

Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Hodgkin and Non-Hodgkin Lymphomas

Thursday, June 17, 2021
5:00 PM – 6:00 PM ET

Faculty

Carla Casulo, MD
Jacklyn Gideon, MSN, AGPCNP-BC

Moderator

Neil Love, MD

Faculty



Carla Casulo, MD

Associate Professor of Medicine
Division of Hematology/Oncology
Director, Hematology/Oncology Fellowship
Program
University of Rochester
Wilmot Cancer Institute
New York, New York



Jacklyn Gideon, MSN, AGPCNP-BC

University of Chicago Hematopoietic
Cellular Therapy Program
Lead Apheresis APP
Chicago, Illinois

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, 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, 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.

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.

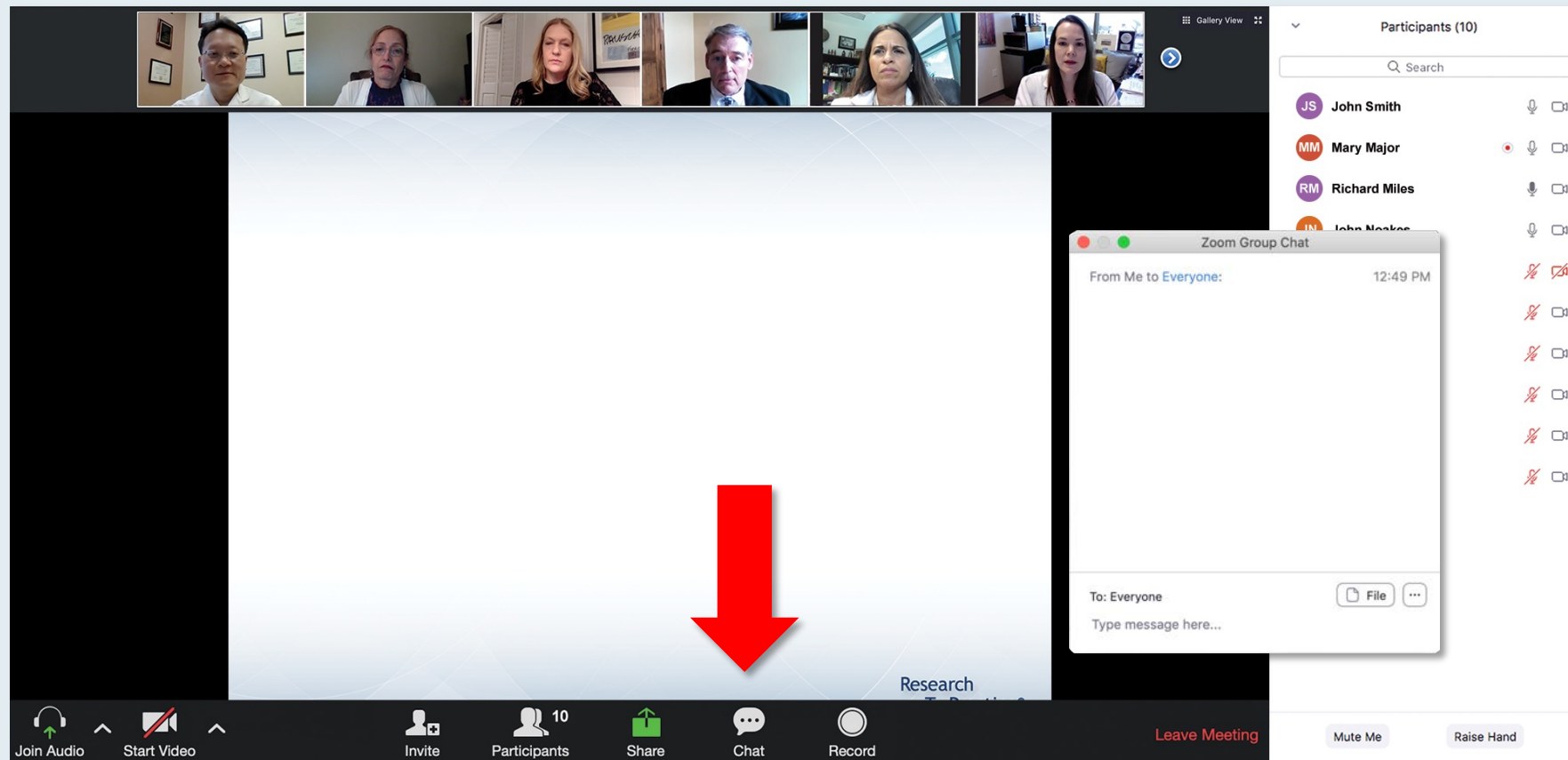
Dr Casulo — Disclosures

No relevant conflicts of interest to disclose.

Ms Gideon — Disclosures

Speakers Bureau	Bristol-Myers Squibb Company, Pharmacyclics LLC, an AbbVie Company, Sanofi Genzyme
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We Encourage Clinicians in Practice to Submit Questions



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How to answer poll questions

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What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?

Quick Poll

- ☐ Carfilzomib +/- dexamethasone
- ☐ Pomalidomide +/- dexamethasone
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- ☐ Daratumumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + bortezomib +/- dexamethasone
- ☐ Ixazomib + Rd
- ☐ Other

Submit

Co-provided by USF Health Research To Practice®

Participants (10)

- JS John Smith
- MM Mary Major
- RM Richard Miles
- JN John Noakes
- AS Alice Suarez
- JP Jane Perez
- RS Robert Stiles
- JF Juan Fernandez
- AK Ashok Kumar
- JS Jeremy Smith







When a poll question pops up, click your answer choice from the available options.

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

The screenshot displays a Zoom meeting interface. At the top, a video bar shows participants: RTP Coordinat..., Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. Below the video bar, a 'Recording...' indicator is visible. The main content area shows a presentation slide titled 'Meet The Professor Program Steering Committee'. The slide lists six members of the steering committee, each with a portrait photo and their name and affiliation. The chat window on the right is open, showing messages from 'Me to Panelists' and 'Me to Panelists and Attendees'. A red arrow points to the white line above the chat submission box, indicating where to drag to expand the box.

Meet The Professor Program Steering Committee

 John N Allan, MD Assistant Professor of Medicine Weill Cornell Medicine New York, New York	 Ian W Flinn, MD, PhD Director of Lymphoma Research Program Sarah Cannon Research Institute Tennessee Oncology Nashville, Tennessee
 Steven Coutre, MD Professor of Medicine (Hematology) Stanford University School of Medicine Stanford, California	 Prof John G Gribben, MD, DSc, FMedSci Chair of Medical Oncology Barts Cancer Institute Queen Mary University of London Charterhouse Square London, United Kingdom
 Matthew S Davids, MD, MMSc Associate Professor of Medicine Harvard Medical School Director of Clinical Research Division of Lymphoma Dana-Farber Cancer Institute Boston, Massachusetts	 Brian T Hill, MD, PhD Director, Lymphoid Malignancy Program Cleveland Clinic Taussig Cancer Institute Cleveland, Ohio

Chat

Me to Panelists 4:31 PM

Welcome and thank you for attending! To access the slides from today's session please use the link below.
http://images.researchtopractice.com/2021/Meetings/Slides/MTP_ToGo_CLL_2021_April1.pdf

Me to Panelists and Attendees 4:32 PM

Welcome and thank you for attending! To access the slides from today's session please use the link below.
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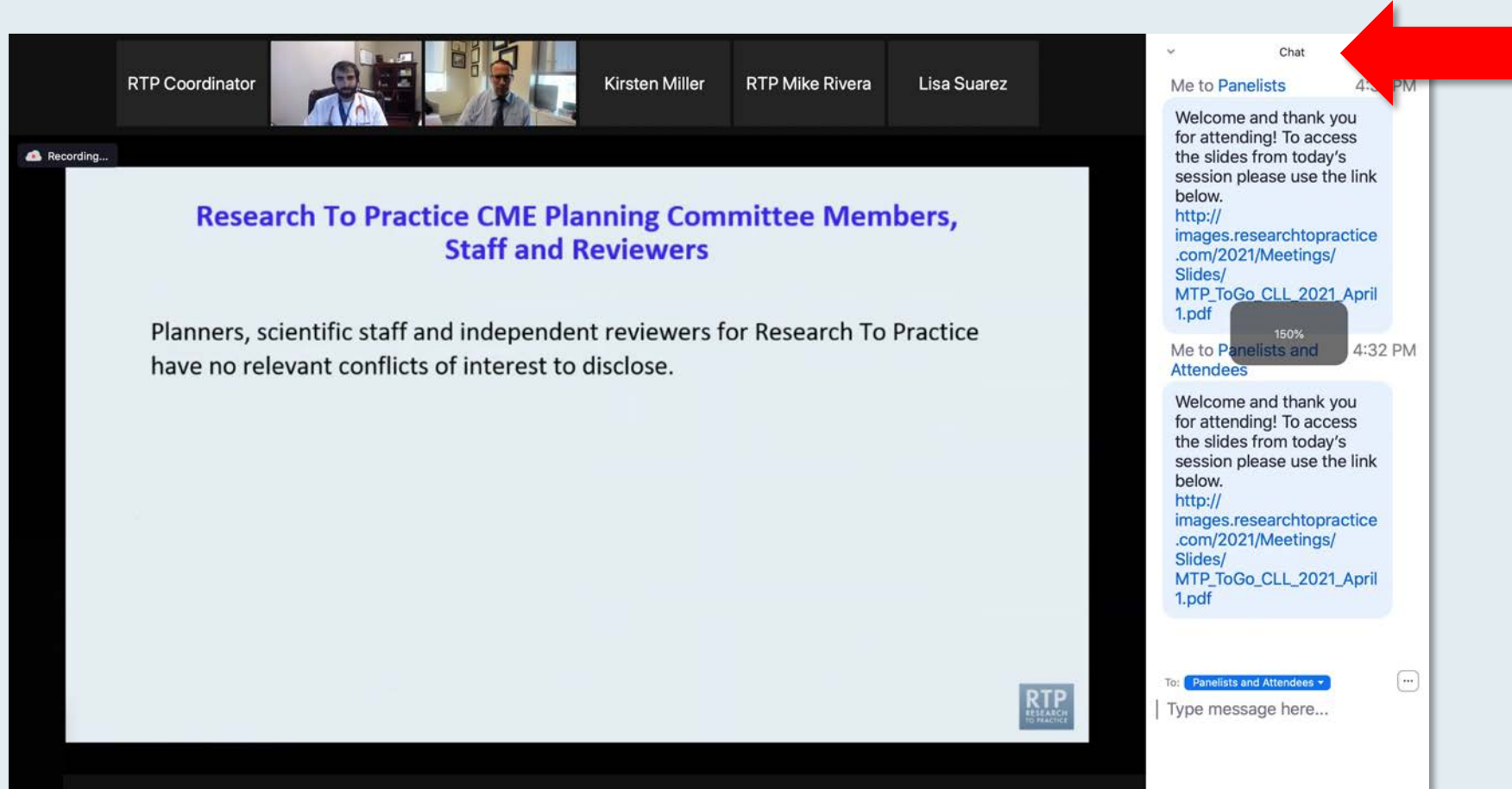
To: Panelists and Attendees ▼

Type message here...

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

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



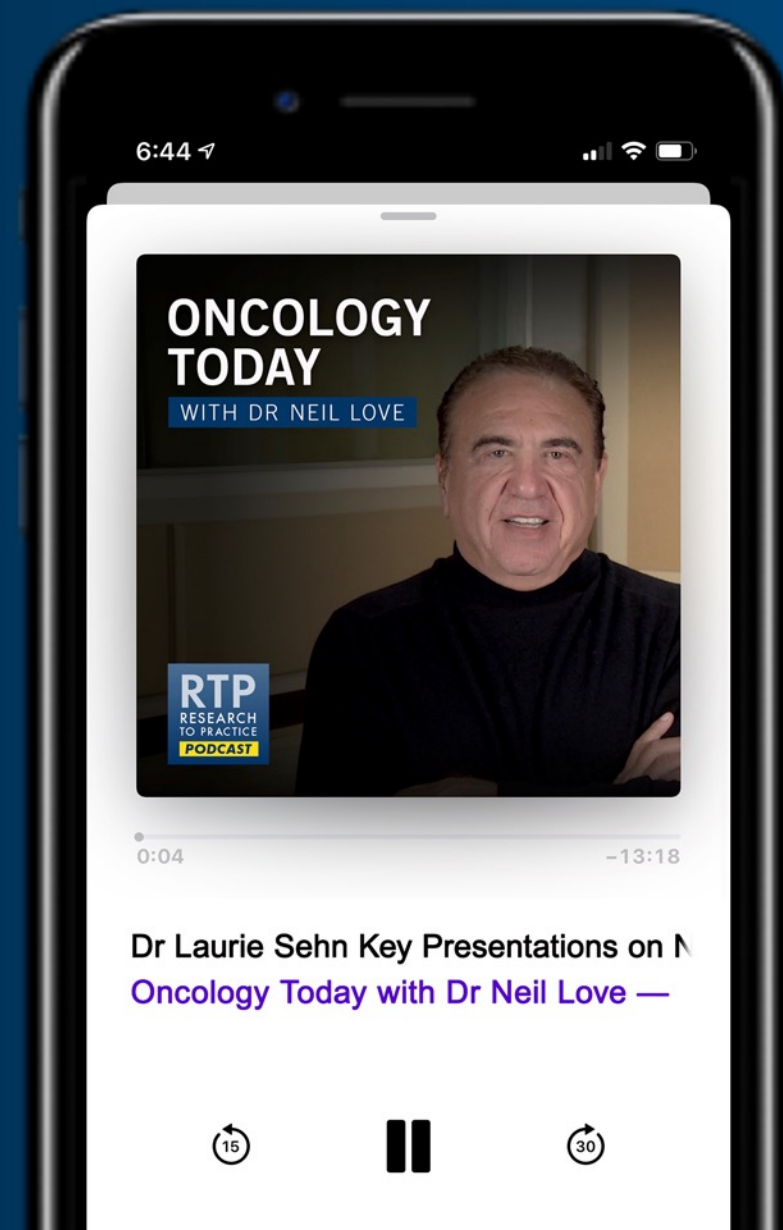
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17 Exciting CME/MOC Events You Do Not Want to Miss

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HER2-Positive Breast Cancer

Tuesday, June 22

5:00 PM – 6:00 PM ET

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Ovarian Cancer

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Hormonal Therapy for Prostate Cancer

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Alli McClanahan, MSN, APRN, ANP-BC

Moderator

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ASCO Highlights and More: Investigators Review Recent Data Sets and Provide Perspectives on Current Oncology Care

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Prostate Cancer: Session 1

Thursday, July 1, 2021

5:00 PM – 6:00 PM ET

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Charles J Ryan, MD

Brenda Martone, MSN, NP-BC, AOCNP

Moderator

Neil Love, MD

Ask the Expert: Clinical Investigators Provide Perspectives on the Management of Renal Cell Carcinoma

In Partnership with Project Echo® and Florida Cancer Specialists

**Tuesday, July 6, 2021
5:00 PM – 6:00 PM ET**

Faculty

David I Quinn, MBBS, PhD

Moderator

Neil Love, MD

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Non-Small Cell Lung Cancer

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5:00 PM – 6:00 PM ET

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Zofia Piotrowska, MD, MHS

Tara Plues, APRN, MSN

Moderator

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Thank you for joining us!

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

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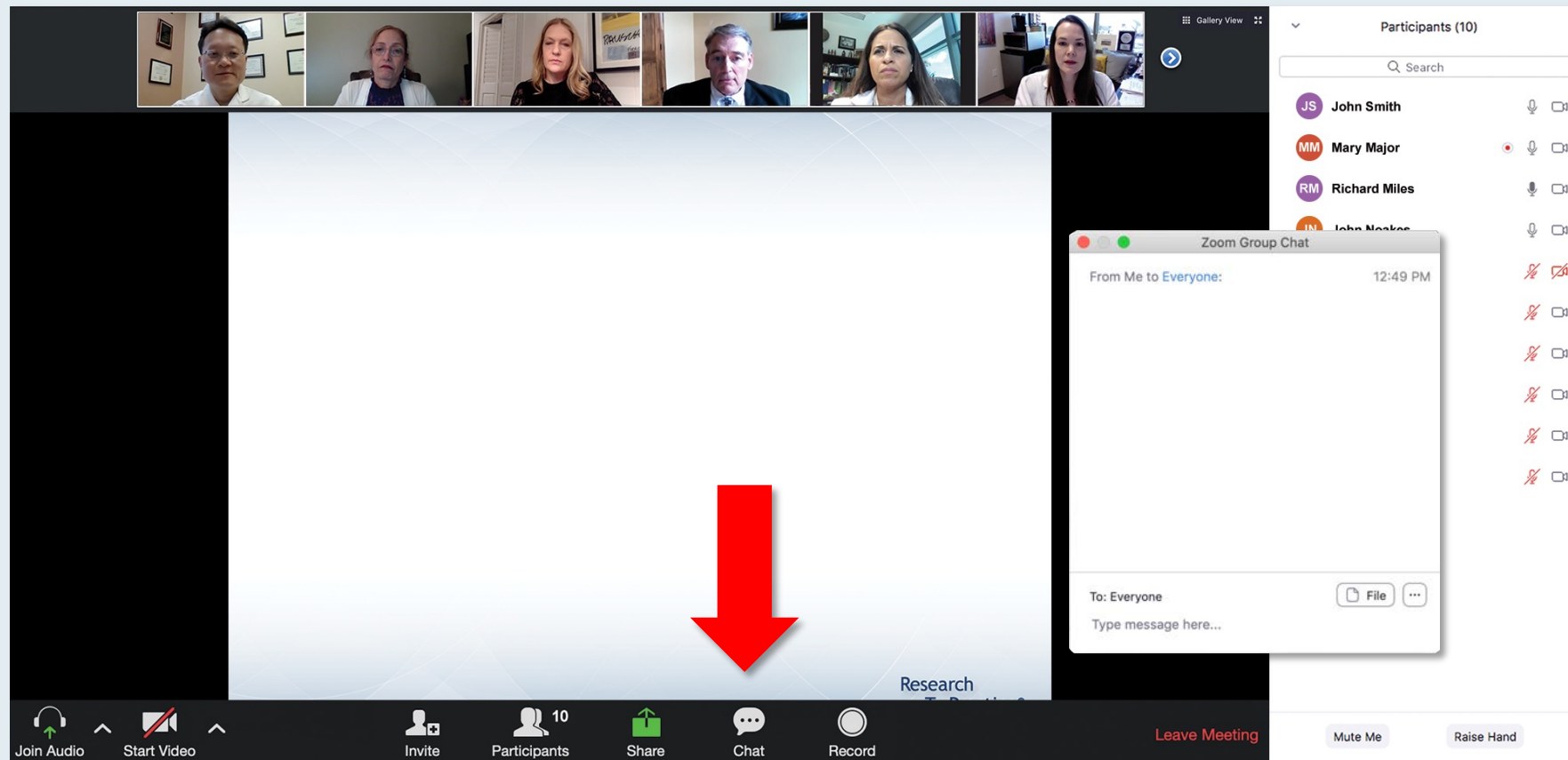
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Co-provided by USF Health Research To Practice®

Join Audio Start Video Invite Participants 10 Share Chat Record Leave Meeting Mute Me Raise Hand

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Oncology Grand Rounds Nursing Webinar Series

April 2021

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

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



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?

Agenda

Module 1: Diffuse Large B-Cell Lymphoma

- Dr Casulo: A 76-year-old man with advanced-stage diffuse large B-cell lymphoma
- Ms Gideon: A 66-year-old woman with high-grade, Stage IV diffuse large B-cell lymphoma

Module 2: Hodgkin Lymphoma

- Dr Casulo: A 35-year-old woman with advanced-stage Hodgkin lymphoma
- Ms Gideon: A 38-year-old man with relapsed/refractory classical Hodgkin lymphoma

Module 3: Follicular Lymphoma

- Dr Casulo: A 54-year-old woman with recurrent Grade I-II follicular lymphoma
- Ms Gideon: A 69-year-old man with recurrent Grade IIIA follicular lymphoma

Module 4: Mantle Cell Lymphoma

- Dr Casulo: A 64-year-old man with advanced-stage mantle cell lymphoma
- Ms Gideon: A 70-year-old man with relapsed/refractory mantle cell lymphoma

Positive Top-Line Results Announced from Phase III TRANSFORM Trial: Lisocabtagene Maraleucel versus Chemotherapy → ASCT

Press Release – June 10, 2021

“ Today positive topline results [were announced] from TRANSFORM, a global, randomized, multicenter Phase 3 study evaluating lisocabtagene maraleucel as a second-line treatment in adults with relapsed or refractory large B-cell lymphoma (LBCL) compared to salvage therapy followed by high-dose chemotherapy and hematopoietic stem cell transplant, which is currently considered a gold standard treatment for these patients. Results of a pre-specified interim analysis conducted by an independent review committee showed the study met its primary endpoint of demonstrating a clinically meaningful and highly statistically significant improvement in event-free survival, as well as key secondary endpoints of complete response rate and progression-free survival compared to standard of care. Overall survival data were immature at the time of this interim analysis. Safety results were consistent with the known safety profile of lisocabtagene maraleucel for the treatment of LBCL in the third-line setting, and no new safety concerns were identified in this second-line setting.

The results represent the first time a therapy has shown a benefit over standard of care high-dose chemotherapy and stem cell transplant in relapsed or refractory LBCL, and the first time a CD19-directed CAR T cell therapy has demonstrated potential as a second-line therapy in this patient population. The company will complete an evaluation of the TRANSFORM data and looks forward to sharing the results at an upcoming medical conference, as well as with health authorities. ”

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Case Presentation – Dr Casulo: A 76-year-old man with advanced-stage diffuse large B-cell lymphoma

- 5 years prior at age 71 patient was treated with R-CHOP x 6 cycles
 - Experienced a complete response
- Patient experienced disease progression 1 year later
 - Treated with ICE and autologous stem cell transplant (ASCT)
- One year post ASCT developed disease progression and poor PS
- Patient was then treated with tafasitamab/lenalidomide and is faring well

Case Presentation – Dr Casulo: A 76-year-old man with advanced-stage diffuse large B-cell lymphoma (continued)

What tumor-related or clinical factors were most important in influencing your decision to use tafasitamab/lenalidomide for this patient?

1. Patient had few options given his age and comorbidities
2. Patient was seeking oral therapy if possible
3. Patient was not eligible for clinical trial due to poor PS

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?

Chimeric antigen receptor (CAR) T-cell therapy is commonly associated with...

1. Cytokine release syndrome
2. Neurotoxicity
3. Rash
4. Peripheral neuropathy
5. I don't know

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

1. Agree
2. Disagree
3. I don't know

Case Presentation – Ms Gideon: A 66-year-old woman with high-grade, Stage IV diffuse large B-cell lymphoma

- 5/2020: Initial diagnosis of DLBCL of germinal center origin
- 11/2020: Disease relapse following initial treatment (R-CHOP → dose adjusted R-EPOCH)
- 12/1/2020: R-ICE initiated
- 12/16/20: Worsening back pain and elevated LDH clinically concerning for progression
- 12/30/20: T-cell apheresis for axicabtagene ciloleucel (axi-cel)
- 12/31/20: C1D1 of BR + polatuzumab vedotin bridging therapy initiated
- 1/11/21-1/15/21: IFRT to left paraspinal mass (20Gy in 5 fractions)
- 1/27/21: Patient receives axi-cel infusion
- 2/25/21: D+30 PET/CT imaging with PR (Deauville 4)

Case Presentation – Ms Gideon: A 66-year-old woman with high-grade, Stage IV diffuse large B-cell lymphoma (continued)

What education issues do you generally discuss with a patient with DLBCL who is about to begin treatment with CAR T-cell therapy?

- Typically advise patients that CAR T cell offers a different treatment approach where chemotherapy is not the backbone and that its toxicities are unique including CRS and neurotoxicity
- Patients will need 24/7 caregiver support, must be within 2 hours of treating institution for 4 weeks following the infusion
- Patients can anticipate being unable to drive for 8 weeks post infusion

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?

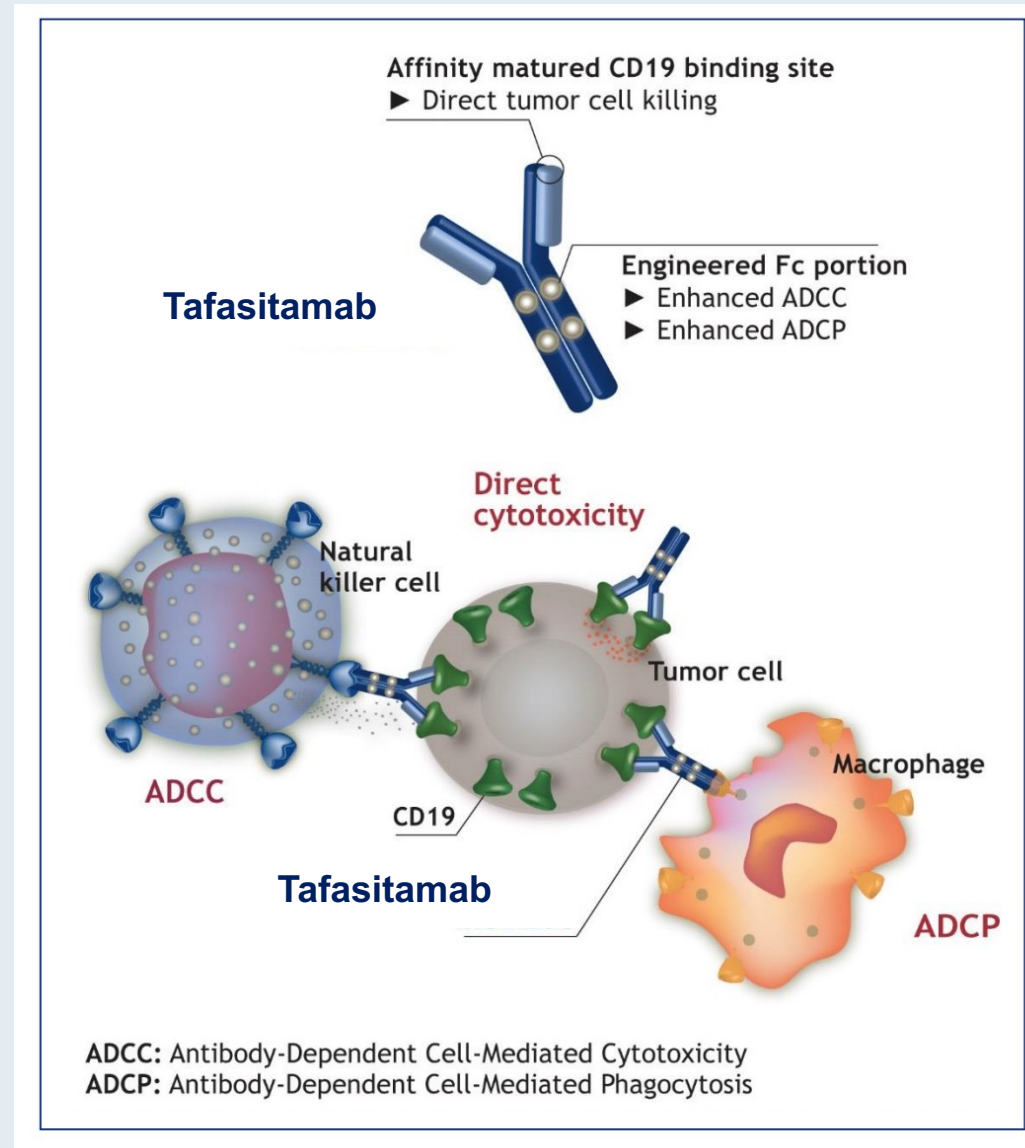
FDA Grants Accelerated Approval to Tafasitamab-cxix for Diffuse Large B-Cell Lymphoma

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.”

Tafasitamab (MOR208)



**Lenalidomide enhances
NK function with
enhanced ADCC in vitro**

Salles et al. Lancet Onc 2020

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%

Phase II L-MIND Trial: Tafasitamab Combined with Lenalidomide (LEN) for Relapsed or Refractory (R/R) DLBCL

Conclusions

- Combination treatment with tafasitamab and LEN followed by tafasitamab monotherapy provided durable responses in patients with R/R DLBCL not eligible for ASCT
- These data suggest that this chemotherapy-free combination may have the potential to achieve prolonged remission and survival benefit in the patient population, especially at first relapse
- The long-term safety data indicate the favorable benefit-risk profile of tafasitamab and LEN followed by tafasitamab until disease progression

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

Press Release – February 5, 2021

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

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

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.

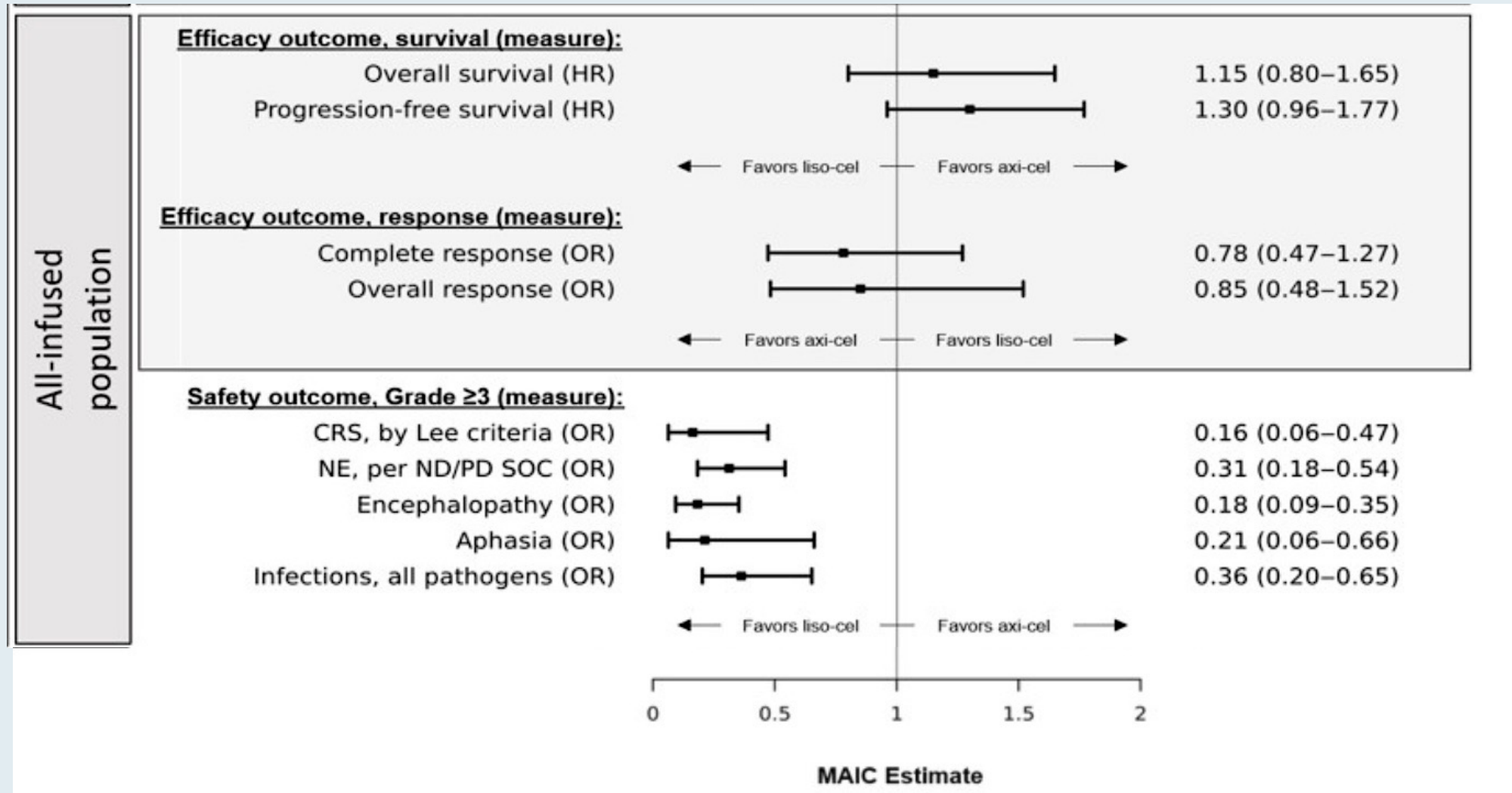
Abramson JS et al; TRANSCEND NHL 001 Investigators. *Proc ASCO* 2018;Abstract 7505.

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

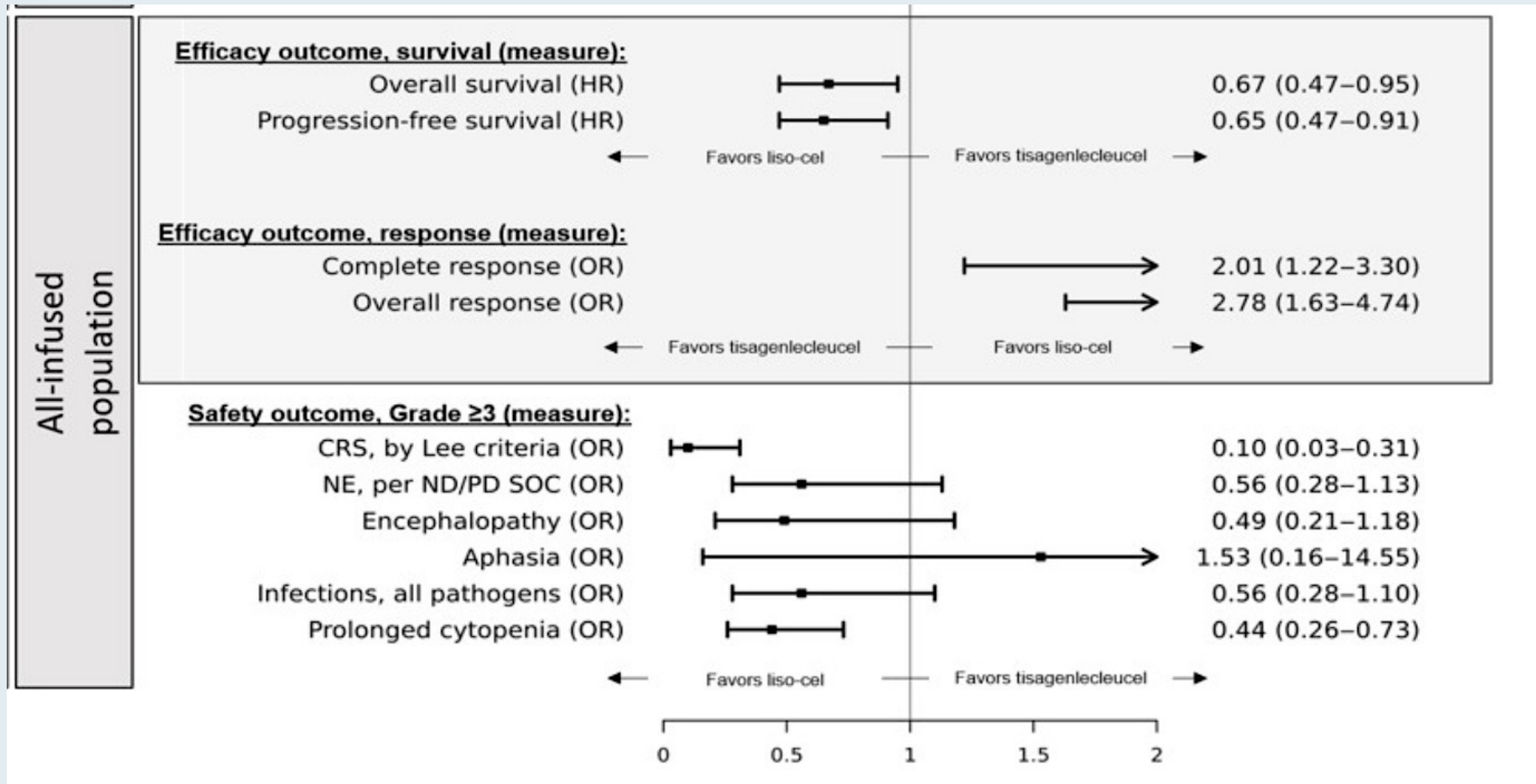
Maloney DG et al.

ASH 2020;Abstract 2116.

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



Matching-Adjusted Indirect Comparison of Liso-cel versus Tisagenlecleucel



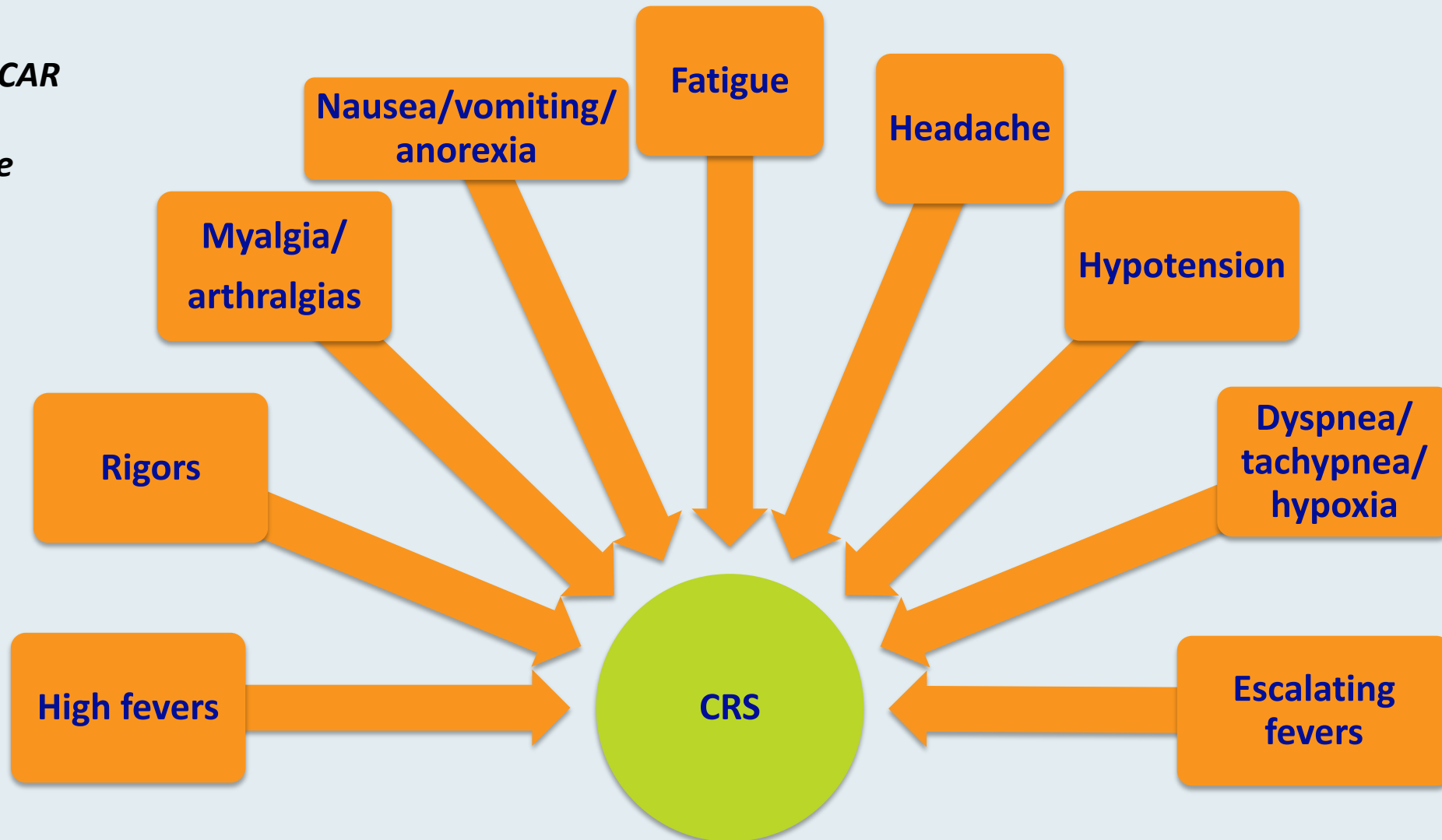
CAR T-Cell Therapy-Associated Cytokine Release Syndrome (CRS)

CRS — May be mild or life-threatening

- Occurs with CART19 activation and expansion
- Dramatic cytokine elevations (IL-6, IL10, IFN γ , 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%

Cytokine Release Syndrome (CRS): Common Symptoms

*Based on CAR
T-cell
experience*



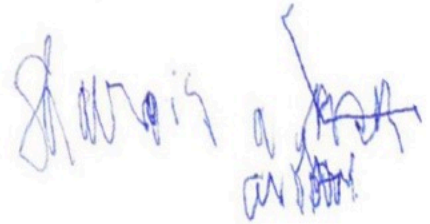
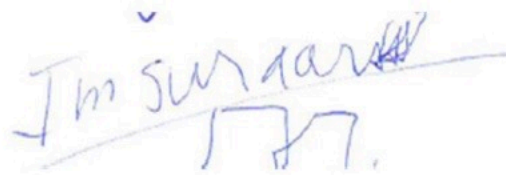
Diagnosis based on clinical symptoms and events

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

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

Day 4 9 am	I love Shawnee, KS.	MMSE score 29/30
Day 5 01:30 PM Toci 8 mg/kg		27/30
Day 5 03:30 PM		27/30
Day 6 9 am	I miss my kids.	29/30

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

- Dr Casulo: A 76-year-old man with advanced-stage diffuse large B-cell lymphoma
- Ms Gideon: A 66-year-old woman with high-grade, Stage IV diffuse large B-cell lymphoma

Module 2: Hodgkin Lymphoma

- Dr Casulo: A 35-year-old woman with advanced-stage Hodgkin lymphoma
- Ms Gideon: A 38-year-old man with relapsed/refractory classical Hodgkin lymphoma

Module 3: Follicular Lymphoma

- Dr Casulo: A 54-year-old woman with recurrent Grade I-II follicular lymphoma
- Ms Gideon: A 69-year-old man with recurrent Grade IIIA follicular lymphoma

Module 4: Mantle Cell Lymphoma

- Dr Casulo: A 64-year-old man with advanced-stage mantle cell lymphoma
- Ms Gideon: A 70-year-old man with relapsed/refractory mantle cell lymphoma

Based on the results of the Phase III ECHELON-1 trial, which of the following regimens resulted in a progression-free survival advantage over standard ABVD as first-line therapy for patients with Stage III or IV classical Hodgkin lymphoma (HL)?

1. ABVD + bendamustine
2. ABVD + nivolumab
3. AVD + brentuximab vedotin
4. Brentuximab vedotin + nivolumab
5. I don't know

Patients at high risk for disease progression after undergoing transplant for relapsed HL may receive 1 year of consolidation treatment with...

1. Nivolumab
2. Brentuximab vedotin
3. Nivolumab + brentuximab vedotin
4. Chemotherapy
5. Other
6. I don't know

Case Presentation – Dr Casulo: A 35-year-old woman with advanced-stage Hodgkin lymphoma

- Advanced stage HL involving bone and liver
- Otherwise very healthy except she is a smoker
- Began therapy on SWOG-S1826: Phase III trial of nivolumab or brentuximab vedotin with combination chemotherapy for newly diagnosed Stage III-IV cHL
 - Randomly assigned to BV-AVD arm

Case Presentation – Dr Casulo: A 35-year-old woman with advanced-stage Hodgkin lymphoma (continued)

What tumor-related or clinical factors were most important in influencing your decision to use BV-AVD for this patient?

1. Off study, BV-AVD does not require PET adapted therapy and possibility of dose escalation
2. Avoidance of bleomycin given smoking history was important
3. High risk disease makes adding brentuximab appealing

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?

Case Presentation – Ms Gideon: A 38-year-old man with relapsed/refractory classical Hodgkin lymphoma

- Multiagent/regimen refractory disease
- 12/2016: Nivolumab initiated → stable disease
- 01/2018: Evidence of disease progression; nivolumab discontinued
- 02/2018: Patient received palliative treatment with GND x 2 → partial response
- 05/2018: Patient underwent a second MRD SCT with fludarabine, melphalan and alemtuzumab conditioning therapy
 - PET/CT scan day +30 consistent with CR
 - PET/CT scan day +180 consistent with disease relapse
 - Course complicated by severe ITP, refractory to steroids, IVIG, rituximab, N-plate, and fostamatinib
- 04/2019: Began palliative treatment with brentuximab vedotin
 - Treatment tolerated well with evidence of response
 - Disease eventually progressed approximately 1 year later

Case Presentation – Ms Gideon: A 38-year-old man with relapsed/refractory classical Hodgkin lymphoma (continued)

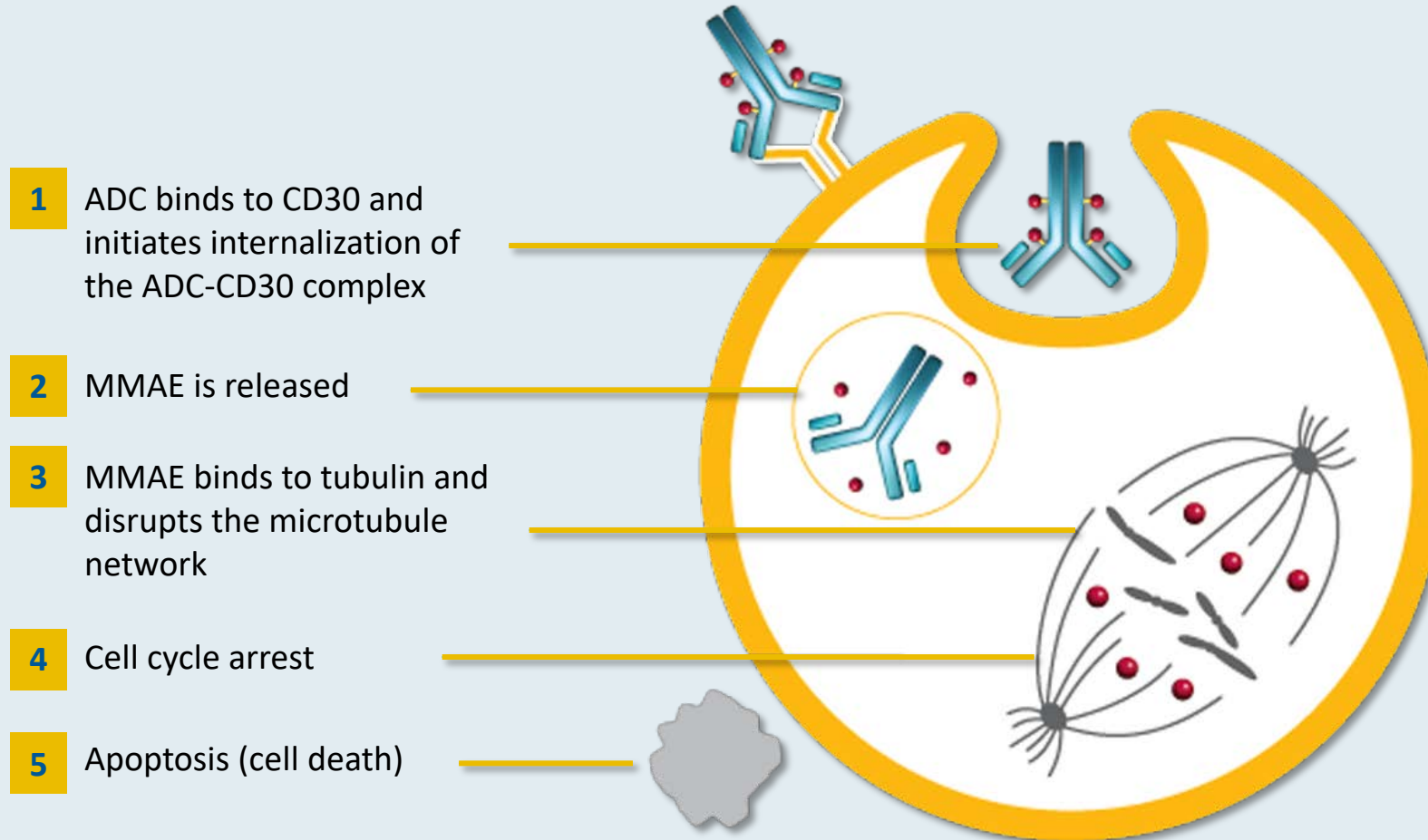
What education issues did you discuss with this patient or do you generally discuss with a patient with HL who is about to begin treatment with brentuximab vedotin?

- This particular patient had failed induction, salvage and relapsed post allotransplant. We discussed how BV is an antibody-drug conjugate and how it was different to the prior therapies he had received (ie, follow-up less intensive than allotransplant); plan was for 2nd allo if response to BV given his young age
- This patient had PN prior to BV treatment, so we discussed the importance of close monitoring during BV treatment for worsening neuropathy and need for potential dose reduction
- In general we also discuss side effects including peripheral neuropathy, low blood counts (might have more cytopenias given prior tx), abnormal liver function tests, GI SEs, fatigue
- PML should also be mentioned even though it is rare

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



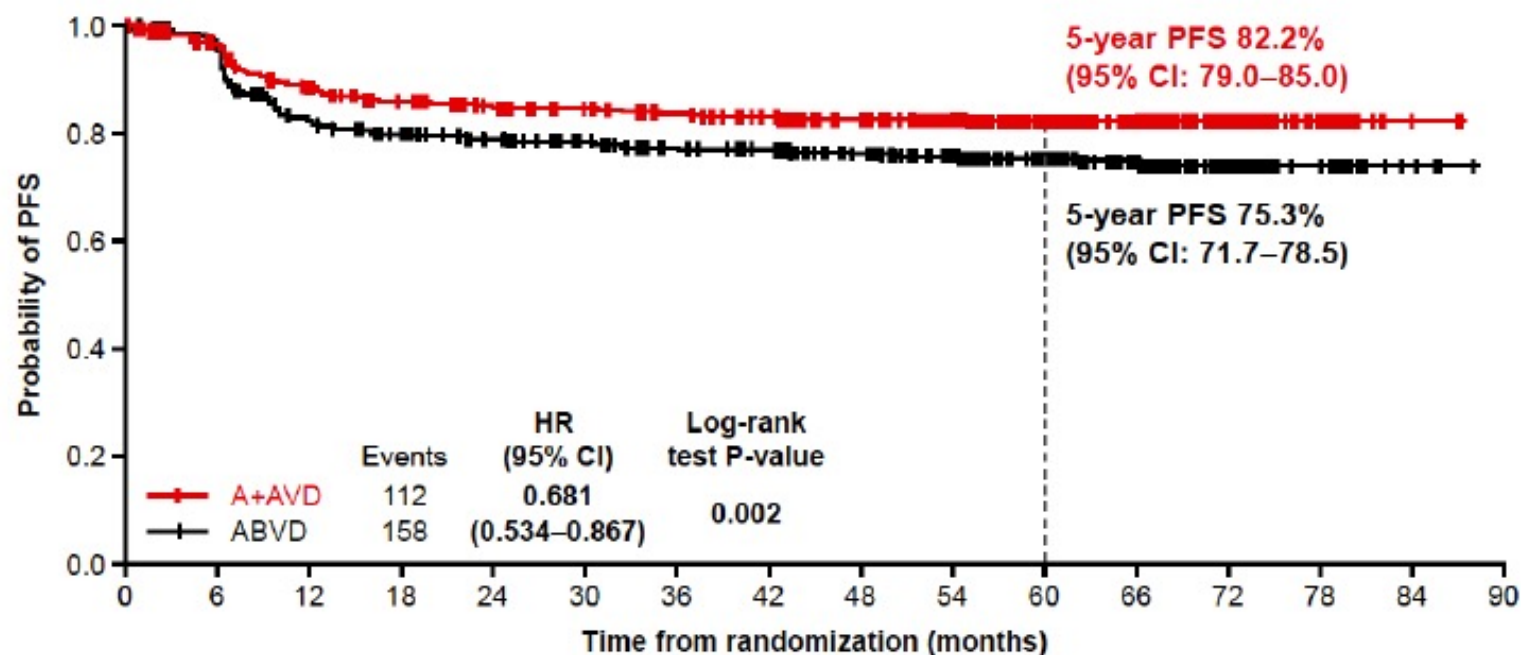
Brentuximab Vedotin with Chemotherapy for Patients with Previously Untreated, Stage III/IV Classical Hodgkin Lymphoma: 5-Year Update of the ECHELON-1 Study

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.

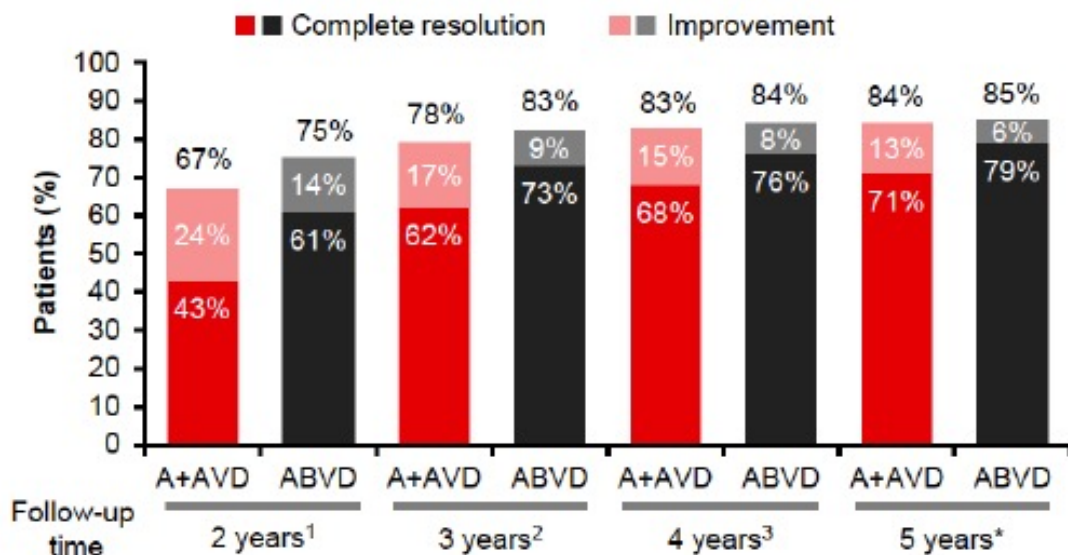
*September 14, 2020 data cut-off.



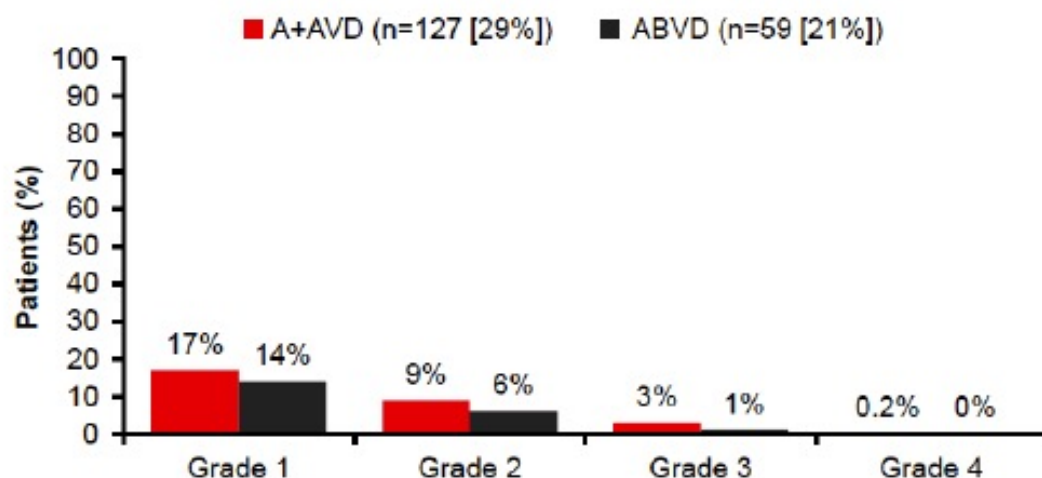
ECHELON-1: PN resolution and improvement

- 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 (%)^{*}

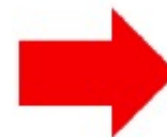


Patients with ongoing PN by grade at last follow-up[†]



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.

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

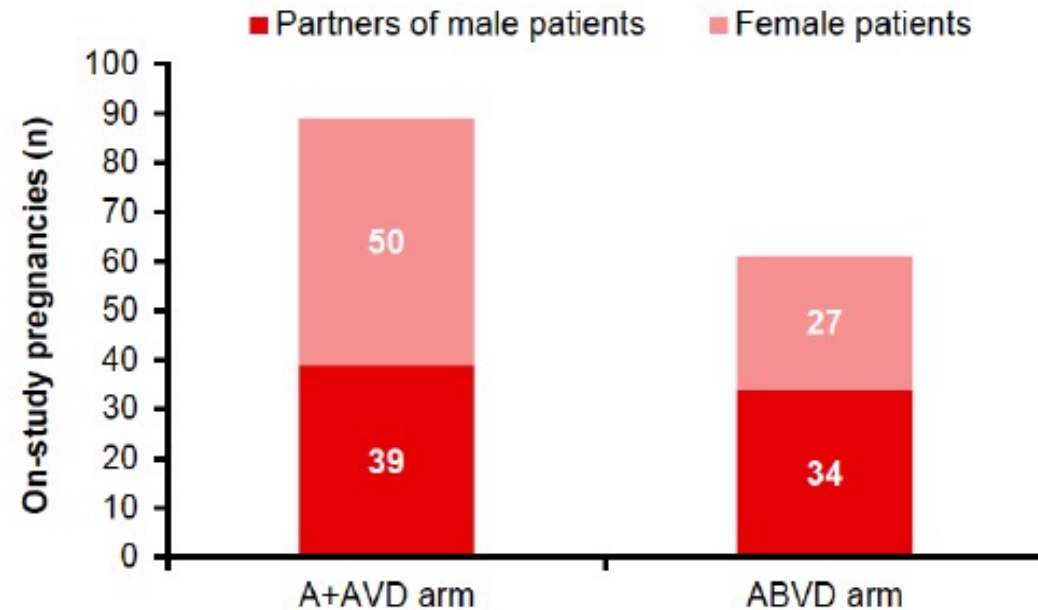




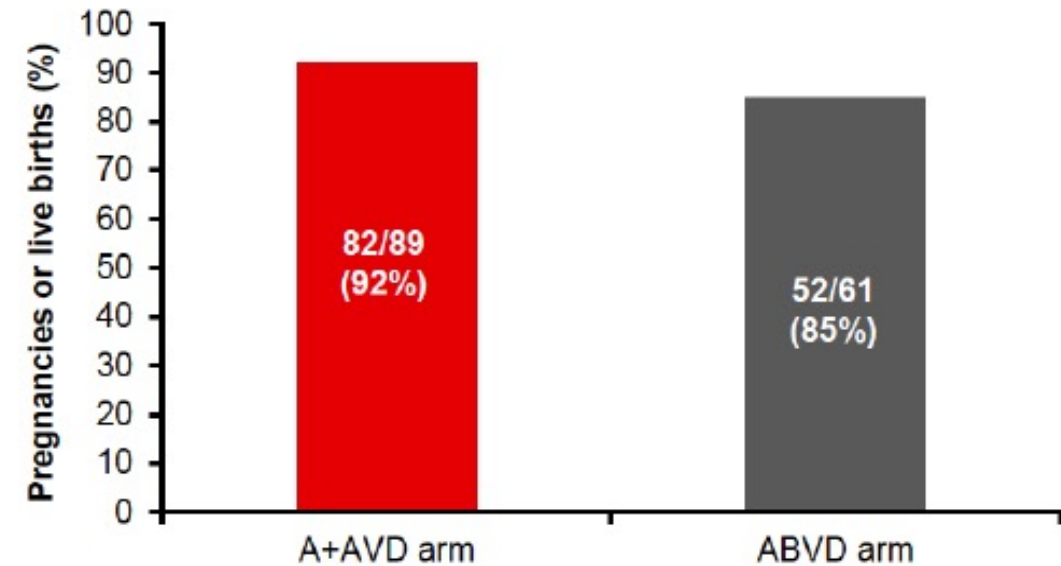
ECHELON-1: Pregnancies

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

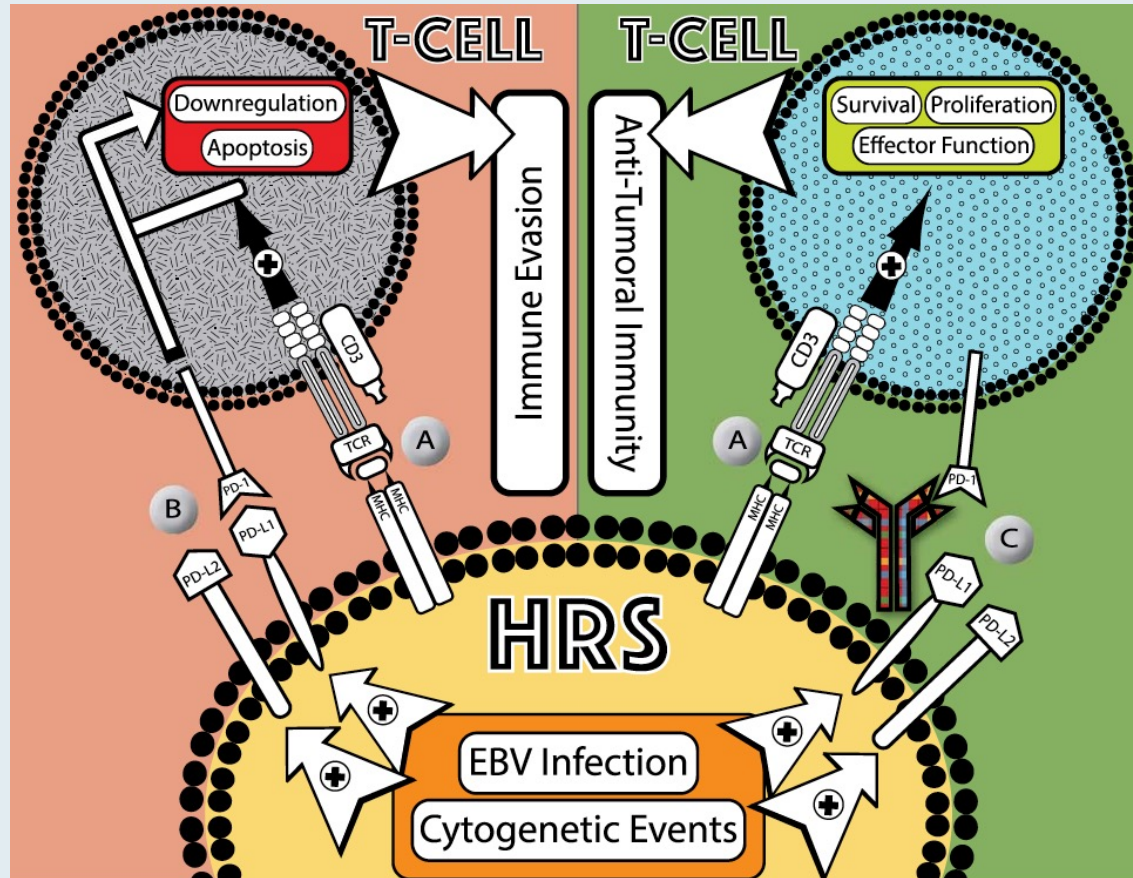
On-study pregnancies in patients or their partners



Ongoing pregnancies or live births

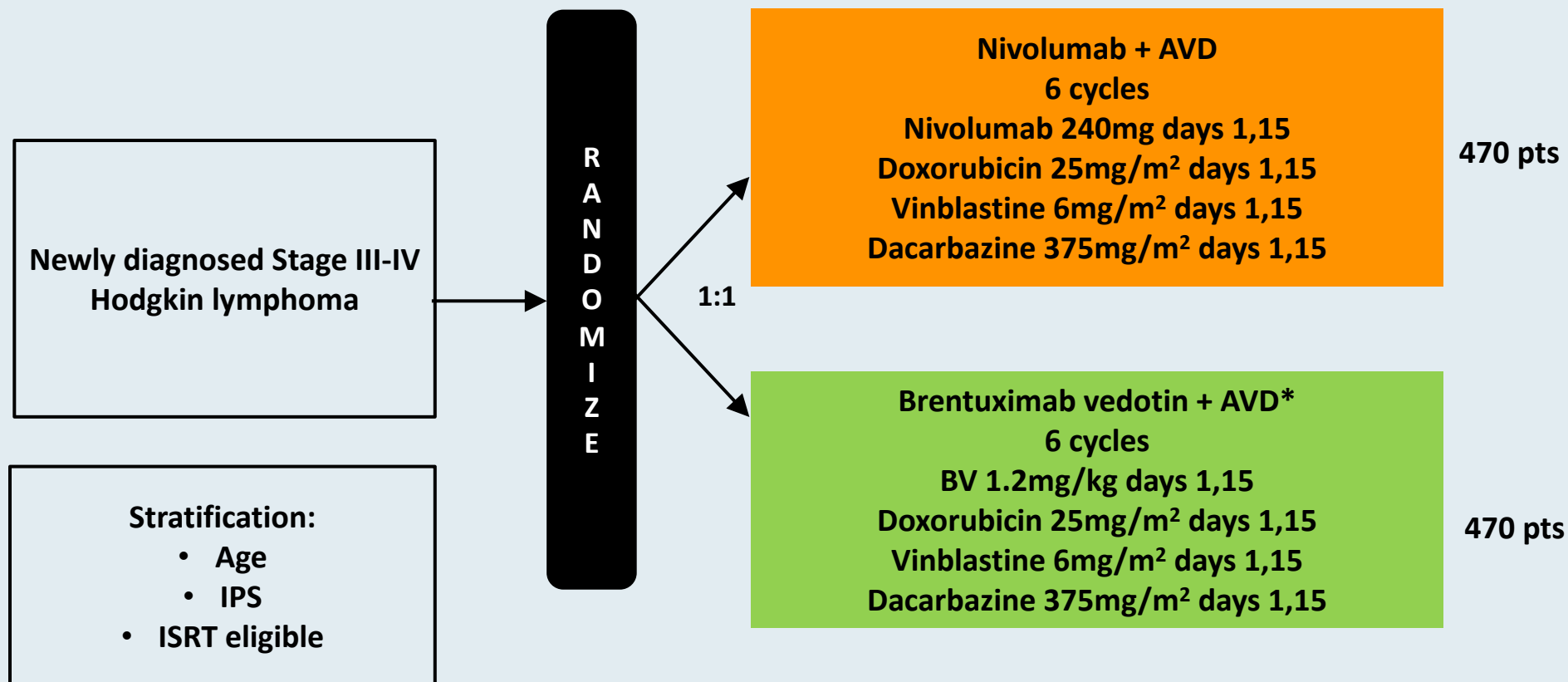


Targeting the PD-1/PD-L1 Axis in HL



- 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)

SWOG-1826: Ongoing Phase III Trial of Nivolumab or Brentuximab Vedotin with Combination Chemotherapy for Newly Diagnosed Stage III-IV Classical HL



* G-CSF is mandatory in BV-AVD arm, optional in N-AVD

Agenda

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- Ms Gideon: A 70-year-old man with relapsed/refractory mantle cell lymphoma

Which of the following regimens appears to have the same efficacy as bendamustine/rituximab (BR) as first-line treatment for symptomatic follicular lymphoma (FL)?

1. Rituximab alone
2. Lenalidomide/rituximab
3. Obinutuzumab
4. R-CHOP
5. None of the above
6. I don't know

What is the usual second-line therapy for a patient with FL who experiences disease progression on first-line BR?

1. Re-treatment with BR
2. Obinutuzumab/bendamustine
3. Rituximab/lenalidomide
4. A PI3K inhibitor (eg, idelalisib, copanlisib, duvelisib, umbralisib)
5. I don't know

Case Presentation – Dr Casulo: A 54-year-old woman with recurrent Grade I-II follicular lymphoma

- Initially treated with first-line BR
- Experienced early disease relapse and entered SWOG-S1608: Phase II trial of obinutuzumab +/- umbralisib, lenalidomide, or combination chemotherapy for early relapsing or refractory Grade I-IIIa FL
 - Randomly assigned to umbralisib and obinutuzumab
- Patient experienced a partial response, but disease progressed shortly thereafter
- She then received R-CHOP x 6 and autologous stem cell transplant → disease progression 1 year later
- Tazemetostat initiated

Case Presentation – Dr Casulo: A 54-year-old woman with recurrent Grade I-II follicular lymphoma (continued)

What tumor-related or clinical factors were most important in influencing your decision to use tazemetostat for this patient?

1. Lack of other options
2. Low grade FL
3. Patient needed low toxicity therapy

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?

Case Presentation – Ms Gideon: A 69-year-old man with recurrent Grade IIIA follicular lymphoma

- 5/2018 - 9/2018: R-CHOP x 6 cycles → maintenance rituximab (complete response)
- 1/2019: Patient developed recurrent RLE edema, decreased energy, night sweats
- 1/14/19: CT C/A/P w/ RP and inguinal lymphadenopathy
- 1/28/19: Right inguinal LN, Grade IIIA FL
- 5/1/19: CAR T-cell infusion for FL on IRB18-123 trial (complete response)
- 10/2020: 18-month imaging with progression with worsening right inguinal LAD, new sclerotic focus w/i posterior left iliac bone, erythematous skin nodule R anterior thigh
- 12/3/20: C1D1 lenalidomide/rituximab
 - Tolerating therapy well; disease restaging following 4 cycles

Case Presentation – Ms Gideon: A 69-year-old man with recurrent Grade IIIA follicular lymphoma (continued)

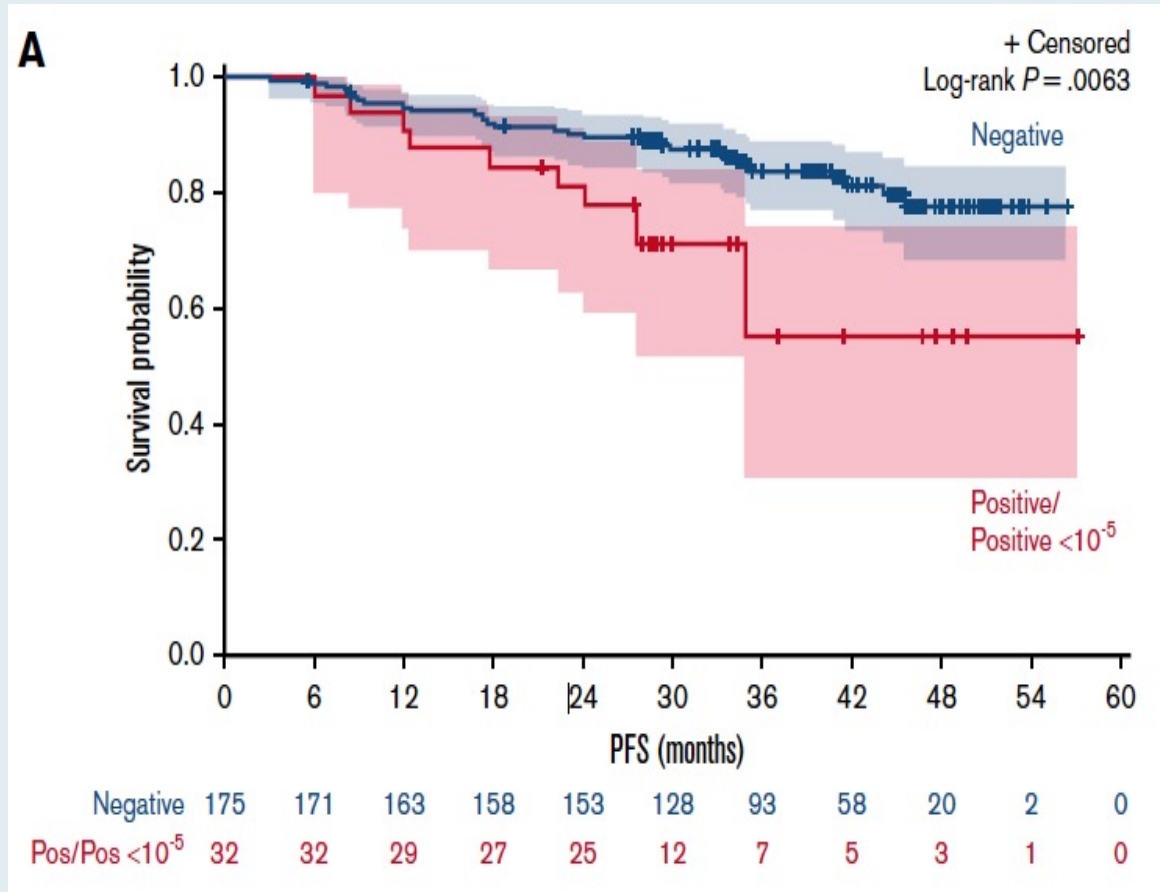
What education issues do you generally discuss with a patient with follicular lymphoma who is about to begin treatment with lenalidomide/rituximab?

- We discuss the fixed duration schedule; the first cycle is the most intensive with weekly lenalidomide, but follow-up spreads out with subsequent cycles.
- Dose reductions of lenalidomide are not uncommon due to cytopenias, but the regimen still efficacious even with lower dosing.
- Focus on fatigue (take lenalidomide in the evening), GI changes (diarrhea/constipation) and how to manage, rash, infection precautions, risk for secondary malignancies. Adverse events don't necessarily mean drug needs to be discontinued. Can manage with supportive care, dose interruption or dose reduction. Risk for DVT, appropriate VTE prophylaxis is patient specific. Always need to discuss contraception depending on patient age and reproductive potential.

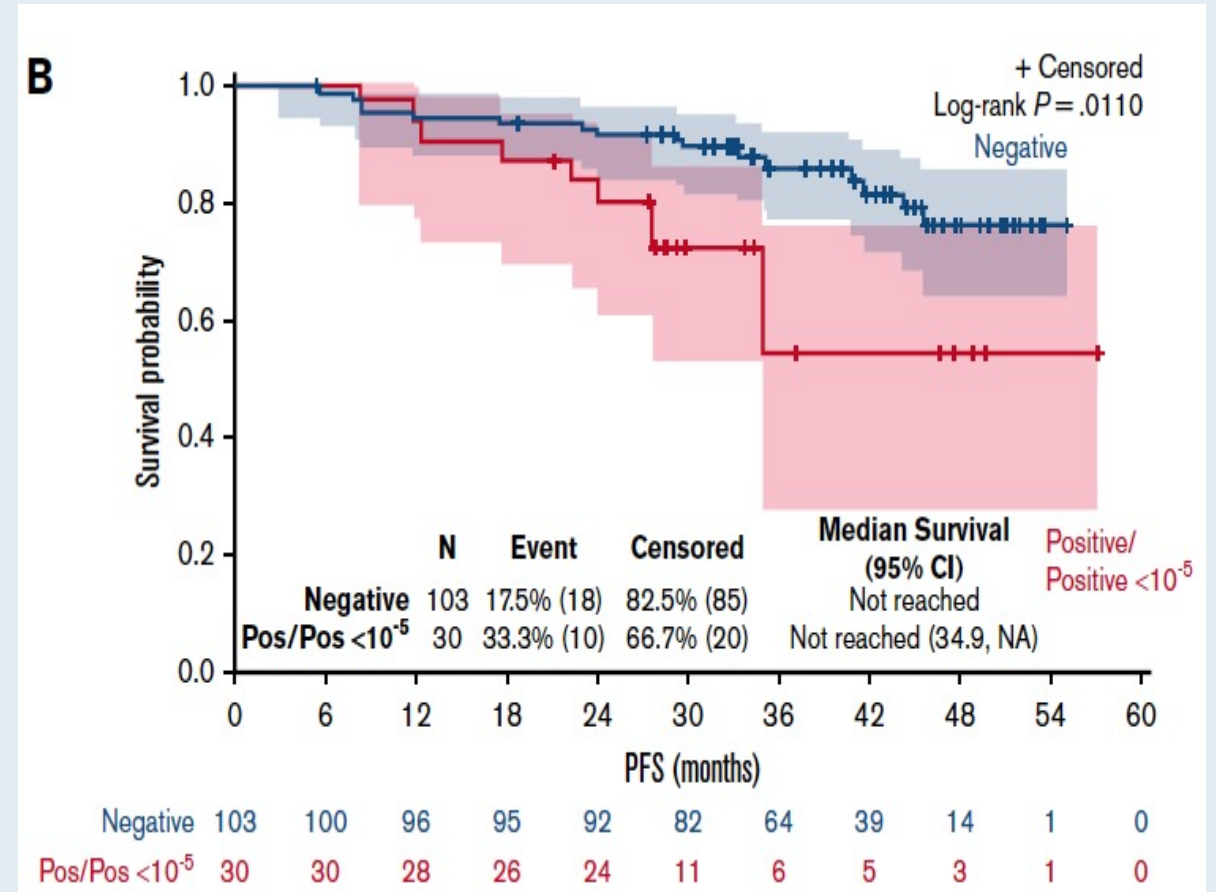
How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

RELEVANCE Trial: R² Induces High Molecular Response in Untreated FL

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

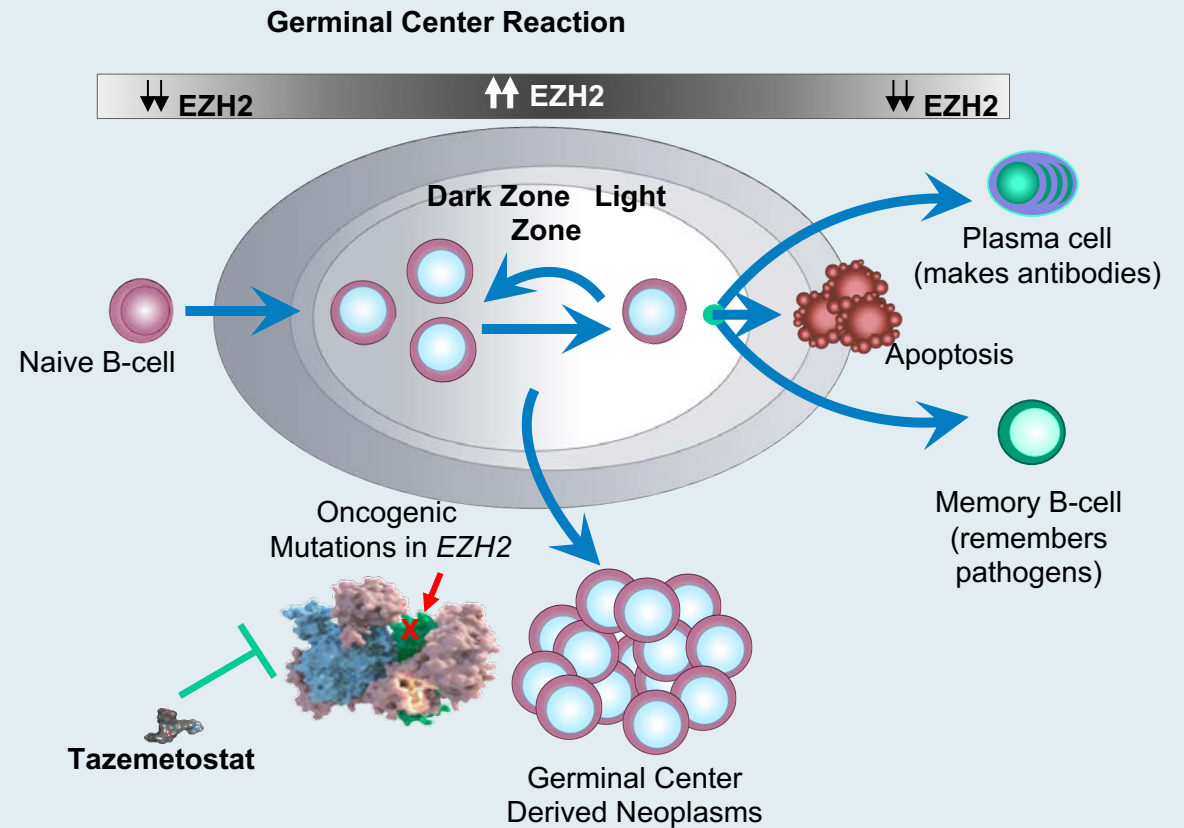


Impact of positive MRD at week 24 on PFS in BM



Follicular Lymphoma and EZH2

- ***EZH2*** an epigenetic regulator of gene expression and cell fate decisions¹
- ***EZH2*** is required for normal B-cell biology and germinal center formation²
 - Oncogenic mutations in ***EZH2*** suppress exit from germinal state and “lock” B cells in this state thereby transforming into a cancer²
- ***EZH2*** biology relevant in both mutant (MT) and wild-type (WT) ***EZH2*** FL
 - ~20% of patients with FL also have ***EZH2*** gain of function mutations³



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.

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 <i>EZH2</i> (N=99)	WT <i>EZH2</i> (n=54) ¹	MT <i>EZH2</i> (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* groups¹
- 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 status¹

^aORR, 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.



American Society of Hematology

Ongoing Phase Ib/III Trial of Tazemetostat + Lenalidomide/Rituximab (R²) 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

R

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graph LR; R((R)) --> A[Tazemetostat + R2]; R --> B[Placebo + R2];
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Tazemetostat

+

R²

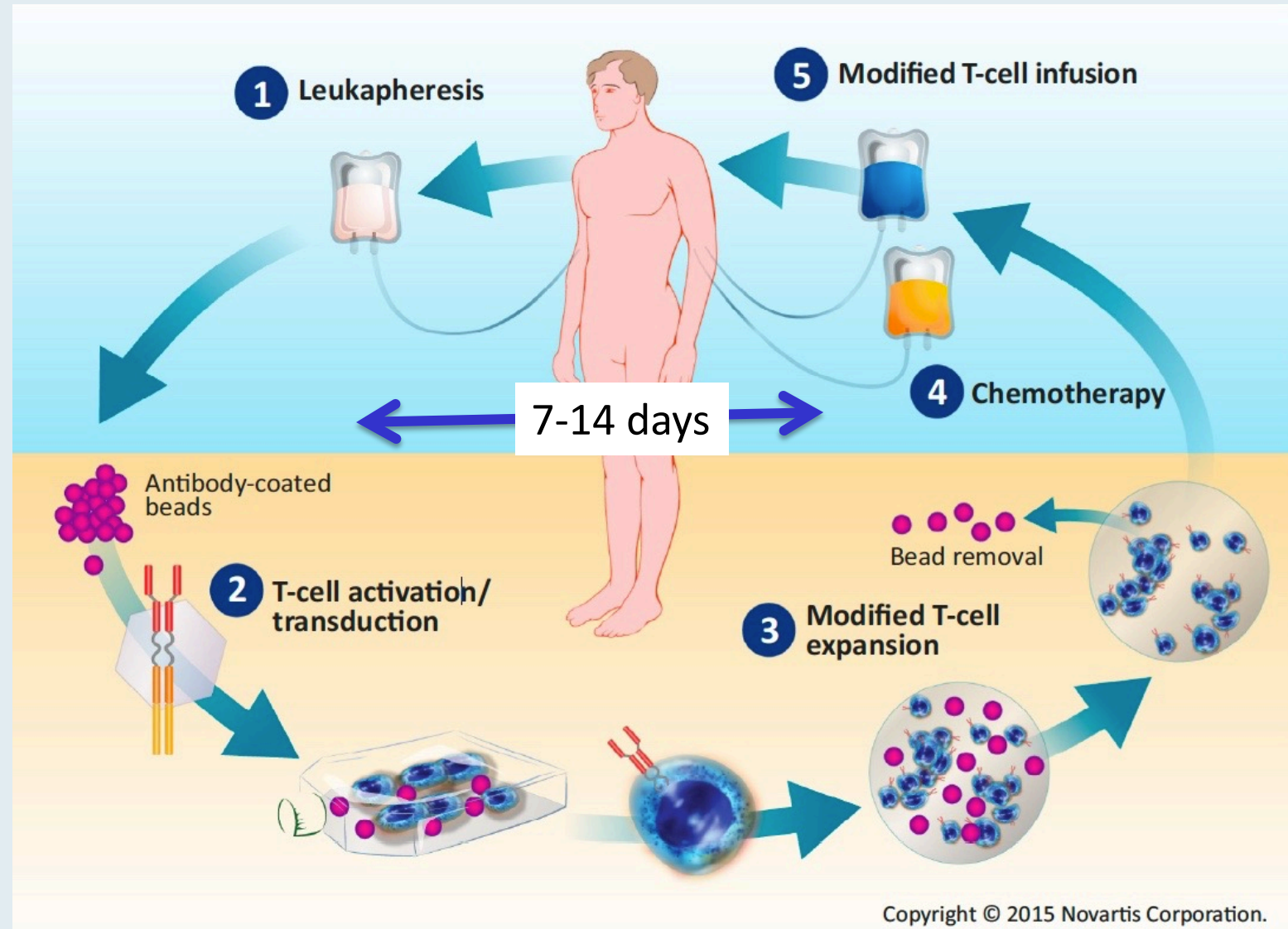
Placebo

+

R²

- Primary endpoint:
 - Stage 1: RP3D of tazemetostat in combination with R²
 - Stage 2: PFS

Overview of CAR T-Cell Therapy



Efficacy and Safety of Tisagenlecleucel in Adult Patients with Relapsed/Refractory Follicular Lymphoma: Interim Analysis of the Phase 2 Elara Trial

Fowler NH et al.

ASH 2020;Abstract 1149.

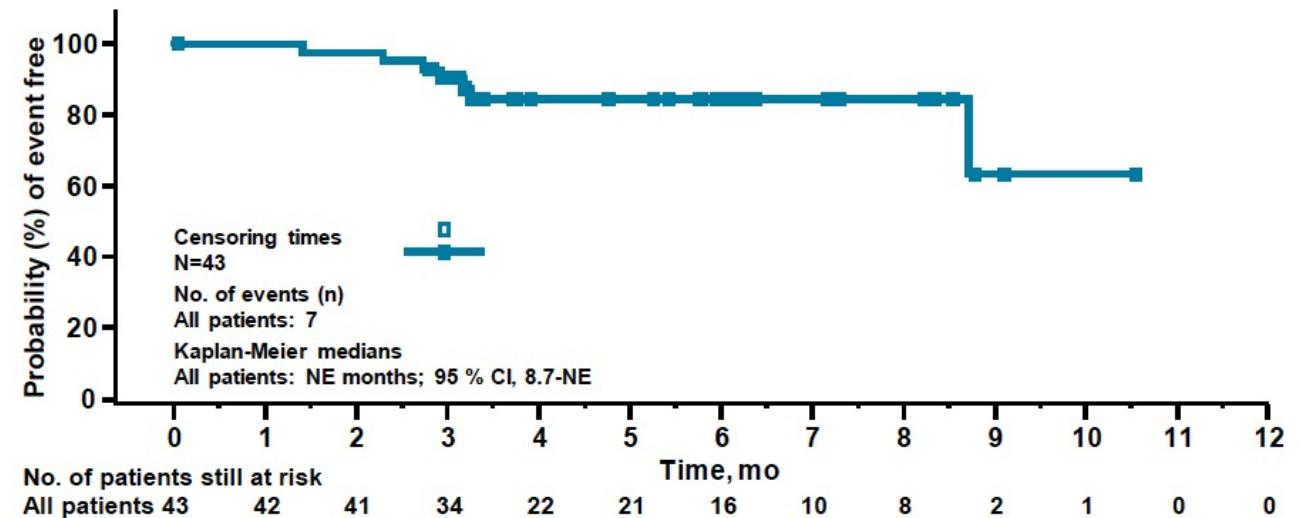
ELARA Interim Analysis: Primary CR Endpoint

Best Overall Response Rate

Response Rate, %	Patients Evaluable for Efficacy ^a (n=52)
CR	65.4 ^a
PR	17.3
ORR (CR + PR)	82.7

- Investigator-assessed CR rate was 67.3%^b (ORR 88.5%)
- ORR was consistent across subgroups, including prior SCT, disease status, and high-risk features

At 10 Months Median Follow-up for Efficacy, Median DOR Not Reached



- Median follow-up for efficacy (n=52): 9.9 months (6.0-15.6)
- Probability for a responding patient to remain in response ≥ 6 months was 84.4%
- 8 of 18 PRs (44%) converted to CRs; all but 1 occurred between Month 3 and Month 6
- Median time to next antilymphoma treatment was not reached
- 69% (36/52) had ongoing responses at the time of data cutoff

ELARA: Overall Safety Profile

Adverse Events, n (%)	Treated Patients N=97
Any AE (all grade)	92 (94.8)
AEs suspected to be drug-related	71 (73.2)
Any SAE	37 (38.1)
Suspected to be drug-related	26 (26.8)
Any grade 3/4 AE	68 (70.1)
Suspected to be drug-related	37 (38.1)
Death	3 (3.1)
Deaths due to study indication	3 (3.1)
Deaths within 30 days post infusion	0

	Treated Patients N=97	
AESI (within 8 weeks of infusion)	All grades, %	Grade ≥3, %
Cytokine release syndrome ^a	48.5	0
Serious neurological adverse reactions	9.3	1.0
Infections	18.6	4.1
Tumor lysis syndrome	1.0	0
Prolonged depletion of B cells/ agammaglobulinemia	9.3	0
Hematologic disorders including cytopenias		
Neutropenia ^{b,c}	28.9	24.7
Anemia ^b	22.7	12.4
Thrombocytopenia ^b	15.5	8.2

- Median onset of neurological events was 8.5 (4-190^d) days
- Only 1 case of serious ICANS within the first 8 weeks
- CRS median onset was 4.0 (1-14) days

- **All neurological and CRS events resolved with appropriate management**

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

Dreyling M et al.

EHA 2021;Abstract S210.

Phase II ELARA Trial: Tisagenlecleucel for Relapsed/Refractory Follicular Lymphoma (FL)

Conclusions

- Tisagenlecleucel demonstrated high rates of durable responses with an ORR of 86% and CR rate of 66%
- Data from the ELARA study suggest that tisagenlecleucel is effective in patients with relapsed/refractory FL (including the high-risk subgroup)
- Safety data are consistent with the established favorable safety profile of tisagenlecleucel
 - No cases of high-grade CRS were reported
 - One case (1%) of high-grade neurotoxicity was reported
 - No treatment-related mortalities were observed
- Tisagenlecleucel is a promising therapy for adult patients with relapsed/refractory FL after ≥ 2 lines of therapy

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.

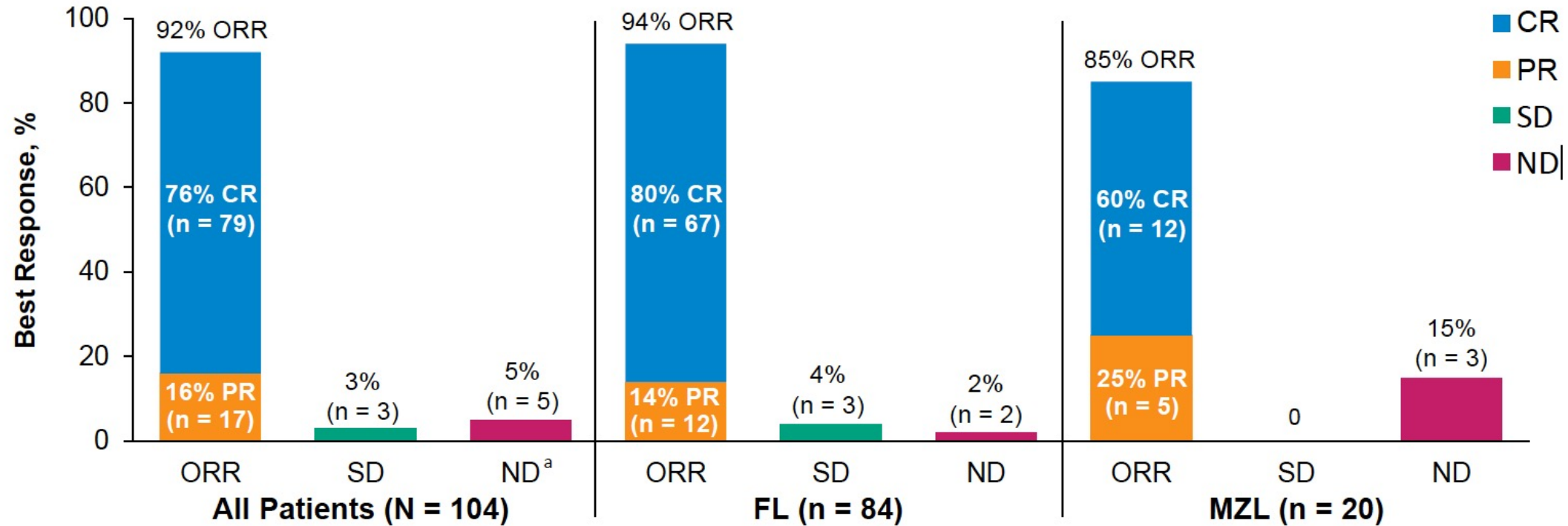
The main efficacy measures were objective response rate (ORR) and duration of response (DOR) as determined by an independent review committee. Among 81 patients in the primary efficacy analysis, the ORR was 91% with a complete remission (CR) rate of 60% and a median time-to-response of 1 month. The median 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%.”

Primary Analysis of Zuma-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-cel) in Patients with Relapsed/Refractory (R/R) Indolent Non-Hodgkin Lymphoma (iNHL)

Jacobson CA et al.

ASH 2020;Abstract 700.

ZUMA-5 Primary Endpoint: ORR by IRRC Assessment



- 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)

A Comparison of Updated Clinical Outcomes from ZUMA-5 (Axicabtagene Ciloleucel) and the International SCHOLAR-5 External Control Cohort in Relapsed/Refractory Follicular Lymphoma (R/R FL)

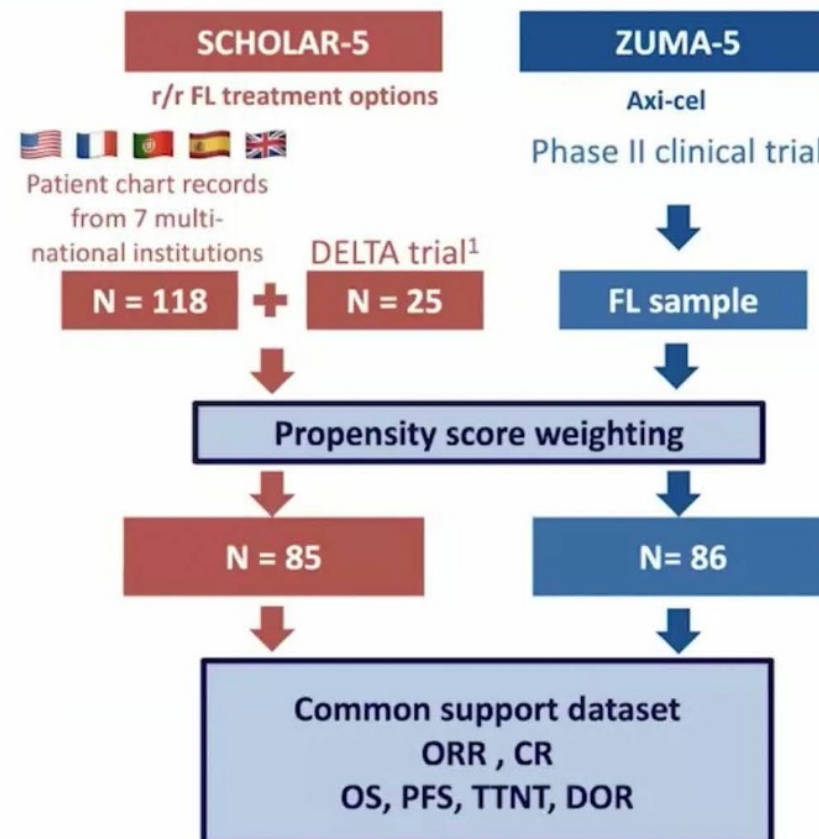
Gribben J et al.

EHA 2021;Abstract LBA1904.

ZUMA-5 Comparison to SCHOLAR-5: Study Design

Study Design

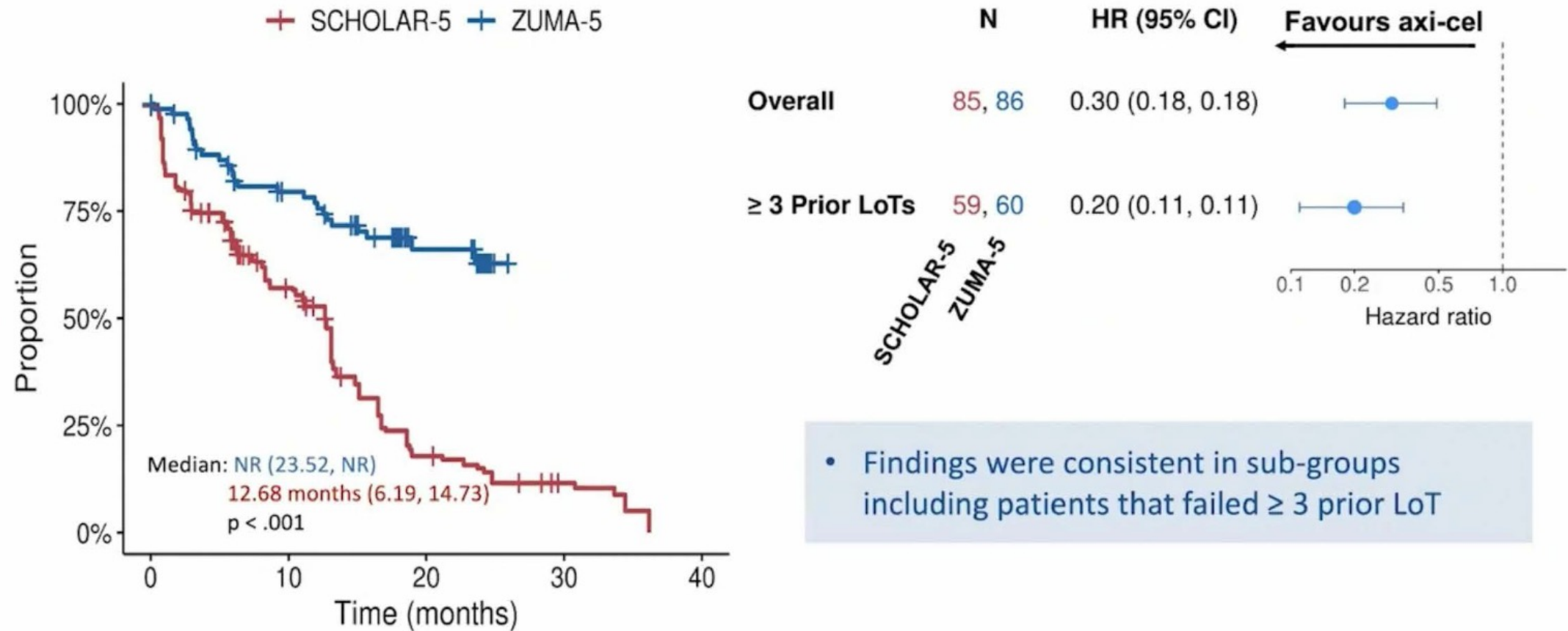
- Cross-study comparisons of a retrospective study versus a prospective clinical trial may be difficult to interpret or prone to bias
- Therefore, propensity score methods were used to create balance between ZUMA-5 and SCHOLAR-5 for a broad set of prognostic covariates
- In the setting of a single-arm study compared to external control data, these methods allow for balanced comparisons



¹Gopal, et al. "PI3K5 inhibition by idelalisib in patients with relapsed indolent lymphoma." New England Journal of Medicine 370.11 (2014): 1008-1018.
axi-cel: axicabtagene ciloleucel; CAR: chimeric antigen receptor; CR: complete response; DOR: duration of response; FL: follicular lymphoma;
ORR: overall response rate; OS, overall survival; PFS: progression-free survival; R/R: relapsed/refractory; TTNT: Time to next treatment.

EHA2021
VIRTUAL

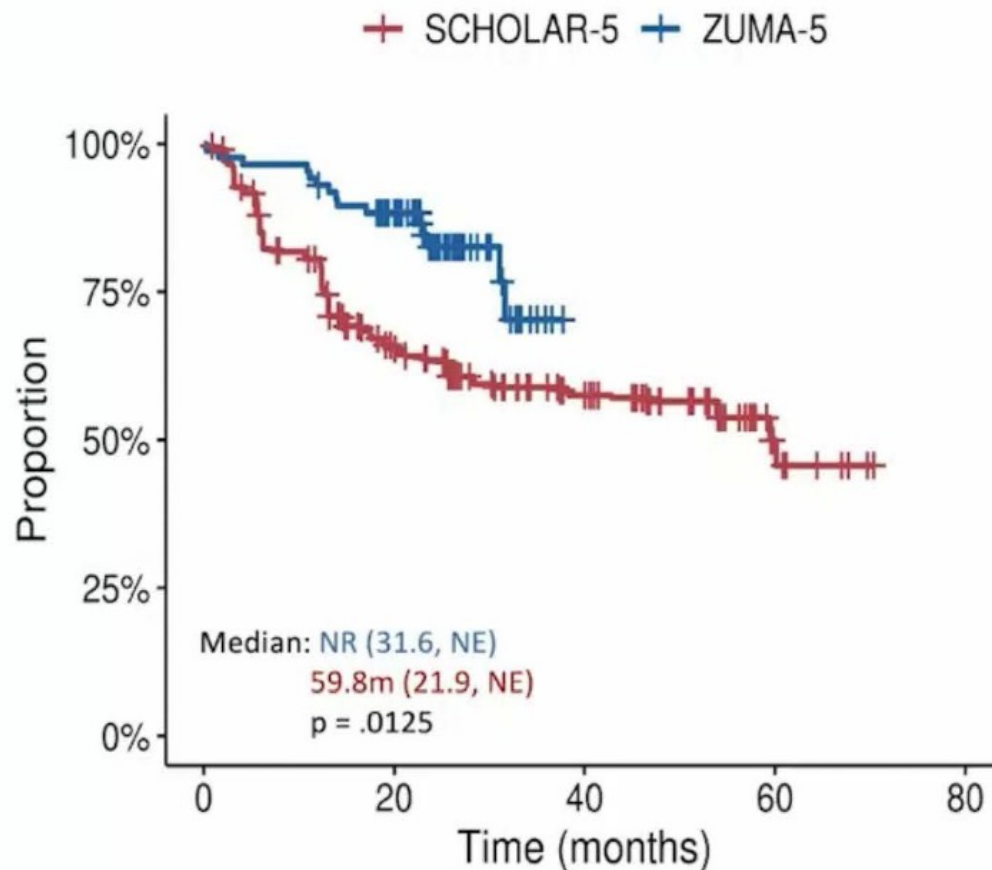
ZUMA-5 Comparison to SCHOLAR-5: Progression-Free Survival



NR = Not reached
Median follow-up time for ZUMA-5 was 23.3 months and for SCHOLAR-5 was 26.2 months



ZUMA-5 Comparison to SCHOLAR-5: Overall Survival



	N	HR (95% CI)	Favours axi-cel
Overall	85, 86	0.42 (0.21, 0.21)	←
≥ 3 Prior LoTs	59, 60	0.31 (0.15, 0.15)	←

SCHOLAR-5
 ZUMA-5

Hazard ratio

- Point estimate HR was improved in sub-group analysis of patients who failed ≥ 3 prior LoT
- Findings were maintained across 5 pre-specified sensitivity analyses



S-5= SCHOLAR-5, Z-5= ZUMA-5
 Median follow-up time for ZUMA-5 was 23.3 months and for SCHOLAR-5 was 26.2 months
 Sensitivity analyses included removal of DELTA trial data, use of matching rather than

EHA2021
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Agenda

Module 1: Diffuse Large B-Cell Lymphoma

- Dr Casulo: A 76-year-old man with advanced-stage diffuse large B-cell lymphoma
- Ms Gideon: A 66-year-old woman with high-grade, Stage IV diffuse large B-cell lymphoma

Module 2: Hodgkin Lymphoma

- Dr Casulo: A 35-year-old woman with advanced-stage Hodgkin lymphoma
- Ms Gideon: A 38-year-old man with relapsed/refractory classical Hodgkin lymphoma

Module 3: Follicular Lymphoma

- Dr Casulo: A 54-year-old woman with recurrent Grade I-II follicular lymphoma
- Ms Gideon: A 69-year-old man with recurrent Grade IIIA follicular lymphoma

Module 4: Mantle Cell Lymphoma

- Dr Casulo: A 64-year-old man with advanced-stage mantle cell lymphoma
- Ms Gideon: A 70-year-old man with relapsed/refractory mantle cell lymphoma

What is generally the most common second-line therapy for patients with mantle cell lymphoma who experience disease progression on first-line BR?

1. A BTK inhibitor (eg, ibrutinib, acalabrutinib, zanubrutinib)
2. Lenalidomide/rituximab
3. Bortezomib
4. Venetoclax
5. I don't know

Acalabrutinib may result in fewer of the toxicities commonly associated with ibrutinib, but it is noteworthy for the occurrence of _____ during the first month of treatment.

1. Hair loss
2. Headache
3. Constipation
4. Visual disturbances
5. I don't know

Case Presentation – Dr Casulo: A 64-year-old man with advanced-stage mantle cell lymphoma

- Initially received BR approximately 7 years ago for advanced stage disease
- Upon disease recurrence he was treated with ibrutinib + checkpoint inhibitor on a clinical trial
- Patient experienced CR and underwent ASCT with remission lasting approximately 3 years
- Upon disease progression, patient entered the Phase II ZUMA-2 trial: Brexucabtagene autoleucel (KTE-X19) for relapsed/refractory MCL
 - Experienced a CR

Case Presentation – Dr Casulo: A 64-year-old man with advanced-stage mantle cell lymphoma (continued)

What tumor-related or clinical factors were most important in influencing your decision to use CAR T-cell therapy for this patient?

1. Patient was previously treated with ibrutinib and ASCT
2. Patient was willing to participate in a clinical trial
3. Patient was young and fit so a good candidate for CAR T-cell therapy

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?

Case Presentation – Ms Gideon: A 70-year-old man with relapsed/refractory mantle cell lymphoma

- 2/2020: Diagnosed with Stage IV MCL
 - Initially treated with R-CHOP x 6
 - Referred for consolidative ASCT
- 10/8/2020: Presented with leptomeningeal disease
 - Ibrutinib (560 mg qd) initiated
- 12/24/20: Venetoclax ramp-up initiated for disease progression on ibrutinib (ibrutinib continued)
- 1/20/21: Initiated leukapheresis for CAR T-cell therapy (while on ibrutinib and venetoclax)
- 2/7/21: Patient received brexucabtagene autoleucel infusion
 - G1 CRS and G3 ICANS requiring 3 doses tocilizumab and high dose steroids
- 3/17/21: Day 30 PET/CT and brain MRI:
 - PR w/ some residual disease in left inguinal region which is likely inflammatory in nature; CSF NED

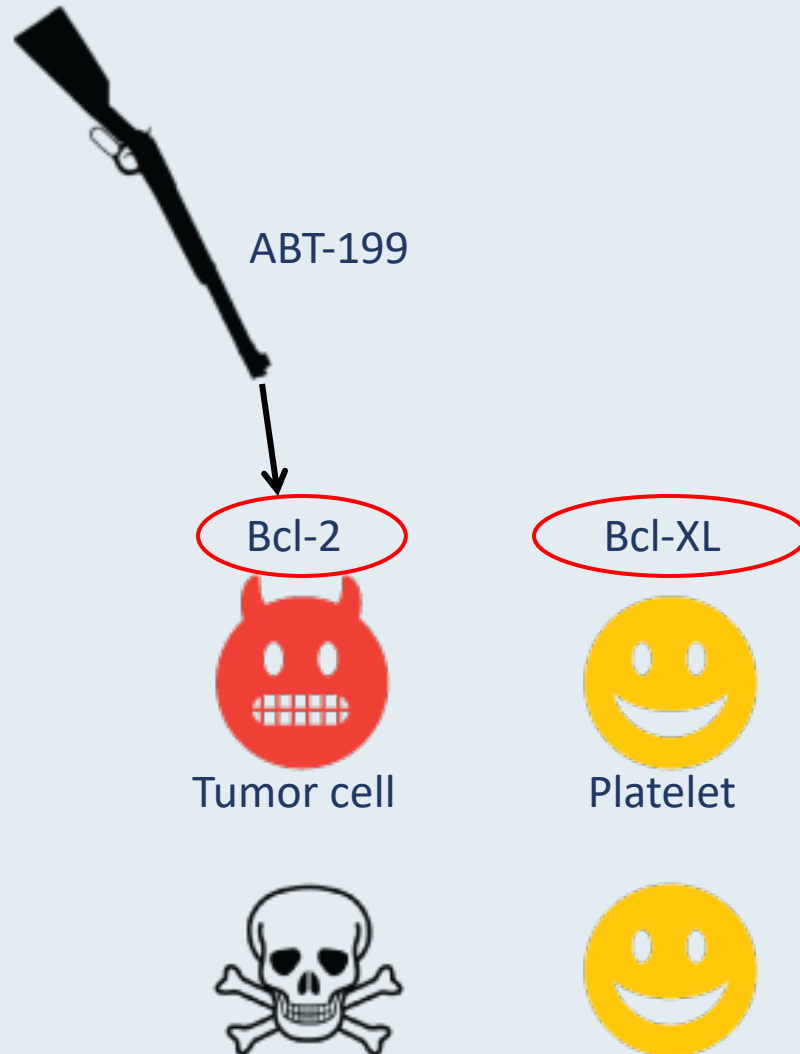
Case Presentation – Ms Gideon: A 70-year-old man with relapsed/refractory mantle cell lymphoma (continued)

What education issues did you discuss with this patient or do you generally discuss with patients with MCL who are about to begin treatment with CAR T-cell therapy?

- Typically discuss toxicities unique to CAR T-cell therapy including CRS and neurotoxicity; outline the follow-up schedule and required outpatient visits after hospital discharge
- Need for 24/7 caregiver support, must be within 2 hours of treating institution for 4 weeks following the infusion
- Unable to drive for 8 weeks post infusion (this particular patient was not driving at the time given PN, but given frequent follow-up, required a lot of coordination for transportation to clinic given that his mother does not drive long distances and sisters had to return to work)

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 Venetoclax (ABT-199)



- Bcl-2 functions to prevent cell death by apoptosis
- Venetoclax is specific for Bcl-2 and inhibits its function, thereby removing the block on apoptosis

Venetoclax Monotherapy for BTK Inhibitor-Resistant MCL: Results Summary

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

No cases of clinical TLS were observed.

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

Expert Second Opinion: HER2-Positive Breast Cancer

**Tuesday, June 22, 2021
5:00 PM – 6:00 PM ET**

Faculty

**Erika Hamilton, MD
Ian E Krop, MD, PhD
Joyce O'Shaughnessy, MD**

Moderator

Neil Love, MD

Thank you for joining us!

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