Consensus or Controversy? Clinical Investigator Perspectives on the Current and Future Management of Mantle Cell, Diffuse Large B-Cell and Hodgkin Lymphoma

Monday, August 2, 2021
5:00 PM – 6:00 PM ET

Faculty

Stephen M Ansell, MD, PhD
Craig Moskowitz, MD
Laurie H Sehn, MD, MPH

Moderator

Neil Love, MD

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Faculty

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

Laurie H Sehn, MD, MPH
Chair, Lymphoma Tumour Group
BC Cancer Centre for Lymphoid Cancer
Clinical Professor of Medicine
Division of Medical Oncology
University of British Columbia
Associate Editor, *Blood*
Vancouver, British Columbia, Canada

Craig Moskowitz, MD
Physician in Chief, Oncology Service Line
Sylvester Comprehensive Cancer Center
Professor of Medicine, Miller School of Medicine
University of Miami Health System
Miami, Florida

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Commercial Support

This activity is supported by educational grants from AbbVie Inc, Adaptive Biotechnologies Corporation, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Genentech, a member of the Roche Group, GlaxoSmithKline, Incyte Corporation, Oncopeptides, Pharmacyclics LLC, an AbbVie Company and Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Sanofi Genzyme, Seagen Inc, and Takeda Oncology.

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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Dr Ansell — Disclosures

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Dr Moskowitz — Disclosures

No relevant conflicts of interest to disclose.

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Dr Sehn — Disclosures

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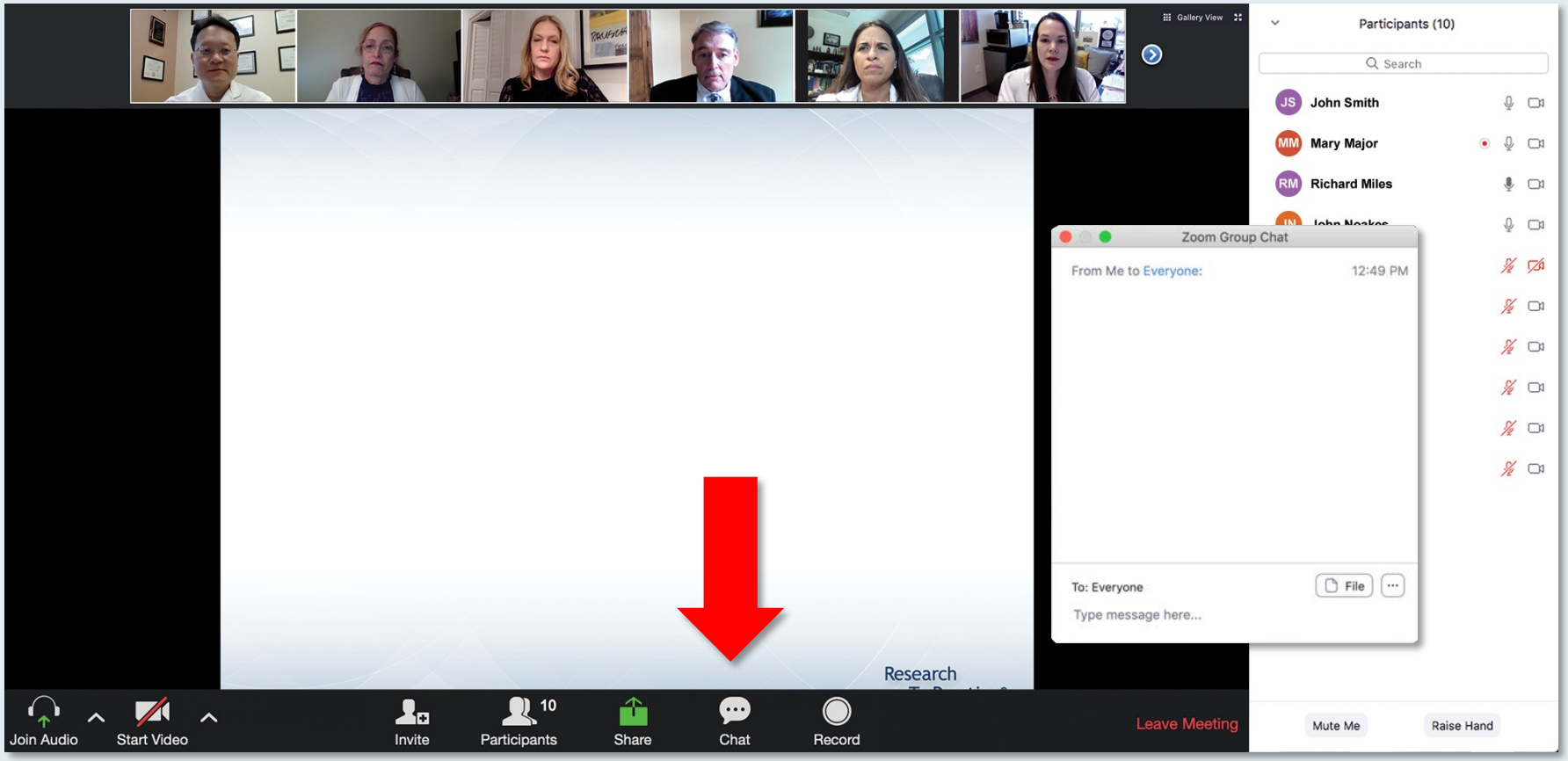
We Encourage Clinicians in Practice to Submit Questions



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

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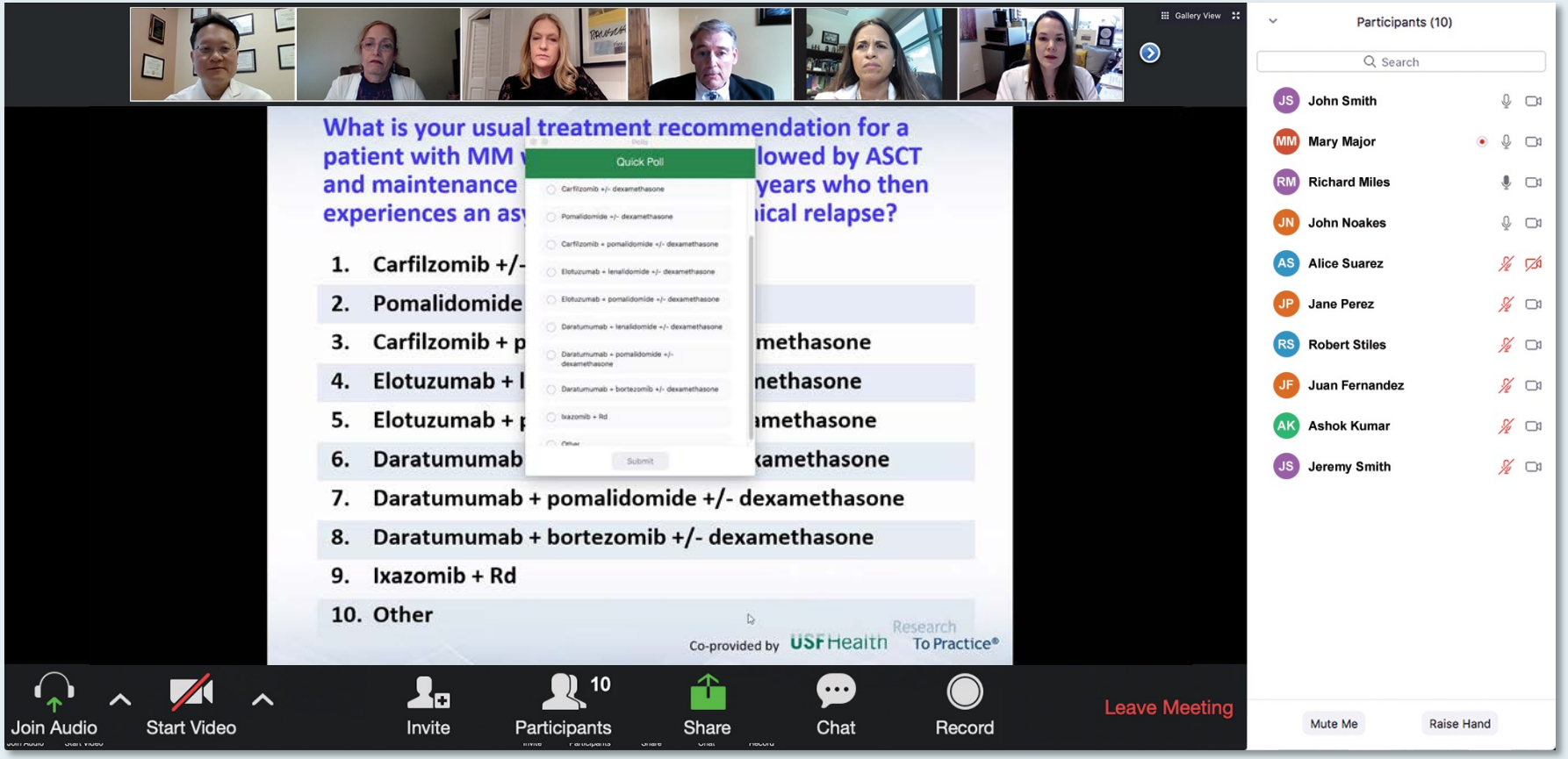
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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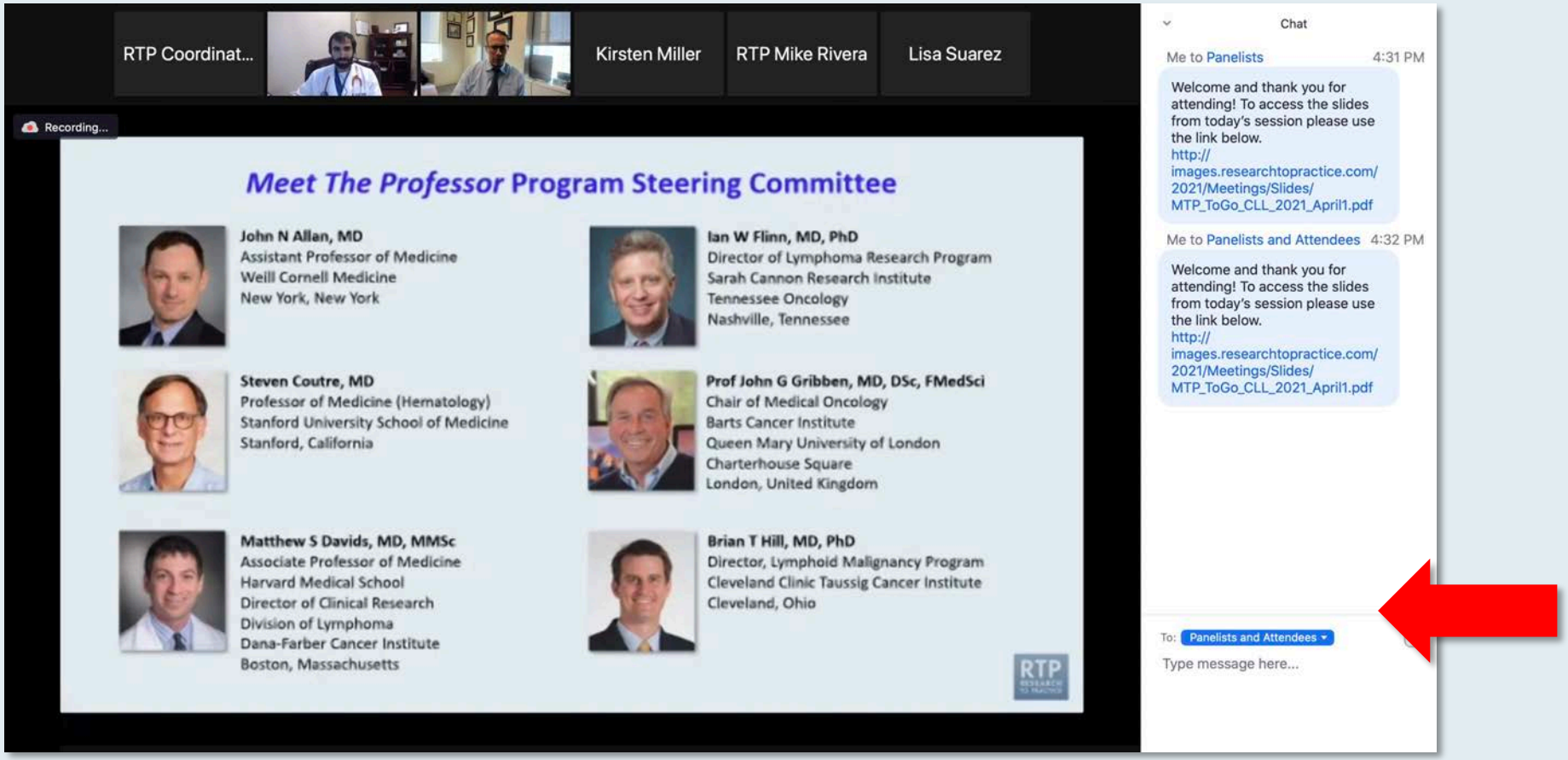
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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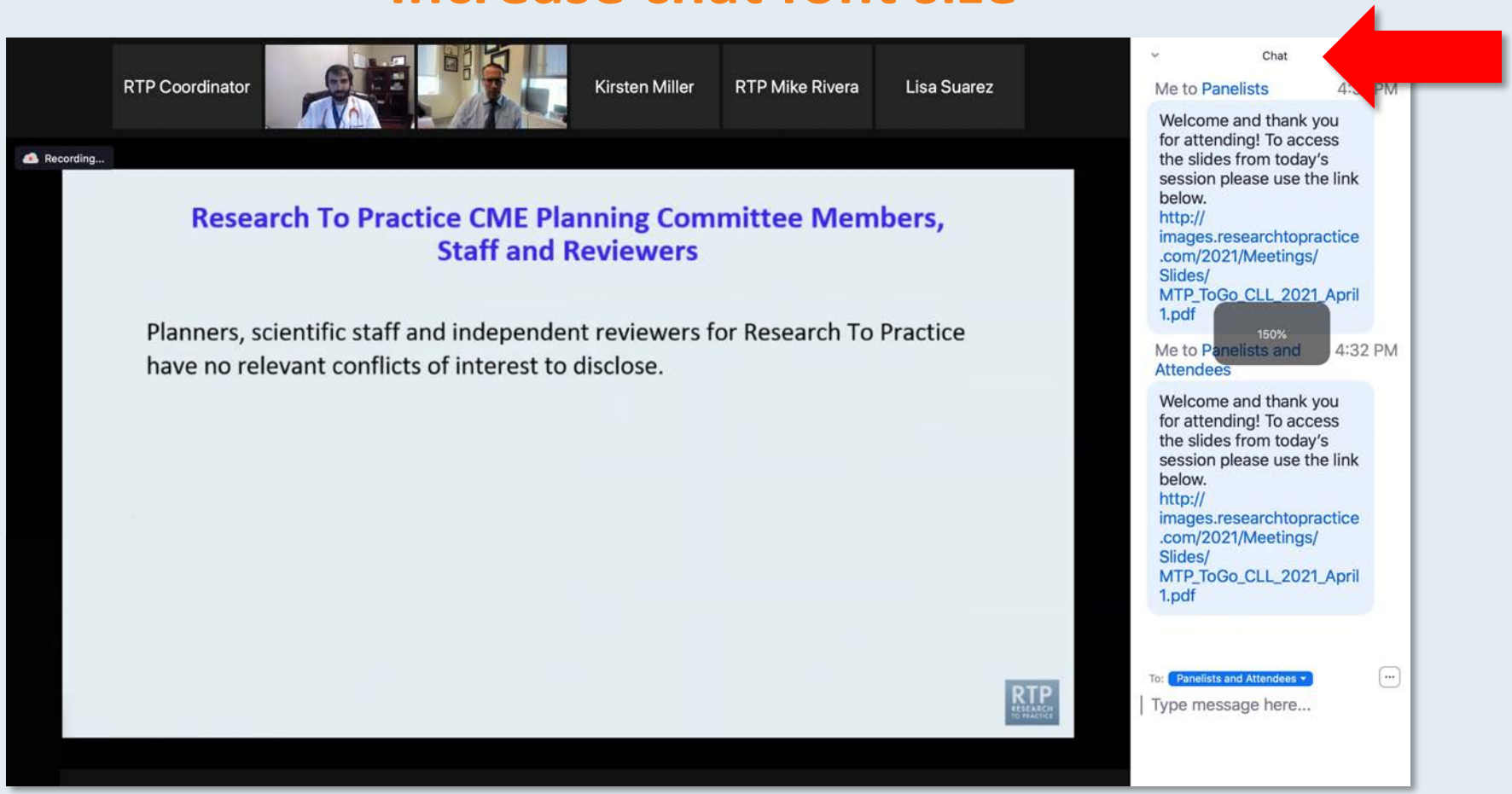
Familiarizing Yourself with the Zoom Interface

Increase chat font size



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

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WITH DR NEIL LOVE

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

DR LAURIE SEHN

BC CANCER CENTRE FOR LYMPHOID CANCER

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

A Live Webinar Series Held in Conjunction with the 2021 ASCO Annual Meeting

Mantle Cell, Diffuse Large B-Cell and Hodgkin Lymphoma
Monday, August 2
5:00 PM – 6:00 PM ET

Hepatocellular Carcinoma and Pancreatic Cancer
Wednesday, August 4
5:00 PM – 6:30 PM ET

Colorectal and Gastroesophageal Cancers
Tuesday, August 3
5:00 PM – 6:30 PM ET

Head and Neck Cancer
Wednesday, August 11
5:00 PM – 6:00 PM ET

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Consensus or Controversy? Clinical Investigator Perspectives on the Current and Future Management of Colorectal and Gastroesophageal Cancers

Tuesday, August 3, 2021
5:00 PM – 6:30 PM ET

Faculty

Chloe E Atreya, MD, PhD
Dustin Deming, MD
Eric Van Cutsem, MD, PhD
Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Consensus or Controversy? Clinical Investigator Perspectives on the Current and Future Management of Hepatocellular Carcinoma and Pancreatic Cancer

Wednesday, August 4, 2021
5:00 PM – 6:30 PM ET

Faculty

Tanios Bekaii-Saab, MD
Kim A Reiss Binder, MD
Eileen M O'Reilly, MD
Philip A Philip, MD, PhD, FRCP

Moderator

Neil Love, MD

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Meet The Professor

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

Friday, August 6, 2021
12:00 PM – 1:00 PM ET

Faculty

Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

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Three Exciting Educational Events Held in Conjunction with the 2021 Pan Pacific Lymphoma Conference

In Partnership with the University of Nebraska Medical Center

Expert Second Opinion — Acute Myeloid Leukemia and Myelodysplastic Syndromes

Monday, August 9, 2021
7:00 PM – 8:30 PM ET

Faculty
Krishna Gundabolu, MD
Richard M Stone, MD
Eunice S Wang, MD

Moderator
Harry Paul Erba, MD, PhD

Beyond the Guidelines — Chronic Lymphocytic Leukemia

Tuesday, August 10, 2021
7:00 PM – 9:00 PM ET

Faculty
Alexey V Danilov, MD, PhD
Susan O'Brien, MD
Sonali M Smith, MD
Julie M Vose, MD, MBA

Moderator
Matthew S Davids, MD, MMSc

Cases from the Community — Multiple Myeloma

Thursday, August 12, 2021
7:00 PM – 8:30 PM ET

Faculty
Muhamed Baljevic, MD
Joseph Mikhael, MD
Nina Shah, MD

Moderator
Robert Z Orlowski, MD, PhD

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Meet The Professor

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

Tuesday, August 10, 2021
12:00 PM – 1:00 PM ET

Faculty

Karen A Gelmon, MD

Moderator

Neil Love, MD

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A Conversation with the Investigators: Perspectives on the Management of Head and Neck Cancer

Wednesday, August 11, 2021
5:00 PM – 6:00 PM ET

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Barbara Burtness, MD
Ezra Cohen, MD
Robert L Ferris, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 2-3 business days.

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Consensus or Controversy Consulting Investigators

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Ian W Flinn, MD, PhD

Christopher R Flowers, MD, MS

John P Leonard, MD

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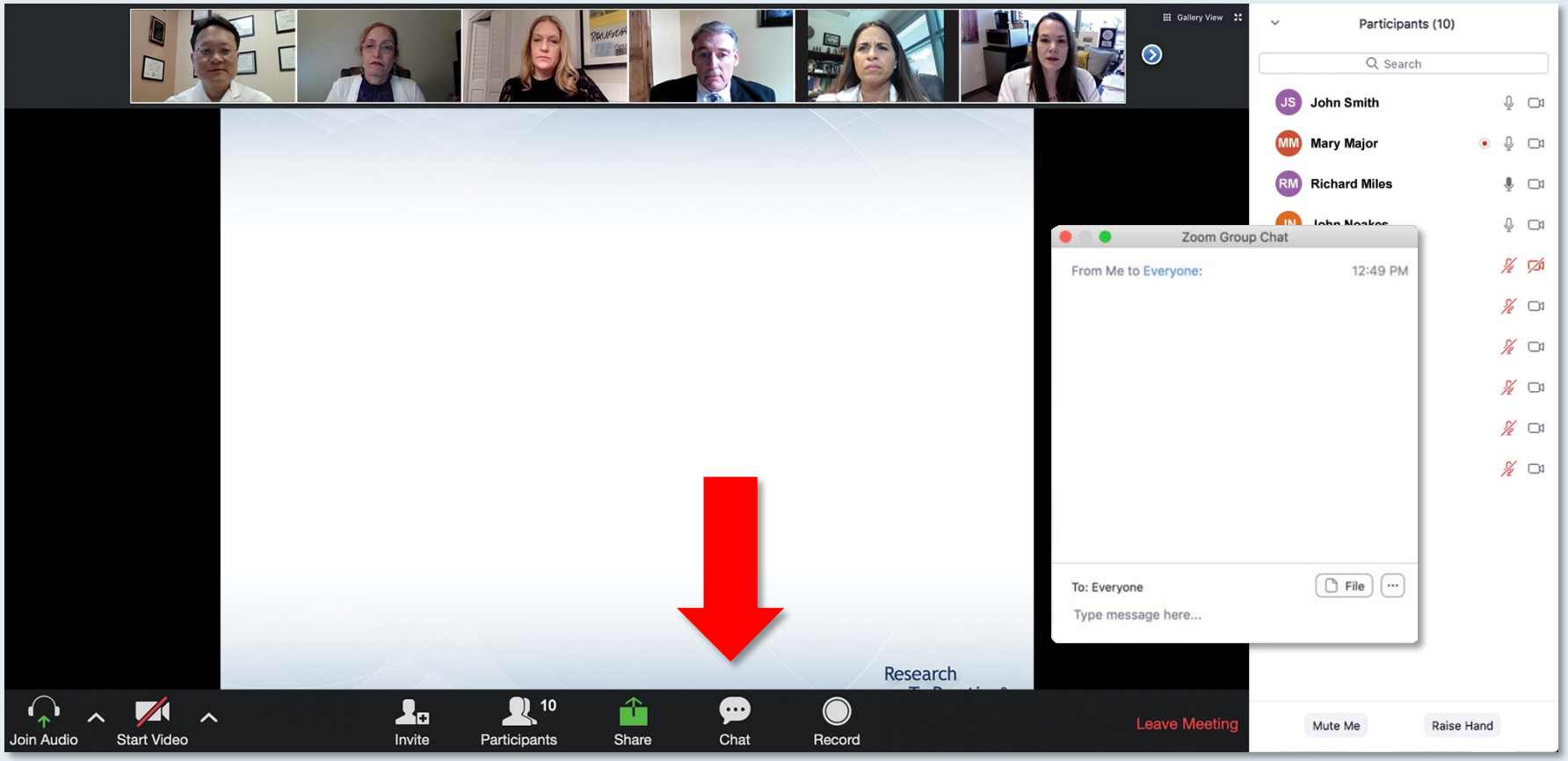

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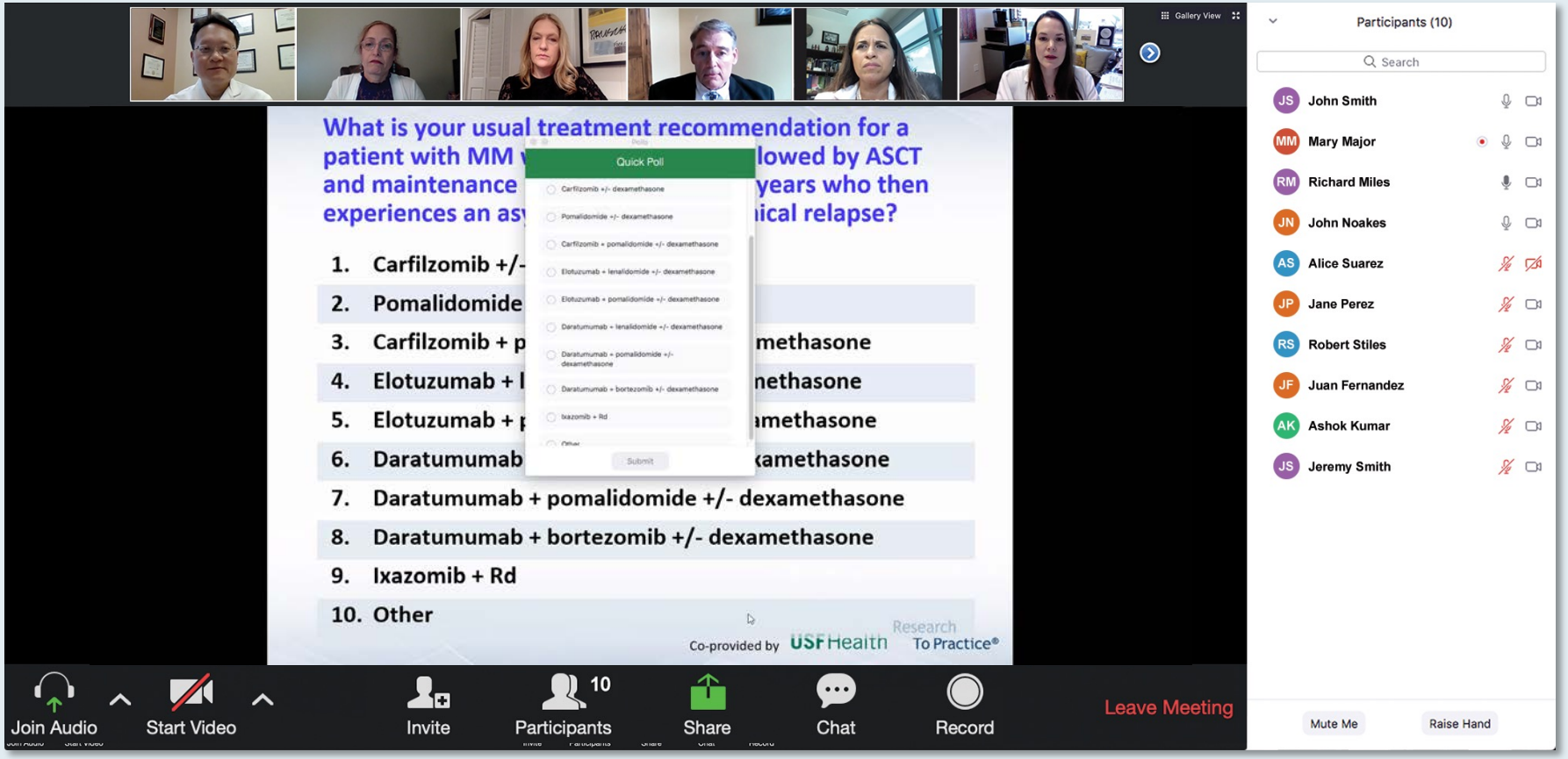

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ASCO 2021 Mantle Cell, Diffuse Large B-Cell and Hodgkin Lymphoma Presentation Library

Mantle Cell Lymphoma

Laurie H Sehn, MD, MPH

Download Slides

Diffuse Large B-Cell Lymphoma

Stephen M Ansell, MD, PhD

Download Slides

Hodgkin Lymphoma

Craig Moskowitz, MD

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Agenda

Module 1: Mantle Cell Lymphoma (MCL)

- What is your current approach to second-line treatment of MCL?
- How do you currently integrate venetoclax into the management of progressive MCL?
- Do you approach the management of MCL differently for patients with TP53-mutated disease?

Module 2: Diffuse Large B-Cell Lymphoma (DLBCL)

- How does CAR T-cell therapy currently fit into your management of DLBCL?
- At this point, are there discernible clinical differences in the 3 available CAR T-cell products for DLBCL?
- Aside from CAR T-cell therapy, how do you approach sequencing of the other agents and regimens available for second-line treatment and beyond in DLBCL?

Module 3: Hodgkin Lymphoma (HL)

- How do you select up-front systemic treatment for younger patients with advanced-stage HL?
- How do you select up-front systemic treatment for elderly patients with advanced-stage HL?

Agenda

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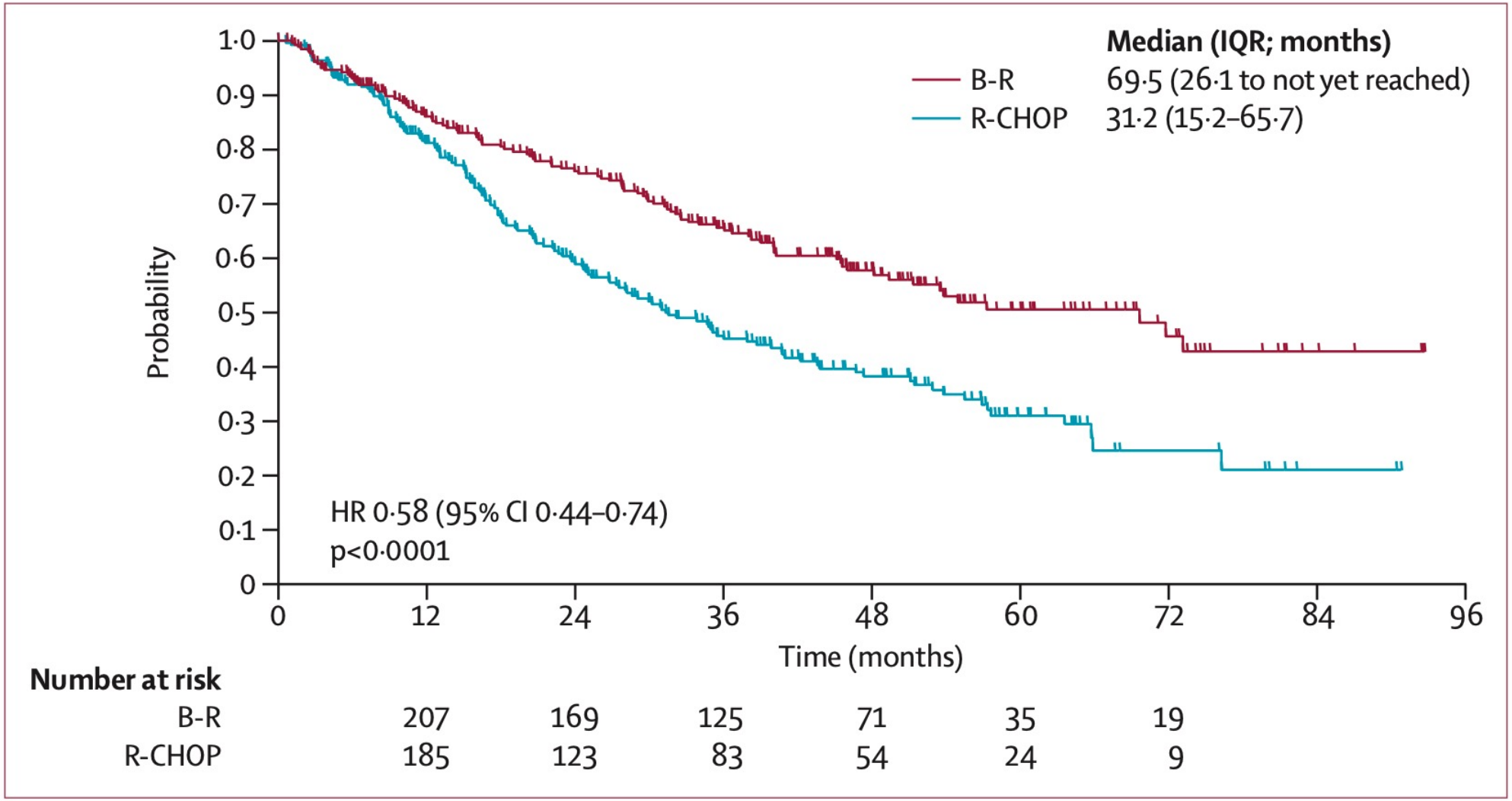
- How do you select up-front systemic treatment for younger patients with advanced-stage HL?
- How do you select up-front systemic treatment for elderly patients with advanced-stage HL?

Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: an open-label, multicentre, randomised, phase 3 non-inferiority trial

Mathias J Rummel, Norbert Niederle, Georg Maschmeyer, G Andre Banat, Ulrich von Grünhagen, Christoph Losem, Dorothea Kofahl-Krause, Gerhard Heil, Manfred Welslau, Christina Balser, Ulrich Kaiser, Eckhart Weidmann, Heinz Dürk, Harald Ballo, Martina Stauch, Fritz Roller, Juergen Barth, Dieter Hoelzer, Axel Hinke, Wolfram Brugger, on behalf of the Study group indolent Lymphomas (StiL)

***Lancet* 2013;381(12):1203-10.**

BR versus R-CHOP: Progression-Free Survival



Rummel MJ et al. *Lancet* 2013;381(12):1203-10.

What is your current approach to second-line treatment of MCL?

Dr Jeff Sharman

Dr Ian Flinn

Dr Christopher Flowers

Dr John Leonard

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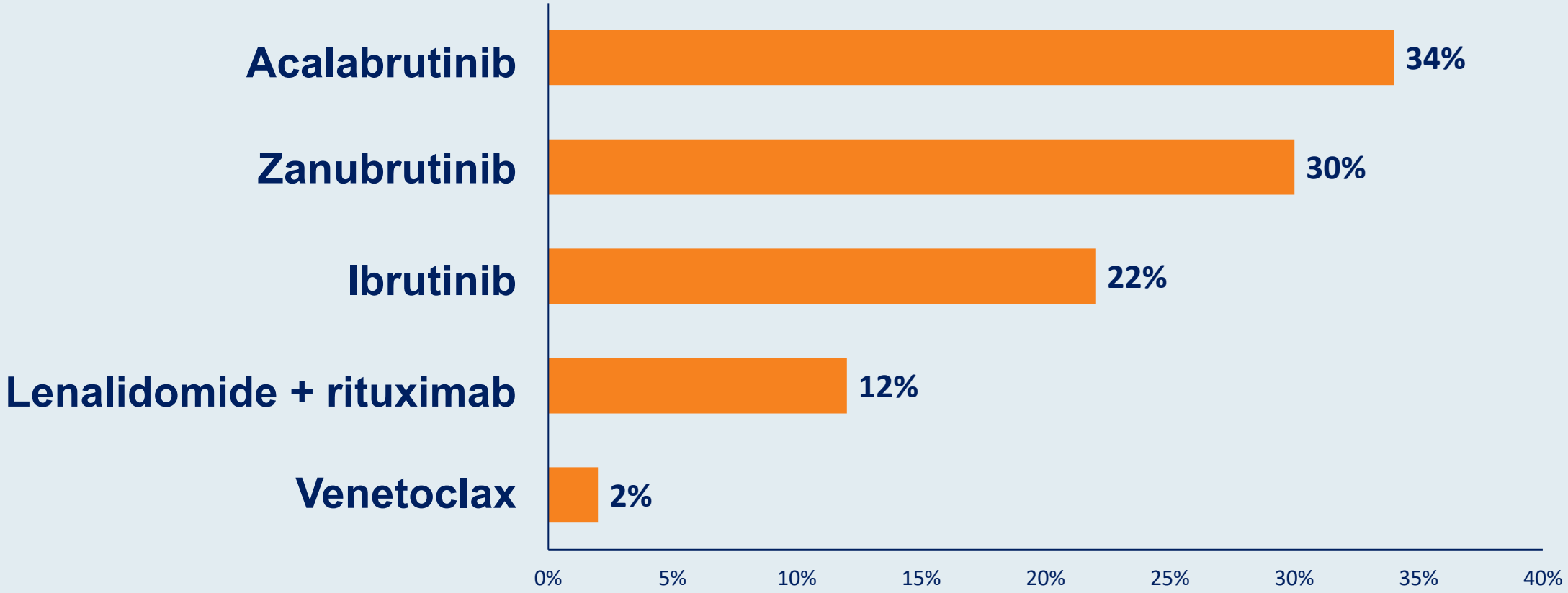
A 78-year-old patient with MCL initially treated with BR followed by 2 years of rituximab maintenance experiences disease relapse 3 years later. What would you recommend?



Premeeting survey: July 2021

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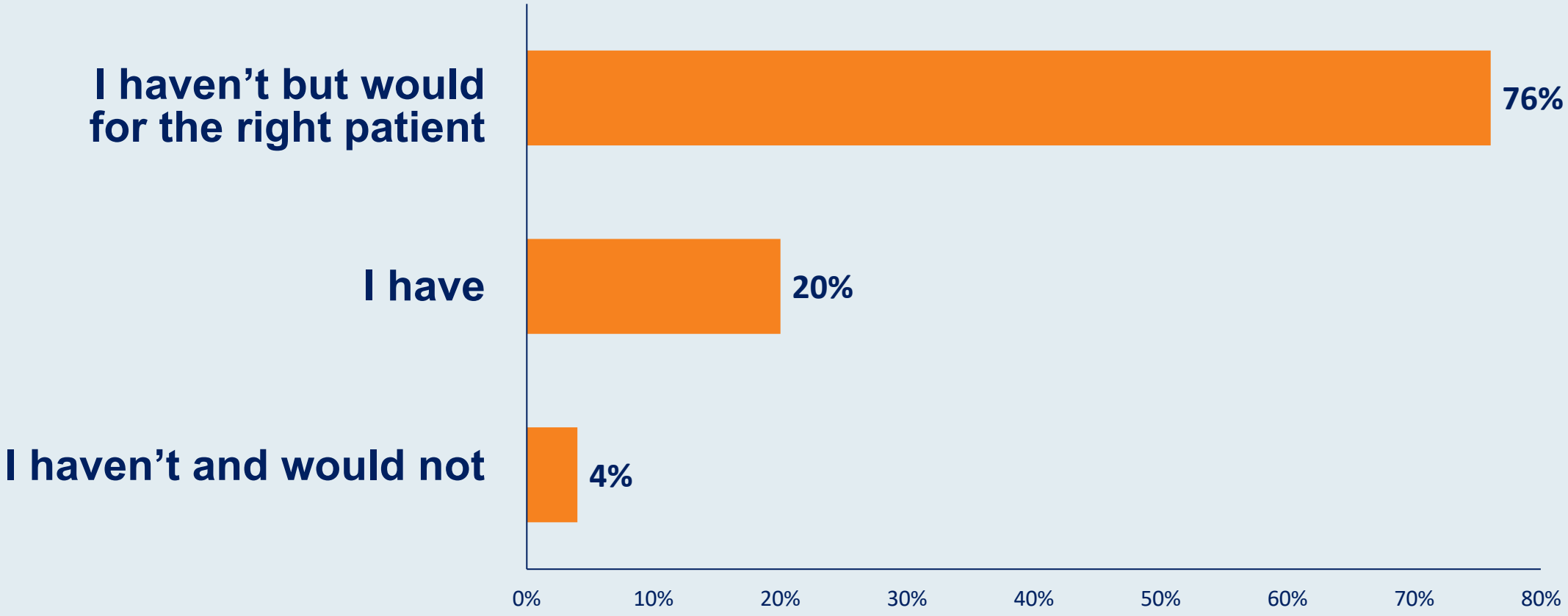
A 78-year-old patient with mantle cell lymphoma (MCL) initially treated with bendamustine/rituximab (BR) followed by 2 years of maintenance rituximab experiences disease relapse 3 years later. What would you recommend?

 Dr Ansell	Acalabrutinib	 Dr Flowers	Acalabrutinib
 Dr Moskowitz	Acalabrutinib	 Prof Gribben	Acalabrutinib
 Dr Sehn	Acalabrutinib	 Dr Kahl	Zanubrutinib
 Dr Fowler	Acalabrutinib	 Dr Leonard	Acalabrutinib
 Dr Flinn	Acalabrutinib Zanubrutinib	 Dr Sharman	Zanubrutinib

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



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

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

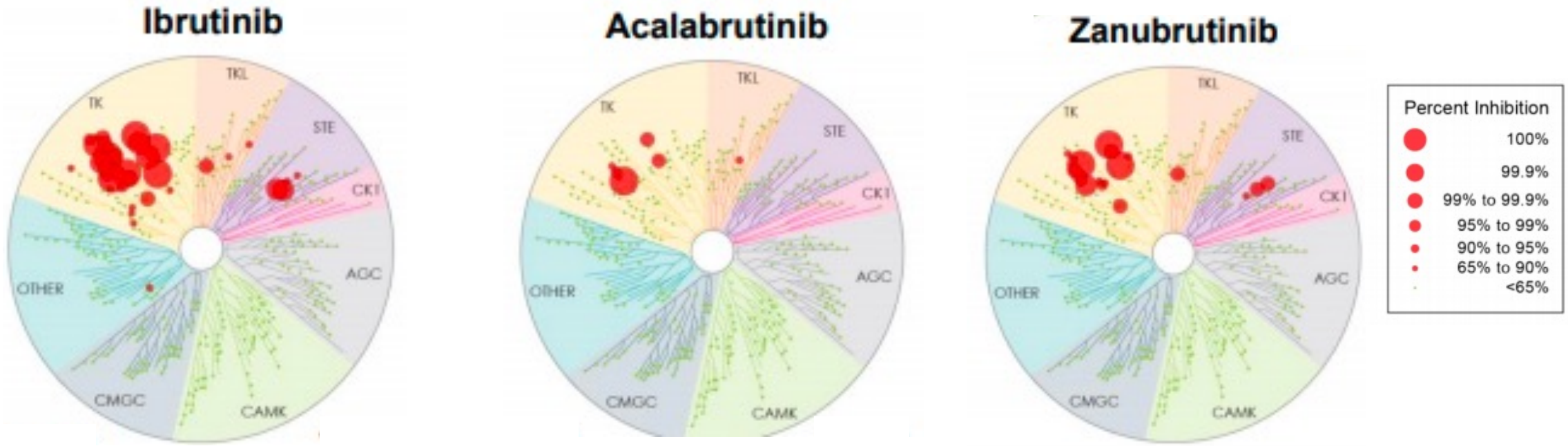
 Dr Ansell	I have	 Dr Flowers	I have
 Dr Moskowitz	I have	 Prof Gribben	I have
 Dr Sehn	I have	 Dr Kahl	I haven't but would for the right patient
 Dr Fowler	I have	 Dr Leonard	I haven't but would for the right patient
 Dr Flinn	I haven't but would for the right patient	 Dr Sharman	I have

Do you believe that there are discernible differences in terms of efficacy or tolerability that make one of the three FDA-approved BTK inhibitors for MCL a better therapeutic option?

	Ibrutinib (median 3 prior tx)	Acalabrutinib (median 2 prior tx)	Zanabrutinib (median 2 prior tx)
Efficacy			
ORR	68%	81%	84%
CR	21%	43%	69%
Median PFS (m)	13.9	20	22
Pooled Safety Data			
Headache, any (grade ≥3)	10% (0%)	42% (2%)	4% (NR)
Diarrhea, any (grade ≥3)	40% (4%)	38% (2%)	18% (1%)
Hypertension, grade ≥3	5%	<3%	3%
Atrial Fibrillation, any (grade ≥3)	11% (6%)	2% (1%)	2% (1%)
Bleeding, serious or grade ≥3	5%	3%	3%
Discontinuation due to AEs	10%	6%	10%

- **No comparative trials, all agents effective**
- **Second generation drugs likely have improved safety profile**

FDA-Approved BTK Inhibitors in Relapsed MCL



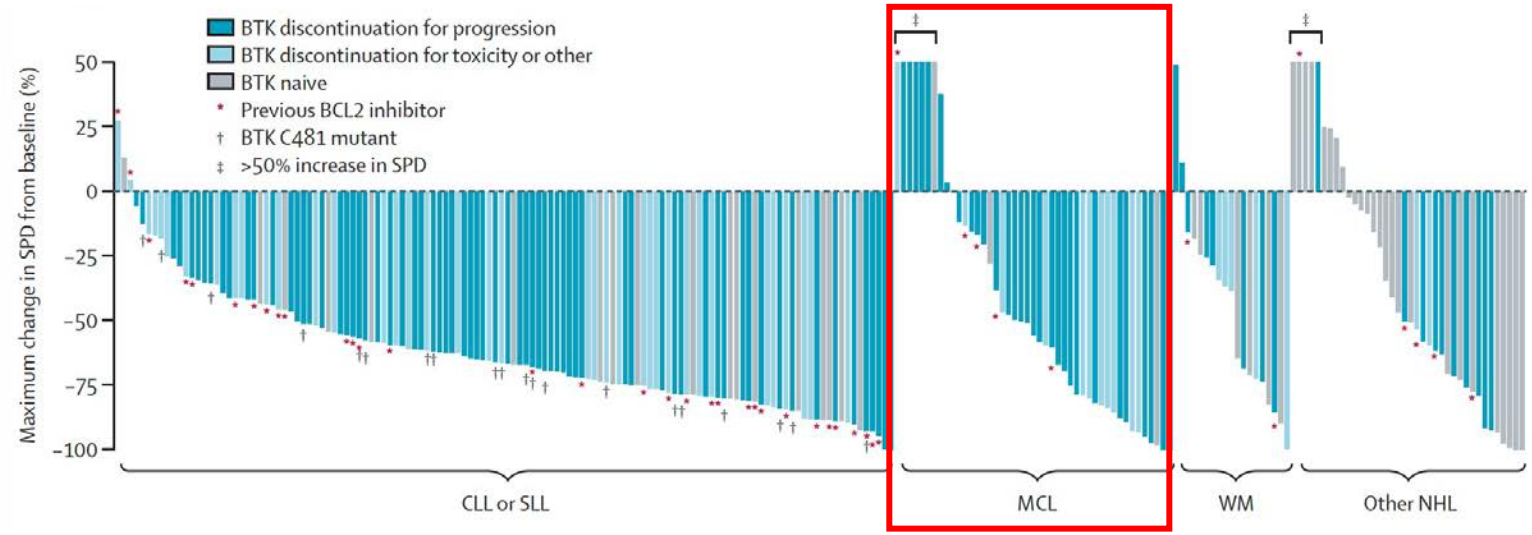
Second generation BTKi were designed to maximize BTK occupancy and minimize off-target inhibition of TEC- and EGFR-family kinases

Kaptein A et al, ASH 2018. Abstract 1871.

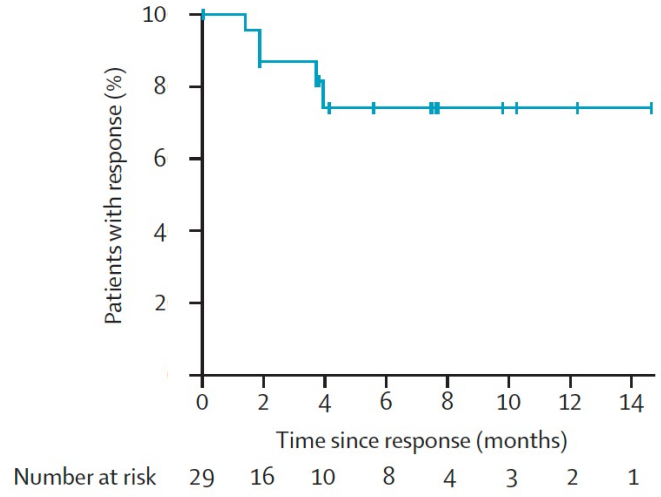
Courtesy of Laurie H Sehn MD, MPH

BRUIN: Pirtobrutinib (LOXO-305) Efficacy

Change in tumor burden from baseline



Duration of Response (MCL)



MCL	Number of previous lines of therapy	Treated	Efficacy evaluable	Responders	ORR
All patients	3 (2-4)	61	56	29	52% (38-65)
Patients who received at least a BTK inhibitor	3 (2-4)	57	52	27	52% (38-66)

Mato AR, et al. *Lancet.* 2021;397:892-901.

Courtesy of Laurie H Sehn MD, MPH

How do you currently integrate venetoclax into the management of progressive MCL?

Dr Jeff Sharman

Dr Ian Flinn

Dr Christopher Flowers

Dr John Leonard

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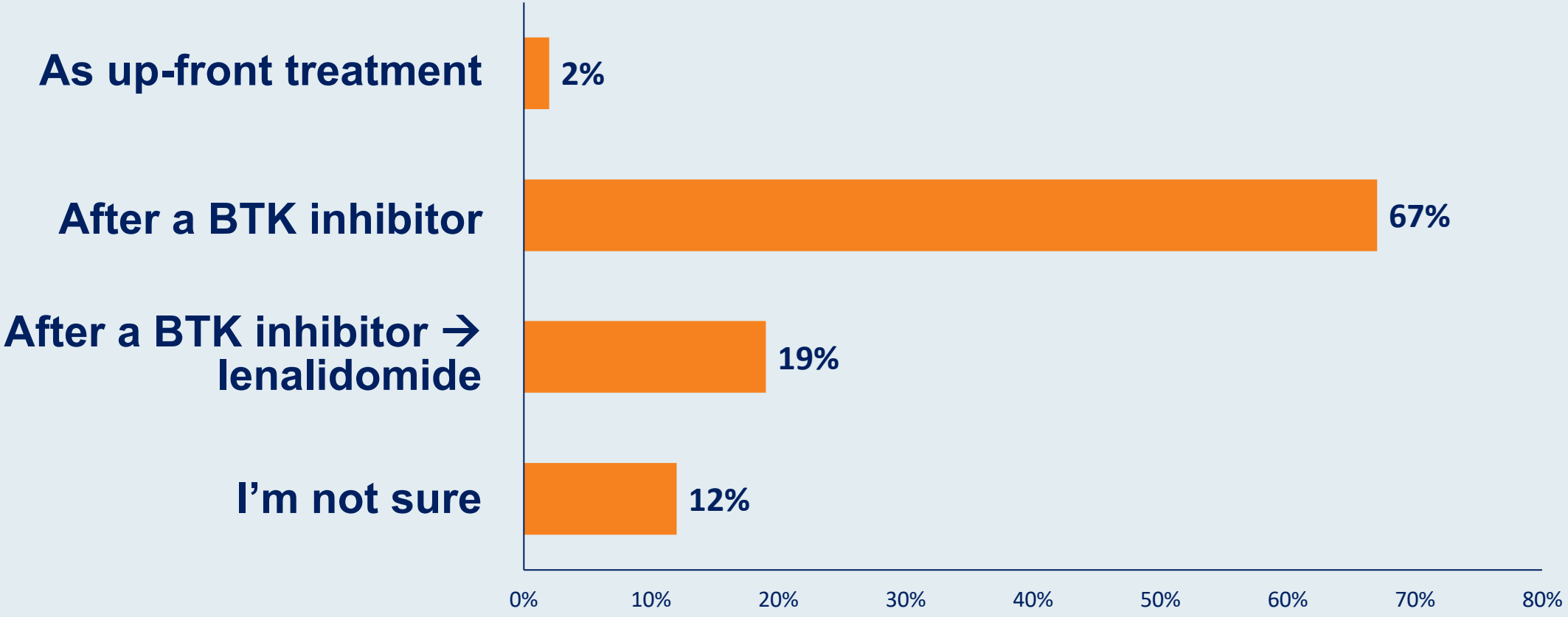
Outside of a clinical trial setting, where in the treatment sequence is the appropriate time to administer venetoclax to a patient with relapsed MCL?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

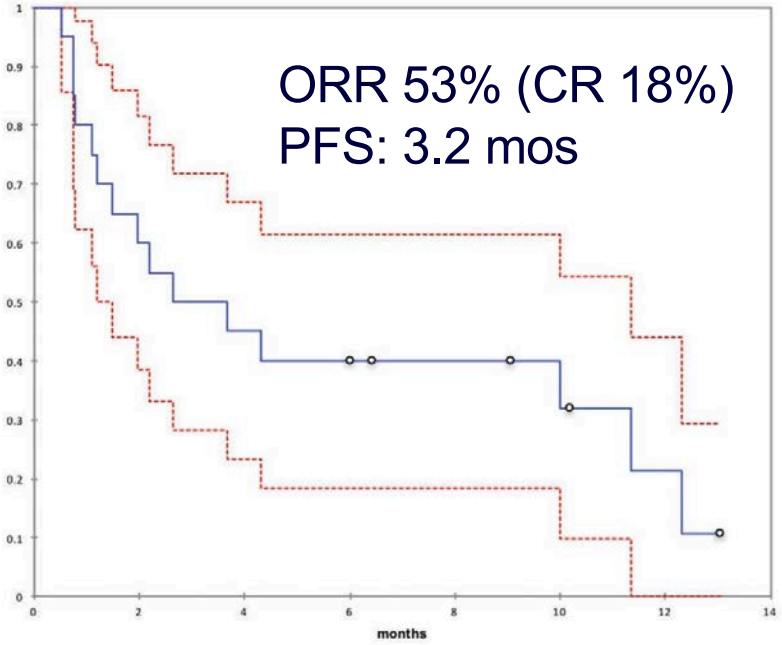
Outside of a clinical trial setting, where in the treatment sequence is the appropriate time to administer venetoclax to a patient with relapsed MCL?

 Dr Ansell	After a BTK inhibitor	 Dr Flowers	After a BTK inhibitor
 Dr Moskowitz	As a bridge to CAR T-cell therapy or allo-transplant	 Prof Gribben	After a BTK inhibitor
 Dr Sehn	Consider 3rd line after chemoimmune therapy, BTK inhibitor and CAR T-cell therapy	 Dr Kahl	After a BTK inhibitor → lenalidomide
 Dr Fowler	After a BTK inhibitor → lenalidomide	 Dr Leonard	After a BTK inhibitor XX in some cases
 Dr Flinn	After a BTK inhibitor → lenalidomide if not CAR-T candidate	 Dr Sharman	After a BTK inhibitor and R^2 for CAR-T ineligible

Outside of a clinical trial setting, where in the treatment sequence is the appropriate time to administer venetoclax to a patient with relapsed/refractory MCL?

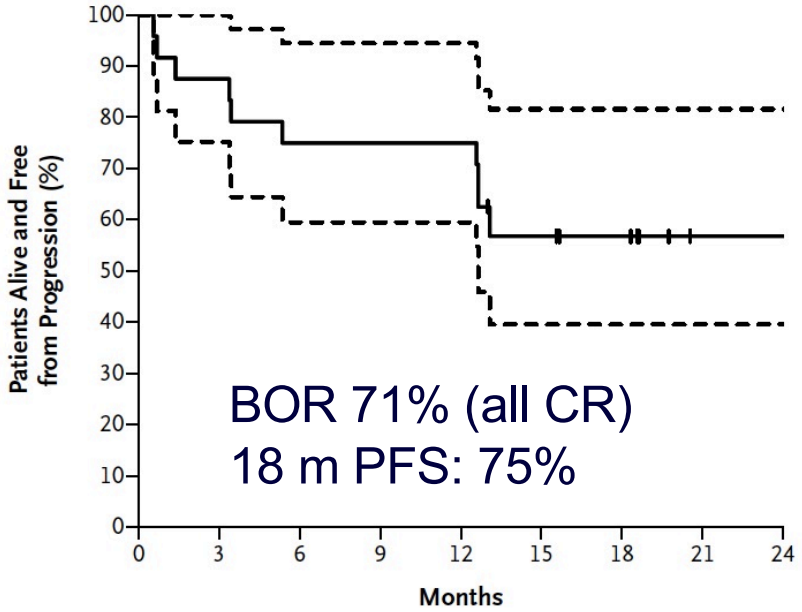
- **Single-agent venetoclax has modest activity in R/R MCL**
- **Combination of ibrutinib + venetoclax shows promise**
- **Phase 3 SYMPATICO trial is assessing ibrutinib +/- venetoclax in R/R MCL**

Venetoclax after BTKi



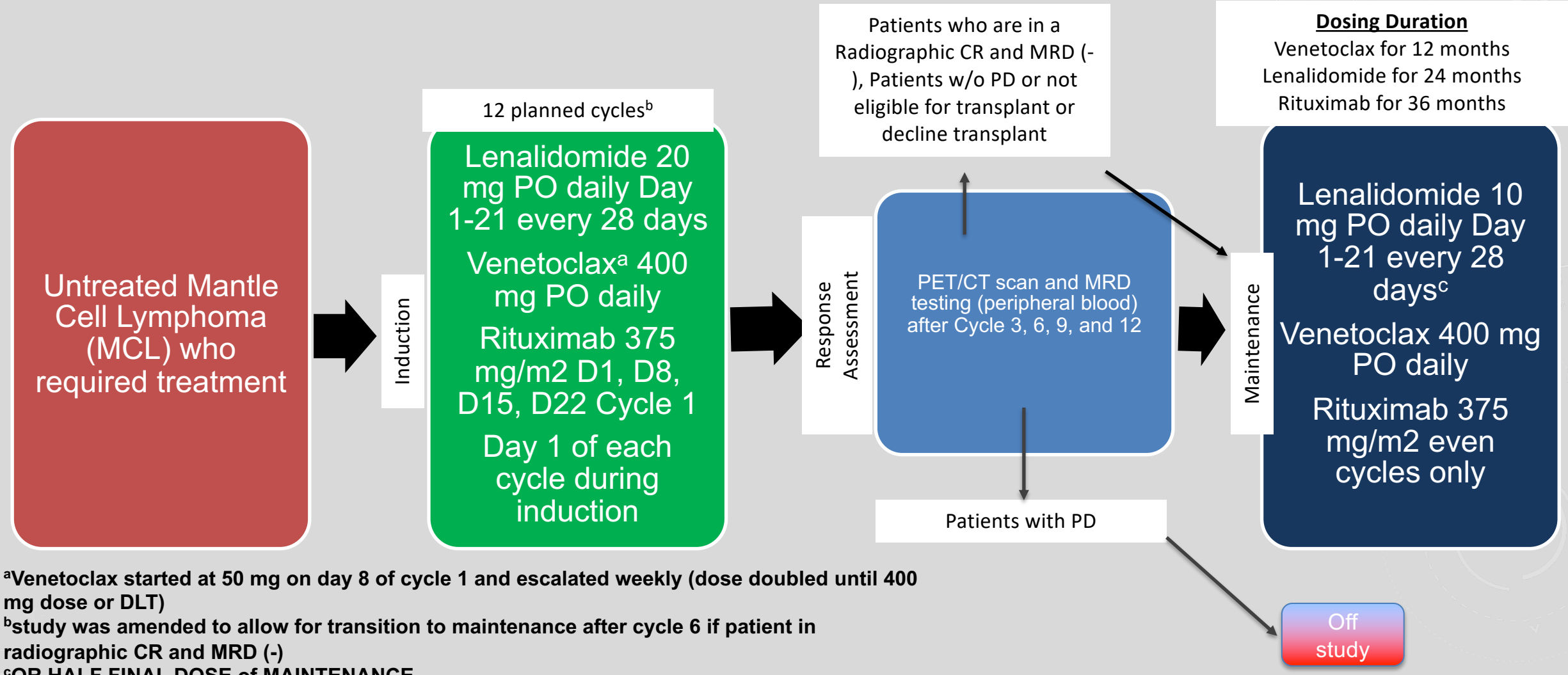
Eyre et al, Haematologica 2019

Ibrutinib + Venetoclax in R/R MCL



Tam et al, NEJM 2018

Venetoclax + Lenalidomide and Rituximab for Untreated MCL



[a]Venetoclax started at 50 mg on day 8 of cycle 1 and escalated weekly (dose doubled until 400 mg dose or DLT)
[b]study was amended to allow for transition to maintenance after cycle 6 if patient in radiographic CR and MRD (-)
[c]OR HALF FINAL DOSE of MAINTENANCE.

Phillips, ASCO 2021

Courtesy of Laurie H Sehn MD, MPH

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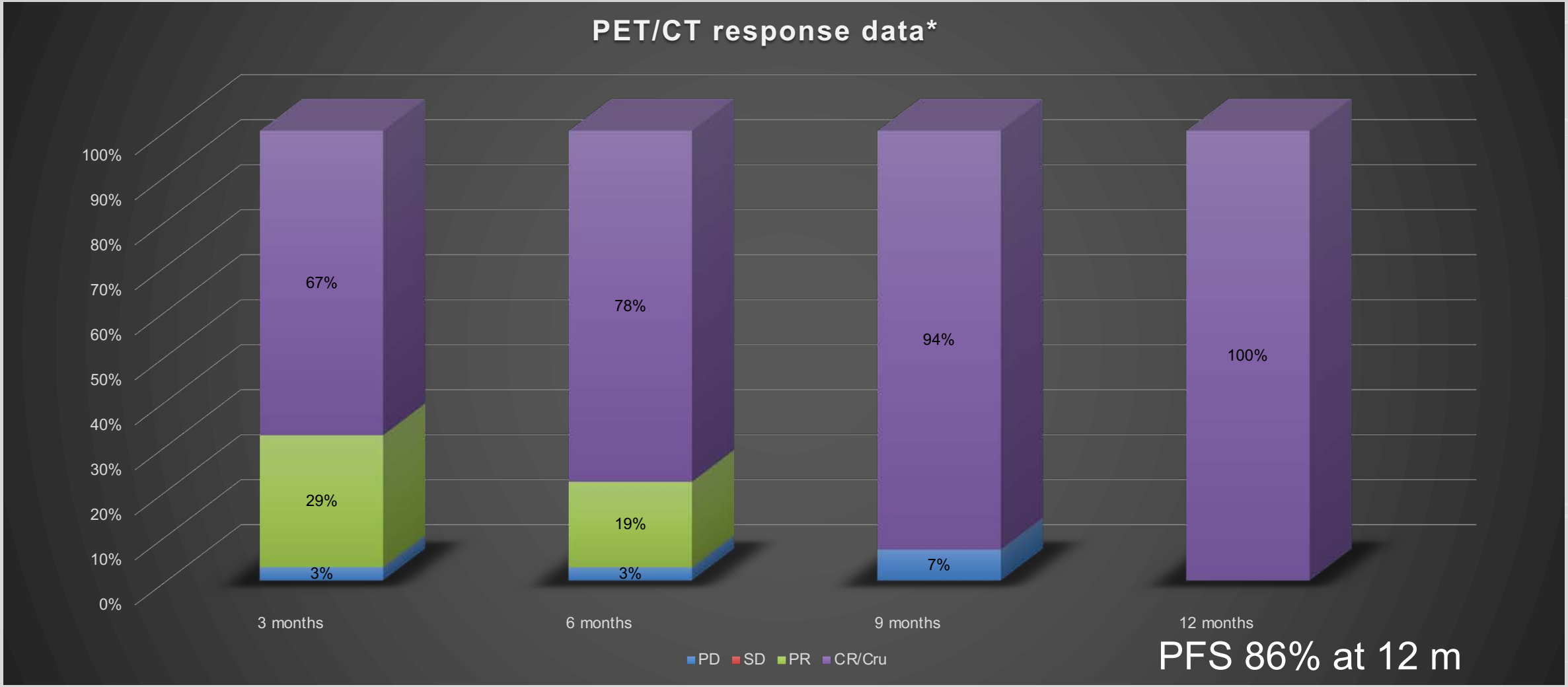
Radiographic Response



N= 28 N= 27 N= 16 N= 12

*Responses reflective # of patients who received assessments at time points

Phillips, ASCO 2021

Courtesy of Laurie H Sehn MD, MPH

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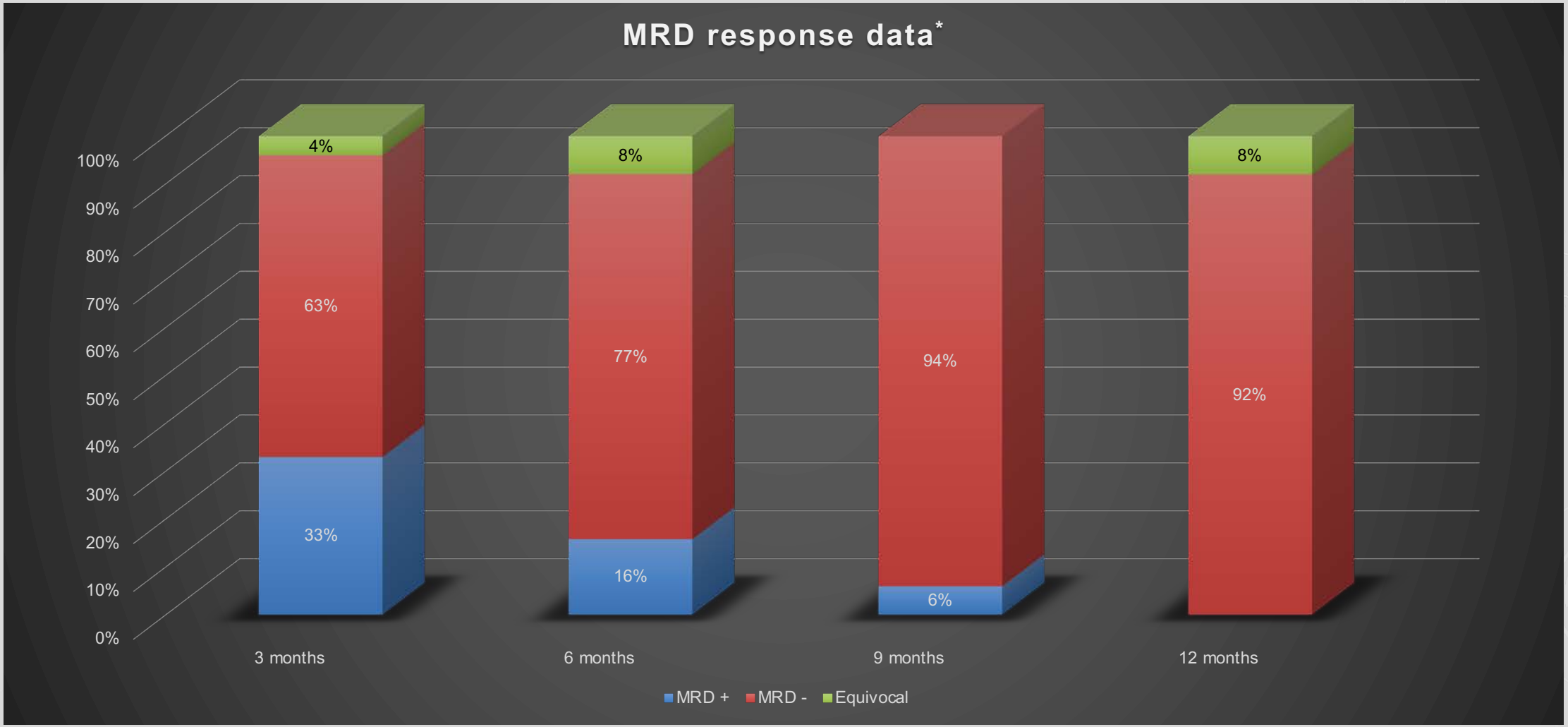
MRD Results (negative if < (10^{-6}))



N= 27 N= 25 N= 16 N= 12

*Responses reflective # of patients who received assessments at time points

Phillips, ASCO 2021

Courtesy of Laurie H Sehn MD, MPH

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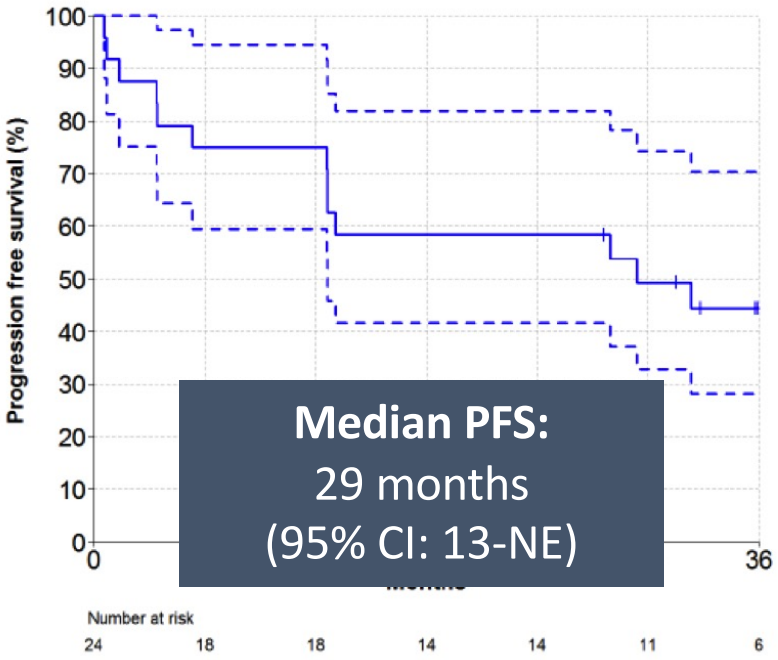
AIM Trial: Venetoclax + Ibrutinib Efficacy and Safety (3-Year Update)

PFS

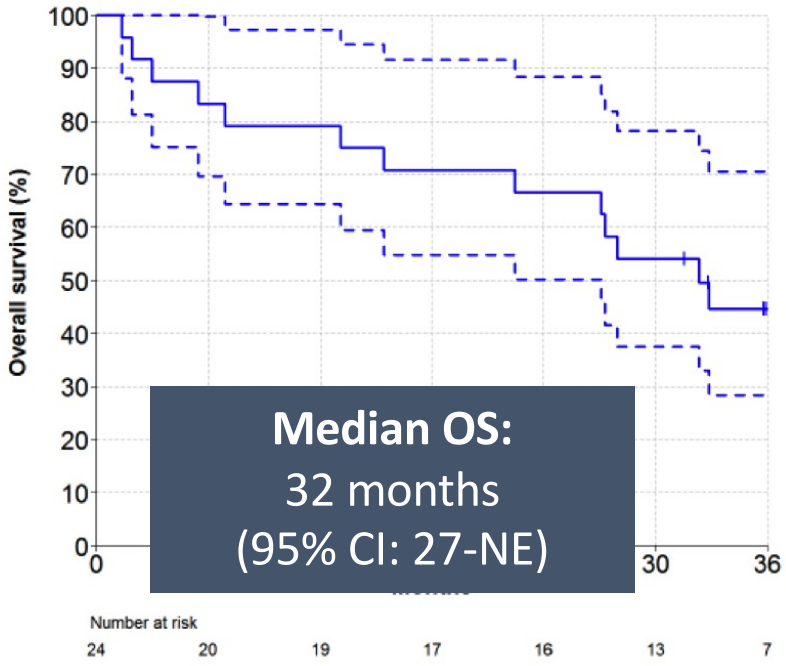
(dashed lines represent 95% CI)



Median PFS:
29 months
(95% CI: 13-NE)

OS

(dashed lines represent 95% CI)



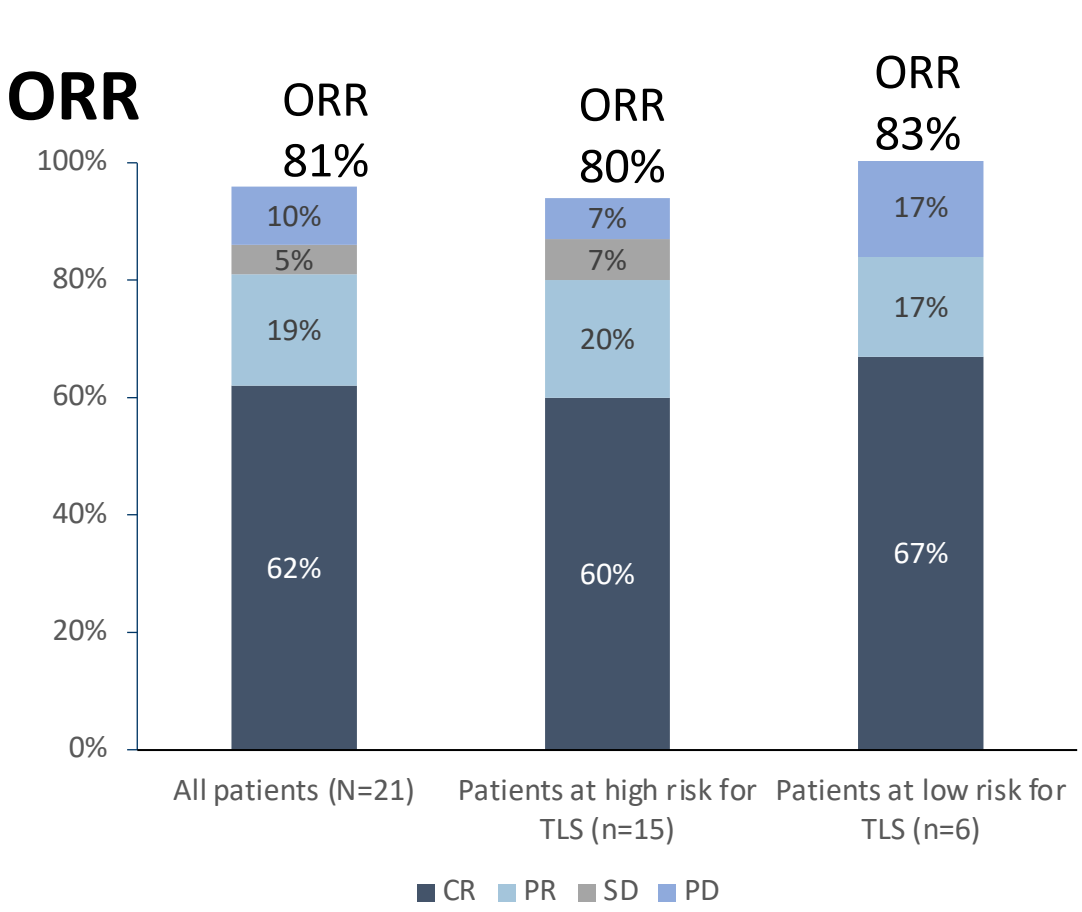
Median OS:
32 months
(95% CI: 27-NE)

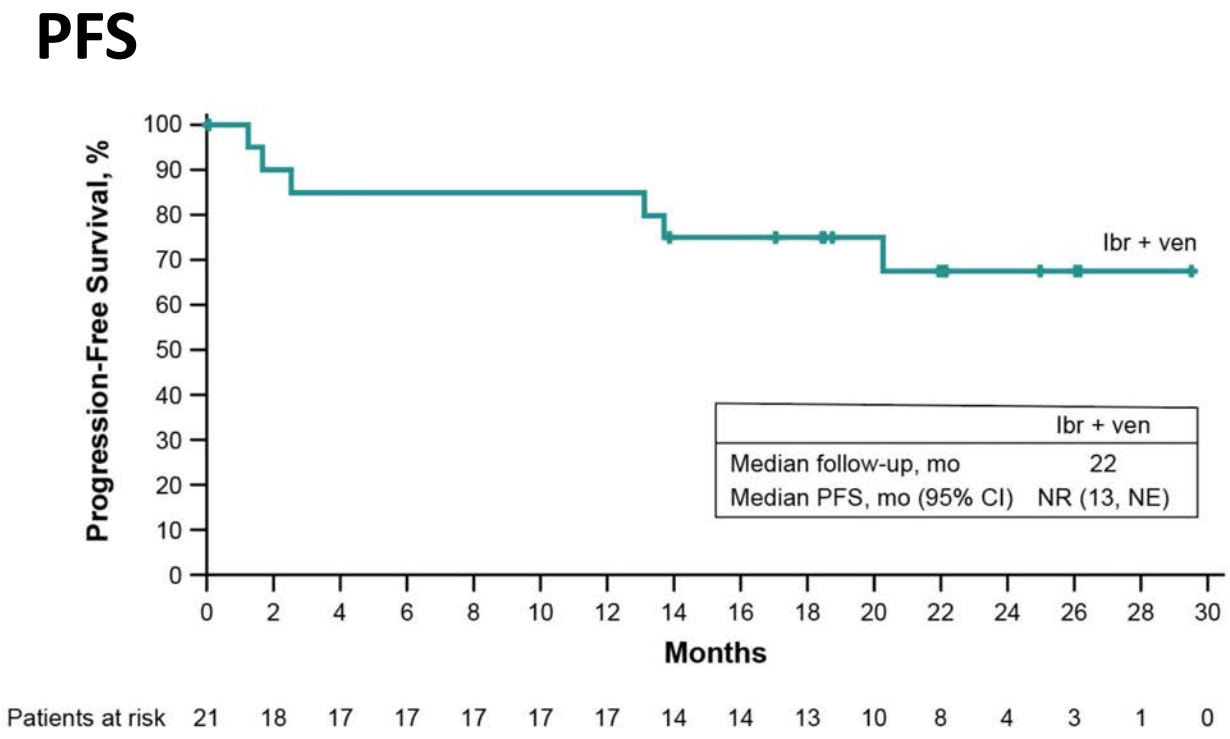
- **TP53-aberrant MCL (n=12)**
  - CRR (with and without PET): 50% (95% CI 21-79) (with and without PET_
  - ORR without PET: 58% (95% CI 28-85)
  - ORR with PET: 50% (21-79)
- **Non TP53-mutated MCL (n=10)**
  - CRR (with and without PET): 90% (95% CI 55-100)
  - ORR (with and without PET): 90% (95% CI 55-100)
- **Deaths**
  - Of 13 deaths, 8 were due to PD
  - Of the other 5 deaths, 2 were due to infection and 1 each to cardiac failure, glioblastoma, and GVHD after an allograft that occurred after PD on trial

Handunnetti SM, et al. Blood. 2019;134(Suppl_1):756.

Courtesy of Laurie H Sehn MD, MPH

SYMPATICO: Venetoclax and Ibrutinib in R/R MCL Safety Run-In Efficacy





Tam CS, et al. ASH 2020 Annual Meeting. Abstract 2938.

Courtesy of Laurie H Sehn MD, MPH

Do you approach the management of MCL differently for patients with TP53-mutated disease?

Dr Jeff Sharman

Dr Ian Flinn

Dr Christopher Flowers

Dr John Leonard

RTP
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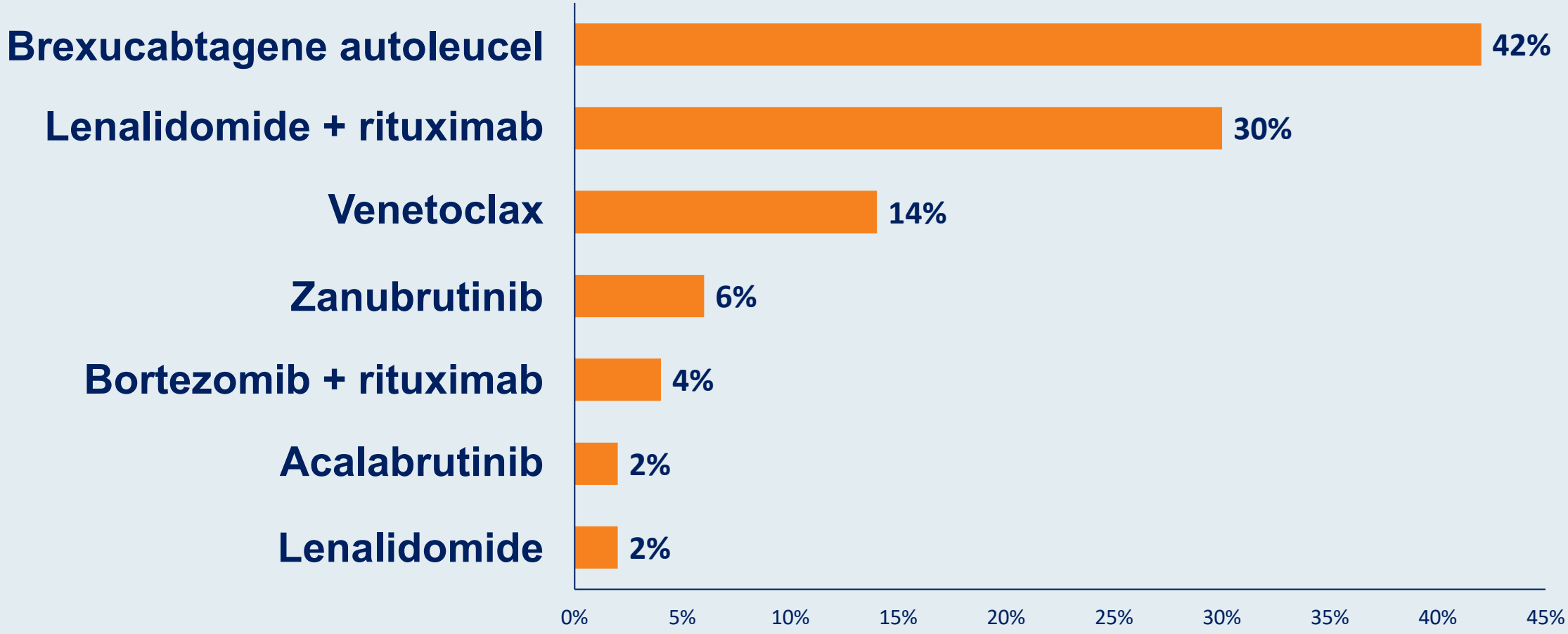
TO PRACTICE

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



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

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

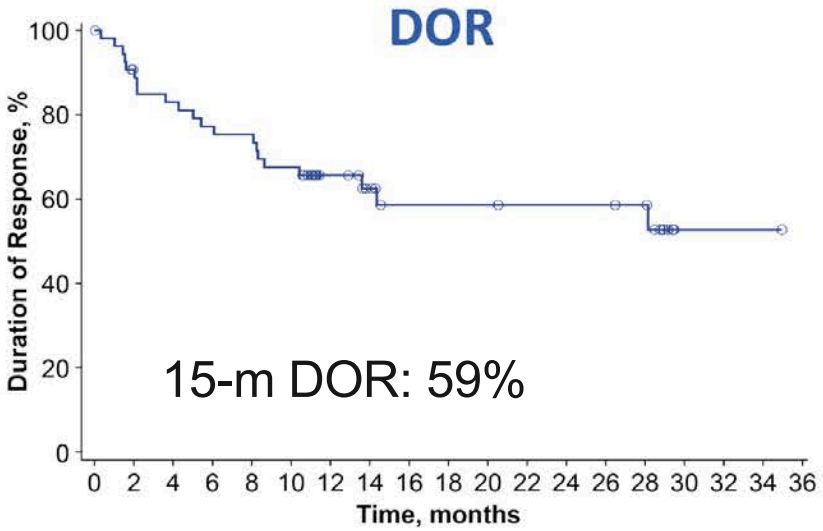
 Dr Ansell	Brexucabtagene autoleucel	 Dr Flowers	Brexucabtagene autoleucel
 Dr Moskowitz	R-CHOP	 Prof Gribben	Venetoclax
 Dr Sehn	Brexucabtagene autoleucel	 Dr Kahl	Brexucabtagene autoleucel
 Dr Fowler	Brexucabtagene autoleucel	 Dr Leonard	Brexucabtagene autoleucel
 Dr Flinn	Brexucabtagene autoleucel	 Dr Sharman	Brexucabtagene autoleucel

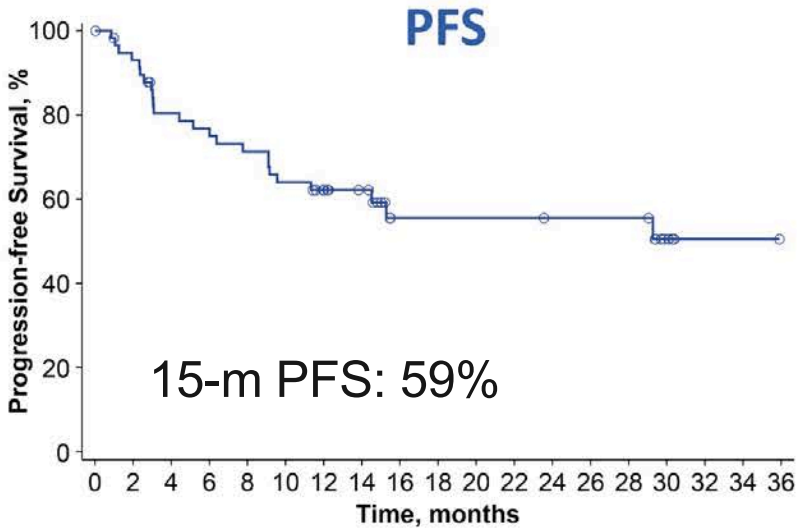
At what point in the treatment course is the appropriate time to refer a patient with relapsed/refractory MCL for CAR T-cell therapy?

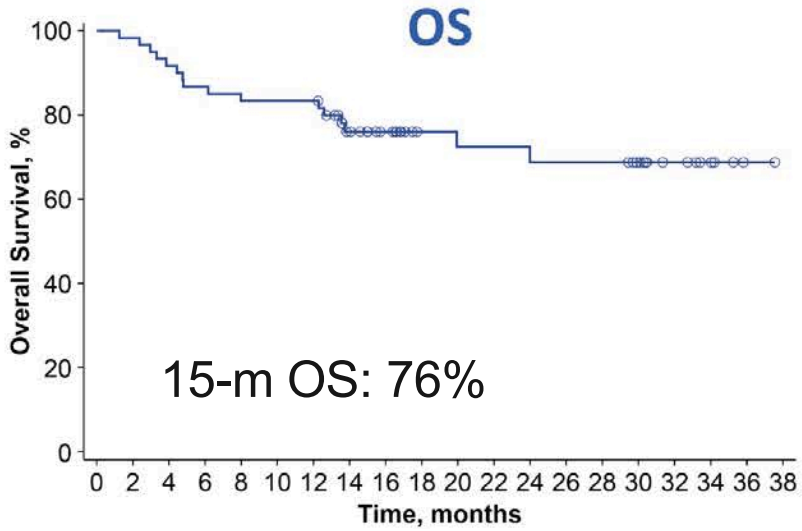
- **Immunochemotherapy (+/- ASCT) and maintenance rituximab is standard of care for untreated MCL**
- **BTK inhibitors are highly effective and commonly used second-line**
- **Outcomes following BTKi's are poor and no standard of care exists**

Update of ZUMA-2: Brexucabtagene Autoleucel (KTE-X19) in MCL (median f/up: 17.5 m)

Wang et al, ASH 2020

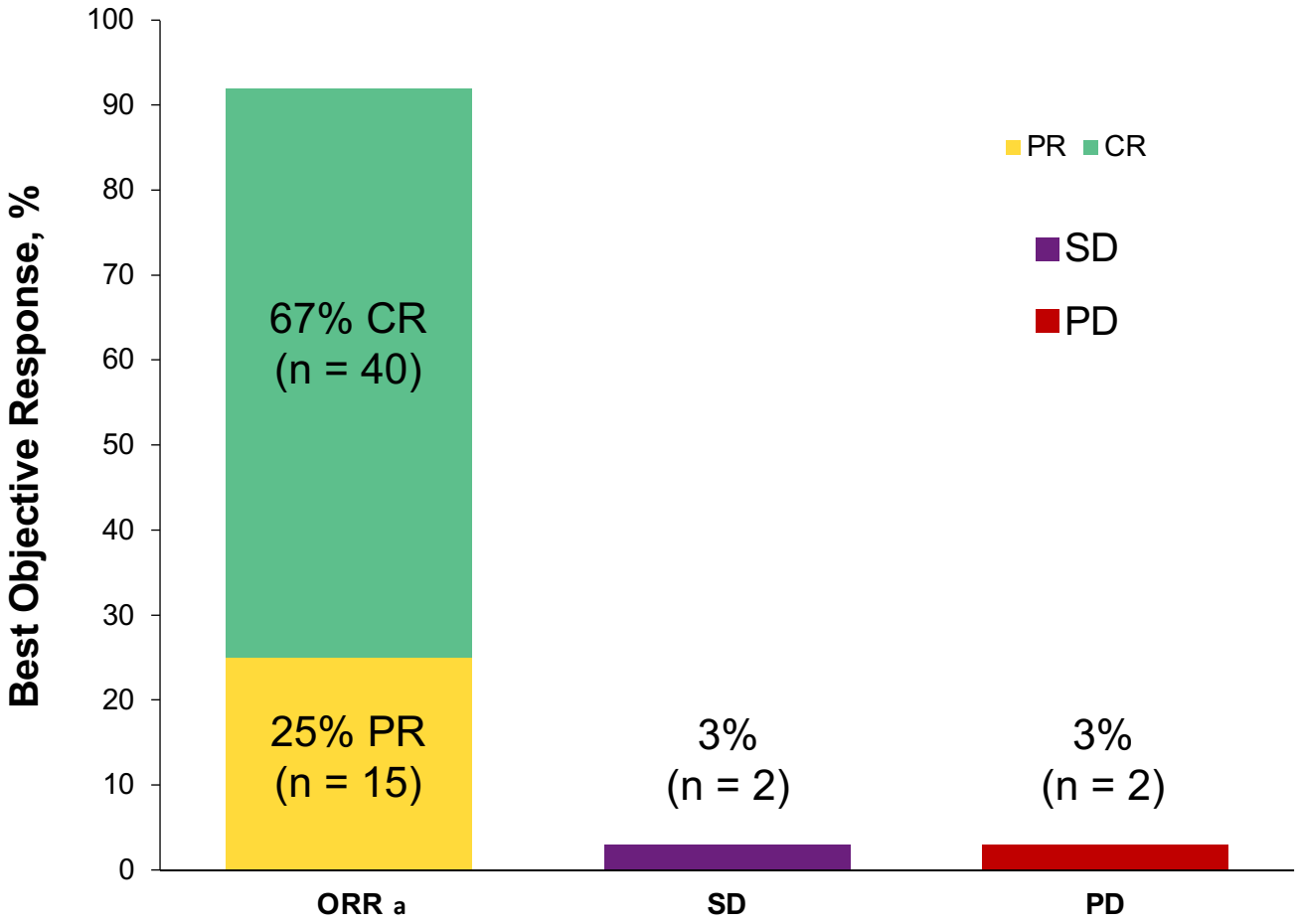






N=60, ORR 92%, CR 67%

ZUMA-2: ORR by IRRC Assessment Was 92% (95% CI, 82 – 97) and CR Rate Was 67% (95% CI, 53 – 78)



- At a median follow-up of 17.5 months (range, 12.3 – 37.6), 29 of 60 evaluable patients (48%) remain in ongoing responses
  - 28 of 40 patients who achieved CR (70%) remain in response
- The first 28 patients treated had a median follow-up of 32.3 months (range, 30.6 – 37.6)
  - 39% of patients remain in continued remission with no further therapy
- In all enrolled patients (N = 74), ORR was 84% (59% CR rate)

[a] Assessed by an IRRC according to the Lugano Classification.[1] One patient was not evaluable.

1. Cheson BD, et al. *J Clin Oncol*. 2014;32:3059-3068.

CR, complete response; IRRC, Independent Radiology Review Committee; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Courtesy of Laurie H Sehn MD, MPH

Wang, ASH 2020

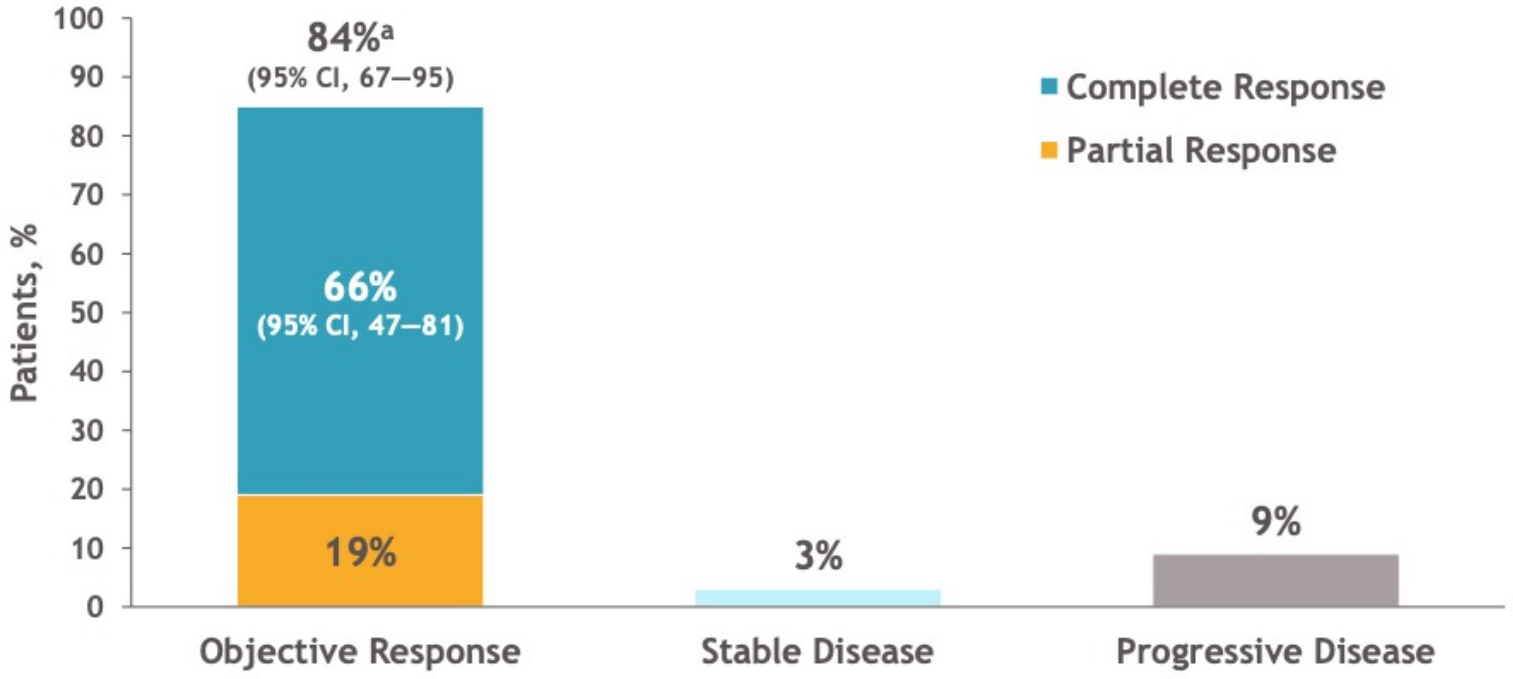
Safety and Preliminary Efficacy in Patients with Relapsed/Refractory Mantle Cell Lymphoma Receiving Lisocabtagene Maraleucel in TRANSCEND NHL 001

M. Lia Palomba,[1] Leo I. Gordon,[2] Tanya Siddiqi,[3] Jeremy Abramson,[4] Manali Kamdar,[5] Matthew Lunning,[6] David G. Maloney,[7] Charalambos Andreadis,[8] Jon E. Arnason,[9] Nilanjan Ghosh,[10] Amitkumar Mehta,[11] Scott R. Solomon,[12] Thalia Farazi,[13] Jacob Garcia,[13] Christine Dehner,[13] Ken Ogasawara,[14] Jie Gao,[13] Michael Wang[15]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Northwestern University Feinberg School of Medicine, Robert H. Lurie Comprehensive Cancer Center, Chicago, IL, USA; [3]City of Hope National Medical Center, Duarte, CA, USA; [4]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [5]University of Colorado Cancer Center, Aurora, CO, USA; [6]University of Nebraska Medical Center, Omaha, NE, USA; [7]Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [8]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, San Francisco, CA, USA; [9]Beth Israel Deaconess Medical Center, Boston, MA, USA; [10]Levine Cancer Institute, Atrium Health, Charlotte, NC, USA; [11]University of Alabama at Birmingham, Birmingham, AL, USA; [12]Immunotherapy Program, Northside Hospital Cancer Institute, Atlanta, GA, USA; [13]Bristol Myers Squibb, Seattle, WA, USA; [14]Bristol Myers Squibb, Princeton, NJ, USA; [15]University of Texas MD Anderson Cancer Center, Houston, TX, USA

Palomba ML et al. ASH 2020;Abstract 118.

NHL 001: Overall Response by Investigator Assessment

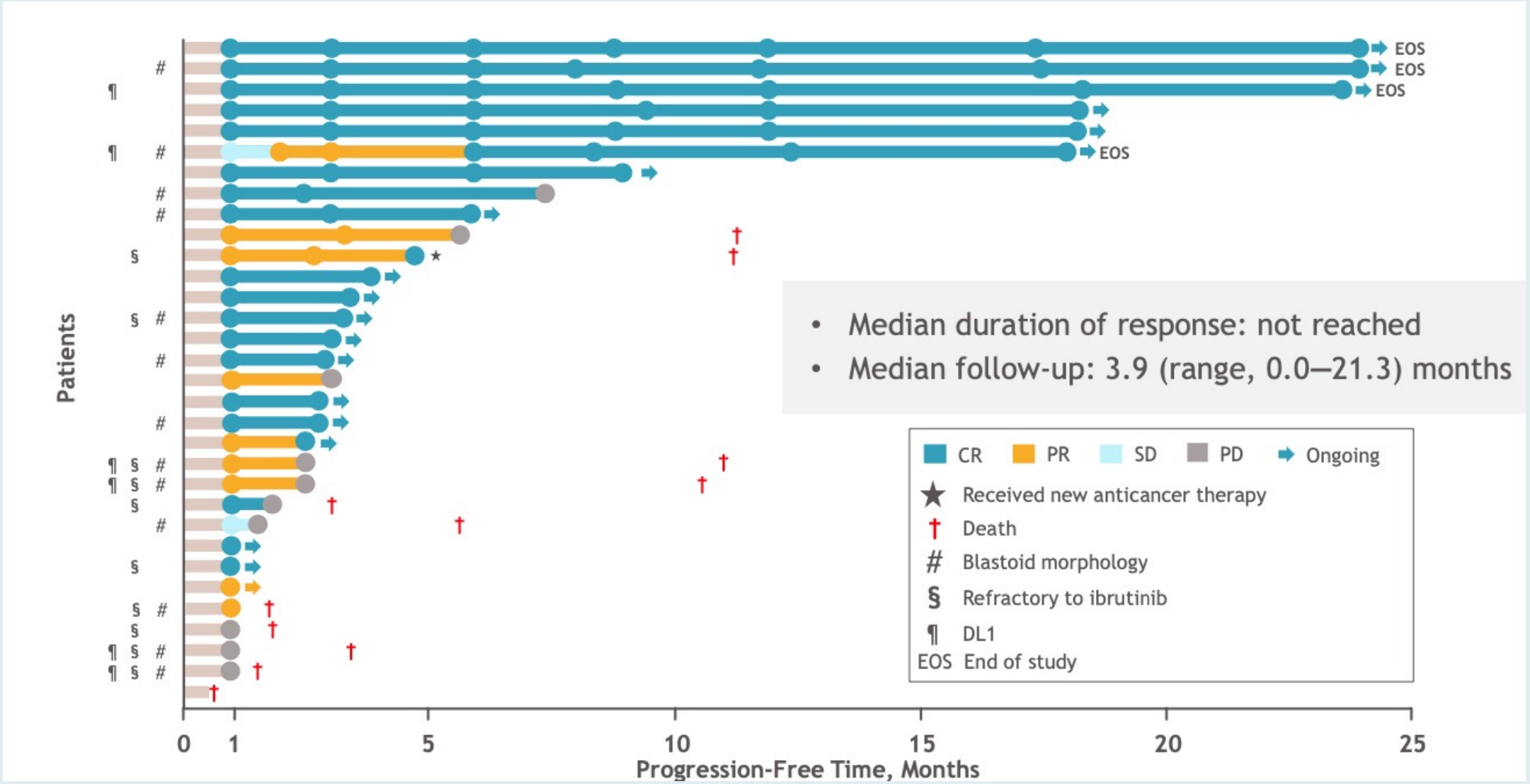


- Median on-study follow-up: 5.9 (range, 0.4–24.8) months
- Median time to first CR or PR: 0.95 (range, 0.9–2.0) months

- ORR and CR rate, respectively, for patients with high-risk features:
  - Ki67 ≥30% (n = 23): 83% and 65%
  - Blastoid morphology (n = 13): 77% and 54%
  - *TP53* mutations (n = 7): 100% and 57%

Palomba ML et al. ASH 2020;Abstract 118.

NHL 001: Patient Responses over Time



Palomba ML et al. ASH 2020;Abstract 118.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Mantle Cell Lymphoma (MCL)

- What is your current approach to second-line treatment of MCL?
- How do you currently integrate venetoclax into the management of progressive MCL?
- Do you approach the management of MCL differently for patients with TP53-mutated disease?

Module 2: Diffuse Large B-Cell Lymphoma (DLBCL)

- How does CAR T-cell therapy currently fit into your management of DLBCL?
- At this point, are there discernible clinical differences in the 3 available CAR T-cell products for DLBCL?
- Aside from CAR T-cell therapy, how do you approach sequencing of the other agents and regimens available for second-line treatment and beyond in DLBCL?

Module 3: Hodgkin Lymphoma (HL)

- How do you select up-front systemic treatment for younger patients with advanced-stage HL?
- How do you select up-front systemic treatment for elderly patients with advanced-stage HL?

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RESEARCH
TO PRACTICE

How does CAR T-cell therapy currently fit into your management of DLBCL?

Dr Jeff Sharman

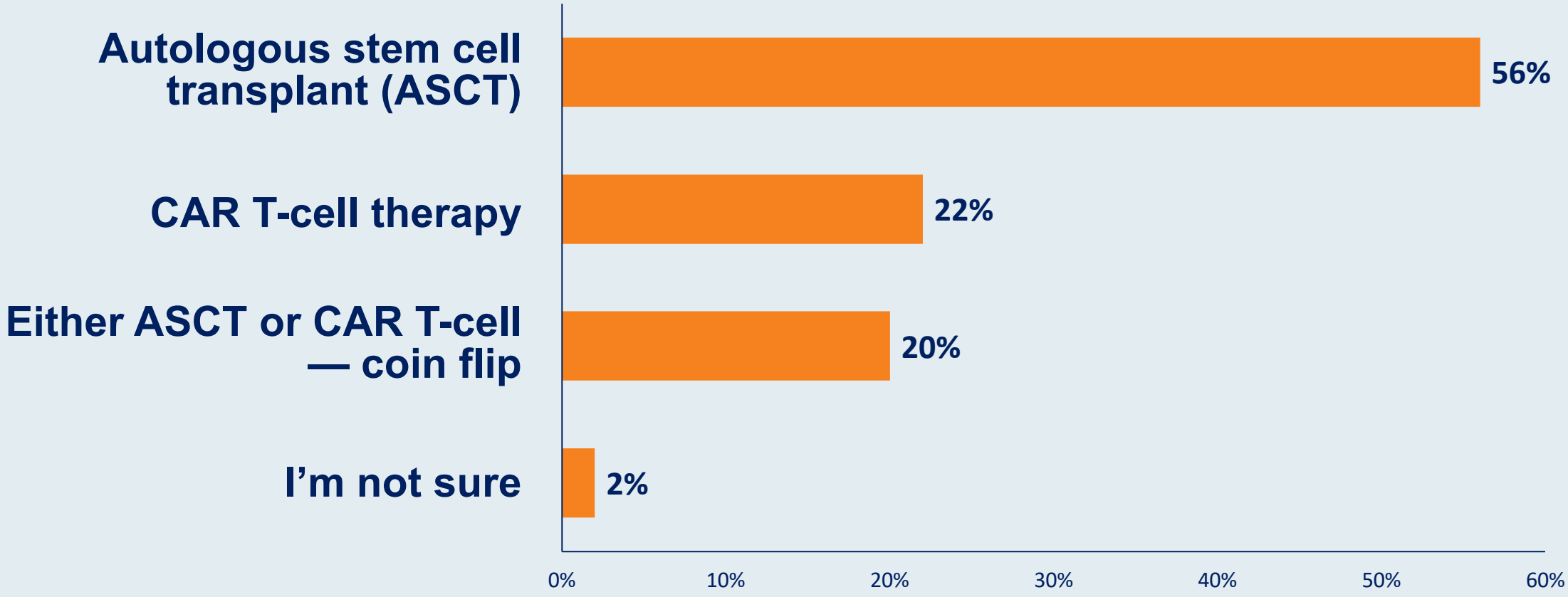
Dr Ian Flinn

Dr Christopher Flowers

Dr John Leonard

RTP
RESEARCH
TO PRACTICE

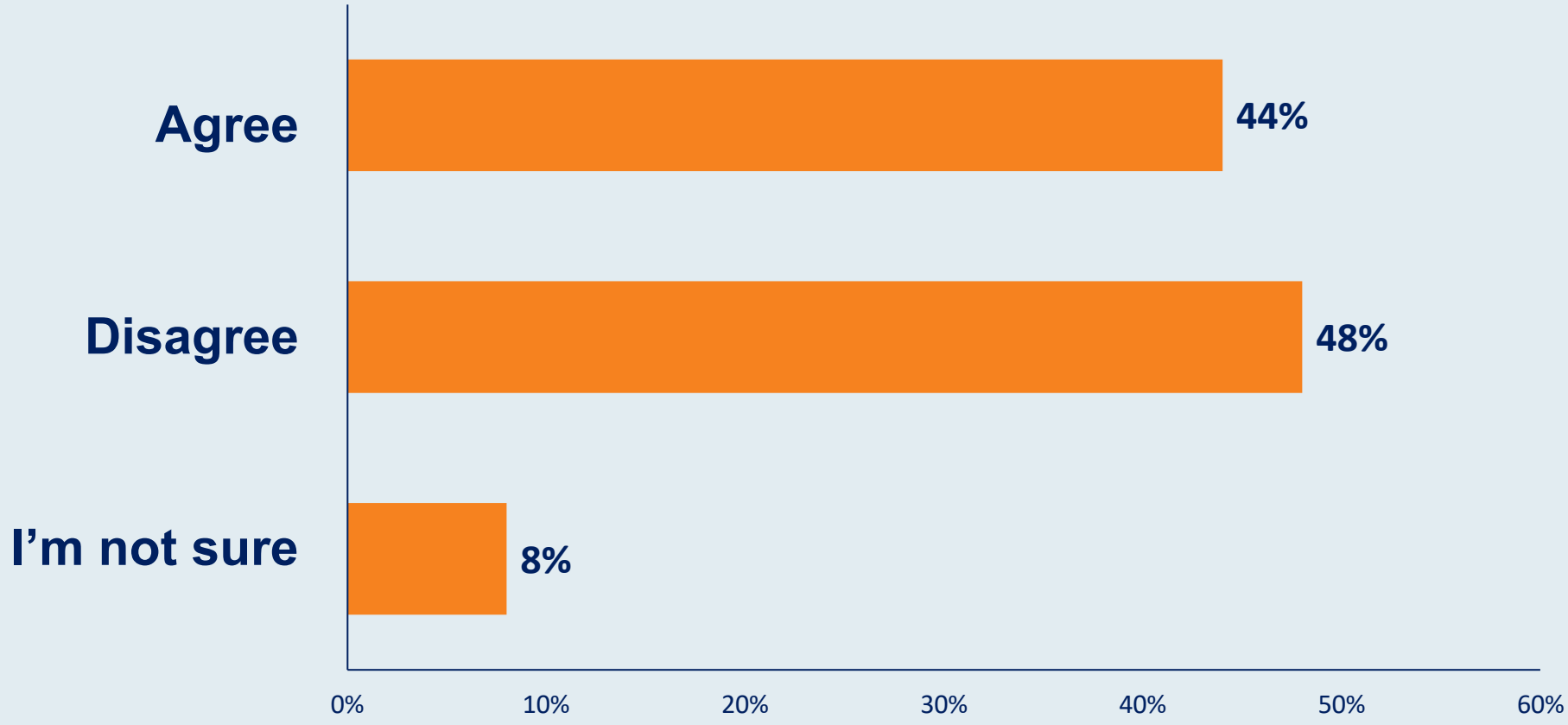
In general, what is the optimal treatment for a younger, transplant-eligible patient with DLBCL who experiences disease relapse after R-CHOP?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

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



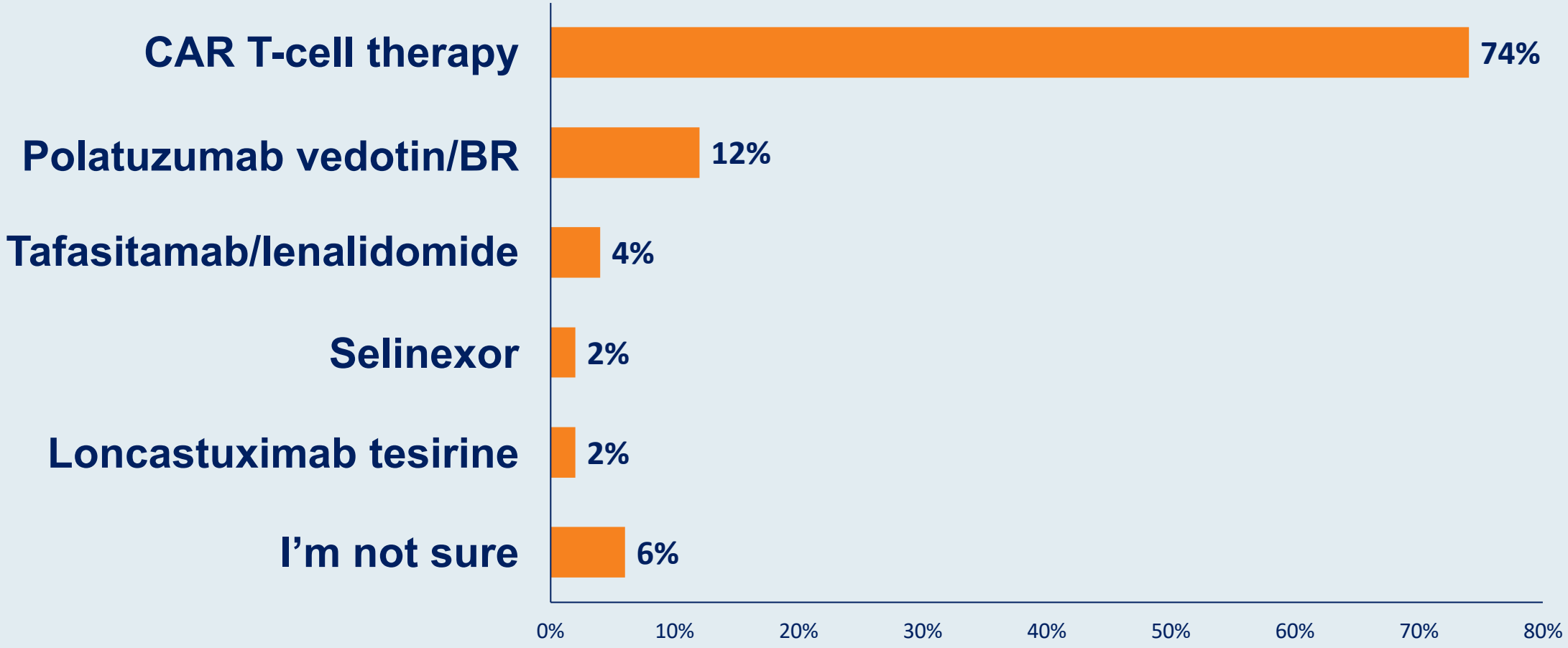
Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

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

 Dr Ansell	Disagree	 Dr Flowers	Disagree
 Dr Moskowitz	Agree	 Prof Gribben	Disagree
 Dr Sehn	Disagree	 Dr Kahl	Disagree
 Dr Fowler	Agree	 Dr Leonard	Disagree
 Dr Flinn	Agree	 Dr Sharman	Disagree

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



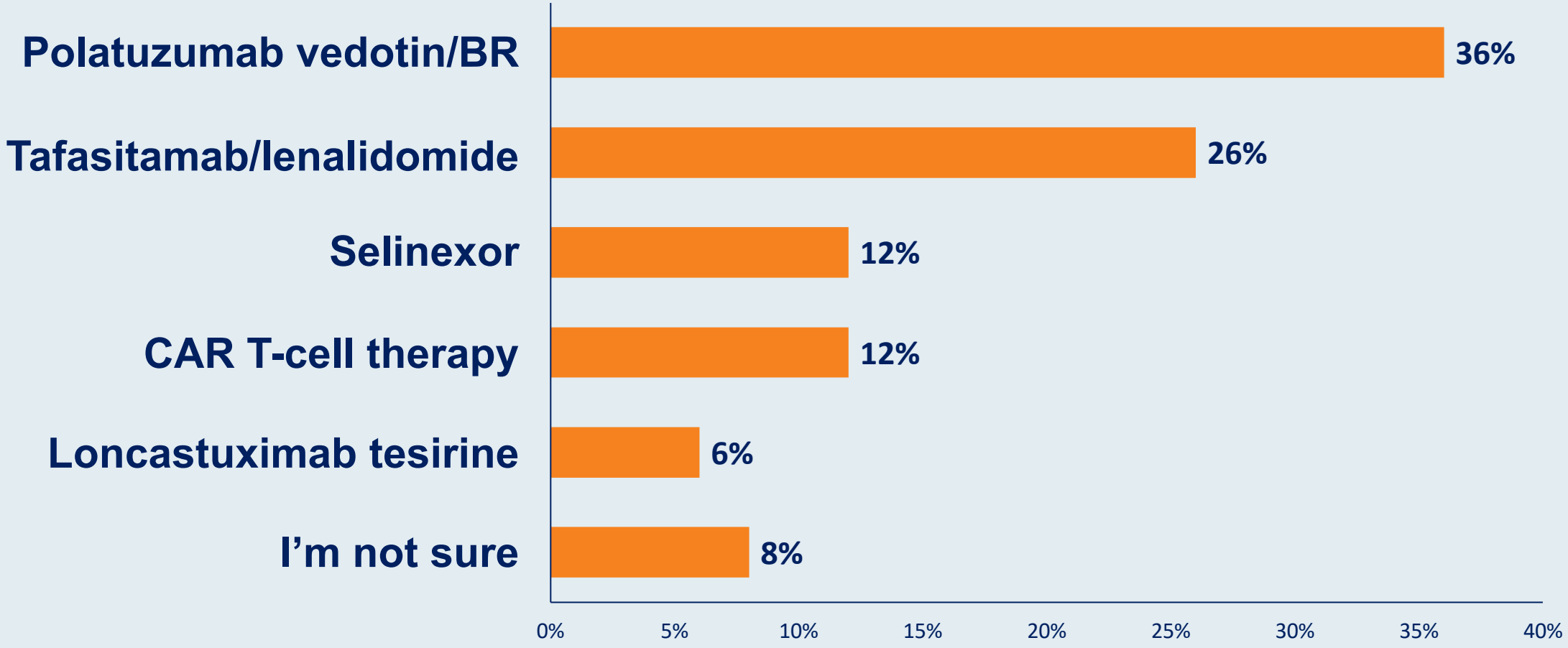
Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

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

 Dr Ansell	Tafasitamab/ lenalidomide	 Dr Flowers	CAR T-cell therapy
 Dr Moskowitz	Polatuzumab vedotin/BR	 Prof Gribben	CAR T-cell therapy
 Dr Sehn	CAR T-cell therapy	 Dr Kahl	CAR T-cell therapy
 Dr Fowler	CAR T-cell therapy	 Dr Leonard	CAR T-cell therapy
 Dr Flinn	CAR T-cell therapy	 Dr Sharman	CAR T-cell therapy

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



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

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

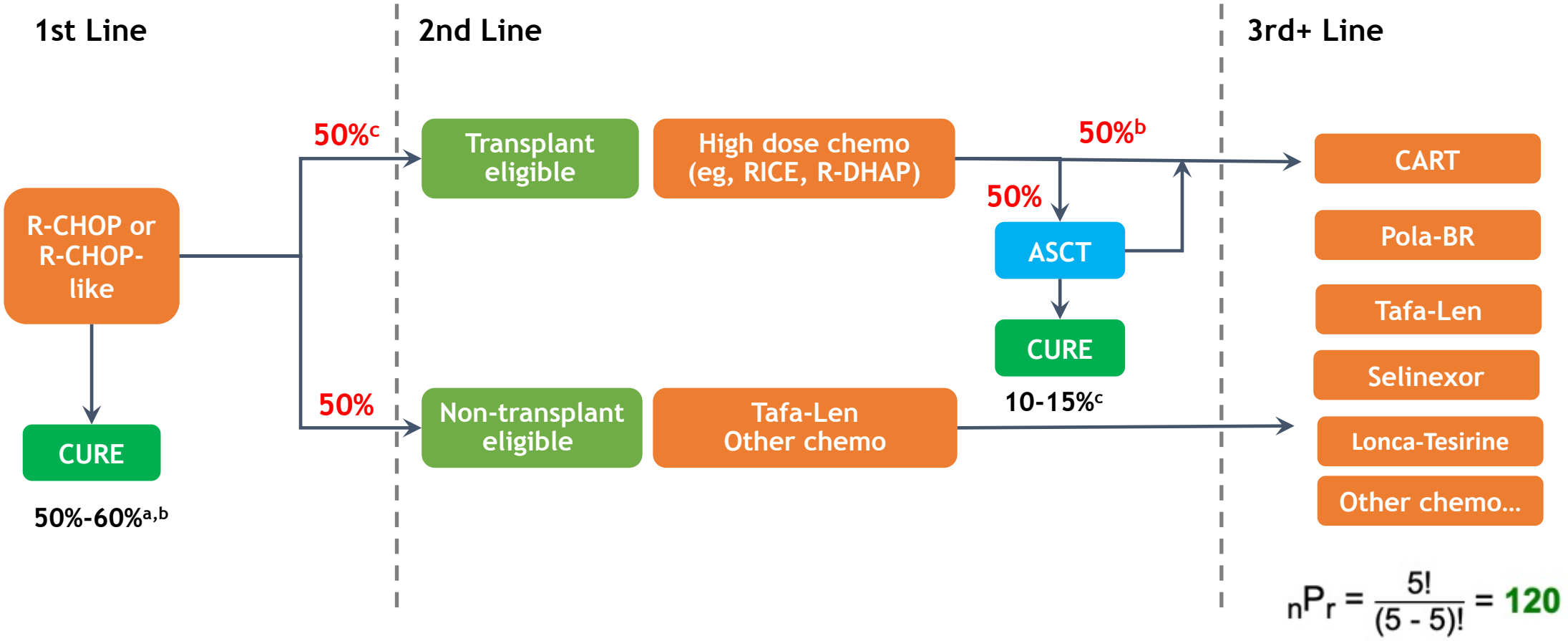
 Dr Ansell	Tafasitamab/ lenalidomide	 Dr Flowers	Tafasitamab/ lenalidomide
 Dr Moskowitz	Loncastuximab tesirine	 Prof Gribben	Polatuzumab vedotin/BR
 Dr Sehn	Polatuzumab vedotin/BR	 Dr Kahl	Tafasitamab/ lenalidomide
 Dr Fowler	Tafasitamab/ lenalidomide	 Dr Leonard	Tafasitamab/ lenalidomide
 Dr Flinn	Tafasitamab/ lenalidomide	 Dr Sharman	Polatuzumab vedotin/BR

For a patient with relapsed/refractory DLBCL, do you believe there is an optimal approach to the therapeutic sequencing of polatuzumab vedotin, tafasitamab/lenalidomide, selinexor, loncastuximab tesirine and CAR T-cell therapy?

- Issues to consider –
  - How soon is next therapy needed?
  - What previous therapy has the patient received?
  - Could the patient still be cured?
  - Is there evidence of antigen loss?
  - What residual toxicities does the patient have?

For a Pt with R/R DLBCL, do you believe there is an optimal approach to of polatuzumab vedotin, tafasitamab/lenalidomide, selinexor, loncastuximab tesirine and CAR T-cell therapy? – continued.

There are choices…how to choose?

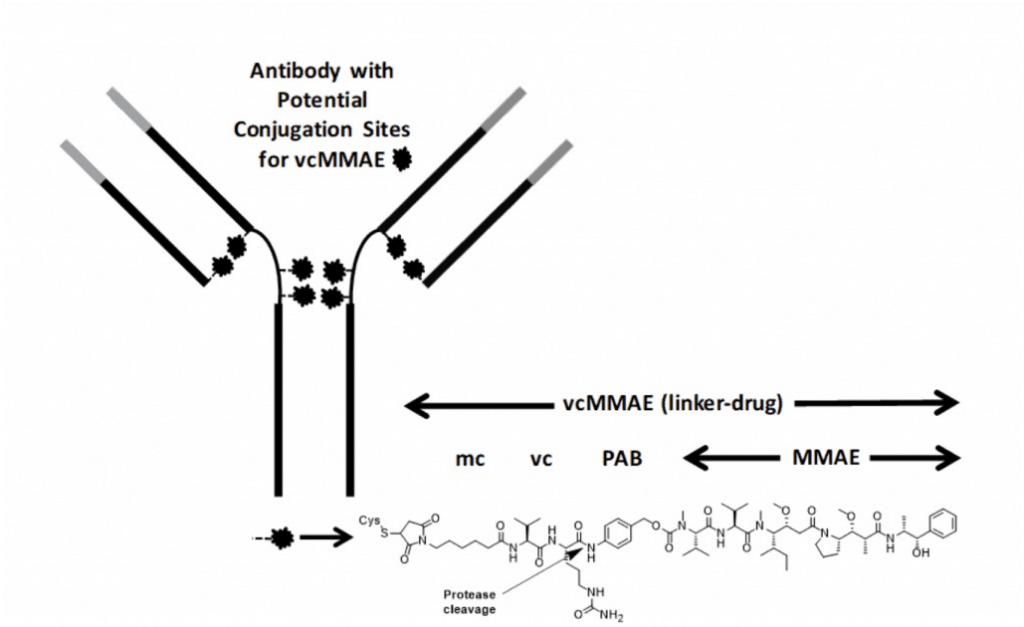


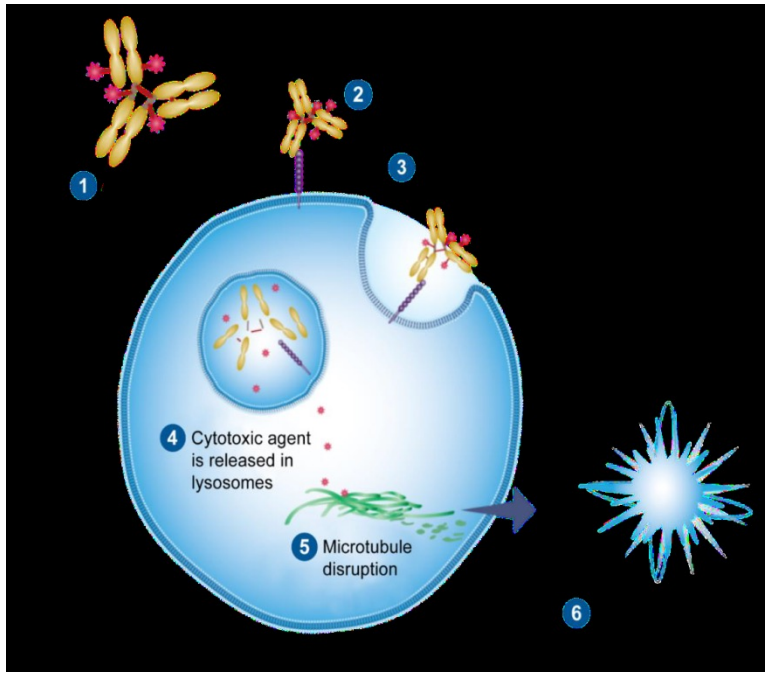
SCT=stem-cell transplantation.
[a] Decisions Resource Group. DLBCL Epidemiology data; [b] Sehn LH, Gascoyne RD. *Blood*. 2015;125:22-32;
[c] Friedberg JW, et al. *Hematology Am Soc Hematol Educ Program*. 2011;2011:498-505;

Courtesy of G. S. Nowakowski MD

Using Antibody Drug Conjugates to Target Lymphoma B cells - Polatuzumab vedotin

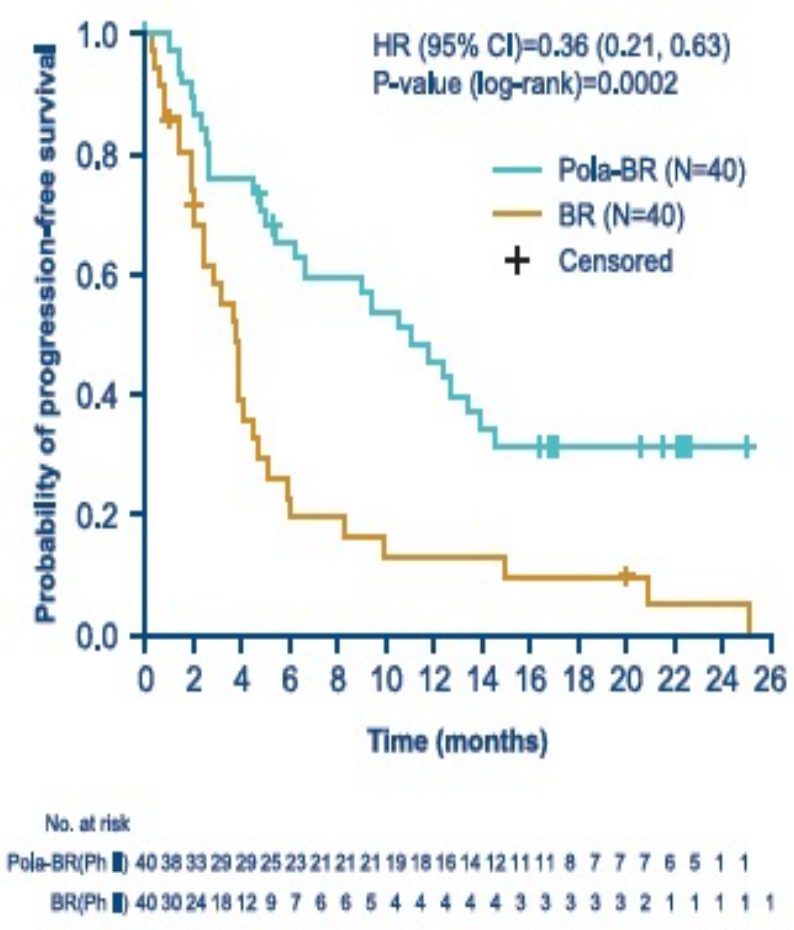
Targets CD79b
Also has the MMAE payload

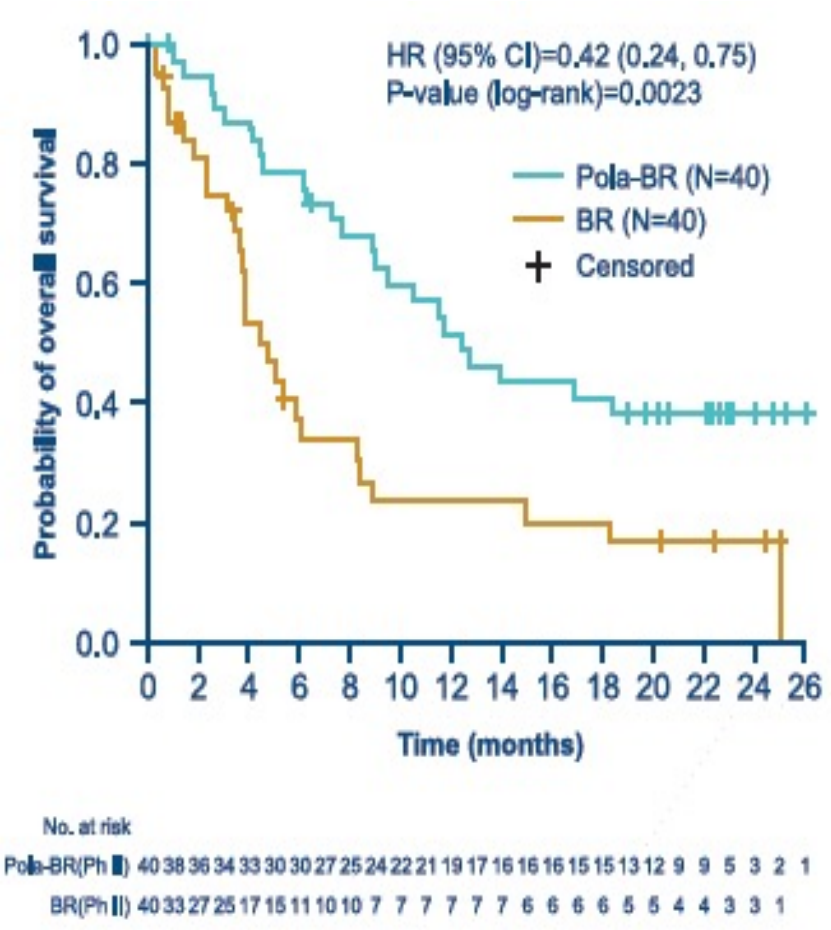




Courtesy of Stephen M Ansell, MD, PhD

Phase Ib/II Study of Polatuzumab Vedotin + Bendamustine/Rituximab for R/R DLBCL





- PET-CR and survival were significantly better with Pola + BR vs BR alone (all $P<0.05$)
  - Improvement was observed regardless of COO or DE status

Courtesy of Stephen M Ansell, MD, PhD

Sehn et al. J Clin Oncol. 2020;38(2):155-165

At this point, are there discernible clinical differences in the 3 available CAR T-cell products for DLBCL?

Dr Jeff Sharman

Dr Ian Flinn

Dr Christopher Flowers

Dr John Leonard

RTP
RESEARCH
TO PRACTICE

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

 Dr Ansell	Yes	 Dr Flowers	Yes
 Dr Moskowitz	No	 Prof Gribben	Yes
 Dr Sehn	No	 Dr Kahl	Yes
 Dr Fowler	Yes	 Dr Leonard	Yes
 Dr Flinn	Yes	 Dr Sharman	No

Do you view the three available CD19-directed CAR T-cell therapies as equivalent therapeutic options, or are there distinct differences between these agents that would lead you to refer patients for one versus the other?

- Issues to consider –
  - What product does your center have access to?
  - What is the patient's histology?
  - Will you need to give bridging chemotherapy?
  - How soon do you need the product?
  - How frail is the patient?
  - How concerned are you about toxicity?
    - CRS and neurotoxicity
    - HLH and neutropenia
  - Cost effectiveness?

Do you view the three available CD19-directed CAR T-cell therapies as equivalent therapeutic options, or are there distinct differences between these agents that would lead you to refer patients for one versus the other? - Continued

Comparative efficacy of tisagenlecleucel (tisa-cel) and lisocabtagene maraleucel (liso-cel) in patients with relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL).

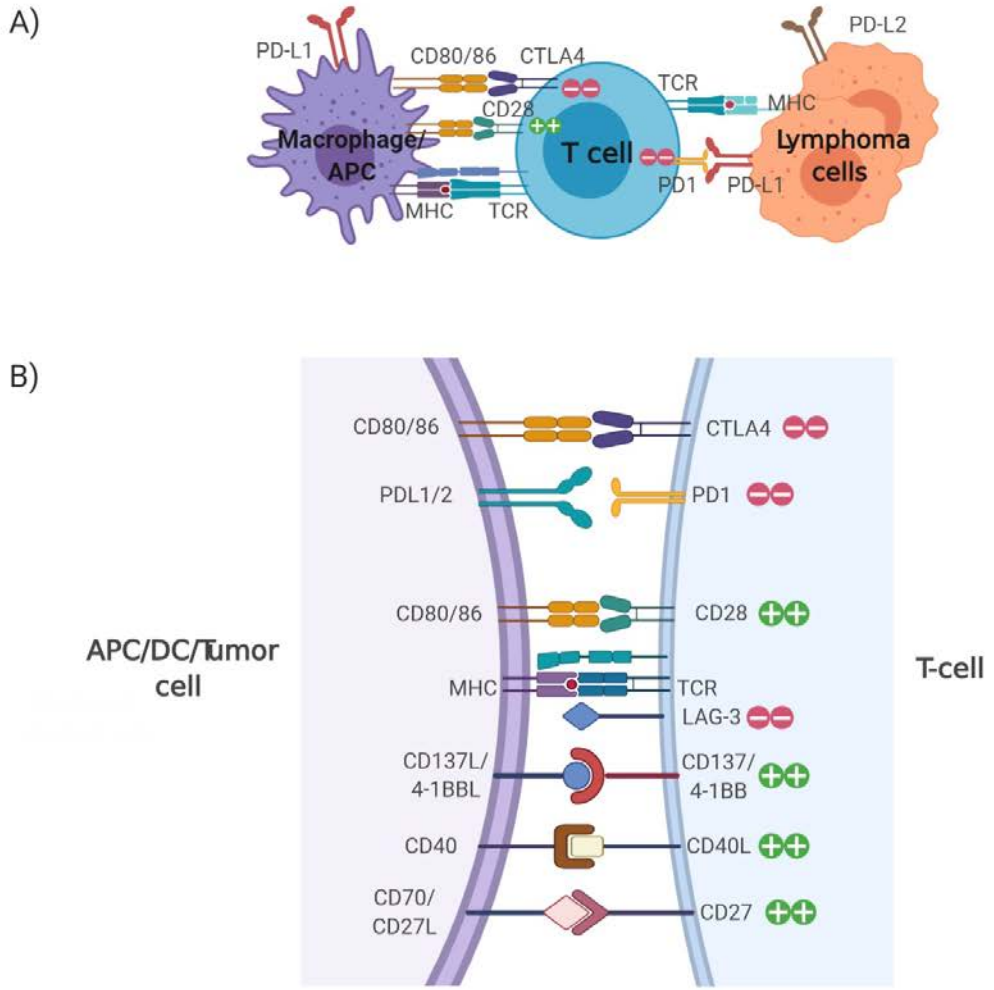
No evidence suggesting differences in OS, PFS and CR between tisa-cel and liso-cel in R/R DLBCL.

MAIC of Tisa-cel Infused vs. Liso-cel Efficacy-evaluable set.

	Tisa-cel vs. liso-cel (95% CI); p-value
OS, hazard ratio (HR)	1.12 (0.62, 2.05); p=0.71; 1-year OS rate: 55.1% vs 57.9%
PFS, HR	1.16 (0.64, 2.09); p=0.63; 1-year PFS rate: 47.4% vs 44.1%
CR, rate difference	-5.4% (-15.5%, 4.7%); p=0.29
OR, rate difference	-9.7% (-20.0%, 0.6%); p=0.07

Schuster S, et al ASCO 2021; abstr 7535

Targeting T-cells to Promote an Effective Anti-Tumor Immune Response in Lymphoma



Courtesy of Stephen M Ansell, MD, PhD

Ansell SM. J Clin Oncol. 2021 Feb 10;39(5):525-533.

Comparative efficacy of tisagenlecleucel (tisa-cel) and lisocabtagene maraleucel (liso-cel) in patients with relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL).

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PFS, HR	1.16 (0.64, 2.09); p=0.63; 1-year PFS rate: 47.4% vs 44.1%
CR, rate difference	-5.4% (-15.5%, 4.7%); p=0.29
OR, rate difference	-9.7% (-20.0%, 0.6%); p=0.07

Schuster S, et al ASCO 2021; abstr 7535

Courtesy of Stephen M Ansell, MD, PhD

Aside from CAR T-cell therapy, how do you approach sequencing of the other agents and regimens available for second-line treatment and beyond in DLBCL?

Dr Jeff Sharman

Dr Ian Flinn

Dr Christopher Flowers

Dr John Leonard

RTP
RESEARCH
TO PRACTICE

Is it reasonable to treat a patient who has experienced disease progression on or after CD19-directed CAR T-cell therapy with tafasitamab/lenalidomide, and vice versa?

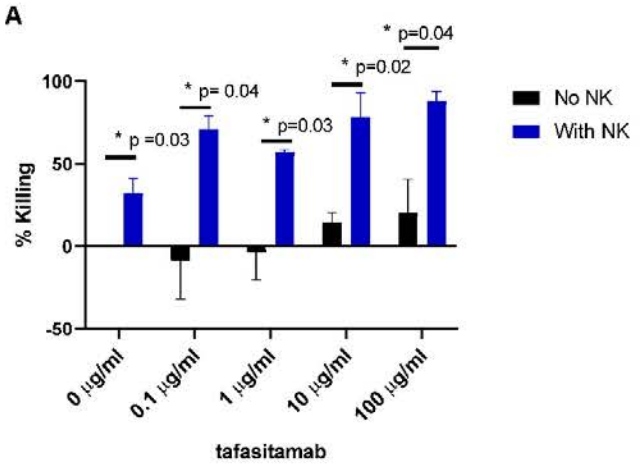
 Dr Ansell	Yes	 Dr Flowers	Yes
 Dr Moskowitz	Yes	 Prof Gribben	Yes
 Dr Sehn	Yes	 Dr Kahl	Yes
 Dr Fowler	Yes	 Dr Leonard	Yes
 Dr Flinn	Yes	 Dr Sharman	Yes

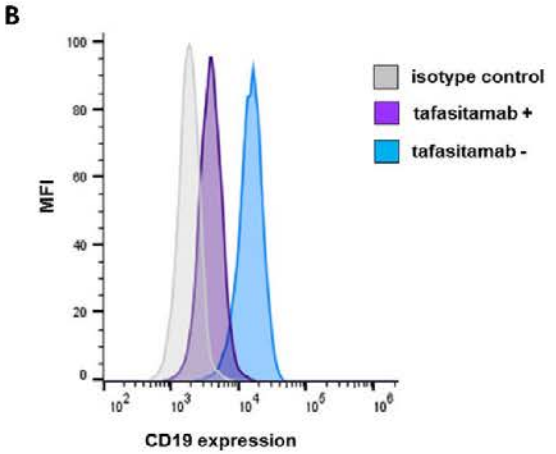
Is it reasonable to treat a patient who has experienced disease progression on or after CD19-directed CAR T-cell therapy with tafasitamab/lenalidomide and vice versa?

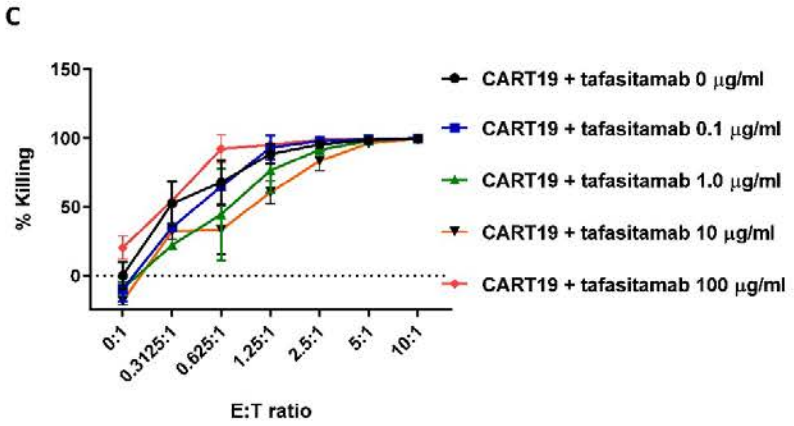
- Issues to consider –
  - What previous therapy has the patient received?
  - Is there evidence of antigen loss?
  - Could the patient still be cured?

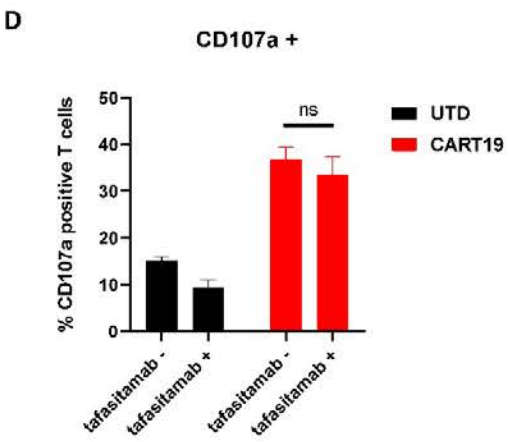
Is it reasonable to treat a Pt who has experienced PD on or after CD19-directed CAR T-cell therapy with tafasitamab/lenalidomide and vice versa? - Continued

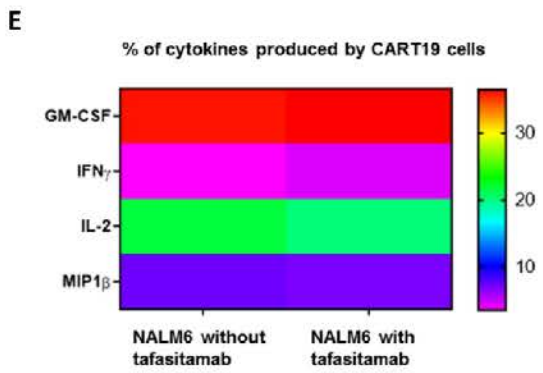
Targeting of CD19 By Tafasitamab Does Not Impair CD19-Directed Chimeric Antigen Receptor T-Cell Activity in Vitro

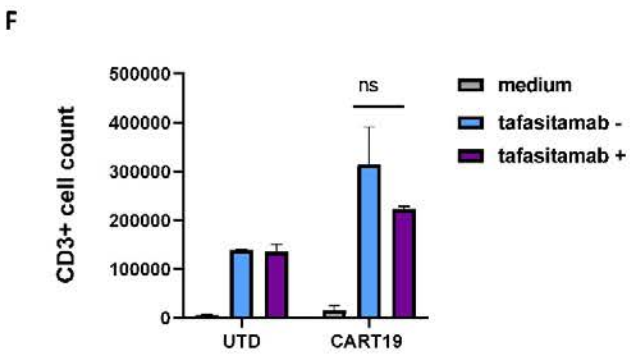








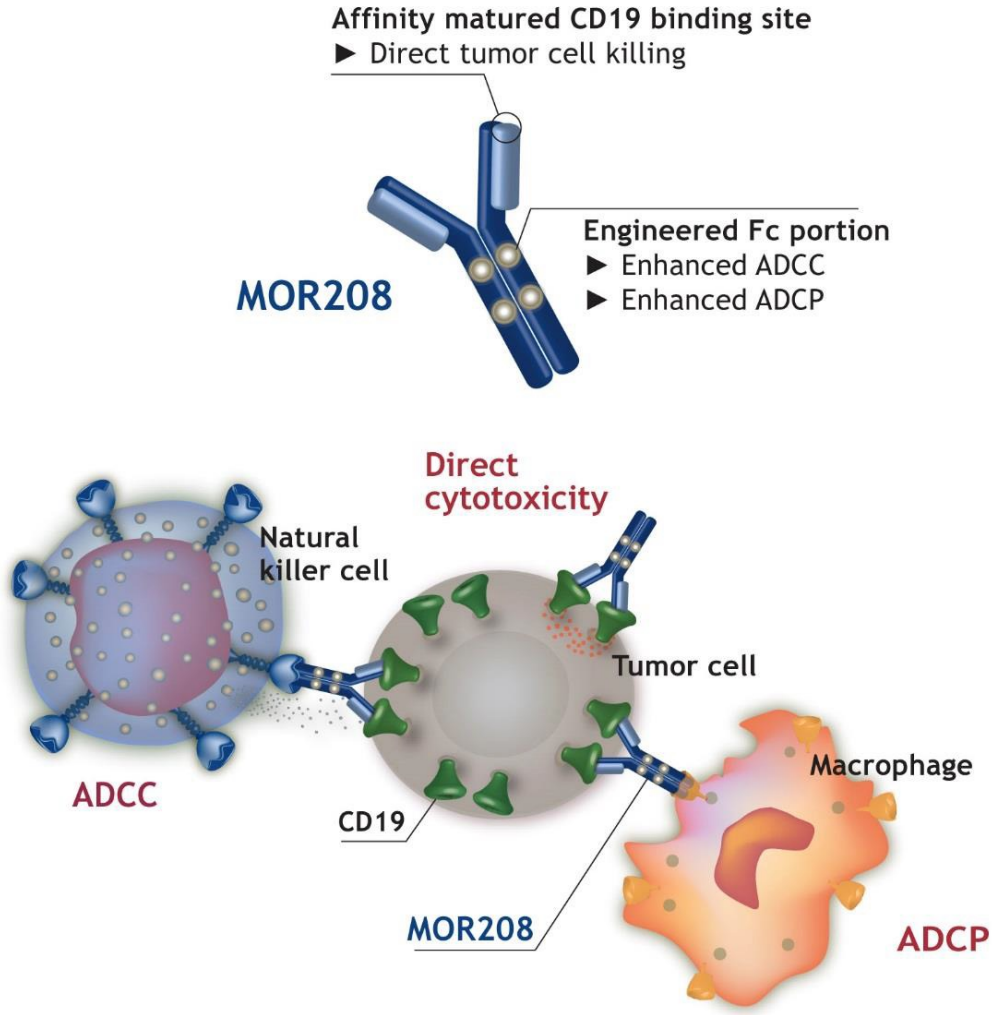




Horvei et al. Blood (2019) 134 (Supplement_1): 2859

Targeting lymphoma B-cells directly with antibodies to CD19

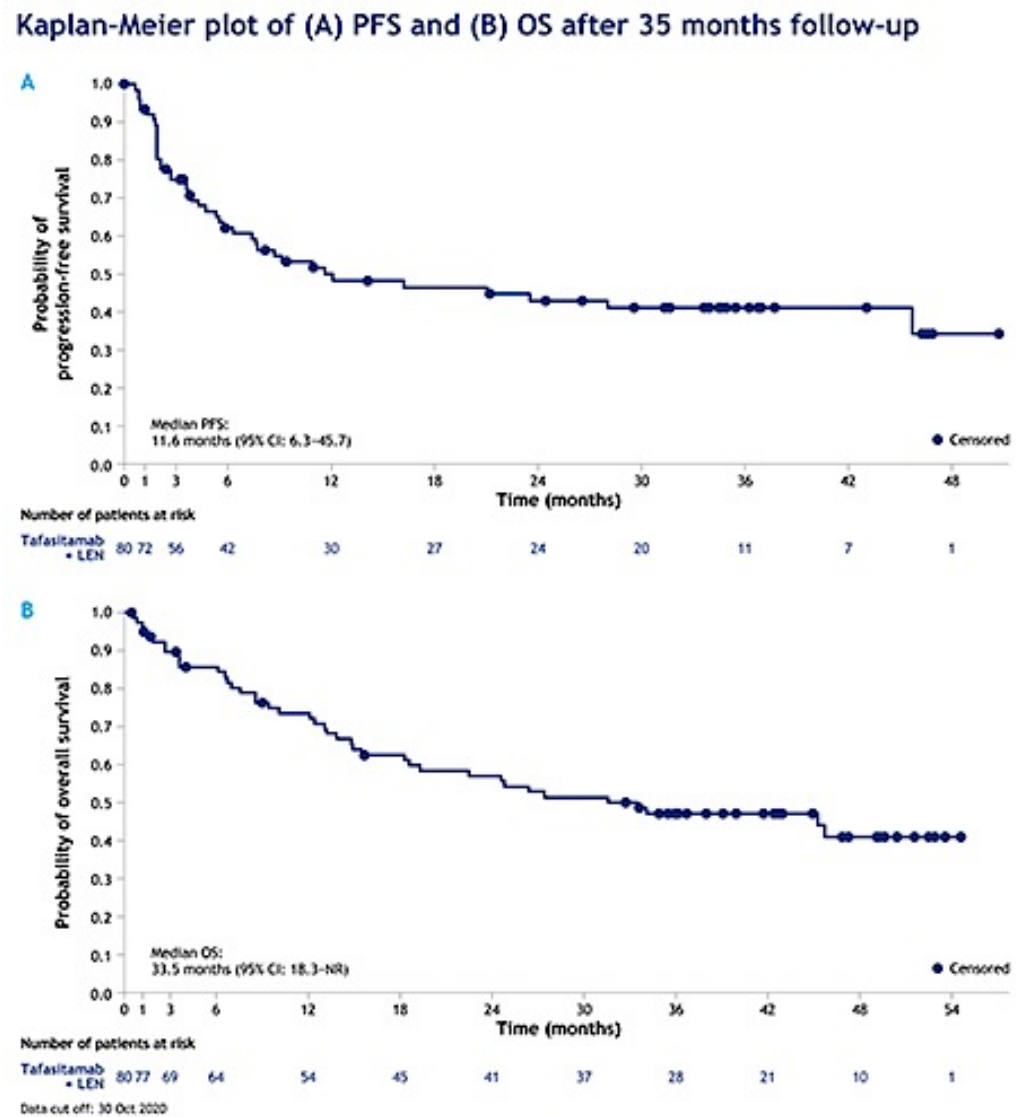
MOR208 = Tafasitamab



ADCC: Antibody-Dependent Cell-Mediated Cytotoxicity
ADCP: Antibody-Dependent Cell-Mediated Phagocytosis

Courtesy of Stephen M Ansell, MD, PhD

LONG-TERM ANALYSES FROM L-MIND, A PHASE II STUDY OF TAFASITAMAB (MOR208) WITH LENALIDOMIDE IN R/R DLBCL



Courtesy of Stephen M Ansell, MD, PhD

Düll J. EHA. 06/09/21; 324124; PB1444

Agenda

Module 1: Mantle Cell Lymphoma (MCL)

- What is your current approach to second-line treatment of MCL?
- How do you currently integrate venetoclax into the management of progressive MCL?
- Do you approach the management of MCL differently for patients with TP53-mutated disease?

Module 2: Diffuse Large B-Cell Lymphoma (DLBCL)

- How does CAR T-cell therapy currently fit into your management of DLBCL?
- At this point, are there discernible clinical differences in the 3 available CAR T-cell products for DLBCL?
- Aside from CAR T-cell therapy, how do you approach sequencing of the other agents and regimens available for second-line treatment and beyond in DLBCL?

Module 3: Hodgkin Lymphoma (HL)

- How do you select up-front systemic treatment for younger patients with advanced-stage HL?
- How do you select up-front systemic treatment for elderly patients with advanced-stage HL?

How do you select up-front systemic treatment for younger patients with advanced-stage HL?

Dr Jeff Sharman

Dr Ian Flinn

Dr Christopher Flowers

Dr John Leonard

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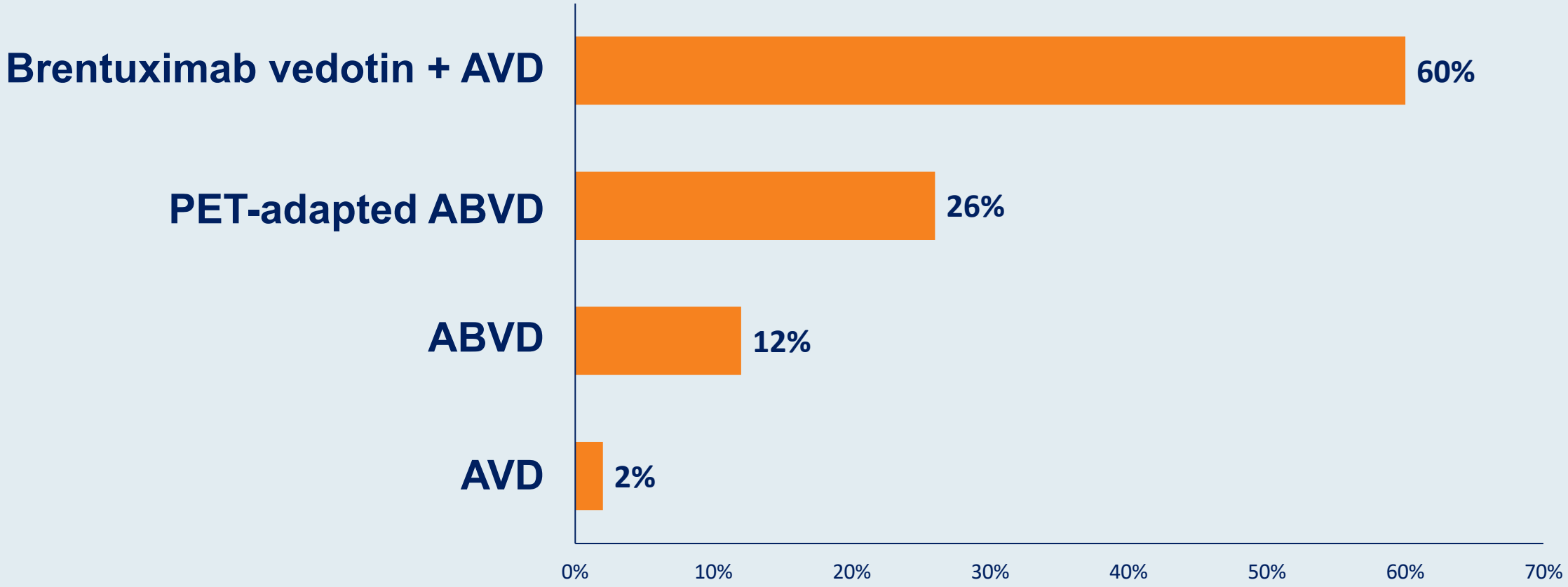
What initial treatment would you recommend for a 26-year-old patient with classical HL with anemia, diffuse adenopathy, hepatosplenomegaly and diffuse bone marrow involvement?



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

Premeeting survey: July 2021

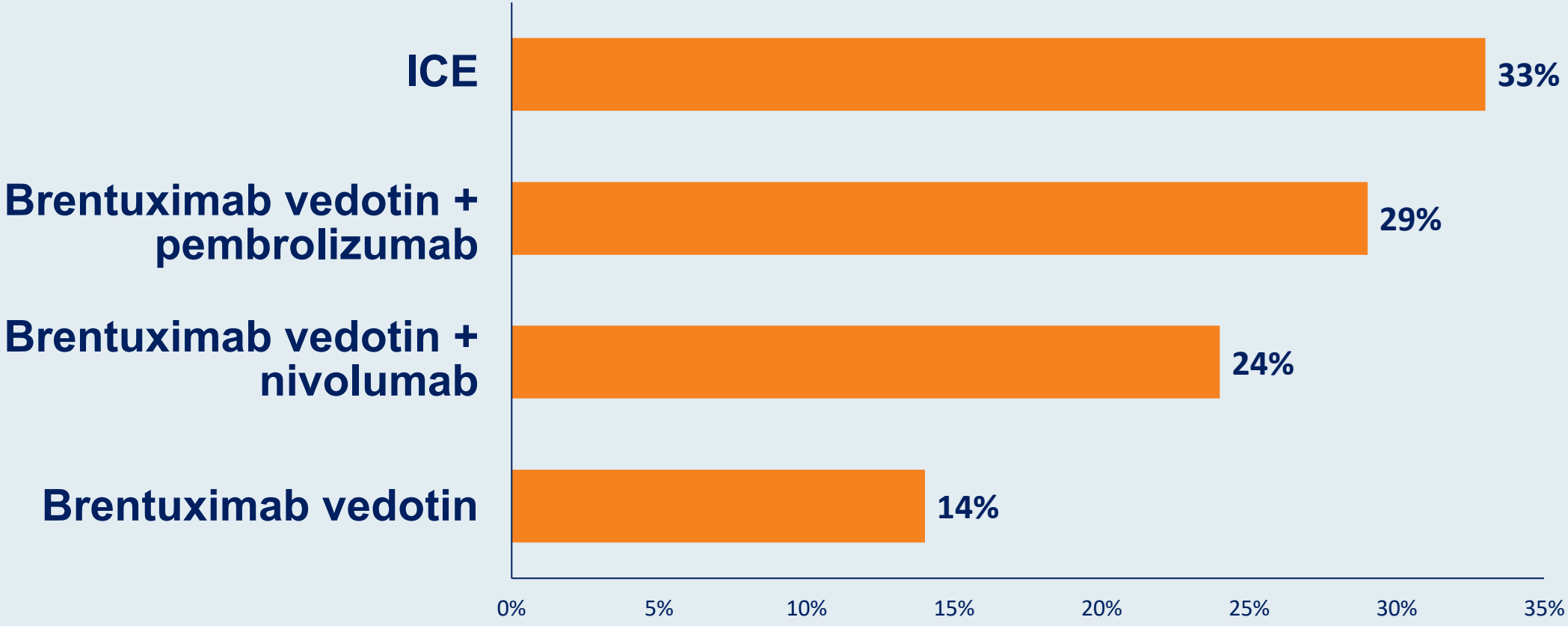
RTP RESEARCH TO PRACTICE

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

 Dr Ansell	Brentuximab vedotin + AVD	 Dr Flowers	Brentuximab vedotin + AVD
 Dr Moskowitz	Brentuximab vedotin + AVD	 Prof Gribben	Brentuximab vedotin + AVD
 Dr Sehn	Brentuximab vedotin + AVD	 Dr Kahl	Brentuximab vedotin + AVD
 Dr Fowler	Brentuximab vedotin + AVD	 Dr Leonard	Brentuximab vedotin + AVD
 Dr Flinn	Brentuximab vedotin + AVD	 Dr Sharman	Brentuximab vedotin + AVD

AVD = doxorubicin/vinblastine/dacarbazine

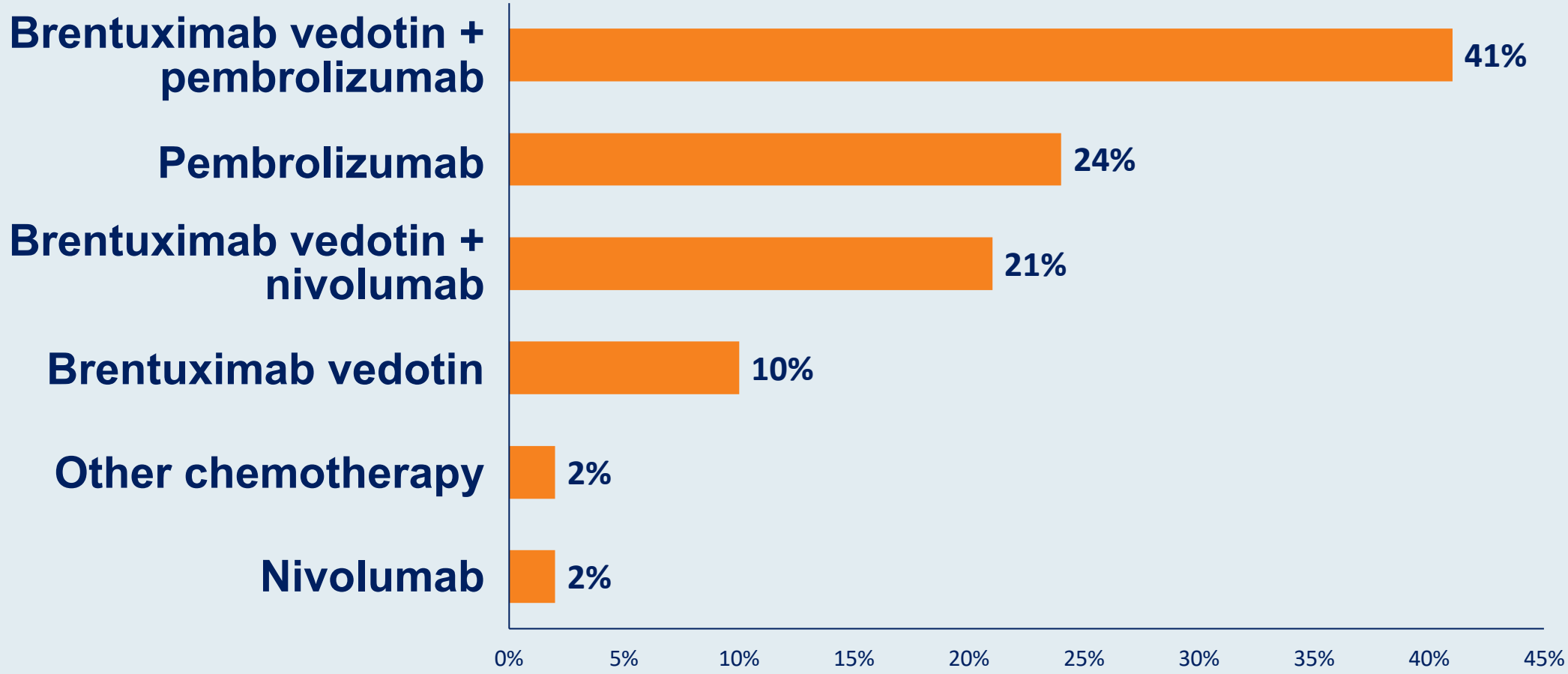
Regulatory and reimbursement issues aside, in general, what would be your preferred bridge to transplant for a patient with HL who is experiencing relapse after up-front ABVD?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

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



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

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

 Dr Ansell	Brentuximab vedotin + nivolumab	 Dr Flowers	Brentuximab vedotin + nivolumab
 Dr Moskowitz	Brentuximab vedotin + nivolumab	 Prof Gribben	Nivolumab
 Dr Sehn	Nivolumab	 Dr Kahl	Brentuximab vedotin + nivolumab
 Dr Fowler	Brentuximab vedotin + nivolumab	 Dr Leonard	Pembrolizumab
 Dr Flinn	Nivolumab	 Dr Sharman	Brentuximab vedotin + nivolumab

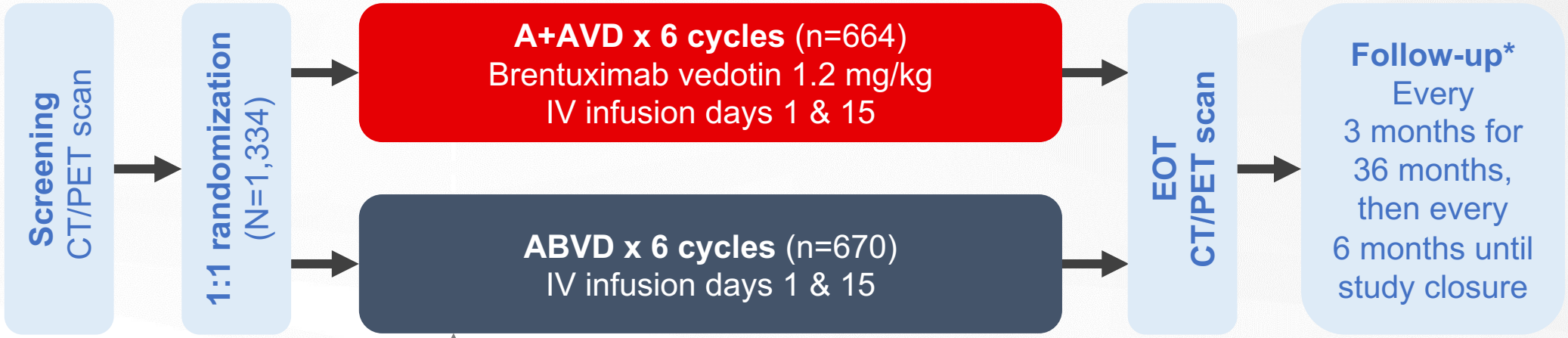
How do you approach first-line treatment for younger patients with advanced HL, and how does risk status factor in? For which patients with newly diagnosed advanced-stage HL do you recommend brentuximab vedotin in combination with AVD as first-line therapy?

How do you treat advanced stage HL?
Stage III/IV

- ABVD x 6
- Escalated BEACOPP x 6
- BV-AVD x 6
- ABVD x 2 followed by an interim PET after 2 cycles to inform further therapy
- Escalated BEACOPP x 2 followed by an interim PET after 2 cycles to inform further therapy

- **Many studies include stage IIA poor risk and IIB: This is not advanced stage HL!**

ECHELON-1 is an open-label, international, randomized, phase 3 trial comparing A+AVD vs ABVD in patients with advanced cHL



Primary endpoint: modified PFS per IRF

Key secondary endpoints: OS, rate of PET2-negativity, safety

Long-term follow-up assessments

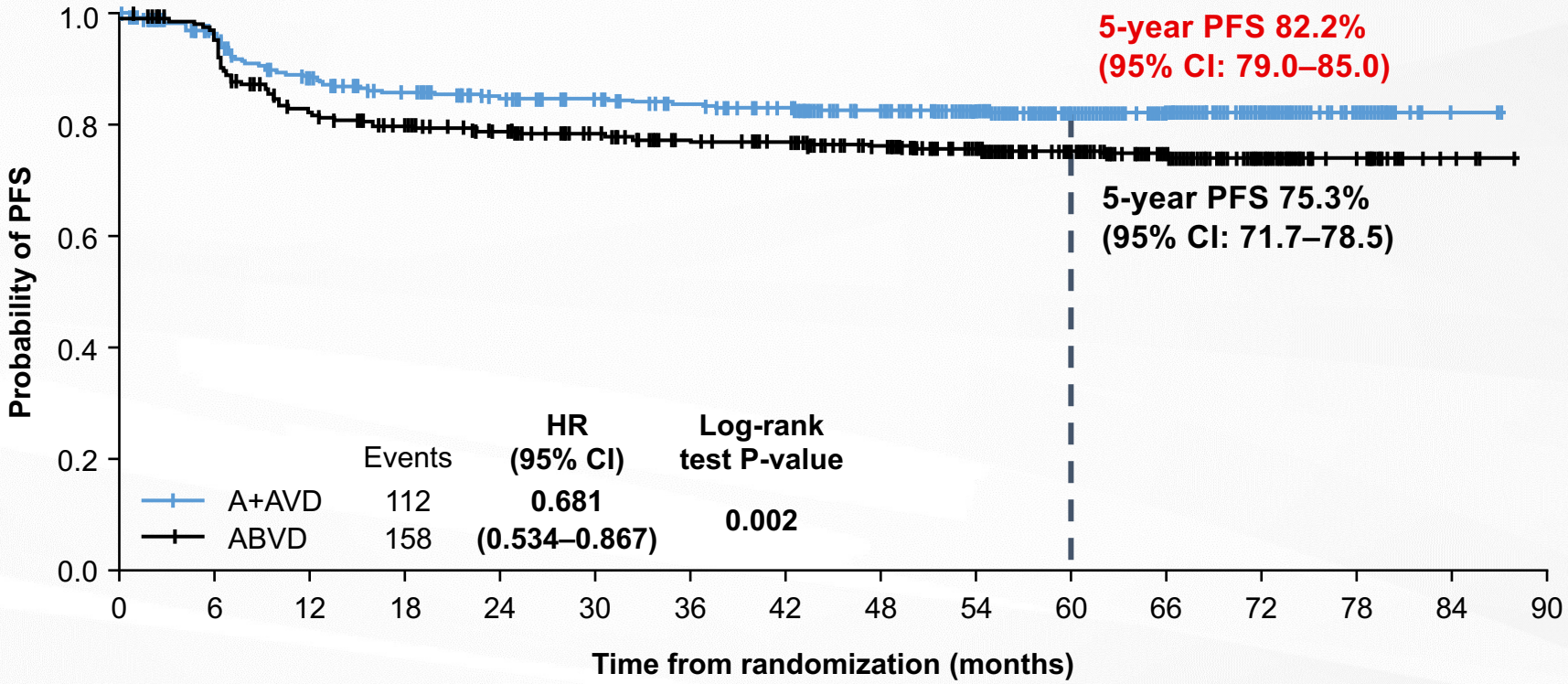
- PFS per investigator in the ITT population was assessed at a median follow-up of approximately 5 years' follow-up.
- Patients are followed for survival until death or for a minimum of 10 years after enrollment of the last patient.
- Post-treatment follow-up for secondary malignancies and other safety events performed Q3M until 36 months after EOT, then Q6M.

*Per protocol: During post-treatment follow-up, patients are to be followed for survival and disease status Q3M for 36 months and then Q6M until death/study closure. Investigators are requested to document response assessed from any scans performed either as standard of care or based on clinical judgment before initiation of any subsequent anticancer therapy for cHL. Investigators are also requested to document best response to any subsequent salvage anticancer therapies and any multimodality therapy that includes brentuximab vedotin as a component of the regimen.
CT, computed tomography; EOT, end of treatment; IV, intravenous; OS, overall survival; PET2, PET status after 2 cycles of treatment; Q3M, every 3 months; Q6M, every 6 months.

Courtesy of Craig Moskowitz, MD

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

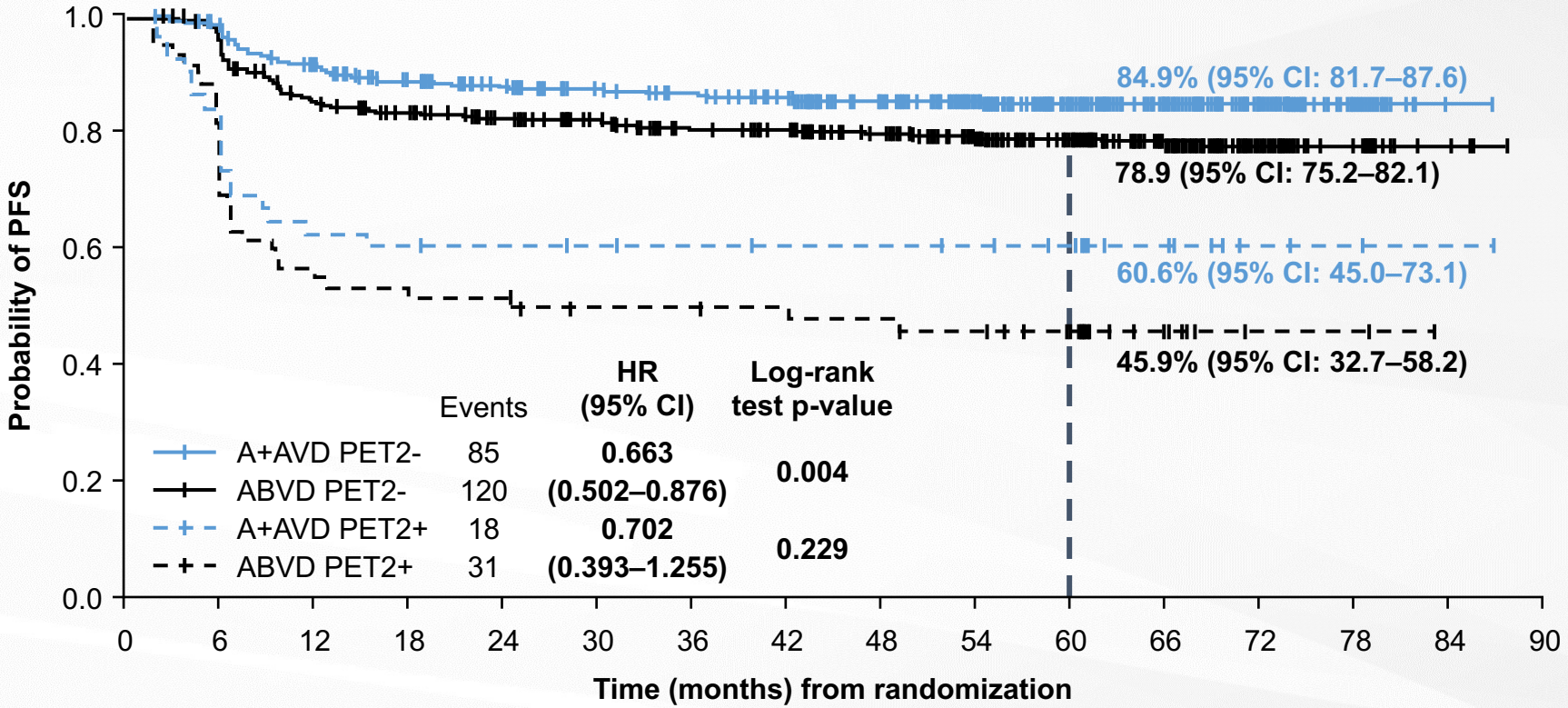
- As of the 5-year follow-up, the prespecified number of events required to trigger an OS analysis have not been reached
- OS was a prespecified key secondary endpoint

*September 14, 2020 data cut-off.

Courtesy of Craig Moskowitz, MD

Straus DJ et al. ASH 2020;Abstract 2973

ECHELON-1: 5-year PFS rates by PET2 status



Number of patients at risk

A+AVD PET2-	588	572	526	500	484	472	460	444	417	386	312	189	98	36	1	0
ABVD PET2-	578	558	483	463	442	424	400	392	368	334	271	170	70	20	4	0
A+AVD PET2+	47	39	28	27	26	25	24	23	23	22	18	10	3	2	1	0
ABVD PET2+	58	46	32	31	30	26	26	25	24	22	18	8	2	2	0	0

Courtesy of Craig Moskowitz, MD

Straus DJ et al. ASH 2020;Abstract 2973

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

How do you select up-front systemic treatment for elderly patients with advanced-stage HL?

Dr Jeff Sharman

Dr Ian Flinn

Dr Christopher Flowers

Dr John Leonard

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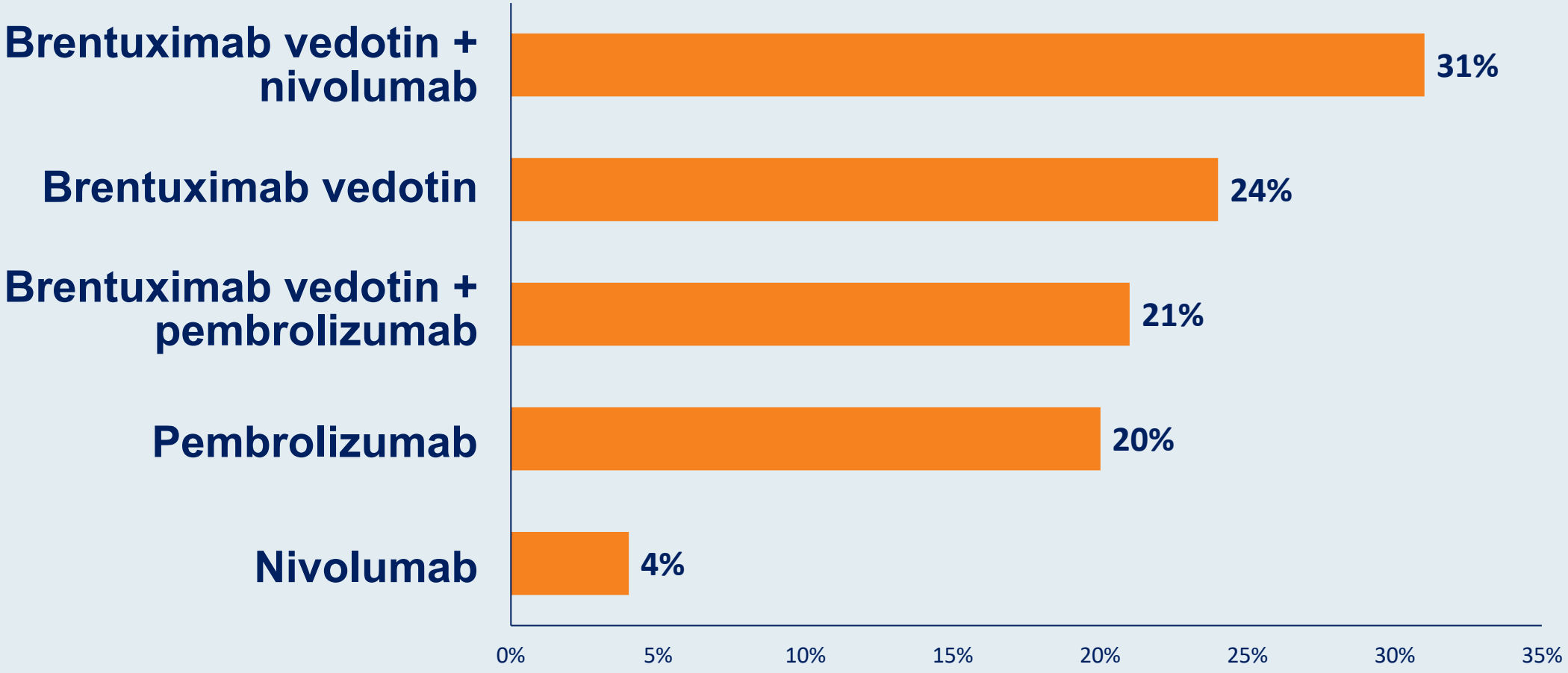
An 85-year-old frail patient with advanced-stage symptomatic HL is not a candidate for aggressive chemotherapy but is seeking active treatment. Regulatory and reimbursement issues aside, what would you recommend?



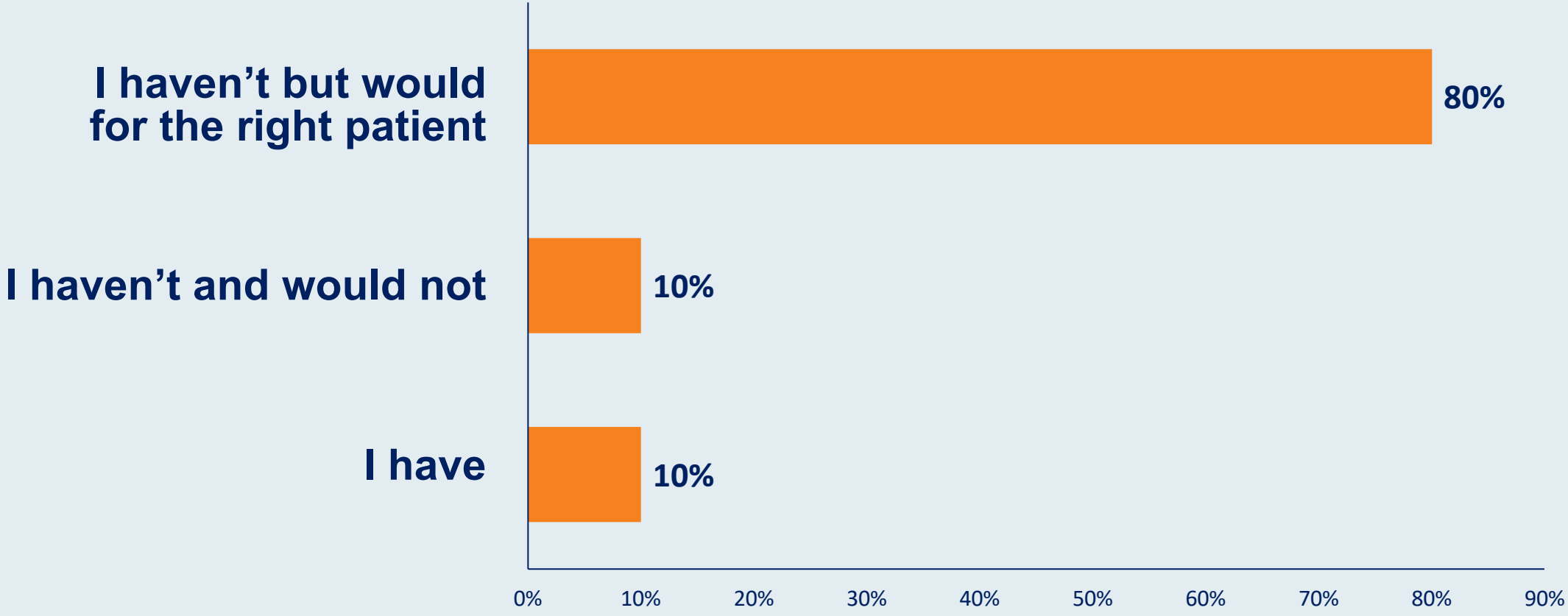
Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

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

 Dr Ansell	Brentuximab vedotin/dacarbazine	 Dr Flowers	Brentuximab vedotin/dacarbazine
 Dr Moskowitz	Pembrolizumab	 Prof Gribben	Nivolumab
 Dr Sehn	Brentuximab vedotin	 Dr Kahl	Pembrolizumab
 Dr Fowler	Brentuximab vedotin	 Dr Leonard	Brentuximab vedotin/dacarbazine
 Dr Flinn	Brentuximab vedotin/dacarbazine	 Dr Sharman	Brentuximab vedotin/dacarbazine Brentuximab vedotin + nivolumab

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



Premeeting survey: July 2021

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

 Dr Ansell	I have	 Dr Flowers	I haven't but would for the right patient
 Dr Moskowitz	I have	 Prof Gribben	I haven't and would not
 Dr Sehn	I haven't and would not	 Dr Kahl	I have
 Dr Fowler	I haven't but would for the right patient	 Dr Leonard	I haven't but would for the right patient
 Dr Flinn	I have	 Dr Sharman	I haven't but would for the right patient

What is the optimal first-line therapy for an older patient with newly diagnosed advanced-stage HL?

How do I treat ASHL?

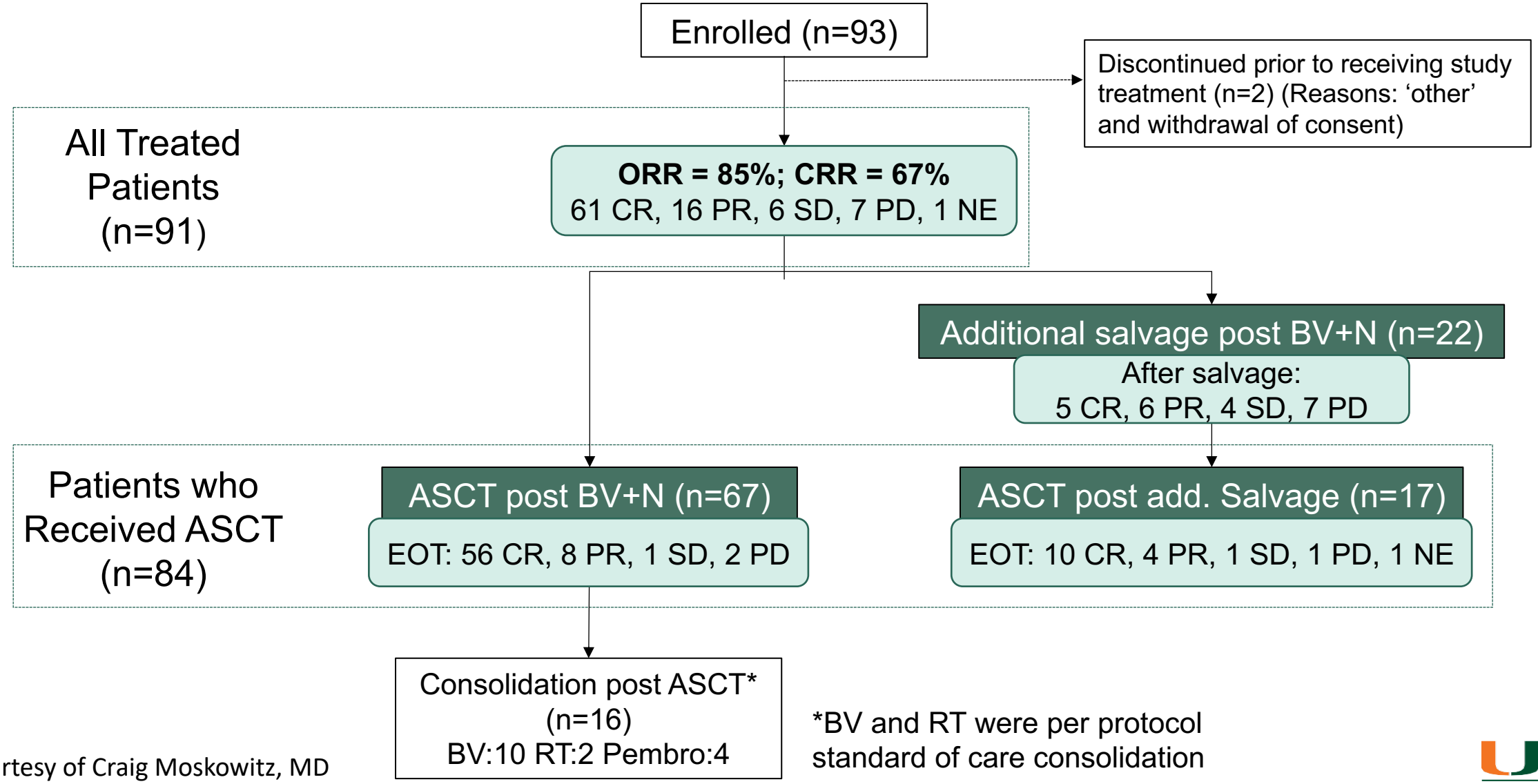
1. Enroll on national study
2. Off protocol BV-AVD for stage IIIB and IV, PET-adapted IIIA
3. Pts older than 60 get a variation on theme

Let's remember the intergroup study does not have an arm for PET-adapted therapy; the field is moving on

Is it reasonable to treat a patient with BV in combination with an anti-PD-1 antibody in any HL clinical situation outside of a clinical trial?

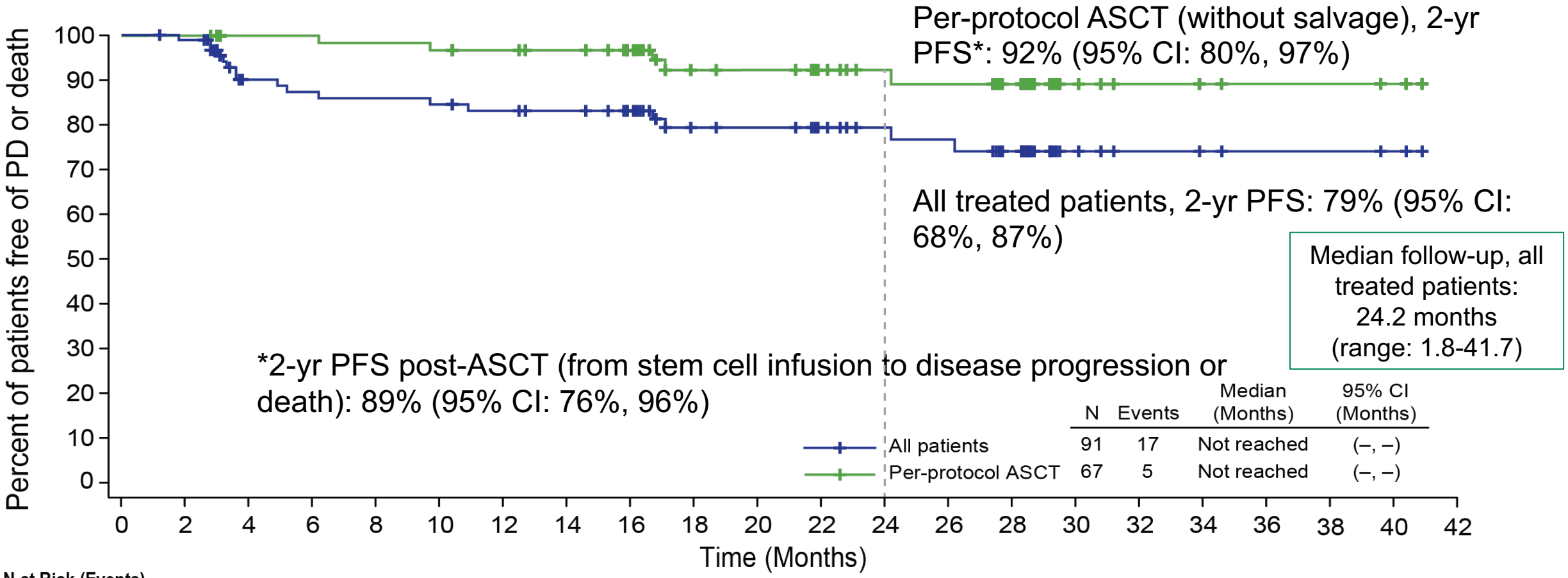
- Pts that have received BV-AVD and had primary refractory disease or short remission duration: I do not re-treat with BV
- Pts that have not received BV upfront: I always treat off protocol with BV in first salvage
- Historically this has been in combination with ICE, which we published in *Lancet Oncology* as well as *Blood*
- But it is very clear that the combination of BV and Nivo has equivalent efficacy as outpatient treatment and has a better safety profile
- Therefore, it is my treatment of choice in first relapse HL, and PMBL off study

Phase 1/II Trial: Brentuximab Vedotin in combination with Nivolumab therapy following study treatment, including ASCT



Courtesy of Craig Moskowitz, MD

Phase 1/II Trial: Progression-free survival in all treated patients versus patients who received per-protocol ASCT (without salvage)

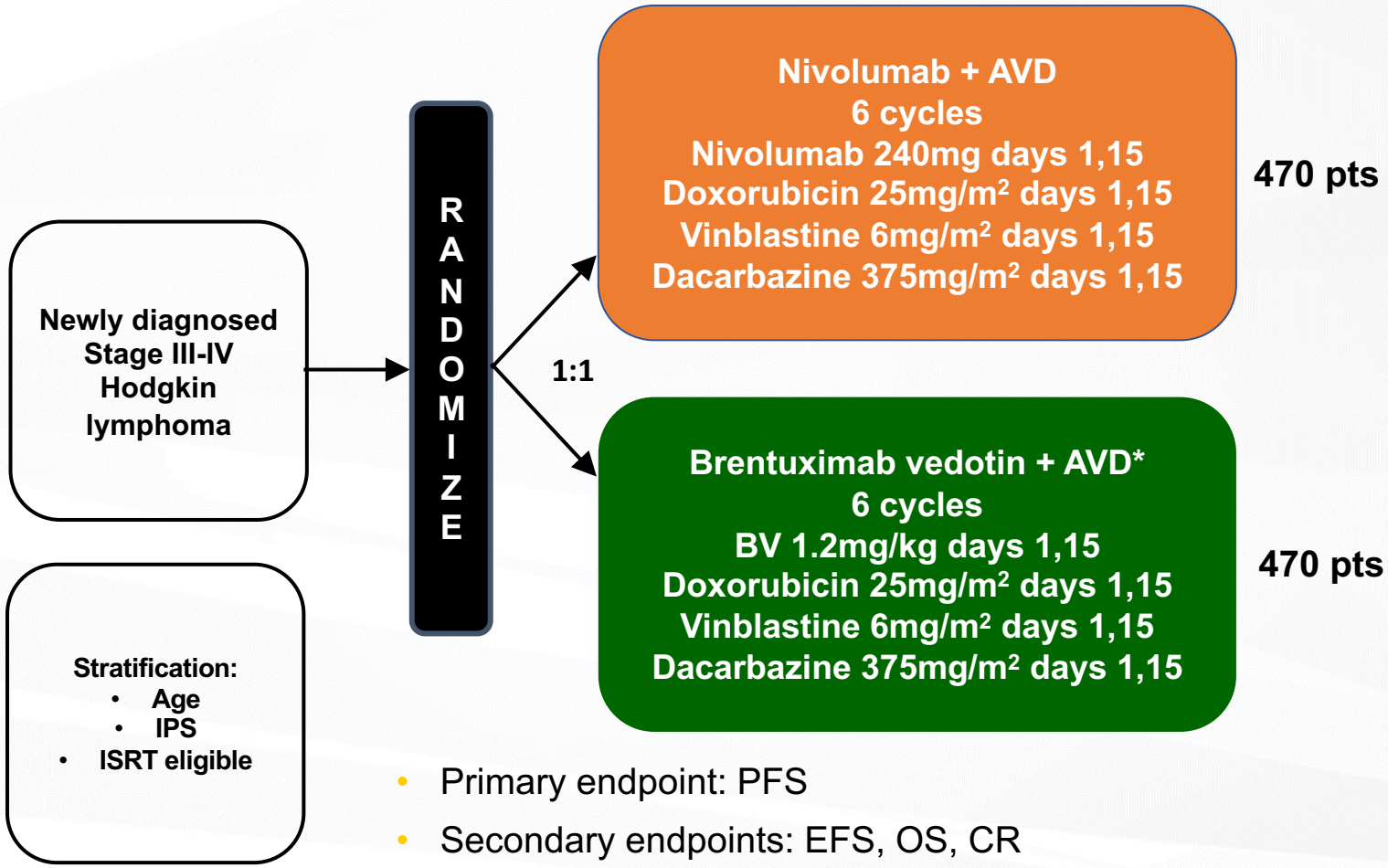


N at Risk (Events)

All patients	91(0)	89(1)	65(8)	63(10)	62(11)	61(12)	58(13)	56(13)	51(13)	39(15)	38(15)	34(15)	30(15)	29(16)	24(17)	8(17)	5(17)	4(17)	3(17)	3(17)	2(17)	0(17)
Per-protocol ASCT	67(0)	67(0)	61(0)	61(0)	60(1)	59(2)	57(2)	55(2)	50(2)	38(4)	37(4)	33(4)	29(4)	28(5)	24(5)	8(5)	5(5)	4(5)	3(5)	3(5)	2(5)	0(5)

Courtesy of Craig Moskowitz, MD

SWOG-S1826: Treatment/Schema



Post-Tx ISRT allowed for pts declared ISRT-eligible prior to randomization with EOT:

- DS 4-5
- ≥ 30% reduction in max transverse diameter

AND

- Residual LN ≥ 2.5cm

OR

- Residual extranodal > 1cm

- Primary endpoint: PFS
- Secondary endpoints: EFS, OS, CR

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

Courtesy of Craig Moskowitz, MD

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

Consensus or Controversy? Clinical Investigator Perspectives on the Current and Future Management of Colorectal and Gastroesophageal Cancers

Tuesday, August 3, 2021
5:00 PM – 6:30 PM ET

Faculty

Chloe E Atreya, MD, PhD
Dustin Deming, MD
Eric Van Cutsem, MD, PhD
Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 2-3 business days.

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