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

Lymphomas

Thursday, January 14, 2021
5:00 PM – 6:00 PM ET

Faculty

Christopher R Flowers, MD, MS
Sonali M Smith, MD

Moderator

Neil Love, MD

RTP Year in Review 2020

YiR Lymphomas Faculty

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Chair, Professor
Department of Lymphoma/Myeloma
The University of Texas MD Anderson Cancer Center
Houston, Texas

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Interim Chief, Section of Hematology/Oncology
Co-Leader, Cancer Service Line
Director, Lymphoma Program
The University of Chicago
Chicago, Illinois

Commercial Support

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Contracted Research	AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Burroughs Wellcome Fund, Cancer Prevention and Research Institute of Texas, Celgene Corporation, Eastern Cooperative Oncology Group, Genentech, a member of the Roche Group, Gilead Sciences Inc, Janssen Biotech Inc, National Cancer Institute, Pharmacyclics LLC, an AbbVie Company, Takeda Oncology, TG Therapeutics Inc, V Foundation for Cancer Research

Dr Smith — Disclosures

Consulting Agreements	Bristol-Myers Squibb Company, Genentech, a member of the Roche Group, Incyte Corporation, Janssen Biotech Inc, Karyopharm Therapeutics, MorphoSys, TG Therapeutics Inc
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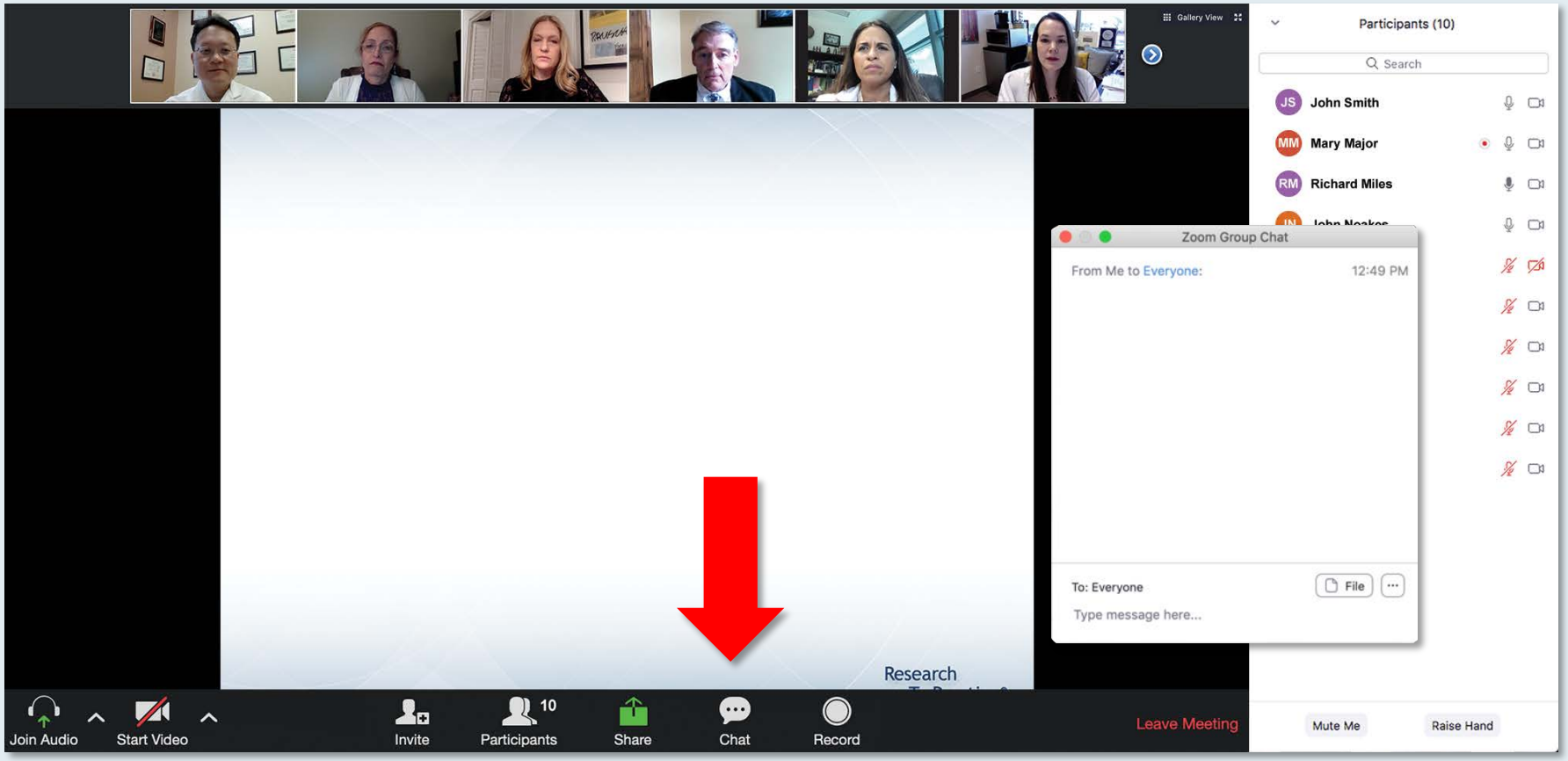
We Encourage Clinicians in Practice to Submit Questions



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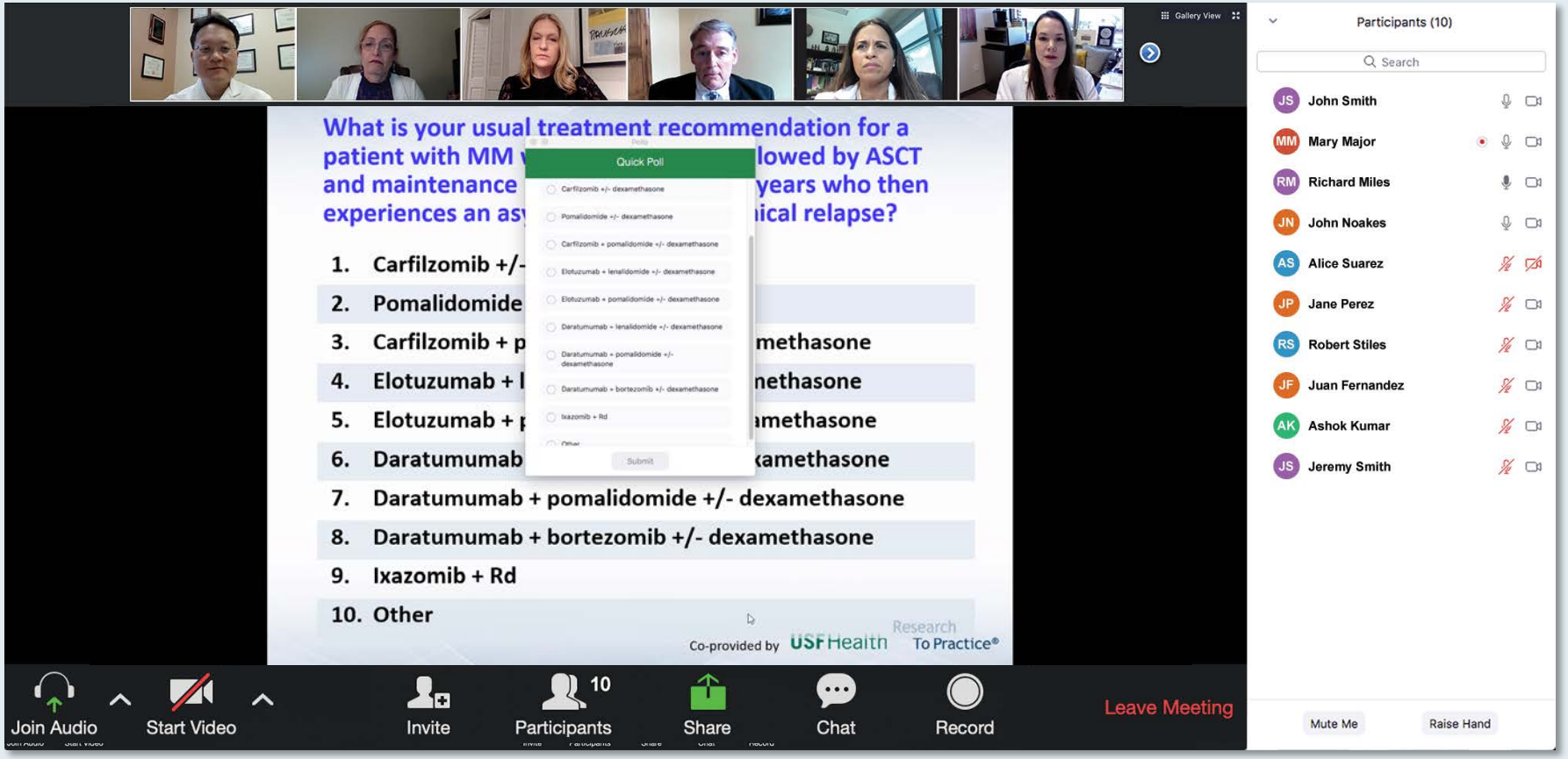

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FRONT-LINE TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA

DR JOHN PAGEL
SWEDISH CANCER INSTITUTE
SEATTLE, WASHINGTON

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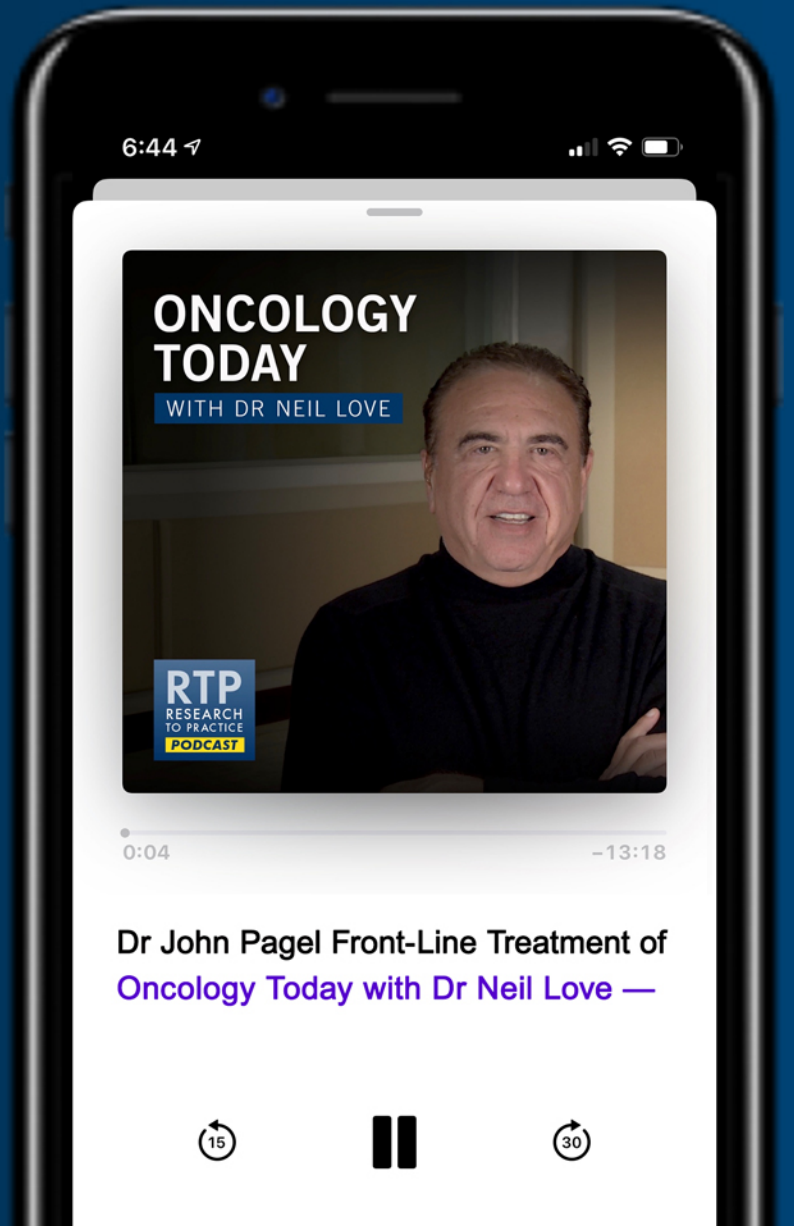

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Recent Advances in Hematologic Oncology: A 4-Part Live Webinar Series Reviewing Key Data and Presentations from the 62nd ASH Annual Meeting

Part 1 — Acute Myeloid Leukemia

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Meet The Professor
Management of Ovarian Cancer

Friday, January 22, 2021
1:15 PM – 2:15 PM ET

Faculty

Professor Jonathan A Ledermann, MD

Moderator

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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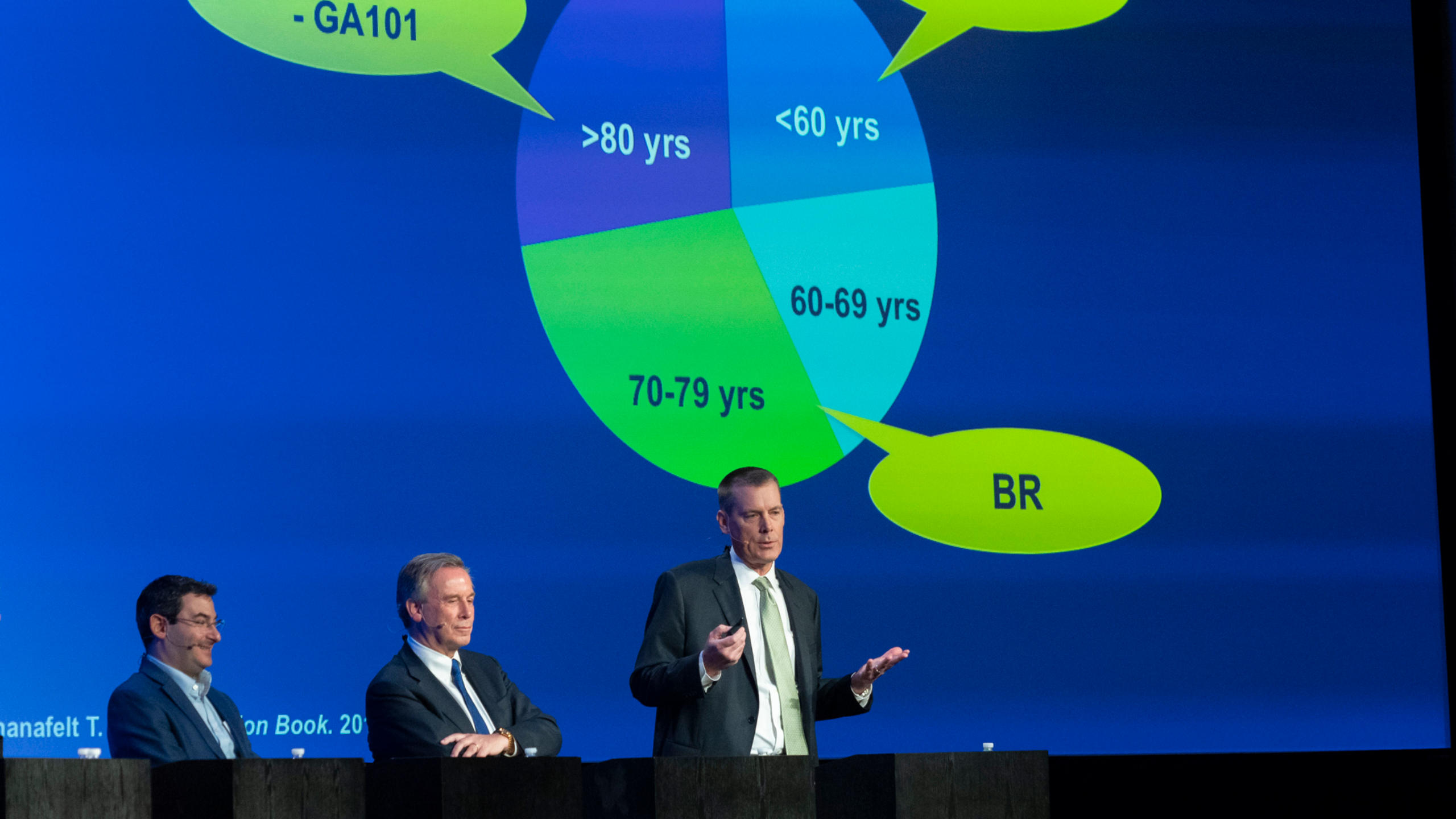
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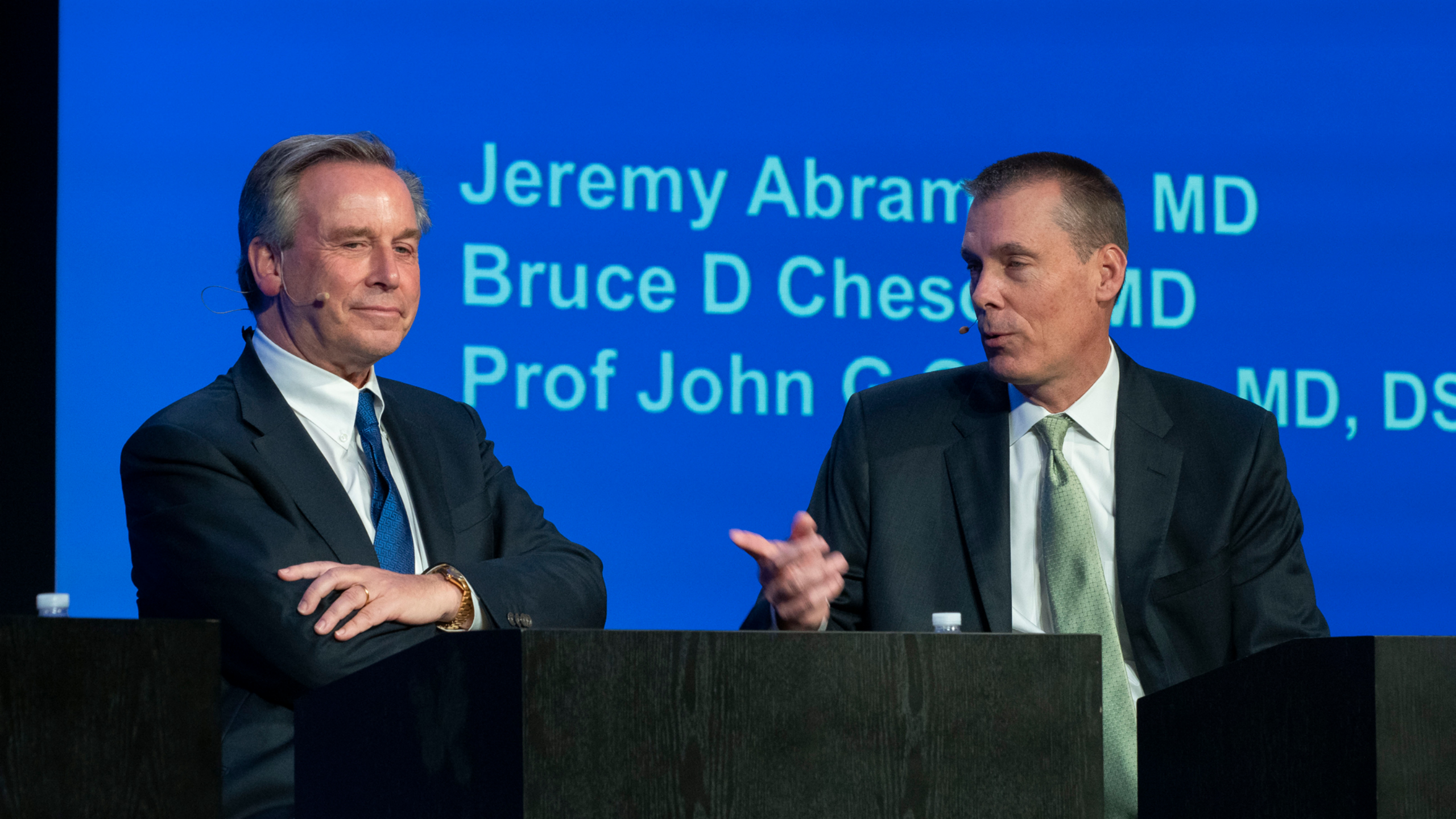
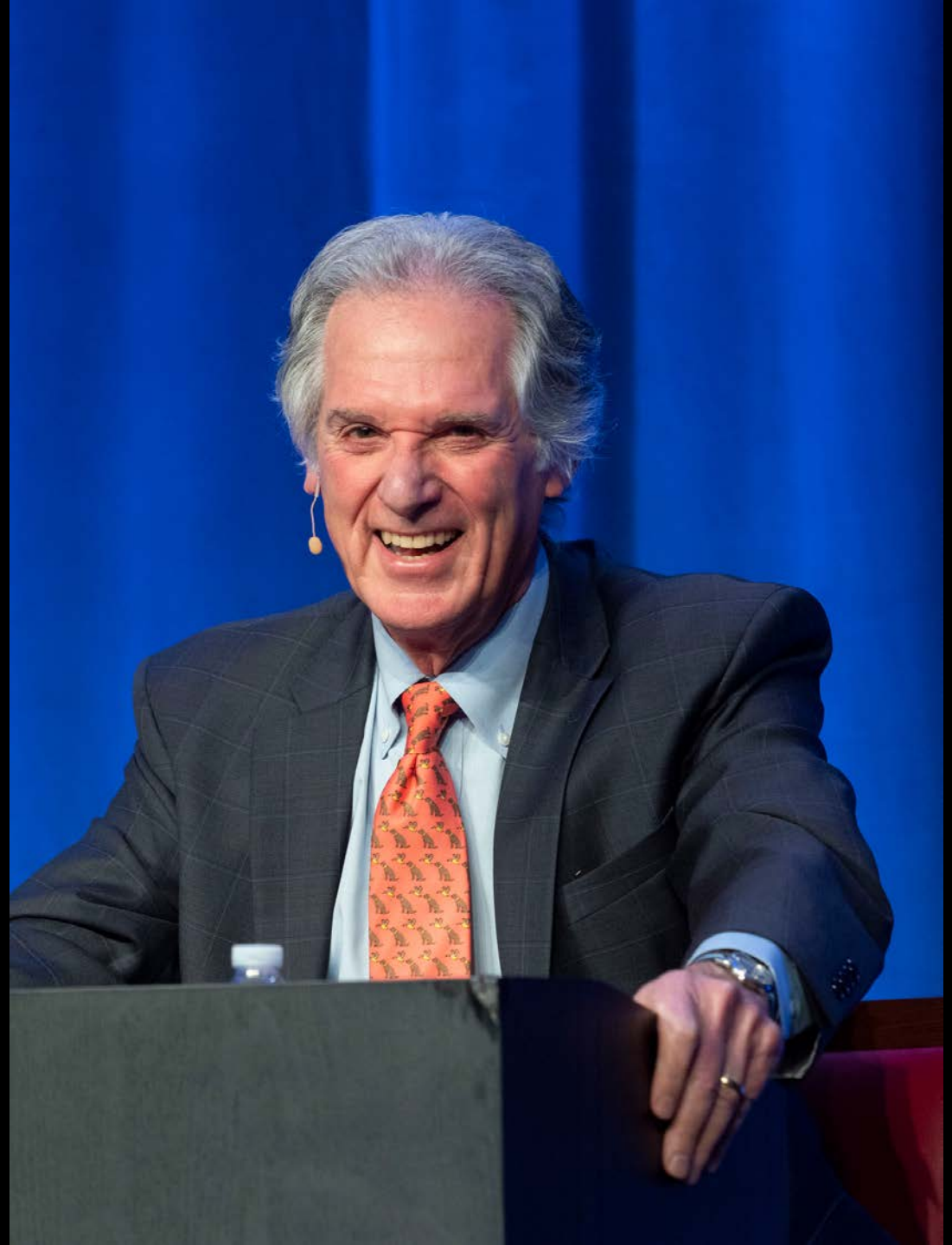
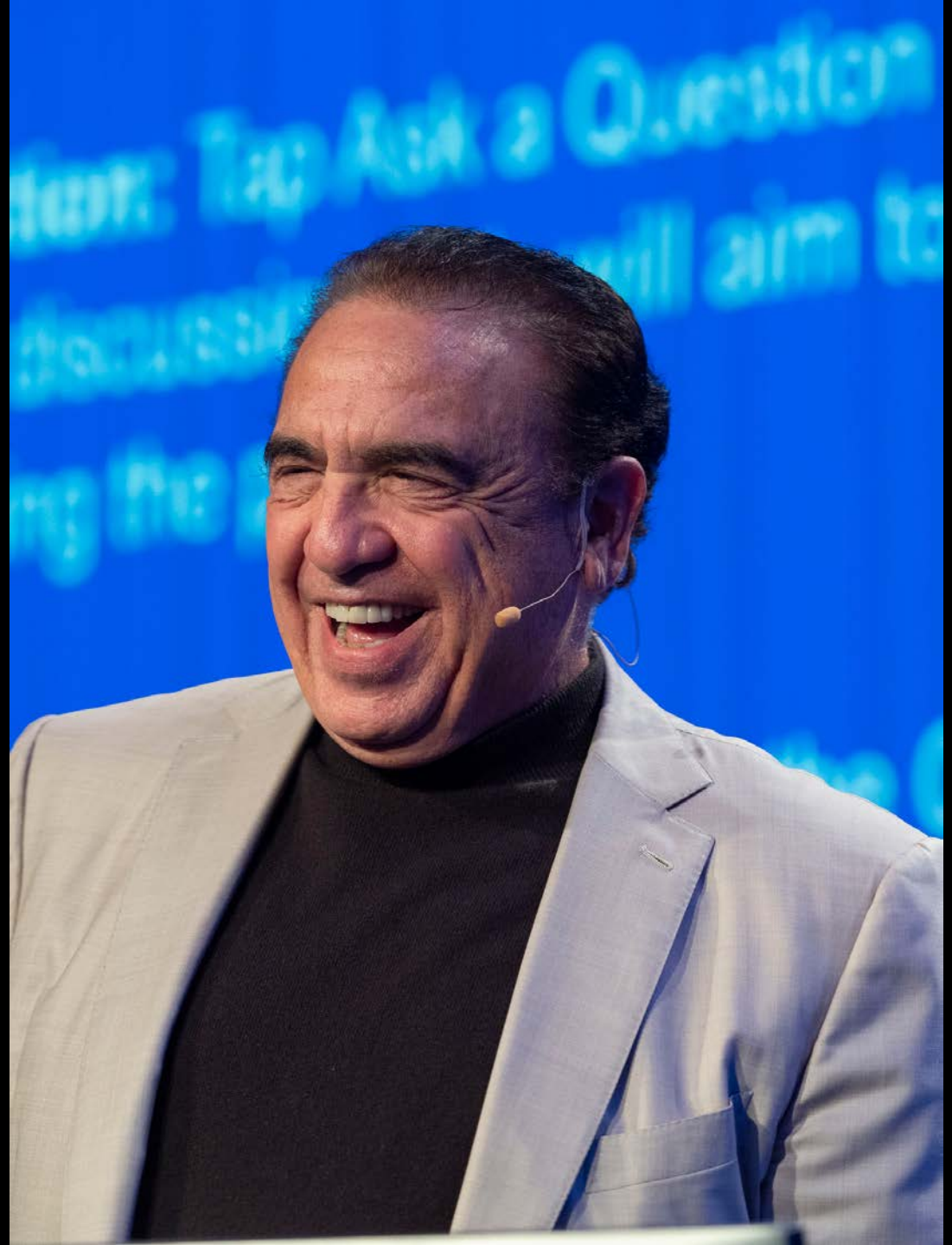

Jeremy Abram MD
Bruce D Ches MD
Prof John C MD, DS





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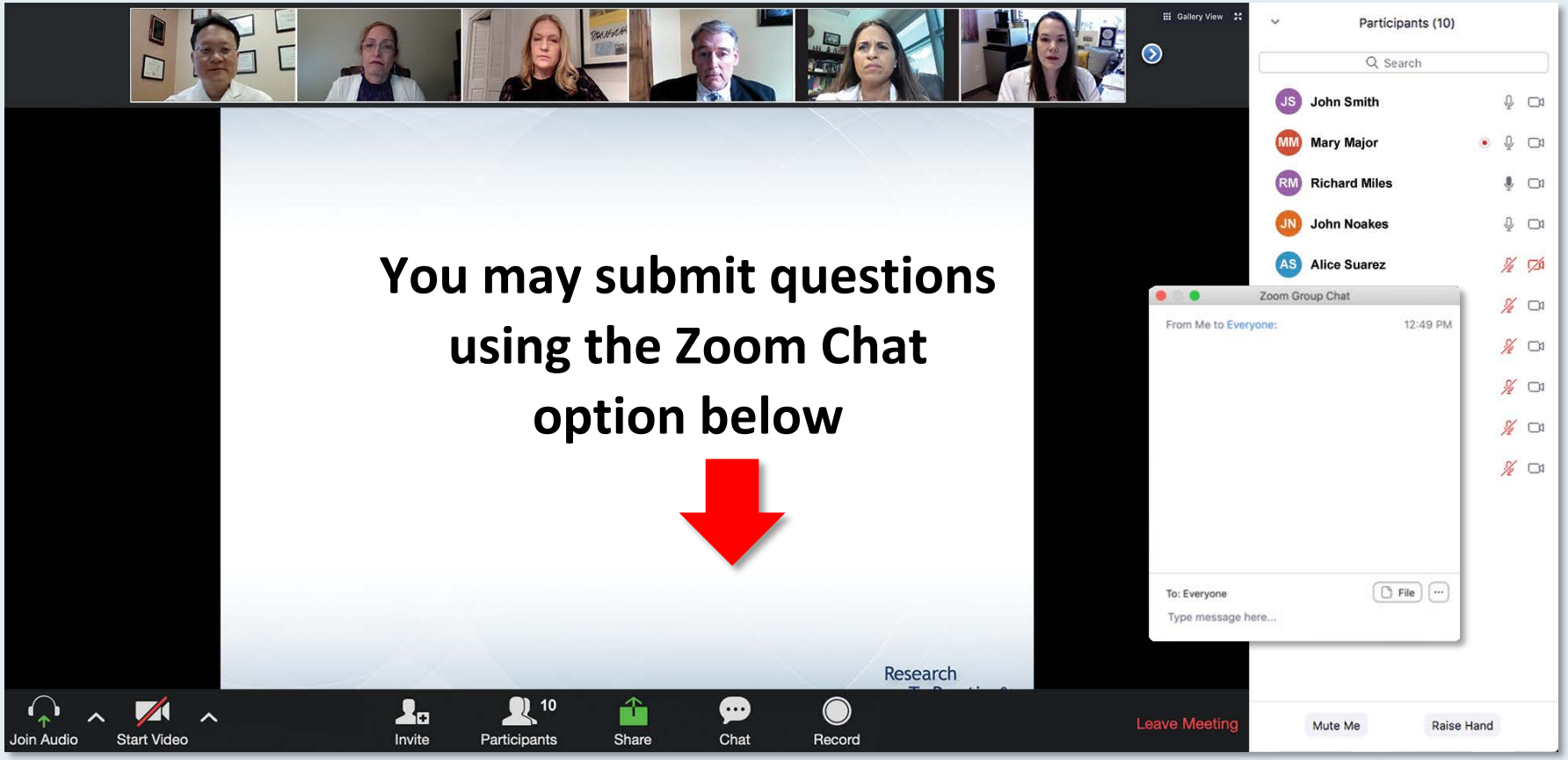

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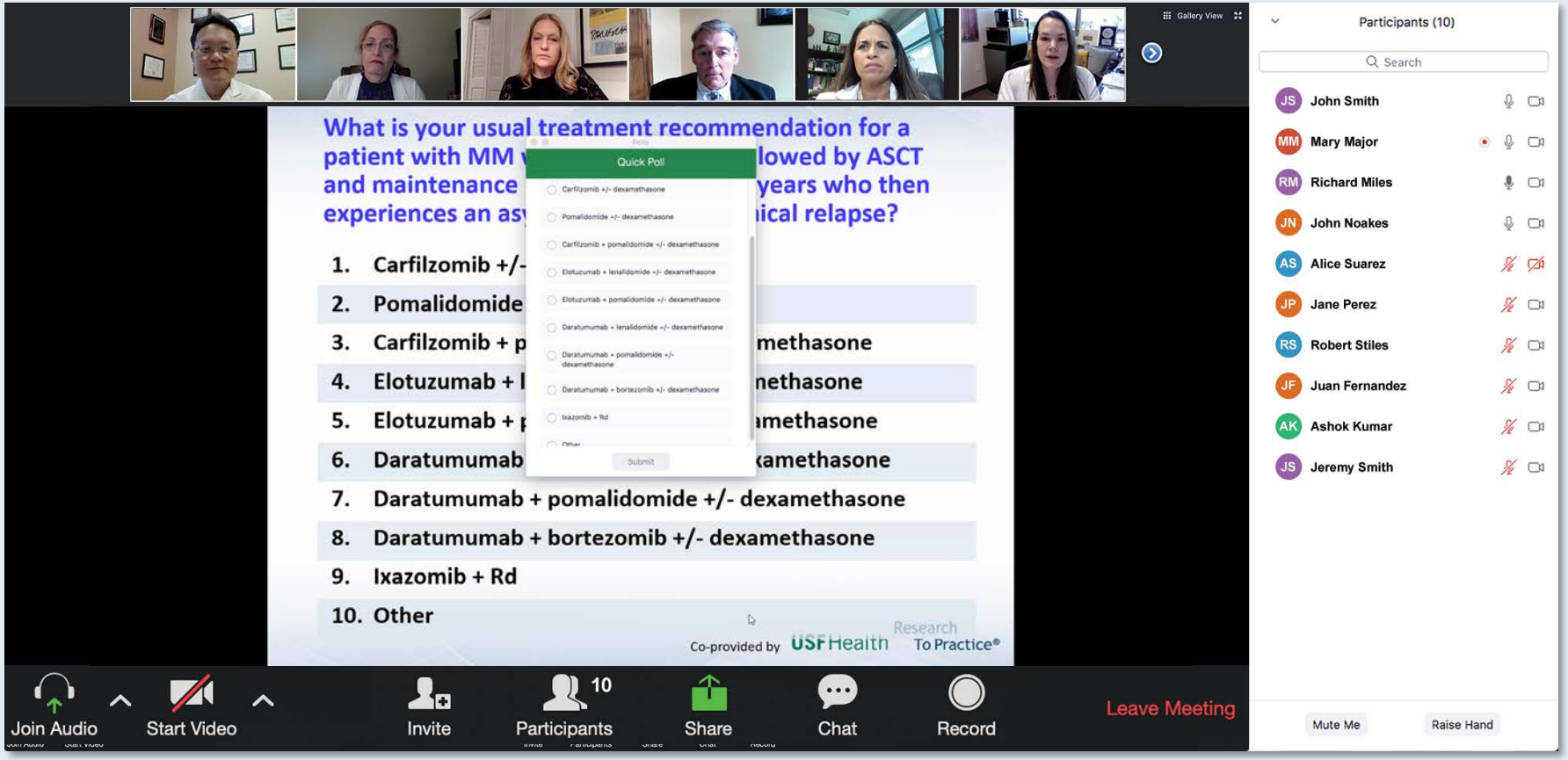

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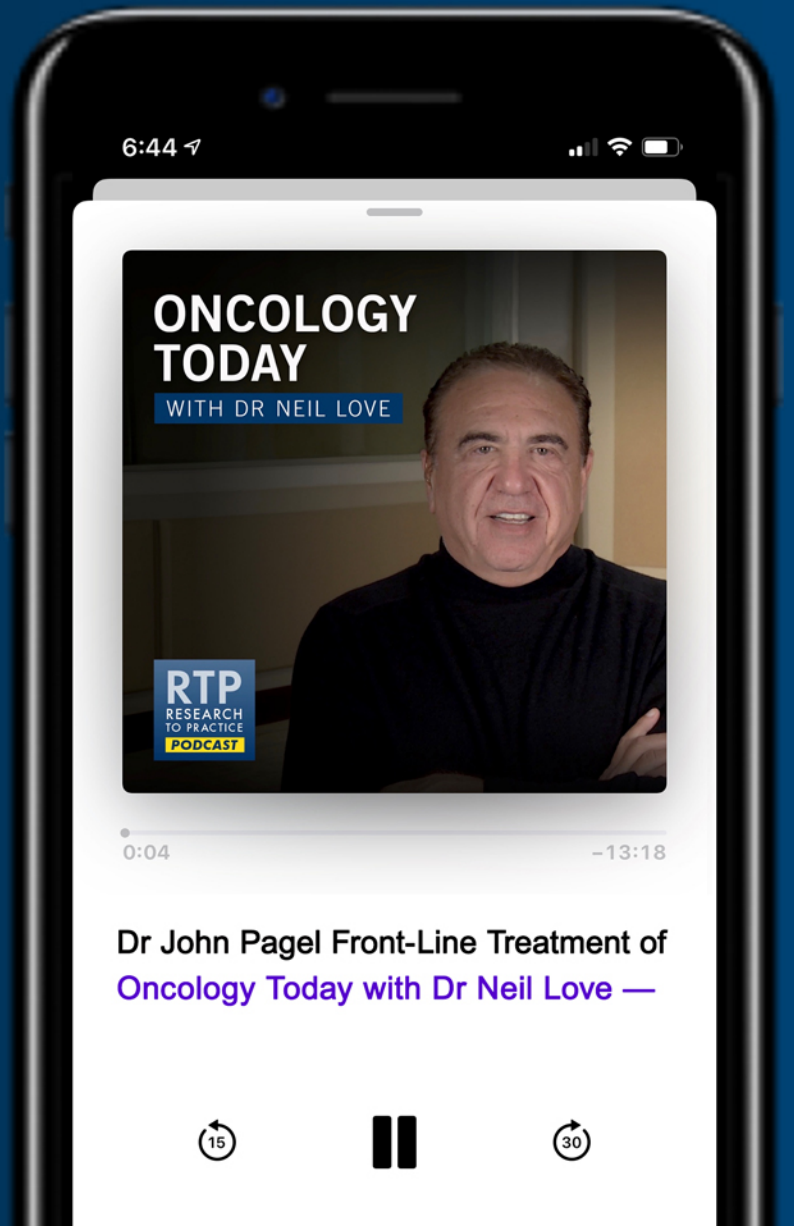

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Agenda

Module 1: Follicular lymphoma

Module 2: Mantle cell lymphoma

Module 3: Diffuse large B-cell lymphoma

Module 4: Hodgkin lymphoma

Module 5: CAR T-cell therapy in DLBCL and other lymphoma subtypes

Agenda

Module 1: Follicular lymphoma

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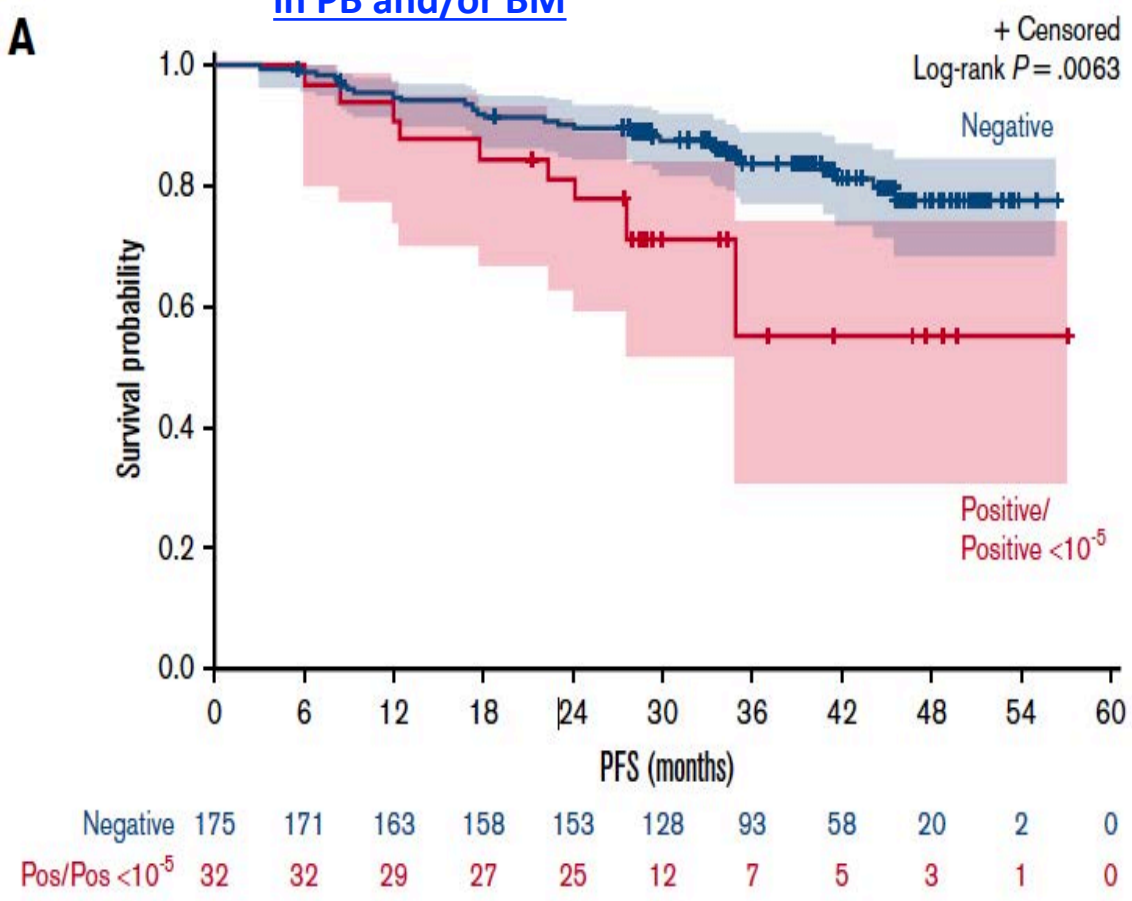
Module 1: Follicular lymphoma

- **Key Relevant Data Sets**
  - RELEVANCE: R^2 for untreated follicular lymphoma
  - Tazemetostat +/- lenalidomide/rituximab
  - CHRONOS: Copanlisib + rituximab for untreated and relapsed/refractory disease

RELEVANCE Trial: R^2 induces high molecular response in untreated FL

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



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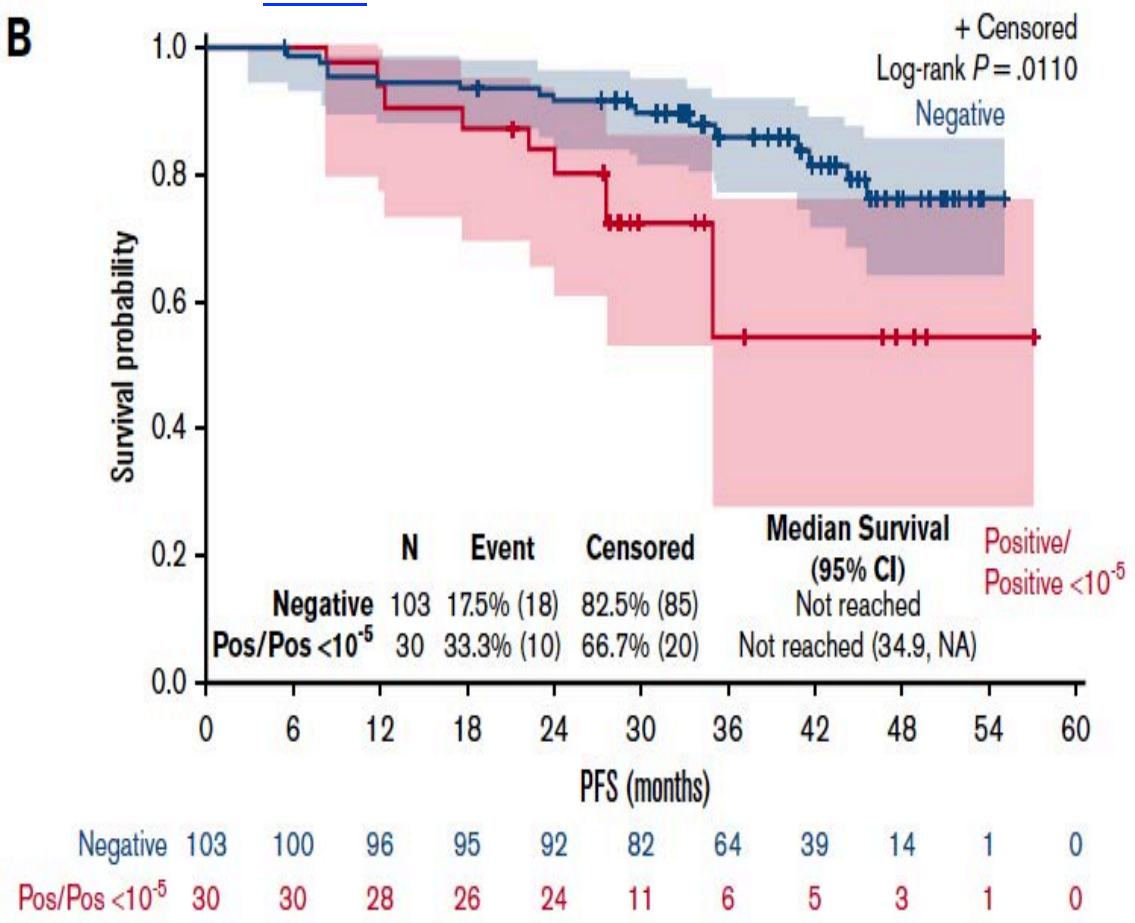
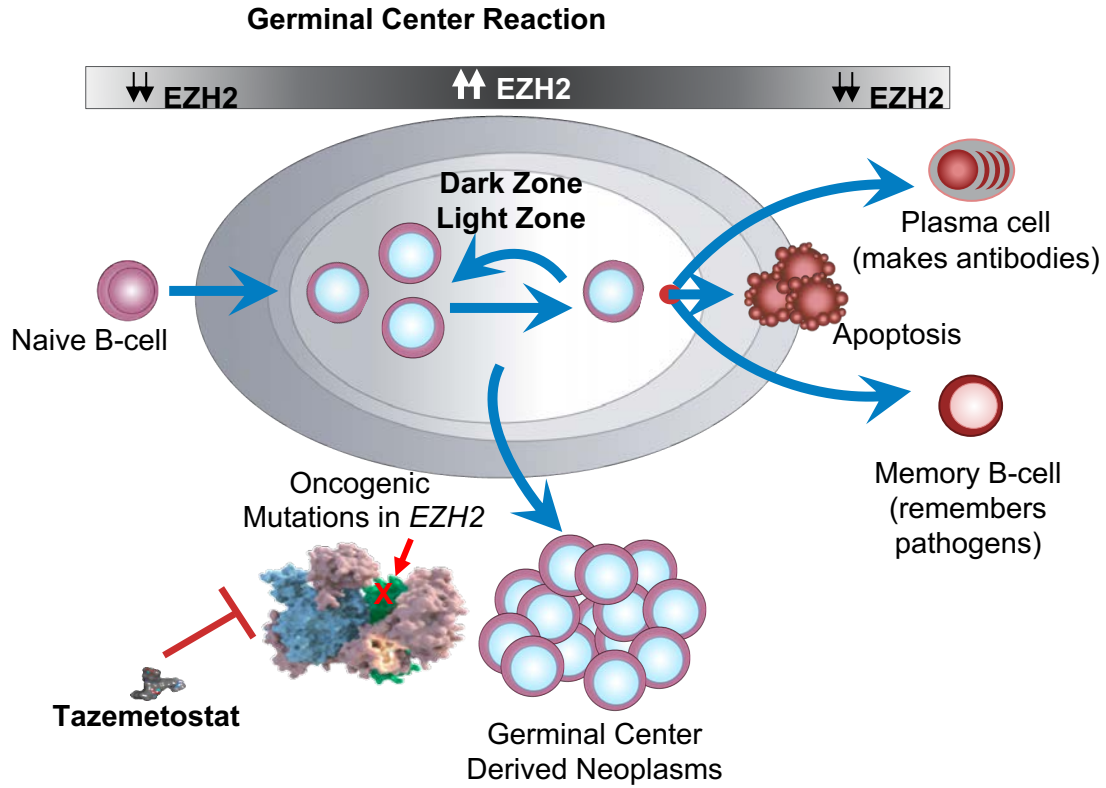


Delfau-Larue MH et al. *Blood Adv* 2020;4(14):3217-3223.

Courtesy of Christopher R Flowers, MD, MS

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

Phase II Trial of the Oral EZH2 Inhibitor Tazemetostat for R/R FL - Response

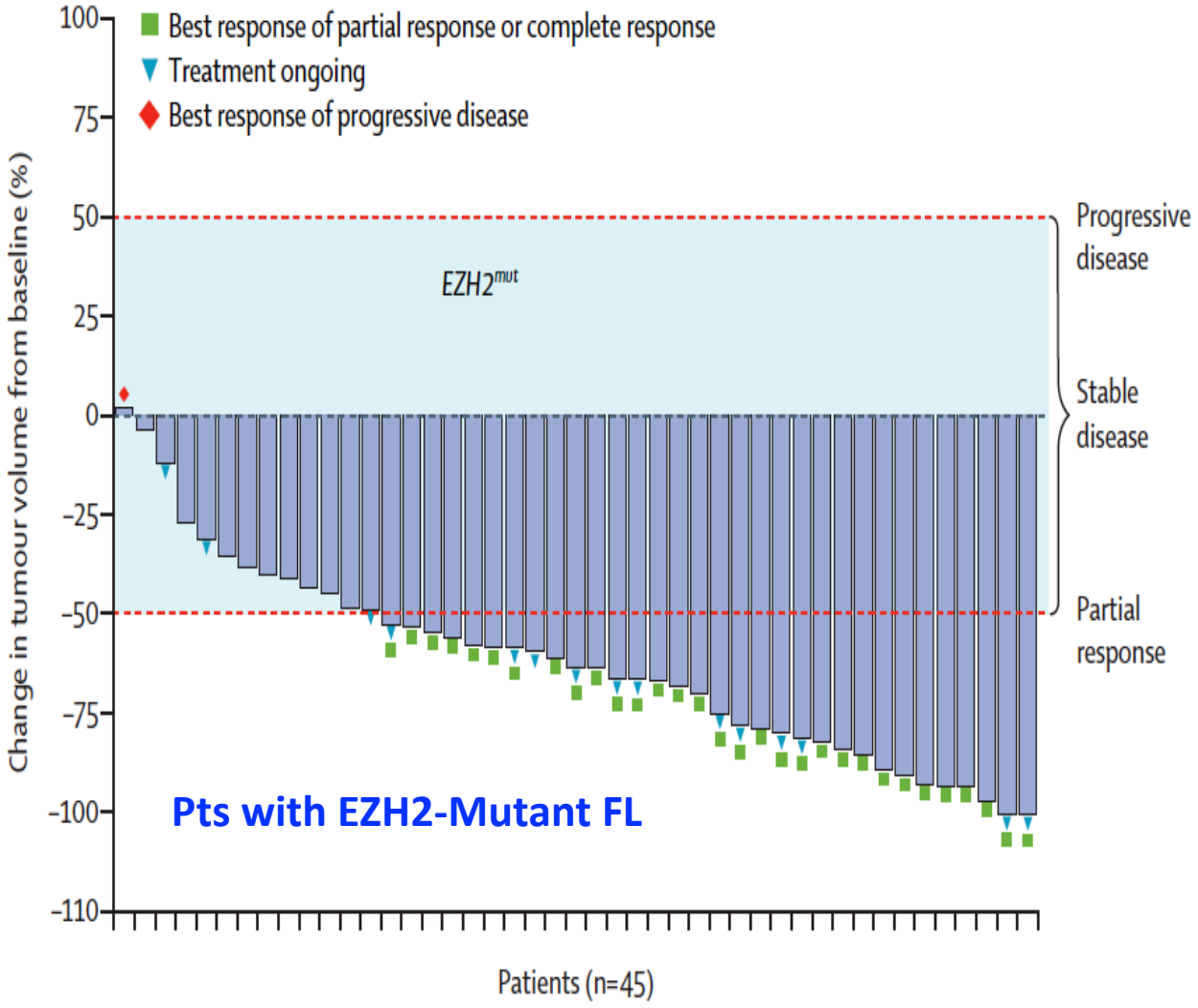
Tumor Response by EZH2 mutation status	*EZH2*^{mut} (n=45)		*EZH2*^{WT} (n=54)	
	IRC-assessed	Investigator-assessed	IRC-assessed	Investigator-assessed
Objective response rate*	31 (69%; 53–82)	35 (78%; 63–89)	19 (35%; 23–49)	18 (33%; 21–48)
Overall disease control rate†	44 (98%)	45 (100%)	37 (69%)	34 (63%)
Best overall response				
Complete response	6 (13%)	4 (9%)	2 (4%)	3 (6%)
Partial response	25 (56%)	31 (69%)	17 (31%)	15 (28%)
Stable disease	13 (29%)	10 (22%)	18 (33%)	16 (30%)
Progressive disease	1 (2%)	0	12 (22%)	16 (30%)
Not estimable or unknown	0	0	5 (9%)	4 (7%)

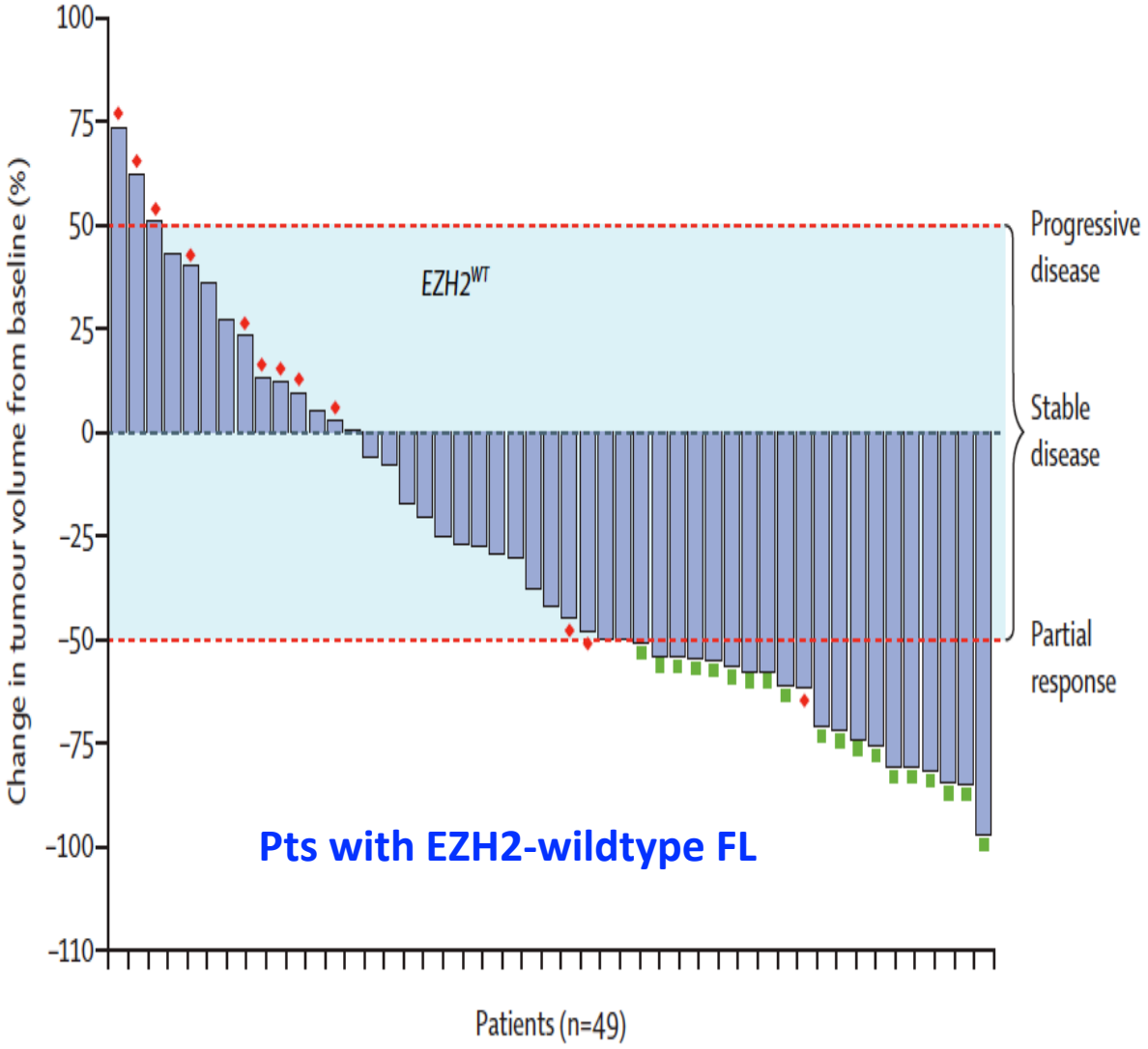
Data are n (%; 95% CI) or n (%). IRC=independent radiology committee. *Objective response rate includes patients with a complete or partial response. †Overall disease control rate includes patients with a complete response, partial response, or stable disease.

Morschhauser F et al. *Lancet Oncol* 2020;21(11):1433-1442.

Courtesy of Christopher R Flowers, MD, MS

Phase II Trial of Tazemetostat in R/R FL – Change in Tumor Volume from Baseline





Morschhauser F et al. *Lancet Oncol* 2020;21(11):1433-1442.

Courtesy of Christopher R Flowers, MD, MS

Ongoing Phase Ib/III Trial of Tazemetostat + Len/Rituximab in R/R FL

Target accrual (N = 518)

- Must have Grade 1 to 3A FL
- Received at least 1 prior line of therapy
- No prior EZH2 inhibitor
- No prior lenalidomide for FL

R

Tazemetostat + Rituximab/Lenalidomide (R^2)

Placebo + R^2

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

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

Courtesy of Christopher R Flowers, MD, MS

CHRONOS-3 Trial: Copanlisib + Rituximab Meets Primary Endpoint in Relapsed iNHL

Press Release: October 14, 2020

- The Phase III study CHRONOS-3 evaluating copanlisib in combination with rituximab in indolent Non-Hodgkin's Lymphoma (iNHL) patients (n=458) who have relapsed after one or more prior lines of rituximab-containing therapy has met its primary endpoint of prolonged progression-free survival (PFS). The study predominantly included patients with follicular lymphoma (FL) and marginal zone lymphoma, as well as patients with small lymphocytic lymphoma and lymphoplasmacytoid lymphoma/Waldenström macroglobulinemia.
- Safety observed in the trial was generally consistent with previously published data on the individual components of the combination and no new safety signals were identified.

https://bayer2019tf.q4web.com/news/news-details/2020/Aliqopa-copanlisib-in-Combination-With-Rituximab-Meets-Primary-Endpoint-in-Patients-With-Relapsed-Indolent-Non-Hodgkins-Lymphoma/default.aspx.

Courtesy of Christopher R Flowers, MD, MS

If you were to administer rituximab/lenalidomide as first-line treatment for a patient with FL, what would be the duration of treatment, including maintenance therapy if used?

1. 1 year
2. 18 months
3. 2 years
4. 2.5 years
5. Other

Have you used or would you use obinutuzumab/lenalidomide to treat FL?

1. Yes, as first line treatment and beyond
2. Yes, as second line treatment and beyond
3. No

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 → autologous stem cell transplant
8. Other

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

1. Idelalisib
2. Copanlisib
3. Duvelisib
4. Tazemetostat
5. R-CHOP
6. Radioimmunotherapy
7. Obinutuzumab
8. Obinutuzumab + chemotherapy
9. Other

Agenda

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Module 2: Mantle cell lymphoma

Module 3: Diffuse large B-cell lymphoma

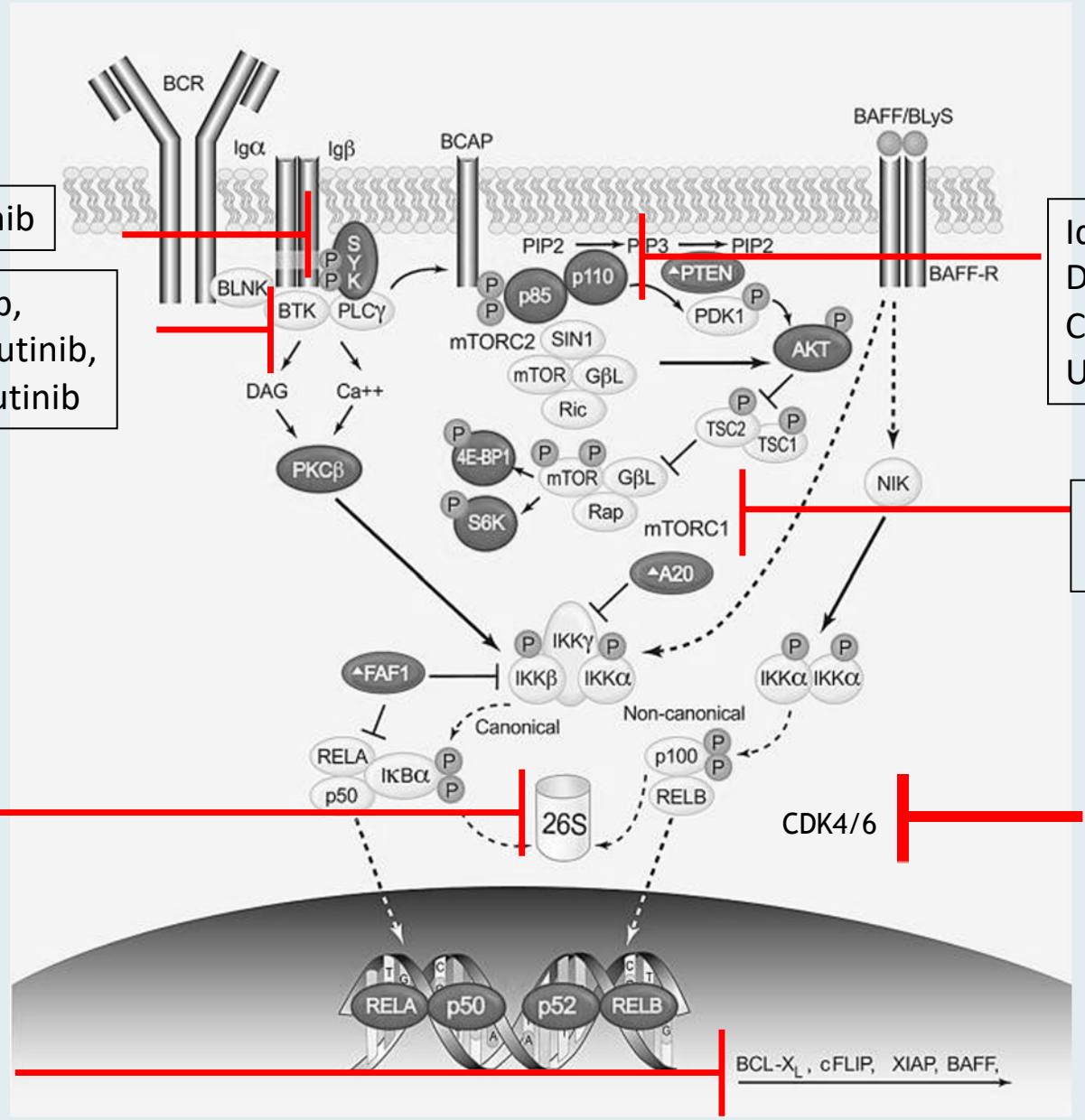
Module 4: Hodgkin lymphoma

Module 5: CAR T-cell therapy in DLBCL and other lymphoma subtypes

Module 2: Mantle cell lymphoma

- **Key Relevant Data Sets**
  - FDA-approved BTK inhibitors for mantle cell lymphoma (MCL)
  - BRUIN: LOXO-305 for previously treated MCL, Waldenström macroglobulinemia
  - ZUMA-2: Brexucabtagene autoleucel for R/R MCL

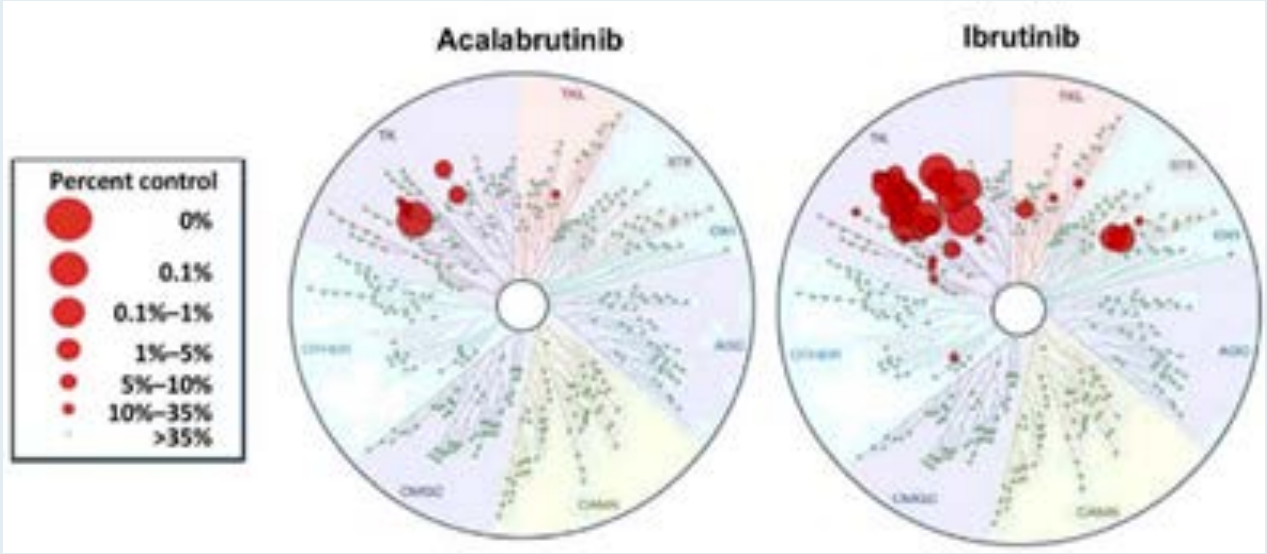
The B-cell receptor pathway: Selected inhibitors



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

Overview of FDA-Approved BTK Inhibitors 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**



Herman et al, Clin Ca Res 2017

Courtesy of Michael E Williams, MD, ScM

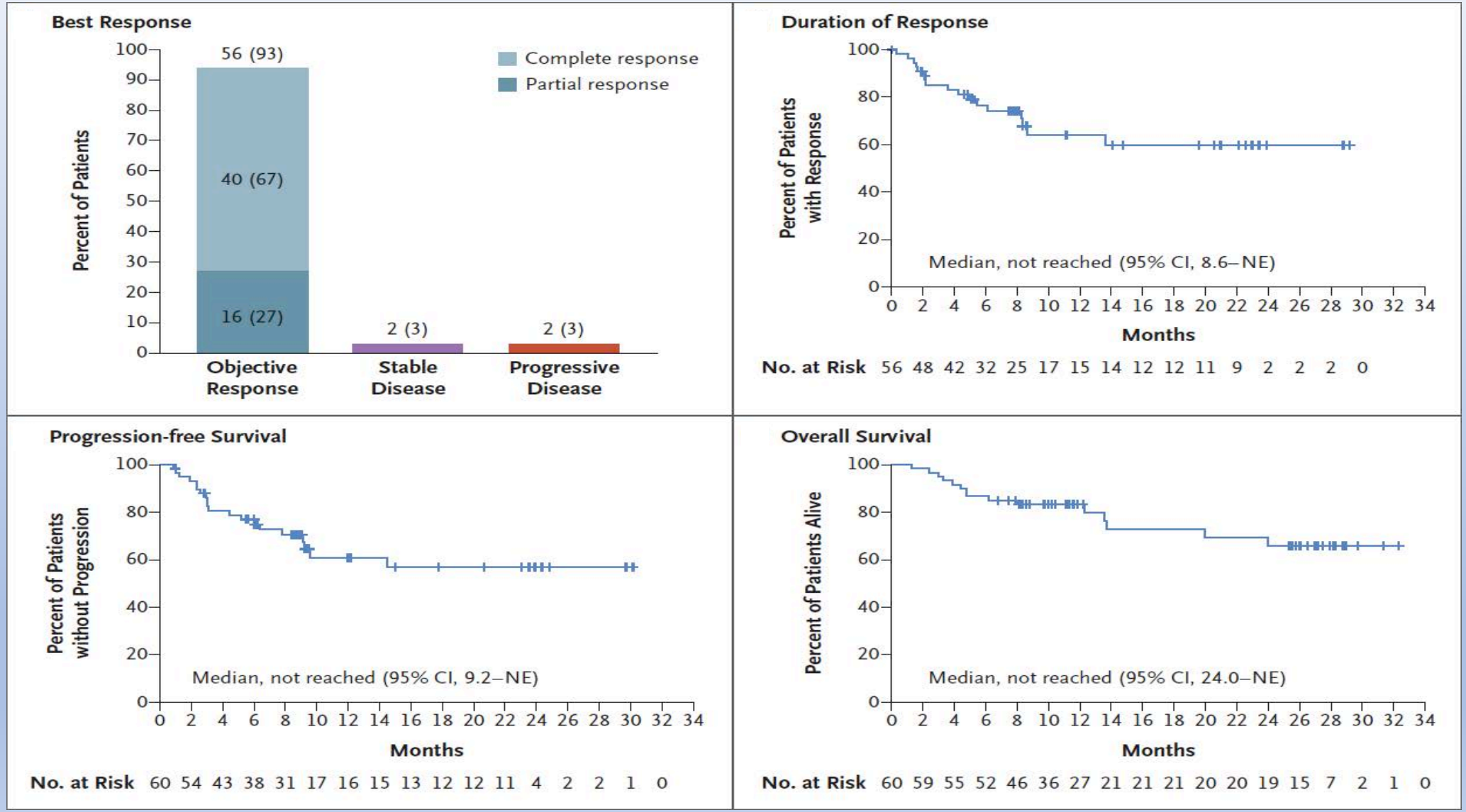
Phase I/II BRUIN Trial of LOXO-305 in Previously Treated MCL, Waldenström's Macroglobulinemia, and Other Non-Hodgkin Lymphomas

- LOXO-305 is a highly selective, non-covalent BTK inhibitor that inhibits both wild type and C481-mutated BTK with equal low nanomolar potency
- Median number of prior lines of therapy was 2 for MCL (range 2-8)
- Responses were observed at the first dose level of 25 mg QD.
- RP2D of 200 mg QD was selected for future studies.
- **Among 35 evaluable pts with MCL**
  - ORR = 51%
  - CR = 9 (25.7%)
  - Among the 20 efficacy evaluable pts who started at RP2D, ORR was 65% with 7 CRs
- Responses in MCL were observed in pts who received prior cell therapy, including 3 of 7 patents with prior SCT, and 1 of 2 with prior CAR-T
- There were no DLTs or dose reductions.
- The only TEAEs regardless of attribution or grade seen in $\geq$10% of pts (n=186) were fatigue (n=29, 16%) and diarrhea (n=28, 15%).

Wang M et al. ASH 2020; Abstract 117.

Courtesy of Christopher R Flowers, MD, MS

Results from the ZUMA-2 Trial of KTE-X19 CAR T-Cell Therapy in R/R MCL (7-Month Follow-Up)



Wang M et al. *N Engl J Med* 2020;382(14):1331-1342.

Courtesy of Christopher R Flowers, MD, MS

ZUMA-2: One-Year Follow-Up Results for 60 Pts

- **The ORR = 92%**
  - CR rate = 67%
- Of all efficacy-evaluable patients, 48% had ongoing responses at the data cutoff. Median DoR, PFS and OS = Not reached
  - 15-month PFS = 59.2%
  - 15-month OS = 76.0%

Wang M et al. ASH 2020; Abstract 1120.

Courtesy of Christopher R Flowers, MD, MS

ZUMA-2: One-Year Follow-Up Results for 60 Pts

- **Common grade ≥ 3 AEs:** Neutropenia (85%), thrombocytopenia (53%), anemia (53%), and infections (34%).
- Grade ≥ 3 cytopenias were reported in 60% of patients ≥ 30 days post-infusion.
- Grade ≥ 3 CRS occurred in 15% of patients; 59% received tocilizumab
- Grade ≥ 3 neurologic events (NEs) were reported in 31% of patients; 8% received steroids
- All CRS events and most NEs (37/43) resolved, as previously reported.
- There were no Grade 5 CRS events or NEs, and no new Grade 5 events occurred with additional follow-up.

Wang M et al. ASH 2020; Abstract 1120.

Courtesy of Christopher R Flowers, MD, MS

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 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

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 tumor progression?

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

Agenda

Module 1: Follicular lymphoma

Module 2: Mantle cell lymphoma

Module 3: Diffuse large B-cell lymphoma

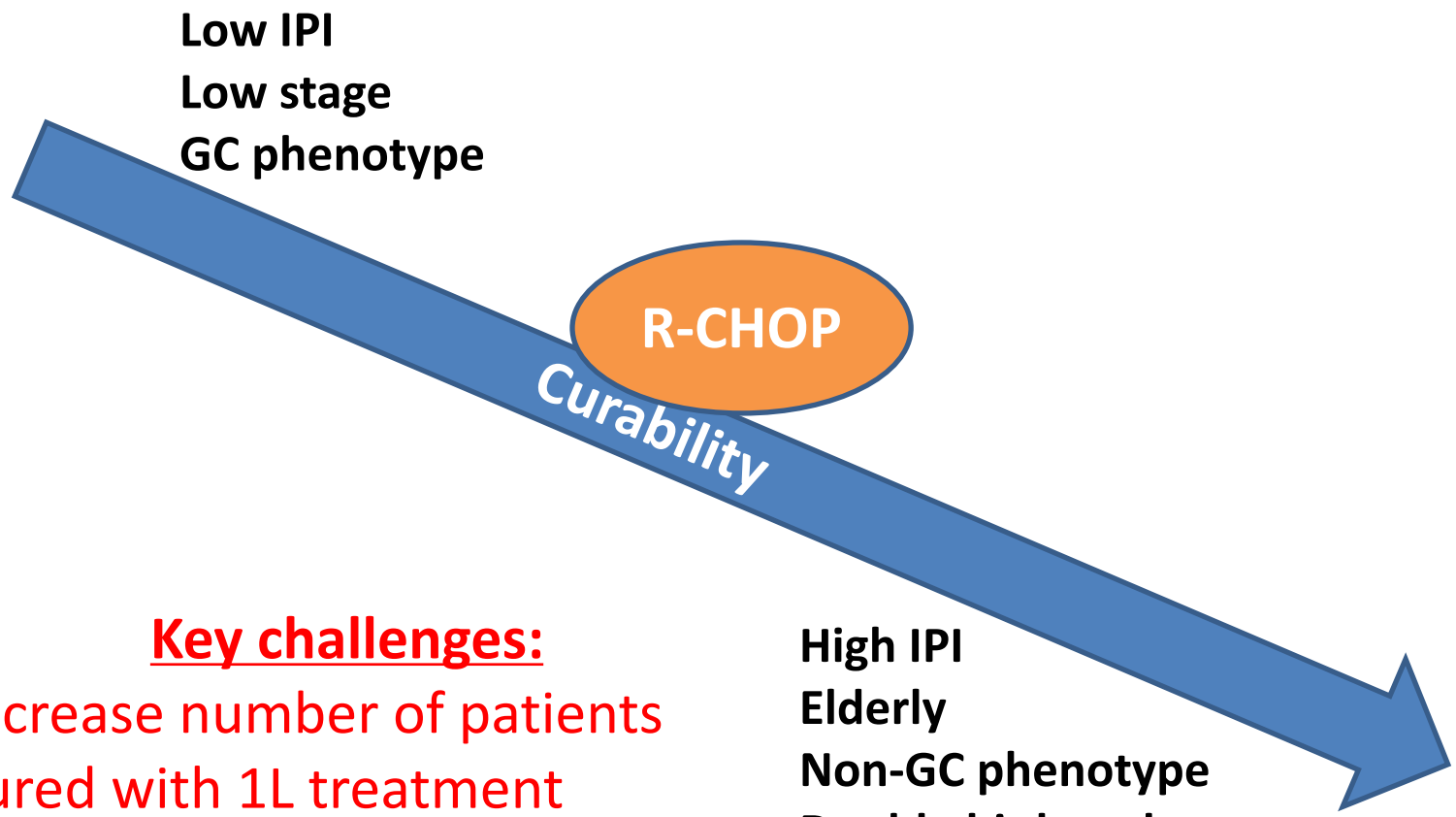
Module 4: Hodgkin lymphoma

Module 5: CAR T-cell therapy in DLBCL and other lymphoma subtypes

Module 3: Diffuse large B-cell lymphoma

- **Key Relevant Data Sets**
  - SADAL: Selinexor for relapsed/refractory DLBCL
  - L-MIND: Tafasitamab + lenalidomide
  - Investigational bispecific agents

Many subsets of DLBCL are not cured with R-CHOP

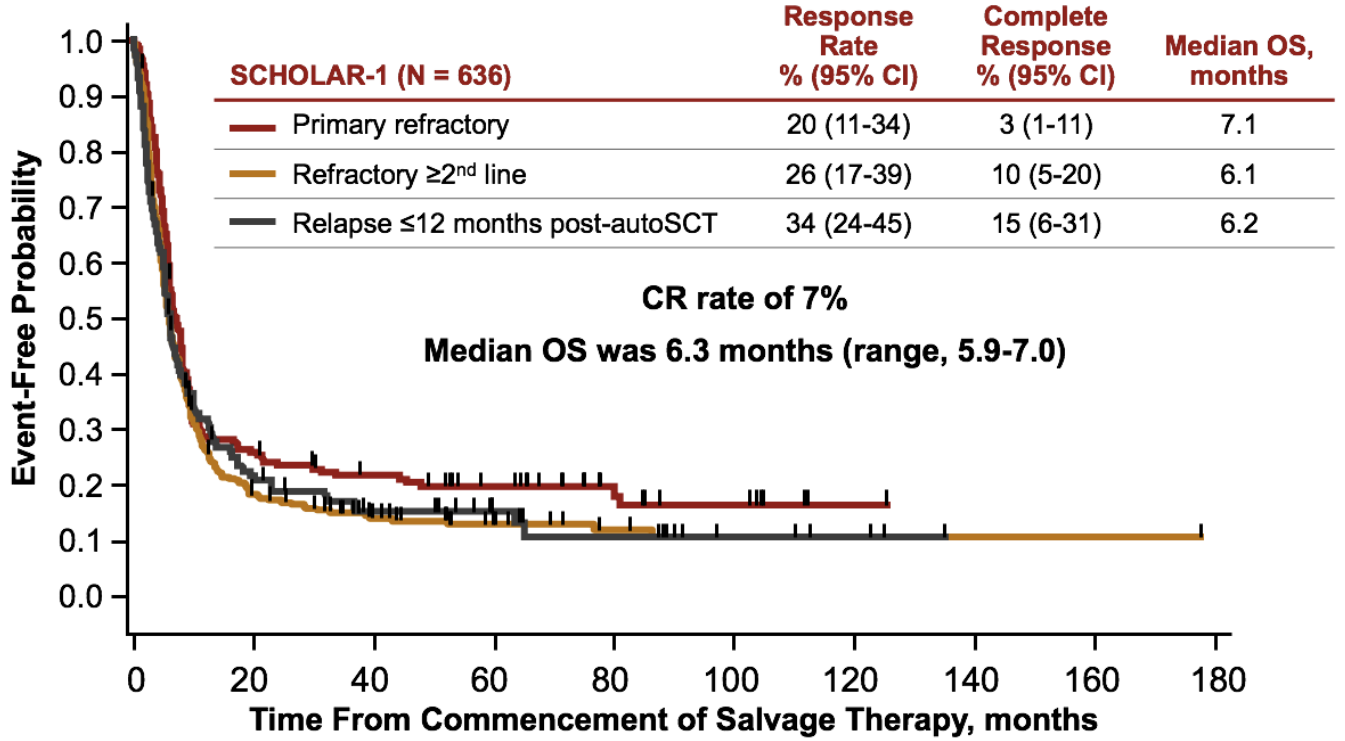


Key challenges:

- Increase number of patients cured with 1L treatment
- Improve options for patients 2L+

Courtesy of Sonali M Smith, MD

Expected Survival for R/R DLBCL Treated with Salvage Chemotherapy



SCHOLAR-1 (N = 636)	Response Rate % (95% CI)	Complete Response % (95% CI)	Median OS, months
Primary refractory	20 (11-34)	3 (1-11)	7.1
Refractory ≥2nd line	26 (17-39)	10 (5-20)	6.1
Relapse ≤12 months post-autoSCT	34 (24-45)	15 (6-31)	6.2

CR rate of 7%

Median OS was 6.3 months (range, 5.9-7.0)

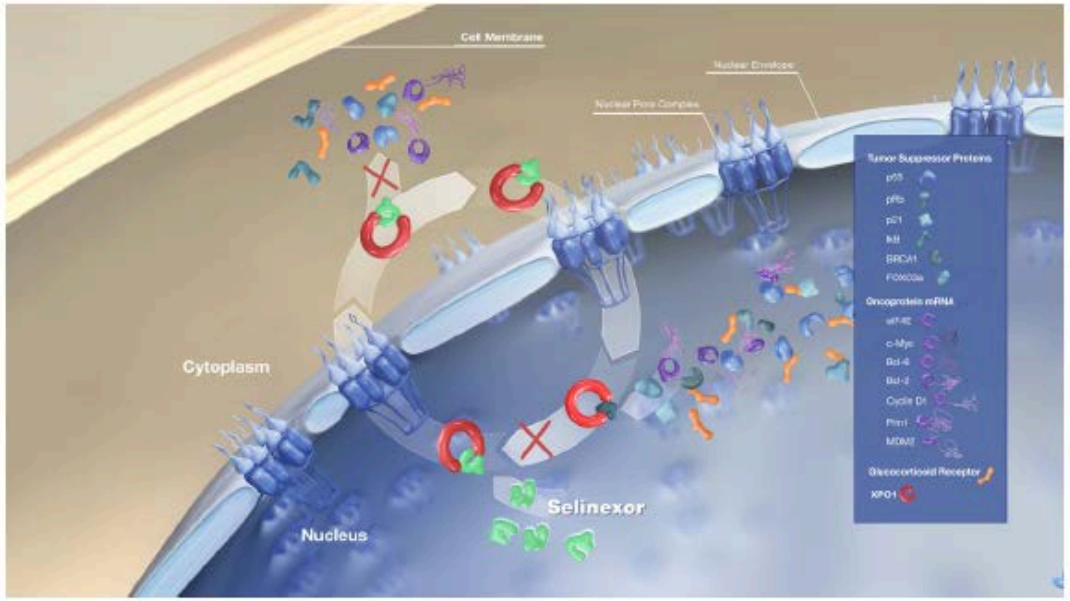
Patients unable to undergo autologous stem cell transplant have median survivals < 1 year

Crump M, et al. *Blood*. 2017;130:1800-1808

Courtesy of Sonali M Smith, MD

Selinexor: oral XPO1 inhibitor

Selinexor: Mechanism of Action



Exportin 1 (XPO1 or CRM1) mediates the nuclear export of proteins, mRNAs, rRNAs, snRNAs and impacts

- **Tumor suppressor proteins** (p53, IκB, FOXO etc.)
- **eIF4E** (Translational initiation factor) bound oncogenic mRNAs (c-Myc, Bcl-xL, cyclins etc.)

Selinexor is an oral selective **XPO1** inhibitor; preclinical data support that XPO1 inhibition:

- Reactivates multiple TSPs relevant to NHL, (p53, p21, IκB, FOXO etc.)
- Disrupts localization of eIF4e (overexpressed in most B-cell lymphomas[1]
- Reduces c-Myc, Bcl-2, and Bcl-6 levels[2-3]

1. Kodali 2011 2. Kuruvilla 2014 3. Schmidt 2013

Courtesy of Sonali M Smith, MD

SADAL: phase 2 trial of selinexor monotherapy in R/R DLBCL

Patient characteristics:

N=127 with med age 67y

45% of pts ≥ 70y

72% refractory to last regimen

Results:

ORR 28%

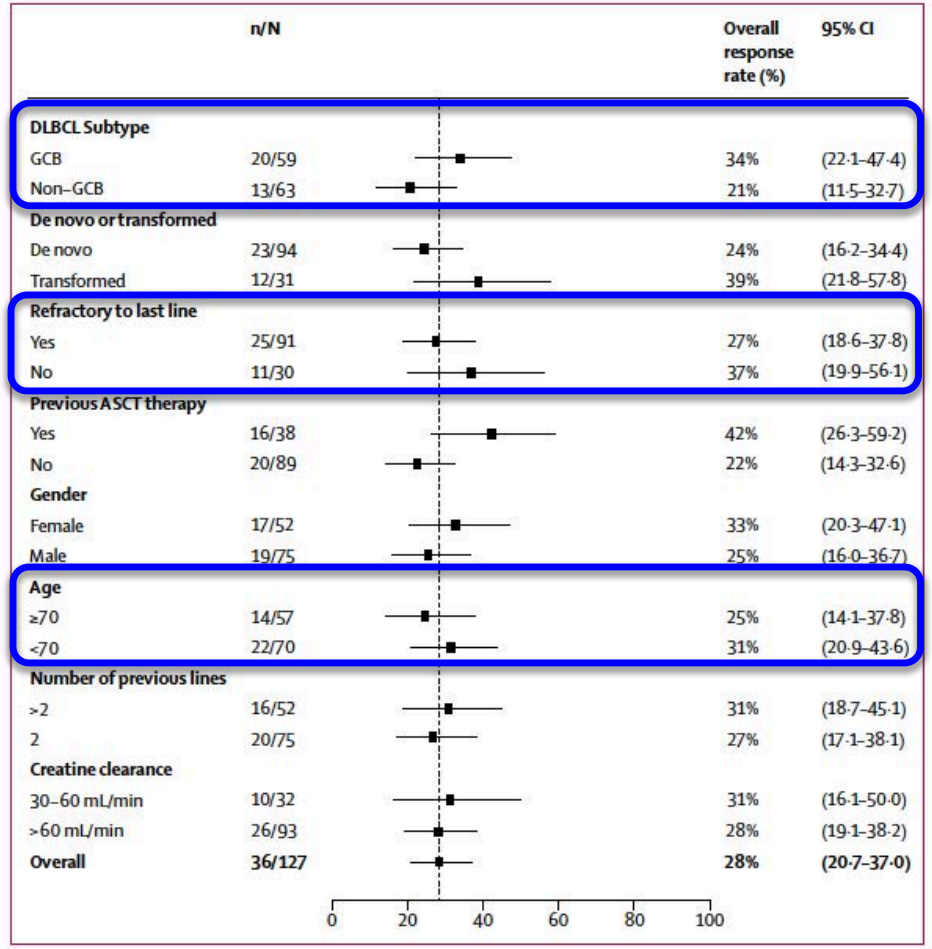
CR 12%

Med DR 9.3m

--med DR for CR pts 23m

--med DR for PR pts 4.4m

No impact of COO



Kalakonda N et al. *Lancet Haematol* 2020;7(7):e511-22.

Courtesy of Sonali M Smith, MD

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Kalakonda N et al. *Lancet Haematol* 2020;7(7):e511-22.

Courtesy of Sonali M Smith, MD

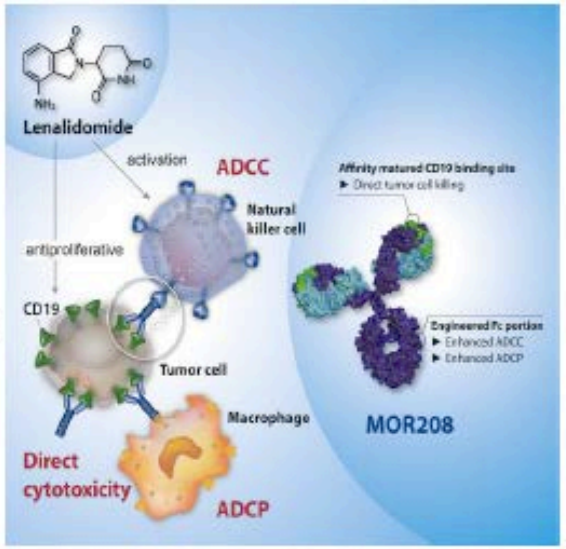
Tafasitamab MOA

Tafasitamab
Fc-enhanced, anti-CD19 mAb

+

Lenalidomide

- ADCC ↑
- ADCP ↑
- Direct Cell Death
- Encouraging single agent activity in NHL patients with long DoR in R/R DLBCL



- T and NK Cell Activation/Expansion
- Direct Cell Death
- Demonstrated activity as an anti-lymphoma agent, alone or in combination
- Approved for treatment of MCL and FL/MZL

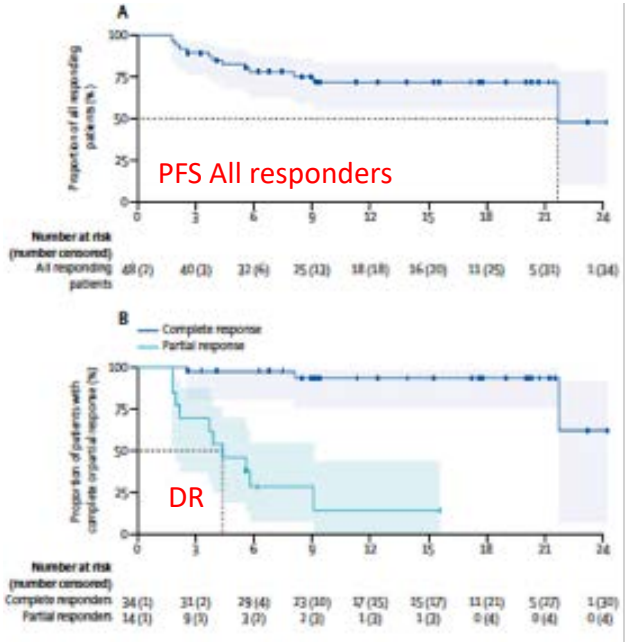
Potentiation of activity by combining Tafasitamab & LEN in vivo and in vitro

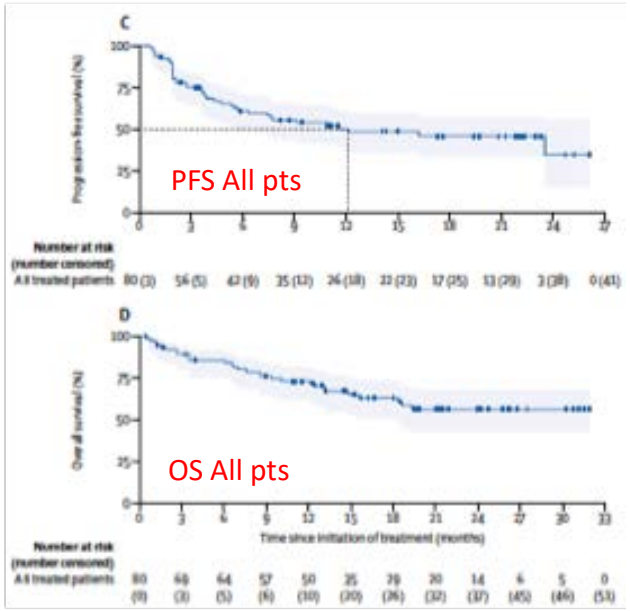
L-MIND trial: phase 2 trial of tafa-len x 12 cycles in R/R DLBCL

Salles et al. ICML 2019. #124.
Hortonet al., 2008; Awanet al., 2010; Richter et al., 2013; MorphoSys data on file; Wu et al., 2008; Lapalombella et al., 2008; Zhang et al., 2013, Wiernik et al., 2008; Witzig et al., 2011; Czuczman et al., 2017; Jurczak et al, 2018

Courtesy of Sonali M Smith, MD

L-MIND Results: very long response duration for CR pts





Patient characteristics:

N=81 with med age 72y

50% of pts 2L

42% R-ref, 44% ref

Results:

ORR 60%, CR 43%

Med DR 22m but NR for CR pts

Salles G et al. Lancet Oncol. 2020 Jul;21(7):978-988

Courtesy of Sonali M Smith, MD

L-MIND Results: very long response duration for CR pts

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N=81 with med age 72y

50% of pts 2L

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Results:

ORR 60%, CR 43%

Med DR 22m but NR for CR pts

Salles G et al. Lancet Oncol. 2020 Jul;21(7):978-988

Courtesy of Sonali M Smith, MD

ASH 2020: Advent of Bispecifics in Lymphoma

- **CD20 x CD3**
  - REGN1979 — Bannerji ASH 2020 #400
  - Mosunetuzumab — Olszewski ASH 2020 #401
  - Epcoritamab — Hutchings ASH 2020 #402
  - Glofitamab — Hutchings ASH 2020 #403

- **CD19 x CD3**
  - MB-CART2019.1 — Borchman ASH 2020 #404

Courtesy of Sonali M Smith, MD

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

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

Agenda

Module 1: Follicular lymphoma

Module 2: Mantle cell lymphoma

Module 3: Diffuse large B-cell lymphoma

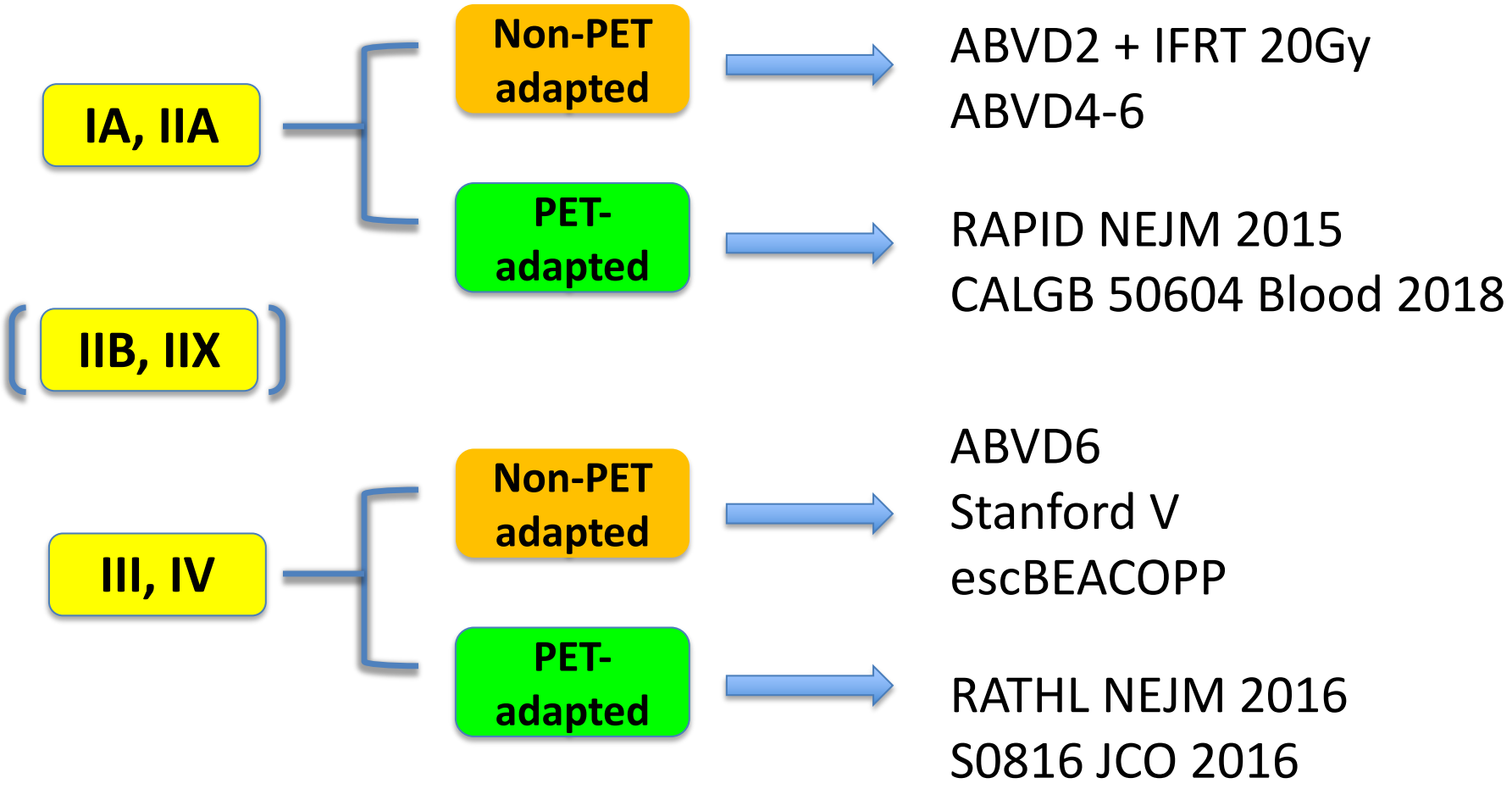
Module 4: Hodgkin lymphoma

Module 5: CAR T-cell therapy in DLBCL and other lymphoma subtypes

Module 4: Hodgkin lymphoma

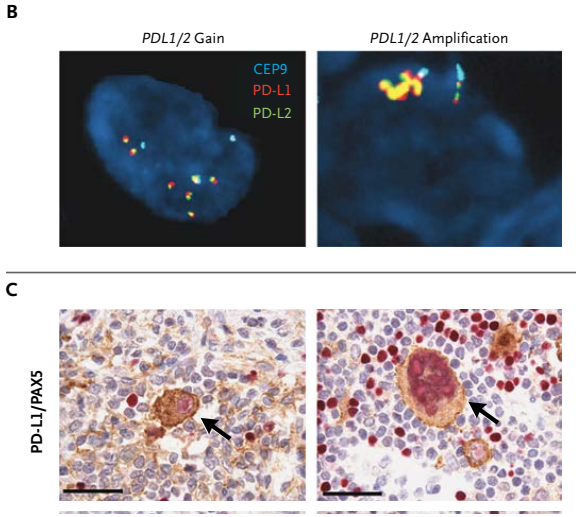
- **Key Relevant Data Sets**
  - ECHELON-1: Five-year update
  - AETHERA: Five-year follow-up
  - Brentuximab vedotin (BV) + nivolumab as first-line therapy
  - KEYNOTE-204: Pembrolizumab versus BV for R/R classical HL

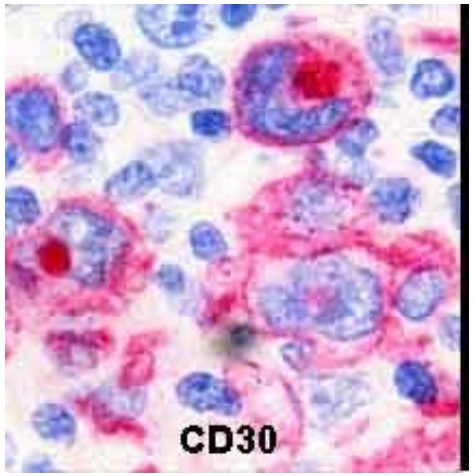
Snapshot of frontline standard treatment approach prior to targeted agents



Courtesy of Sonali M Smith, MD

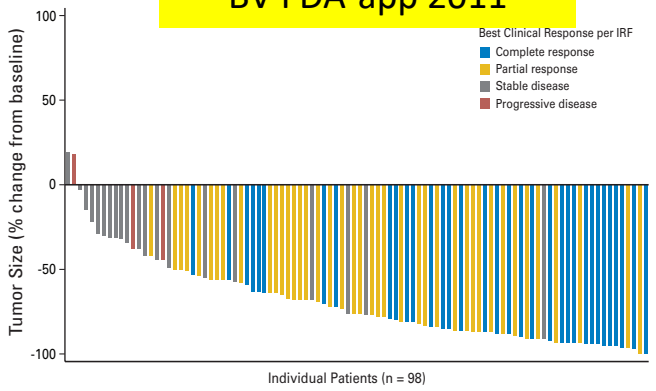
Evolution of care: two “new” targets



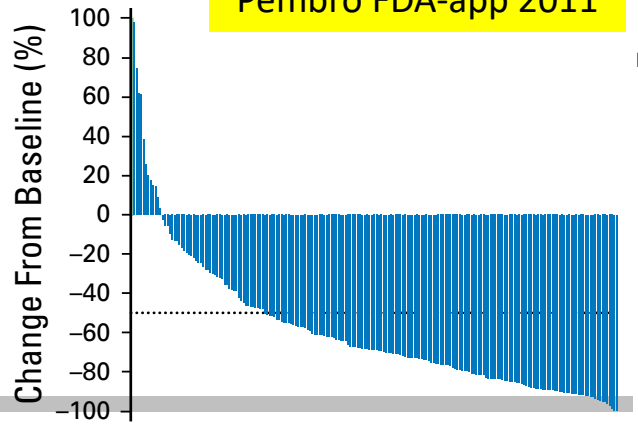


http://pleiad.umdnj.edu/~dweiss/hd_types/hdImmuno_img.html

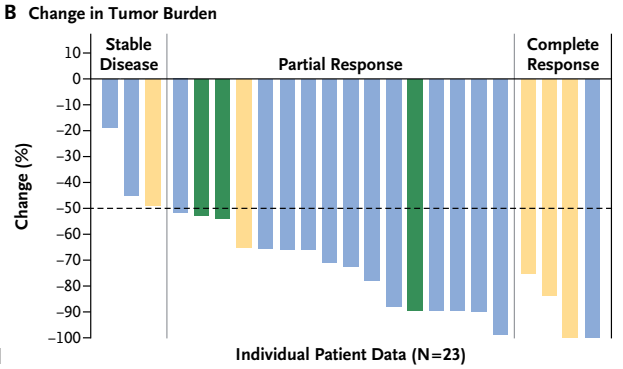
BV FDA-app 2011



Pembro FDA-app 2011



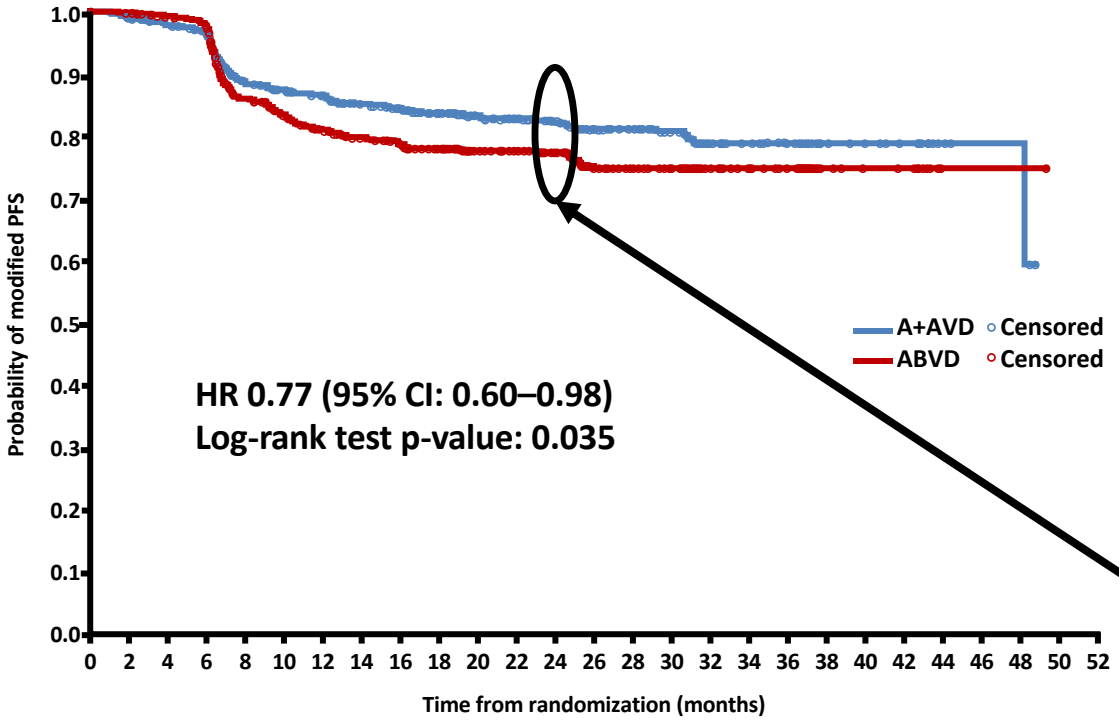
Nivo FDA-app 2016



Ansell et al. N Engl J Med. 2015 Jan 22;372(4):311-9; Younes et al. J Clin Oncol. 2012 Jun 20;30(18):2183-9; J Clin Oncol. 2017 Jul 1;35(19):2125-2132

Courtesy of Sonali M Smith, MD

Integration of targeted agents into frontline management of advanced stage cHL: ECHELON-1



Number of events

Category	A+AVD N=117	ABVD N=146
Progression	90	102
Death	18	22
Modified progression	9	22
Chemotherapy	7	15
Radiotherapy	2	7

Modified PFS estimates

Time	A+AVD (95% CI)	ABVD (95% CI)
2-year	82.1 (78.7–85.0)	77.2 (73.7–80.4)

Median follow-up (range): 24.9 months (0.0–49.3)

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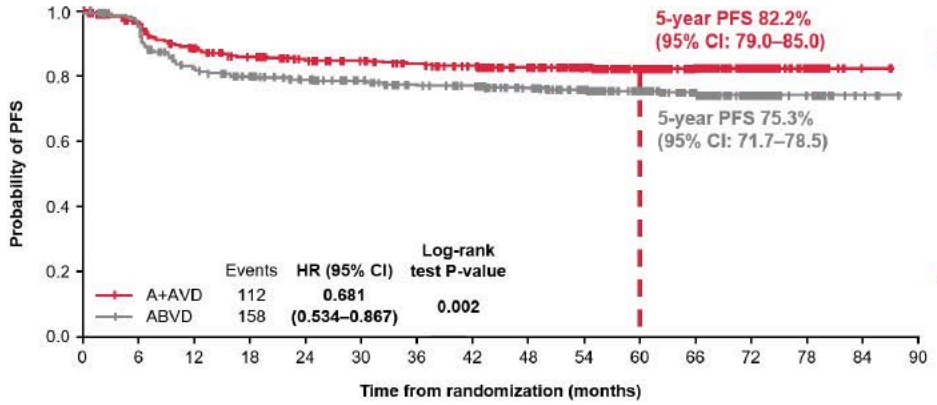
Connors et al. *NEJM* online 2017; slide courtesy of Alex Herrera

Courtesy of Sonali M Smith, MD

ASH 2020: 5-year follow up of ECHELON-1

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



- 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

Author Conclusions

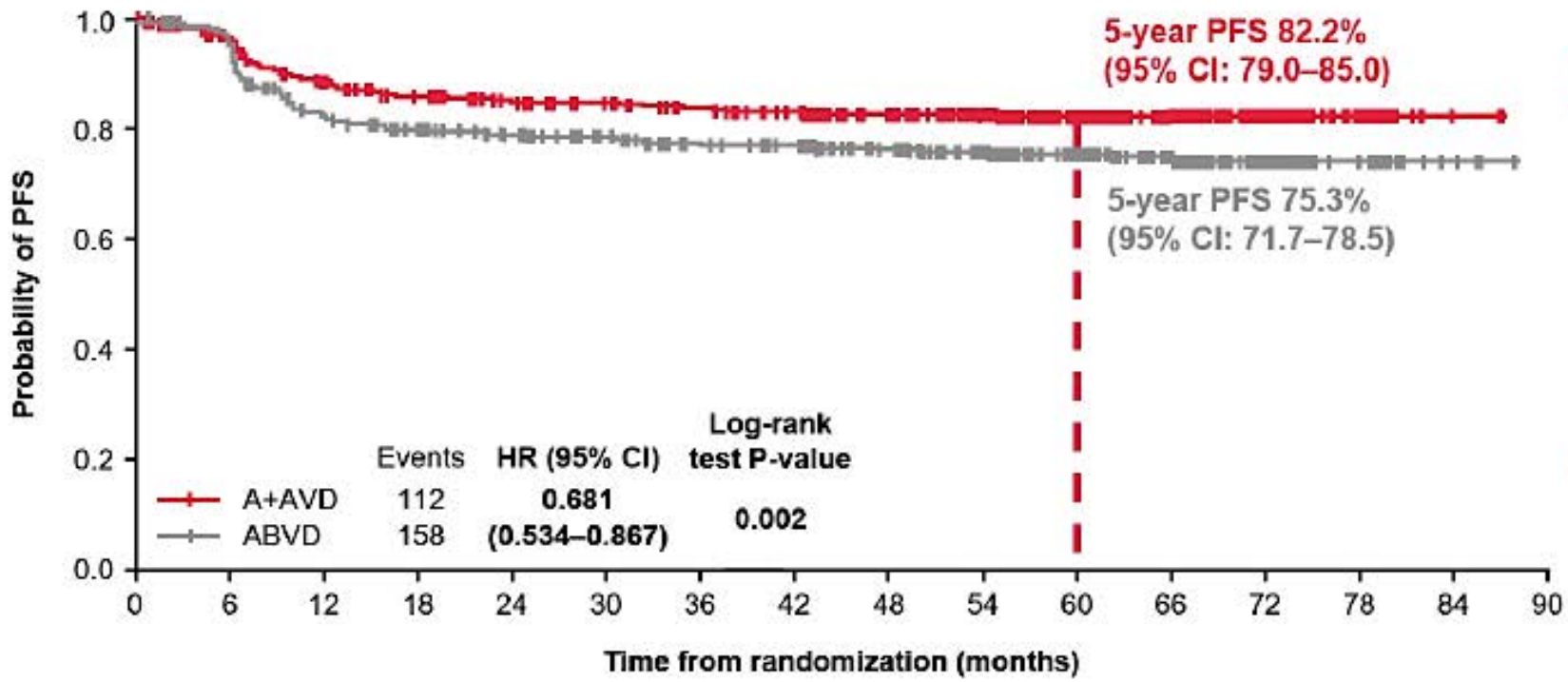
- At 5 years A+AVD continues to demonstrate a robust and durable treatment benefit independent of disease stage, risk factor score, and PET2 status, without requiring change of therapy based on interim PET assessment and without exposure to bleomycin.
- The sustained PFS benefit with A+AVD is coupled with:
  - A manageable long-term safety profile
  - A low rate of secondary malignancies
  - No observed impact on the rate of successful pregnancies compared with ABVD
  - A high rate of resolution and improvement of PN, with symptoms of PN resolving or improving over time.
- As most relapses in cHL occur within 5 years of frontline treatment, these long-term PFS data suggest that more patients may have been cured of their disease with A+AVD versus ABVD.
- A+AVD should be considered a preferred treatment option for all patients with previously untreated Stage III or IV cHL.

Strauss DJ et al. Brentuximab Vedotin with Chemotherapy for Patients with Previously Untreated, Stage III/IV Classical Hodgkin Lymphoma: 5-Year Update of the ECHELON-1 Study. ASH 2020; Abstract 2973. Poster

Courtesy of Sonali M Smith, MD

ASH 2020: 5-year follow up of ECHELON-1

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



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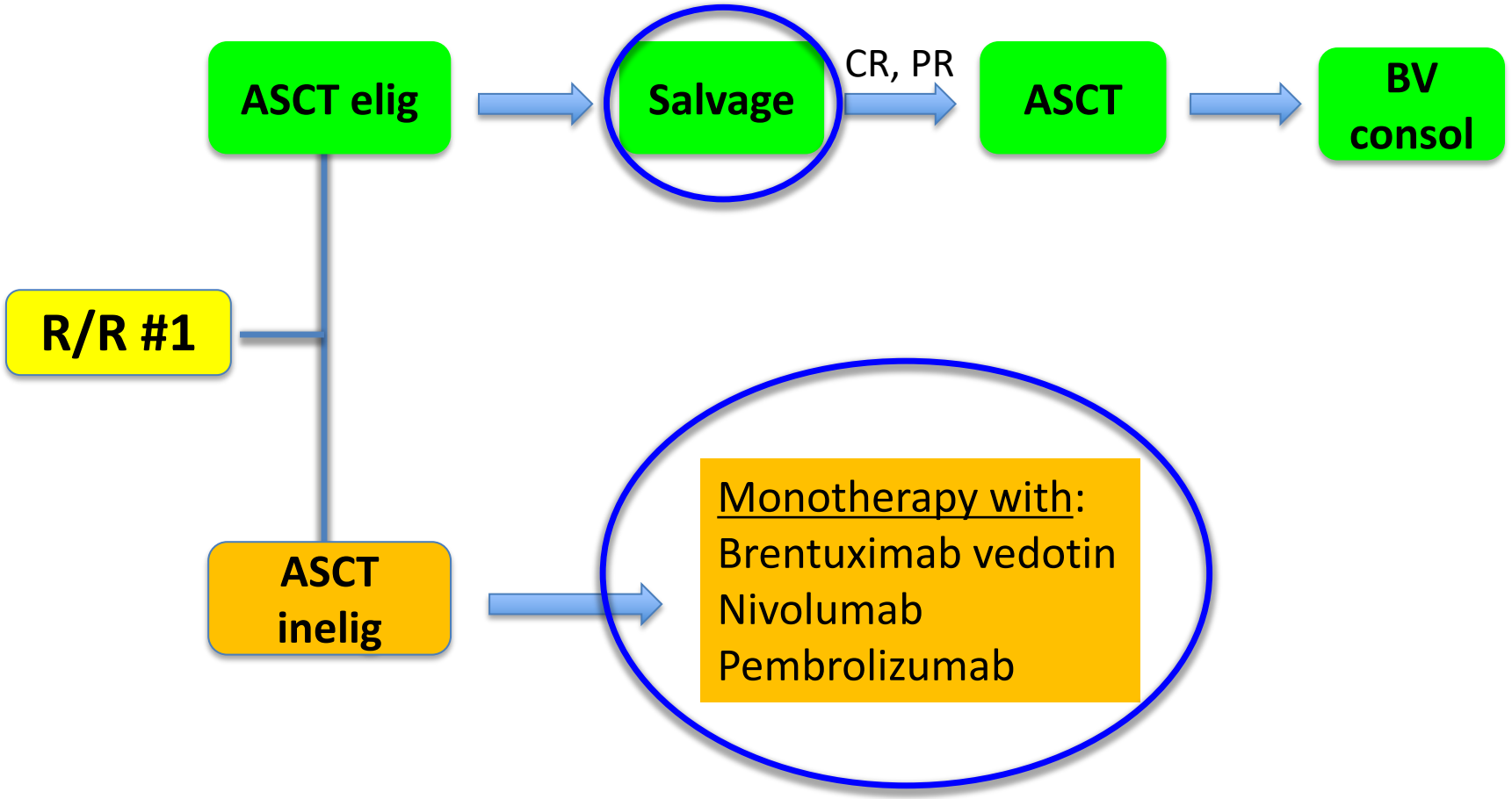
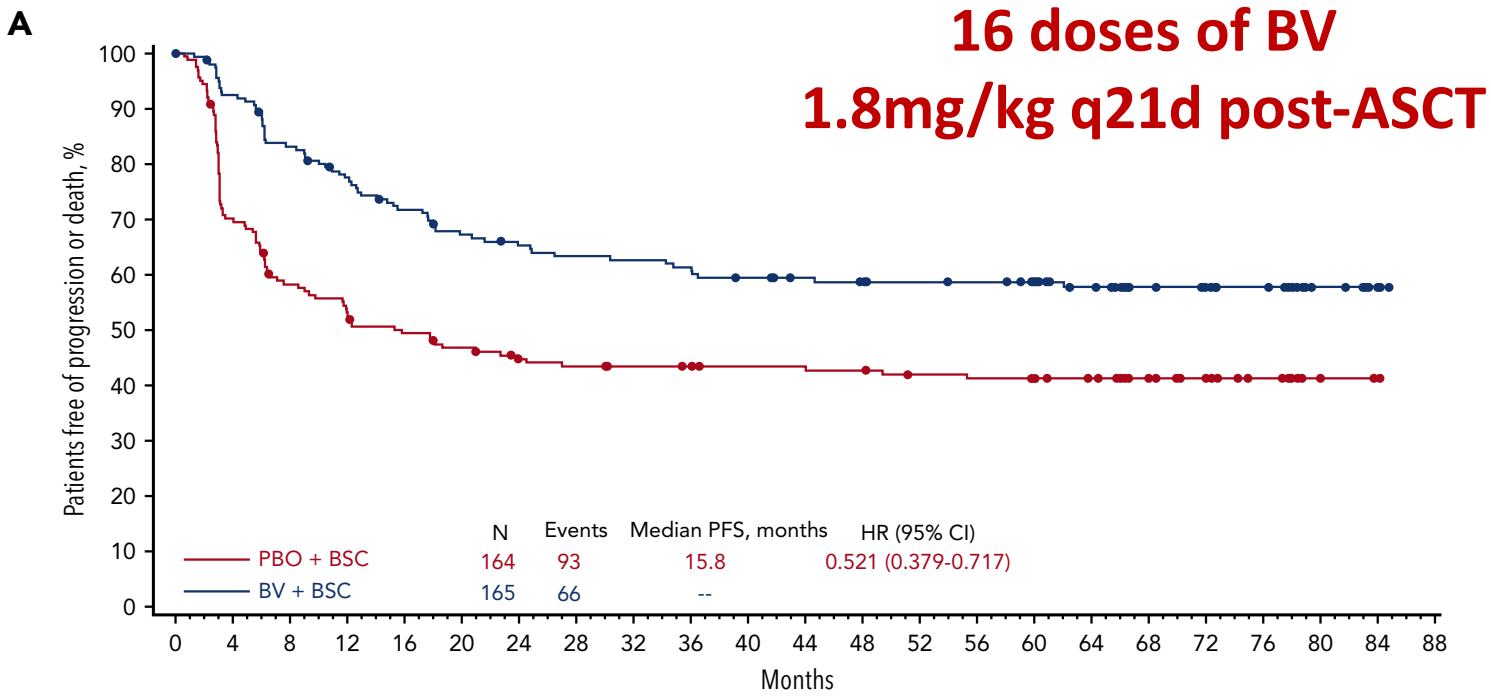
Courtesy of Sonali M Smith, MD

Treatment approach for relapsed cHL



Courtesy of Sonali M Smith, MD

5-year follow up of post-ASCT BV (AETHERA TRIAL)



Moskowitz et al. Blood. 2018 Dec 20;132(25):2639-2642.

Courtesy of Sonali M Smith, MD

Is there a shorter, less toxic post-transplant option?

Treatment:

30-75 days post AHCT

1.8mg/kg BV and 3mg/kg nivo q21d x 8 doses

Primary endpoint 18m PFS

Patients:

N=59

Med age 30 (18-72y)

32% primary refractory disease

39% EN disease

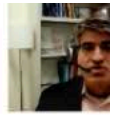
51% prior BV

42% prior PD-1 inhibitors

Herrera AF et al. ASH 2020; Abstract 472

Courtesy of Sonali M Smith, MD

Post-autologous stem cell transplant BV + nivo



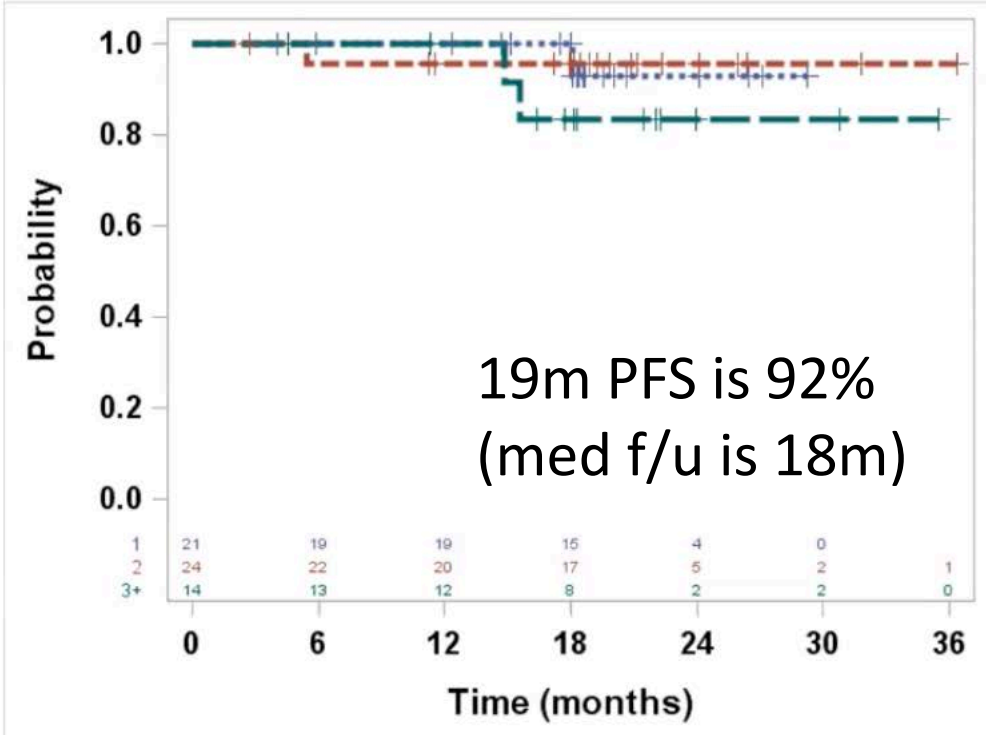
PFS according to number of risk factors

19-month PFS in pts with:

1 risk factor (n=21) – 93%
(95 CI 59-99%)

2 risk factors (n=24) – 96%
(95 CI 73-99%)

3+ risk factors (n=14) – 83%
(95 CI 48-96%)



Only 49% completed both agents

Most common AEs were neuropathy, neutropenia

27% had immune-related AE's requiring steroids

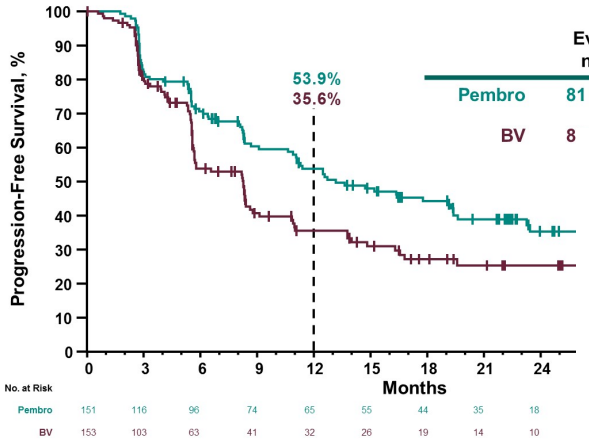
Herrera AF et al. ASH 2020; Abstract 472

Courtesy of Sonali M Smith, MD

KEYNOTE-204: Pembro vs. BV in R/R cHL

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

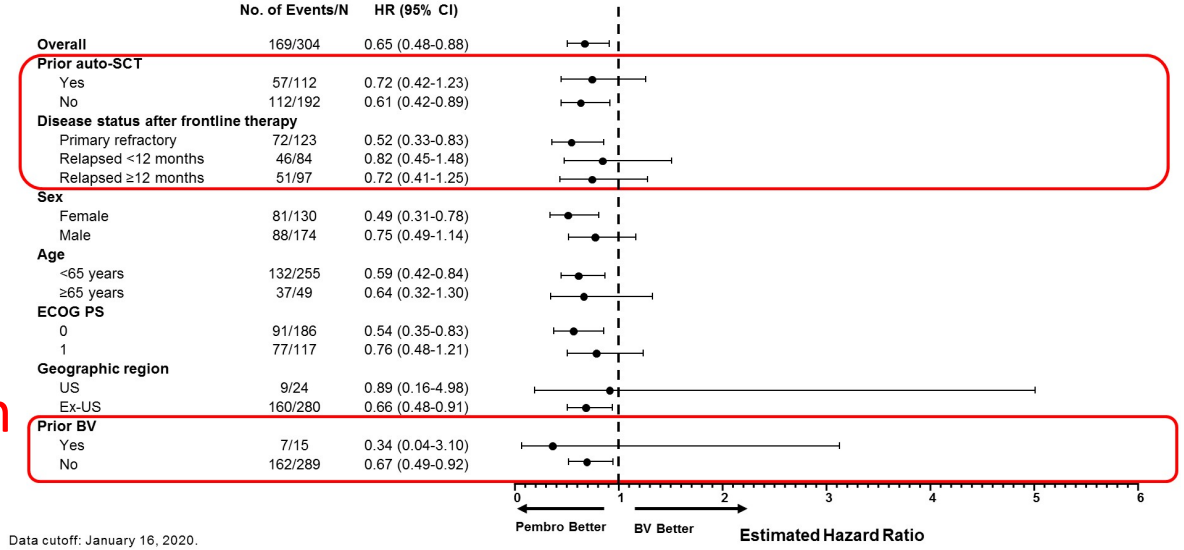
Including Clinical and Imaging Data Following Auto-SCT or Allo-SCT



	Events n (%)	HR (95% CI)	*P* value
Pembro	81 (53.6)	0.65 (0.48-0.88)	0.00271
BV	8		

Data cutoff: January 16, 2020.

Progression-Free Survival in Key Subgroups



Data cutoff: January 16, 2020.

- Med PFS 13.2 vs. 8.3m favoring pembro
- Most pts BV-naive

Kuruvilla J et al. ASCO 2020; Abstract 8005. Oral, HoD
Zinzani P et al. EHA 2020; Abstract LB2600. Late Breaking
Kuruvilla J et al.. ASH 2020; Abstract 1158. Poster

Courtesy of Sonali M Smith, MD

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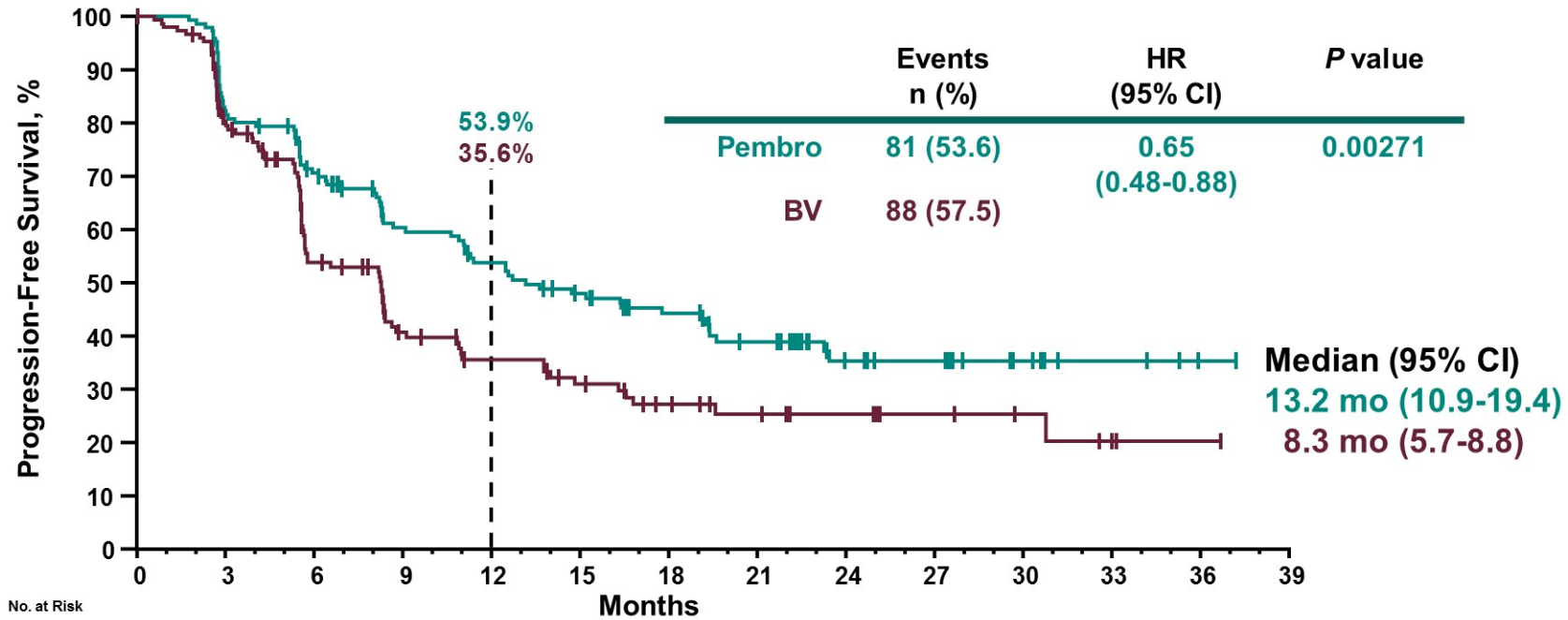

Data cutoff: January 16, 2020.

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Kuruvilla J et al. ASCO 2020; Abstract 8005. Oral, HoD
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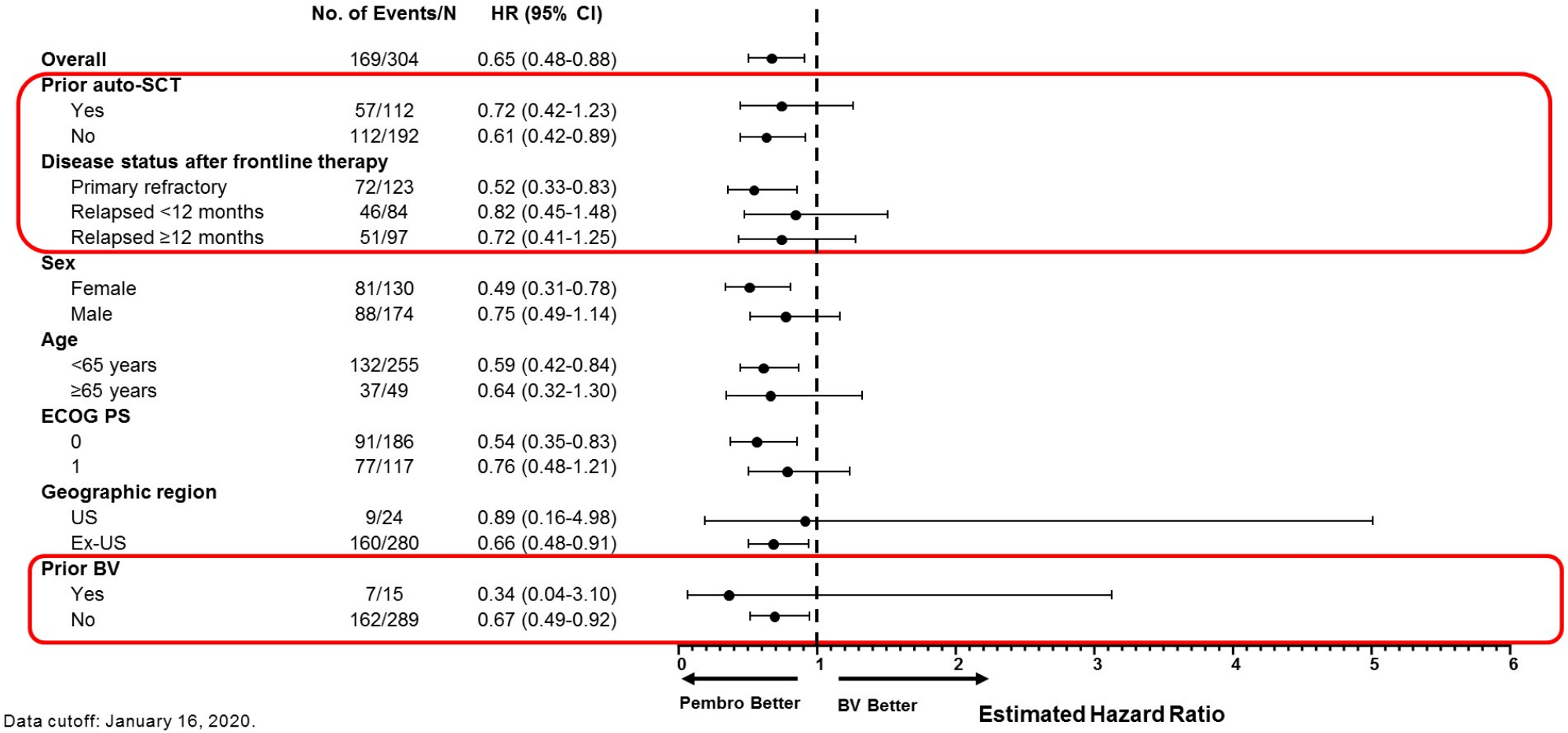
Courtesy of Sonali M Smith, MD

KEYNOTE-204: Pembro vs. BV in R/R cHL

Progression-Free Survival in Key Subgroups



Data cutoff: January 16, 2020.

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Kuruvilla J et al. ASCO 2020; Abstract 8005. Oral, HoD
Zinzani P et al. EHA 2020; Abstract LB2600. Late Breaking
Kuruvilla J et al.. ASH 2020; Abstract 1158. Poster

Courtesy of Sonali M Smith, MD

Combination targeted therapy in R/R cHL

Grade 3-4 AE's seen in all groups
- slightly higher in Ipi-groups
- (43% ipi vs. 50% in triplet vs. 16% in nivo groups)

Grade 5 toxicity
- 2 deaths from pneumonitis (nivo group and triplet group)

Houot R, Merryman RW, Morschhauser F.. Lancet Haematol. 2020 Sep;7(9):e629-e630

Courtesy of Sonali M Smith, MD

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

Agenda

Module 1: Follicular lymphoma

Module 2: Mantle cell lymphoma

Module 3: Diffuse large B-cell lymphoma

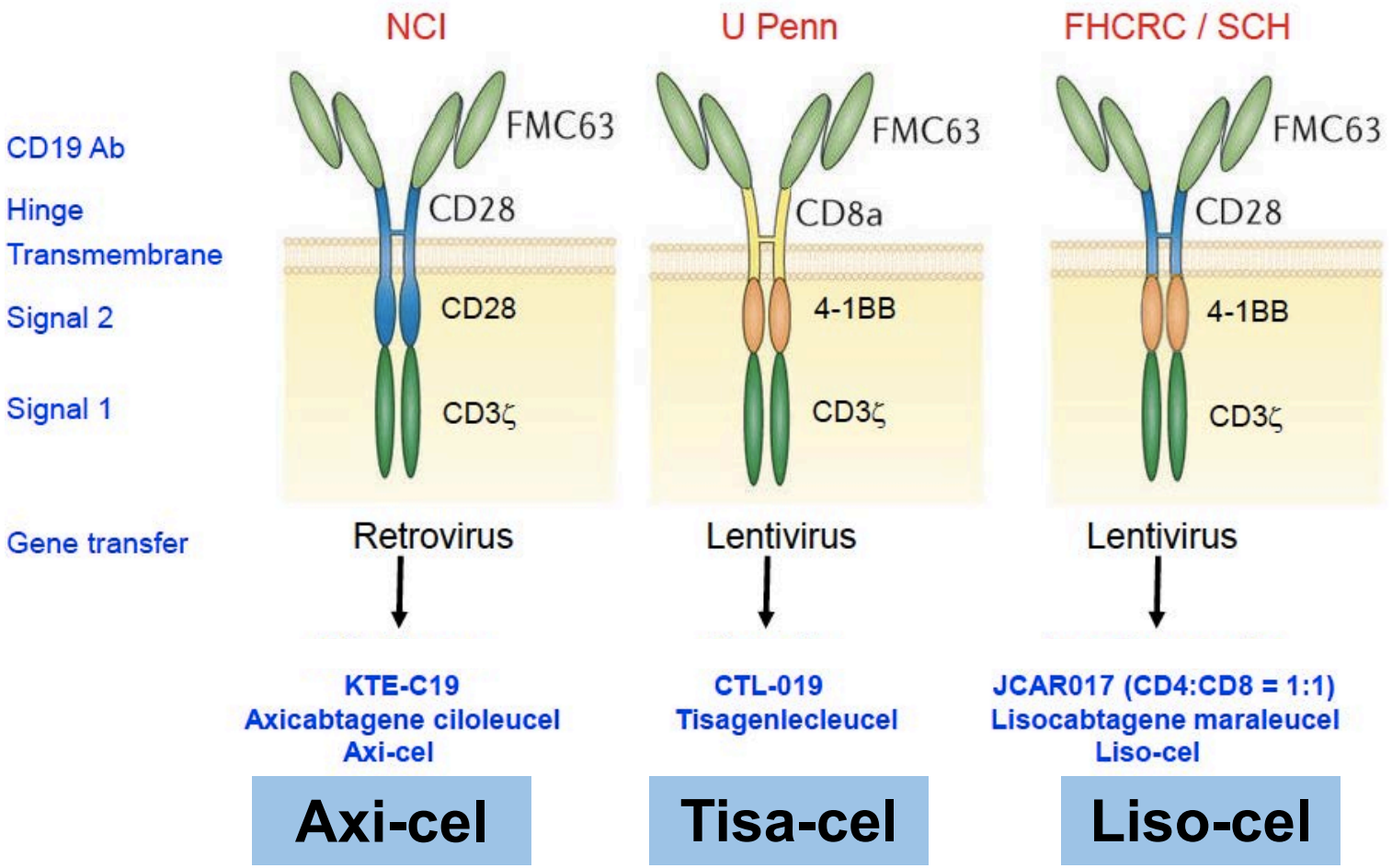
Module 4: Hodgkin lymphoma

Module 5: CAR T-cell therapy in DLBCL and other lymphoma subtypes

Module 5: CAR T-cell therapy

- **Key Relevant Data Sets**
  - Lisocabtagene maraleucel versus axicabtagene ciloleucel (axi-cel) + tisagenlecleucel for R/R large B-cell lymphoma (LBCL)
  - ZUMA-12: First-line axi-cel for high-risk LBCL
  - TRANSCEND NHL 001: Lisocabtagene maraleucel for R/R LBCL
  - JULIET: Tisagenlecleucel for R/R DLBCL
  - ELARA: Tisagenlecleucel for R/R FL
  - ZUMA-5: Axi-cel for R/R indolent non-Hodgkin lymphoma

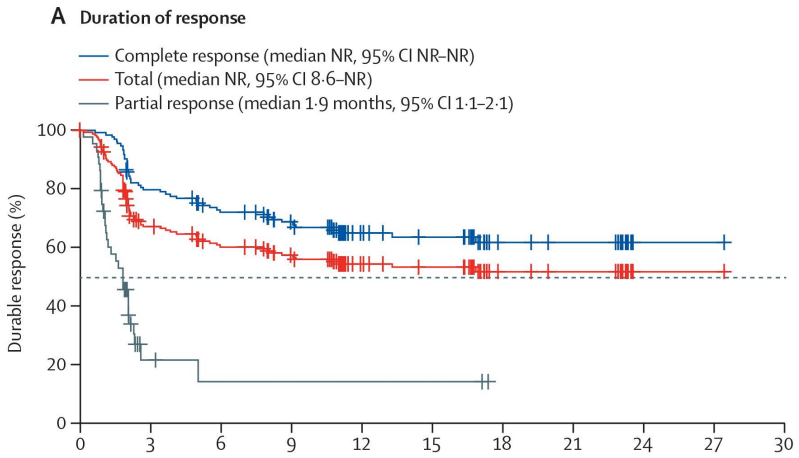
CD19 Directed CAR T Cell Products in Clinical Development



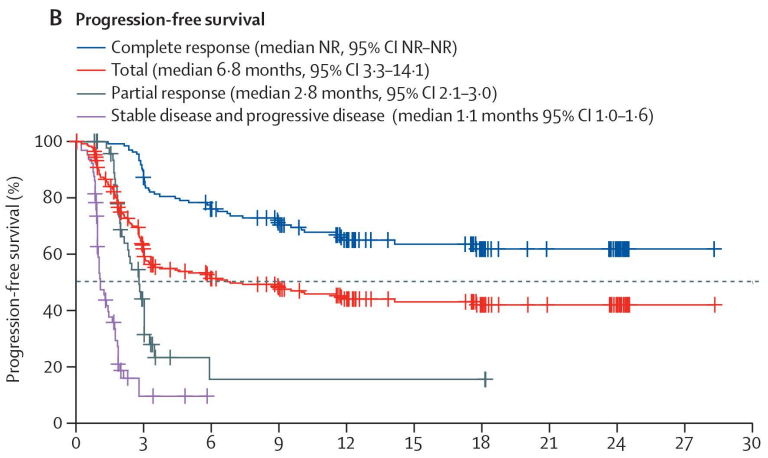
Adapted from van der Steegan et al. Nat Rev Drug Discov, 2015

Courtesy of Sonali M Smith, MD

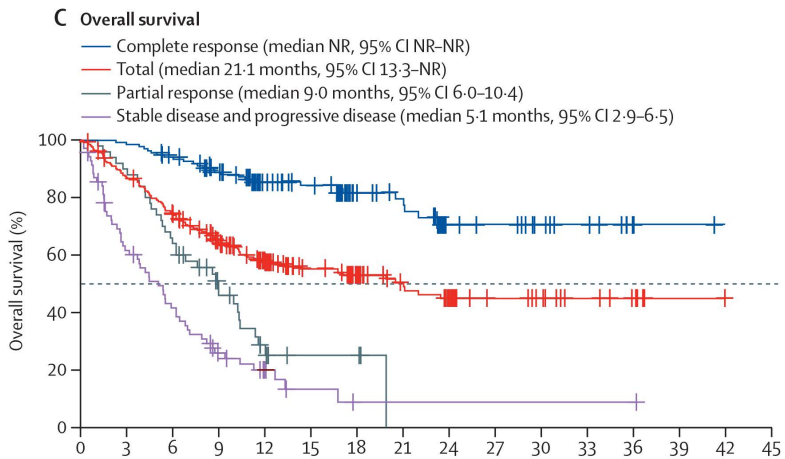
Liso-cel (TRANSCEND NHL-001)



Duration of Response



Overall Survival



Progression-free survival

Key patient features:

269 of 344 pts received product

42% over age 65y

67% chemo-refractory

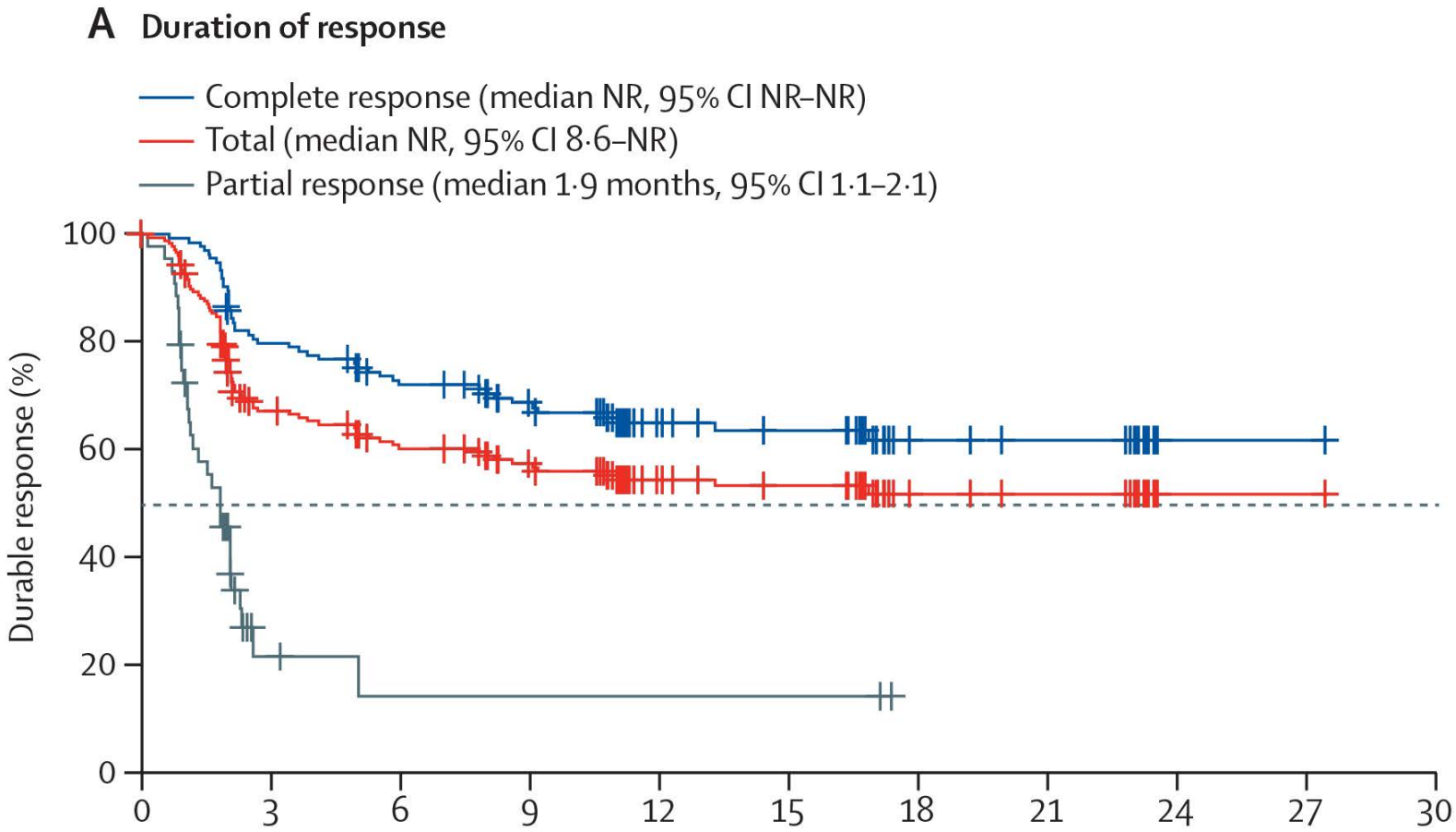
7 pts with secondary CNSL

	Patients (n=269)
Cytokine release syndrome, neurological events, or both	127 (47%)
Cytokine release syndrome*	
Any grade	113 (42%)
Grade 3	4 (1%)
Grade 4	2 (1%)
Time to onset, days	5 (1–14)
Time to resolution, days	5 (1–17)
Neurological events†	
Any grade	80 (30%)
Grade 3	23 (9%)
Grade 4	4 (1%)
Time to onset, days	9 (1–66)
Time to resolution, days	11 (1–86)

Abramson JS et al. Lancet. 2020 Sep 19;396(10254):839-852

Courtesy of Sonali M Smith, MD

Liso-cel (TRANSCEND NHL-001)



Duration of Response

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Abramson JS et al. Lancet. 2020 Sep 19;396(10254):839-852

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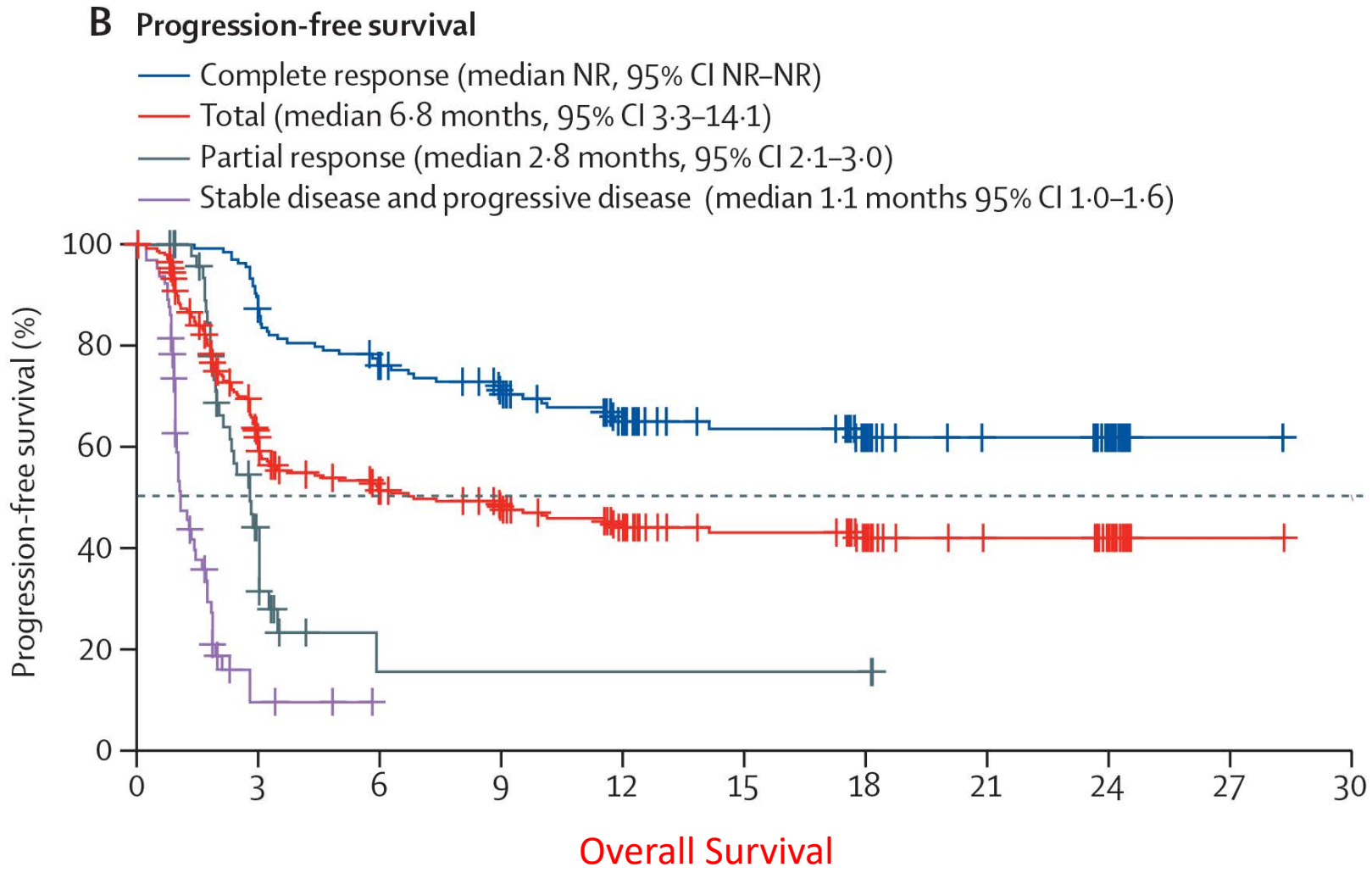

Overall Survival

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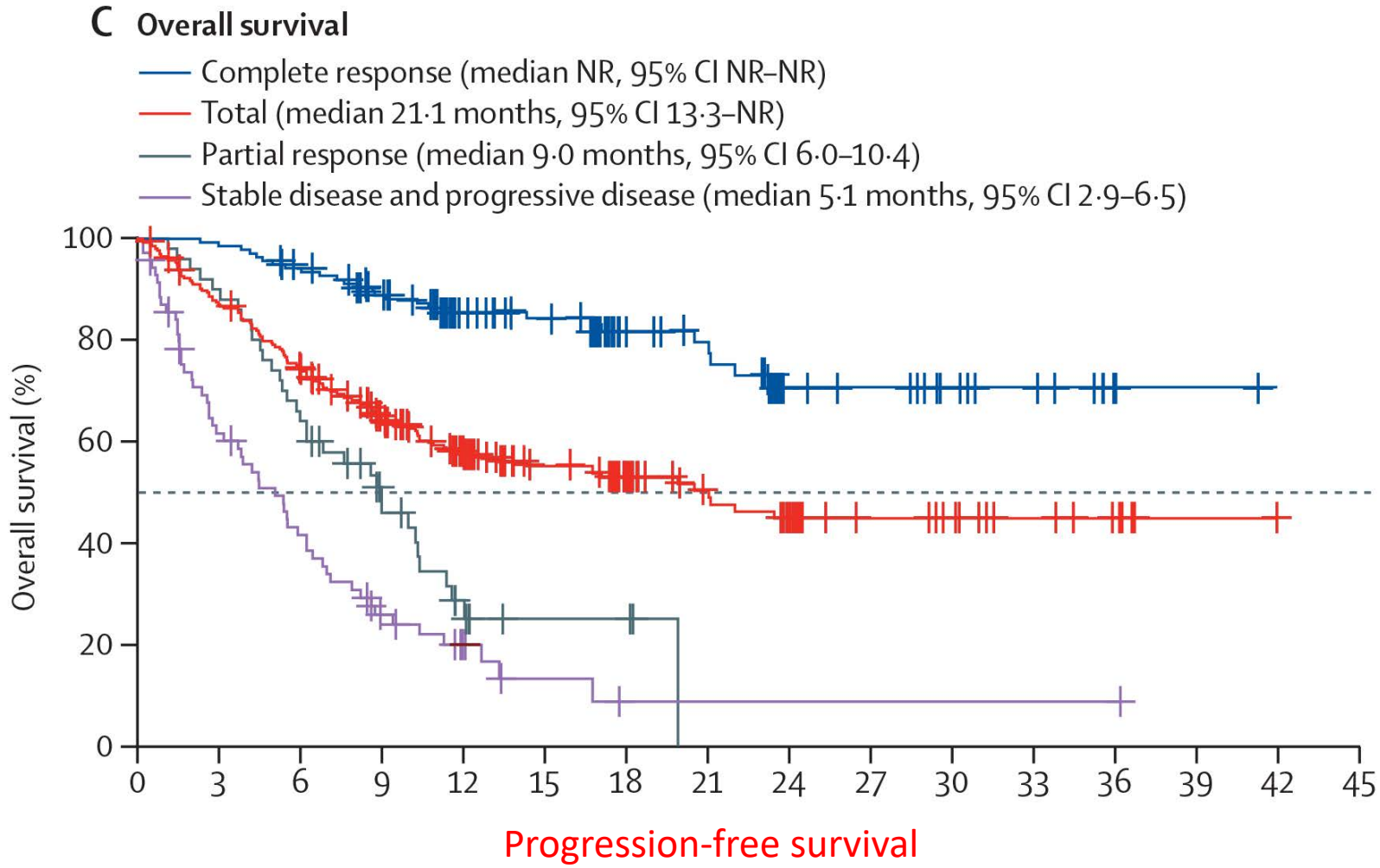

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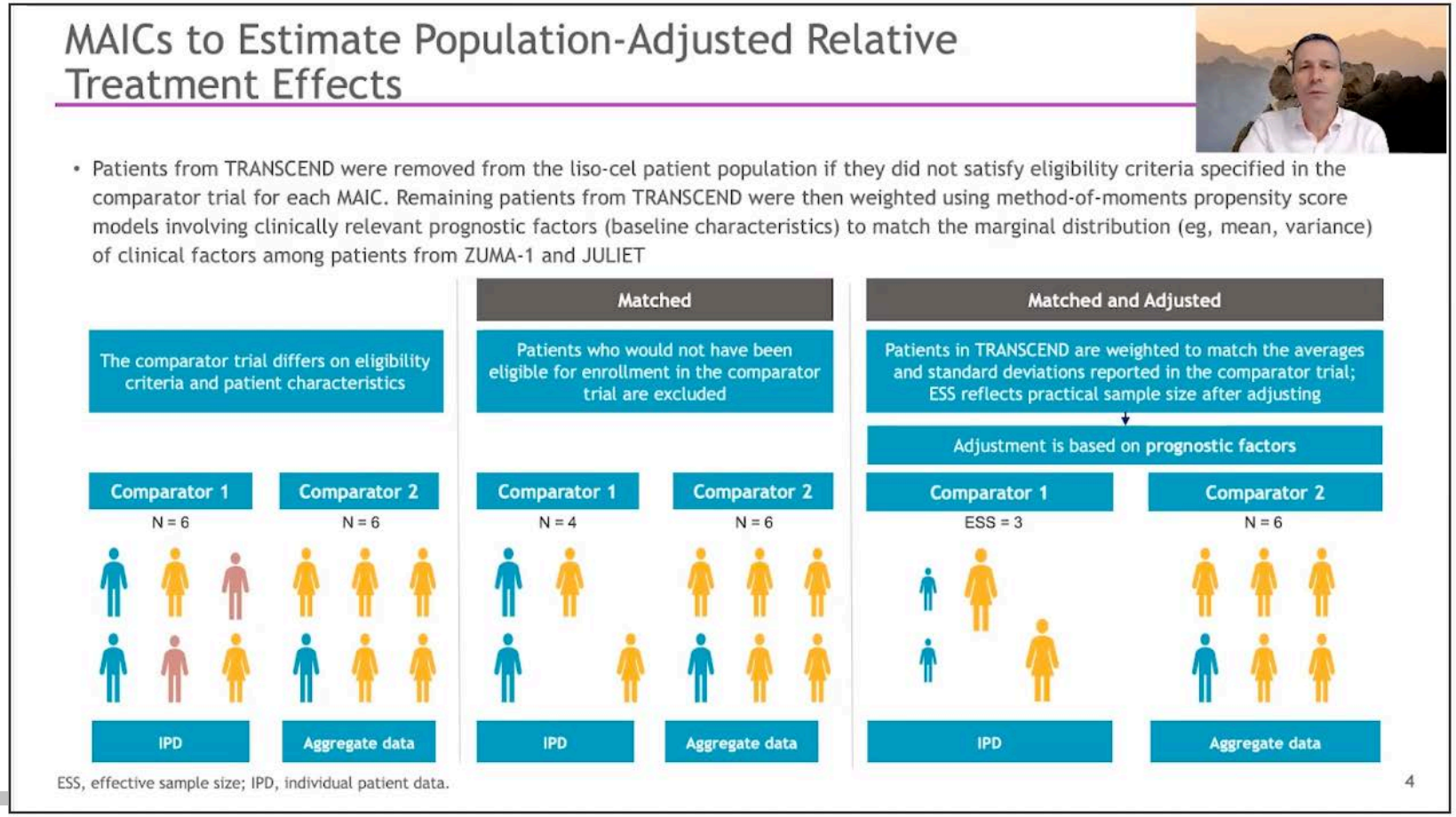
Courtesy of Sonali M Smith, MD

Matching-Adjusted Indirect Comparison (MAIC) of Liso-cel vs Axi-cel and Tisagenlecleucel in R/R Large B-Cell Lymphoma
Is there a "best-in-class" CAR-T product?



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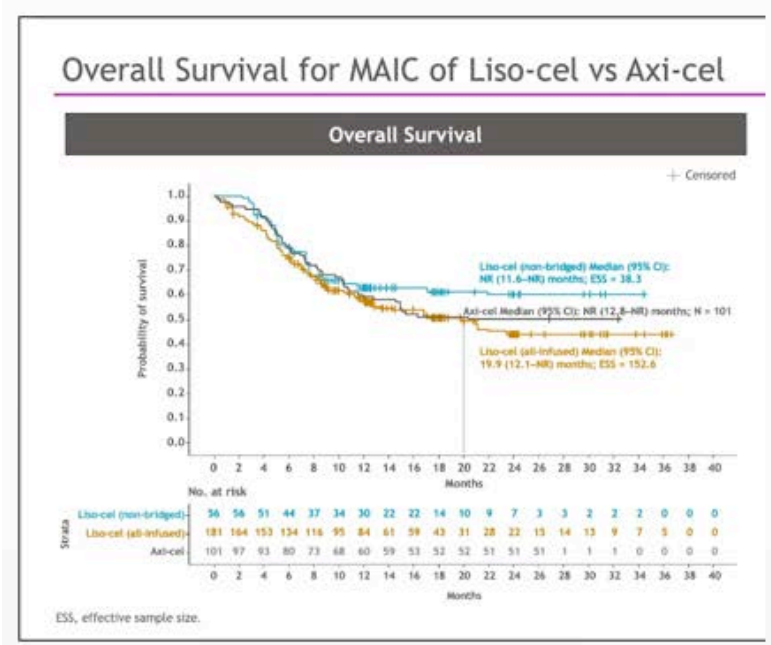
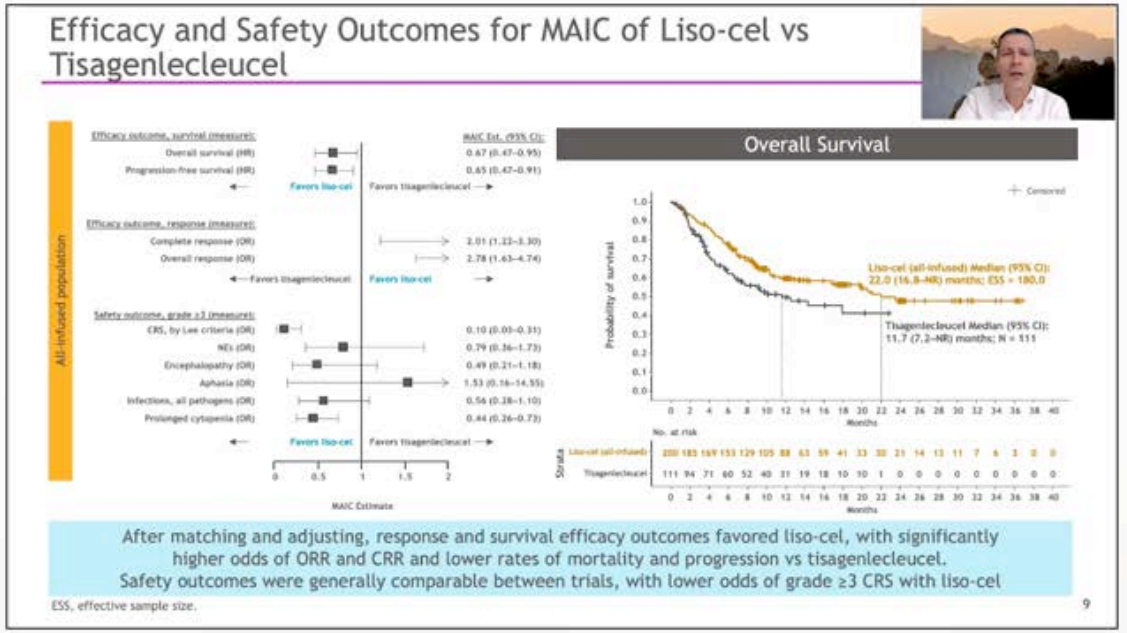
Cartron G et al. ASH 2020; Abstract 2116

Courtesy of Sonali M Smith, MD

Liso-cel vs. Axi-cel and Liso-cel vs. Tisa-cel





- Pairwise matching-adjusted comparison study with matching and then adjustment of ZUMA-1, TRANSCEND, JULIET
- Better safety and comparable efficacy: liso-cel versus axi-cel
- Better efficacy and comparable safety: liso-cel versus tisa-cel

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Cartron G et al. ASH 2020; Abstract 2116

Courtesy of Sonali M Smith, MD

Liso-cel vs. Axi-cel and Liso-cel vs. Tisa-cel

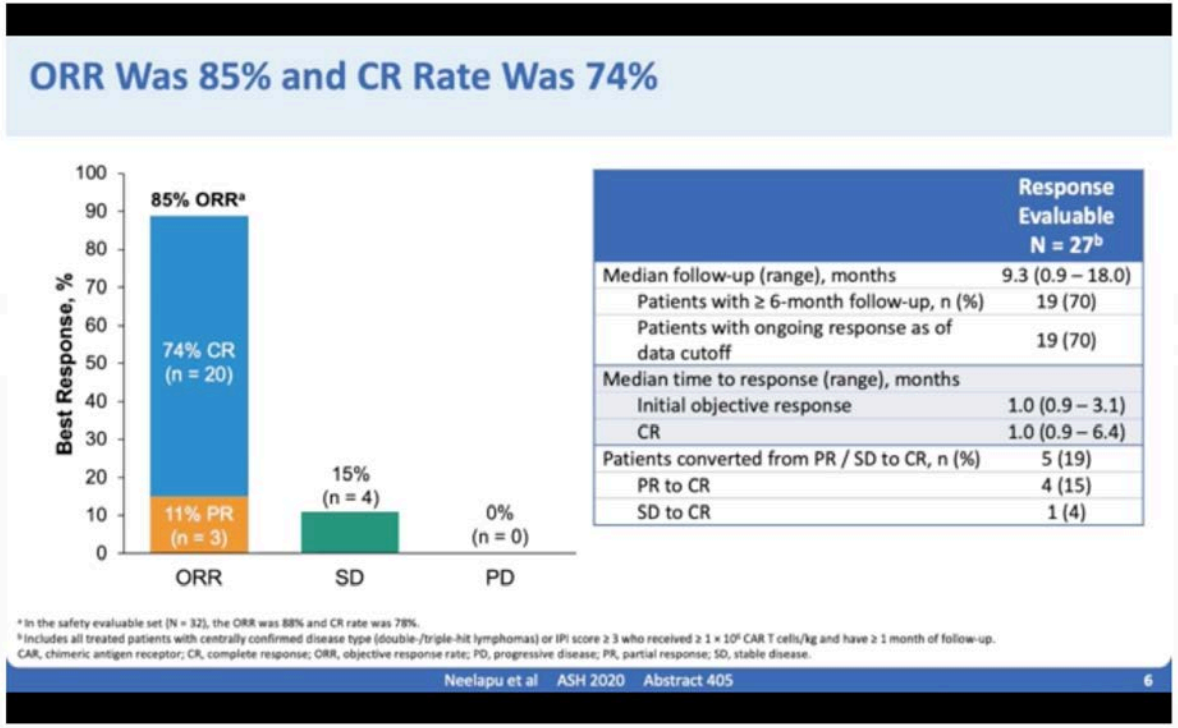
- Pairwise matching-adjusted comparison study with matching and then adjustment of ZUMA-1, TRANSCEND, JULIET
- Better safety and comparable efficacy: liso-cel versus axi-cel
- Better efficacy and comparable safety: liso-cel versus tisa-cel

Cartron G et al. ASH 2020; Abstract 2116

Courtesy of Sonali M Smith, MD

Interim Analysis of ZUMA-12 Trial of Axi-cel as First-Line Therapy for Patients with High-Risk Large B-Cell Lymphoma

Moving CAR T-cell therapy earlier: high-risk DLBCL



Med f/u 9.5m

Are CAR-T cells “better” if utilized earlier?

- Higher frequency of CCR7+CD45RA+ T-cells
- Greater CAR-T cell expansion

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Neelapu SS et al. ASH 2020; Abstract 405

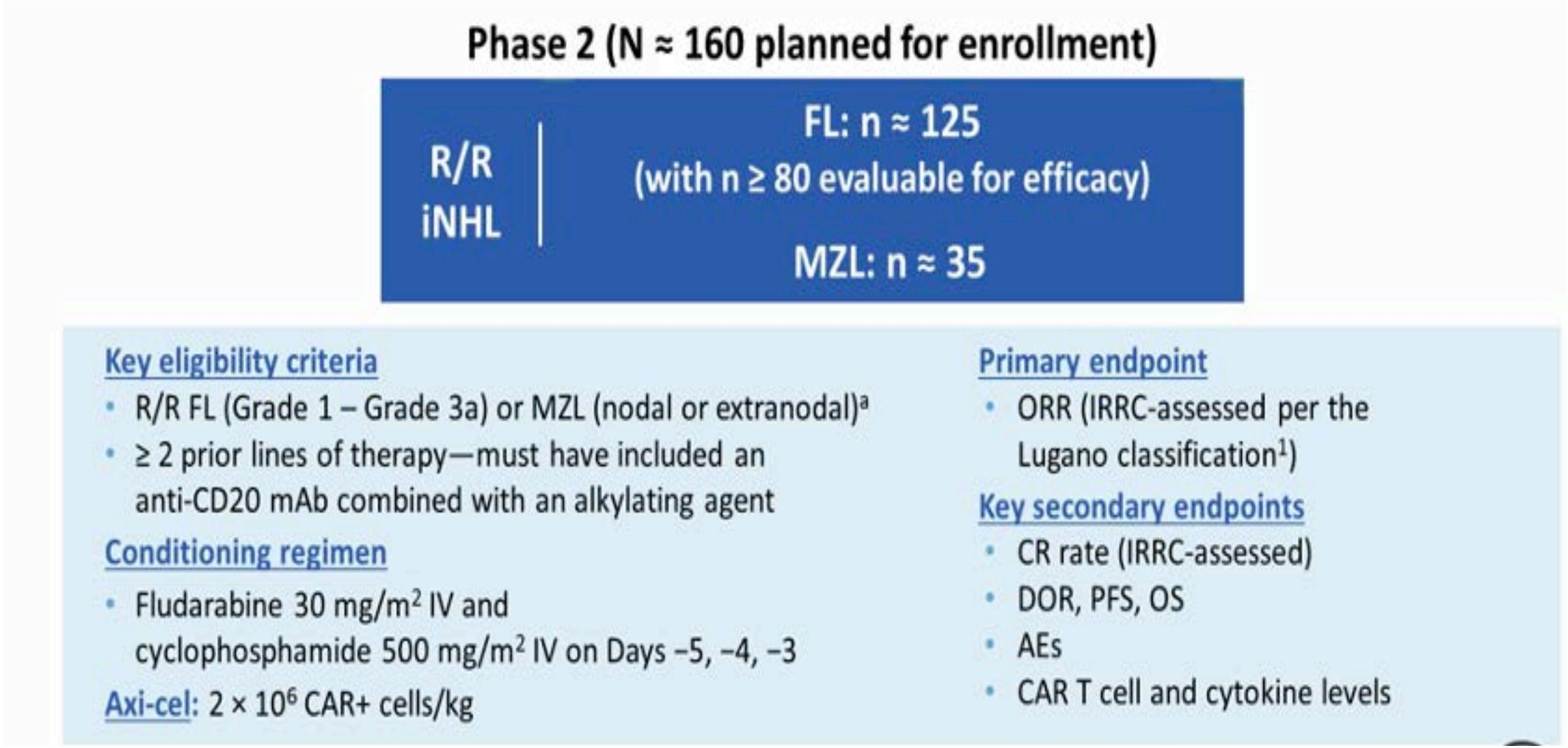
Courtesy of Sonali M Smith, MD

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

Fowler NH et al.

ASH 2020;Abstract 1149.

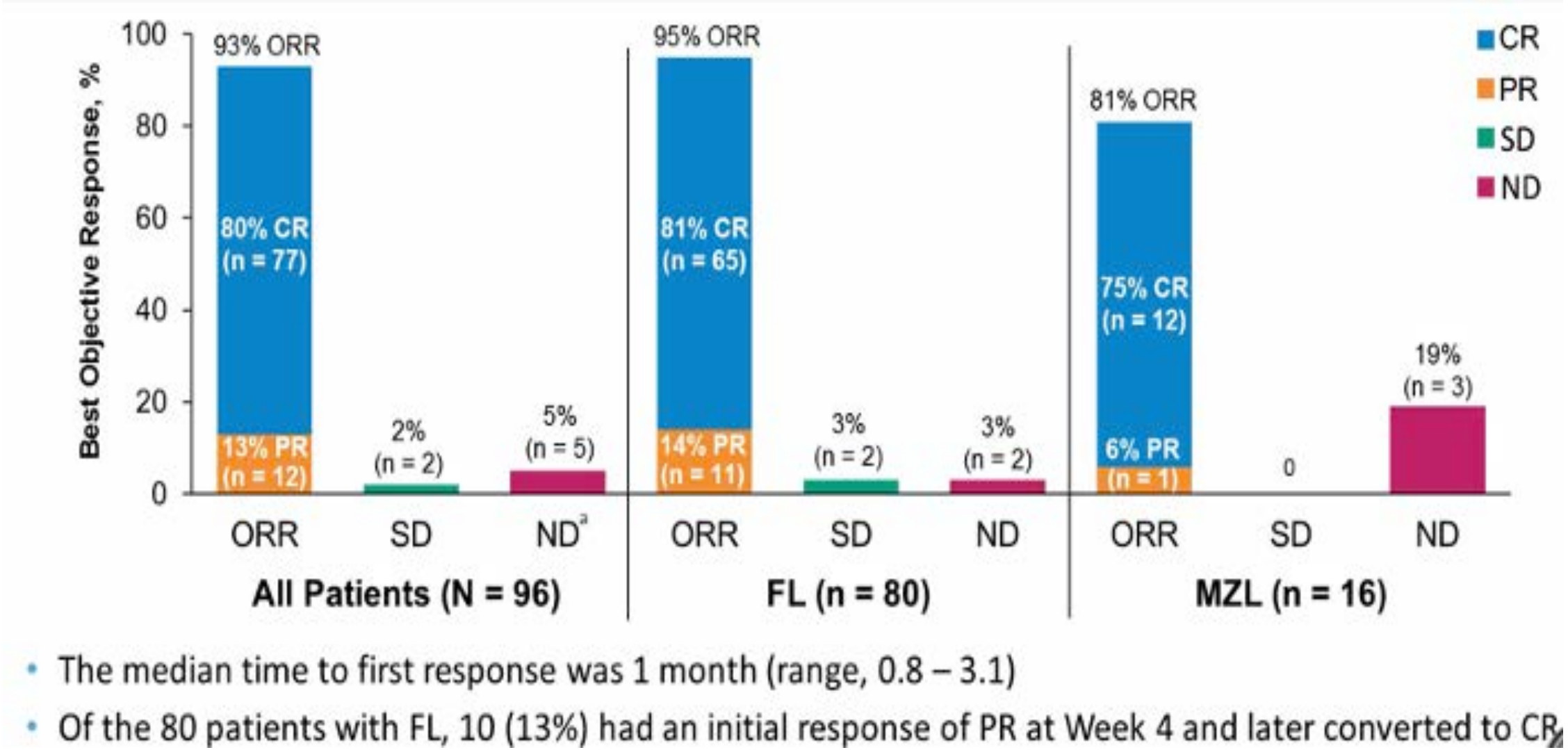
Phase II ZUMA-5 Trial of Axicabtagene Ciloleucel



Jacobson CA et al. ASCO 2020; Abstract 8008.

Courtesy of Christopher R Flowers, MD, MS

ZUMA-5: Response



- The median time to first response was 1 month (range, 0.8 – 3.1)
- Of the 80 patients with FL, 10 (13%) had an initial response of PR at Week 4 and later converted to CR

Jacobson CA et al. ASCO 2020; Abstract 8008.

Courtesy of Christopher R Flowers, MD, MS

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

Nontargeted Therapy for Lung Cancer

Tuesday, January 19, 2021
5:00 PM – 6:00 PM ET

Faculty

Matthew Gubens, MD, MS
Suresh S Ramalingam, MD

Moderator

Neil Love, MD

RTP Year in Review 2020

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

RTP Year in Review 2020