Consensus or Controversy? Investigators Discuss Clinical Practice Patterns and Available Research Data Guiding the Management of Hematologic Cancers

Hodgkin and Non-Hodgkin Lymphoma

Friday, December 4, 2020
7:00 PM – 8:30 PM Pacific Time

Faculty

Jonathan W Friedberg, MD, MMSc
John Kuruvilla, MD
Ann S LaCasce, MD, MMSc
John P Leonard, MD
Michael E Williams, MD, ScM

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Genentech, a member of the Roche Group, Incyte Corporation, Karyopharm Therapeutics 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 commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies Corporation, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Epizyme Inc, Exelixis Inc, Foundation Medicine, Genentech, a member of the Roche Group, Genmab, Genomic Health Inc, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Guardant Health, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seagen Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, Teva Oncology, Tokai Pharmaceuticals Inc and Verastem Inc.

RTP
RESEARCH
TO PRACTICE

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 Friedberg — Disclosures

Data and Safety Monitoring Board/Committee	Acerta Pharma — A member of the AstraZeneca Group, Bayer HealthCare Pharmaceuticals

RTP
RESEARCH
TO PRACTICE

Dr Kuruvilla — Disclosures

Consulting Agreements	AbbVie Inc, Bristol-Myers Squibb Company, Gilead Sciences Inc, Karyopharm Therapeutics, Merck, Roche Laboratories Inc, Seagen Inc
Contracted Research	AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Celgene Corporation, Gilead Sciences Inc, Janssen Biotech Inc, Karyopharm Therapeutics, Merck, Novartis, Roche Laboratories Inc, Seagen Inc
Honoraria	Amgen Inc, Antengene, AstraZeneca Pharmaceuticals LP, Celgene Corporation, Gilead Sciences Inc, Janssen Biotech Inc, Karyopharm Therapeutics, Merck, Novartis, Pfizer Inc, Roche Laboratories Inc, Seagen Inc, TG Therapeutics Inc

RTP
RESEARCH
TO PRACTICE

Dr LaCasce — Disclosures

Data and Safety Monitoring Board/Committee	Bristol-Myers Squibb Company

Dr Leonard — Disclosures

Consulting Agreements	ADC Therapeutics SA, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, BeiGene, Celgene Corporation, Genentech, a member of the Roche Group, Gilead Sciences Inc, Karyopharm Therapeutics, MEI Pharma Inc, MorphoSys, Nordic Nanovector, Novartis, Roche Laboratories Inc, Sutro Biopharma
Data and Safety Monitoring Board/Committee	Biotest Pharmaceuticals Corporation, Bristol-Myers Squibb Company

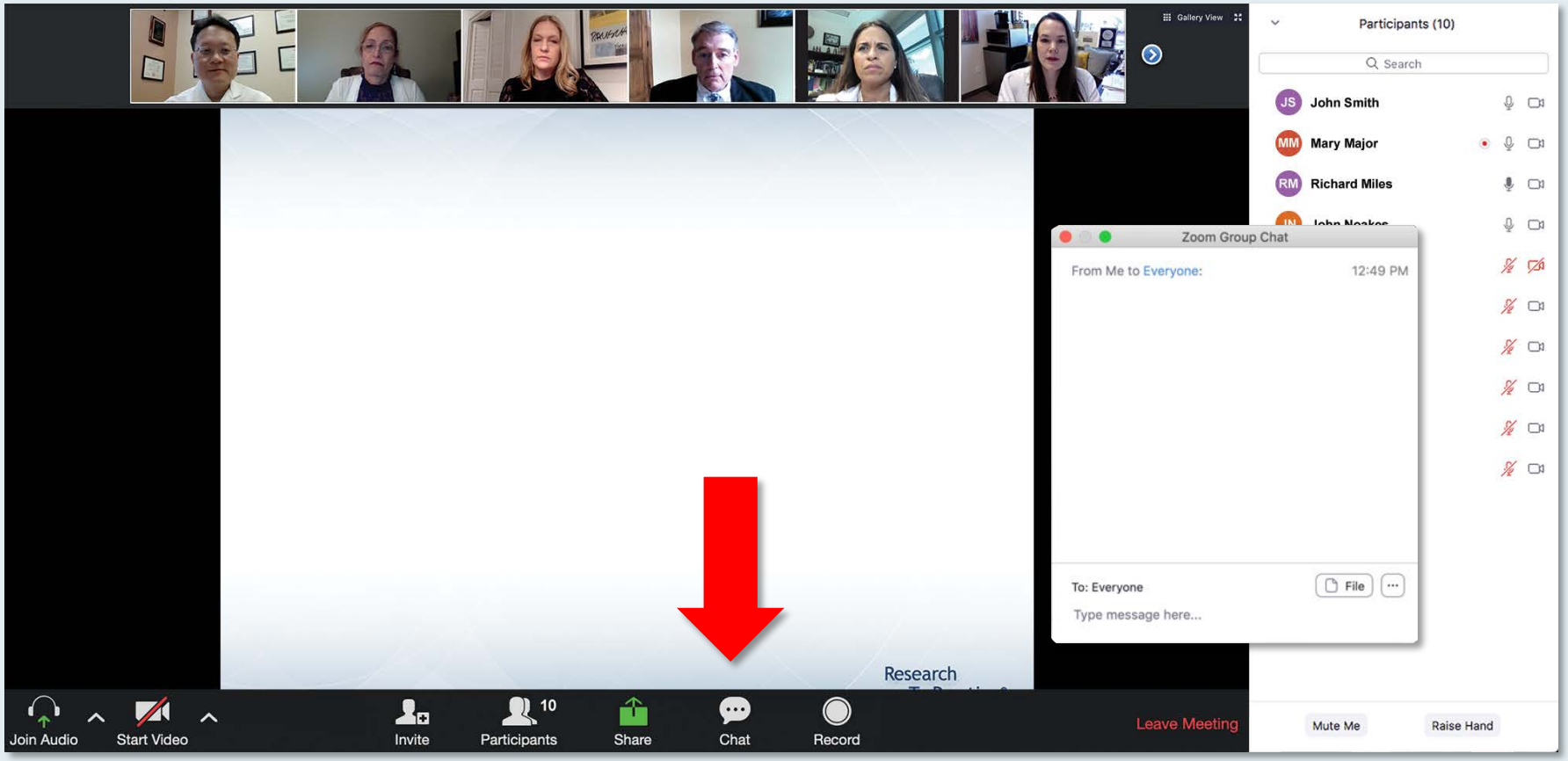
RTP
RESEARCH
TO PRACTICE

Dr Williams — Disclosures

Advisory Committee	AbbVie Inc
Consulting Agreements	Celgene Corporation, Gilead Sciences Inc, TG Therapeutics Inc
Contracted Research	Allos Therapeutics, Celgene Corporation, Gilead Sciences Inc, Janssen Biotech Inc, Pharmacyclics LLC, an AbbVie Company, TG Therapeutics Inc
Speakers Bureau	Xian Janssen Pharmaceutical Ltd

RTP
RESEARCH
TO PRACTICE

We Encourage Clinicians in Practice to Submit Questions

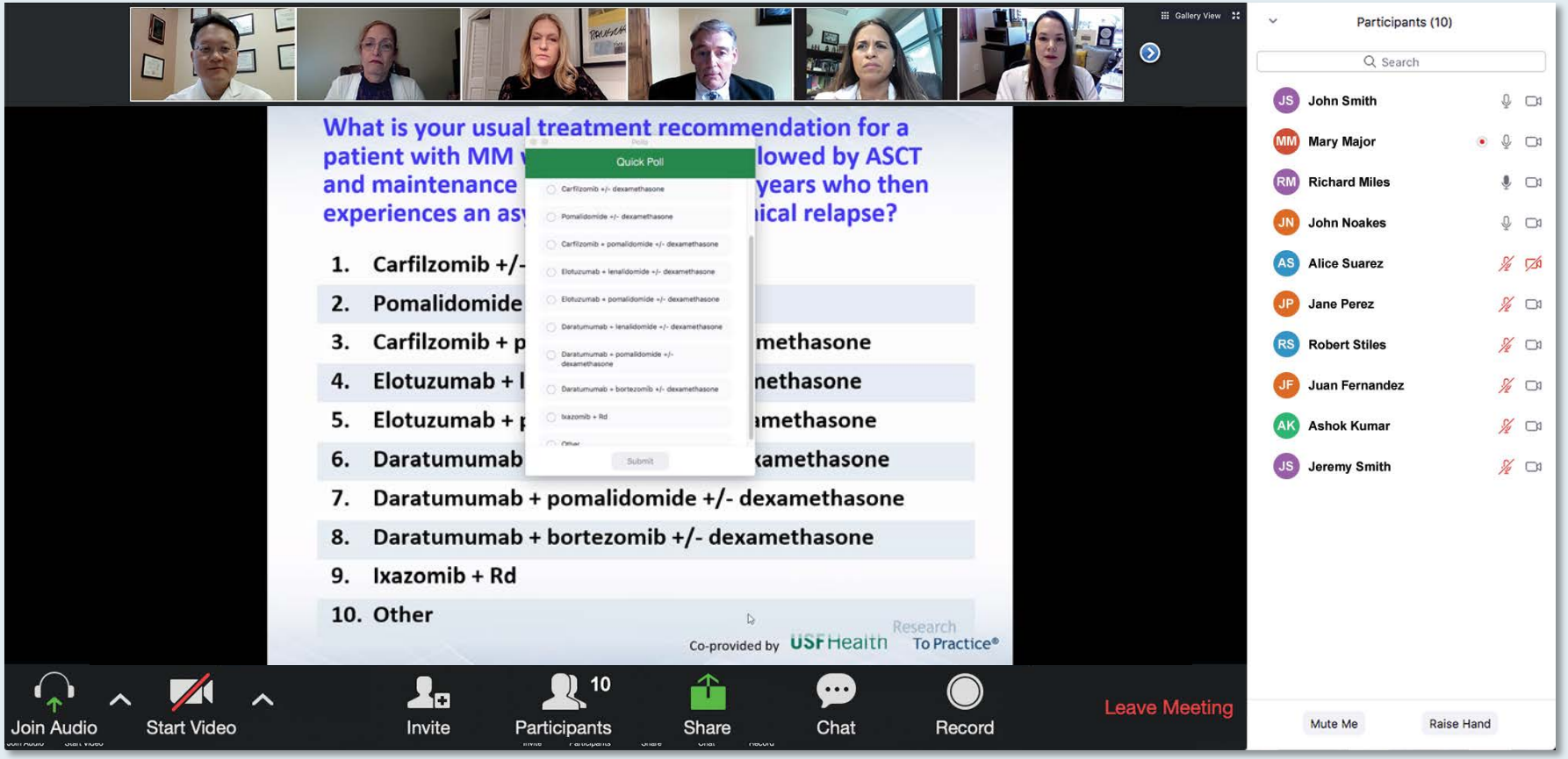


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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

Results will be shown after everyone has answered.

RTP RESEARCH TO PRACTICE

Upcoming Webinars

Tuesday, December 8, 2020
5:00 PM – 6:00 PM ET

Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology
Colorectal and Gastroesophageal Cancers

Faculty
Peter C Enzinger, MD
Zev Wainberg, MD, MSc

Moderator
Neil Love, MD

Wednesday, December 9, 2020
12:30 PM – 1:30 PM ET

Meet The Professor: Immunotherapy and Novel Agents in Gynecologic Cancers

Faculty
Gottfried E Konecny, MD

Moderator
Neil Love, MD

Upcoming Webinars

Thursday, December 10, 2020
8:30 PM – 10:00 PM ET

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Positive Breast Cancer

Faculty

Carey K Anders, MD
Erika Hamilton, MD
Sara Hurvitz, MD
Mark D Pegram, MD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

Friday, December 11, 2020
8:30 PM – 10:00 PM ET

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Triple-Negative Breast Cancer

Faculty

P Kelly Marcom, MD
Joyce O'Shaughnessy, MD
Hope S Rugo, MD
Professor Peter Schmid, MD, PhD

Moderator

Neil Love, MD

Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.

ONCOLOGY TODAY

WITH DR NEIL LOVE

CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY IN NON-HODGKIN LYMPHOMA

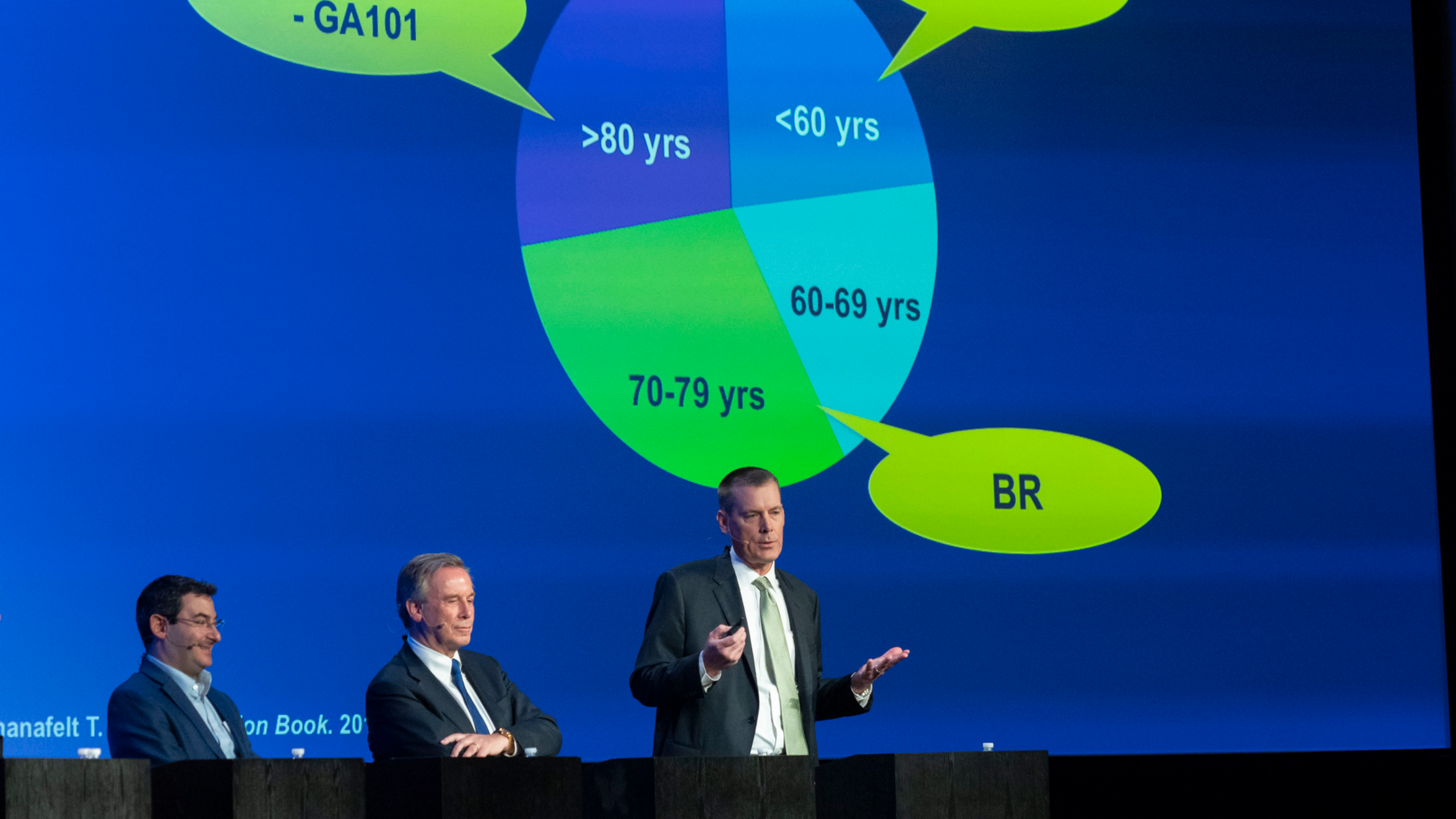
DR TANYA SIDDIQI

CITY OF HOPE NATIONAL MEDICAL CENTER

Listen on Apple Podcasts

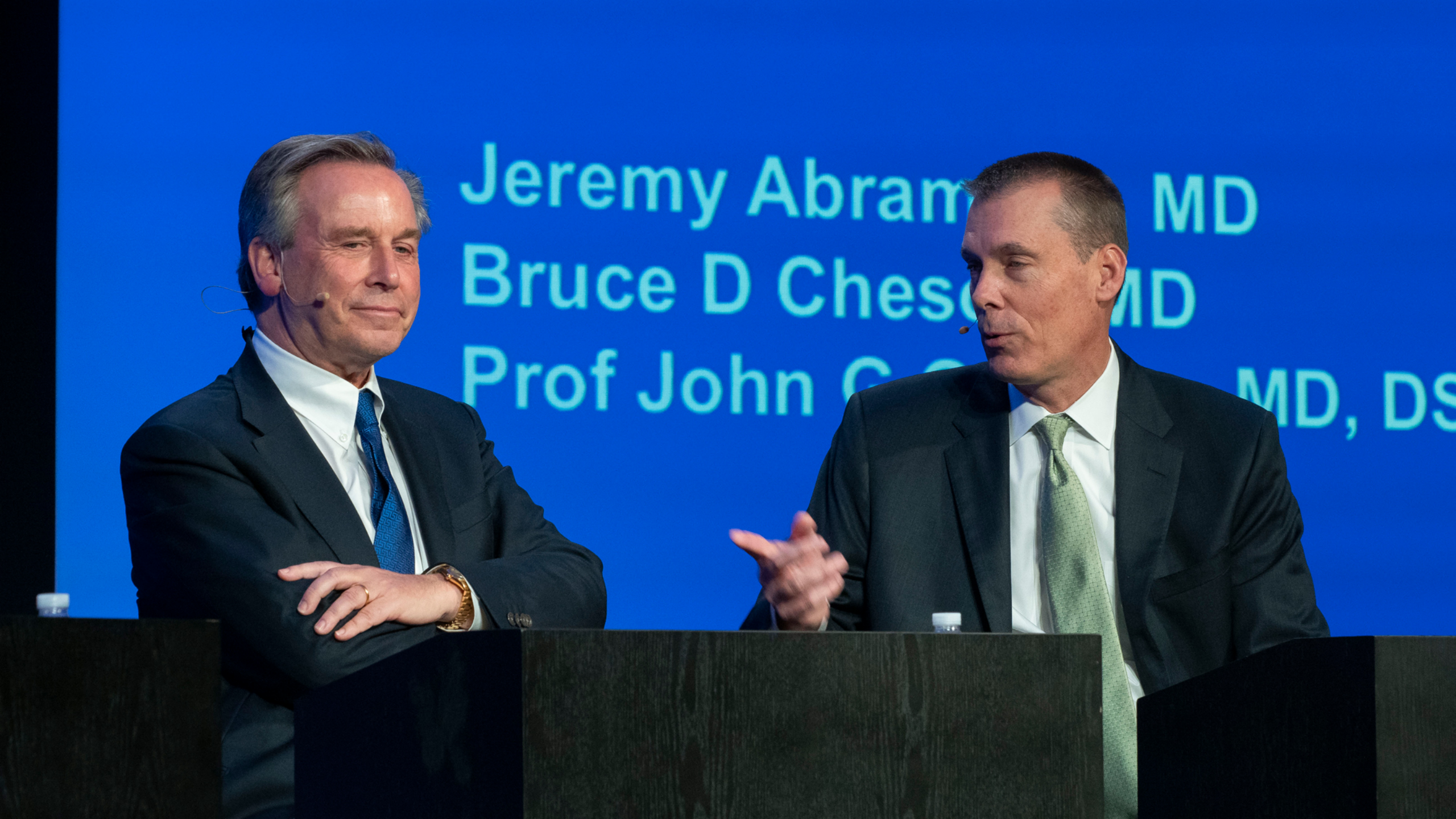
Spotify

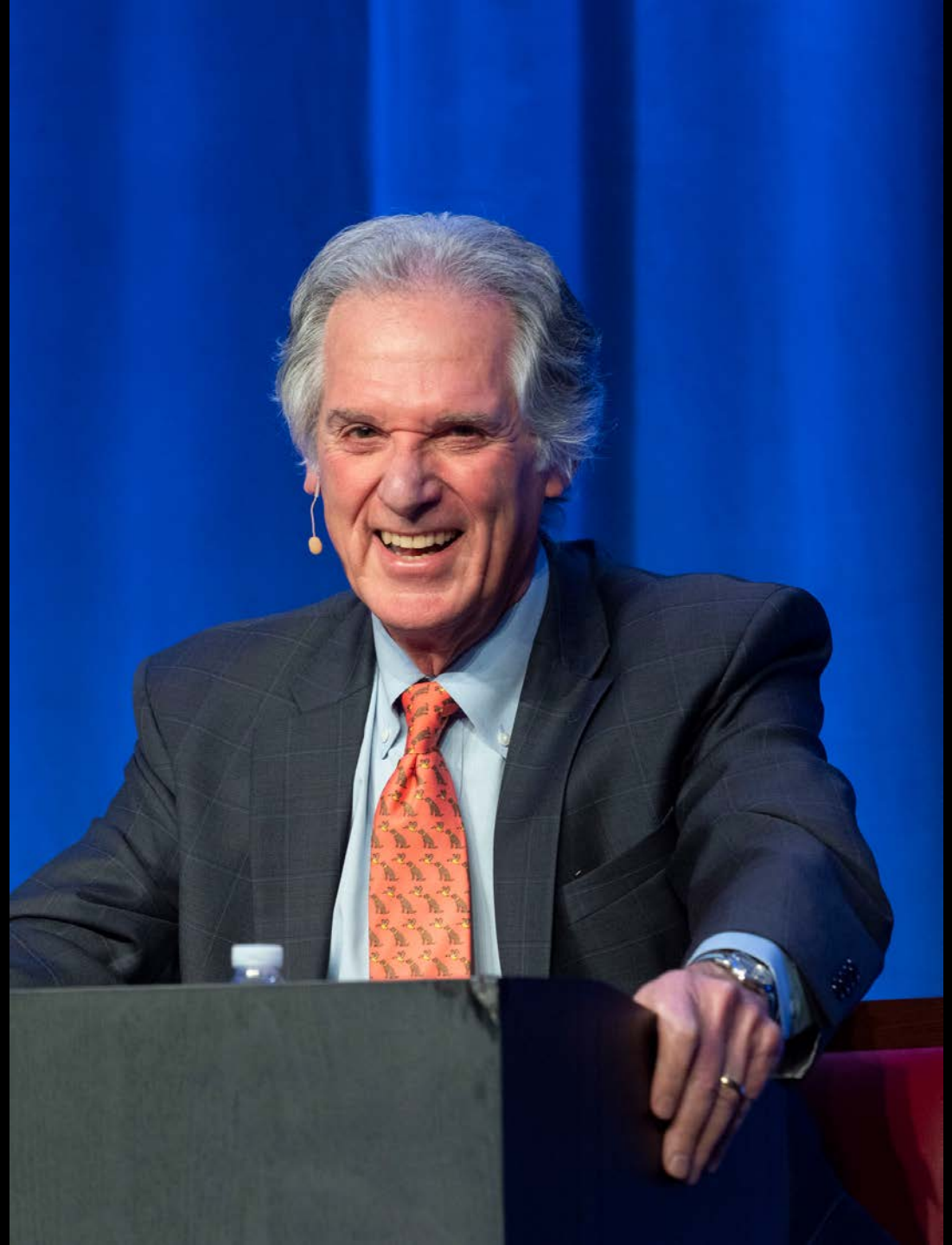
Listen on Google Podcasts

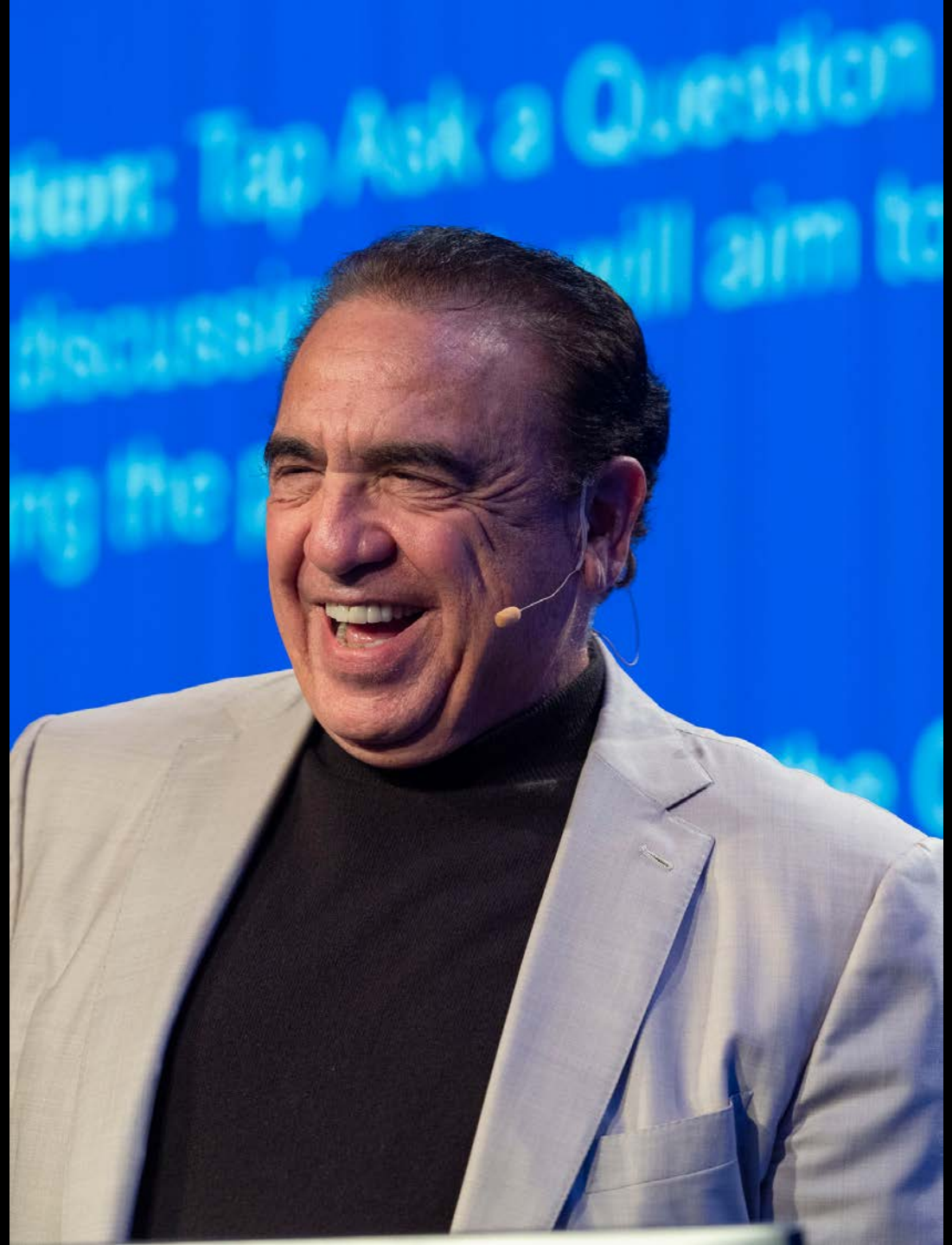

- GA101
>80 yrs
<60 yrs
60-69 yrs
70-79 yrs
BR


ıab
ıcil


Acalabruti
obinutuzuma
Obinutuz
+ chlorambuc
Vene
uzumab


Jeremy Abram MD
Bruce D Ches MD
Prof John C MD, DS





Consensus or Controversy? Investigators Discuss Clinical Practice Patterns and Available Research Data Guiding the Management of Hematologic Cancers

Hodgkin and Non-Hodgkin Lymphoma

Friday, December 4, 2020
7:00 PM – 8:30 PM Pacific Time

Faculty

Jonathan W Friedberg, MD, MMSc
John Kuruvilla, MD
Ann S LaCasce, MD, MMSc
John P Leonard, MD
Michael E Williams, MD, ScM

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

Jonathan W Friedberg, MD, MMSc
Samuel E Durand Professor of Medicine
Director, James P Wilmot Cancer Institute
University of Rochester
Rochester, New York

Ann S LaCasce, MD, MMSc
Director, Dana-Farber/Mass General Brigham Fellowship in Hematology/Oncology
Associate Professor of Medicine
Harvard Medical School
Lymphoma Program
Dana-Farber Cancer Institute
Boston, Massachusetts

John Kuruvilla, MD
Hematologist, Princess Margaret Cancer Centre
Associate Professor, University of Toronto
Toronto, Ontario, Canada

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

RTP
RESEARCH TO PRACTICE

Faculty

Michael E Williams, MD, ScM
Byrd S Leavell Professor of Medicine
Chief, Hematology/Oncology Division
Physician Lead, Cancer Service Line
University of Virginia School of Medicine
Charlottesville, Virginia

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

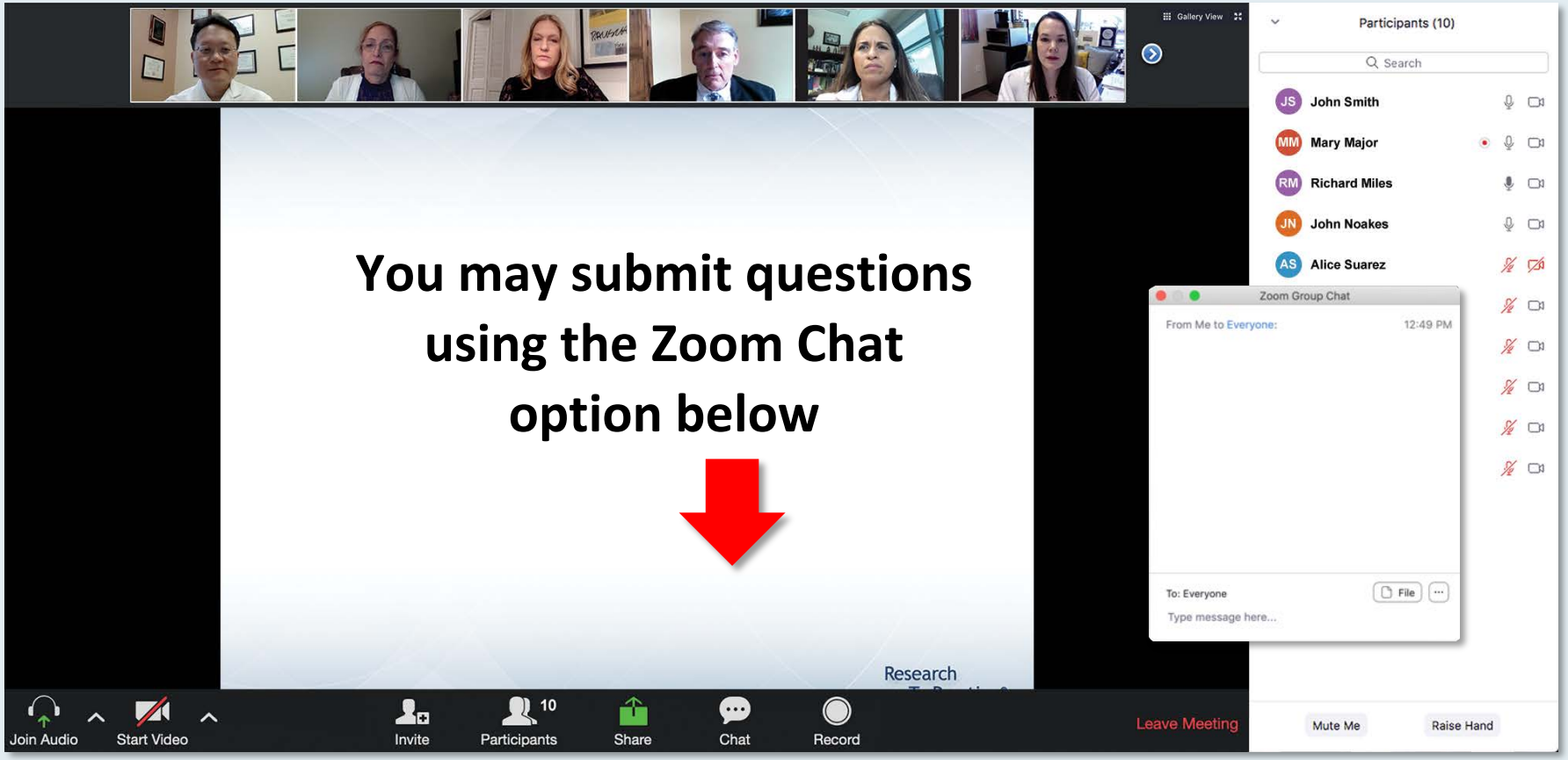
Consensus or Controversy Survey Participants (in Addition to Our Faculty)

Craig Moskowitz, MD
Sylvester Comprehensive Cancer Center
University of Miami Health System
Miami, Florida

Loretta Nastoupil, MD
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Laurie H Sehn, MD, MPH
BC Cancer Agency and University of British Columbia
Vancouver, British Columbia, Canada

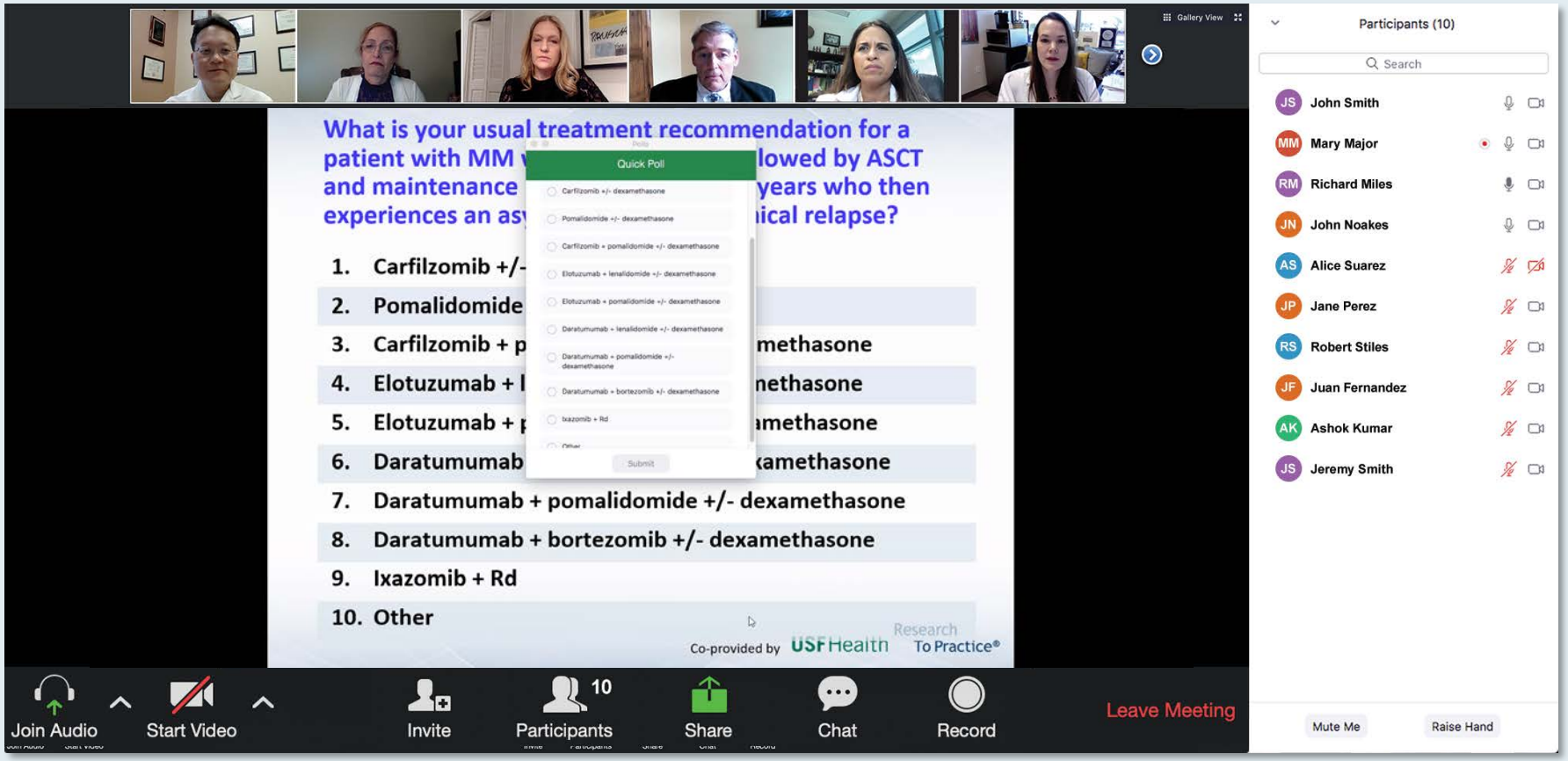
We Encourage Clinicians in Practice to Submit Questions



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

Familiarizing Yourself with the Zoom Interface

How to answer poll questions



When a poll question pops up, click your answer choice from the available options. Results will be shown after everyone has answered.

ONCOLOGY TODAY

WITH DR NEIL LOVE

CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY IN NON-HODGKIN LYMPHOMA

DR TANYA SIDDIQI

CITY OF HOPE NATIONAL MEDICAL CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology

Colorectal and Gastroesophageal Cancers

Tuesday, December 8, 2020
5:00 PM – 6:00 PM ET

Faculty

Peter C Enzinger, MD
Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor
Immunotherapy and Novel Agents in Gynecologic Cancers

Wednesday, December 9, 2020
12:30 PM – 1:30 PM ET

Faculty

Gottfried E Konecny, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Positive Breast Cancer

Thursday, December 10, 2020
8:30 PM – 10:00 PM ET

Faculty

Carey K Anders, MD
Erika Hamilton, MD
Sara Hurvitz, MD
Mark D Pegram, MD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Triple-Negative Breast Cancer

Friday, December 11, 2020
8:30 PM – 10:00 PM ET

Faculty

P Kelly Marcom, MD
Joyce O'Shaughnessy, MD
Hope S Rugo, MD
Professor Peter Schmid, MD, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Recent Advances in Hematologic Oncology: A 4-Part Live Webinar Series Reviewing Key Data and Presentations from the 62nd ASH Annual Meeting

Acute Myeloid Leukemia

Wednesday, January 20, 2021
5:00 – 6:00 PM ET

Faculty
Daniel A Pollyea, MD, MS
Andrew H Wei, MBBS, PhD
Additional faculty to be announced

Multiple Myeloma

Wednesday, February 10, 2021
5:00 – 6:00 PM ET

Faculty
Robert Z Orlowski, MD, PhD
Edward A Stadtmauer, MD
Additional faculty to be announced

Hodgkin and Non-Hodgkin Lymphoma

Wednesday, February 3, 2021
5:00 – 6:00 PM ET

Faculty
John Kuruvilla, MD
John P Leonard, MD
Michael E Williams, MD, ScM

Chronic Lymphocytic Leukemia

Wednesday, February 24, 2021
5:00 – 6:00 PM ET

Faculty
Matthew S Davids, MD, MMSc
Additional faculty to be announced

RTP RESEARCH TO PRACTICE

Consensus or Controversy? Investigators Discuss Clinical Practice Patterns and Available Research Data Guiding the Management of Hematologic Cancers

Hodgkin and Non-Hodgkin Lymphoma

Friday, December 4, 2020
7:00 PM – 8:30 PM Pacific Time

Faculty

Jonathan W Friedberg, MD, MMSc
John Kuruvilla, MD
Ann S LaCasce, MD, MMSc
John P Leonard, MD
Michael E Williams, MD, ScM

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

ASH Lymphomas 2020 Presentation Library

Evolving treatment paradigm for patients with diffuse large B-cell lymphoma (DLBCL)
Ann S LaCasce, MD, MMSc

Download Slides

Optimal management of newly diagnosed and relapsed/ refractory (R/R) follicular lymphoma (FL)
John P Leonard, MD

Download Slides

Available and emerging approaches for mantle cell lymphoma (MCL)
Michael E Williams, MD, ScM

Download Slides

Selection and sequencing of therapies for patients with advanced Hodgkin lymphoma (HL)
John Kuruvilla, MD

Download Slides

Advances in chimeric antigen receptor T-cell therapy for DLBCL and other lymphoma subtypes
Jonathan W Friedberg, MD, MMSc

Download Slides

RTP
RESEARCH TO PRACTICE

Agenda

Module 1: Evolving treatment paradigm for patients with diffuse large B-cell lymphoma (DLBCL) – Dr LaCasce

Module 2: Optimal management of newly diagnosed and relapsed/refractory follicular lymphoma – Dr Leonard

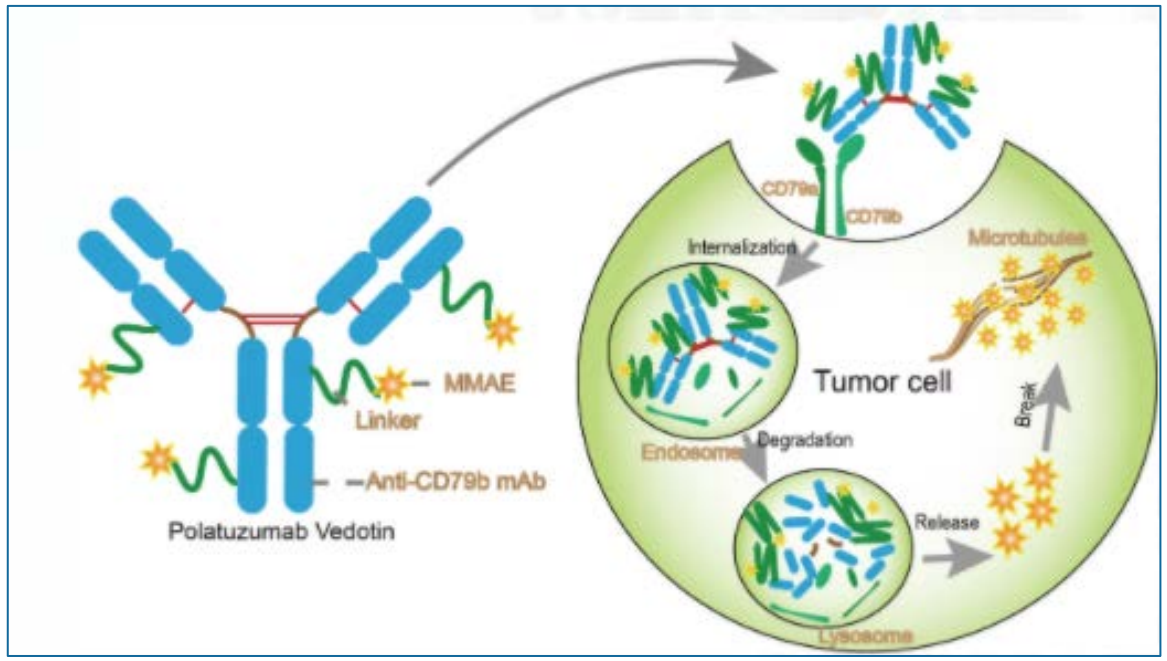
Module 3: Available and emerging approaches for mantle cell lymphoma – Dr Williams

Module 4: Selection and sequencing of therapies for patients with advanced Hodgkin lymphoma – Dr Kuruvilla

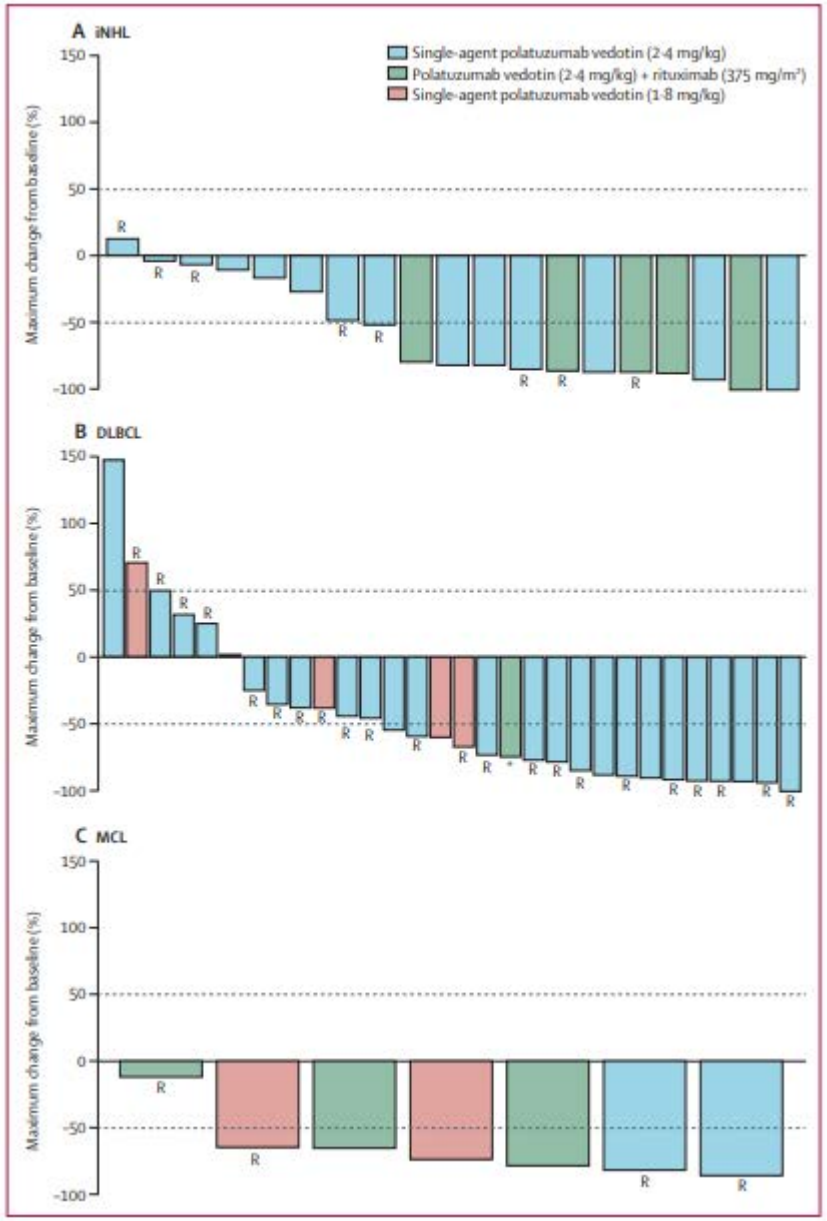
Module 5: Advances in chimeric antigen receptor T-cell therapy for DLBCL and other lymphoma subtypes – Dr Friedberg

RTP
RESEARCH
TO PRACTICE

Polatuzumab vedotin phase I trial for R/R B-cell NHL and CLL



AEs in NHL 2.4 mg/kg	Gr 1-2	Gr 3	Gr 4
Neutropenia	4%	24%	16%
PN sensory	27%	7%	2%



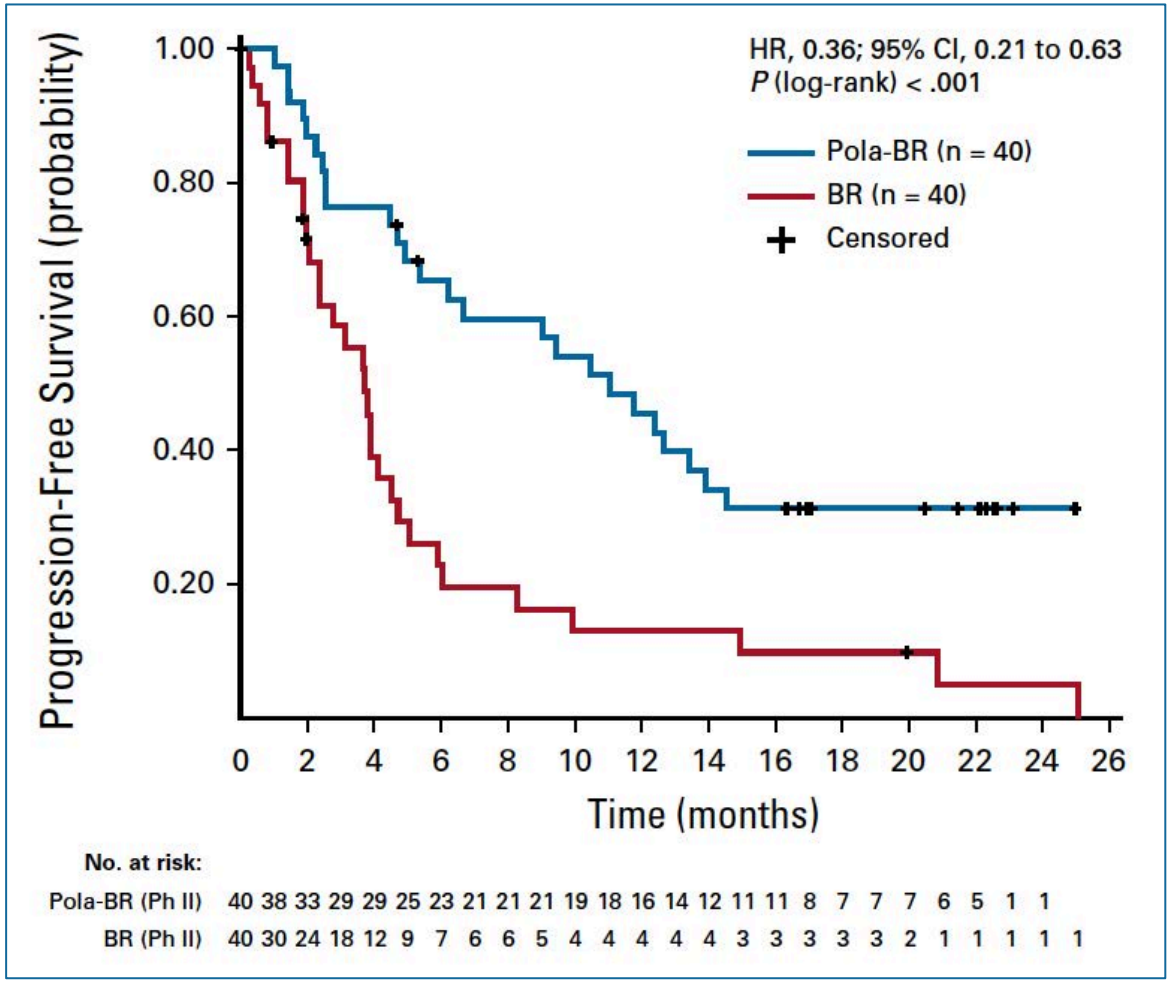
Palanca-Wessels et al. Lancet Oncol 2015

Courtesy of Ann S LaCasce, MD, MMSc

Polatuzumab vedotin + bendamustine + rituximab approved in relapsed/refractory DLBCL

Lines of prior therapy, median (range)	2 (1-7)	2 (1–5)
1	11 (27.5)	12 (30)
2	11 (27.5)	9 (22.5)
≥ 3	18 (45.0)	19 (47.5)
Prior bone marrow transplantation	10 (25.0)	6 (15.0)

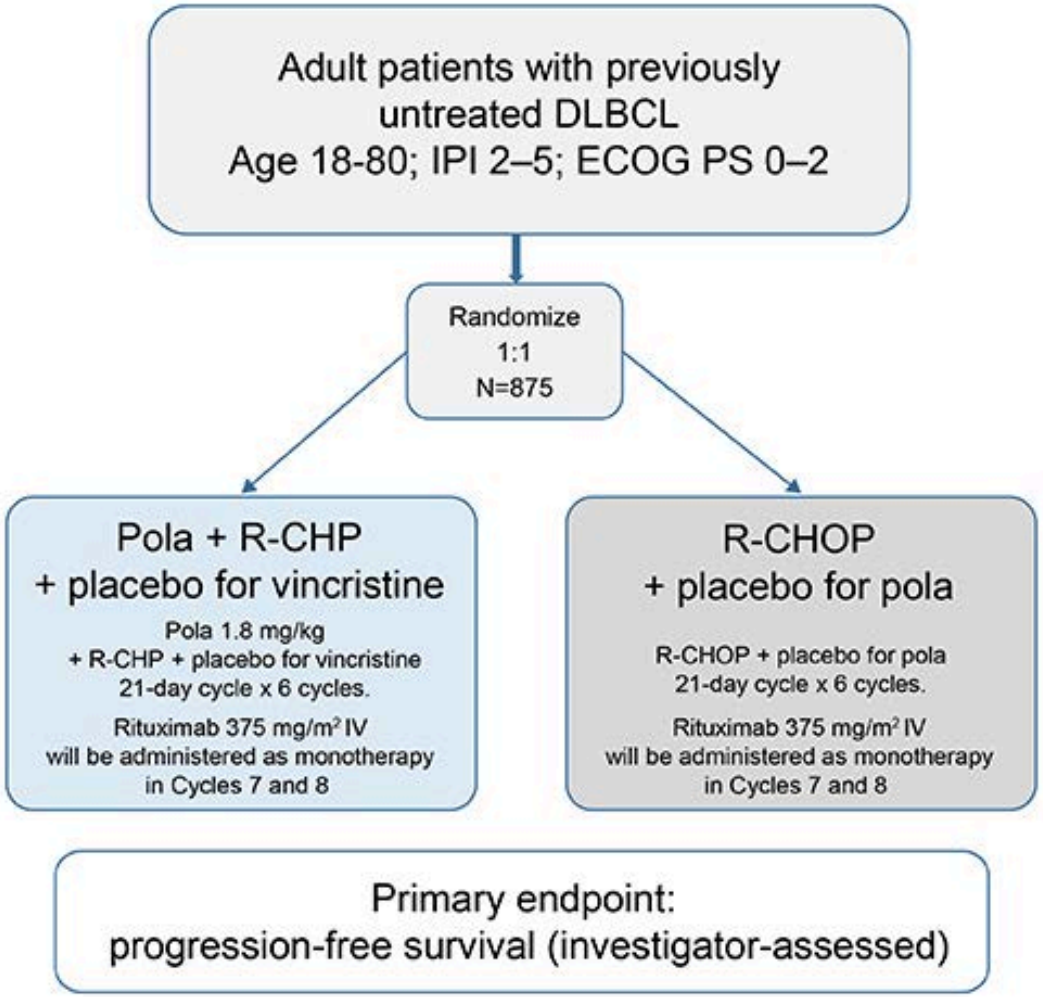
ORR 62.5%
CR rate 50%



Sehn et al. JCO 2019

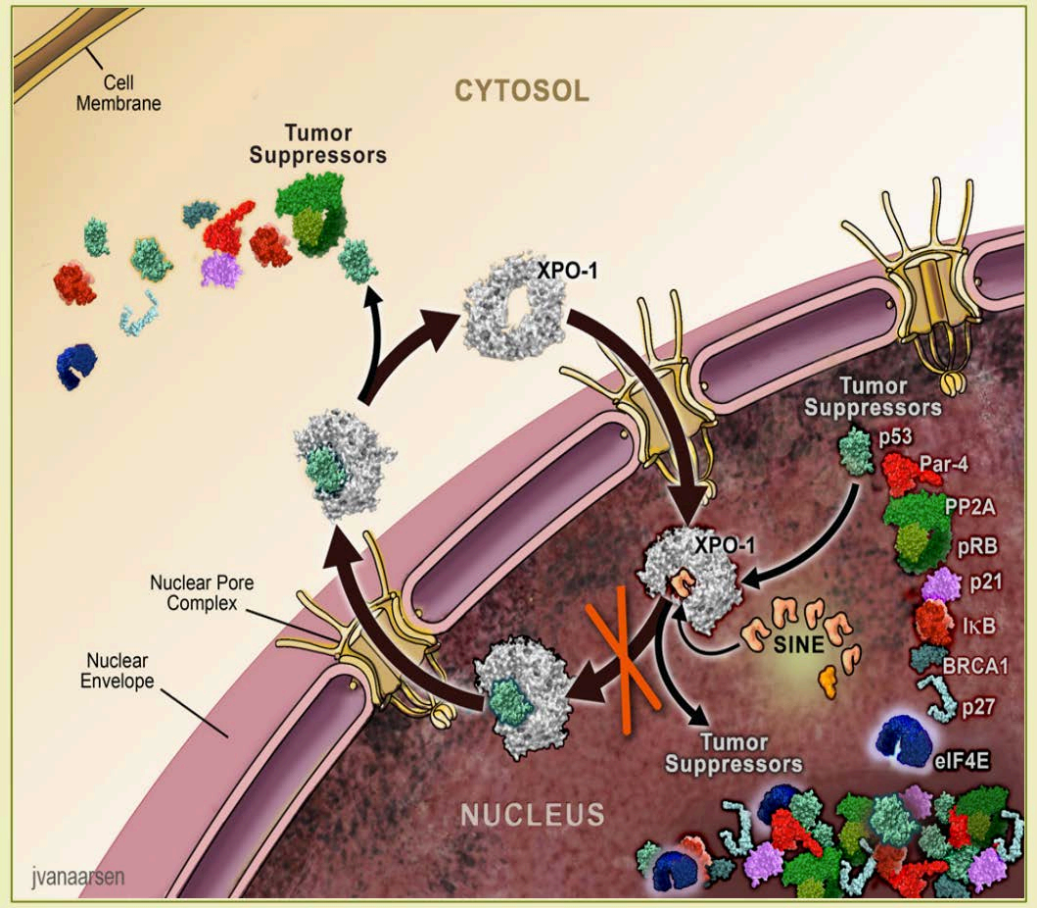
Courtesy of Ann S LaCasce, MD, MMSc

Ongoing Phase 3 POLARIX Study DLBCL



Courtesy of Ann S LaCasce, MD, MMSc

Selinexor has a novel mechanism of action: XPO-1 inhibitor



XPO1 over-expressed in DLBCL and correlates with poor prognosis

Induces nuclear accumulation of tumor suppressors including p53, p73, IkBk and FOXO

Decreases production of oncoproteins including c-MYC, BCL2, BCL6 and BCL-XL

Kalakonda. Lancet Heme 2020

Courtesy of Ann S LaCasce, MD, MMSc

Phase II SADAL Trial: Selinexor in highly selected population of patients with DLBCL

60 mg D1,3 weekly

Key eligibility:
- **60 days after CR/PR**
- **98 days after refractory disease**

	Total (N=127)
Number of previous systemic regimens for DLBCL	
2	75 (59%)
>3	52 (41%)
Time since most recent progression from previous regimen to start of selinexor, weeks	8·1 (4·57–15·14)
Previous ASCT therapy for DLBCL	
Yes	38 (30%)
No	89 (70%)
Refractory to the most recent systemic treatment regimen for DLBCL	
Yes	91 (72%)
No	29 (23%)
Unknown	7 (6%)
Refractory or relapse DLBCL less than 1 year after last ASCT therapy	21 (17%)

Kalakonda. Lancet Heme 2020

Courtesy of Ann S LaCasce, MD, MMSc

SADAL: Activity is modest with high rates of low grade GI toxicity

	Overall response rate	Complete response	Partial response	Stable disease	Progressive disease or no response recorded
All patients	36/127 (28%) (20·7–37·0)	15 (12%) (6·8–18·7)	21 (17%) (10·5–24·2)	11 (9%) (4·4–15·0)	80 (63%) (54·0–71·4)
GCB subtype	20/59 (34%) (22·1–47·4)	8 (14%) (6·0–25·0)	12 (20%) (11·0–32·8)	7 (12%) (4·9–22·9)	32 (54%) (40·8–67·3)
Non-GCB subtype	13/63 (21%) (11·5–32·7)	6 (10%) (3·6–19·6)	7 (11%) (4·6–21·6)	3 (5%) (1·0–13·3)	47 (75%) (62·1–84·7)
Unclassified	3/5 (60%) (14·7–94·7)	1 (20%) (0·5–71·6)	2 (40%) (5·3–85·3)	1 (20%) (0·5–71·6)	1 (20%) (0·5–71·6)

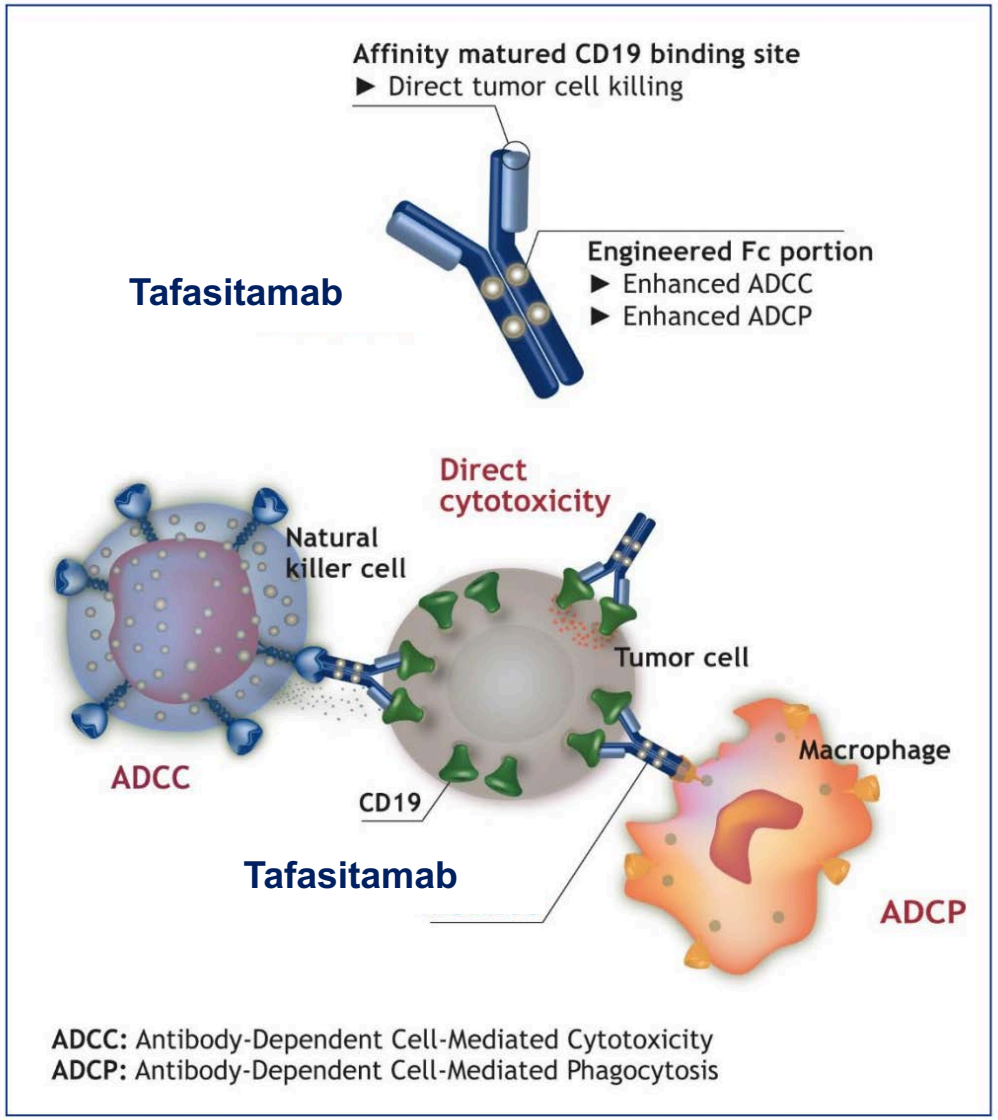
Data are n/N (%; 95% CI). Responses were adjudicated according to central imaging assessment. GCB=germinal centre B cell. See results section in main text for one-sided 97·5% CI.

Table 2: **Responses in evaluable patients**

On June 22, 2020, the FDA granted accelerated approval to selinexor for pts with R/R DLBCL, NOS, including DLBCL arising from FL, after at least 2 lines of systemic therapy.

	Grade 1–2	Grade 3	Grade 4
Thrombocytopenia	20 (16%)	39 (31%)	19 (15%)
Nausea	66 (52%)	8 (6%)	0
Fatigue	46 (36%)	14 (11%)	0
Anaemia	26 (21%)	27 (21%)	1 (1%)
Decreased appetite	42 (33%)	5 (4%)	0
Diarrhoea	41 (32%)	4 (3%)	0
Constipation	39 (31%)	0	0
Neutropenia	7 (6%)	20 (16%)	11 (9%)
Weight loss	38 (30%)	0	0
Vomiting	35 (28%)	2 (2%)	0
Pyrexia	23 (18%)	5 (4%)	0
Asthenia	21 (17%)	6 (5%)	0
Cough	23 (18%)	0	0
Upper respiratory tract infection	18 (14%)	1 (1%)	0
Dizziness	18 (14%)	0	0
Hypotension	13 (10%)	4 (3%)	0
Oedema peripheral	14 (11%)	1 (1%)	0
Dyspnoea	12 (10%)	1 (1%)	1 (1%)
Hyponatraemia	4 (3%)	10 (8%)	0

Tafasitamab (MOR208)



Lenalidomide enhances NK function with enhanced ADCC in vitro

Salles et al. Lancet Onc 2020

Courtesy of Ann S LaCasce, MD, MMSc

Phase II L-MIND Trial: Tafasitamab plus lenalidomide with durable responses in CR

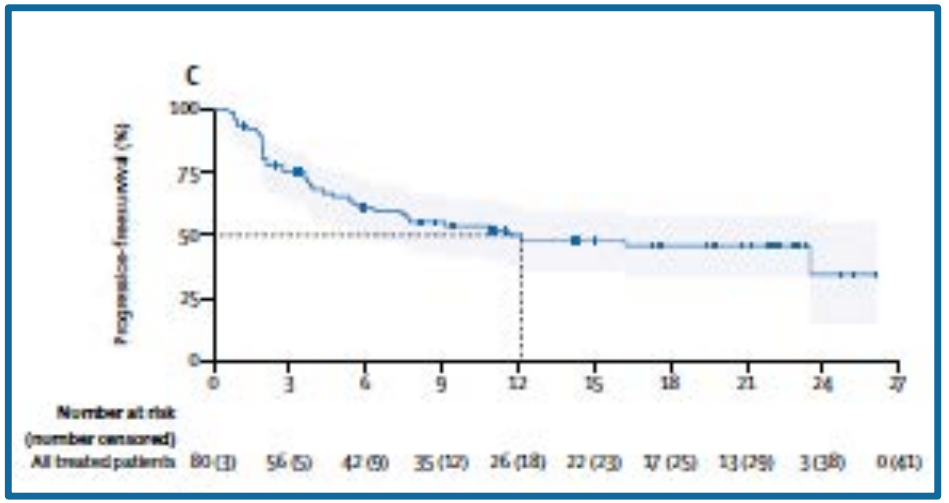
	Patients treated with tafasitamab plus lenalidomide (n=80)*
Best objective response	
Complete response	34 (43%; 32–54)
Partial response	14 (18%; 10–28)
Stable disease	11 (14%; 7–23)
Progressive disease	13 (16%; 9–26)
Not evaluable†	8 (10%; 4–19)
PET-confirmed complete response	30/34 (88%; 73–97)
Objective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

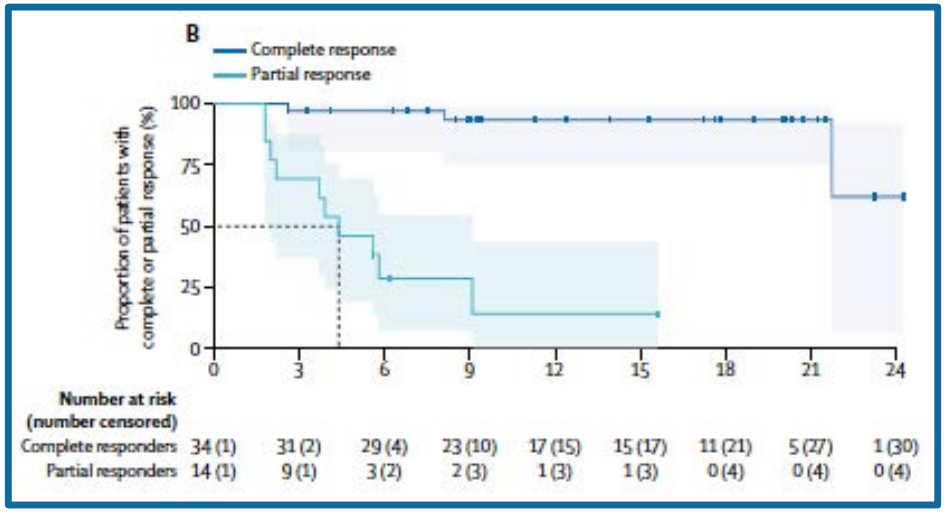
60% of patients received one year of both agents.

46% required dose reduction of lenalidomide and 22% permanently discontinued.

Most common TEAEs (Grade ≥3): Neutropenia, thrombocytopenia and febrile neutropenia

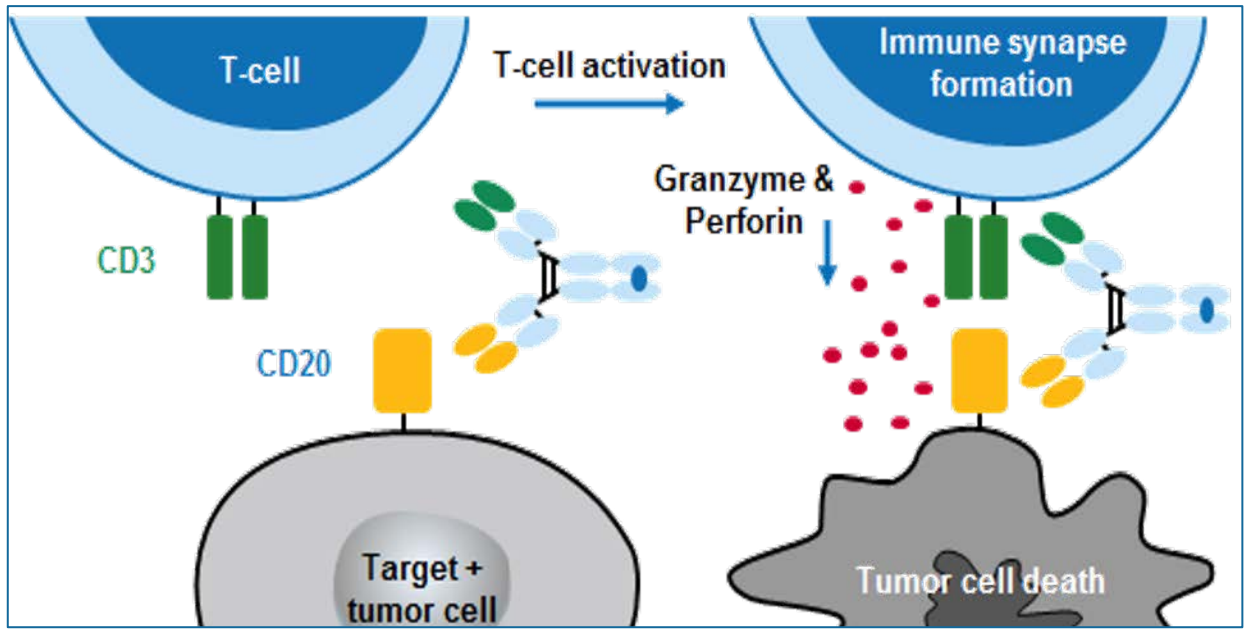
Serious AEs include pneumonia, febrile neutropenia, pulmonary embolism, bronchitis, atrial fibrillation and congestive cardiac failure



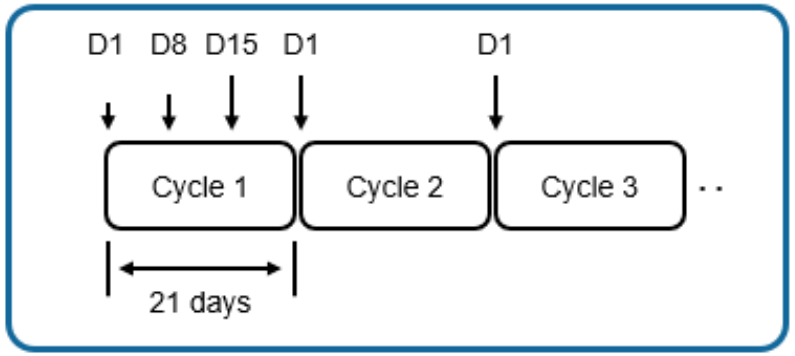


On July 31, 2020, the FDA granted accelerated approval to tafasitamab/len for R/R DLBCL NOS, including DLBCL arising from low-grade lymphoma, and pts who are not eligible for ASCT.

Mosunetuzumab: full length CD20/CD3 bispecific antibody



Mosunetuzumab regimen



Phase I/Ib GO29781 Trial

Initial treatment = 8 cycles; if CR achieved, treatment discontinued; if PR or SD, treatment continued for up to 17 cycles

Retreatment allowed for CR patients who relapse

- Schuster et al. ASH 2019

Courtesy of Ann S LaCasce, MD, MMSc

GO29781 Trial: CRS is 30% and NT is 44% but mostly low grade

All Gr AEs in >15% pts	*N=270*
Cytokine release syndrome	78 (28.9%)
Neutropenia‡	65 (24.1%)
Fatigue	55 (20.4%)
Hypophosphatemia	52 (19.3%)
Diarrhea	45 (16.7%)
Pyrexia	44 (16.3%)
Headache	42 (15.6%)
Nausea	41 (15.2%)

Gr 3–4 AEs in >5% pts	*N=270*
Neutropenia‡	59 (21.8%)
Hypophosphatemia	36 (13.3%)
Anemia	24 (8.9%)

	NAEs	
n (%) with ≥1 AE	*Safety evaluable pts (N=270)*	*Prior CAR-T pts (n=30)*
Any Grade	118 (43.7%)	13 (43.3%)
Gr 1	74 (27.4%)	7 (23.3%)
Gr 2	34 (12.6%)	3 (10.0%)
Gr 3	10 (3.7%)	3 (10.0%)
Related Gr 3	3 (1.1%)	1 (3.3%)
ICANS-like NAE	3 (1.1%)	0
Gr 1	2 (0.7%)	0
Gr 2	1 (0.4%)	0
AE characteristics	• Most common NAEs: headache (15.6%), insomnia (9.3%), dizziness (9.3%) • ICANS-like NAEs: 2 confusion (1 related), 1 lethargy (related); all resolved ≤3 days	

Schuster et al. ASH 2019

Courtesy of Ann S LaCasce, MD, MMSc

GO29781 Trial: Efficacy in aggressive, indolent lymphoma and s/p CAR-T

Investigator-assessed best objective response (pooled data from 2.8mg to 40.5mg cohorts)

	N*	ORR, n (%)	CR, n (%)
Aggressive NHL	124	46 (37.1%)	24 (19.4%)
DLBCL/trFL after ≥ 2 lines	98	37 (37.8%)	20 (20.4%)
• Refractory to anti-CD20	88/98	32 (36.4%)	18 (20.5%)
• With prior auto SCT	32/98	17 (53.1%)	11 (34.3%)

s/p CAR-T	N*	ORR, n (%)	CR, n (%)
All histologies	18	7 (38.9%)	4 (22.2%)
• DLBCL	9	2 (22.2%)	2 (22.2%)
• trFL	5	1 (20.0%)	0 (0.0%)
• FL	4	4 (100%)	2 (50.0%)

Investigator-assessed best objective response (pooled data from 2.8mg to 13.5mg cohorts)

	N*	ORR, n (%)	CR, n (%)
Indolent NHL	67	42 (62.7%)	29 (43.3%)
FL after ≥ 2 lines	61	39 (63.9%)	27 (44.3%)
• Double refractory	43/61	28 (65.1%)	19 (44.2%)
• History of POD24	33/61	20 (60.6%)	14 (42.4%)
• PI3Ki refractory	9/61	8 (88.9%)	7 (77.8%)

Schuster et al. ASH 2019

Courtesy of Ann S LaCasce, MD, MMSc

Which therapy would you generally recommend first for a patient with DLBCL who experiences disease progression on front-line R-CHOP and is unfit for high-dose therapy?

1. Polatuzumab vedotin/BR
2. Tafasitamab/lenalidomide
3. Selinexor
4. CAR T-cell therapy
5. I don’t know

RTP
RESEARCH
TO PRACTICE

Which therapy would you generally recommend first for a patient with DLBCL who experiences disease progression on front-line R-CHOP and is unfit for high-dose therapy?

 JONATHAN W FRIEDBERG, MD, MMSC	Tafasitamab/lenalidomide
 JOHN KURUVILLA, MD	Depends on fitness for CAR-T
 ANN S LACASCE, MD, MMSC	Polatuzumab vedotin/BR
 JOHN P LEONARD, MD	Tafasitamab/lenalidomide
 MICHAEL E WILLIAMS, MD, SCM	Tafasitamab/lenalidomide
 CRAIG MOSKOWITZ, MD	Tafasitamab/lenalidomide
 LORETTA NASTOUPIL, MD	Tafasitamab/lenalidomide
 LAURIE H SEHN MD, MPH	Polatuzumab vedotin/BR
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Polatuzumab vedotin/BR, Tafasitamab/lenalidomide

Which therapy would you generally recommend first for a patient with DLBCL who experiences disease progression on front-line R-CHOP and is unfit for high-dose therapy and CAR T-cell therapy?

 JONATHAN W FRIEDBERG, MD, MMSC	Tafasitamab/lenalidomide
 JOHN KURUVILLA, MD	Polatuzumab vedotin/BR
 ANN S LACASCE, MD, MMSC	Polatuzumab vedotin/BR
 JOHN P LEONARD, MD	Tafasitamab/lenalidomide
 MICHAEL E WILLIAMS, MD, SCM	Tafasitamab/lenalidomide
 CRAIG MOSKOWITZ, MD	Tafasitamab/lenalidomide
 LORETTA NASTOUPIL, MD	Tafasitamab/lenalidomide
 LAURIE H SEHN MD, MPH	Polatuzumab vedotin/BR
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Polatuzumab vedotin/BR, Tafasitamab/lenalidomide

Which therapy would you generally recommend first for a patient with DLBCL who experiences disease progression on R-CHOP, R-DHAP followed by transplant and CAR T-cell therapy?

 JONATHAN W FRIEDBERG, MD, MMSC	Polatuzumab vedotin/BR
 JOHN KURUVILLA, MD	Polatuzumab vedotin/BR
 ANN S LACASCE, MD, MMSC	Polatuzumab vedotin/BR
 JOHN P LEONARD, MD	Tafasitamab/lenalidomide
 MICHAEL E WILLIAMS, MD, SCM	Tafasitamab/lenalidomide
 CRAIG MOSKOWITZ, MD	Tafasitamab/lenalidomide
 LORETTA NASTOUPIL, MD	Polatuzumab vedotin/BR
 LAURIE H SEHN MD, MPH	Polatuzumab vedotin/BR
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Polatuzumab vedotin/BR, Tafasitamab/lenalidomide

Case Presentation – Dr LaCasce: A 77-year-old-woman with relapsed/refractory non-GCB DLBCL

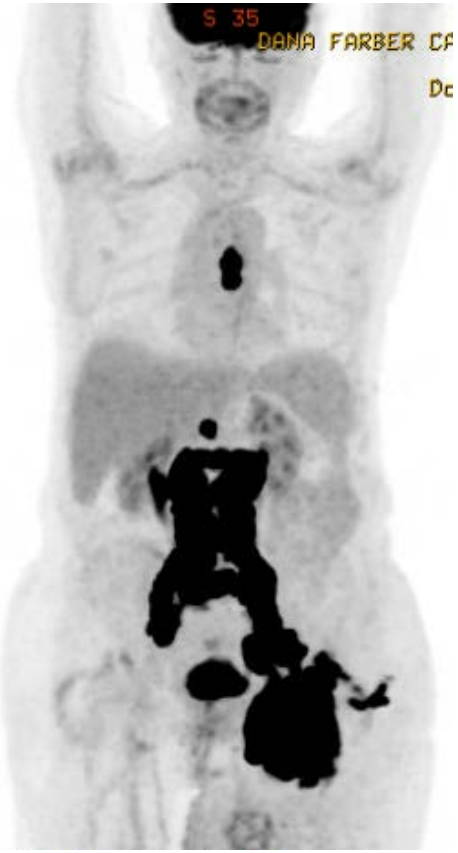
- 77-year-old woman initially presented with stage IV non-GCB DLBCL with extensive disease above and below the diaphragm with splenic and multi-focal bony disease. IPI 5. She was treated with RCHOP x 6 with systemic methotrexate x 3 cycles with a complete remission.

- Unfortunately, she developed recurrent disease 6 months later. She received RICE x 2. Subsequent PET scan showed improvement but with persistent uptake in a solitary soft tissue mass in the abdominal wall.

- She underwent T-cell pheresis, followed by lymphodepletion and CAR-T cell infusion. Her course was complicated by grade 2 CRS.

- One year later, she developed biopsy recurrent disease in the left thigh. She was enrolled on a clinical trial with a bi-specific antibody and achieved a near complete response. Her course was complicated by grade 1 neurotoxicity.

- Within 3 months, however, she had recurrent, severe leg swelling and scan showed high burden disease.



Courtesy of Ann S LaCasce, MD, MMSc

Case Presentation – Dr LaCasce: A 77-year-old-woman with relapsed/refractory non-GCB DLBCL (continued)

- She was treated with polatuzumab plus rituximab.
- Bendamustine was withheld given the persistent cytopenias after CAR-T and her prior therapies.
- She achieved a metabolic CR and had no toxicity.
- She remains in remission, now about 9 months post therapy.

Courtesy of Ann S LaCasce, MD, MMSc

Agenda

Module 1: Evolving treatment paradigm for patients with diffuse large B-cell lymphoma (DLBCL) – Dr LaCasce

Module 2: Optimal management of newly diagnosed and relapsed/refractory follicular lymphoma – Dr Leonard

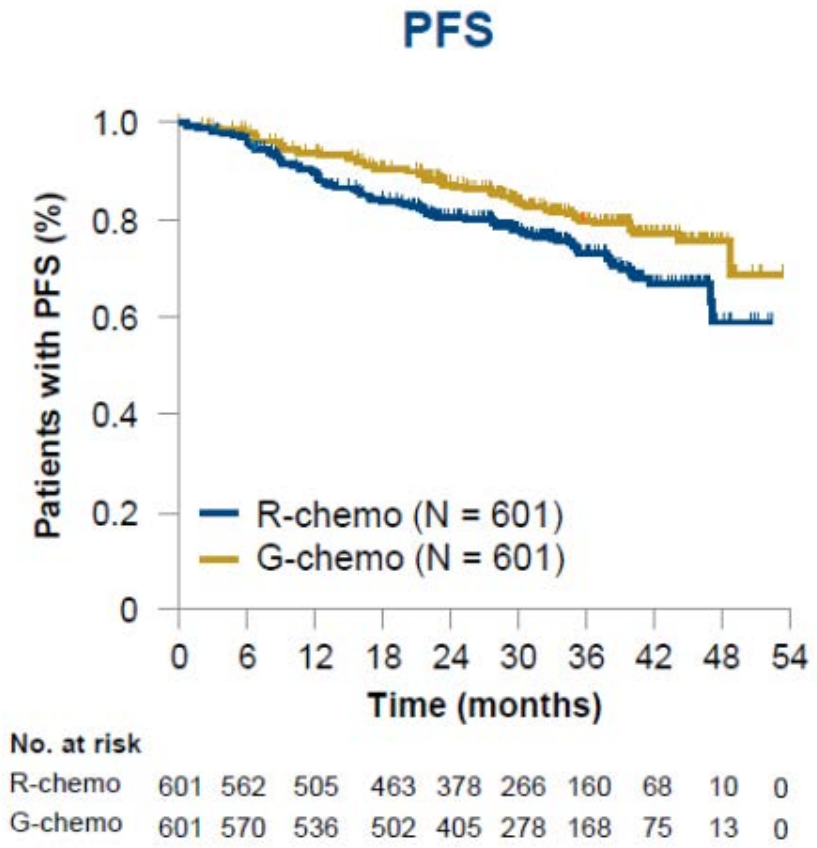
Module 3: Available and emerging approaches for mantle cell lymphoma – Dr Williams

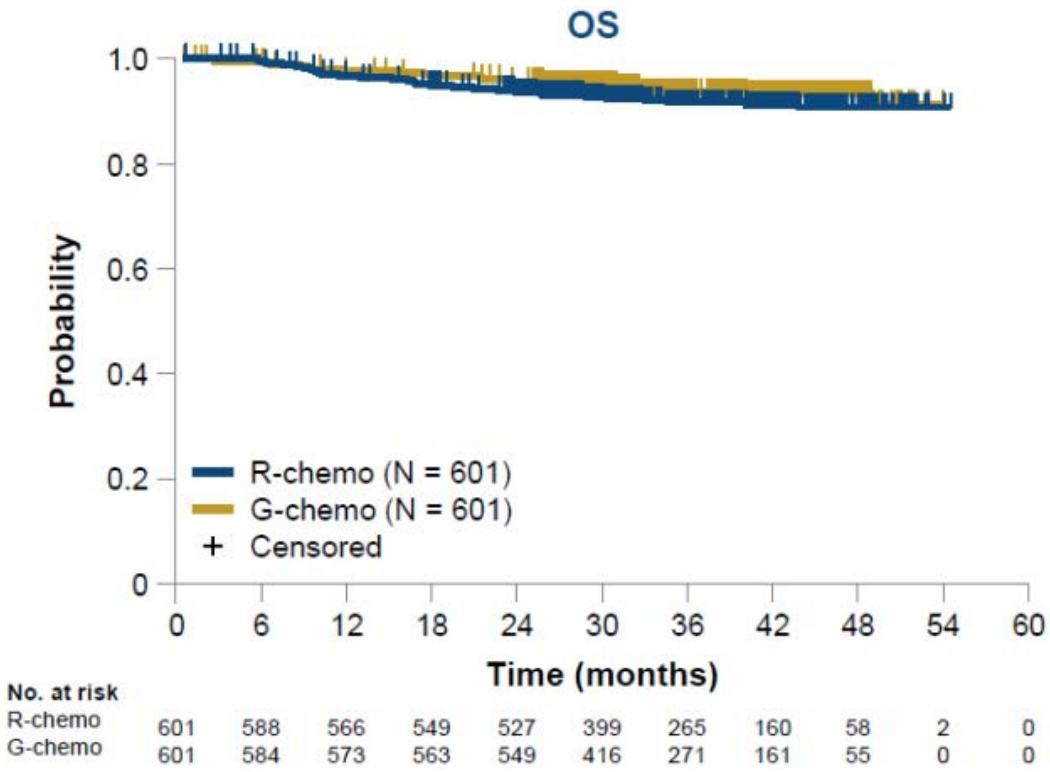
Module 4: Selection and sequencing of therapies for patients with advanced Hodgkin lymphoma – Dr Kuruvilla

Module 5: Advances in chimeric antigen receptor T-cell therapy for DLBCL and other lymphoma subtypes – Dr Friedberg

RTP
RESEARCH
TO PRACTICE

GALLIUM: Obinutuzumab vs Rituximab with chemotherapy (and as maintenance) improves PFS but not OS



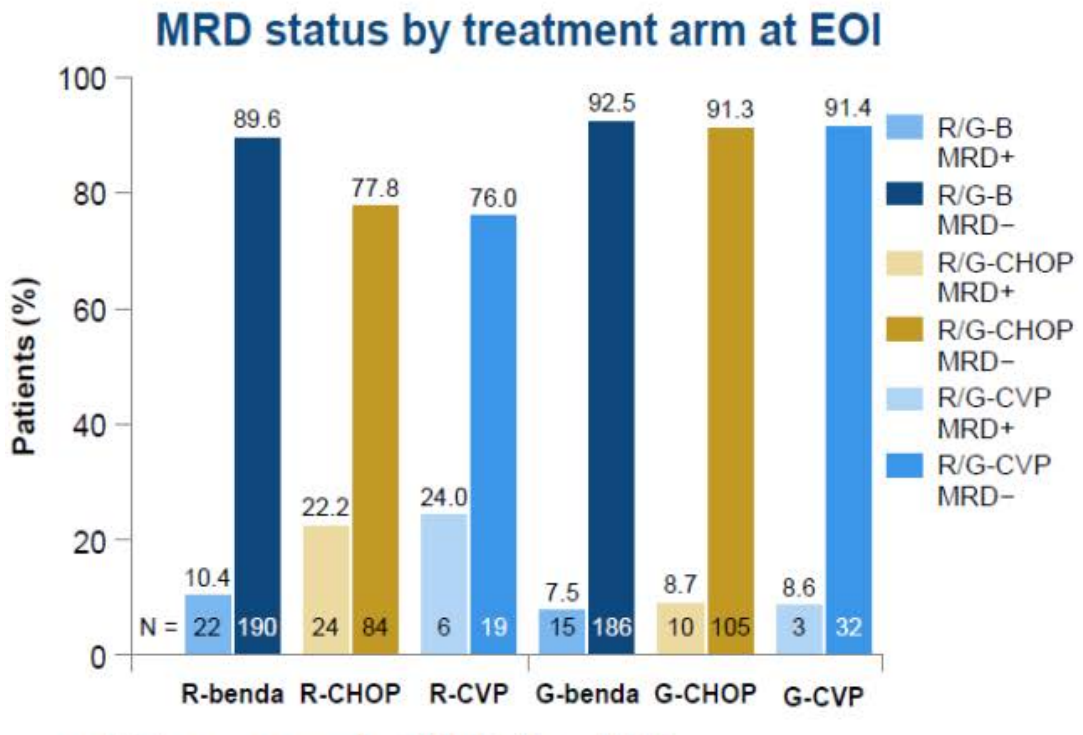


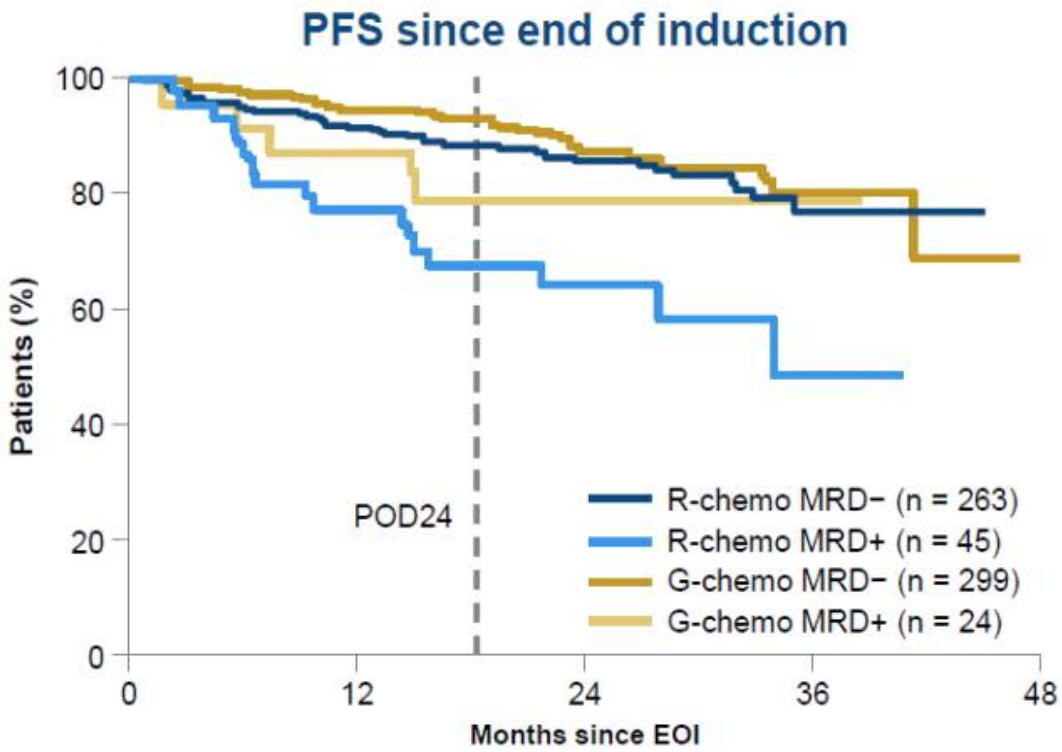
Marcus R, et al. N Engl J Med. 2017; 377:1331-44.

Courtesy of John P Leonard, MD

Weill Cornell Medicine NewYork-Presbyterian

GALLIUM: Obinutuzumab vs Rituximab with chemotherapy (and as maintenance): MRD negativity



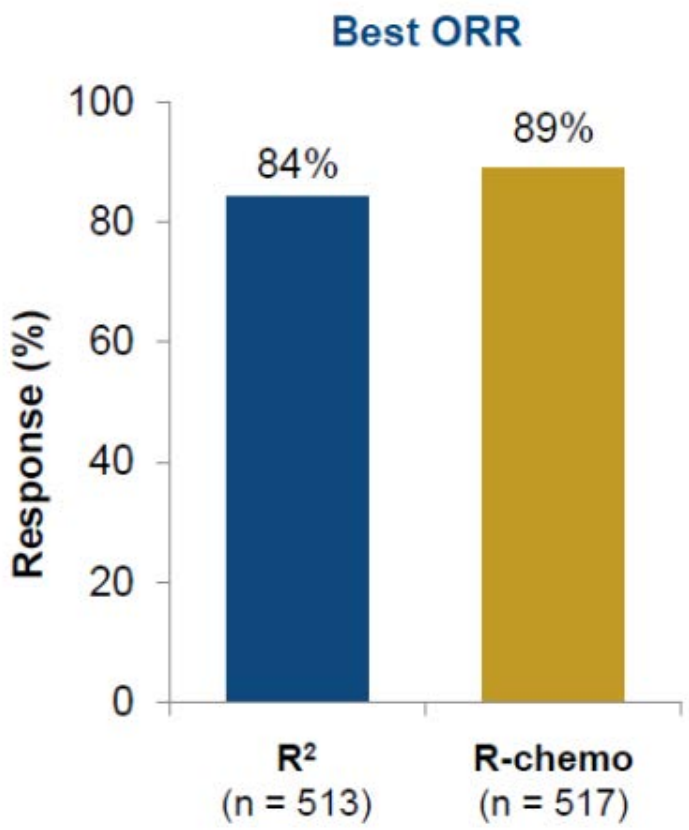


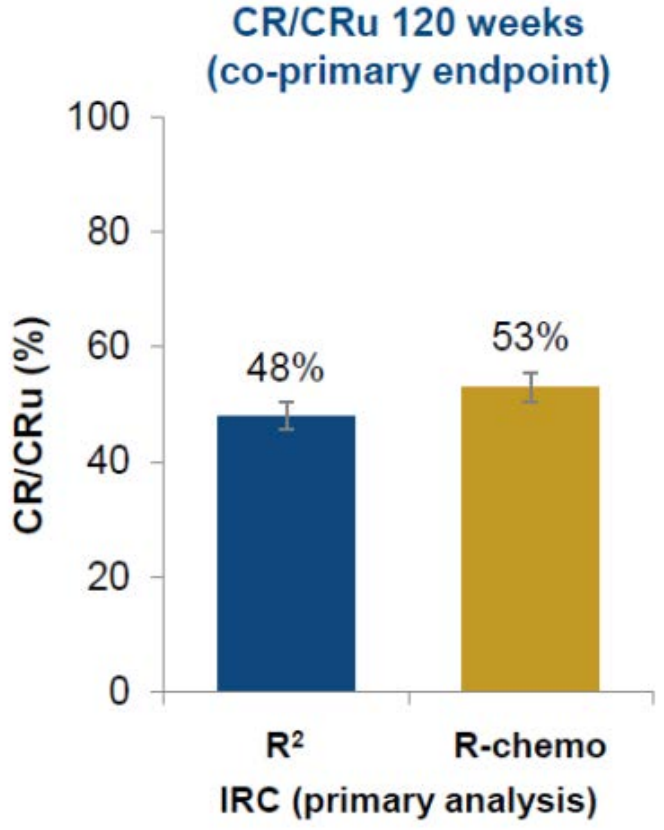
- PD or death due to PD at 24-mos post randomization events occurred in less pts on the G-chemo arm (9.5% vs 16.3%)
  - The cumulative incidence rates were lower on the G-chemo arm (10.1% vs 17.4%)
- The average HR-based reduction in the risk of a POD24 event with G-chemo relative to R-chemo was 46.0%
- The risk of a PFS event in the 24 mos after randomization was lower on the G-chemo arm (12.5% vs 18.9%)
- The relative risk reduction for PFS events was 33.9%

Courtesy of John P Leonard, MD

Pott C, et al. ASH 2016 ; Seymour et al. Haematologica 2019;104(6):1202-1208.

RELEVANCE: Lenalidomide-Rituximab (R^2) vs Chemo-R
Similar ORR and CR as initial therapy for FL



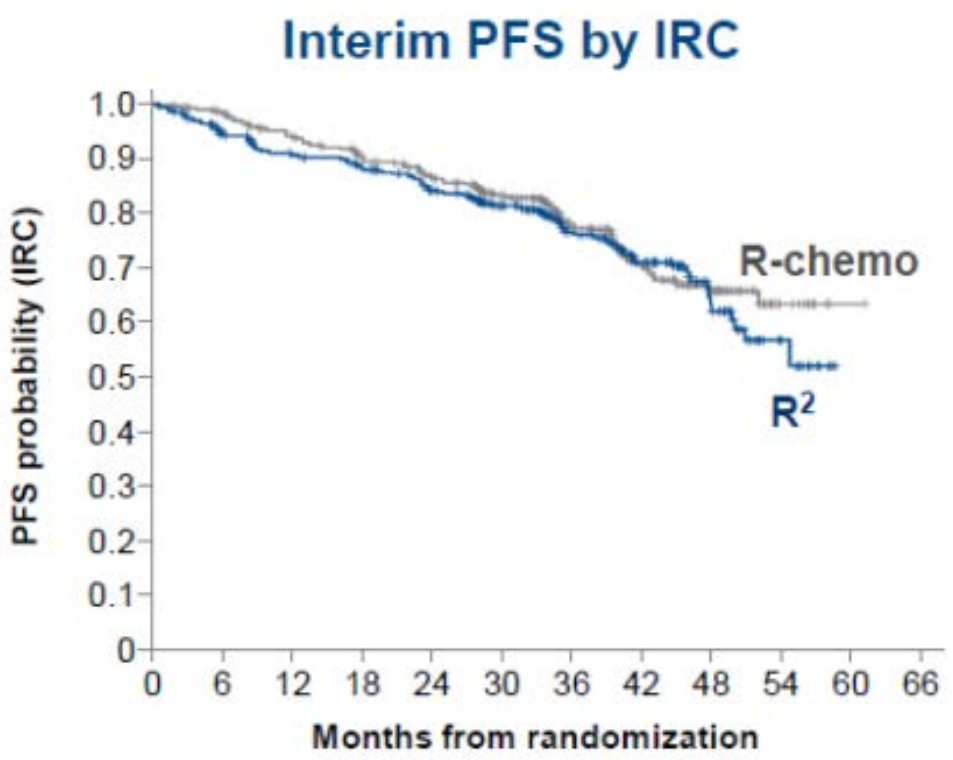


Morschhauser F, et al, NEJM 2018

Courtesy of John P Leonard, MD

Weill Cornell Medicine NewYork-Presbyterian

RELEVANCE: Lenalidomide-Rituximab (R^2) vs Chemo-R
Similar PFS and OS as initial therapy for FL



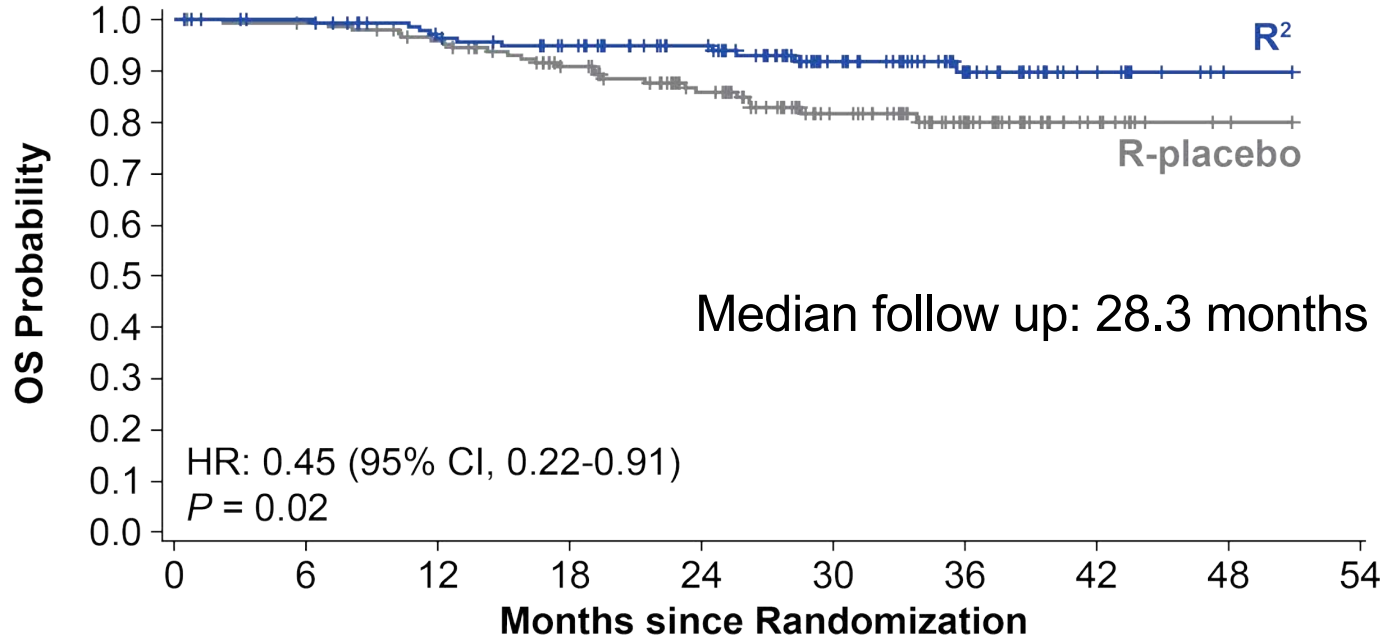
Morschhauser F, et al, NEJM 2018

Courtesy of John P Leonard, MD

Weill Cornell Medicine

NewYork-Presbyterian

AUGMENT: Overall survival in FL patients (prespecified subgroup analysis)



No. at Risk										
R^2	147	142	130	121	105	70	39	13	1	0
R-placebo	148	145	137	117	94	64	35	12	2	0

- 35 total deaths (11 R^2, 24 R-placebo)
- 2-year OS was 95% (95% CI, 90%-98%) for R^2 and 86% (95% CI, 79%-91%) for R-placebo

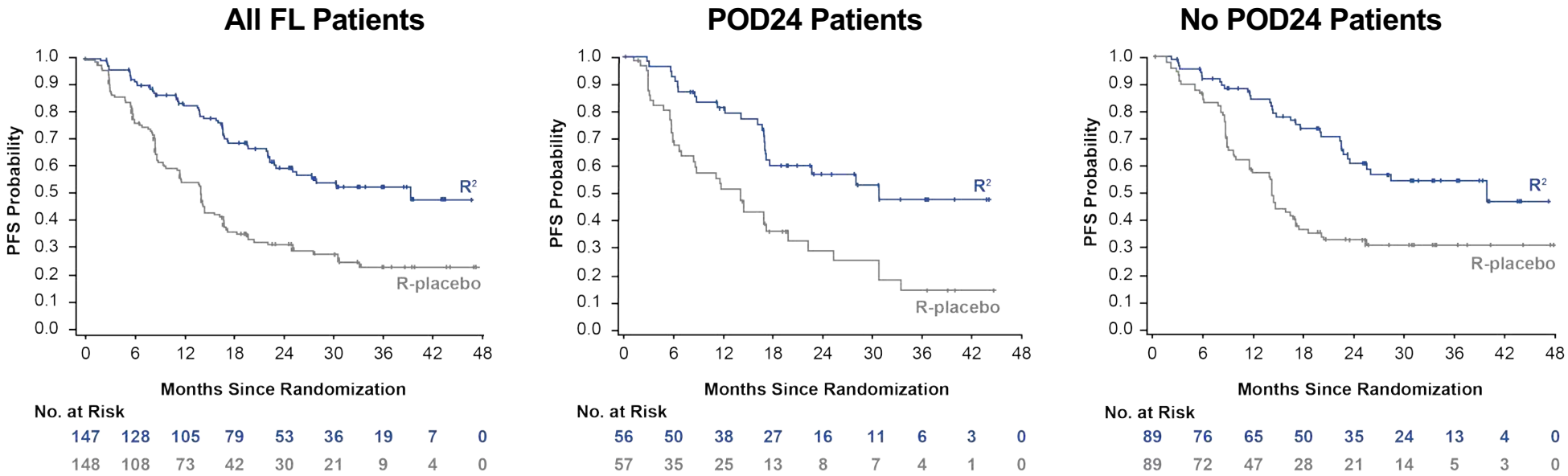
Leonard et al. JCO 2019

Data cutoff June 22, 2018.

Courtesy of John P Leonard, MD

Weill Cornell Medicine NewYork-Presbyterian

AUGMENT: PFS for All FL patients and by POD24 status



Median PFS, mo (95% CI) *(n R^2/n R-placebo)*	All FL Patients *(n = 147/148)*	POD24 *(n = 56/57)*	No POD24 *(n = 89/89)*
R^2	39.4 (23.1-NR)	30.4 (16.8-NR)	39.4 (22.9-NR)
R-placebo	13.9 (11.2-16.0)	13.8 (6.7-16.9)	13.9 (11.2-16.6)
HR (95% CI)	0.40 (0.29-0.56)	0.41 (0.24-0.68)	0.43 (0.28-0.65)
***P* value**	< 0.0001	0.0004	< 0.0001

Data cutoff June 22, 2018. *Censoring rules were based on FDA guidance.

POD24 was defined post-hoc as progression or relapse within 2 years of initial antilymphoma treatment, which included immunotherapy and/or chemotherapy

Courtesy of John P Leonard, MD

Weill Cornell Medicine NewYork-Presbyterian

Combination of Copanlisib and Rituximab Significantly Prolonged Progression-Free Survival for Patients with Relapsed Indolent NHL

Press Release – October 24, 2020

“Phase III study CHRONOS-3 in patients with relapsed indolent non-Hodgkin's Lymphoma (iNHL) who have received one or more lines of prior treatment meets primary endpoint. Safety and tolerability observed in the trial were generally consistent with previously published data on the individual components of the combination and no new safety signals were identified. Copanlisib is already approved in the U.S. under accelerated approval based on overall response rate (ORR) of 104 adult patients with relapsed follicular lymphoma (FL) based on the Phase II CHRONOS-1 study.”

https://media.bayer.com/baynews/baynews.nsf/id/9270FC6817515421C12586000028E06A?open&ref=irrefndcd

RTP RESEARCH TO PRACTICE

Duvelisib in recurrent indolent NHL (Oral PI3K delta/gamma inhibitor)

- Indolent lymphoma patients “double refractory” to rituximab and chemotherapy/radioimmunotherapy
- 25 mg po BID continuous dosing (w/PCP prophylaxis)
- 129 subjects, 83 with FL, median age 65, median 3 prior rx
- ORR 46%, median duration 9.9 months
- Principal toxicities cytopenias, diarrhea
- Led to FDA approval

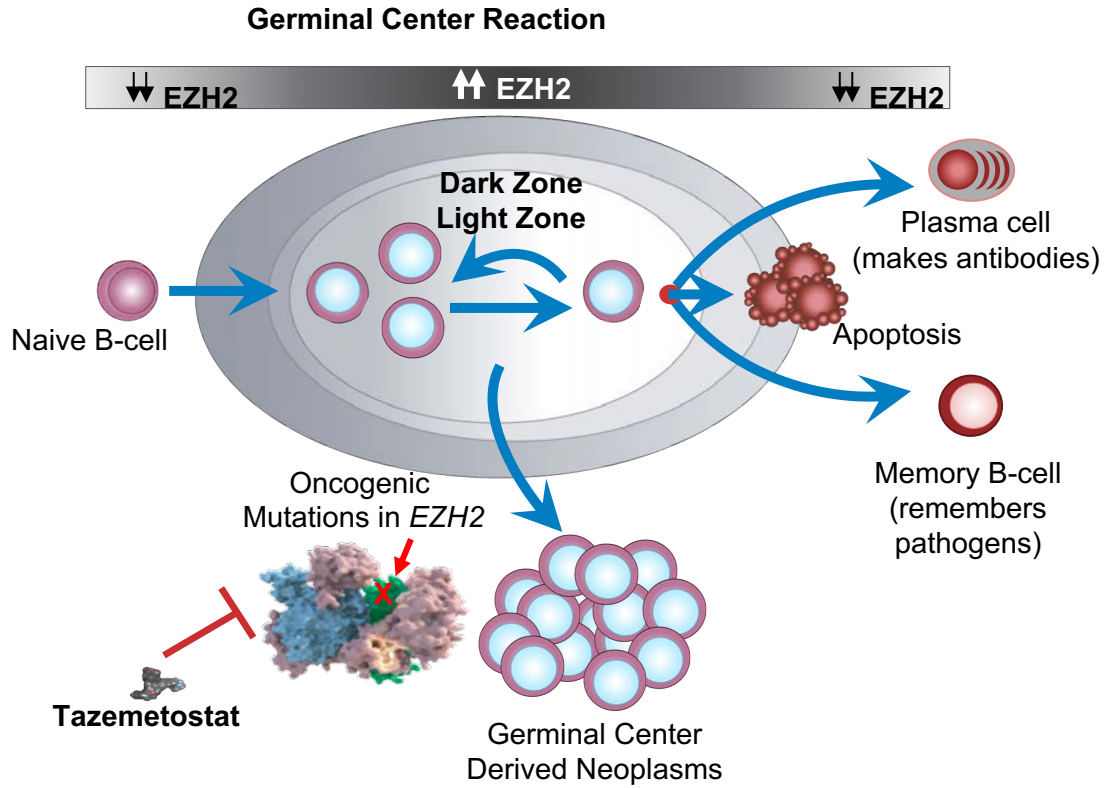
Zinzani et al, ICML 2017

Courtesy of John P Leonard, MD

Weill Cornell Medicine NewYork-Presbyterian

Follicular Lymphoma and EZH2

- *EZH2* an epigenetic regulator of gene expression and cell fate decisions[1]
- *EZH2* is required for normal B-cell biology and germinal center formation[2]
  - Oncogenic mutations in *EZH2* suppress exit from germinal state and "lock" B cells in this state thereby transforming into a cancer[2]
- *EZH2* biology relevant in both mutant (MT) and wild-type (WT) *EZH2* FL
  - ~20% of patients with FL also have *EZH2* gain of function mutations[3]



Tazemetostat, a selective, oral inhibitor of EZH2 has shown antitumor activity in non-Hodgkin's lymphoma patients with either MT or WT EZH2[4,5]

1. Gan L, et al. *Biomark Res*. 2018;6(1):10; 2. Béguelin W, et al. *Cancer Cell*. 2013;23(5)677-692. 3. Bödör C, et al. *Blood*. 2013;122:3165-3168. 4. Italiano A, et al. *Lancet Oncol*. 2018;19(5):649-59; 5. Morschhauser F, et al. *Hematol*

On June 18, 2020, Tazemetostat was granted accelerated FDA approval for R/R FL with EZH2 mutations after at least 2 prior systemic therapies and for R/R FL with no satisfactory alternative treatment options

Courtesy of John P Leonard, MD

Weill Cornell Medicine

NewYork-Presbyterian

Tazemetostat ORR in EZH2 mutant and wild type populations (recurrent FL)

	EZH2 Mutant Cohort (n=45)		*EZH2* WT Cohort (n=54)	
Parameter	**Investigator**	**IRC**	**Investigator**	**IRC**
ORR, n (%)	**35 (78)**	**31 (69)**	**18 (33)**	**19 (35)**
CR, n (%)	4 (9)	6 (13)	3 (6)	2 (4)
PR, n (%)	31 (69)	25 (56)	15 (28)	17 (31)
SD, n (%)	10 (22)	13 (29)	16 (30)	18 (33)
PD, n (%)	0	1 (2)[c]	16 (30)	12 (22)
DOR, months, median (95% CI)	8.3 (5.5–13.8)	10.9 (7.2–NE)	14.7 (7.6–NE)	13.0 (5.6–NE)

Morschhauser, ICML 2019

Courtesy of John P Leonard, MD

Weill Cornell Medicine NewYork-Presbyterian

Regulatory and reimbursement issues aside, what would be your most likely initial treatment choice for a 63-year-old patient with Stage III, Grade I or II follicular lymphoma (FL) with fatigue and symptomatic bulky adenopathy who requires treatment?

 JONATHAN W FRIEDBERG, MD, MMSC	R-bendamustine	 MICHAEL E WILLIAMS, MD, SCM	R-bendamustine
 JOHN KURUVILLA, MD	R-bendamustine → R maintenance	 CRAIG MOSKOWITZ, MD	R-bendamustine
 ANN S LACASCE, MD, MMSC	R-bendamustine	 LORETTA NASTOUPIL, MD	R-bendamustine
 JOHN P LEONARD, MD	R-bendamustine	 LAURIE H SEHN MD, MPH	R-bendamustine
GENERAL MEDICAL ONCOLOGISTS (N = 75)	R-bendamustine		

Regulatory and reimbursement issues aside, what would be your most likely initial treatment choice for a 78-year-old patient with Stage III, Grade I or II FL with fatigue and symptomatic bulky adenopathy who requires treatment?

1. Rituximab
2. R-bendamustine
3. R-CHOP
4. R-CVP
5. Obinutuzumab-bendamustine
6. Obinutuzumab-CHOP
7. Rituximab/lenalidomide
8. Other

RTP
RESEARCH
TO PRACTICE

Regulatory and reimbursement issues aside, what would be your most likely initial treatment choice for a 78-year-old patient with Stage III, Grade I or II FL with fatigue and symptomatic bulky adenopathy who requires treatment?

 JONATHAN W FRIEDBERG, MD, MMSC	R-bendamustine	 MICHAEL E WILLIAMS, MD, SCM	Rituximab/lenalidomide
 JOHN KURUVILLA, MD	R monotherapy → R maintenance	 CRAIG MOSKOWITZ, MD	R-bendamustine
 ANN S LACASCE, MD, MMSC	R-bendamustine	 LORETTA NASTOUPIL, MD	R-bendamustine
 JOHN P LEONARD, MD	R-bendamustine	 LAURIE H SEHN MD, MPH	R-bendamustine
GENERAL MEDICAL ONCOLOGISTS (N = 75)	R-bendamustine		

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

1. Re-treatment with BR
2. Obinutuzumab/bendamustine
3. R-CHOP
4. Rituximab/lenalidomide
5. PI3K inhibitor
6. Tazemetostat
7. Chemotherapy → ASCT
8. Other

RTP RESEARCH TO PRACTICE

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

 JONATHAN W FRIEDBERG, MD, MMSC	Rituximab/lenalidomide or Obinutuzumab/lenalidomide	 MICHAEL E WILLIAMS, MD, SCM	Chemotherapy → autologous transplant
 JOHN KURUVILLA, MD	R-CHOP → R maintenance	 CRAIG MOSKOWITZ, MD	Rituximab/lenalidomide
 ANN S LACASCE, MD, MMSC	Rituximab/lenalidomide	 LORETTA NASTOUPIL, MD	Rituximab/lenalidomide
 JOHN P LEONARD, MD	Rituximab/lenalidomide	 LAURIE H SEHN MD, MPH	Rituximab/lenalidomide
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Rituximab/lenalidomide		

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

 JONATHAN W FRIEDBERG, MD, MMSC	R-CHOP	 MICHAEL E WILLIAMS, MD, SCM	Copanlisib
 JOHN KURUVILLA, MD	Depends on duration of remission	 CRAIG MOSKOWITZ, MD	Copanlisib
 ANN S LACASCE, MD, MMSC	Copanlisib	 LORETTA NASTOUPIL, MD	Copanlisib
 JOHN P LEONARD, MD	Idelalisib	 LAURIE H SEHN MD, MPH	Clinical trial
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Idelalisib		

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

 JONATHAN W FRIEDBERG, MD, MMSC	Tazemetostat	 MICHAEL E WILLIAMS, MD, SCM	Tazemetostat
 JOHN KURUVILLA, MD	Tazemetostat	 CRAIG MOSKOWITZ, MD	Tazemetostat
 ANN S LACASCE, MD, MMSC	Tazemetostat	 LORETTA NASTOUPIL, MD	Tazemetostat
 JOHN P LEONARD, MD	Tazemetostat	 LAURIE H SEHN MD, MPH	Tazemetostat

GENERAL MEDICAL ONCOLOGISTS (N = 75)	Tazemetostat

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

1. PI3K inhibitor → tazemetostat
2. Tazemetostat → PI3K inhibitor
3. I don't know

RTP
RESEARCH
TO PRACTICE

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

 JONATHAN W FRIEDBERG, MD, MMSC	Tazemetostat → PI3K inhibitor	 MICHAEL E WILLIAMS, MD, SCM	Tazemetostat → PI3K inhibitor
 JOHN KURUVILLA, MD	I don't know	 CRAIG MOSKOWITZ, MD	Tazemetostat → PI3K inhibitor
 ANN S LACASCE, MD, MMSC	Tazemetostat → PI3K inhibitor	 LORETTA NASTOUPIL, MD	Tazemetostat → PI3K inhibitor
 JOHN P LEONARD, MD	PI3K inhibitor → tazemotostat	 LAURIE H SEHN MD, MPH	Tazemetostat → PI3K inhibitor

GENERAL MEDICAL ONCOLOGISTS (N = 75)	PI3K inhibitor → tazemetostat, Tazemetostat → PI3K inhibitor

Case Presentation – Dr Leonard: A 67-year-old woman with R/R FL

A 67-year-old woman is diagnosed with follicular lymphoma grade 1 with diffuse lymphadenopathy, 2 cm in multiple sites. Due to cosmetic issues, she decides to pursue treatment with rituximab single agent x 4 doses with a clinical response. 11 months later she develops progression of disease and mild leg swelling. Physical examination shows 2-cm bilateral cervical adenopathy and 3-4 cm unilateral inguinal adenopathy. PET/CT scan confirms the enlarged lymph nodes noted on physical exam, mild splenomegaly, and in addition 2 cm mediastinal and 2.5 cm abdominal lymph nodes are also demonstrated. Maximum SUV is 7.3. Laboratory studies are normal except for mild anemia. Biopsy of inguinal LN shows follicular lymphoma, grade 1. How to treat her?

- This patient opted for Bendamustine/Rituximab. Other options include R retreatment with maintenance, Benda/Obinutuzumab, R^2, R-Obinutuzumab.

Courtesy of John P Leonard, MD

Agenda

Module 1: Evolving treatment paradigm for patients with diffuse large B-cell lymphoma (DLBCL) – Dr LaCasce

Module 2: Optimal management of newly diagnosed and relapsed/refractory follicular lymphoma – Dr Leonard

Module 3: Available and emerging approaches for mantle cell lymphoma – Dr Williams

Module 4: Selection and sequencing of therapies for patients with advanced Hodgkin lymphoma – Dr Kuruvilla

Module 5: Advances in chimeric antigen receptor T-cell therapy for DLBCL and other lymphoma subtypes – Dr Friedberg

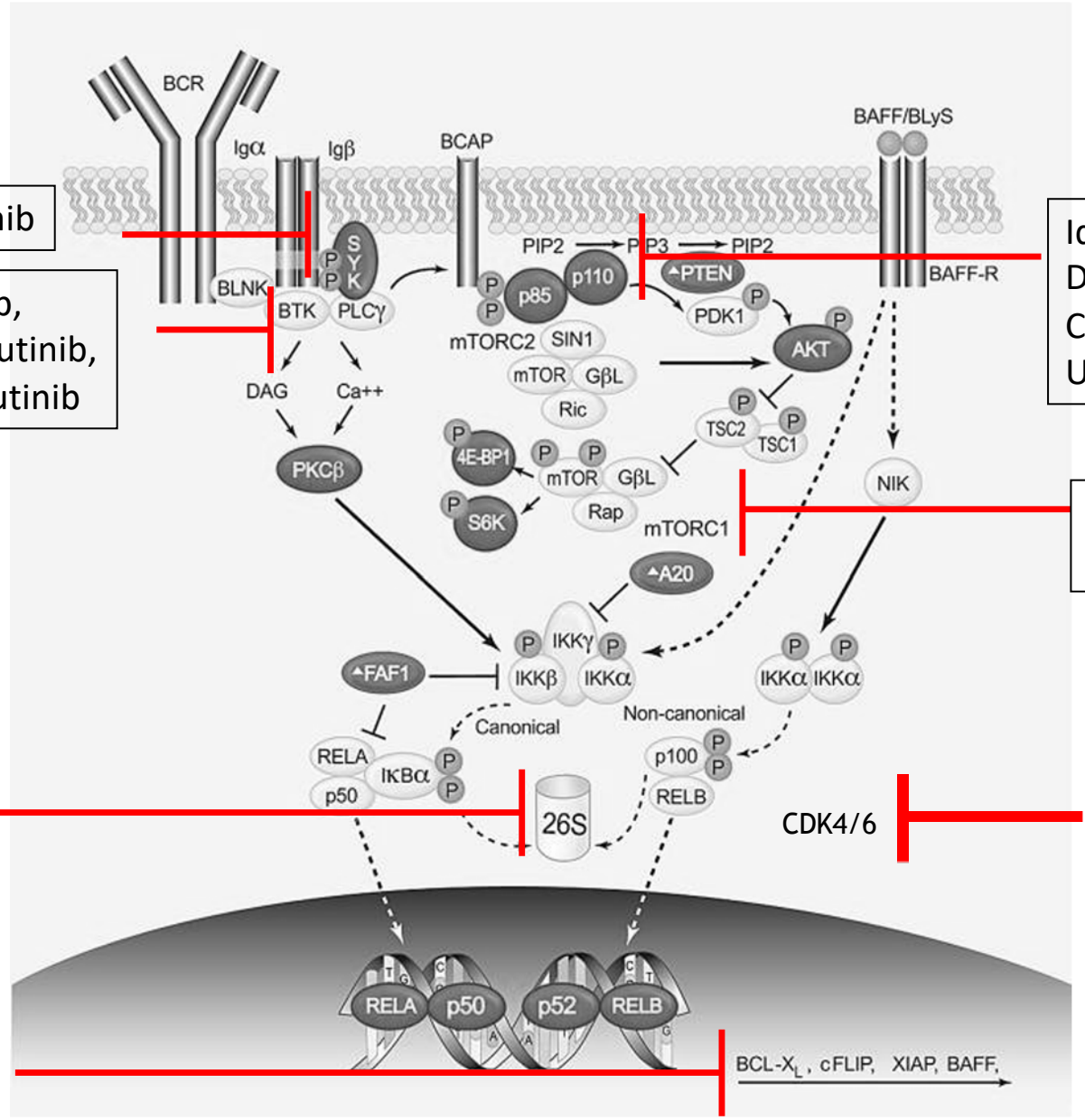
RTP
RESEARCH
TO PRACTICE

MCL Challenges and Opportunities

- Biologic and clinical heterogeneity
  - Many subtypes → complex Rx decisions
- Better treatment endpoints
  - Emerging role for MRD-directed therapy
- Optimize use of targeted agents
  - Chemotherapy-free regimens
- Post-induction SCT vs Maintenance therapy
  - MRD-driven approaches
- Cure

Courtesy of Michael E Williams, MD, ScM

The B-cell receptor pathway: Selected Inhibitors



Fostamatinib

Ibrutinib,
Acalabrutinib,
Zanubrutinib

Idelalisib,
Duvelisib,
Copanlisib,
Umbralisib

Everolimus,
Temsirolimus

Bortezomib,
Carfilzomib,
Ixazomib

Palbociclib,
Ribociclib,
Abemaciclib

Venetoclax

Courtesy of Michael E Williams, MD, ScM

Modified and updated from P. Perez-Galan et al. Blood. 2011

Targeted, non-Chemotherapy Approaches for Relapsed/Refractory MCL

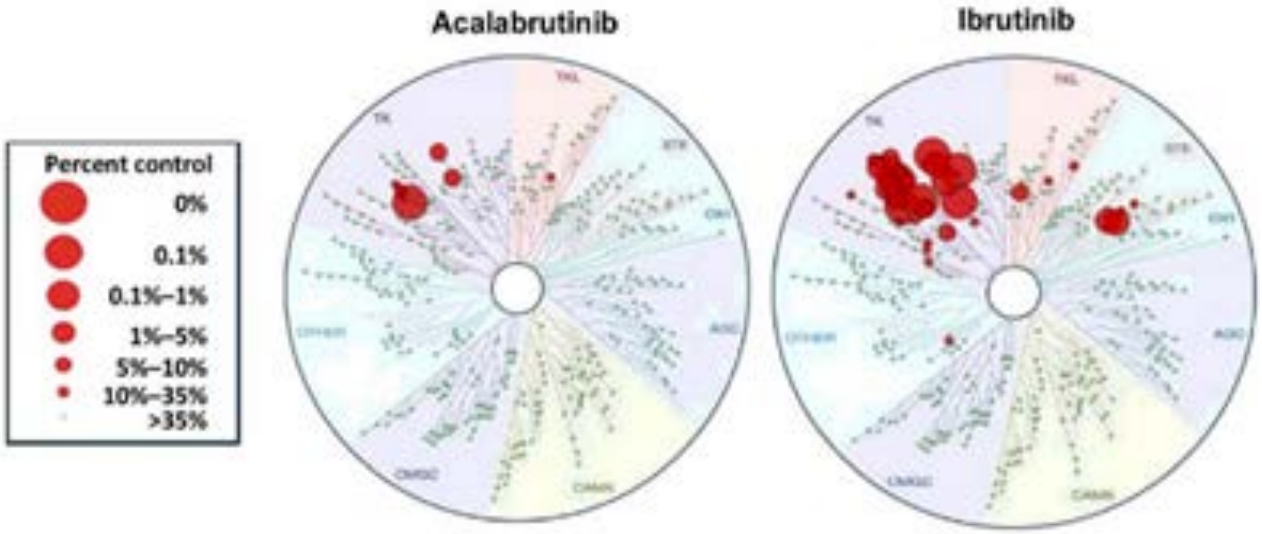
Agent	N	Response Rate	mDOR (mo.)
Bortezomib	155	33%	9.2 m
Temsirolimus	54	22%	7.1 m
Lenalidomide	134	28%	16.6 m
Lenalidomide-rituximab	52	57%	18.9 m
Idelalisib	40	40%	4 m
Ibrutinib	111	68%	17.5 m
Acalabrutinib	124	81%	72% at 12 m
Zanubrutinib	86	84%	16.7 m
Venetoclax	28	75%	12 m
Ibrutinib-Venetoclax	24	71% (all CR)	80% at 12 m

Courtesy of Michael E Williams, MD, ScM

Overview of FDA-approved BTKi for MCL:

Ibrutinib, Acalabrutinib and Zanubrutinib

- Similar overall response rates, ~70-80%
  - Better when used earlier (2nd or 3rd line)
- Improved toxicity profile for acala and zanu
  - More specific BTKi inhibition (Zanu similar to Acala)
  - Less Afib, bruising/bleeding, arthralgia
  - Prefer over ibrutinib if concurrent anticoagulation and/or anti-platelet therapy



Courtesy of Michael E Williams, MD, ScM

Herman et al, Clin Ca Res 2017

Venetoclax after BTKi failure in MCL

- Single-agent Ven (n=20; median 2-5 prior Rx, ASCT 30%)
  - ORR 53%, CR 18%
  - Median PFS 3.2 m, DOR 8.1 m
  - Median OS 9.4 months
- Venetoclax plus anti-CD20 mAb
  - Increases ORR
  - May “rescue” otherwise suboptimal responses to single-agent Veneto

Eyer et al, Haematologica 2019

Courtesy of Michael E Williams, MD, ScM

Update: Ibrutinib/Venetoclax in R/R MCL, median 37.5 m f/u *(ASH 2019, #756)*

Figure 1. Progression free survival (Dashed lines represent 95% confidence interval)

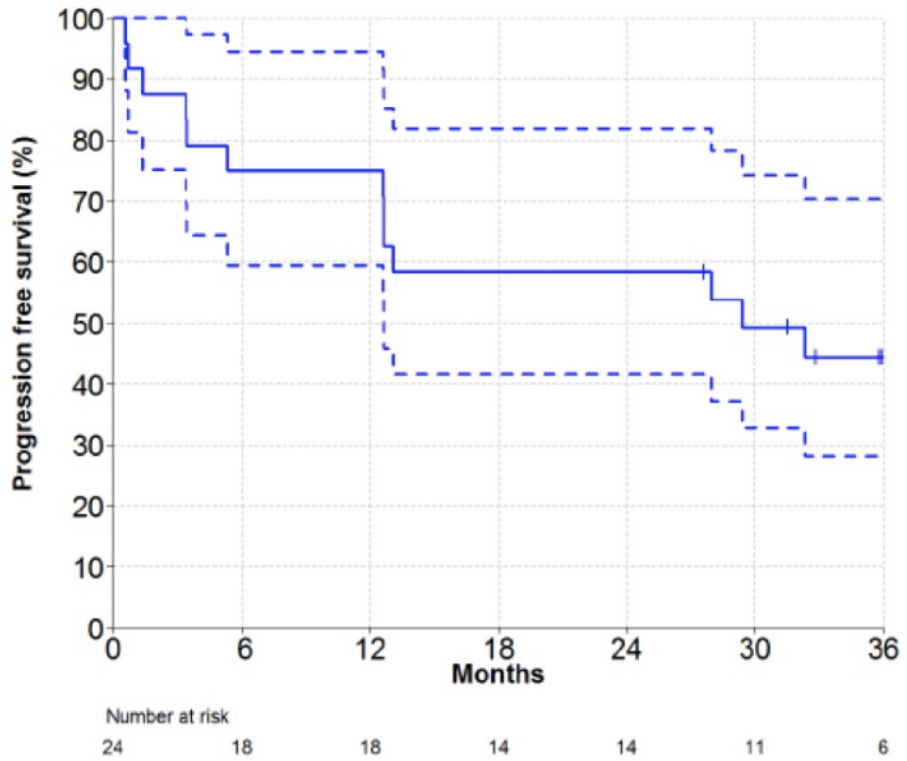
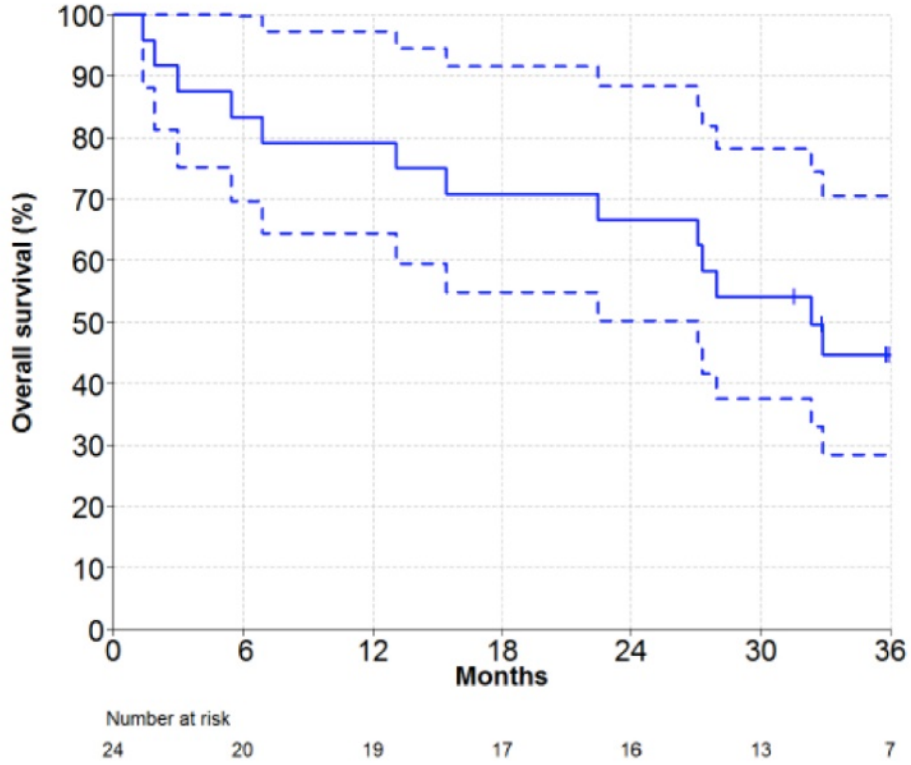


Figure 2. Overall survival (Dashed lines represent 95% confidence interval)

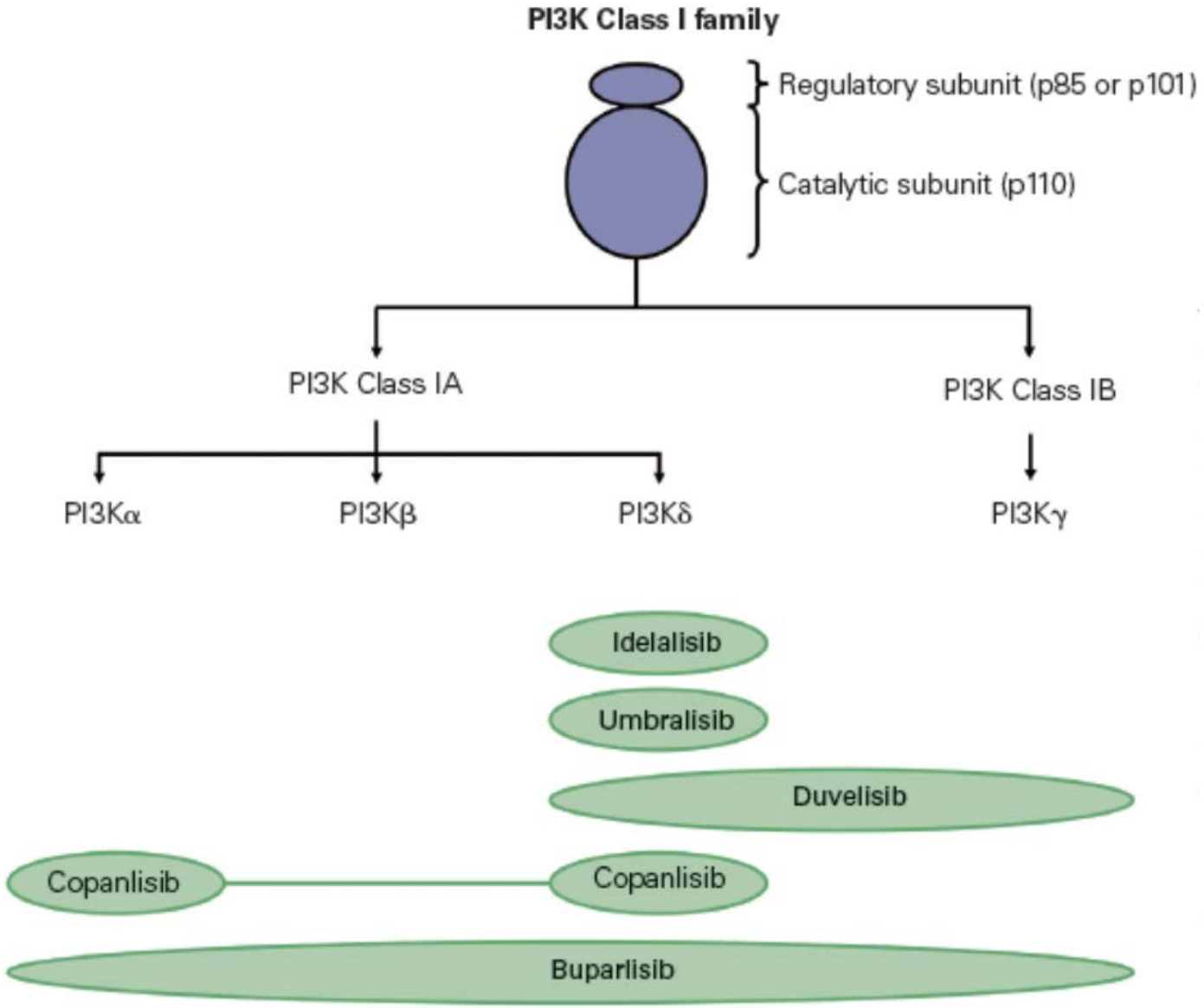


- MRD-negative by flow in 67%, and by ASO-PCR in 38%
- 5 MRD-negative patients discontinued Rx at median of18.5 mo

→4 remained MRD-neg after 6, 13, 17 and 18 months off Rx

Courtesy of Michael E Williams, MD, ScM

PI3Ki (Phosphatidylinositol 3-kinase inhibitors)

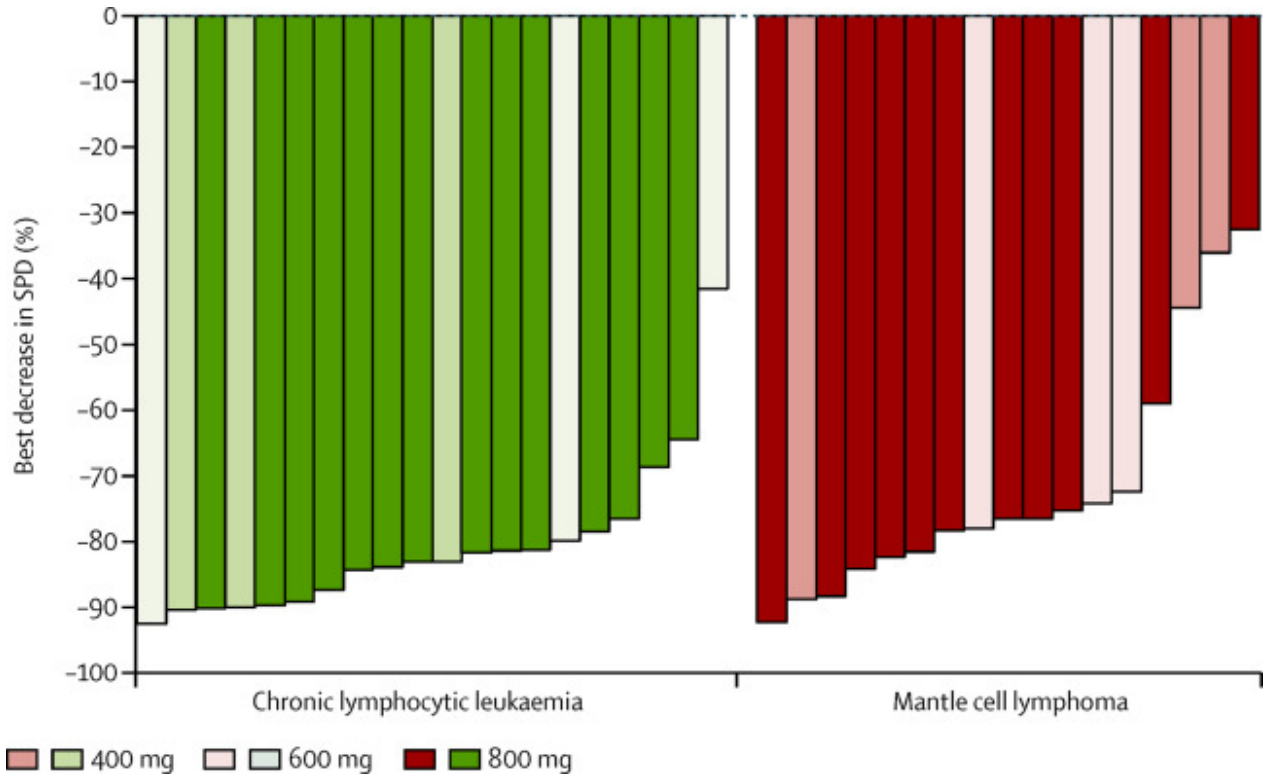


Courtesy of Michael E Williams, MD, ScM

(Greenwell IB et al. Oncology Journal 2017; 31)

Umbralisib in combination with ibrutinib in patients with relapsed or refractory **CLL** or **Mantle Cell Lymphoma**: a multicentre phase 1–1b study

M. Davids et al, Lancet Haematol 2019



MCL, n = 21
ORR 67% (CR = 4/21)
Median PFS 10.5 mo
Median OS 29.7 mo

Recommended phase 2 dose: Umbra 800 mg po qd plus Ibrutinib at standard dose (420 mg or 560 mg qd)
Umbralisib is investigational, not yet FDA approved

Courtesy of Michael E Williams, MD, ScM

Sustained remission with Lenalidomide plus Rituximab as **initial therapy** of MCL

*J Ruan et al, NEJM 2015; **JCO 2018***

- n=38, median f/u 64 mo. (21-78 mo.)
- **ORR 92%, CR 64%** **(by PET +/- BM; med. 11 mo. to reach CR)**
- **3 yr PFS 80%, OS 90%**
- **5 yr estimated PFS 64%, OS 77%**
  - *8/10 patients in CR @ 3 yr are MRD negative*
  - *No difference in ORR for Low- vs High-risk MIPI*
  - *No correlation with Ki-67 score*
- **Toxicity:**
  - Grade 3-4 neutropenia 50%, thrombocytopenia 13%
  - 1 pancreas cancer, 6 non-inv. skin cancer
  - Grade 3 infection in 3 pts
- Relapsing pts respond to second line Rx

Courtesy of Michael E Williams, MD, ScM

Selected Ongoing Combinatorial MCL Trials

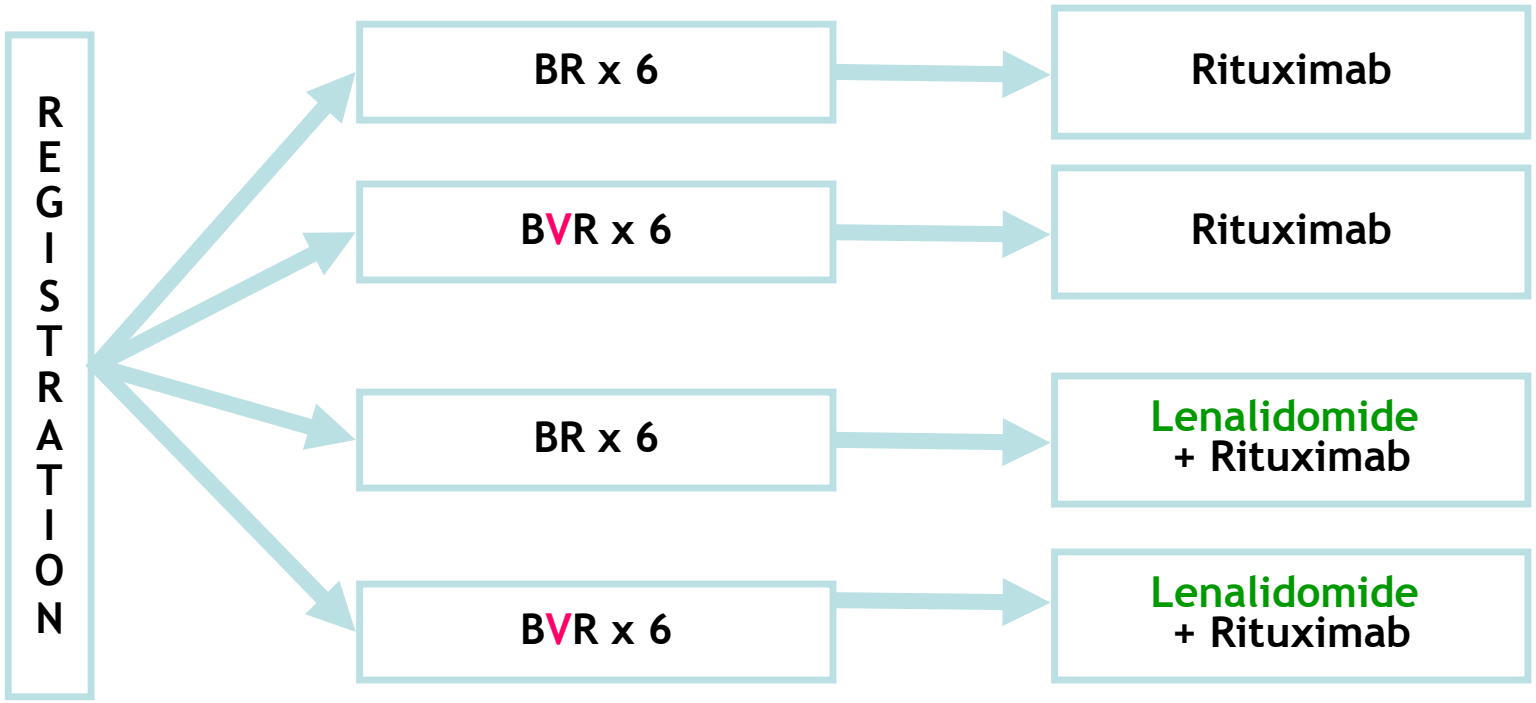
- **Front-line**
  - E4181: BR-HiDAC +/- Acalabrutinib vs BR + Acala
  - PrE0405: BR + Venetoclax (not ASCT eligible)
  - Ibrutinib + Veneto (SYMPATICO)
  - BR vs Zanubrutinib + R (Not ASCT eligible)
  - BR +/- Acalabrutinib
  - Acala + Veneto + R (MDACC)
  - Post-ASCT maintenance with acalabrutinib or ixazomib

  - R/R MCL: PrE0404: Ibrutinib plus ixazomib

  - ***And many more……***

Courtesy of Michael E Williams, MD, ScM

ECOG Trial: E1411 - Phase 2 Intergroup Trial: Initial Therapy of Mantle Cell Lymphoma



BR = Bendamustine, Rituximab

V= Bortezomib

M. Smith, Study PI; *accrual completed September 2016;*
Data analysis in progress as of Sept. 2020

Courtesy of Michael E Williams, MD, ScM

KTE-X19, an Anti-CD19 Chimeric Antigen Receptor T Cell Therapy, in Patients With Relapsed/Refractory Mantle Cell Lymphoma: Results of the Phase 2 ZUMA-2 Study

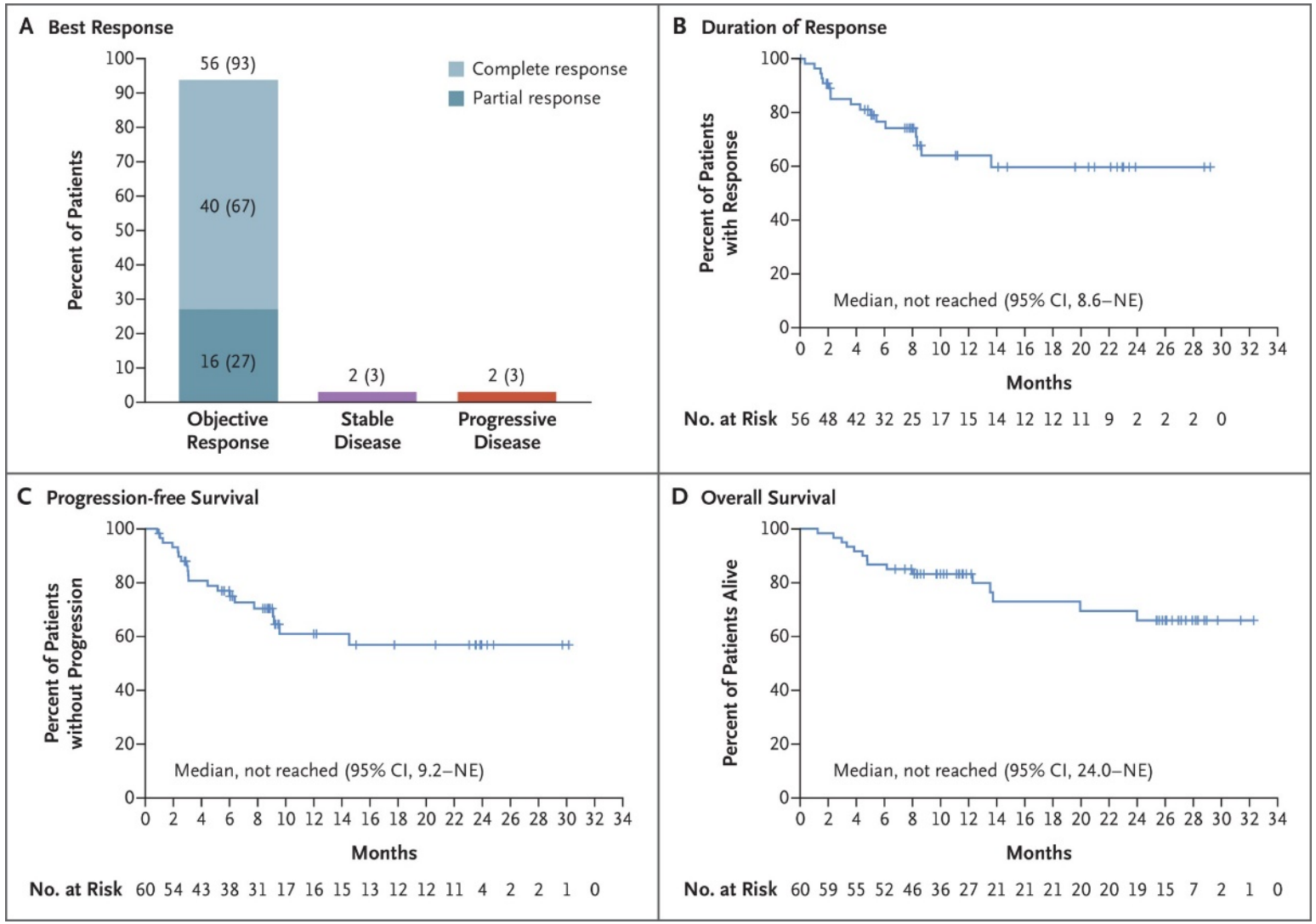
Michael Wang,[1] Javier Munoz,[2] Andre Goy,[3] Frederick L. Locke,[4] Caron A. Jacobson,[5] Brian T. Hill,[6] John M. Timmerman,[7] Houston Holmes,[8] Samantha Jaglowski,[9] Ian W. Flinn,[10] Peter A. McSweeney,[11] David B. Miklos,[12] John M. Pagel,[13] Marie José Kersten,[14] Noel Milpied,[15] Henry Fung,[16] Max S. Topp,[17] Roch Houot,[18] Amer Beitinjaneh,[19] Weimin Peng,[20] Lianqing Zheng,[20] John M. Rossi,[20] Rajul K. Jain,[20] Arati V. Rao,[20] and Patrick M. Reagan[21]

[1]The U… Cancer Cen… ion, Cle… ity Compr… Denver, CO; [12]S… iversity of Am… ance; [16]Fox C… serm & EFS, Rennes, France; [19]University of Miami, Miami, FL, USA; [20]Kite, a Gilead Company, Santa Monica, CA; [21]University of Rochester Medical Center, Rochester, NY

FDA approved CAR T-cell therapy for ***brexucabtagene autoleucel*** to treat relapsed or refractory mantle cell lymphoma. Jul 24, 2020

Courtesy of Michael E Williams, MD, ScM

Results: *from Wang et al, NEJM 2020; 382:1331-1342*



Courtesy of Michael E Williams, MD, ScM

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

1. Ibrutinib
2. Acalabrutinib
3. Zanubrutinib
4. Lenalidomide
5. Lenalidomide + rituximab
6. Venetoclax
7. Venetoclax + rituximab
8. Other

RTP RESEARCH TO PRACTICE

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

 JONATHAN W FRIEDBERG, MD, MMSC	Acalabrutinib	 MICHAEL E WILLIAMS, MD, SCM	Acalabrutinib
 JOHN KURUVILLA, MD	Ibrutinib	 CRAIG MOSKOWITZ, MD	Acalabrutinib
 ANN S LACASCE, MD, MMSC	Zanubrutinib	 LORETTA NASTOUPIL, MD	Acalabrutinib
 JOHN P LEONARD, MD	Acalabrutinib	 LAURIE H SEHN MD, MPH	Ibrutinib
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Ibrutinib, Acalabrutinib		

A 78-year-old patient with MCL initially treated with BR followed by 2 years of maintenance rituximab experiences disease relapse 3 years later. The patient has a history of atrial fibrillation and is receiving anticoagulation therapy. What would you recommend?

 JONATHAN W FRIEDBERG, MD, MMSC	Acalabrutinib	 MICHAEL E WILLIAMS, MD, SCM	Acalabrutinib
 JOHN KURUVILLA, MD	Acalabrutinib	 CRAIG MOSKOWITZ, MD	Zanubrutinib
 ANN S LACASCE, MD, MMSC	Zanubrutinib	 LORETTA NASTOUPIL, MD	Acalabrutinib
 JOHN P LEONARD, MD	Zanubrutinib	 LAURIE H SEHN MD, MPH	Acalabrutinib
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Acalabrutinib		

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?

1. I haven’t and would not
2. I haven’t but would for the right patient
3. I have

RTP
RESEARCH
TO PRACTICE

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?

 JONATHAN W FRIEDBERG, MD, MMSC	I haven't and would not	 MICHAEL E WILLIAMS, MD, SCM	I haven't but would for the right patient
 JOHN KURUVILLA, MD	I haven't but would for the right patient	 CRAIG MOSKOWITZ, MD	I have
 ANN S LACASCE, MD, MMSC	I haven't but would for the right patient	 LORETTA NASTOUPIL, MD	I have
 JOHN P LEONARD, MD	I haven't but would for the right patient	 LAURIE H SEHN MD, MPH	I have

GENERAL MEDICAL ONCOLOGISTS (N = 75)	I haven't but would for the right patient

Regulatory and reimbursement issues aside, would you attempt to access venetoclax for select patients with relapsed/refractory MCL?

1. Yes, as up-front treatment
2. Yes, after a BTK inhibitor
3. Yes, after a BTK inhibitor → lenalidomide
4. Yes, in other situations
5. No

RTP
RESEARCH
TO PRACTICE

Regulatory and reimbursement issues aside, would you attempt to access venetoclax for select patients with relapsed/refractory MCL?

 JONATHAN W FRIEDBERG, MD, MMSC	Yes, after a BTK inhibitor → lenalidomide
 JOHN KURUVILLA, MD	Yes, after a BTK inhibitor
 ANN S LACASCE, MD, MMSC	Yes, after a BTK inhibitor
 JOHN P LEONARD, MD	Yes, after a BTK inhibitor → lenalidomide
 MICHAEL E WILLIAMS, MD, SCM	Yes, after a BTK inhibitor
 CRAIG MOSKOWITZ, MD	Yes, after a BTK inhibitor → lenalidomide
 LORETTA NASTOUPIL, MD	Yes, after a BTK inhibitor
 LAURIE H SEHN MD, MPH	Yes, after a BTK inhibitor
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Yes, after a BTK inhibitor; Yes, after a BTK inhibitor → lenalidomide

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?

1. Lenalidomide
2. Lenalidomide + rituximab
3. Bortezomib
4. Bortezomib + rituximab
5. Venetoclax
6. Acalabrutinib
7. Zanubrutinib
8. Brexucabtagene autoleucel
9. Other

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?

 JONATHAN W FRIEDBERG, MD, MMSC	Brexucabtagene autoleucel	 MICHAEL E WILLIAMS, MD, SCM	Venetoclax
 JOHN KURUVILLA, MD	Brexucabtagene autoleucel	 CRAIG MOSKOWITZ, MD	Bridge therapy to CAR T-cell therapy
 ANN S LACASCE, MD, MMSC	Brexucabtagene autoleucel	 LORETTA NASTOUPIL, MD	Brexucabtagene autoleucel
 JOHN P LEONARD, MD	Brexucabtagene autoleucel	 LAURIE H SEHN MD, MPH	Brexucabtagene autoleucel

GENERAL MEDICAL ONCOLOGISTS (N = 75)	Venetoclax

Case Presentation – Dr Williams: A 72-year-old man with multi-agent refractory MCL

- 72 yo physician referred July 2015 with fatigue, anemia and lymphocytosis 20k
  - Exam: diffuse adenopathy, splenomegaly to umbilicus
- PB flow c/w MCL, typical phenotype
- LN biopsy: MCL, mantle zone pattern, Ki67 30%
- He declined Rx with any cytotoxic agents
- Treated with rituximab weekly x 4 then maint. R → PR, cleared circulating cells
- 2 yr later, PD: orbital mass, diffuse adenopathy
  - → Ibrutinib 560/d → PR
  - Discontinued after 4 mo due to severe rash

Courtesy of Michael E Williams, MD, ScM

Case Presentation – Dr Williams: A 72-year-old man with multi-agent refractory MCL(cont'd)

- Acalabrutinib 100 mg bid → transient decrease in adenopathy x 4 mo, then progressive adenopathy and splenomegaly. No recurrence of rash.
- Venetoclax stepped up dosing to 400 mg/d
  - Nodes and spleen decreased x 3 months, then progressed
  - Lymphocyte count remained normal
- Added obinutuzumab to Veneto, with goal of achieving synergy for apoptotic response
  - Obinu 100 mg IV, given IV fluids and he pushed po fluids, returned on day 2 for 900 mg dose. On allopurinol.
  - Patient asymptomatic, clear decrease in cervical and axillary node size, decreased splenomegaly on exam
  - Laboratory TLS: LDH 2000, phos 6.8, K 4.7, creat 1.1, uric acid 8.4 → resolved with IV and po fluids

Courtesy of Michael E Williams, MD, ScM

Case Presentation – Dr Williams: A 72-year-old man with multi-agent refractory MCL(cont'd)

- Continued Veneto, gave dose 2 obinu 1 week later
  - No further TLS
- Completed obinu induction phase, then q2mo x 1 y
  - Achieved CR by imaging and exam at 3 months from initiation of obinu
- Obinu d/c due to pneumonia in Dec. 2019
- Continues Veneto 400 mg/d
- Oct. 2020: Remains in CR by exam and imaging

Courtesy of Michael E Williams, MD, ScM

Agenda

Module 1: Evolving treatment paradigm for patients with diffuse large B-cell lymphoma (DLBCL) – Dr LaCasce

Module 2: Optimal management of newly diagnosed and relapsed/refractory follicular lymphoma – Dr Leonard

Module 3: Available and emerging approaches for mantle cell lymphoma – Dr Williams

Module 4: Selection and sequencing of therapies for patients with advanced Hodgkin lymphoma – Dr Kuruvilla

Module 5: Advances in chimeric antigen receptor T-cell therapy for DLBCL and other lymphoma subtypes – Dr Friedberg

RTP
RESEARCH
TO PRACTICE

Brentuximab Vedotin with Chemotherapy for Stage III/IV Classical Hodgkin Lymphoma (cHL): 4-Year Update of the ECHELON-1 Study

Nancy L. Bartlett[1], David J. Straus[2], Monika Dlugosz-Danecka[3], Sergey Alekseev[4], Árpád Illés[5], Ewa Lech-Maranda[6], Tatyana A. Feldman[7], Piotr Smolewski[8], Kerry J Savage[9], Jan Walewski[10], Radhakrishnan Ramchandren[11], Pier Luigi Zinzani[12], Martin Hutchings[13], Joseph M. Connors[9], John Radford[14], Javier Munoz[15], Won-Seog Kim[16], Ranjana H. Advani[17], Stephen M Ansell[18], Anas Younes[2], Andrea Gallamini[19], Harry Miao[20], Rachael Liu[20], Keenan Fenton[21], Andres Forero-Torres[21], and Marco Picardi[22]

[1]Washington University School of Medicine Siteman Cancer Center, St Louis, MO; [2]Department of Medicine, Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY; [3]Department of Hematology, Jagiellonian University, Kraków, Poland; [4]Petrov Research Institute of Oncology, St Petersburg, Russia; [5]University of Debrecen, Debrecen, Hungary; [6]Department of Hematology, Institute of Hematology and Transfusion Medicine, Warsaw, Poland; [7]Hackensack University Medical Center, NJ; [8]Medical University of Lodz, Poland; [9]BC Cancer Centre for Lymphoid Cancer, Vancouver, Canada; [10]Maria Sklodowska-Curie Institute and Oncology Centre, Warsaw, Poland; [11]The University of Tennessee Graduate School of Medicine, Knoxville; [12]Seràgnoli Institute of Hematology, Bologna University, Italy; [13]Department of Haematology, Rigshospitalet, Copenhagen University Hospital, Denmark; [14]The University of Manchester and the Christie NHS Foundation Trust, Manchester Academic Health Science Centre, United Kingdom; [15]Banner MD Anderson Cancer Center, Gilbert, AZ; [16]Division of Hematology-Oncology, Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [17]Department of Medicine, Division of Oncology, Stanford University, CA; [18]Division of Hematology, Mayo Clinic, Rochester, MN; [19]Research Innovation and Statistics, Antoine-Lacassagne Cancer Centre, Nice, France; [20]Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceuticals Limited, Cambridge, MA; [21]Seattle Genetics, Inc., Bothell, WA; [22]Hematology Unit, University Federico II, Naples, Italy

Abstract No. 4026

American Society of Hematology Annual Meeting; December 7-10, 2019; Orlando, FL

Landmark PFS per INV

Table 2. Landmark PFS per INV

PFS per INV	A+AVD (95% CI)	ABVD (95% CI)
2-Year follow up (primary analysis)[8]		
2-Year PFS rate (95% CI), %	n=332 84.2 (81.1, 86.9)	n=307 78.0 (74.4, 81.1)
HR (95% CI) P value	0.70 (0.54, 0.91) P=0.006	
3-Year follow up[5]		
3-Year PFS rate (95% CI), %	n=360 83.1 (79.9, 85.9)	n=325 76.0 (72.4, 79.2)
HR (95% CI) P value	0.70 (0.55, 0.90) P=0.005	
4-Year follow up		
4-Year PFS rate (95% CI), %	n=287 81.7 (78.3, 84.6)	n=257 75.1 (71.4, 78.4)
HR (95% CI) P value	0.69 (0.54, 0.88) P=0.003	

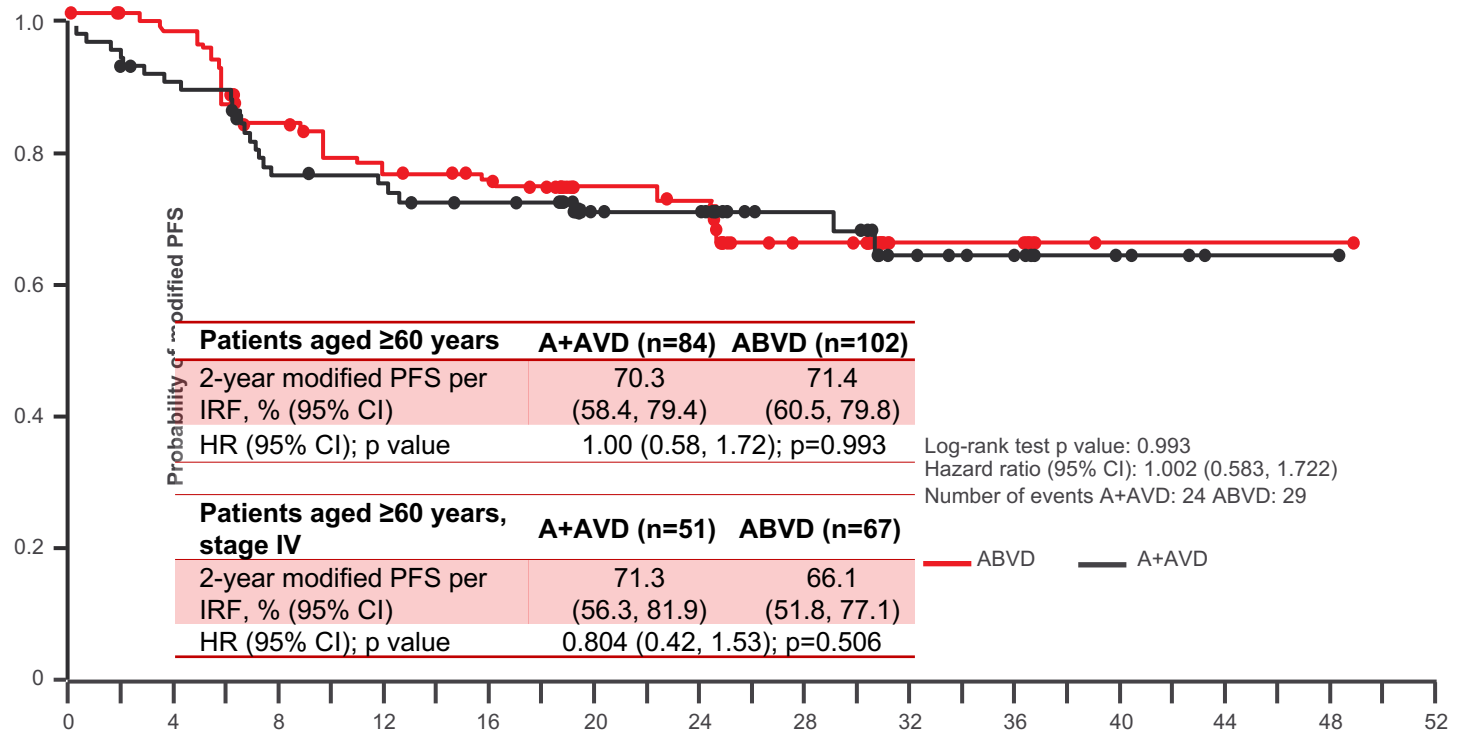
8. Connors JM, et al. ASH 2018 [abstract 2904].

Bartlett ASH 2019

Courtesy of John Kuruvilla, MD

ECHELON-1: Patients Over Age 60

Modified PFS per IRF in patients aged ≥60 years



Patients aged ≥60 years	A+AVD (n=84)	ABVD (n=102)
2-year modified PFS per IRF, % (95% CI)	70.3 (58.4, 79.4)	71.4 (60.5, 79.8)
HR (95% CI); p value	1.00 (0.58, 1.72); p=0.993	

Log-rank test p value: 0.993
Hazard ratio (95% CI): 1.002 (0.583, 1.722)
Number of events A+AVD: 24 ABVD: 29

Patients aged ≥60 years, stage IV	A+AVD (n=51)	ABVD (n=67)
2-year modified PFS per IRF, % (95% CI)	71.3 (56.3, 81.9)	66.1 (51.8, 77.1)
HR (95% CI); p value	0.804 (0.42, 1.53); p=0.506	

Number at risk

A+AVD	84	74	69	68	56	55	54	51	50	49	38	37	37	25	24	23	13	11	10	5	4	3	1	1	1	0	0
ABVD	102	93	90	83	72	68	64	63	60	57	44	44	42	25	23	22	8	8	8	2	1	1	1	1	1	0	0

Evens ASH 2018

Courtesy of John Kuruvilla, MD

Sequential BV-chemotherapy Strategies pre-ASCT

Strategy	N	ORR (CR) BV	ORR (CR) post chemo	PFS	Toxicity
BV → augICE	46	NR (27)	NR (76)	2Y EFS: 80%	BV: G3-4: 7
BV → salvage	37	68 (35)	87 (65)	NR	

Sequential strategy allows less exposure to chemotherapy but conceptually is less likely to lead to very high CR rate

Note: No concerns with PBSC mobilization or engraftment post-ASCT

Moskowitz Lancet Oncol 2015, Chen BBMT 2016

Courtesy of John Kuruvilla, MD

Immune checkpoint inhibitor combinations pre ASCT

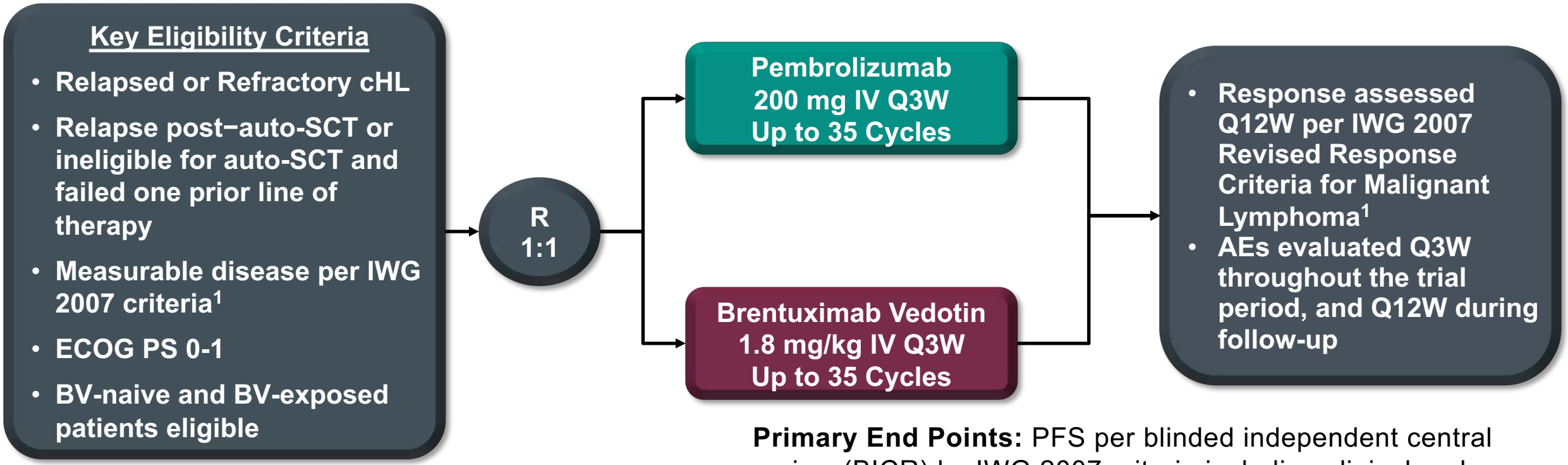
Regimen	N	ORR (CR)	PFS	Toxicity
Nivo + BV*	93	85 (67)	79% @ 24 m 92% @ 24 m (ASCT pp)	Gr3 PN and ANC (1) IrAE: GBS, pneumonia, diarrhea, AST (all n=1)
Nivo + BV + Ipi (E4412)	22	82 (68)	mPFS NR @ 6m	3 DLT (DKA, AST, rash)
Nivo / sequential NICE	43 N=8	90 (58) 100 (88)	74% @ 12 m	1 Gr5 sepsis 1 Grade 4 encephalitis

Note: No concerns with PBSC mobilization or engraftment post-ASCT
* pre-SCT

Moskowitz ASH 2019, Diefenbach ASH 2018; Herrera ASH 2019

Courtesy of John Kuruvilla, MD

KEYNOTE-204 Study Design (NCT02684292)



Stratification Factors

- Prior auto-SCT (yes vs no)
- Status after 1L therapy (primary refractory vs relapsed <12 months vs relapsed ≥12 months after end of 1L therapy)

Primary End Points: PFS per blinded independent central review (BICR) by IWG 2007 criteria including clinical and imaging data following auto-SCT or allogeneic stem cell transplant (allo-SCT); OS

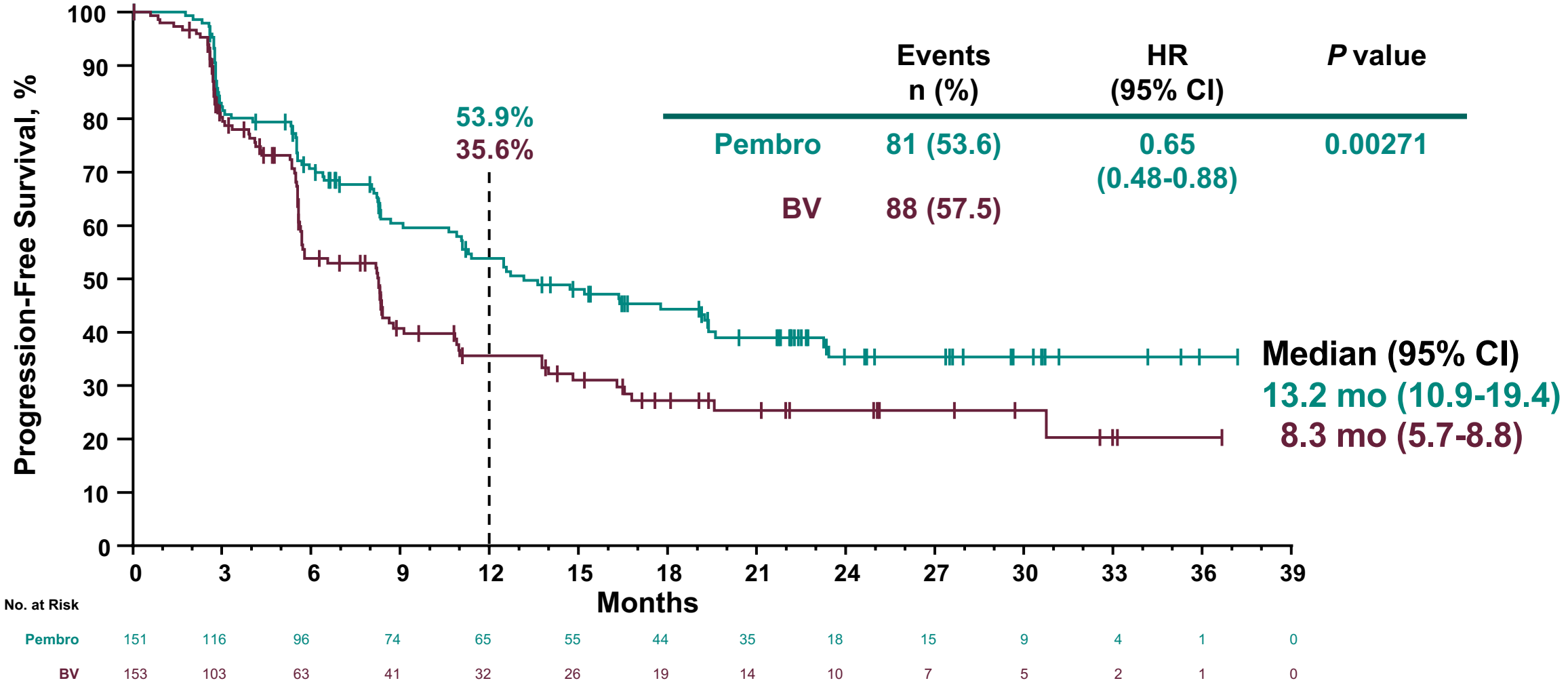
Secondary End Points: PFS per BICR by IWG 2007 criteria excluding clinical and imaging data following auto-SCT or allo-SCT; ORR by BICR per IWG 2007; PFS per investigator review; DOR; safety

1. Cheson BD et al. *J Clin Oncol.* 2007;25:579-586.

Courtesy of John Kuruvilla, MD

Primary End Point: Progression-Free Survival Per Blinded Independent Central Review

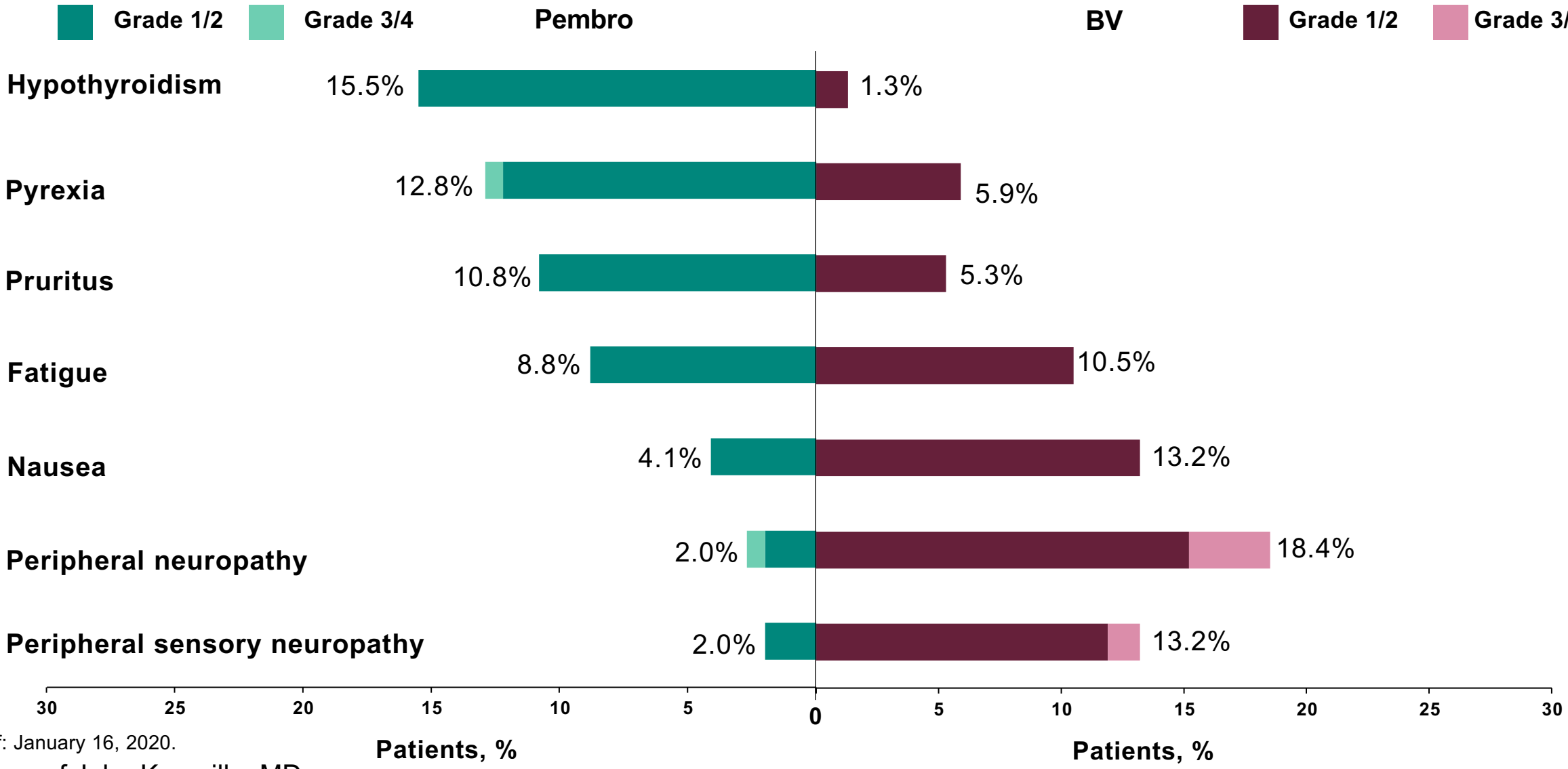
Including Clinical and Imaging Data Following Auto-SCT or Allo-SCT



Data cutoff: January 16, 2020.

Courtesy of John Kuruvilla, MD

Treatment-Related AEs (≥10% Either Arm)



Data cutoff: January 16, 2020.

Courtesy of John Kuruvilla, MD

Selected Novel Strategies in RR-cHL

Regimen	N	ORR (%)	Comment
AFM13 (CD30/CD16A)	28	12 (50% SD) 23 (higher dose)	Proof of concept trial
AFM13 + Pembro	30	83 (37 CR)	Safety and proof of concept
Relatlimab + Nivo	Not published		Safety and proof of concept
MK4280 + Pembro	Not published		Safety and proof of concept
CD30 CAR-T therapy	41	62 (51) 72 (59)	UNC / BCM experience ORR in n=32 receiving fludarabine-based lymphodepletion

Rothe Blood 2015; Bartlett Blood 2020, Ramos JCO 2020

Courtesy of John Kuruvilla, MD

A 27-year-old man is diagnosed with Stage IVB classical HL with nodal, spleen and bone involvement. Albumin is 3.1 g/dL, Hgb is 8.6 g/dL and white blood cell count is 17,500. IPS = 5. What initial treatment would you recommend?

1. Doxorubicin/bleomycin/vinblastine/dacarbazine (ABVD)
2. PET-adapted ABVD
3. Brentuximab vedotin + AVD
4. AVD
5. Other chemotherapy
6. Other

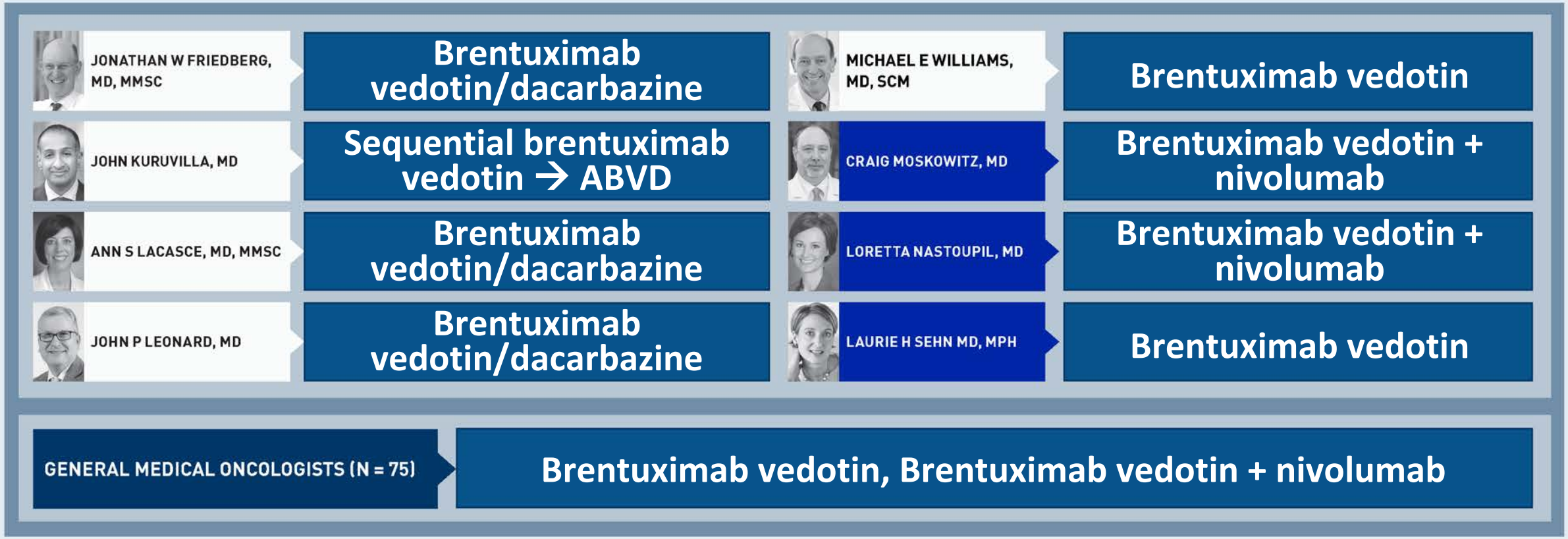
RTP
RESEARCH
TO PRACTICE

A 27-year-old man is diagnosed with Stage IVB classical Hodgkin lymphoma (HL) with nodal, spleen and bone involvement. Albumin is 3.1 g/dL, Hgb is 8.6 g/dL and white blood cell count is 17,500. IPS = 5. What initial treatment would you recommend?

 JONATHAN W FRIEDBERG, MD, MMSC	Brentuximab vedotin + AVD	 MICHAEL E WILLIAMS, MD, SCM	Brentuximab vedotin + AVD
 JOHN KURUVILLA, MD	PET-adapted BEACOPP	 CRAIG MOSKOWITZ, MD	Brentuximab vedotin + AVD
 ANN S LACASCE, MD, MMSC	Brentuximab vedotin + AVD	 LORETTA NASTOUPIL, MD	Brentuximab vedotin + AVD
 JOHN P LEONARD, MD	Brentuximab vedotin + AVD	 LAURIE H SEHN MD, MPH	Brentuximab vedotin + AVD
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Brentuximab vedotin + AVD		

AVD = doxorubicin/vinblastine/dacarbazine; BEACOPP = bleomycin/etoposide/doxorubicin/cyclophosphamide/vincristine/procarbazine/prednisone

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?



ABVD = doxorubicin/bleomycin/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?

1. ICE (ifosfamide/carboplatin/etoposide)
2. Brentuximab vedotin
3. Brentuximab vedotin + nivolumab
4. Brentuximab vedotin + pembrolizumab
5. Other

RTP
RESEARCH
TO PRACTICE

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?

 JONATHAN W FRIEDBERG, MD, MMSC	Brentuximab vedotin + nivolumab
 JOHN KURUVILLA, MD	Gemcitabine/ dexamethasone/cisplatin
 ANN S LACASCE, MD, MMSC	ICE if later relapse; brentuximab vedotin + nivolumab for early relapse
 JOHN P LEONARD, MD	Brentuximab vedotin + bendamustine
 MICHAEL E WILLIAMS, MD, SCM	ICE
 CRAIG MOSKOWITZ, MD	Brentuximab vedotin + nivolumab
 LORETTA NASTOUPIL, MD	Brentuximab vedotin + bendamustine
 LAURIE H SEHN MD, MPH	Brentuximab vedotin
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Brentuximab vedotin, Brentuximab vedotin + nivolumab

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?

1. Other chemotherapy
2. Brentuximab vedotin
3. Brentuximab vedotin + nivolumab
4. Brentuximab vedotin + pembrolizumab
5. Nivolumab
6. Pembrolizumab
7. Other

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?

 JONATHAN W FRIEDBERG, MD, MMSC	Brentuximab vedotin	 MICHAEL E WILLIAMS, MD, SCM	Brentuximab vedotin + nivolumab
 JOHN KURUVILLA, MD	Pembrolizumab	 CRAIG MOSKOWITZ, MD	Brentuximab vedotin + nivolumab
 ANN S LACASCE, MD, MMSC	Brentuximab vedotin + nivolumab	 LORETTA NASTOUPIL, MD	Brentuximab vedotin + nivolumab
 JOHN P LEONARD, MD	Pembrolizumab	 LAURIE H SEHN MD, MPH	Brentuximab vedotin

GENERAL MEDICAL ONCOLOGISTS (N = 75)	Brentuximab vedotin, Brentuximab vedotin + nivolumab

Case Presentation – Dr Kuruvilla: A 32-year-old patient with primary refractory HL

Approach to Management of post-ASCT failure

- You are following a 32-year-old patient who has relapsed HL (primary refractory disease, CR to second-line chemotherapy) and now with biopsy proven relapse approximately 3 months post-ASCT.
- Your next step in management is:
  - BV monotherapy
  - Pembrolizumab monotherapy
  - Combination BV+nivo therapy
  - One of the above but goal includes consolidation with allogeneic transplant

Courtesy of John Kuruvilla, MD

Agenda

Module 1: Evolving treatment paradigm for patients with diffuse large B-cell lymphoma (DLBCL) – Dr LaCasce

Module 2: Optimal management of newly diagnosed and relapsed/refractory follicular lymphoma – Dr Leonard

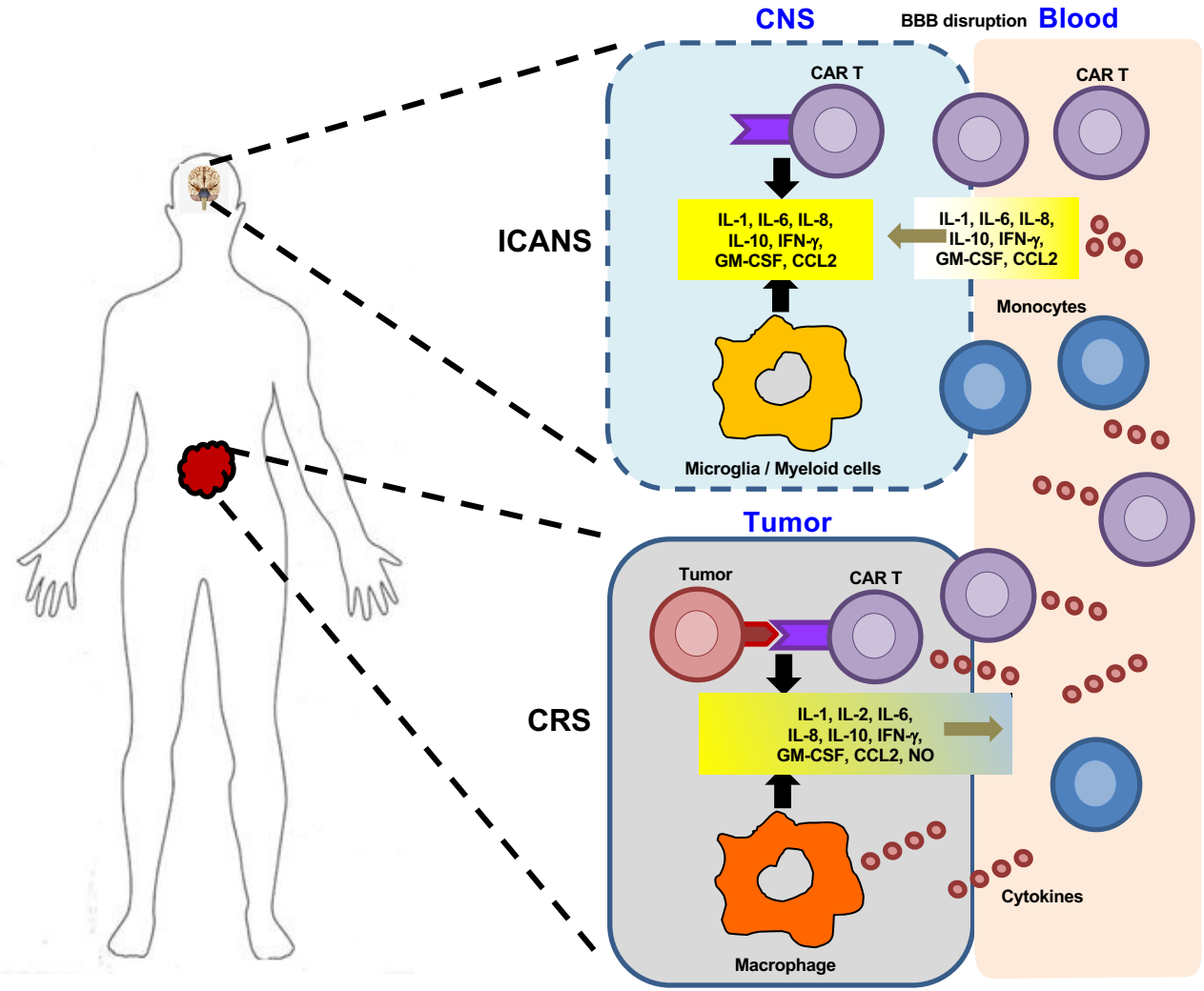
Module 3: Available and emerging approaches for mantle cell lymphoma – Dr Williams

Module 4: Selection and sequencing of therapies for patients with advanced Hodgkin lymphoma – Dr Kuruvilla

Module 5: Advances in chimeric antigen receptor T-cell therapy for DLBCL and other lymphoma subtypes – Dr Friedberg

RTP
RESEARCH
TO PRACTICE

Pathophysiology of CAR T-cell-associated neurotoxicity and cytokine release syndrome



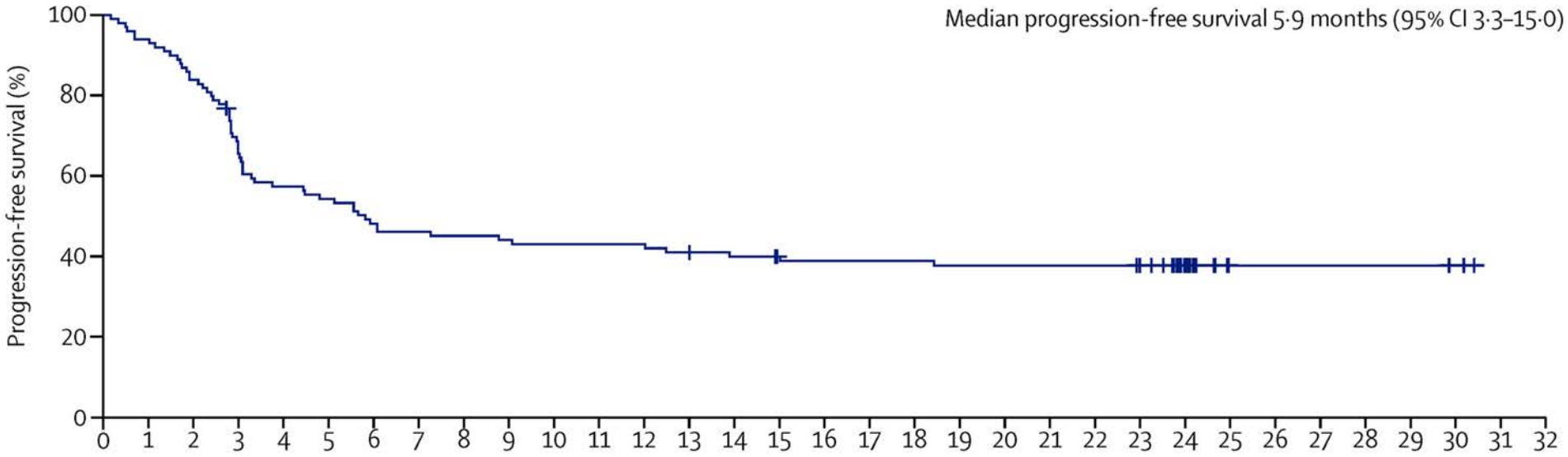
UR MEDICINE
WILMOT CANCER INSTITUTE

Courtesy of Jonathan W Friedberg, MD, MMSc

Reagan and Neelapu, *JCO* in press 2020

Long-term safety and efficacy of axicabtagene ciloleucel in refractory DLBCL (ZUMA-1)

Progression-free survival: Median follow-up 27 months



In patients with CR at 3 months, 24 month PFS was 72%

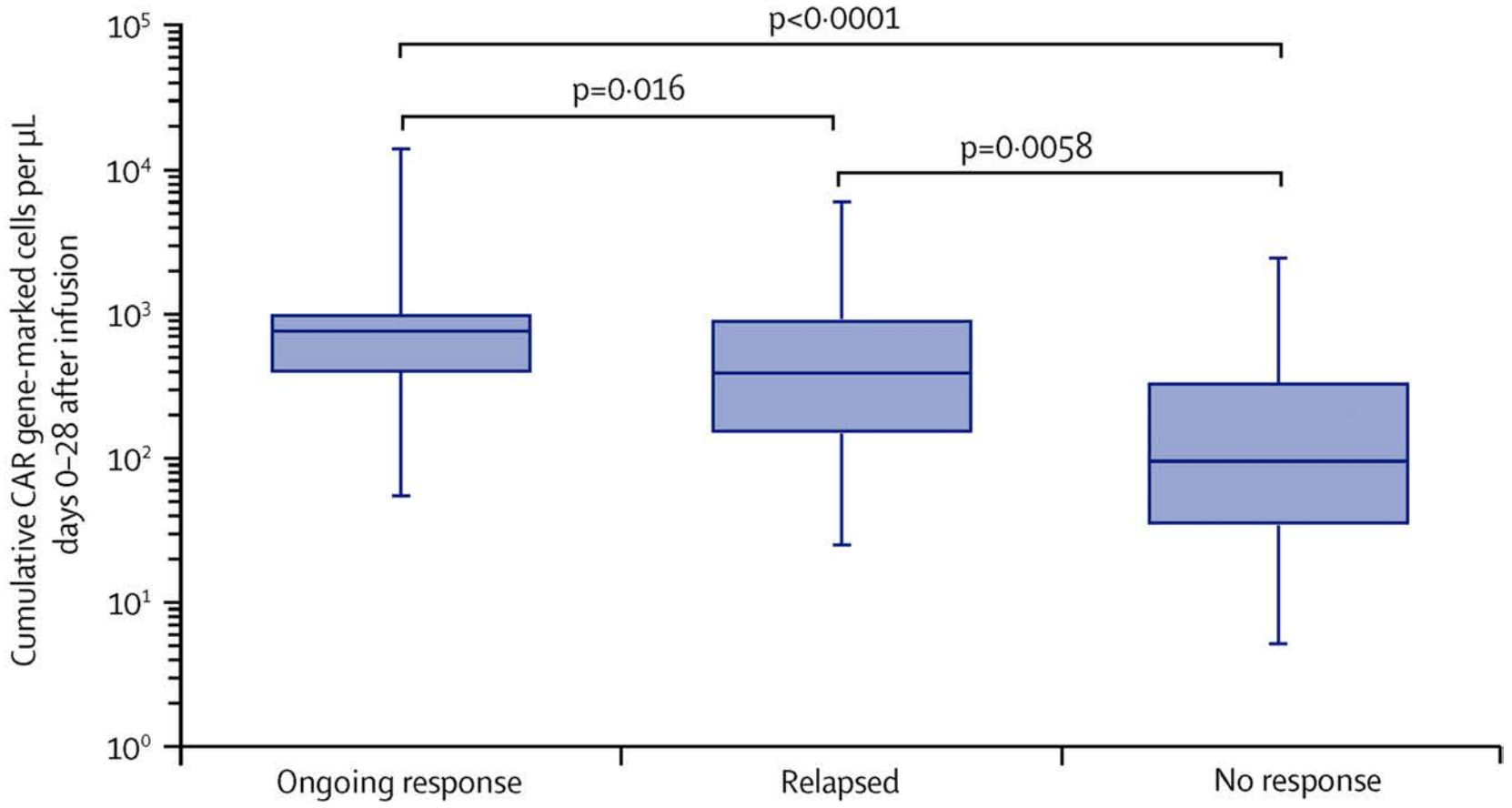
Median OS not reached

UR MEDICINE
WILMOT CANCER INSTITUTE

Courtesy of Jonathan W Friedberg, MD, MMSc

Locke et al, *Lancet Oncol* 20:31-42 2019

Durable responses are correlated with persistent CAR T-cells: ZUMA-1

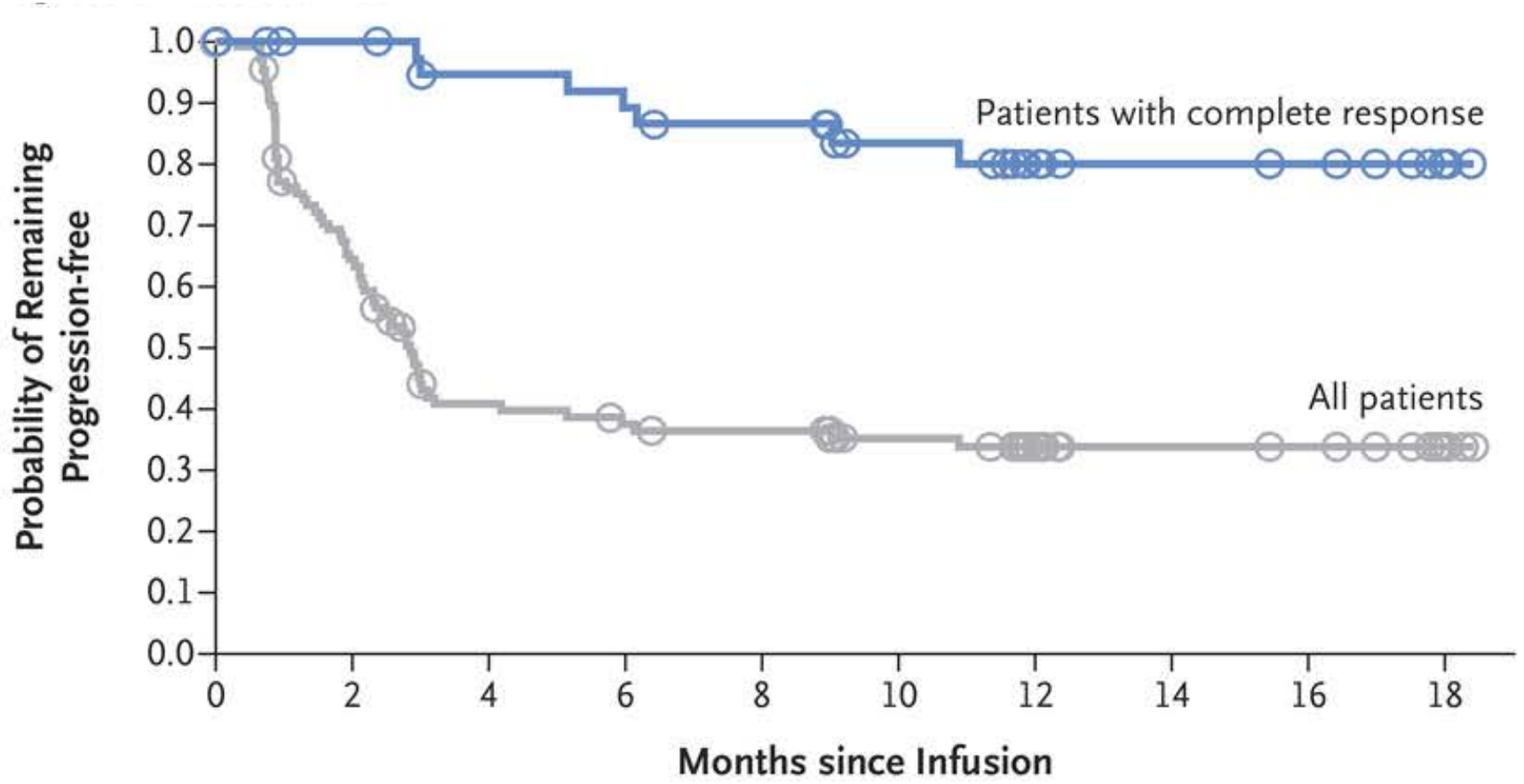


UR MEDICINE
WILMOT CANCER INSTITUTE

Courtesy of Jonathan W Friedberg, MD, MMSc

Locke et al, *Lancet Oncol* 20:31-42 2019

Tisagenlecleucel for DLBCL: JULIET trial
Median follow-up 14 months

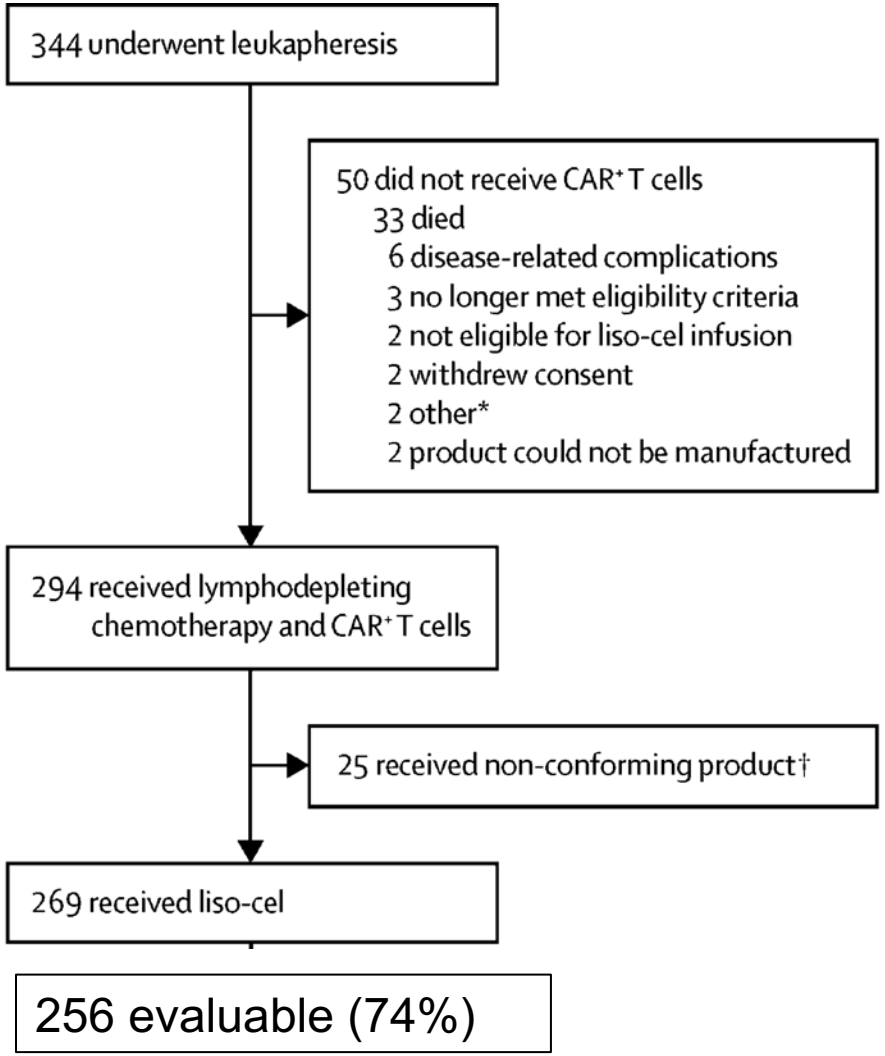


UR MEDICINE
WILMOT CANCER INSTITUTE

Courtesy of Jonathan W Friedberg, MD, MMSc

Schuster et al, *NEJM* 380:45-56 2019

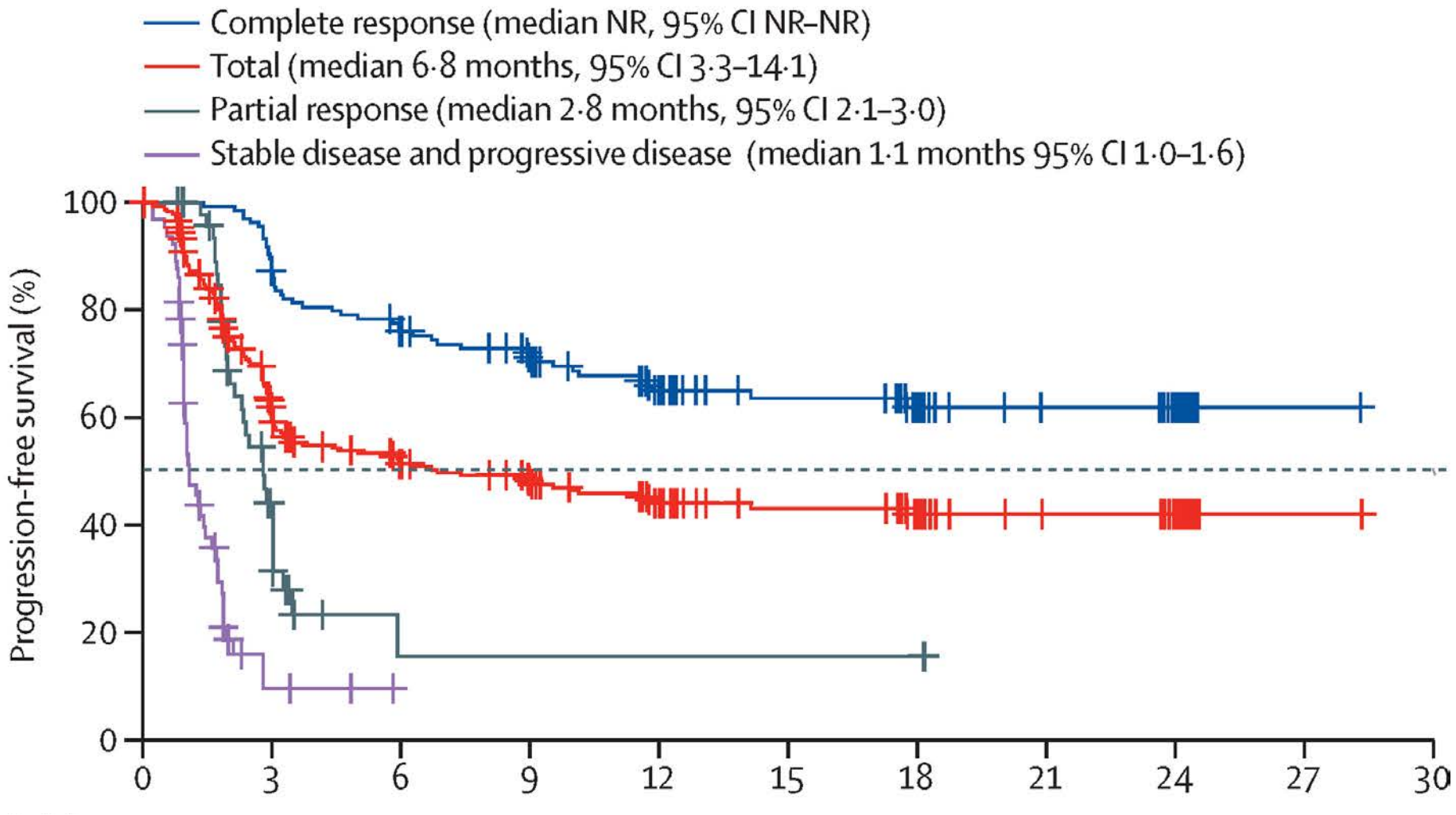
Lisocabtagene maraleucel for relapsed/refractory large cell lymphoma: TRANSCEND NHL 001



Courtesy of Jonathan W Friedberg, MD, MMSc

Abramson et al, *Lancet* 396:839-52 2020

TRANSCEND NHL 001 trial of lisocabtagene maraleucel for large cell lymphoma: Progression-free survival median follow-up 18 mos.

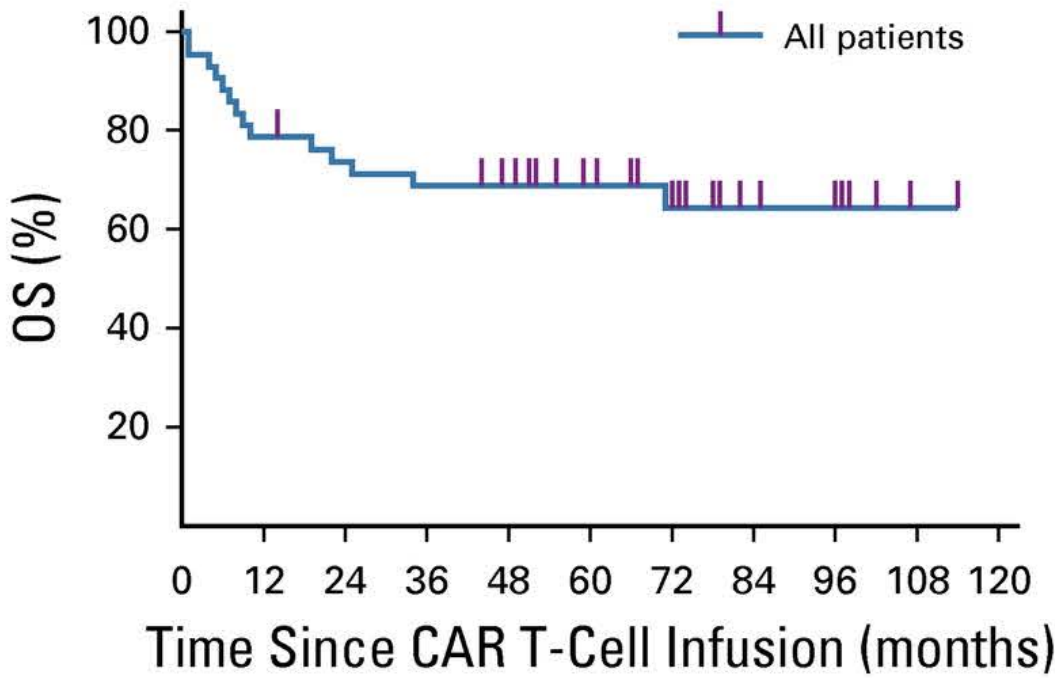


Courtesy of Jonathan W Friedberg, MD, MMSc

Abramson et al, *Lancet* 396:839-52 2020

Are CAR T-cells curative?
Long-term follow-up of NCI experience
Median follow-up 42 months

- No patient with PR/SD as best response had a durable response
- 19/25 CRs (76%) are ongoing
- Overall 51% of CAR T-cell treatments resulted in DOR > 3 years



Courtesy of Jonathan W Friedberg, MD, MMSc

Cappell et al, *JCO* online 2020

ZUMA-5 trial:
CAR-T cell therapy for FL

- High risk Indolent lymphoma:
  - >/= 2 prior lines of therapy
  - 66% POD24
  - 73% refractory to last treatment

N=80 patients with follicular lymphoma
ORR 95%
68% of patients with ongoing responses
CRS grade 3+: 11%
Neuro grade 3+: 19%
Grade 5 events: 2

A supplemental Biologics License Application (sBLA) has been submitted to the FDA to expand the indication for axicabtagene ciloleucel.

UR MEDICINE
WILMOT CANCER INSTITUTE

Courtesy of Jonathan W Friedberg, MD, MMSc

Jacobson et al, *Proc ASCO* 2020

Anti-CD30 CAR-T cell therapy in relapsed/refractory Hodgkin lymphoma

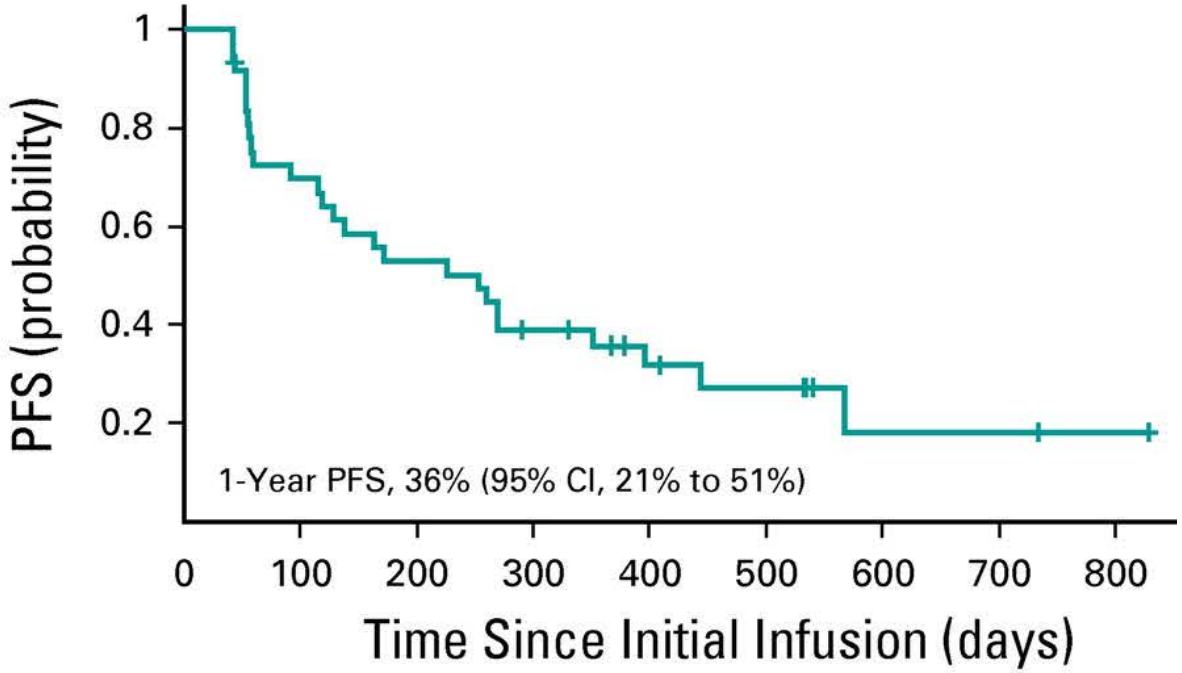
41 patients

Median 7 prior lines of therapy: Checkpoint inhibitors, Brentuximab ASCT/alloSCT.

Low grade CRS; no neurologic toxicity; common skin rash

ORR 72%; CR 59%

One year PFS: 36%



Courtesy of Jonathan W Friedberg, MD, MMSc

Ramos et al, *JCO* online 2020

Patient identification and appropriate referral for CAR-T cell therapy

- EARLY referral is most important
  - Numerous open trials in novel settings
- Considerations:
  - Avoid lymphotoxic therapy (purine analogs, bendamustine)
  - Avoid immunosuppressive therapy, including steroids
  - (?) avoid tafasitamab and other CD19-targeting agents
- For DLBCL:
  - Refer before starting salvage therapy
  - New products may allow treatment of older individuals
  - “Real world” experiences variable

UR MEDICINE
WILMOT CANCER INSTITUTE

Courtesy of Jonathan W Friedberg, MD, MMSc

Jain et al, *BBMT* 25:2305-21 2019

A patient with diffuse large B-cell lymphoma (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

RTP
RESEARCH
TO PRACTICE

A patient with diffuse large B-cell lymphoma (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.

 JONATHAN W FRIEDBERG, MD, MMSC	Agree	 MICHAEL E WILLIAMS, MD, SCM	Agree
 JOHN KURUVILLA, MD	Disagree	 CRAIG MOSKOWITZ, MD	Agree
 ANN S LACASCE, MD, MMSC	Disagree	 LORETTA NASTOUPIL, MD	Disagree
 JOHN P LEONARD, MD	Agree	 LAURIE H SEHN MD, MPH	Disagree

GENERAL MEDICAL ONCOLOGISTS (N = 75)	Agree

How frequently do patients who do not experience cytokine release syndrome or neurologic toxicity when receiving chimeric antigen receptor (CAR) T-cell therapy derive significant treatment benefit?

 JONATHAN W FRIEDBERG, MD, MMSC	Frequently
 JOHN KURUVILLA, MD	Occasionally
 ANN S LACASCE, MD, MMSC	Occasionally
 JOHN P LEONARD, MD	Frequently
 MICHAEL E WILLIAMS, MD, SCM	Frequently
 CRAIG MOSKOWITZ, MD	Frequently
 LORETTA NASTOUPIL, MD	Frequently
 LAURIE H SEHN MD, MPH	Occasionally
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Occasionally

Case Presentation – Dr Friedberg: A 70-year-old woman with recurrent double-hit lymphoma

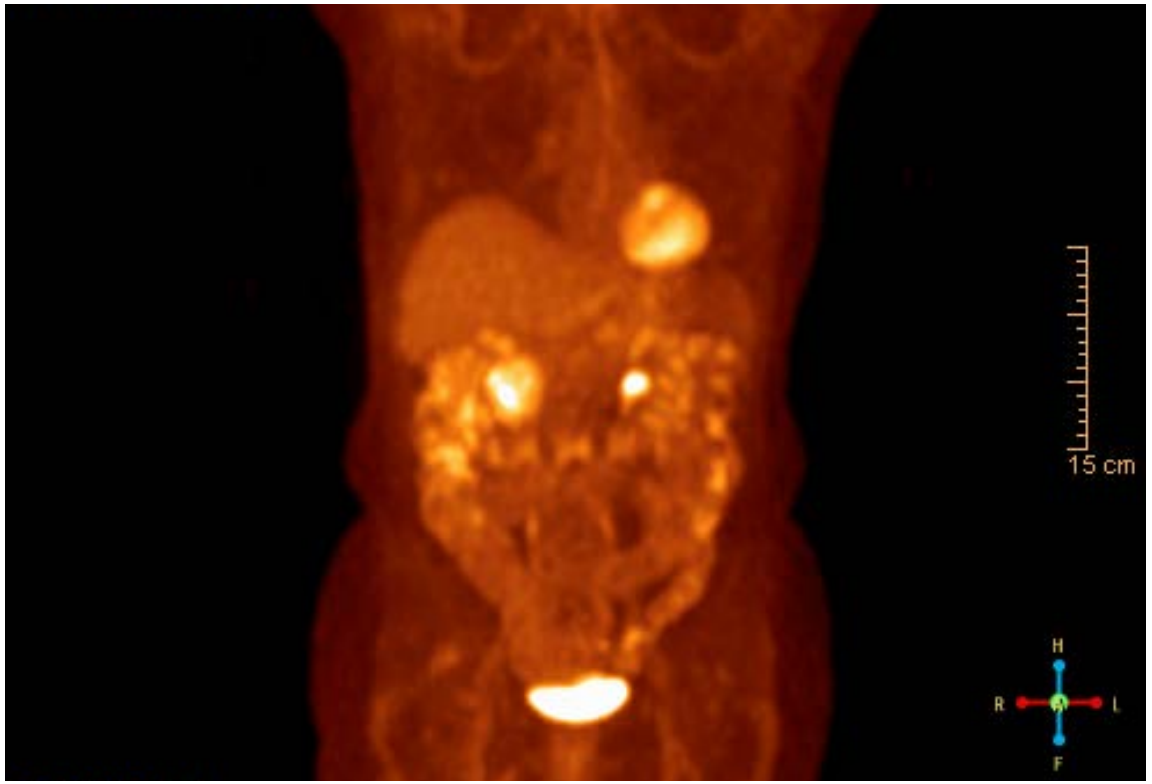
Patient is a 70 y.o. female with history of transformed follicular lymphoma (MYC & BCL-2 translocations) with recurrent disease s/p ASCT.

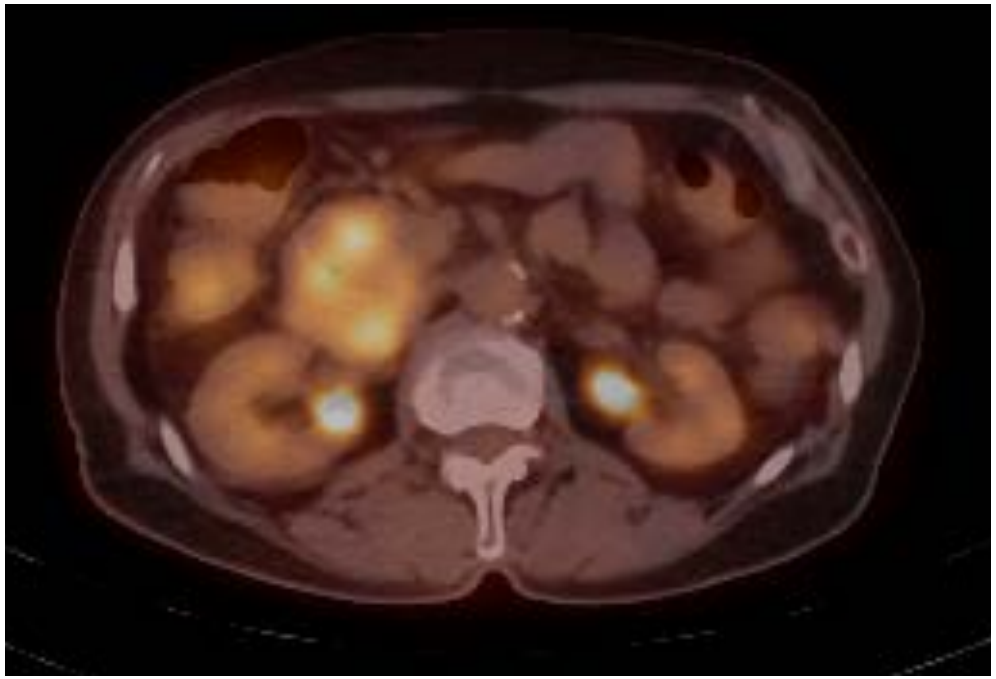
- 2007: Follicular lymphoma, Fludarabine/rituximab x 5
- 2012: Fludarabine/rituximab
- 2013: Double hit transformation, RCHOPx4 followed by BEAM and ASCT
- 7/18/2017: Recurrent transformed follicular lymphoma, Completed 2 cycles of RCHOP initiated then 2 cycles of miniRCHOP due to neutropenic fever
- 11/9/17: Initiated Lenalidomide
- 3/21/2018: Started lymphodepleting chemotherapy with fludarabine and cyclophosphamide
- 3/26/2018: Received axicabtagene ciloleucel 2 x 10^6 cells/kg
- Tolerated treatment well; low grade fever after infusion.
- Remains in complete remission.

Courtesy of Jonathan W Friedberg, MD, MMSc

Case Presentation – Dr Friedberg: A 70-year-old woman with recurrent double-hit lymphoma (continued)

PET/CT Pre CAR T-cell Therapy

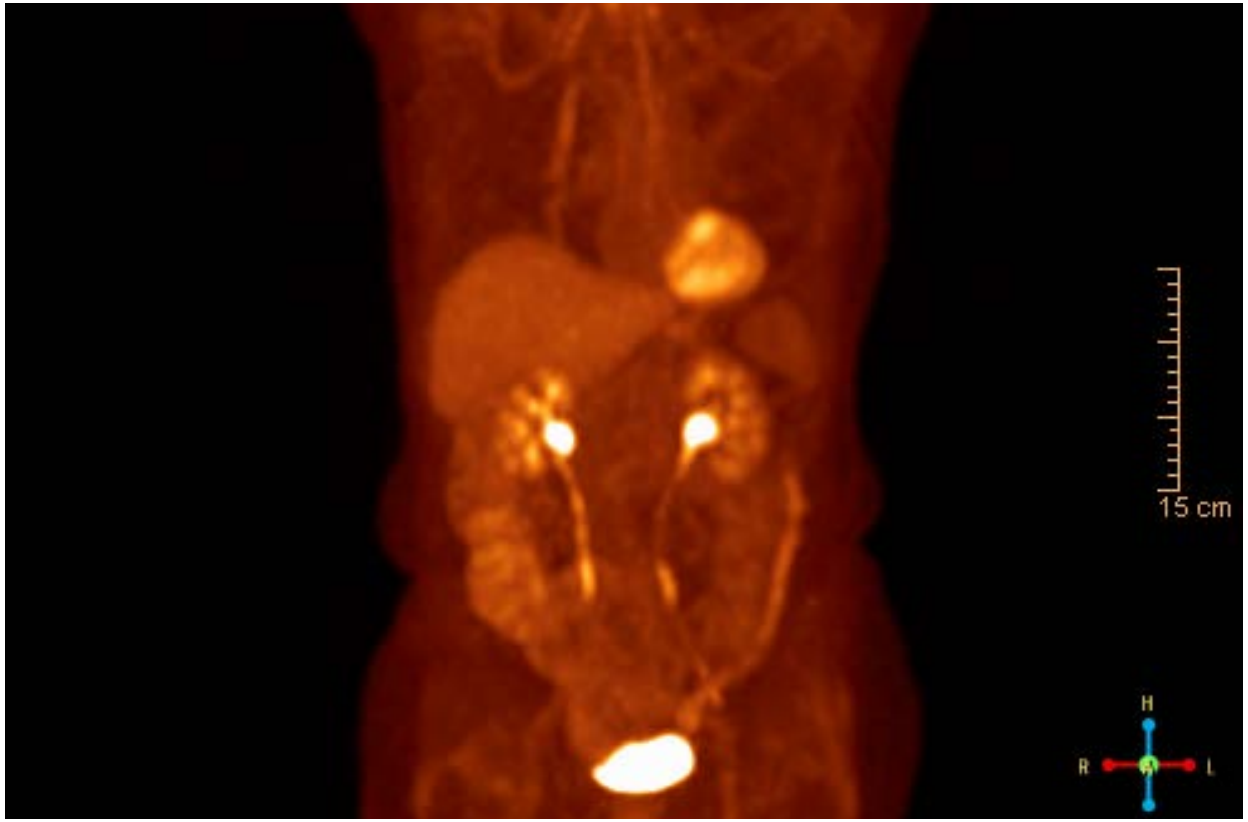


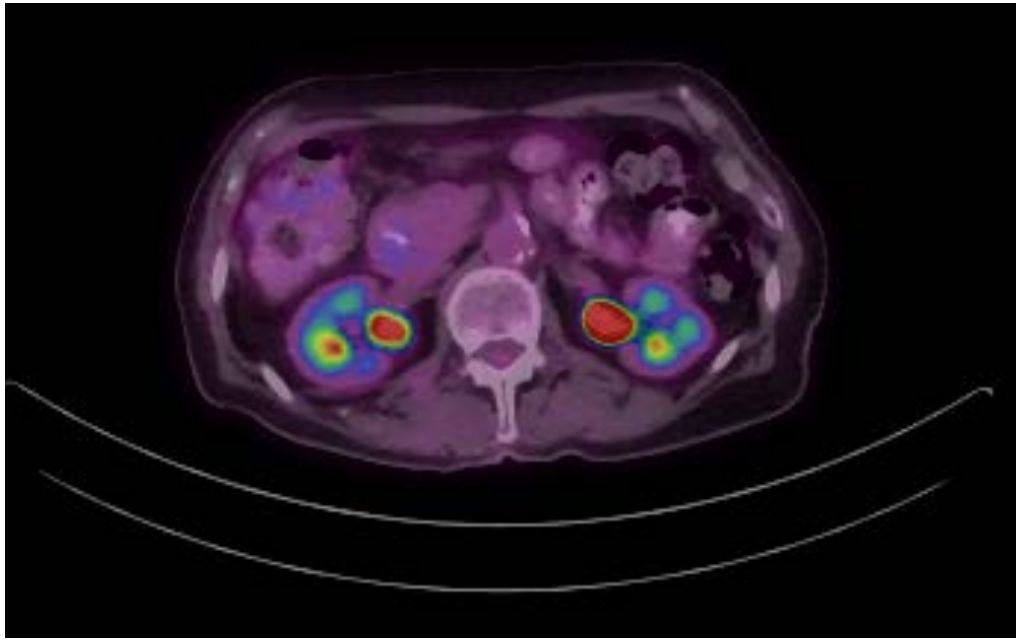


Courtesy of Jonathan W Friedberg, MD, MMSc

Case Presentation – Dr Friedberg: A 70-year-old woman with recurrent double-hit lymphoma (continued)

PET/CT Post CAR T-cell Therapy





Courtesy of Jonathan W Friedberg, MD, MMSc

Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology

Colorectal and Gastroesophageal Cancers

Tuesday, December 8, 2020
5:00 PM – 6:00 PM ET

Faculty

Peter C Enzinger, MD
Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.

RTP
RESEARCH TO PRACTICE