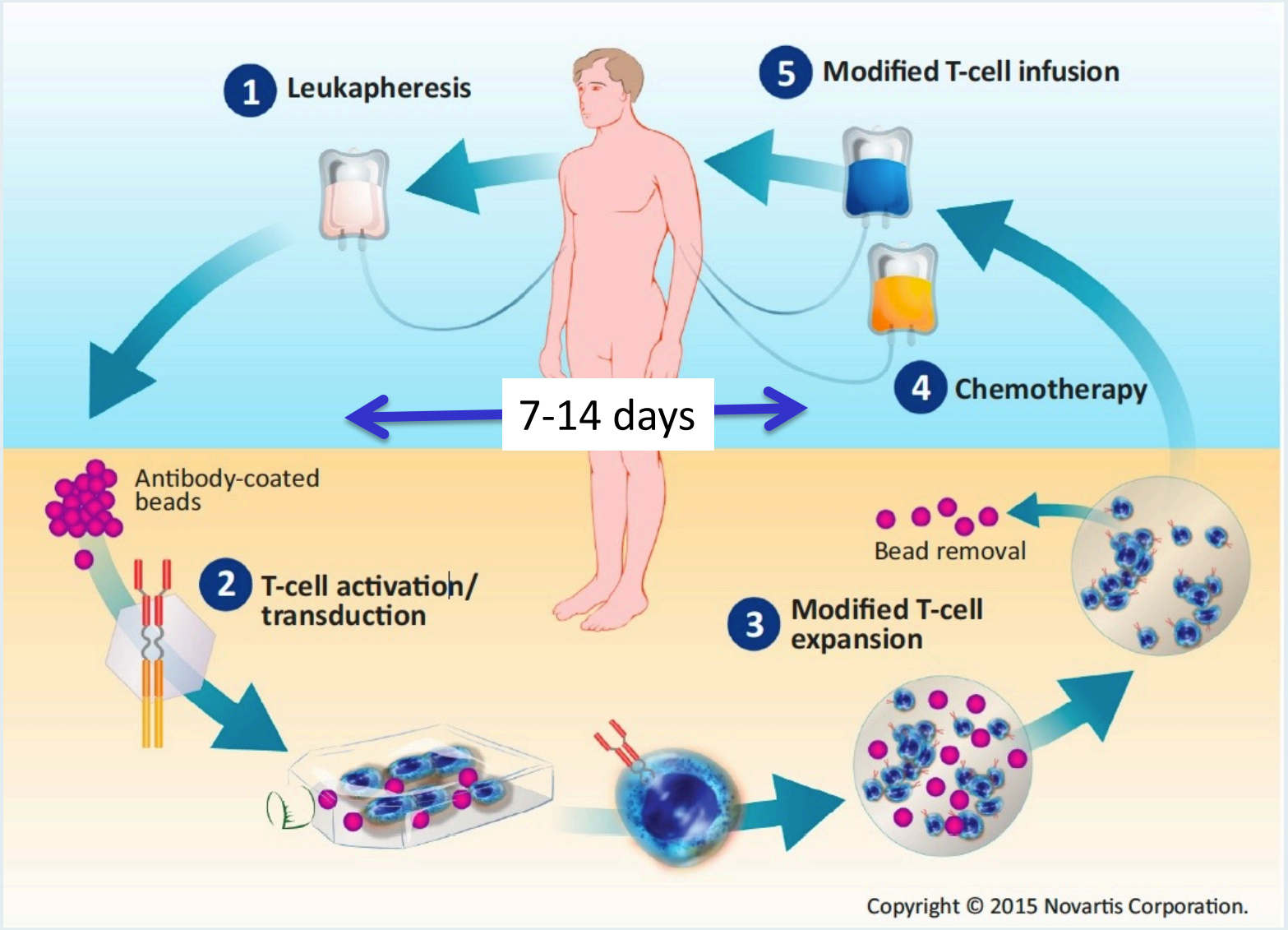
- Must have Grade I to IIIA FL
- Received at least 1 prior line of therapy
- No prior EZH2 inhibitor
- No prior lenalidomide for FL



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

Batlevi CL et al. ASH 2020; Abstract 2052; Clinicaltrials.gov; NCT04224493 (Accessed January 2021).

Overview of CAR T-Cell Therapy



Modification, Courtesy, David Porter, MD

RTP RESEARCH TO PRACTICE

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.

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

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How do you currently approach second-line treatment of MCL, and which BTK inhibitor do you prefer for MCL? How do you currently sequence CAR T therapy?

Case Presentation – A 59-year-old man with Stage IVB mantle cell lymphoma

- Now 59 yo male diagnosed with Stage IVB MCL in 7/2010
- Had been originally diagnosed with ITP a year prior to MCL diagnosis (presented with thrombocytopenia and splenomegaly)
- History of sarcoidosis, CAD (stenting x 3), hypertension and steroid-induced diabetes
- Treated with R-hyper-CVAD in 2010
- Consolidated with autologous stem cell transplant

Case Presentation – A 59-year-old man with Stage IVB mantle cell lymphoma (continued)

- Did well until late 2016, biopsy proven recurrent MCL
- Married, 1 teenage child
- Started ibrutinib in early 2017
- Had early diarrhea, nausea and minor bleeding, all improved or resolved over time
- Progression noted in late 2019
- Went on study with vecabrutinib x 8 months with disease stabilization
- Study closed due to lack of response

Case Presentation – A 59-year-old man with Stage IVB mantle cell lymphoma (continued)

- Developed rapid disease progression immediately upon going off study
- Started R-DHAX in 8/2020 x 4 cycles
- Complete response
- Brexucabtagene autoleucel FDA approved in 7/2020
- Ended up undergoing non-myeloablative allogeneic transplant
- Doing well

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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

The NEW ENGLAND JOURNAL of MEDICINE

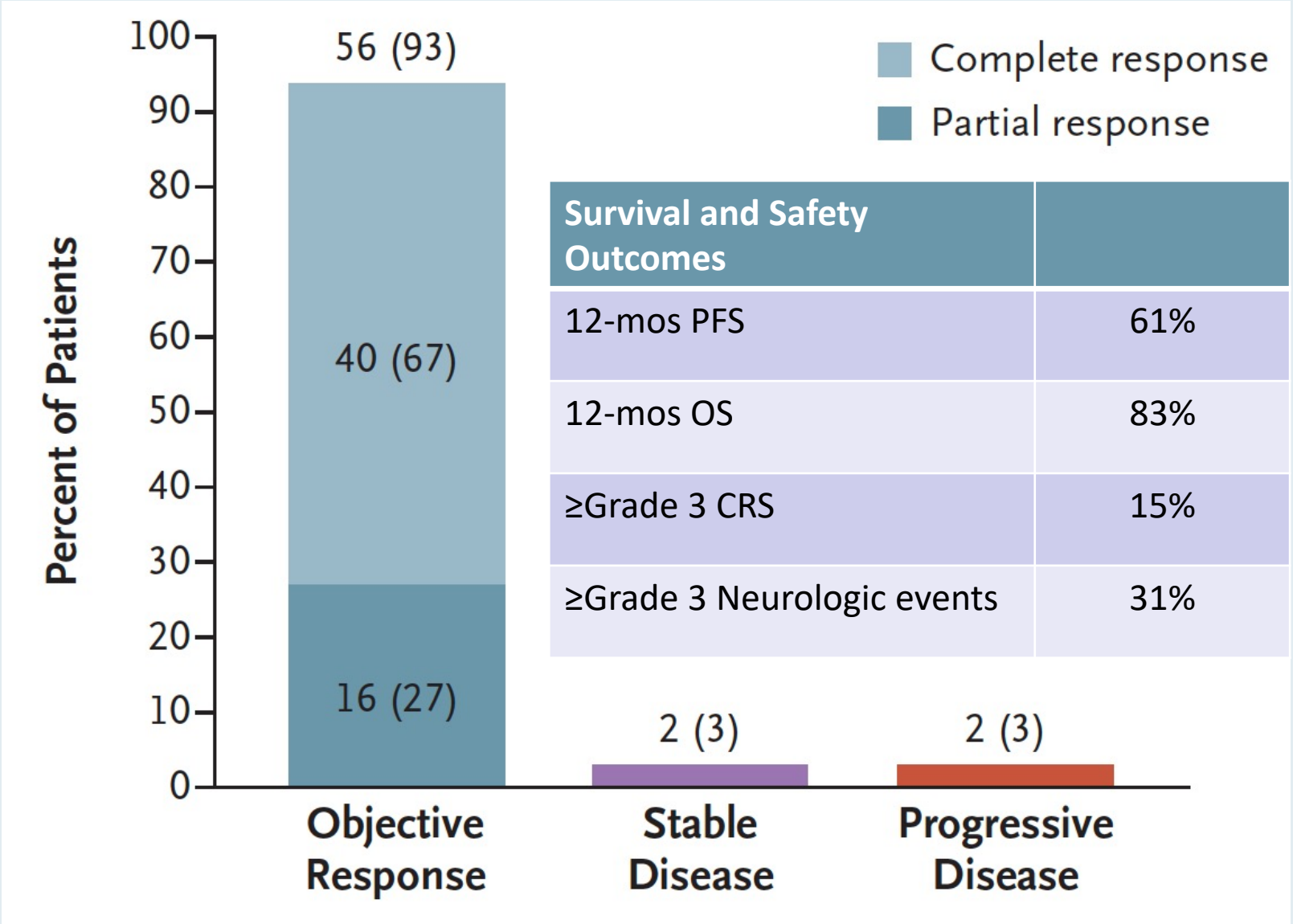
ORIGINAL ARTICLE

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

Immunotherapy and Novel Agents in Gynecologic Cancers

Friday, September 24, 2021
12:00 PM – 1:00 PM ET

Faculty

Martee L Hensley, MD, MSc

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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