Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

Follicular Lymphoma

Tuesday, January 4, 2022
5:00 PM – 6:00 PM ET

Faculty

John P Leonard, MD
Laurie H Sehn, MD, MPH

Moderator

Neil Love, MD

RTP Year in Review 2022

YiR Follicular Lymphoma Faculty

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

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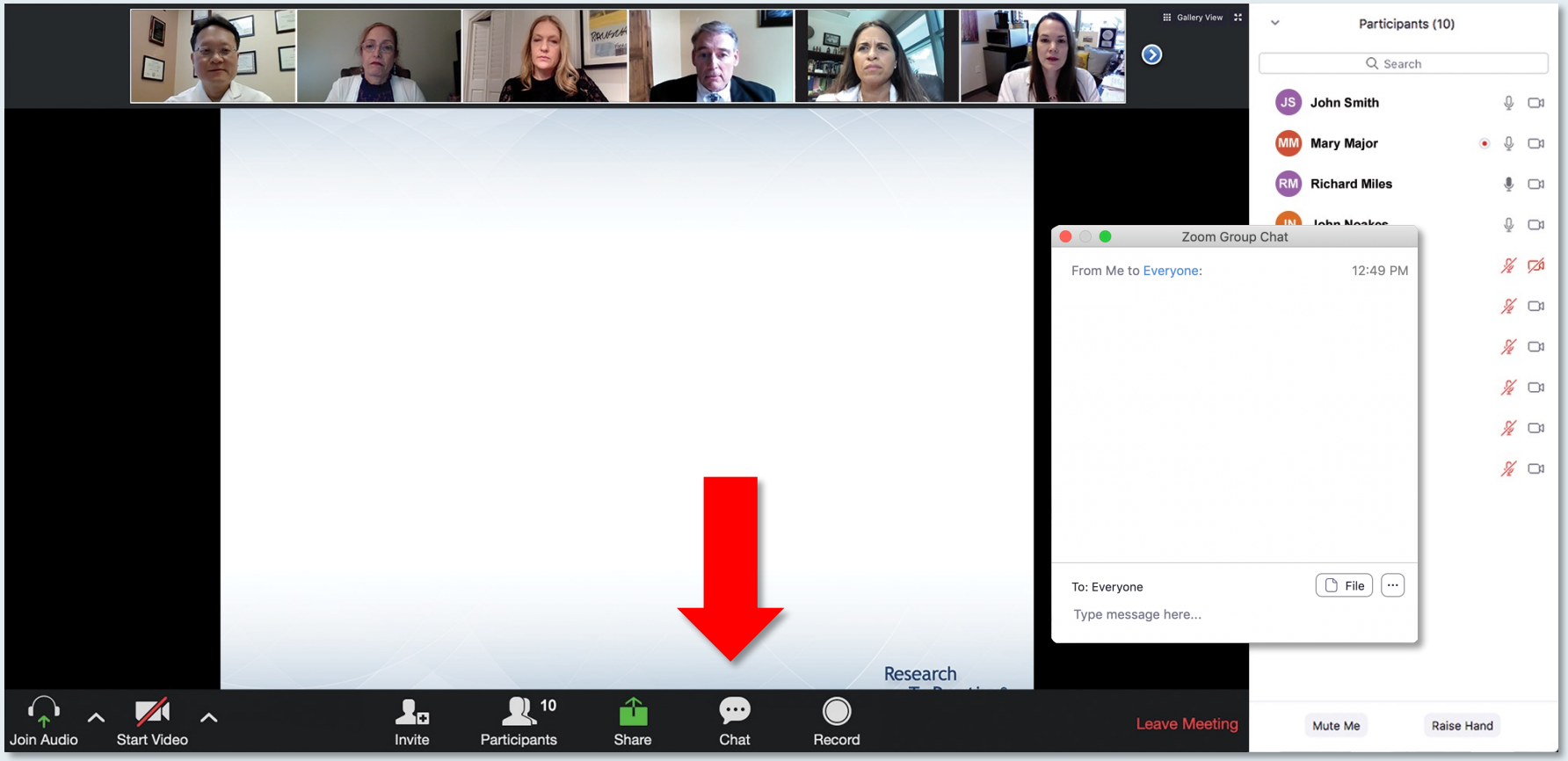

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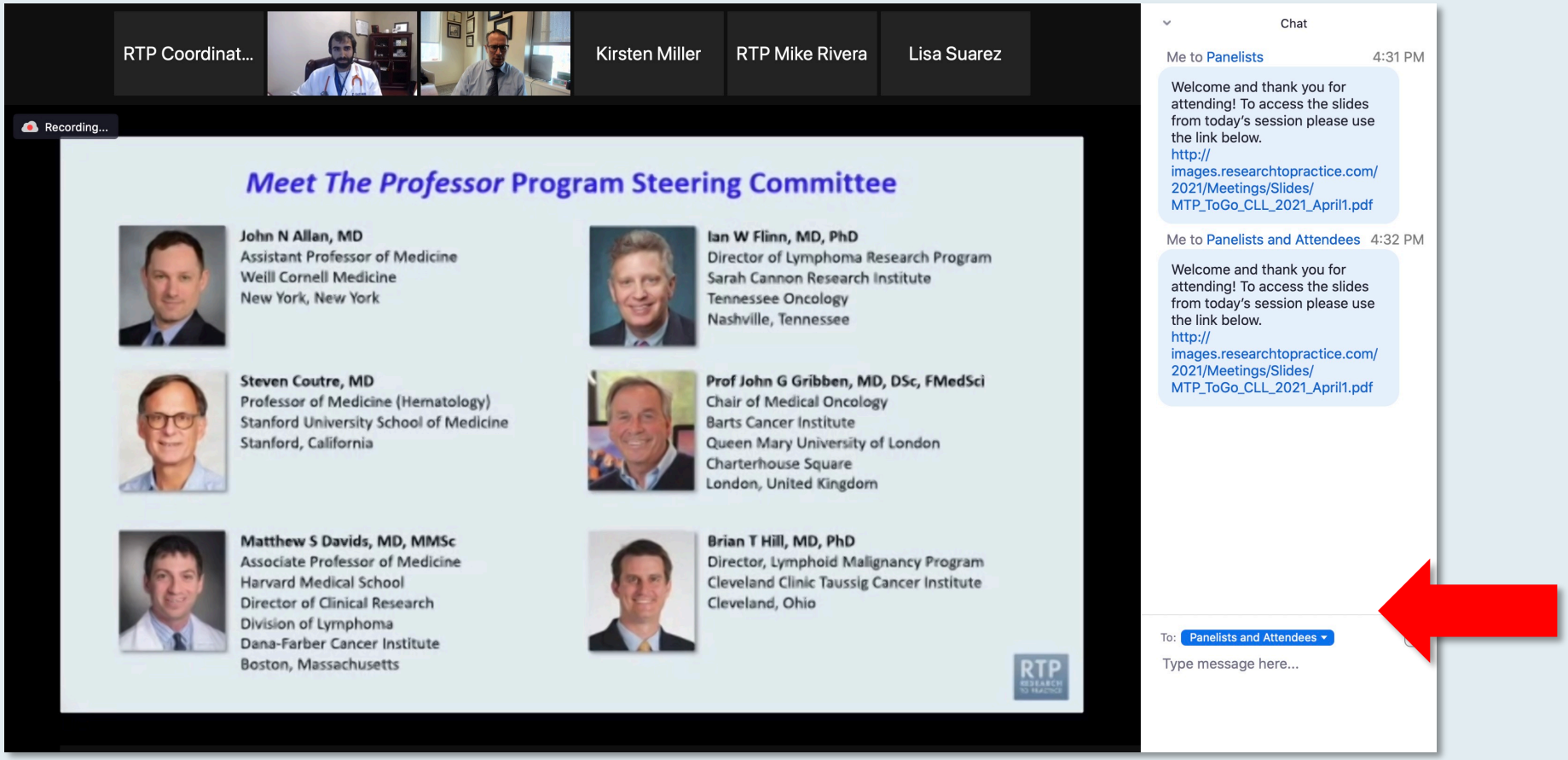

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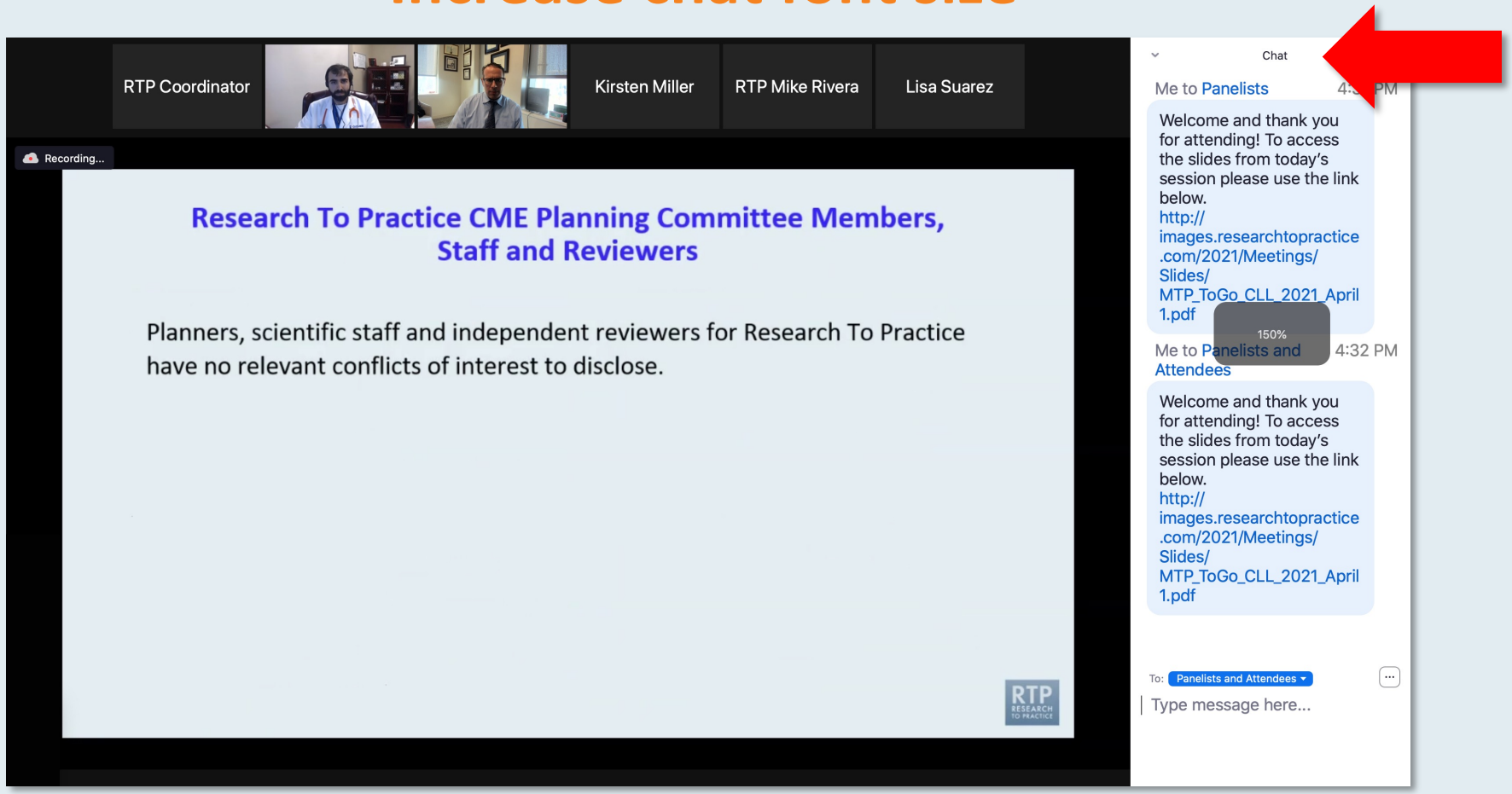

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ONCOLOGY TODAY

WITH DR NEIL LOVE

Recent Advances in the Management of Chronic Lymphocytic Leukemia

PROF DR ARNON KATER
AMSTERDAM UNIVERSITY MEDICAL CENTERS

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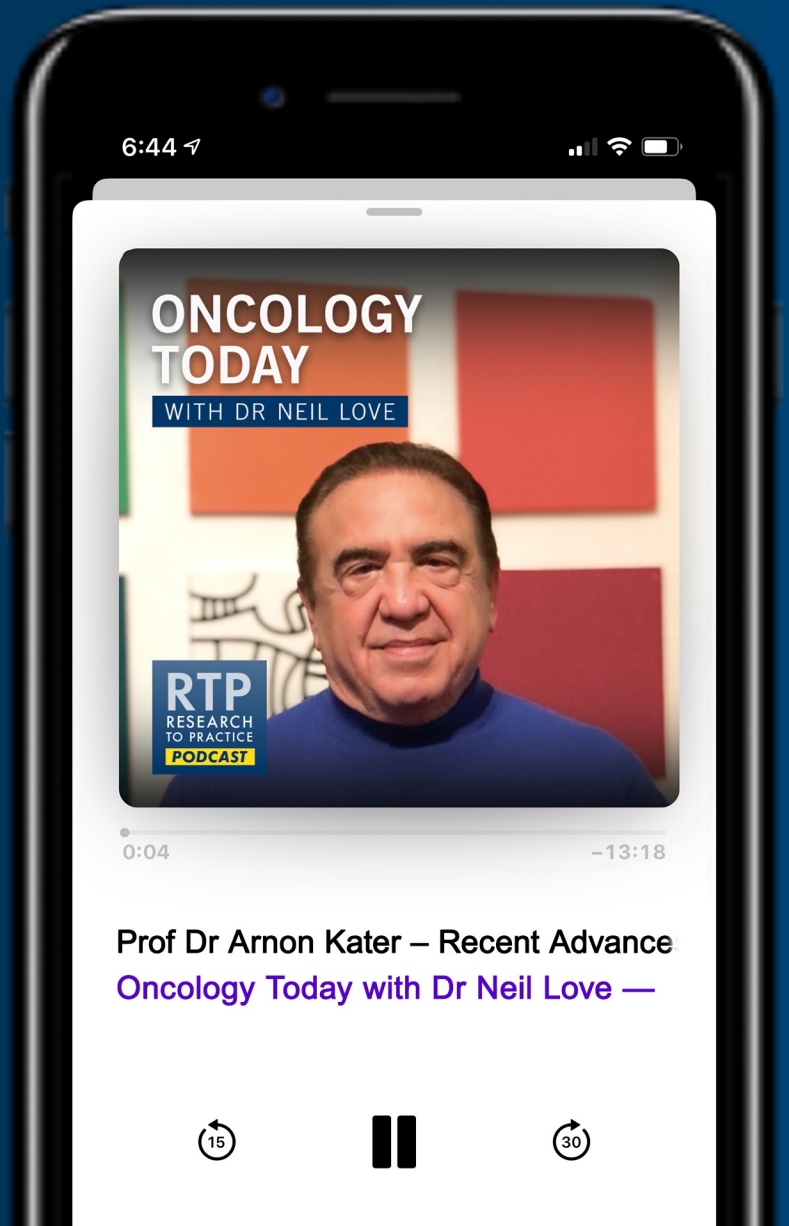

Meet The Professor

Optimizing the Management of Metastatic Castration-Resistant Prostate Cancer

Wednesday, January 5, 2022
12:30 PM – 1:30 PM ET

Faculty

Prof Karim Fizazi, MD, PhD

Moderator

Neil Love, MD

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Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

Breast Cancer

Thursday, January 6, 2022
5:00 PM – 6:00 PM ET

Faculty

Harold J Burstein, MD, PhD

Professor Peter Schmid, FRCP, MD, PhD

Moderator

Neil Love, MD

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Targeted Therapy for Non-Small Cell Lung Cancer

Tuesday, January 11, 2022
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Zofia Piotrowska, MD, MHS

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Neil Love, MD

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Meet The Professor

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

Wednesday, January 12, 2022
6:00 PM – 7:00 PM ET

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Tiffany A Traina, MD

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Neil Love, MD

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Immunotherapy and Other Nontargeted Approaches for Lung Cancer

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Anne S Tsao, MD, MBA

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Colorectal Cancer (Part 1 of a 3-Part Series)

Wednesday, January 19, 2022
10:15 PM – 11:45 PM ET

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Cathy Eng, MD
Christopher Lieu, MD
Alan P Venook, MD

Moderator

Kristen K Ciombor, MD, MSCI

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Gastroesophageal Cancers (Part 2 of a 3-Part Series)

Thursday, January 20, 2022
9:15 PM – 10:45 PM ET

Faculty

Yelena Y Janjigian, MD
Eric Van Cutsem, MD, PhD
Harry H Yoon, MD

Moderator

Samuel J Klempner, MD

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Hepatobiliary Cancers (Part 3 of a 3-Part Series)

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Richard S Finn, MD
Robin K Kelley, MD

Moderator

Tanios Bekaii-Saab, MD

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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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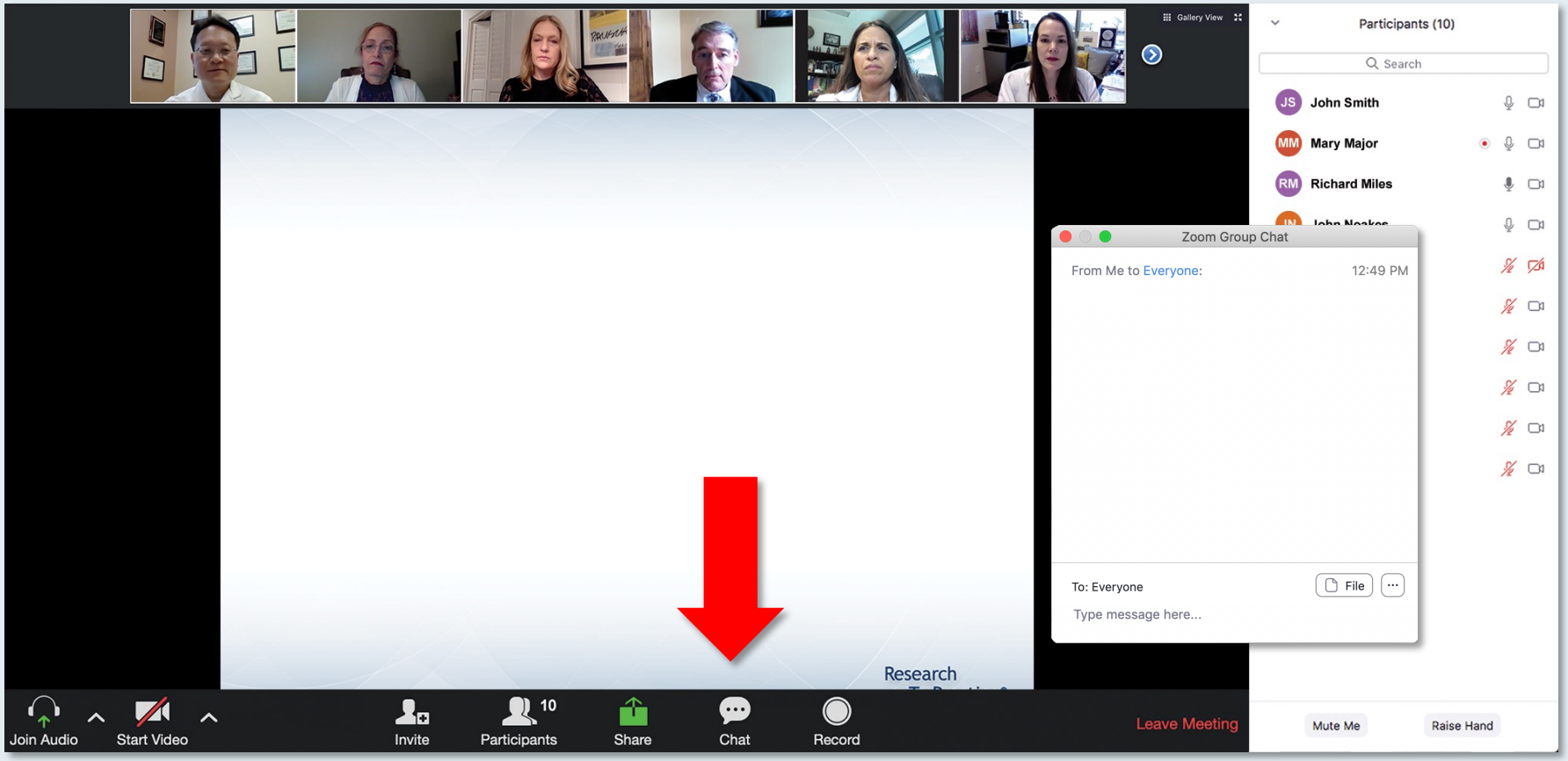

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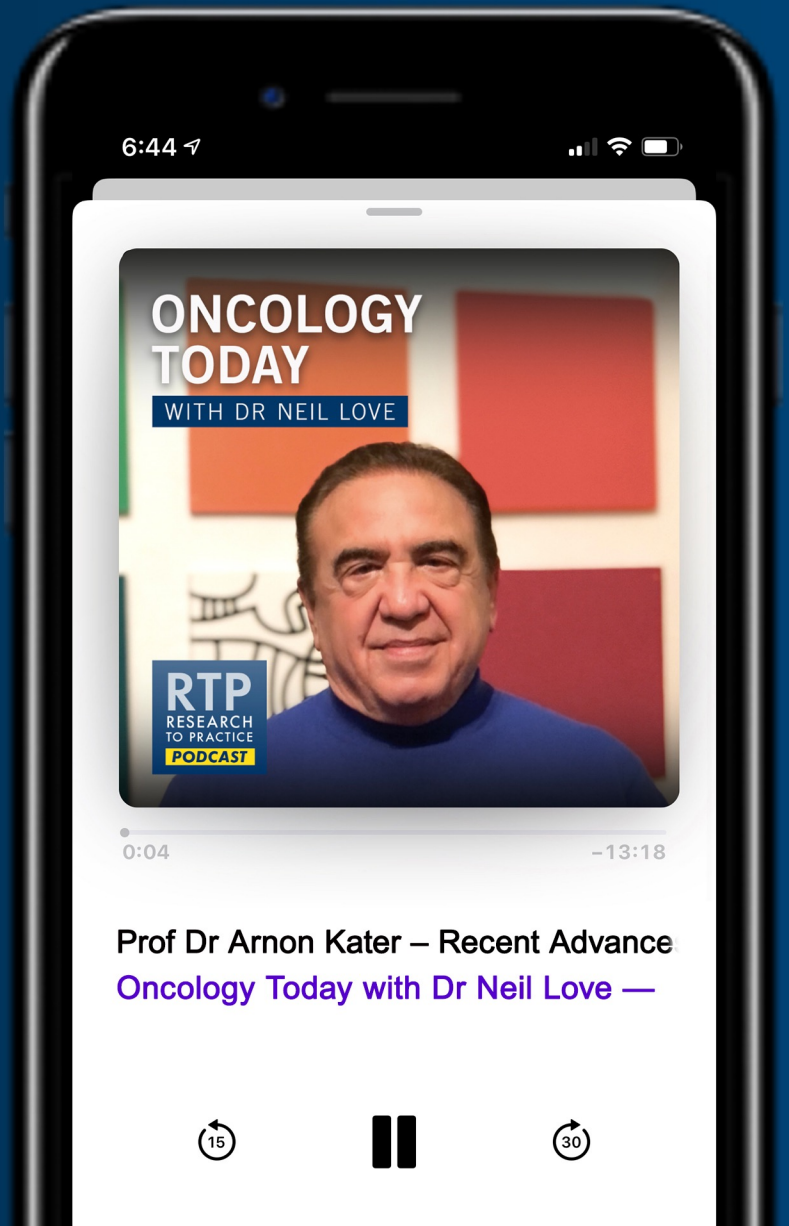

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Module 1: First- and Second-Line Treatment — Chemotherapy, Anti-CD20 Antibodies and IMiDs

Module 2: Sequencing Third Line and Beyond — Bispecific Antibodies, PI3K Inhibitors, Tazemetostat

Module 3: CAR T-Cell Therapy

Agenda

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Module 3: CAR T-Cell Therapy

In the past year approximately how many patients with follicular lymphoma (FL) did you care for clinically?

1. 0
2. 1-5
3. 6-10
4. 11-15
5. 16-20
6. 21-25
7. More than 25

In the past year approximately how many of your patients with FL died from their disease (including those with transformation)?

1. 0
2. 1
3. 2-5
4. 6-10
5. More than 10

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Module 1: First- and Second-Line Treatment — Chemotherapy, Anti-CD20 Antibodies and IMiDs

Key Topics

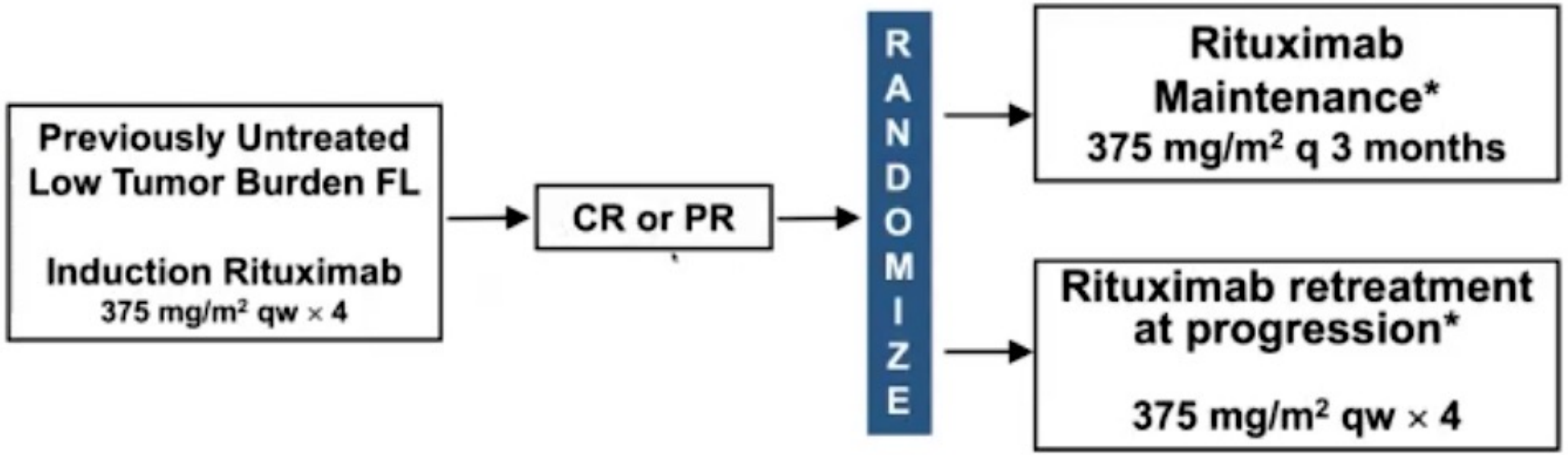
- **Use and duration of anti-CD20 antibodies**
  - RESORT: Long-term follow-up comparing 2 different rituximab doses
    - COVID-19 and vaccine considerations
- **Lenalidomide**
  - RELEVANCE: Lenalidomide/rituximab (R^2) for untreated FL
  - MAGNIFY: R^2 → maintenance for relapsed/refractory disease

To what extent has the risk of COVID-19 affected your use of anti-CD20 antibodies?

When using the combination of lenalidomide and rituximab either up front or in the second line, what is the optimal total duration of treatment, including maintenance, for a patient with FL who achieves a CR in 3-4 months?

When using the combination of lenalidomide and rituximab either up front or in the second line, what is the optimal total duration of treatment, including maintenance, for a patient with FL who achieves a PR in 3-4 months?

Long-Term Follow-Up of the RESORT Trial: A Phase III Study of 2 Different Rituximab Strategies in Low-Tumor-Burden FL



*Continue until treatment failure

No response to retreatment or PD within 6 months of Rituximab

Initiation of cytotoxic therapy or Inability to complete planned R treatment

Courtesy of Laurie H Sehn, MD, MPH

Long-Term Follow-Up of the RESORT Trial: A Phase III Study of 2 Different Rituximab Strategies in Low-Tumor-Burden FL

Original Conclusions: Kahl *J Clin Oncol* 2014

- Rituximab retreatment was as effective as maintenance rituximab for time to treatment failure
- MR was superior of RR for time to cytotoxic therapy
- Both strategies appeared to delay time to chemotherapy compared to historical controls
- 4x more drug administered with MR strategy
- No benefit in QOL or anxiety with MR (Wagner et al, JCO 2015)

- Rituximab retreatment is our recommended strategy if opting for single agent rituximab in LTB FL

Courtesy of Laurie H Sehn, MD, MPH

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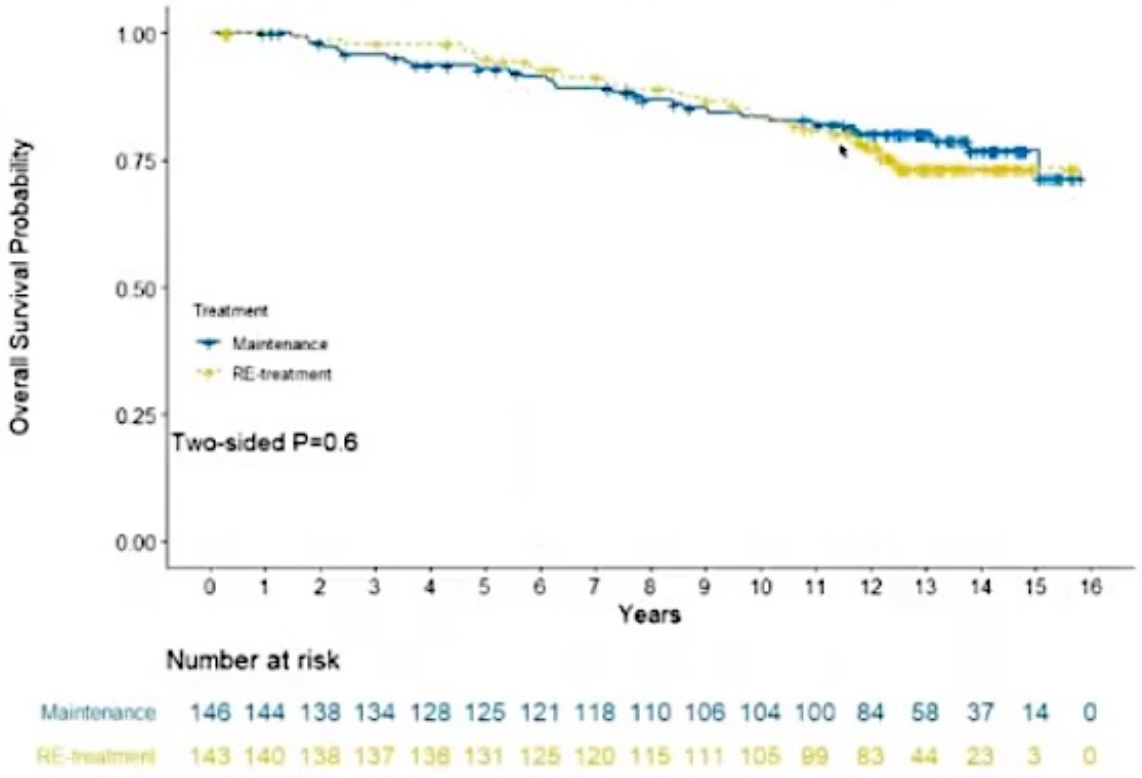


- OS at 10 yrs: 83% vs. 84%
- Transformation risk
  - 11 RR vs. 4 MR (per abstract)
  - Corrected: 6 RR vs. 2 MR (per final analysis)
  - possibly under reported
- 2nd malignancies
  - 19 on RR
  - 17 on MR

*Treatment of asymptomatic low-tumor-burden FL is currently not recommended due to COVID risk

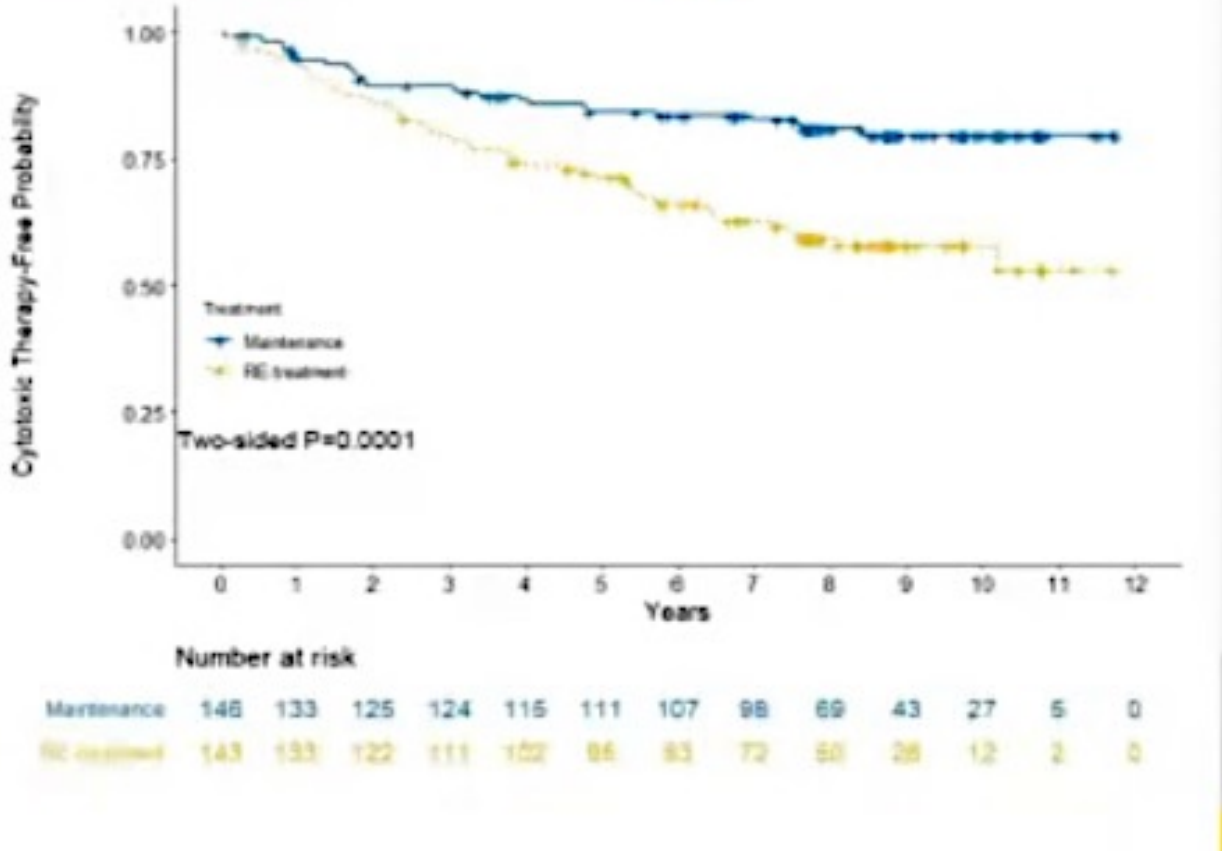
Courtesy of Laurie H Sehn, MD, MPH

Long-Term Follow-Up of the RESORT Trial: Freedom from First Cytotoxic Therapy

	3 years	5 years	7 years
MR	89%	84%	83%
RR	79%	71%	63%

HR 2.37 (1.5-3.76)

Median Follow up – 8.7 years

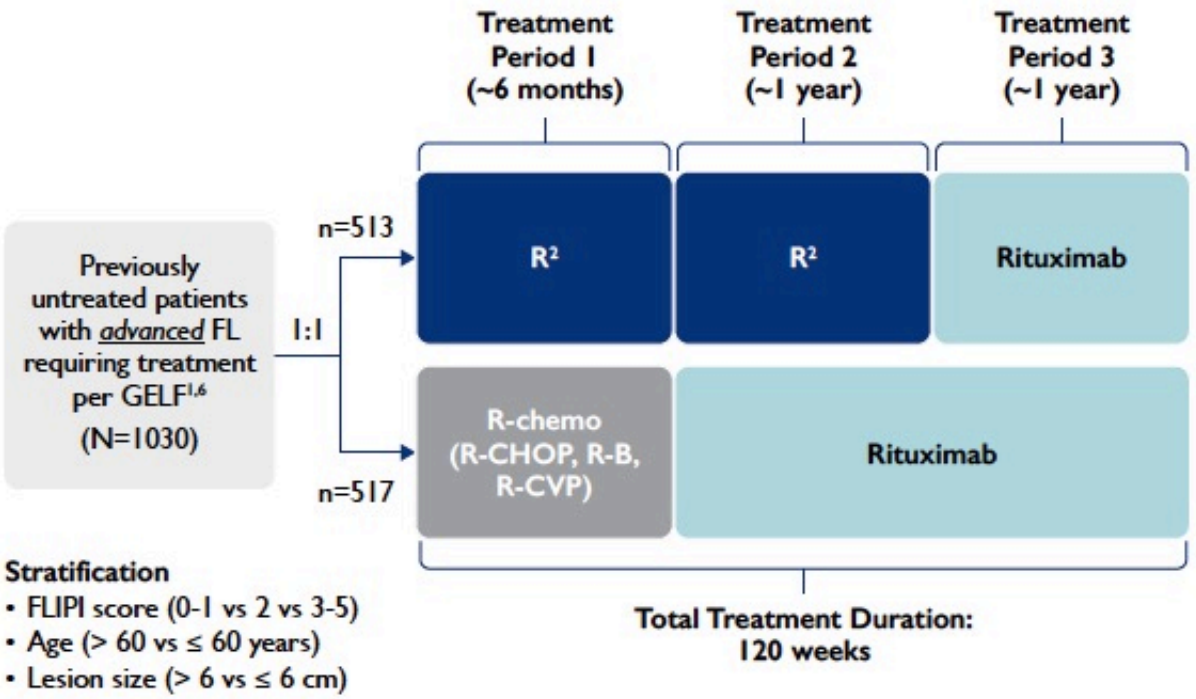


Kahl B et al. ASH 2021;Abstract 815.

Six-Year Results from the Phase III RELEVANCE Study: Similar Outcomes for Previously Untreated Follicular Lymphoma (FL) Receiving Lenalidomide with Rituximab (R^2) versus R-Chemotherapy Followed by Rituximab Maintenance

Morschhauser F, et al ASH 2021

Figure 1. RELEVANCE Study Design



Stratification
- FLIPI score (0-1 vs 2 vs 3-5)
- Age (> 60 vs ≤ 60 years)
- Lesion size (> 6 vs ≤ 6 cm)

- Co-primary endpoints: CR/CRu at 120 weeks and PFS by IRC based on 1999 IWG criteria
- The prespecified second interim analysis was done after 75% of total PFS events were reached

Figure 3: Progression-Free Survival by IRC, FDA Censoring Rules

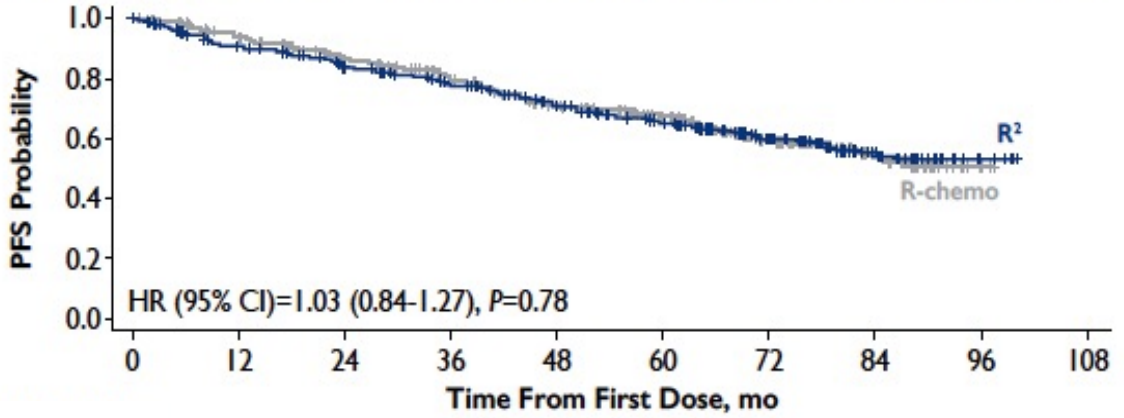
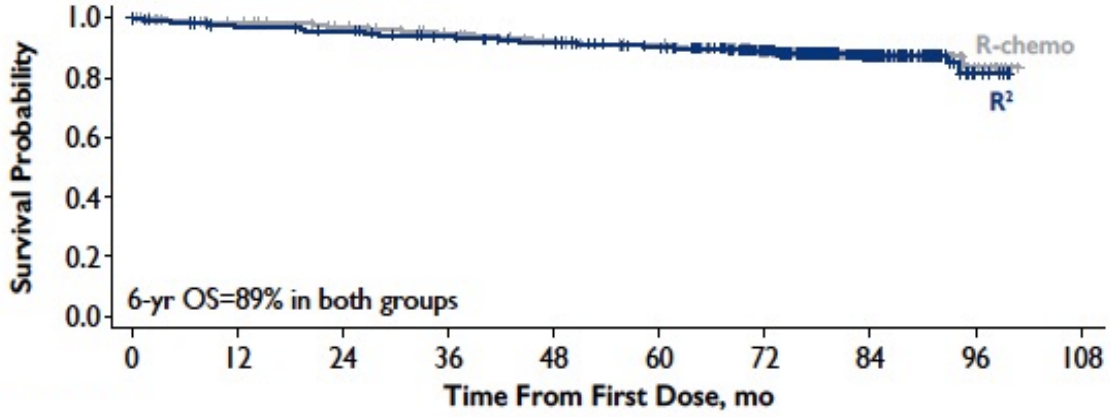


Figure 6: Overall Survival



Courtesy of Laurie H Sehn, MD, MPH

Six-Year Results from the Phase III RELEVANCE Study: Outcomes After Progression

Morschhauser F, et al ASH 2021

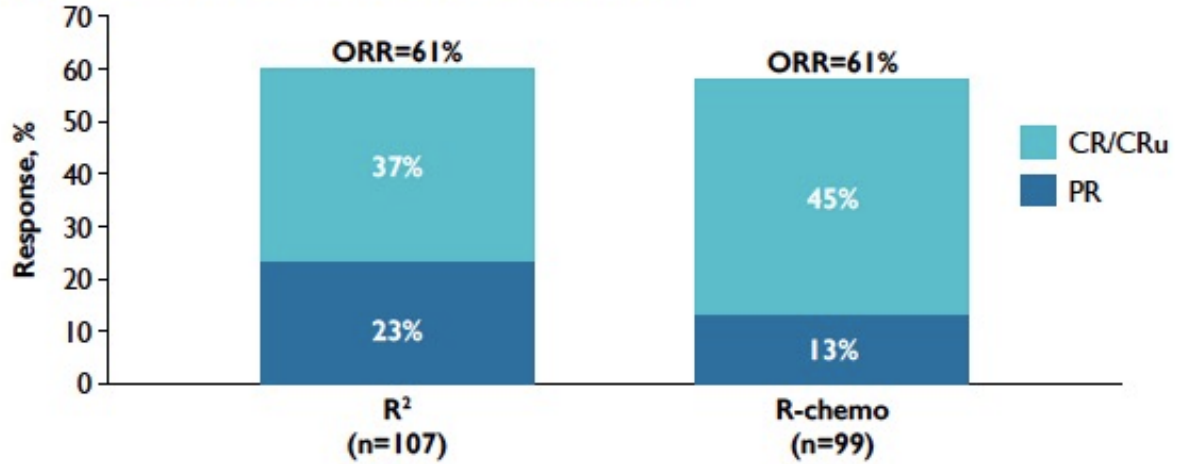
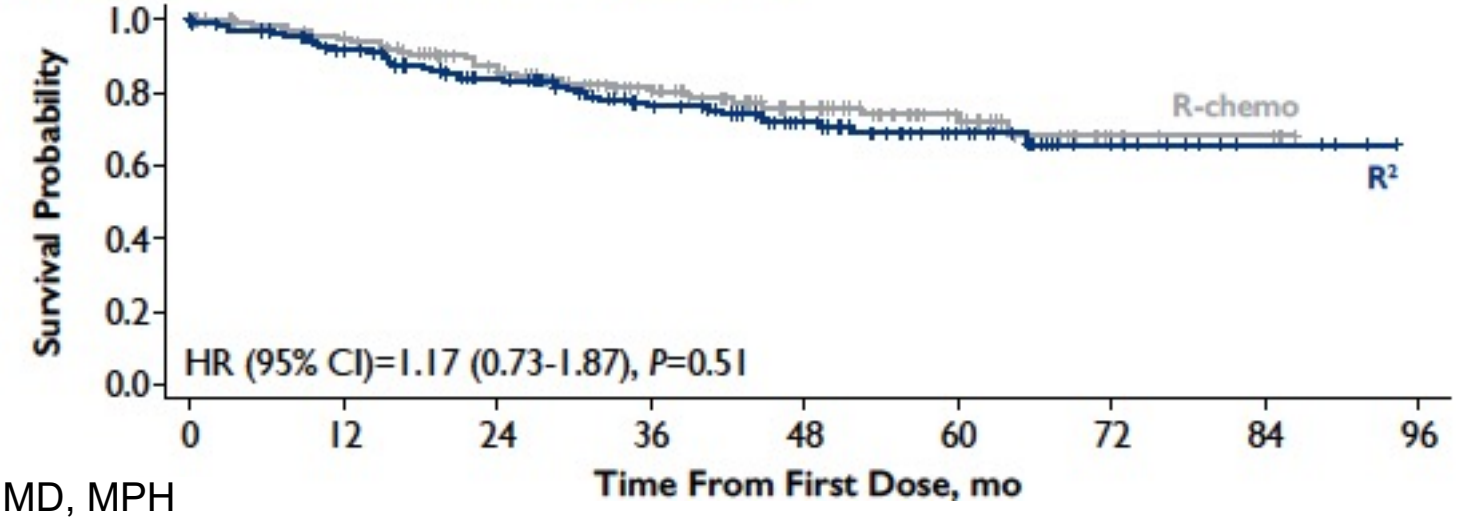
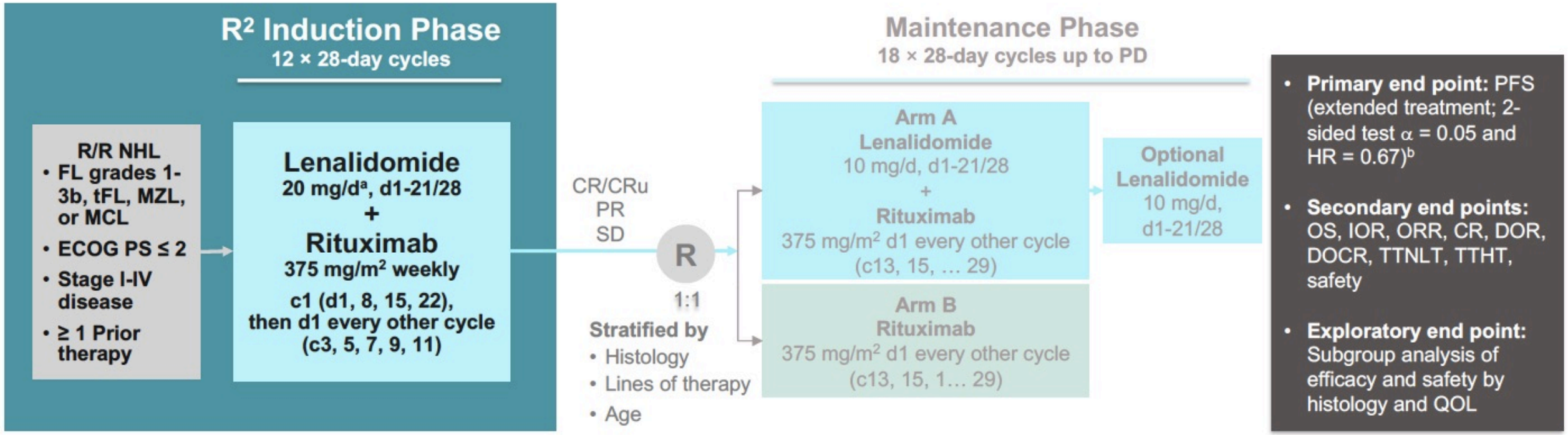


Figure 7: Survival After Progression



Courtesy of Laurie H Sehn, MD, MPH

Completed Induction Analysis of MAGNIFY: A Phase IIIb Study of R² Followed by Maintenance for R/R iNHL



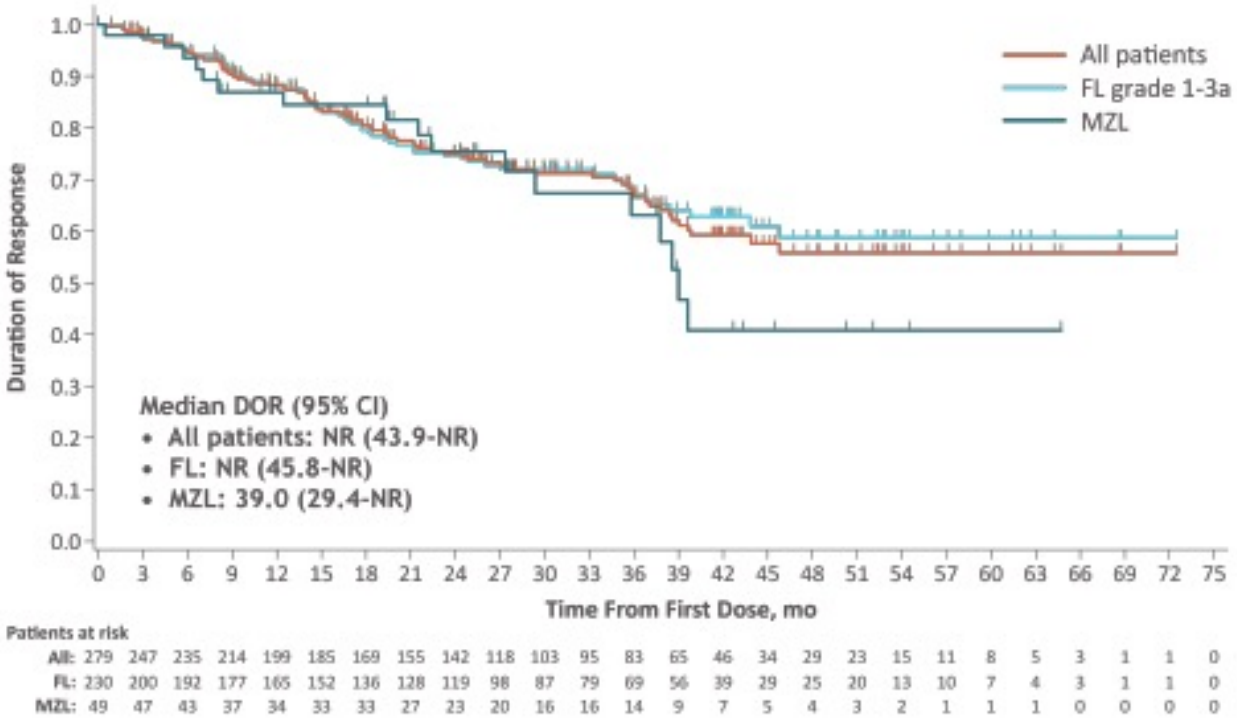
- Data presented here are the complete analysis from the induction phase in patients with FL grades 1-3a or MZL (FL grade 3b, tFL, and MCL not included)[c]
- The focus of this current interim analysis was ORR, DOR, PFS, and safety
  - Response was assessed by 1999 IWG criteria

Courtesy of Laurie H Sehn, MD, MPH

Lansigan et al, ASH 2021

Completed Induction Analysis of MAGNIFY: A Phase IIIb Study of R^2 Followed by Maintenance for R/R Indolent NHL

Duration of Response



- Confirms efficacy of R^2 seen in AUGMENT trial
- Benefit seen in FL and MZL, rituximab-refractory, double-refractory, and early relapsers
- No new safety findings
- Randomized phase with test maintenance with R^2 vs rituximab

Courtesy of Laurie H Sehn, MD, MPH

Lansigan et al, ASH 2021

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Module 2: Sequencing Third Line and Beyond — Bispecific Antibodies, PI3K Inhibitors, Tazemetostat

Key Topics

- **Bispecific antibodies: Efficacy and toxicity**
  - Mosunetuzumab as monotherapy or in combination with polatuzumab vedotin or lenalidomide
  - Glofitamab as monotherapy or in combination with obinutuzumab
  - Dose escalation of subcutaneous epcoritamab
- **Selection of PI3K inhibitor; addition of anti-CD20 antibody**
  - CHRONOS: Copanlisib + rituximab for untreated and relapsed/refractory disease
  - Umbralisib for relapsed/refractory indolent lymphoma
- **Tazemetostat: EZH2 mutated and nonmutated**

To approximately how many patients with FL have you administered a PI3K inhibitor?

1. 0
2. 1
3. 2
4. 3
5. More than 3

To approximately how many patients with FL have you administered tazemetostat?

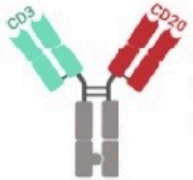
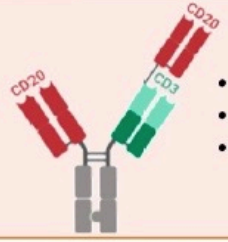
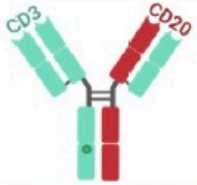
1. 0
2. 1
3. 2
4. 3
5. More than 3

If the bispecific antibody mosunetuzumab was approved by the FDA for patients with FL after 2 lines of treatment, would you use it before a PI3K inhibitor or tazemetostat for a 60-year-old patient?

1. Yes
2. No
3. I'm not sure

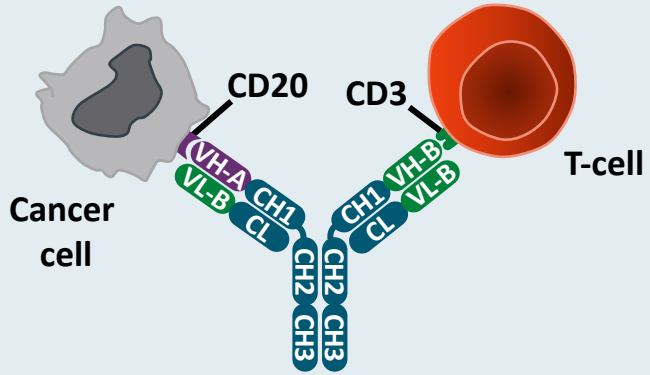
If the bispecific antibody mosunetuzumab was approved by the FDA for patients with FL after 2 lines of treatment, would you use it before a PI3K inhibitor or tazemetostat for an 80-year-old patient?

Structure of Selected Bispecific Antibodies

Bi-Specific Antibody	Targets	Design	Ig Fragment Formats
blinatumomab	CD19 x CD3		• two murine scFv joined by a glycine-serine linker • monovalent CD19 and monovalent CD3 binding • cloned from anti-CD19 (clone HD37) and anti-CD3 (clone L2K-07) murine mAbs
mosunetuzumab	CD20 x CD3		• humanized mouse heterodimeric IgG1-based antibody • monovalent CD20 and monovalent CD3ε binding • modified Fc devoid of FcγR and complement binding
glofitamab	$(CD20)_2$ x CD3		• humanized mouse IgG1-based antibody • bivalent CD20 and monovalent CD3ε binding • modified Fc devoid of FcγR and complement binding
odronextamab	CD20 x CD3		• fully human IgG4-based heterodimeric antibody • monovalent CD20 and monovalent CD3ε binding • Fc-dependent effector function-minimized antibody with Fc of the anti-CD3ε heavy chain modified to reduce Protein A binding • common κ light chain from anti-CD3ε mAb
epcoritamab	CD20 x CD3		• humanized mouse IgG1-based heterodimeric antibody • monovalent CD20 and monovalent CD3 binding • IgG1 Fc modified to minimize Fc-dependent effector functions and to control Fab-arm exchange of mAb half-molecules, resulting in high bispecific product yield

Ig, immunoglobulin; scFv, single-chain variable fragment; mAb, monoclonal antibody; Fc, fragment crystallizable; FcγR, Fc gamma receptor

Anti-CD20/CD3 Bispecific Antibody



Simultaneous binding of CD20 on malignant B cells and CD3 on cytotoxic T cells results in crosslinking of CD3, activation of T cells, and cancer cell killing

Schuster SJ. *Hematol Oncol* 2021;39(S1):113-16.

Courtesy of John P Leonard, MD

FDA Grants Breakthrough Therapy Designation for the CD20 x CD3 Bispecific Cancer Immunotherapy Mosunetuzumab for Follicular Lymphoma

Press Release — July 14, 2020

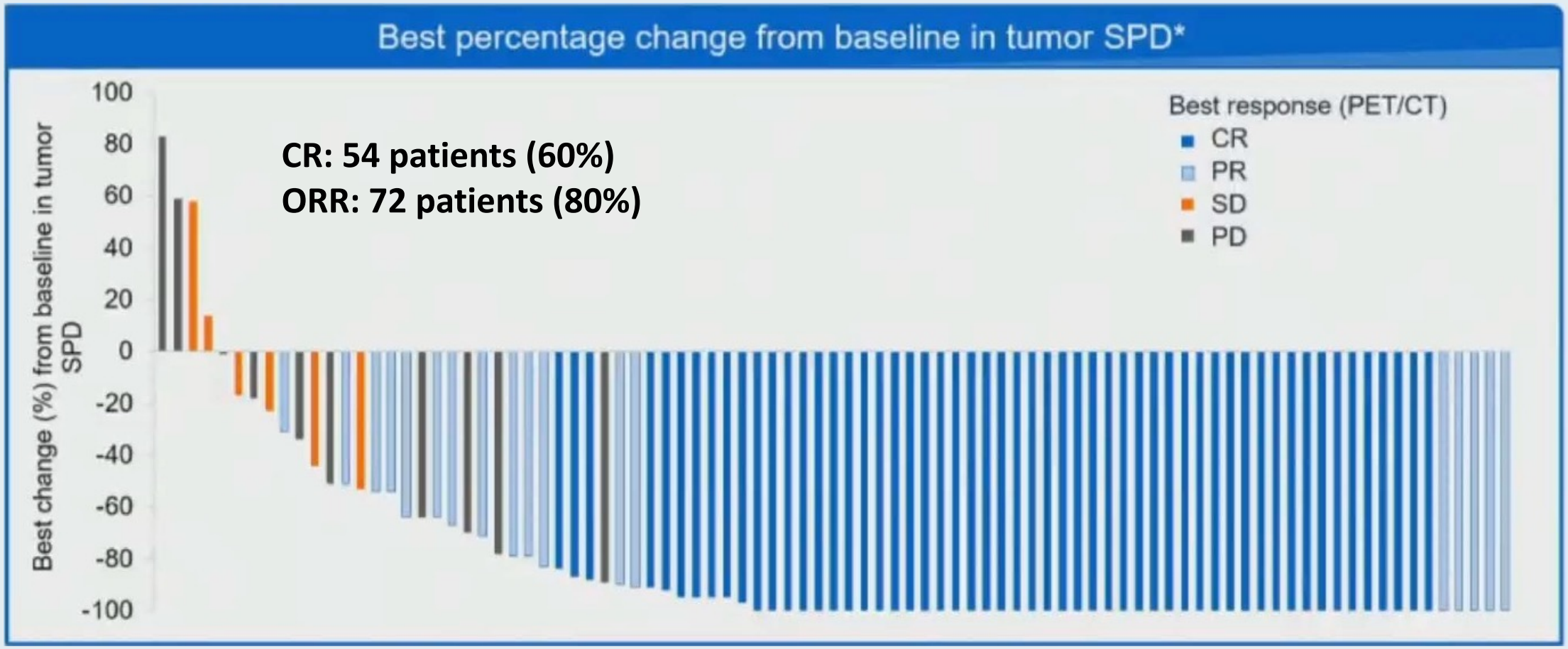
"[The] investigational CD20xCD3 T-cell engaging bispecific mosunetuzumab has been granted Breakthrough Therapy Designation (BTD) by the US Food and Drug Administration (FDA) for the treatment of adult patients with relapsed or refractory (R/R) follicular lymphoma who have received at least two prior systemic therapies.

This designation was granted based on encouraging efficacy results observed in the phase I/Ib GO29781 study [NCT02500407] investigating mosunetuzumab in R/R non-Hodgkin lymphoma (NHL). The safety profile of this T-cell engaging bispecific was consistent with its mechanism of action."

www.roche.com/investors/updates/inv-update-2020-07-14b.htm

Courtesy of John P Leonard, MD

Phase I/II Study of Mosunetuzumab Monotherapy in Patients with R/R FL Who Have Received ≥2 Lines of Therapy



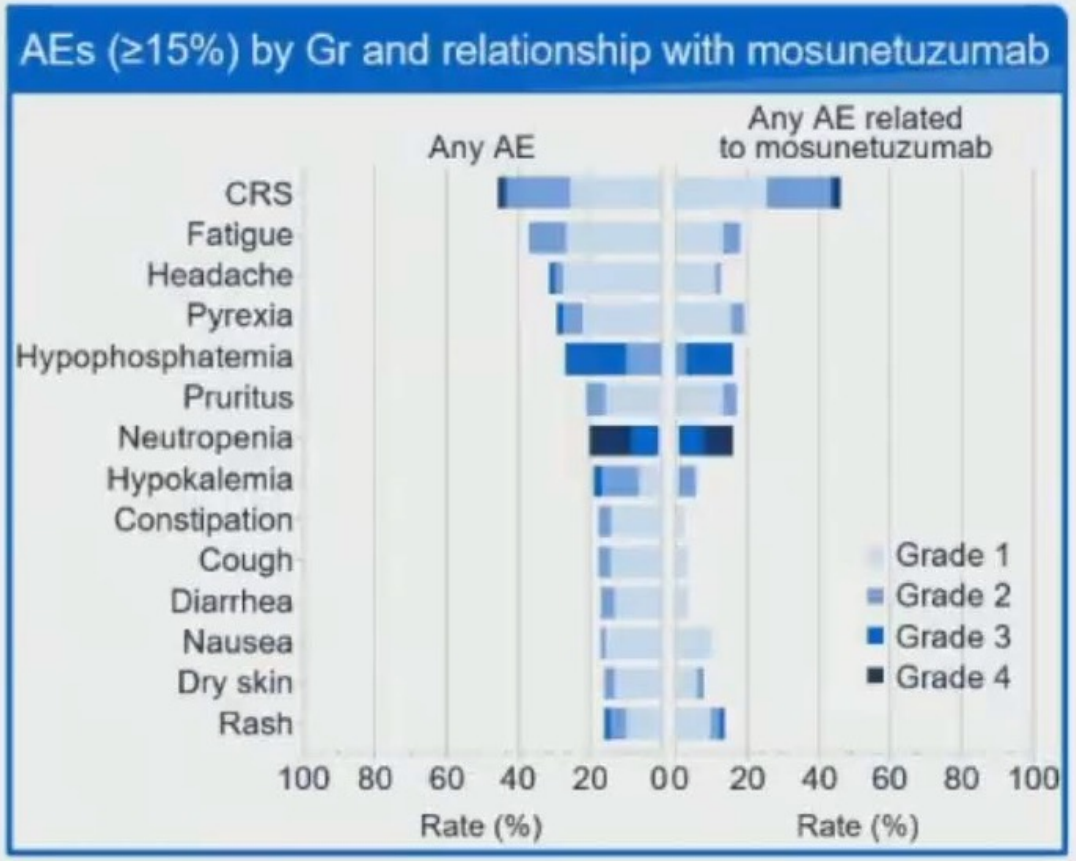
- Median DoR: 22.8 months
- Median PFS: 17.9 months

Budde LE et al. ASH 2021;Abstract 127.

Courtesy of John P Leonard, MD

Safety Profile of Mosunetuzumab Monotherapy for Patients with R/R FL Who Have Received ≥2 Lines of Therapy: *Adverse Events (AEs)*

N (%)	N=90
AE	90 (100%)
Mosunetuzumab related*	83 (92.2%)
Grade 3–4 AE	63 (70.0%)
Mosunetuzumab related*	46 (51.1%)
Serious AE	42 (46.7%)
Mosunetuzumab related*	30 (33.3%)
Grade 5 (fatal) AE	2 (2.2%)†
Mosunetuzumab related*	0
AE leading to discontinuation of treatment	4 (4.4%)‡
Mosunetuzumab related*	2 (2.2%)‡

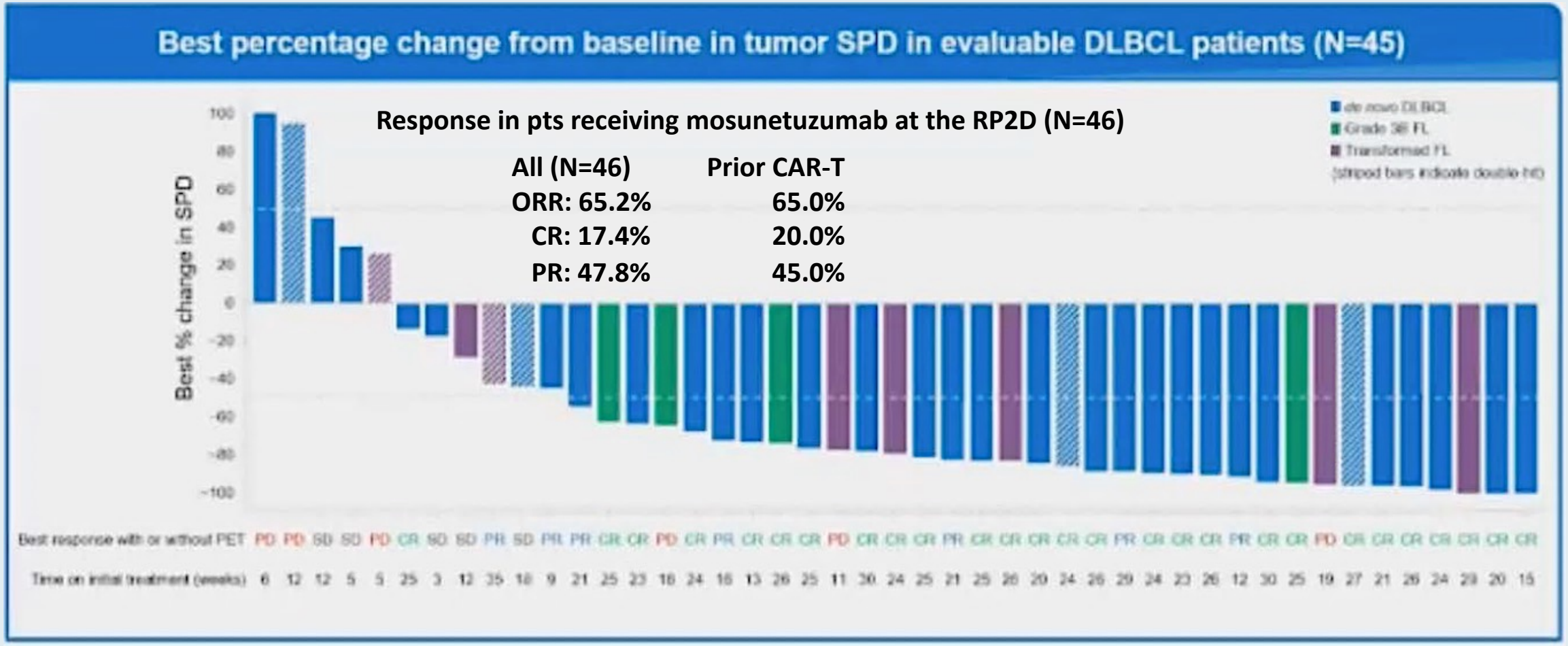


*AE considered related to treatment by the investigator; †mosunetuzumab unrelated: malignant neoplasm progression and unexplained death (1 patient each); ‡mosunetuzumab related: CRS (2 patients); mosunetuzumab unrelated: Esptein-Barr viremia and Hodgkin's disease (1 patient each); AE, adverse event; Gr, Grade

Budde LE et al. ASH 2021;Abstract 127.

Courtesy of John P Leonard, MD

Phase Ib/II Study of Mosunetuzumab with Polatuzumab Vedotin for R/R Aggressive B-Cell NHL: *Response*



Budde LE et al. ASH 2021;Abstract 533.

Courtesy of John P Leonard, MD

Mosunetuzumab with Polatuzumab Vedotin for R/R Aggressive B-Cell NHL: *CRS and Other AEs of Interest*

N (%)	N=63
CRS (any Grade)*	11 (17.5)
Grade 1	10 (15.9)
Grade 2	1 (1.6)
Grade 3	0
Serious AE of CRS (any Grade)†	5 (7.9)
Median time to first CRS onset, days (range)	10 (1–23)
Median CRS duration, days (range)	1 (1–4)
Corticosteroids for CRS management	1 (1.6)
Low-flow oxygen for CRS management	1 (1.6)
Tocilizumab for CRS management	0

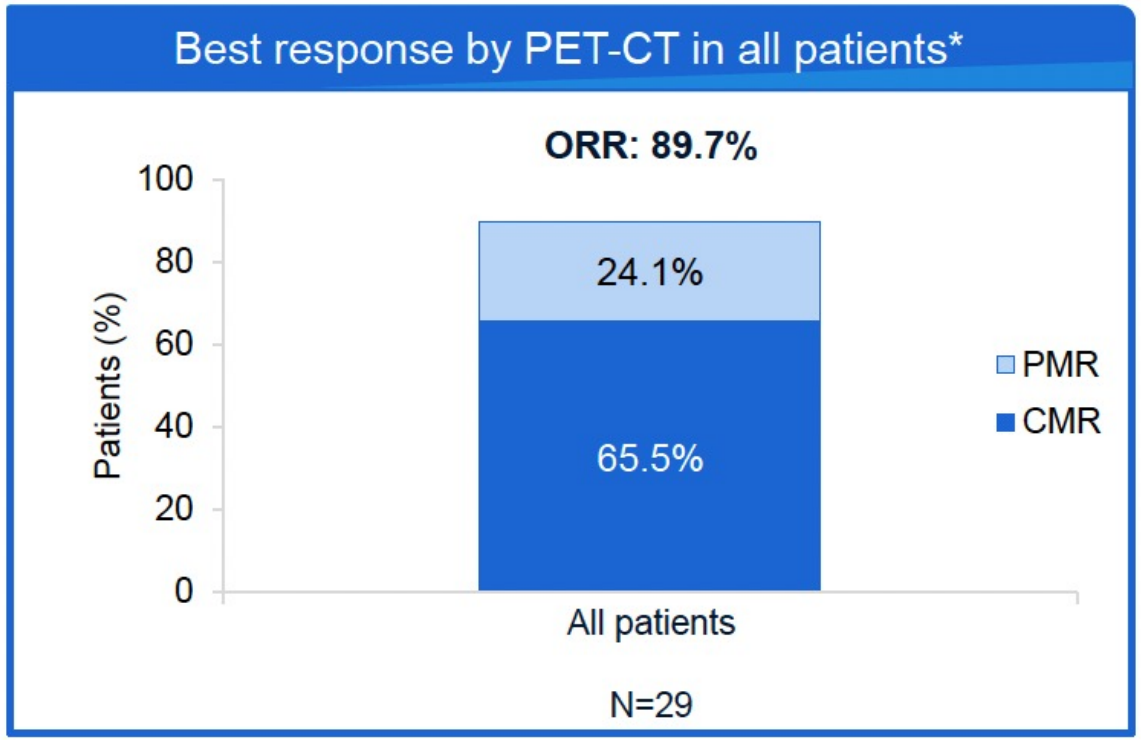
Event	CTCAE Gr	N (%)
ICANS*	Any Gr	5 (7.9)
	Gr 3–4	2 (3.2)
Neuropathy†	Any Gr	21 (33.3)
	Gr 3–4	4 (6.3)
Neutropenia‡	Any Gr	21 (33.3)
	Gr 3–4	14 (22.2)
Serious AE of infection§	Any Gr	9 (14.3)
	Gr 3–4	8 (12.7)
	Gr 5	1 (1.6)

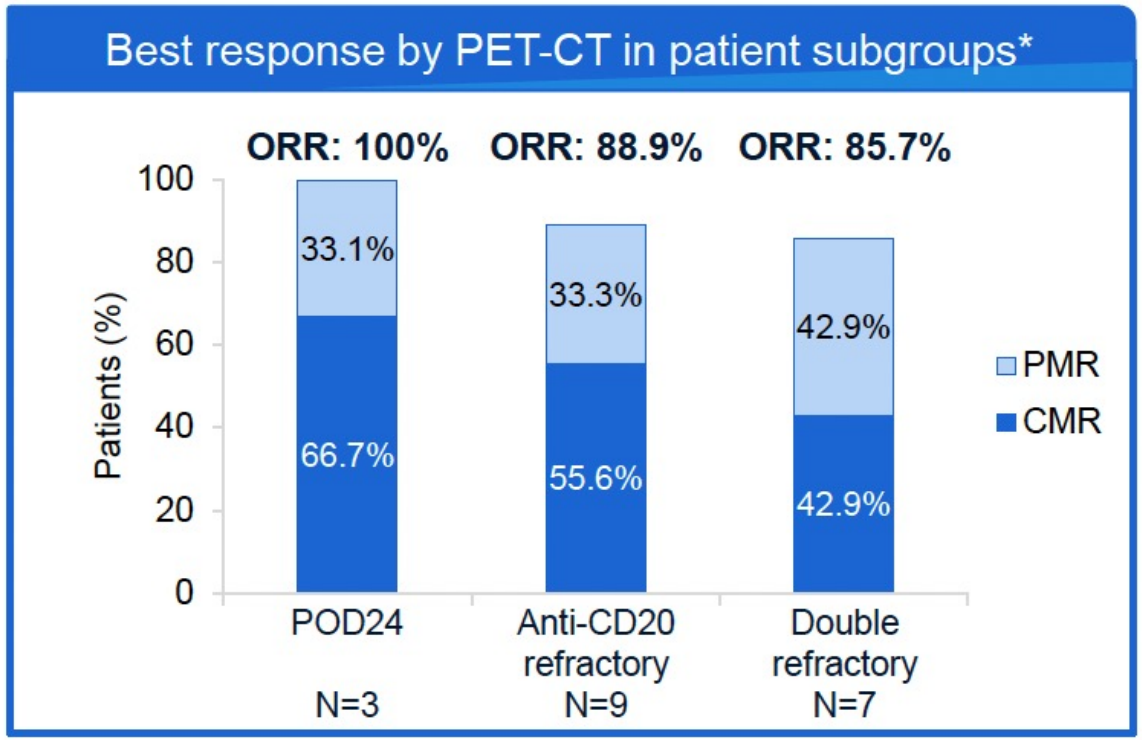
Budde LE et al. ASH 2021;Abstract 533.

Courtesy of John P Leonard, MD

Stage Ib Study of Mosunetuzumab + Lenalidomide for R/R FL: *Response*

- Median time to first / best response: 2.5 mo (range: 1.4–5.3) / 2.5 mo (range: 1.4–10.7)





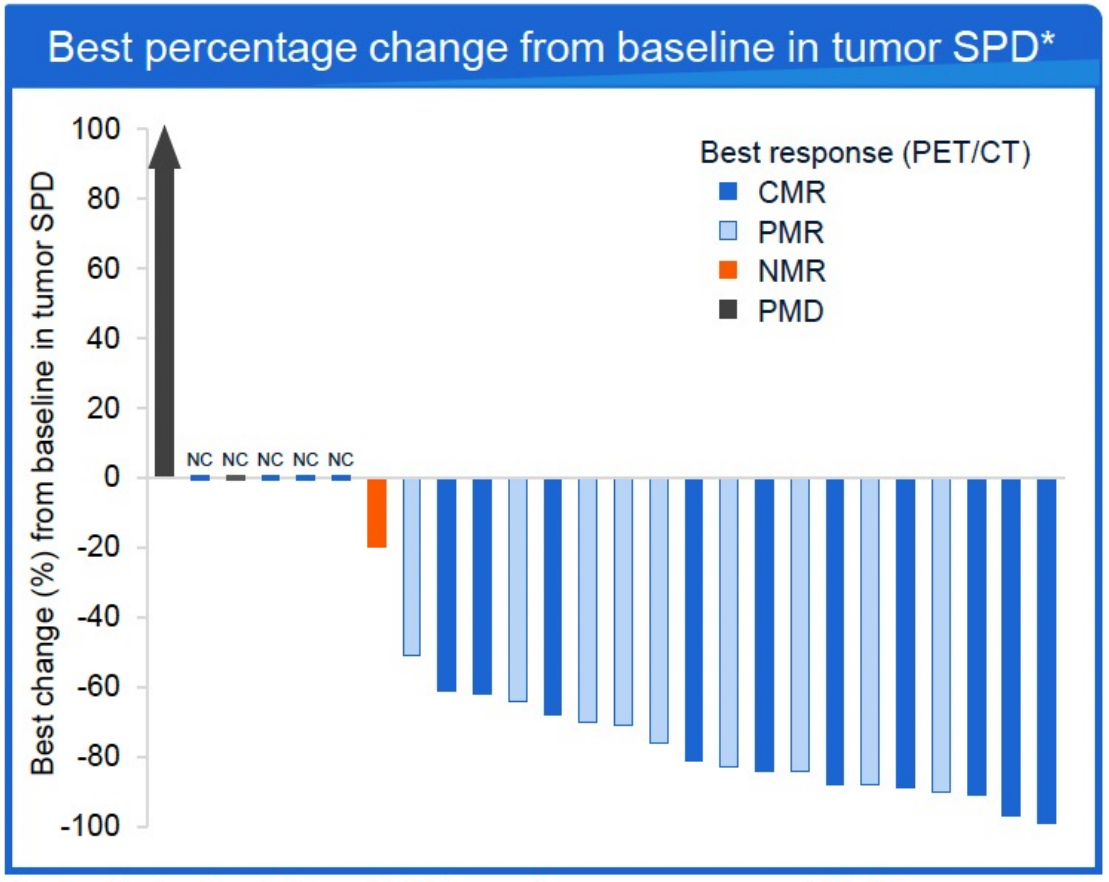
- **High ORR and CMR rate in overall population and in patients with high-risk disease**

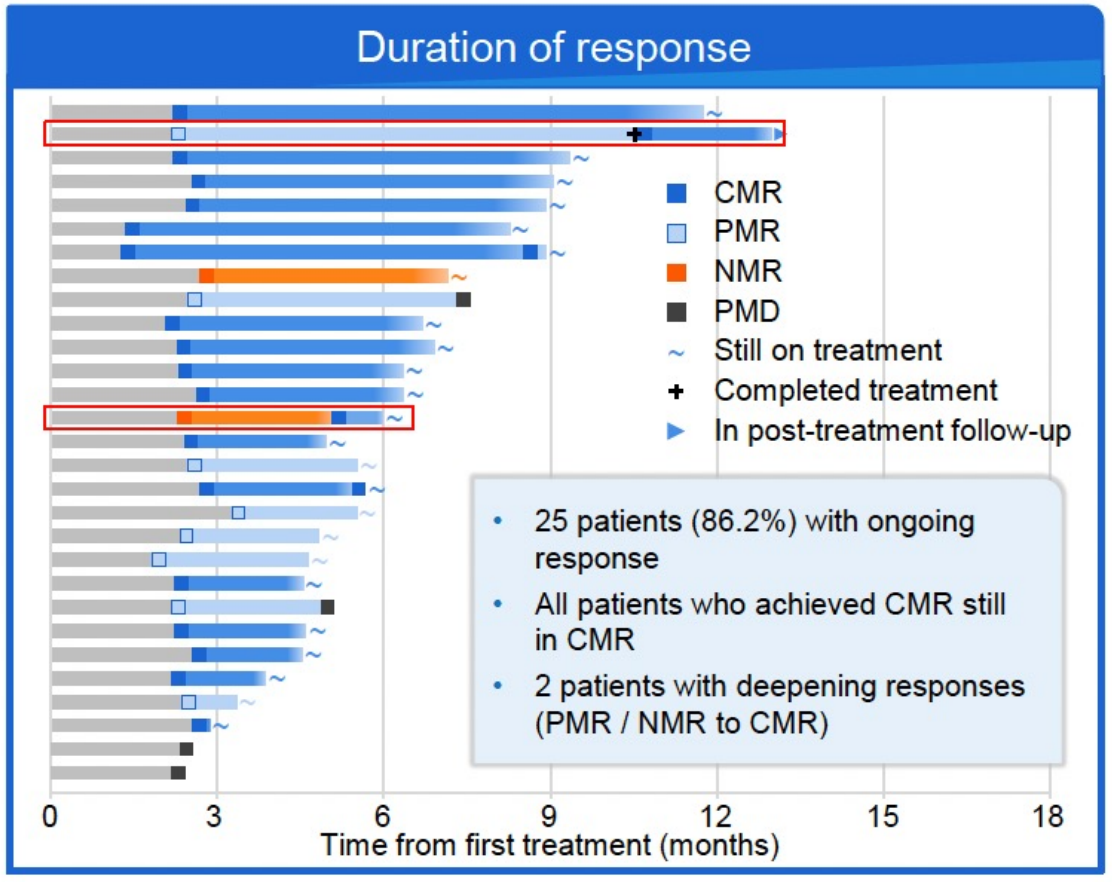
Morschhauser F et al. ASH 2021;Abstract 129.

Courtesy of John P Leonard, MD

Mosunetuzumab + Lenalidomide for R/R FL: *Change in Tumor Sum of Product Diameters and Duration of Response*

- Median duration of follow-up: 5.4 months (range: 3–12)





Morschhauser F et al. ASH 2021;Abstract 129.

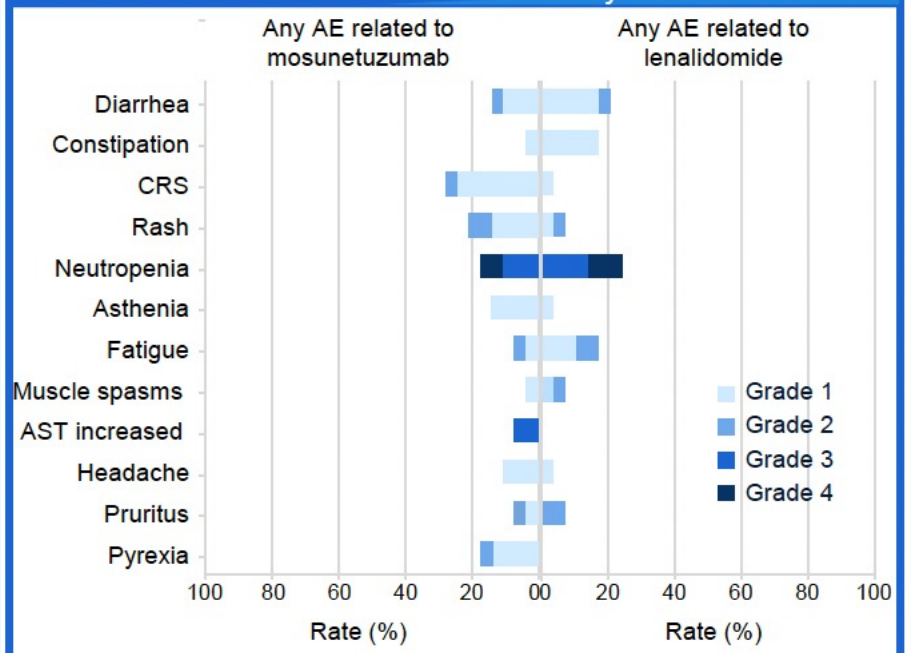
Courtesy of John P Leonard, MD

Mosunetuzumab + Lenalidomide for R/R FL: *Summary of Adverse Events*

- Median duration of follow-up: 5.4 months (range: 3–12)

	N=29
AE Related to mosunetuzumab / lenalidomide	29 (100%) 27 (93.1%) / 23 (79.3%)
Grade 3–4 AE Related to mosunetuzumab / lenalidomide	13 (44.8%) 1 (3.4%) / 1 (3.4%)
Serious AE Related to mosunetuzumab / lenalidomide	9 (31.0%) 6 (20.7%) / 1 (3.4%)
Grade 5 (fatal) AE	0
AE leading to mosunetuzumab / lenalidomide discontinuation	0 / 1 (3.4%)
AE leading to mosunetuzumab dose delay	6 (20.7%)
AE leading to lenalidomide dose reduction	2 (6.9%)
AE leading to lenalidomide temporary dose interruption	6 (20.7%)
AE leading to lenalidomide dose reduction AND temporary dose interruption	4 (13.7%)

AEs with ≥15% incidence overall and corresponding rates of treatment-related events by Grade



- **M-Len had a favorable safety profile. No AEs led to mosunetuzumab discontinuation.**

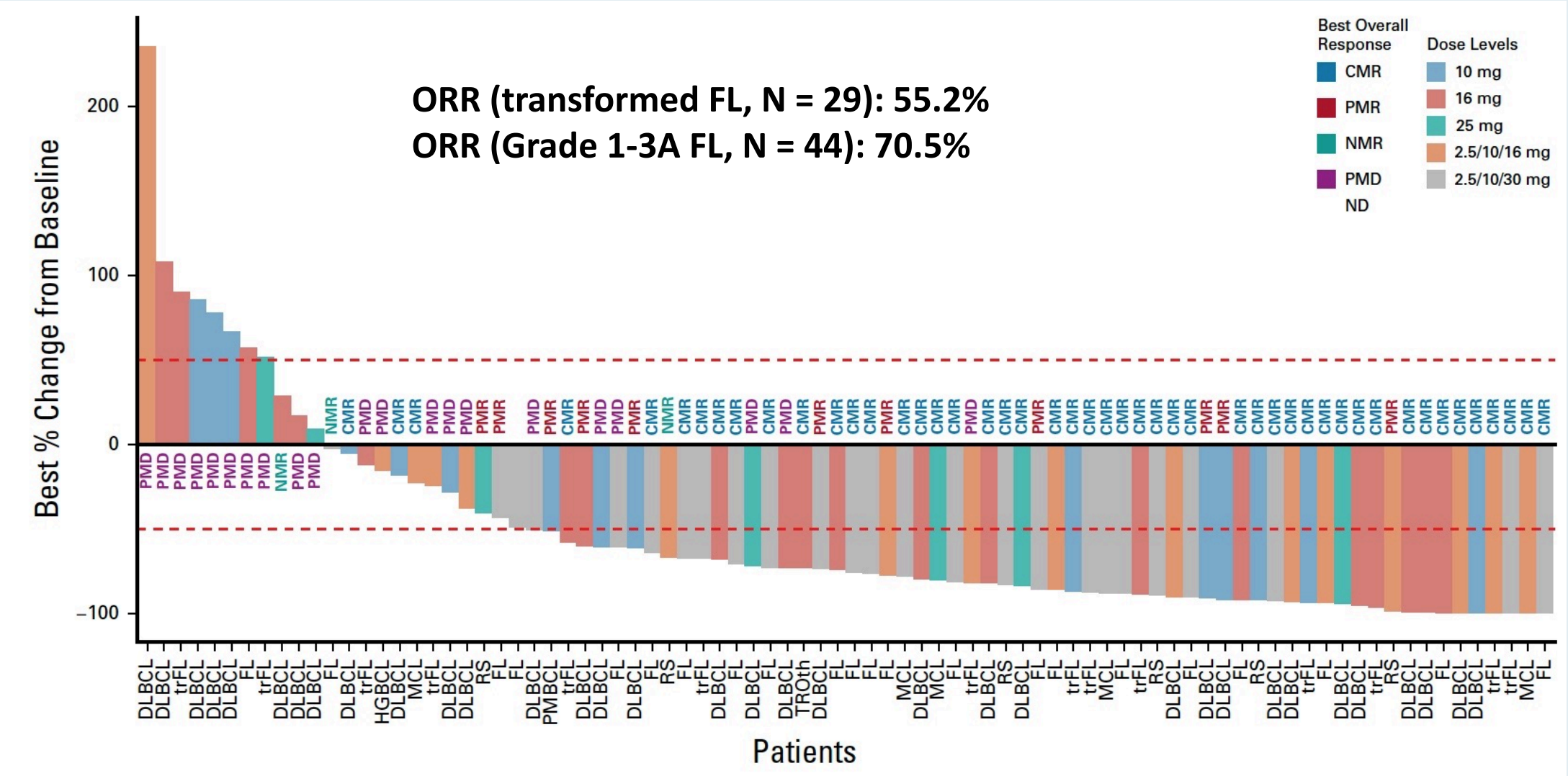
CRS Grade 3-4: 0%
Neutropenia Grade 3-4: 24.1%

ICANS Grade 3-4: 0%
Serious AE of infection Grade 3-4: 6.9%

Morschhauser F et al. ASH 2021;Abstract 129.

Courtesy of John P Leonard, MD

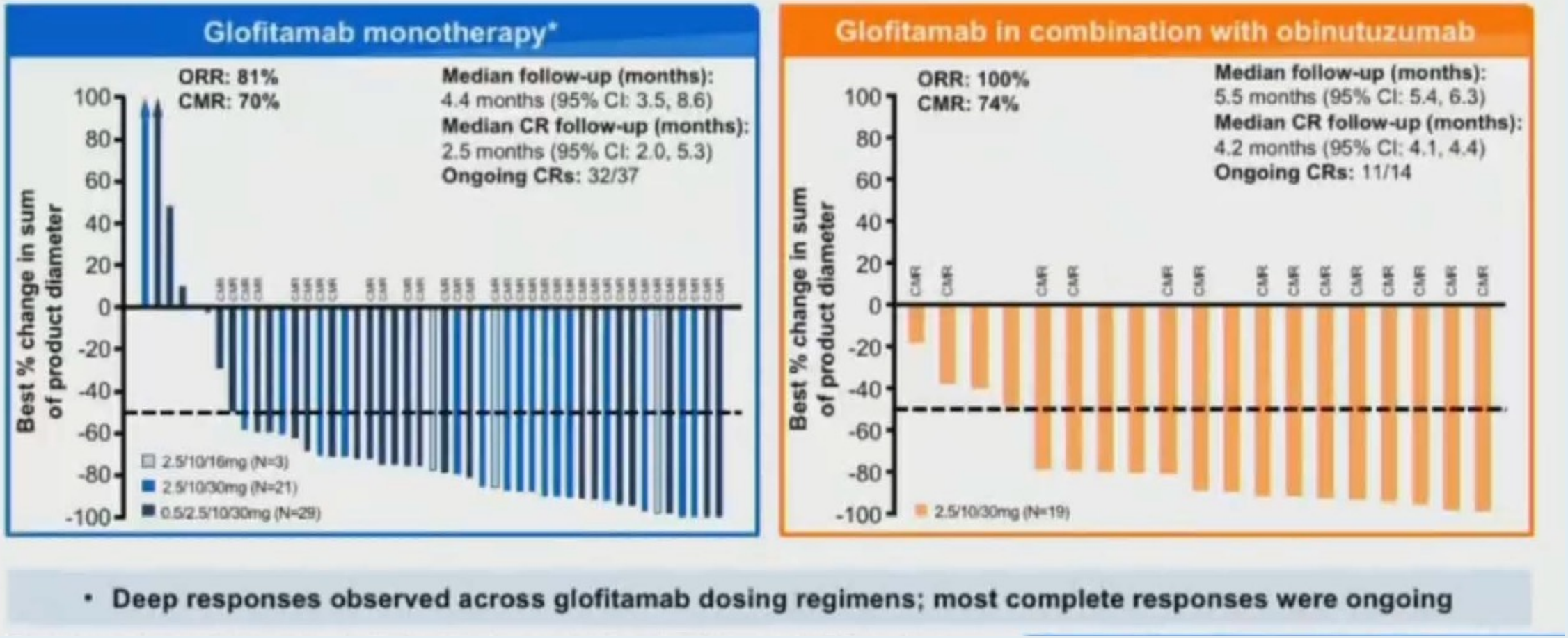
Phase I Study of Glofitamab in R/R B-Cell Lymphomas: *Response*



Hutchings M et al. *J Clin Oncol* 2021;39:1959-70.

Courtesy of John P Leonard, MD

Phase I/II Study of Glofitamab as Monotherapy or in Combination with Obinutuzumab for R/R FL: *Response*

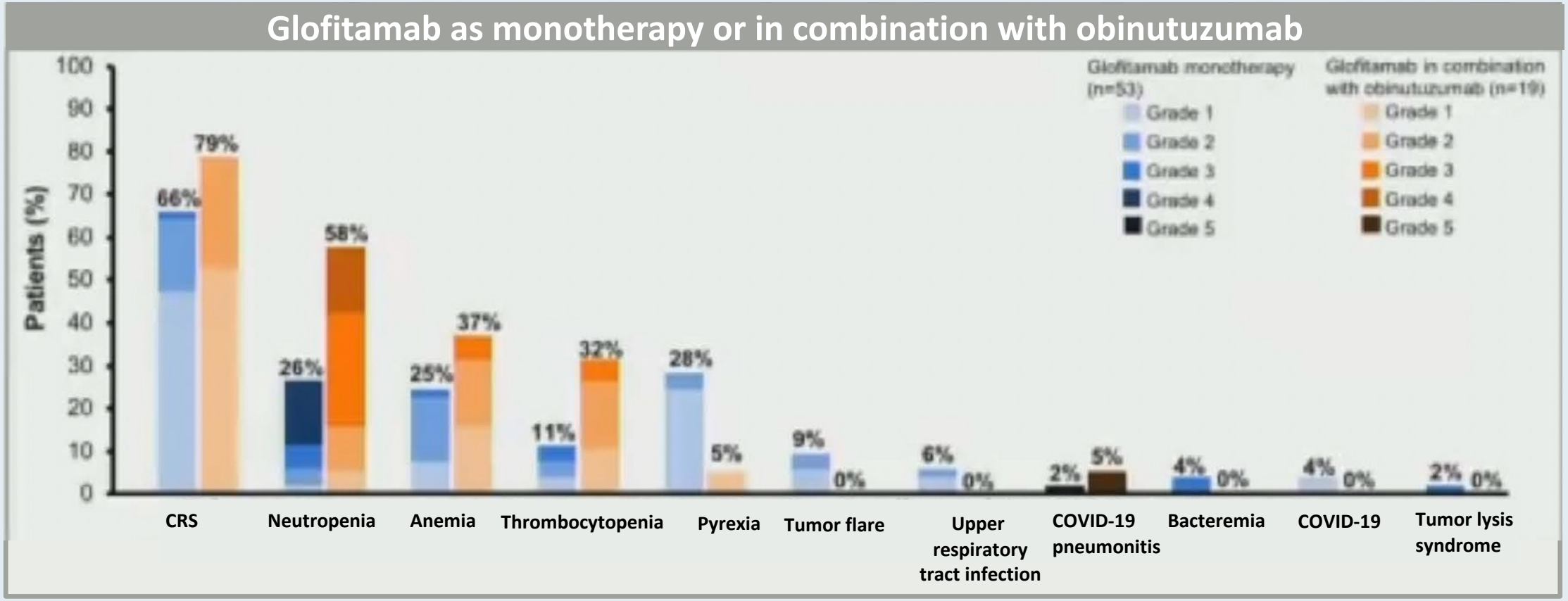


- Myelosuppression was more common with the combination
- CRS rates were high and comparable, and cases were mainly low grade

Morschhauser F et al. ASH 2021;Abstract 128.

Courtesy of John P Leonard, MD

Glofitamab as Monotherapy or in Combination with Obinutuzumab for R/R FL: *Common and Clinical AEs of Interest*



Morschhauser F et al. ASH 2021;Abstract 128.

Courtesy of John P Leonard, MD

Phase I/II Dose Escalation of Subcutaneous Epcoritamab for R/R B-Cell NHL: *Adverse Events of Special Interest*

	Epcoritamab dose			Total (n=68)
	≤24 mg (n=53)	48 mg (n=12)	60 mg (n=3)	
Cytokine release syndrome				
Total	30 (57%)	8 (67%)	2 (67%)	40 (59%)
Grade 1	15 (28%)	4 (33%)	1 (33%)	20 (29%)
Grade 2	15 (28%)	4 (33%)	1 (33%)	20 (29%)
Neurological symptoms				
Total	4 (8%)	0	0	4 (6%)
Grade 1	2 (4%)	0	0	2 (3%)
Grade 3	2 (4%)	0	0	2 (3%)
Clinical tumour lysis syndrome				
Total	0	1 (8%)	0	1 (1%)
Grade 3	0	1 (8%)	0	1 (1%)

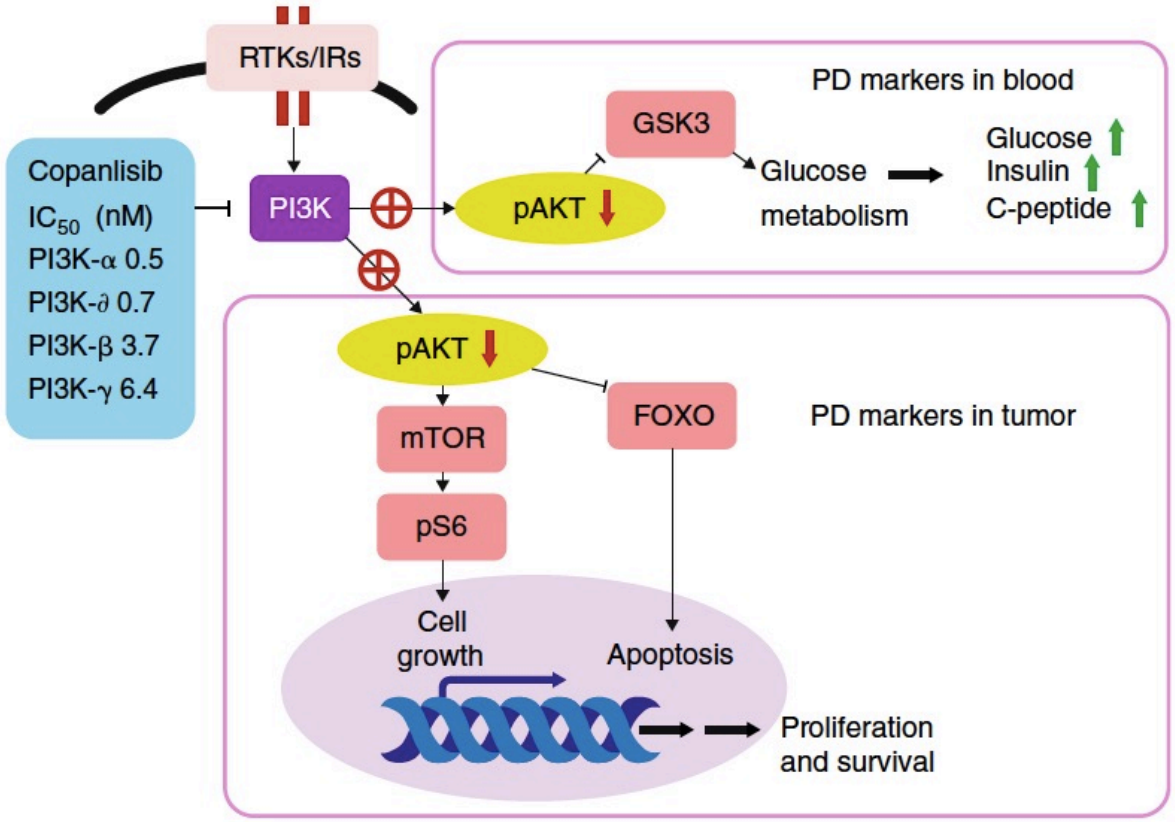
No treatment-related AEs led to discontinuation or death

Hutchings M et al. *Lancet* 2021;398:1157–69.

Courtesy of John P Leonard, MD

Copanlisib + Rituximab vs Placebo + Rituximab in Relapsed Indolent NHL: CHRONOS-3 Double-Blind Placebo Controlled Phase III Trial

Matasar et al, *Lancet Oncol* 2021

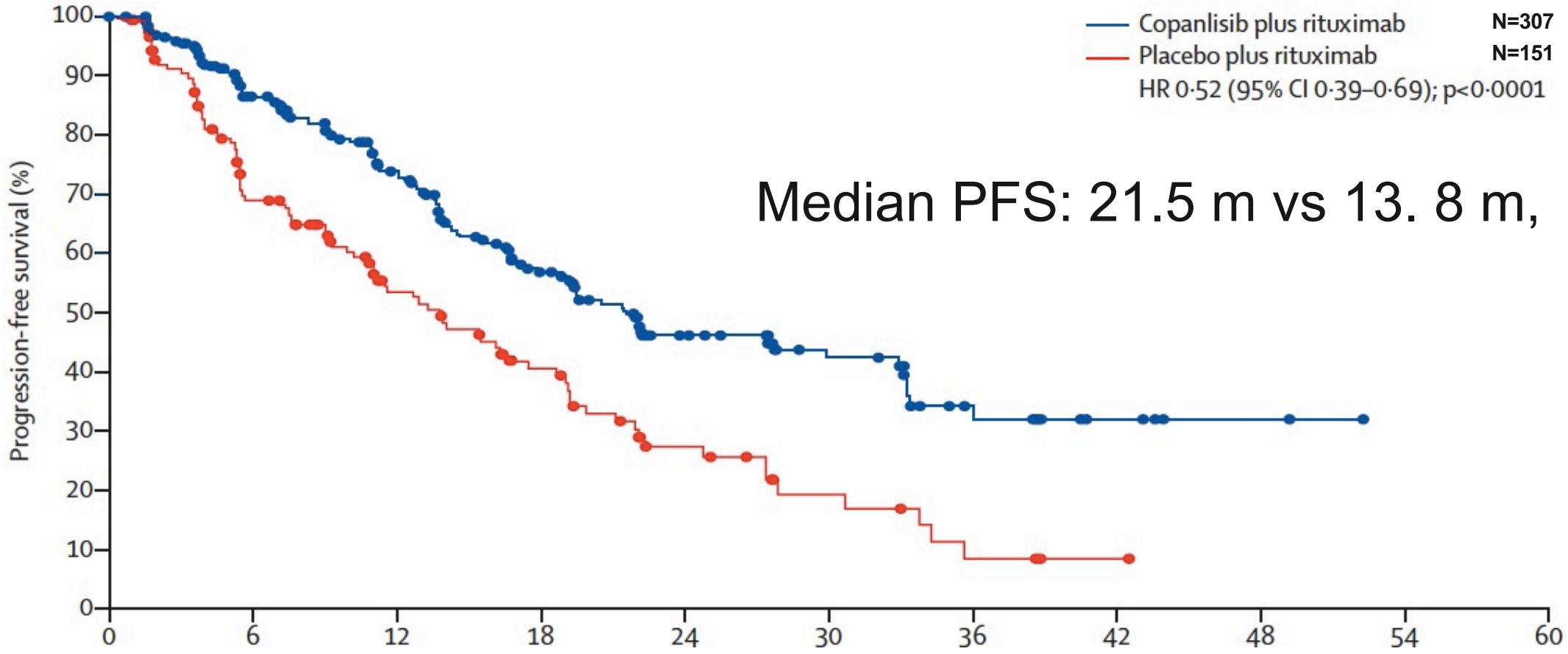


- Pan-class I PI3K inhibitor
- Relapsed indolent non-Hodgkin lymphoma (iNHL) >12 months since last anti-CD20 mAb therapy
- Copanlisib 60 mg IV D1,8,15 of 28-day schedule until progression; rituximab D1,8,15,22 cycle 1, then D1 of cycles 3,5,7,9
- Primary endpoint PFS

Courtesy of Laurie H Sehn, MD, MPH

Copanlisib + Rituximab vs Placebo + Rituximab in Relapsed Indolent NHL: CHRONOS-3 Double-Blind Placebo Controlled Phase III Trial

Matasar et al, *Lancet Oncol* 2021



Median PFS: 21.5 m vs 13. 8 m,

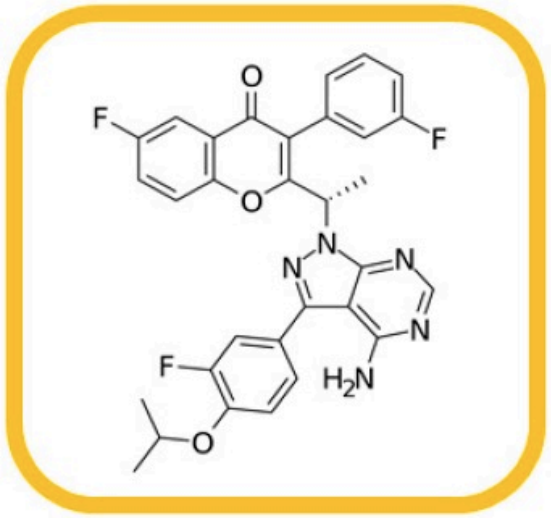
Median follow-up: 19.2 mos

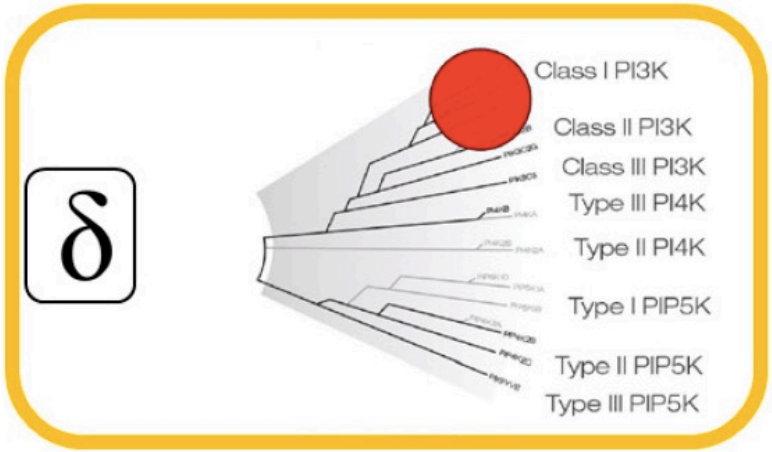
60% of patients had FL

Courtesy of Laurie H Sehn, MD, MPH

Umbralisib, a Dual PI3Kd/CK1ε Inhibitor, in Patients with Relapsed or Refractory Indolent Lymphoma

Fowler et al, *J Clin Oncol* 2021





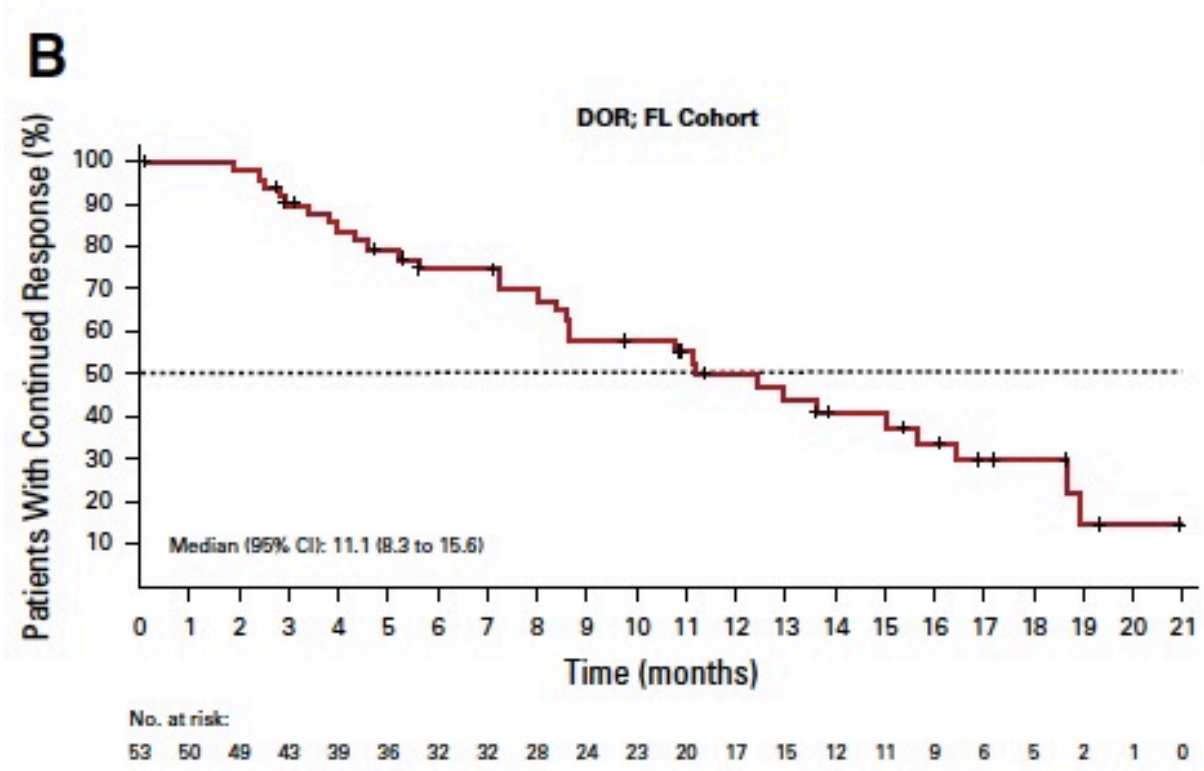
- Umbralisib exhibits improved selectivity for PI3Kd
- Phase 2b study designed to assess the safety and efficacy of umbralisib for relapsed/refractory (R/R) indolent B-cell lymphoma
- Umbralisib 800 mg po qd until progression or intolerance
- FL n=117, median 3 prior lines of therapy (range 1-10)

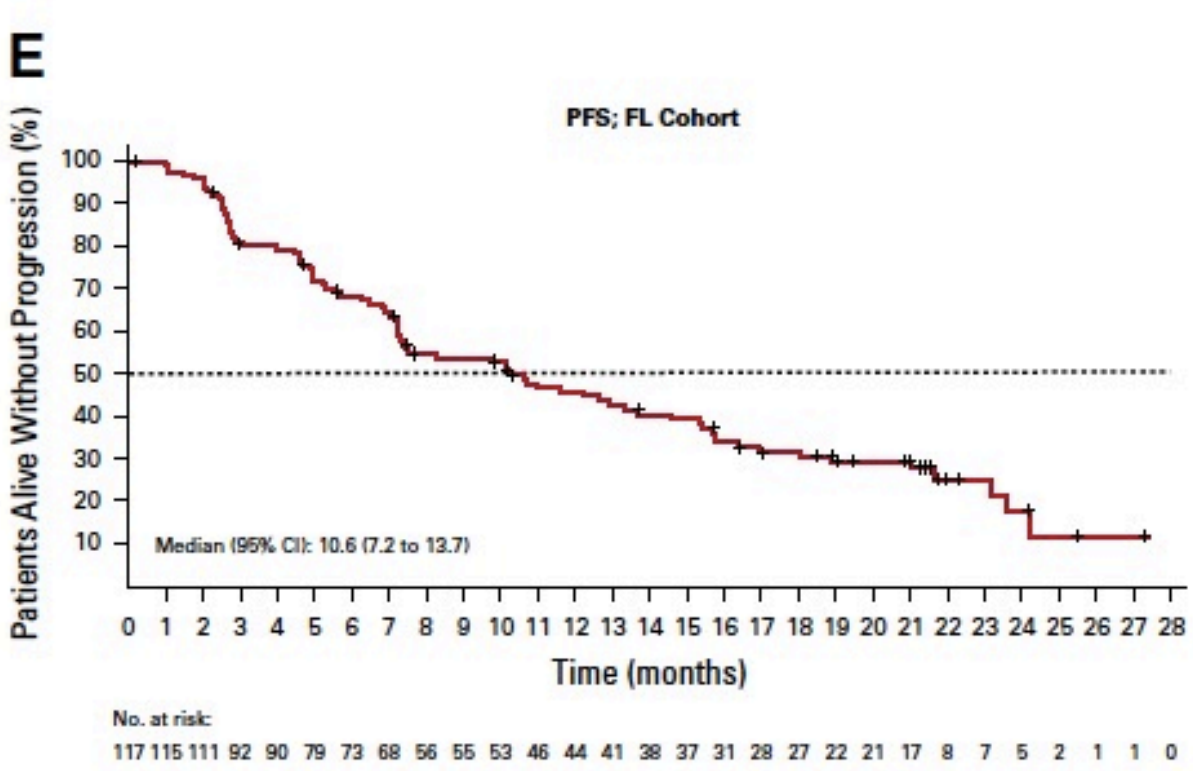
Courtesy of Laurie H Sehn, MD, MPH

Umbralisib, a Dual PI3Kd/CK1ε Inhibitor in Patients with Relapsed or Refractory Indolent Lymphoma

Fowler et al, *J Clin Oncol* 2021

Overall response rate 45.3%, complete response rate 5%





Median follow-up: 27.7 months

Courtesy of Laurie H Sehn, MD, MPH

Agenda

Introduction: Follicular Lymphoma in Clinical Practice

Module 1: First- and Second-Line Treatment — Chemotherapy, Anti-CD20 Antibodies and IMiDs

Module 2: Sequencing Third Line and Beyond — Bispecific Antibodies, PI3K Inhibitors, Tazemetostat

Module 3: CAR T-Cell Therapy

Module 3: CAR T-Cell Therapy

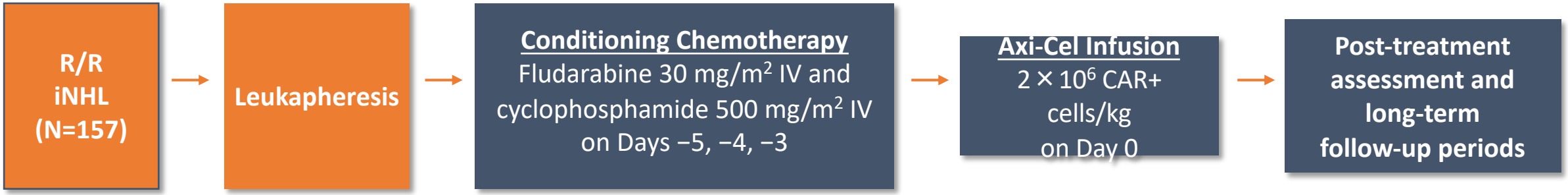
Key Topics

- **CAR T-cell therapy**
  - Efficacy and toxicity
  - Clinical indications

For an otherwise healthy patient with FL with no comorbidities and no other feasible treatment options, what is the maximum age that you would recommend CAR T-cell therapy?

For an otherwise healthy patient with FL with no comorbidities and no other feasible treatment options, what is the maximum age that you would recommend autologous stem cell transplant?

ZUMA-5: A Phase II Study of Axicabtagene Ciloleucel (Axi-Cel) for R/R iNHL — Long-Term Follow-Up



Key ZUMA-5 Eligibility Criteria

- R/R FL (Grades 1–3a) or MZL (nodal or extranodal)[a]
- ≥2 Prior lines of therapy that must have included an anti-CD20 mAb combined with an alkylating agent[b]

Primary Endpoint

- ORR (IRRC assessed per the Lugano classification[1])

Key Secondary Endpoints

- CR rate (IRRC assessed)
- Investigator-assessed ORR[a]
- DOR, PFS, OS
- AEs
- CAR T-cell and cytokine levels

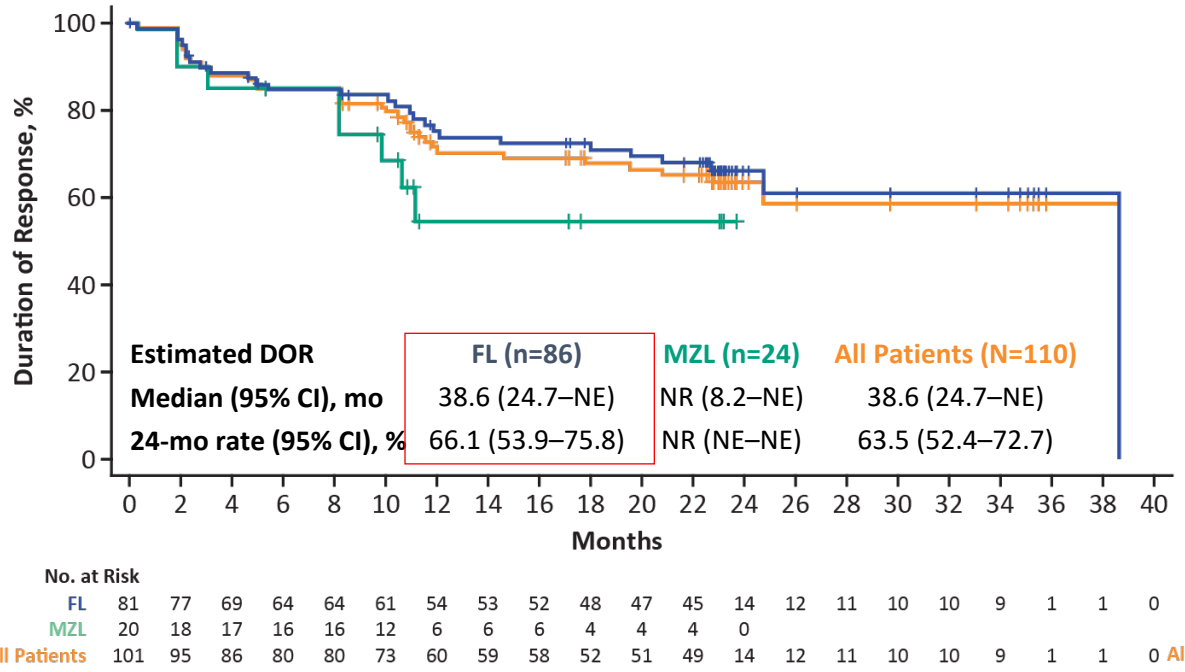
[a] Patients with stable disease (without relapse) >1 year from completion of last therapy were not eligible. [b] Single-agent anti-CD20 antibody did not count as line of therapy for eligibility.

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

AE, adverse event; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CR, complete response; DOR, duration of response; FL, follicular lymphoma; iNHL, indolent non-Hodgkin lymphoma; IRRC, Independent Radiology Review Committee; IV, intravenous; mAb, monoclonal antibody; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed/refractory.

ZUMA-5: Duration of Response and PFS

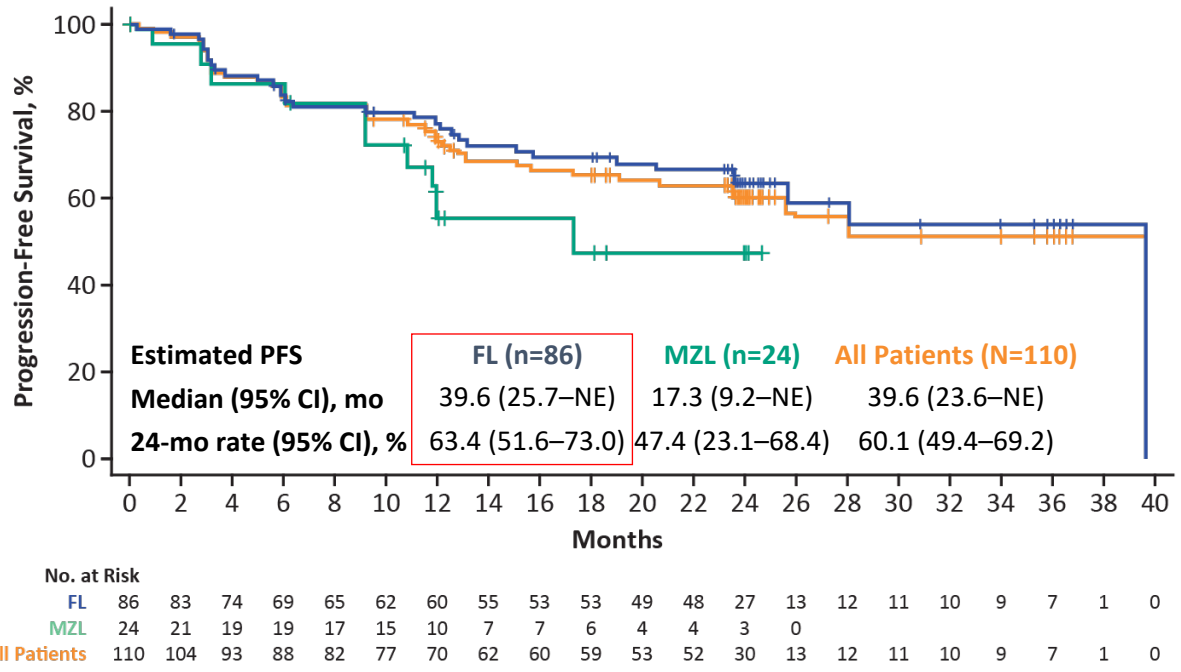
Duration of Response



No. at Risk

FL	81	77	69	64	64	61	54	53	52	48	47	45	14	12	11	10	10	9	1	1	0
MZL	20	18	17	16	16	12	6	6	6	4	4	4	0								
All Patients	101	95	86	80	80	73	60	59	58	52	51	49	14	12	11	10	10	9	1	1	0

Progression-Free Survival



No. at Risk

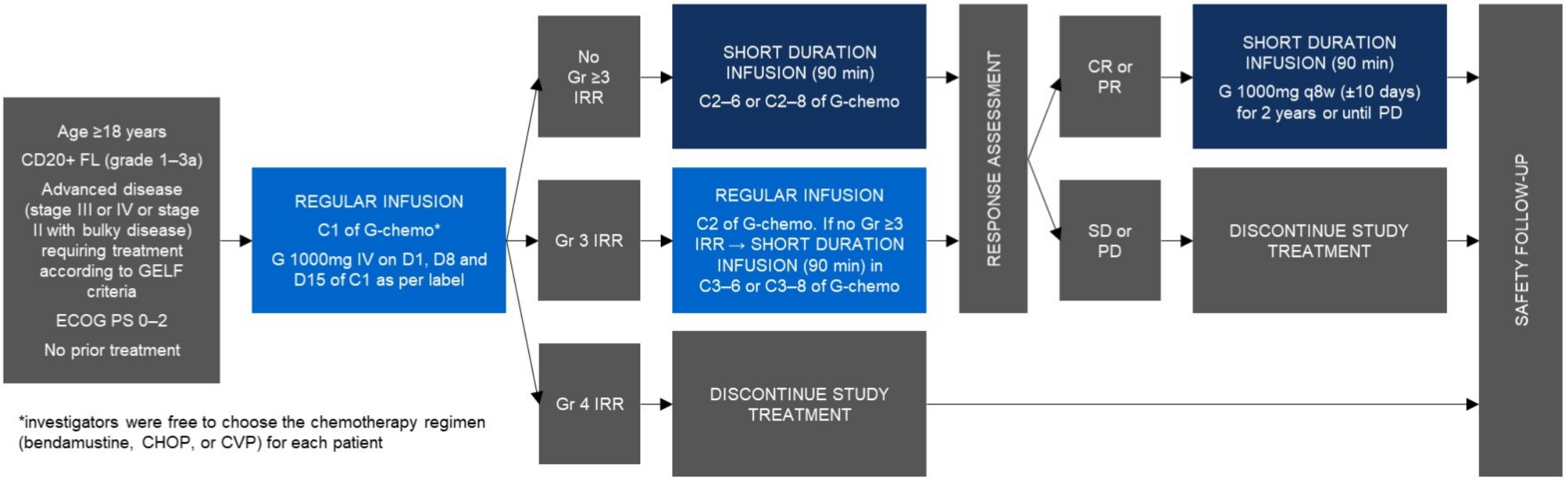
FL	86	83	74	69	65	62	60	55	53	53	49	48	27	13	12	11	10	9	7	1	0
MZL	24	21	19	19	17	15	10	7	7	6	4	4	3	0							
All Patients	110	104	93	88	82	77	70	62	60	59	53	52	30	13	12	11	10	9	7	1	0

- FL n=86
- Updated analysis occurred when ≥80 treated patients with FL had ≥24 months of follow-up
- ORR 94%, CR 79%
- At data cutoff, 57% of efficacy-eligible patients with FL (49 of 86) had ongoing responses

Appendix of Additional Data Slides

GAZELLE study design

International, open-label, Phase IV trial in patients with previously untreated FL (NCT03817853)



Primary endpoint: incidence of Gr ≥3 IRRs during C2

Secondary endpoints include: safety, response, PFS and OS

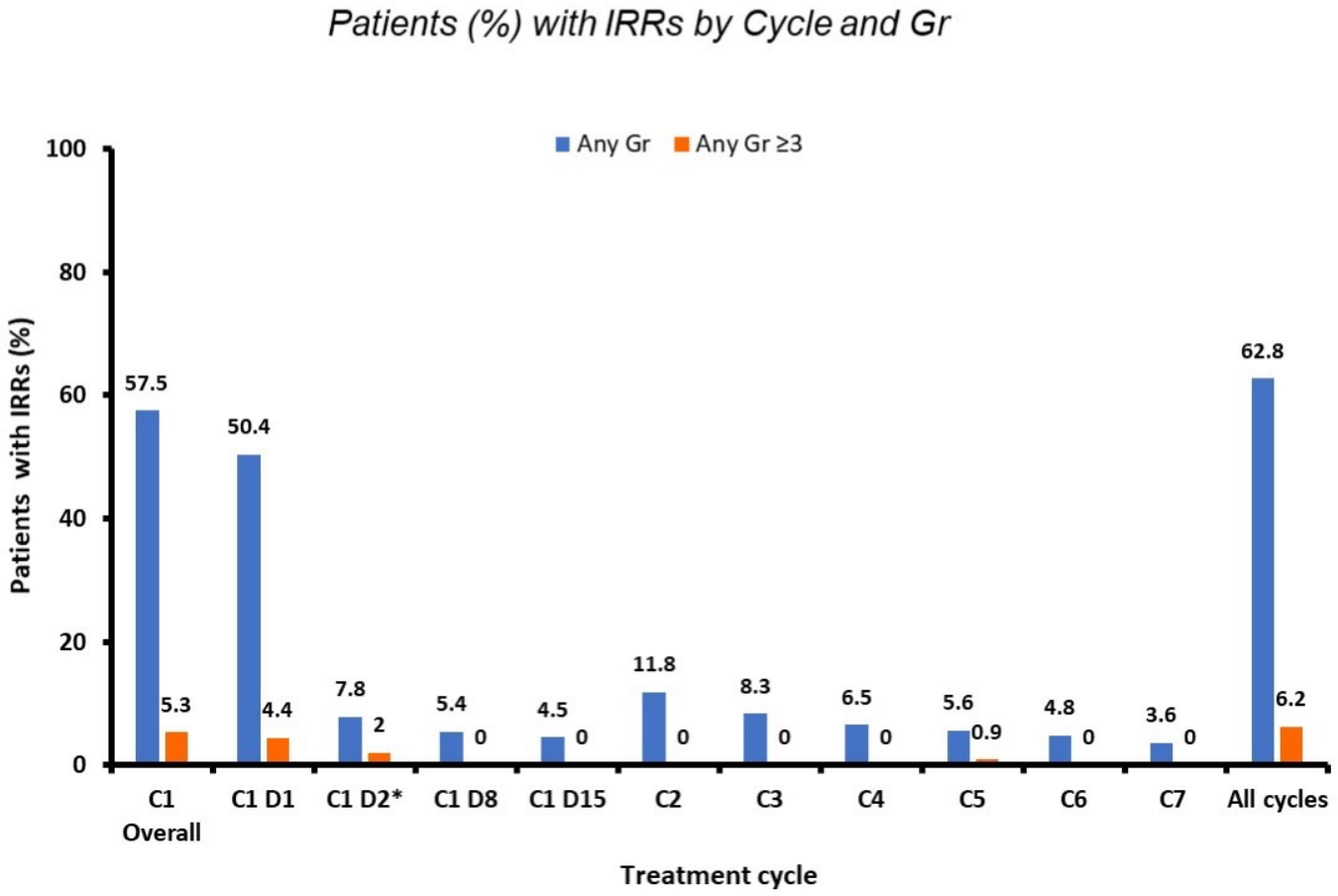
C, cycle; CR, complete response; D, day; FL, follicular lymphoma; G, obinutuzumab; Gr, Grade; IRR, infusion-related reaction; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease

Canales-Albendea MAA et al. ASCO 2021;Abstract 7545.

Courtesy of Laurie H Sehn, MD, MPH

GAZELLE: No patients experienced a Grade 3 or higher IRR with obinutuzumab SDI in C2

- 11.8% (13/110) of patients who received G SDI in C2 experienced an IRR
- All events in C2 were Gr 1 (10.0%) or Gr 2 (1.8%)
- In subsequent cycles, only one patient experienced a Gr ≥3 IRR AE with G SDI (Gr 3 hypertension in C5)

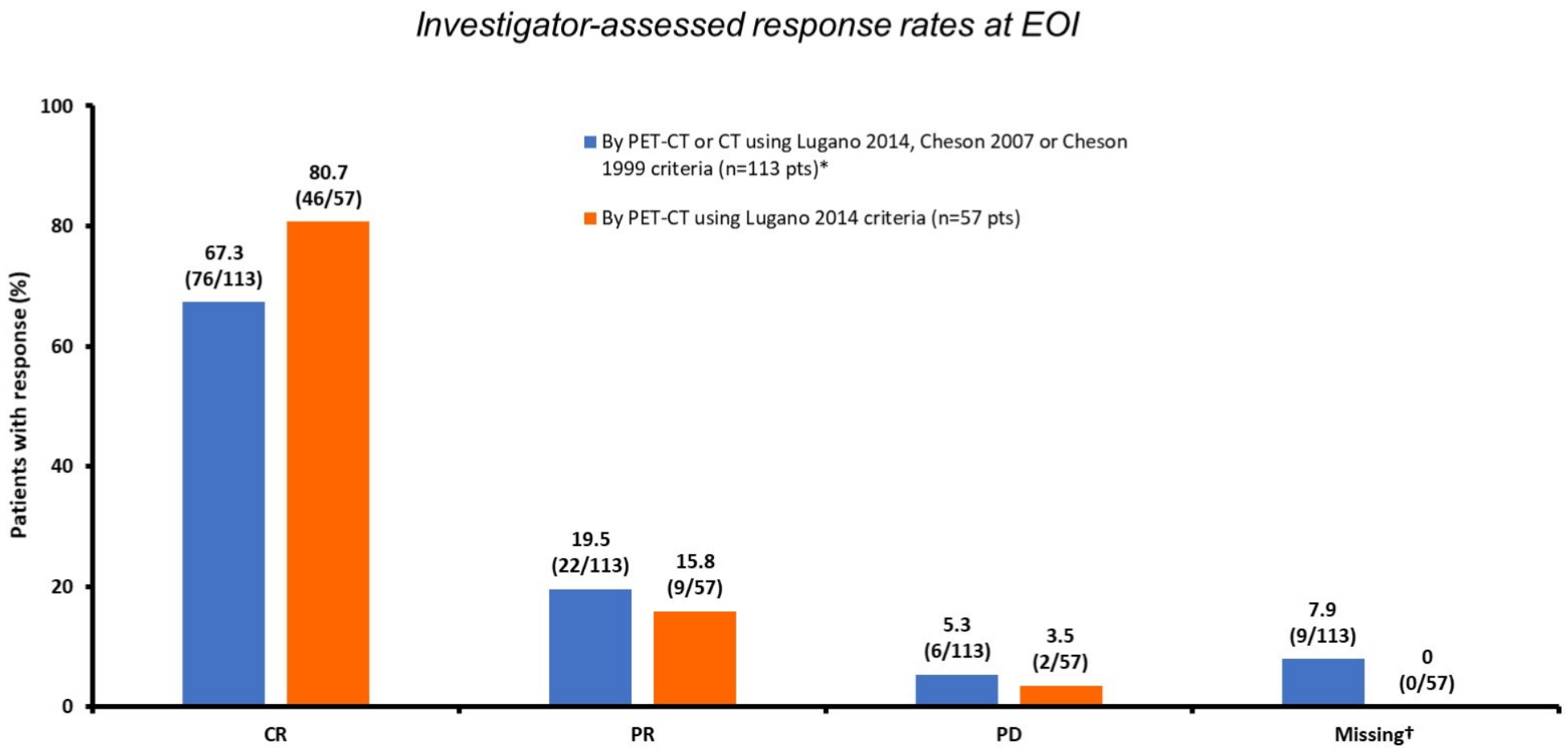


AE, adverse event; C, cycle; D, day; G, obinutuzumab; Gr, Grade; IRR, infusion-related reaction; SDI, short duration infusion

Canales-Albendea MAA et al. ASCO 2021;Abstract 7545.

Courtesy of Laurie H Sehn, MD, MPH

GAZELLE: EOI response rates



*response assessed according to local practice and the criteria used at the site; †no response assessment available at EOI; CR, complete response; EOI, end of induction; PD, progressive disease; PR, partial response

Canales-Albendea MAA et al. ASCO 2021;Abstract 7545.

Courtesy of Laurie H Sehn, MD, MPH

Characteristics of Patients Achieving Complete or Partial Response with Tazemetostat for Wild-Type (WT) R/R FL

Characteristic	Patients With CR/PR (WT *EZH2*) (n=19)	Total Population, WT *EZH2* (n=54)	Patients with CR/PR, MT *EZH2* (n=31)	Total Population, MT *EZH2* (n=45)
POD24, n (%)	8 (42.1)	32 (59.3)	12 (38.7)	19 (42.2)
Refractory to rituximab-containing regimen, n (%)	10 (52.6)	32 (59.3)	13 (41.9)	22 (48.9)
Refractory to last therapy, n (%)	5 (26.3)	22 (40.7)	16 (51.6)	22 (48.9)
Double refractory, n (%)[a]	4 (21.1)	15 (27.8)	7 (22.6)	9 (20.0)
Prior hematopoietic stem cell transplant, n (%)	7 (36.8)	21 (38.9)	3 (9.7)	4 (8.9)

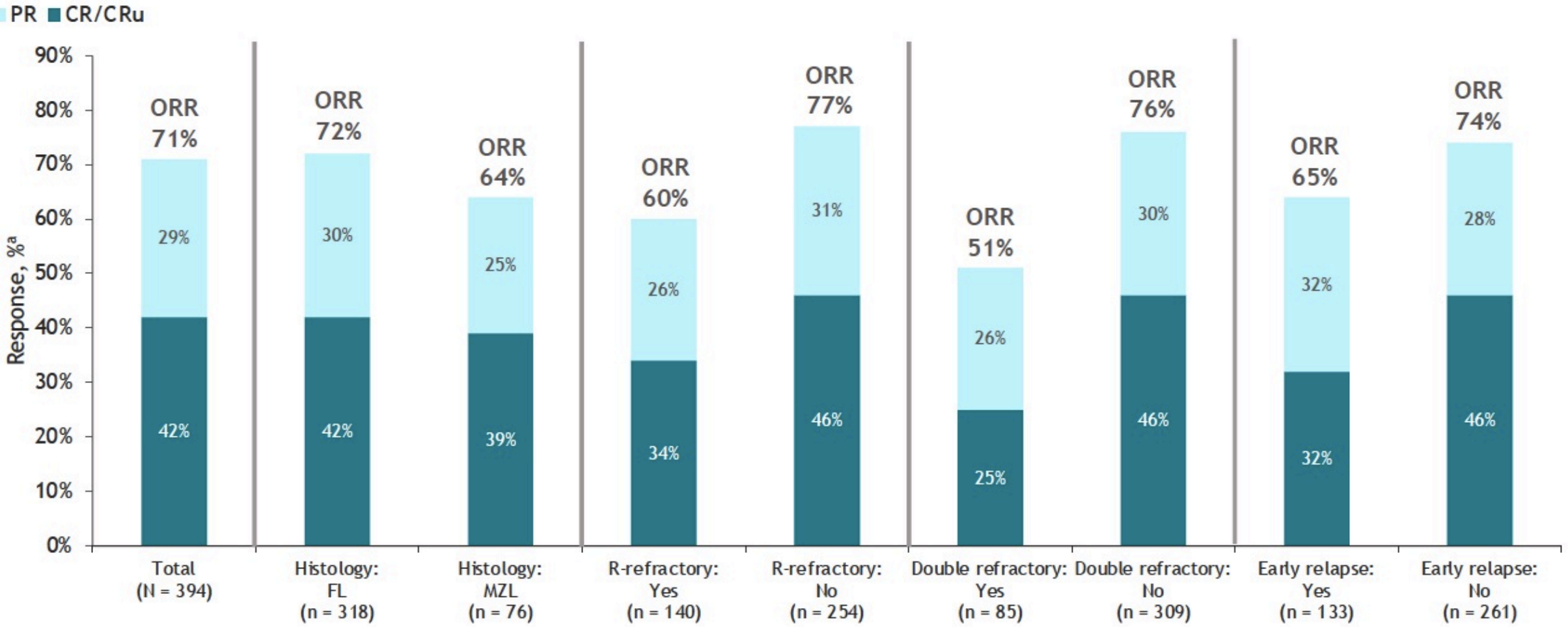
[a]Refractory to rituximab-containing regimen and an alkylating agent-containing regimen.

- Of 99 patients with WT EZH2 or EZH2 mutations, 19 patients with WT EZH2 who received a median of 3 prior lines of therapy responded (2 CR/17 PR)
- Patients with refractoriness to last therapy represented 26.3% and 51.6% of WT and EZH2 mutation responders

Batlevi CL et al. ICML 2021;Abstract 109

Courtesy of Laurie H Sehn, MD, MPH

Best Overall Response in R² Induction Treatment Phase



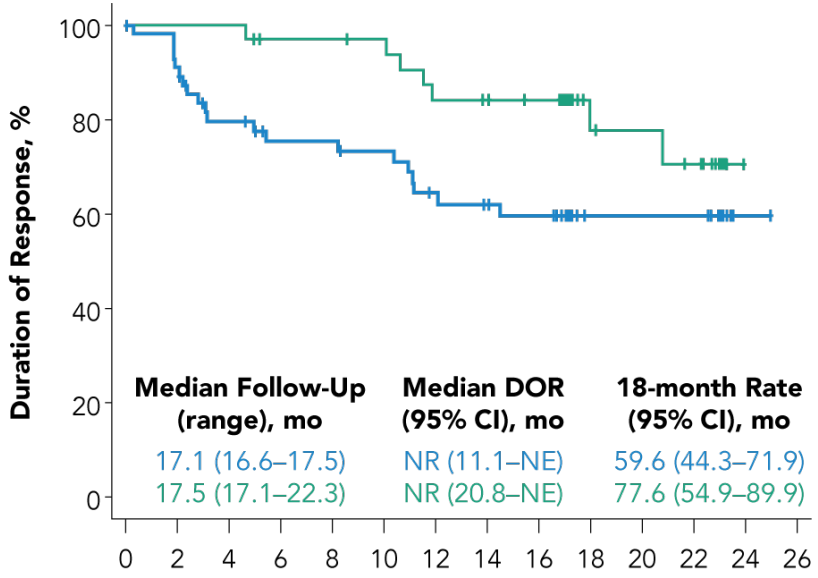
- R² showed clinical activity in patients with R/R iNHL, including those with FL or MZL histology and those refractory to rituximab, double refractory, or early relapse

Lansigan et al, ASH 2021

Courtesy of Laurie H Sehn, MD, MPH

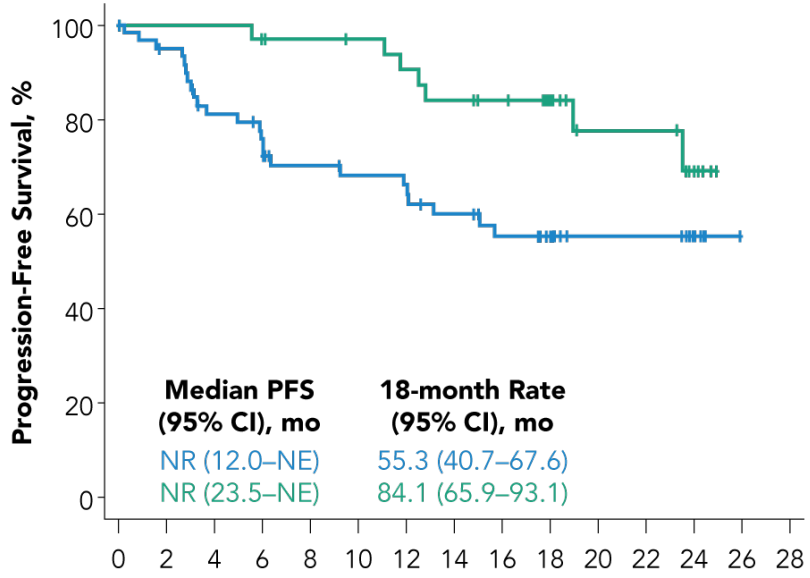
DOR, PFS and OS in Patients with iNHL by POD24 Status

Duration of Response



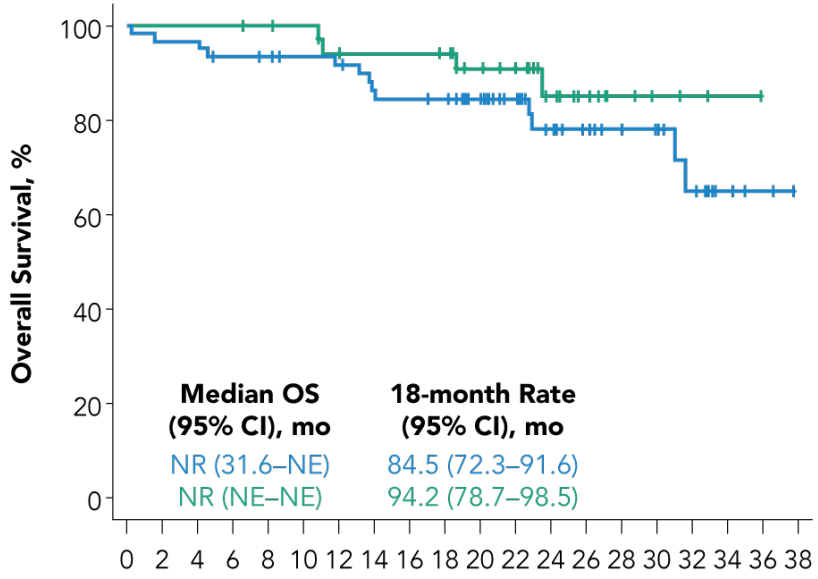
No. at Risk														
With POD24	56	50	41	35	35	33	28	26	24	10	10	10	1	0
Without POD24	34	34	34	31	31	30	26	25	23	12	11	9	0	

Progression-Free Survival



No. at Risk															
With POD24	61	56	46	42	35	33	32	28	24	20	10	10	5	0	
Without POD24	37	34	34	32	31	30	28	26	24	20	11	11	6	0	

Overall Survival



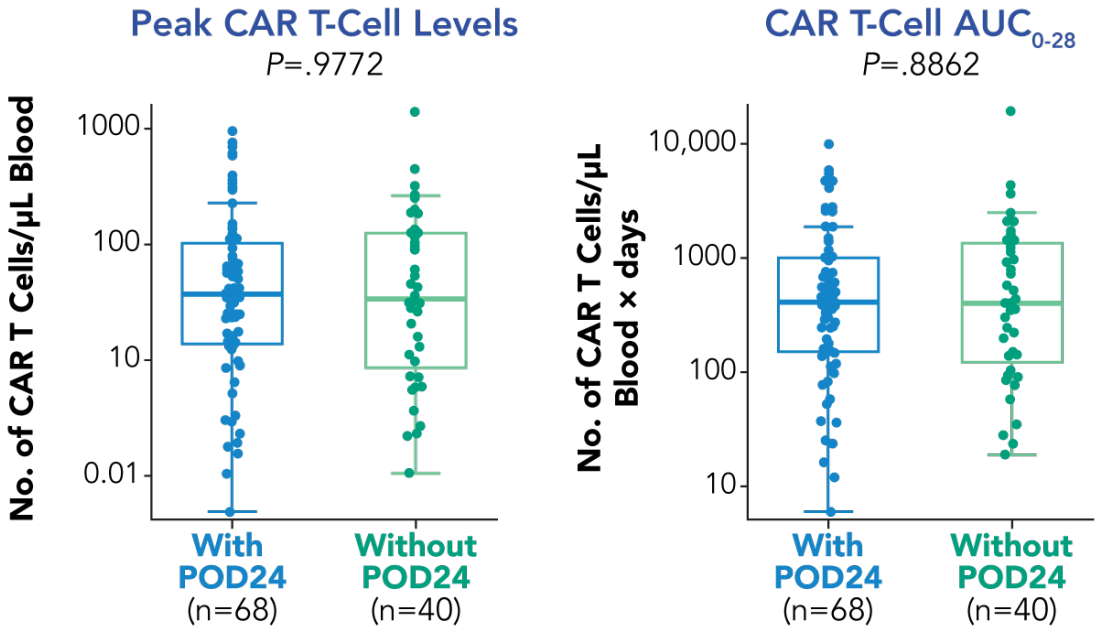
No. at Risk																				
With POD24	61	59	59	56	55	53	52	48	47	46	39	31	23	19	16	14	10	4	2	0
Without POD24	37	37	37	37	36	35	32	31	31	30	25	23	14	9	5	3	2	1	0	

- With median follow-up of 17.1 months and 17.5 months at data cutoff, responses were ongoing in 52% of efficacy-evaluable patients with POD24 and 70% of those without POD24, respectively

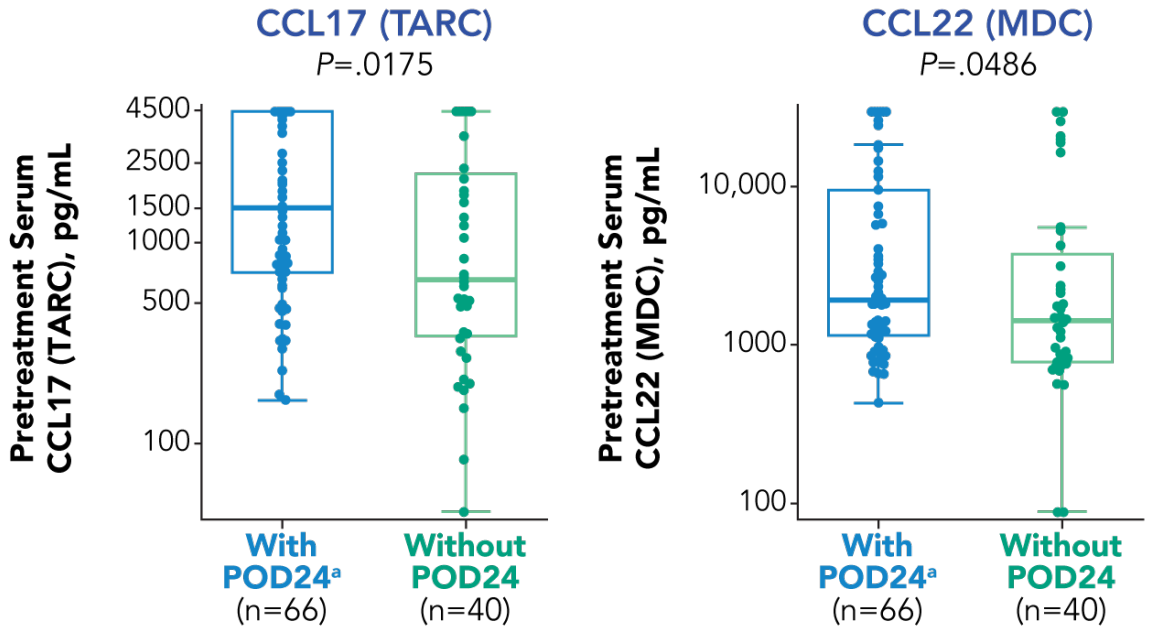
DOR, duration of response; FL, follicular lymphoma; mo, month; MZL, marginal zone lymphoma; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival; POD24, progression of disease <24 months from initiating the first anti-CD20–containing chemoimmunotherapy.

CAR T-Cell Expansion and Key Pretreatment Serum Analytes in Patients with FL by POD24 Status

Peak and AUC_{0-28} CAR T-Cell Levels



Pretreatment Analyte Levels



- In efficacy-evaluable patients with FL, median peak CAR T-cell levels were similar in patients with and without POD24 (36.9 cells/µL and 34.5 cells/µL, respectively)
  - Median AUCs were also similar among patients with and without POD24 (422.5 cells/µL × days and 407.6 cells/µL × days, respectively)
- Pretreatment CCL17 and CCL22 levels appeared higher in patients with POD24 than without POD24

P values were calculated using the Wilcoxon rank sum test. [a] Data were not available for 2 patients with FL before retreatment.
AUC_{0-28}, area under the curve between Day 0 and Day 28; CAR, chimeric antigen receptor; CCL, chemokine (C-C motif) ligand; FL, follicular lymphoma; MDC, macrophage-derived chemokine; POD24, progression of disease <24 months from initiating the first anti-CD20–containing chemoimmunotherapy; TARC; thymus- and activation-regulated chemokine.

ELARA: Efficacy Analysis with Extended Follow-Up

- As of March 29, 2021, 97 patients received tisagenlecleucel and 94 were evaluable for efficacy
- CR rates are consistent and durable for the interim, primary analyses, and this extended follow-up analysis
- Complete response correlated with durability and prolonged PFS
  - **Among patients who achieved CR, 12-month PFS was 85.5% (95% CI, 74-92) and estimated DOR rate at 9 months was 86.5% (95% CI, 75-93)**

Efficacy Results of Extended Follow-up Analysis

Endpoint	% (95% CI)
ORR[a]	**86.2** (77.5-92.4)
CRR[a]	**69.1** (58.8-78.3)
12-mo PFS	**67.0** (56.0-75.8)
9-mo DOR	**76.0** (64.6-84.2)

[a]ORR and CRR were comparable with the primary efficacy analysis (ORR 86.2% and CRR 66.0%).

Thieblemont C et al. ASH 2021;Abstract 131.

Courtesy of John P Leonard, MD

Subcutaneous Epcoritamab for R/R B-Cell NHL: *Treatment Response by Diagnosis*

	Relapsed or refractory diffuse large B-cell lymphoma*			Relapsed or refractory follicular lymphoma†		Relapsed or refractory mantle cell lymphoma‡	
	12–60 mg (n=22)	48 mg (n=8)	60 mg (n=3)	0·76–48 mg (n=10)	48 mg (n=1)	0·76–48 mg (n=4)§	48 mg (n=1)
Overall response, n (%, 95% CI)	15 (68%, 45–86)	7 (88%, 47–100)	3 (100%, 29–100)	9 (90%, 55–100)	0 (0, 0–98)	2 (50%, 7–93)	1 (100%, 3–100)
Complete response	10 (45%)	3 (38%)	3 (100%)	5 (50%)	0	1 (25%)	0
Partial response	5 (23%)	4 (50%)	0	4 (40%)	0	1 (25%)	1 (100%)
Stable disease	1 (5%)	0	0	0	0	1 (25%)	0
Progressive disease	5 (23%)	0	0	1 (10%)	1 (100%)	0	0
Time to response, months	1·4 (1·3–2·6)	1·4 (1·3–2·6)	1·3 (1·1–1·4)	1·9 (1·5–3·5)	NA	1·4 (1·3–1·5)	1·3 (1·3–1·3)
Follow-up duration, months	9·3 (8·2–14·8)	8·2 (7·4–9·9)	9·2 (9·2–9·3)	13·6 (10·4–16·5)	6·6 (6·6–6·6)	10·2 (7·7–10·5)	7·7 (7·7–7·7)

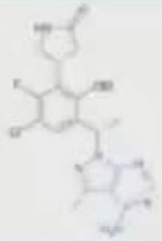
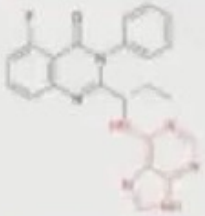
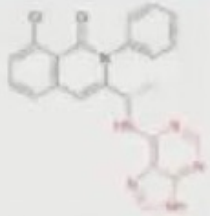
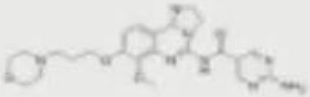
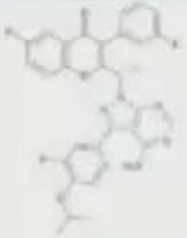
The recommended Phase II dose was 48 mg across B-cell NHL histologies

Hutchings M et al. *Lancet* 2021;398:1157–69.

Courtesy of John P Leonard, MD

Comparative Potency and Isoform Selectivity of PI3K Inhibitors

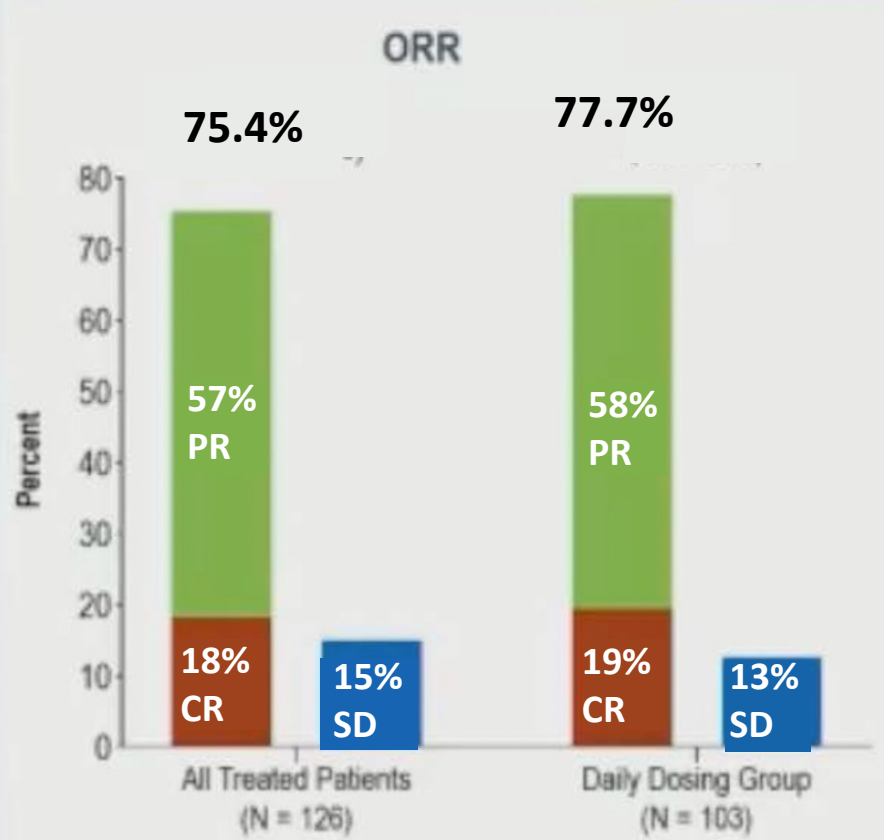
- Parsaclisib was structurally designed to optimize both selectivity and potency, and to avoid the hepatotoxicity associated with the early-generation PI3K inhibitors
- Parsaclisib has more than 10,000-fold greater selectivity for the PI3Kδ isoform than the α, β, and γ isoforms

	Parsaclisib[1]	Idelalisib[2]	Duvelisib[3]	Copanlisib[4]	Umbralisib[5,6]
Structure					
PI3Kδ IC_{50}, nM	1	2.5	2.5	0.7	22.2
Fold selectivity					
PI3Kα	>20,000	>300	1602	1	>1500
PI3Kβ	>20,000	>200	85	5	>1500
PI3Kγ	19,000	>35	27	10	225

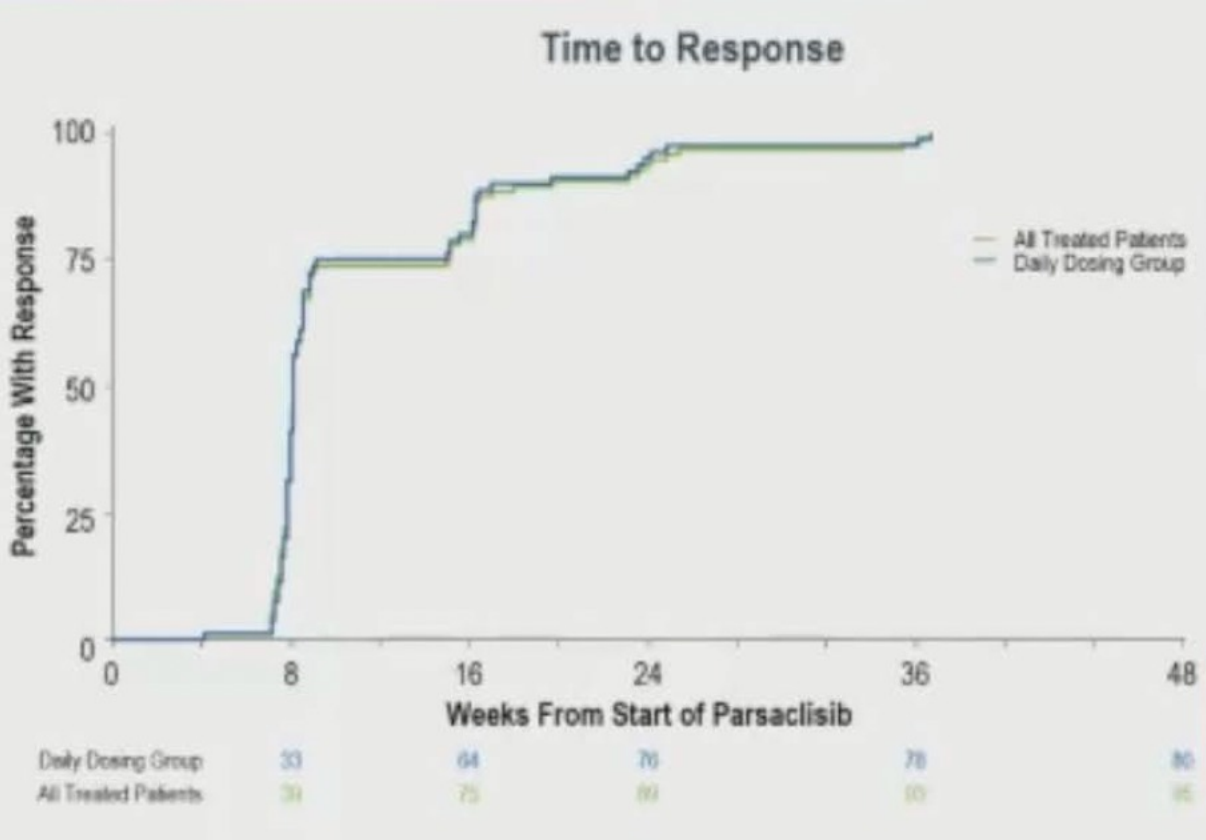
Lynch RC et al. ASH 2021;Abstract 813.

Courtesy of John P Leonard, MD

CITADEL-203 Phase II Study of the Next-Generation PI3K-Delta Inhibitor Parsaclisib in R/R FL: *Objective Response by IRC*



- ORR by investigator assessment: 74.6% in All Treated Patients, 75.7% in Daily Dosing Group



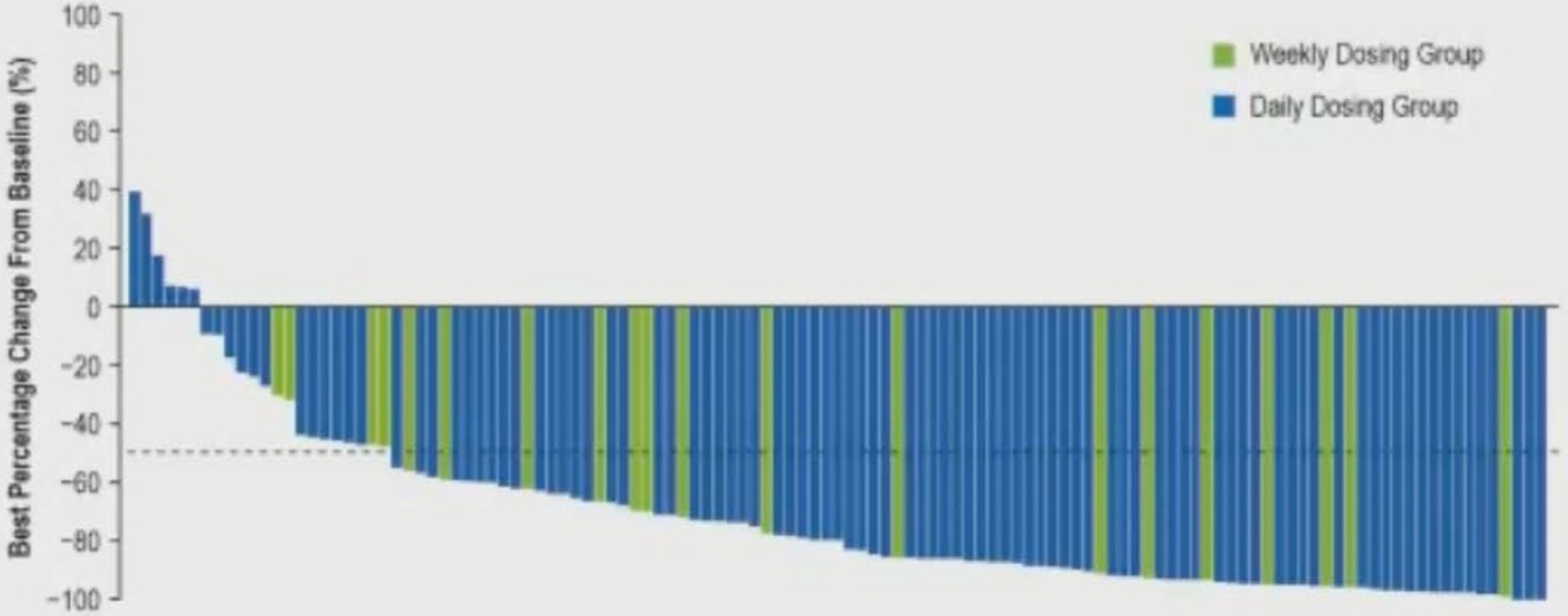
- 74% of all responders had their first response occur at the first disease assessment (8 weeks)

Lynch R et al. ASH 2021;Abstract 813.

Courtesy of John P Leonard, MD

CITADEL-203 Phase II Study of the Next-Generation PI3K-Delta Inhibitor Parsaclisib in R/R FL: *Change from Baseline in Target Lesion*

- 95% (113/119) of evaluable patients had regression at target lesions, 86% (97/113) of whom had >50% reduction in best percentage change from baseline



Lynch R et al. ASH 2021;Abstract 813.

Courtesy of John P Leonard, MD

PrE0403 Phase II Study of Venetoclax + Obinutuzumab + Bendamustine as Front-Line Therapy for High Tumor Burden FL

Primary Endpoint: CR at the End of Induction Therapy

End of Induction Response*		
Complete Response	73.2%	41/56
Overall Response	92.9%	52/56

*3 pts unevaluable due to no post-baseline scans (considered non-responders)

Pre-Planned Primary endpoint of ≥30 CRs was met, thus study positive

*Response based on Lugano Criteria with PET/CT and BM assessment

Estimated 2-year OS: 94.4% **Estimated 2-year PFS: 85.8%**

Portell CA et al. ASH 2021;Abstract 814.

Courtesy of John P Leonard, MD

PrE0403: Venetoclax + Obinutuzumab + Bendamustine as Front-Line Therapy for High Tumor Burden FL

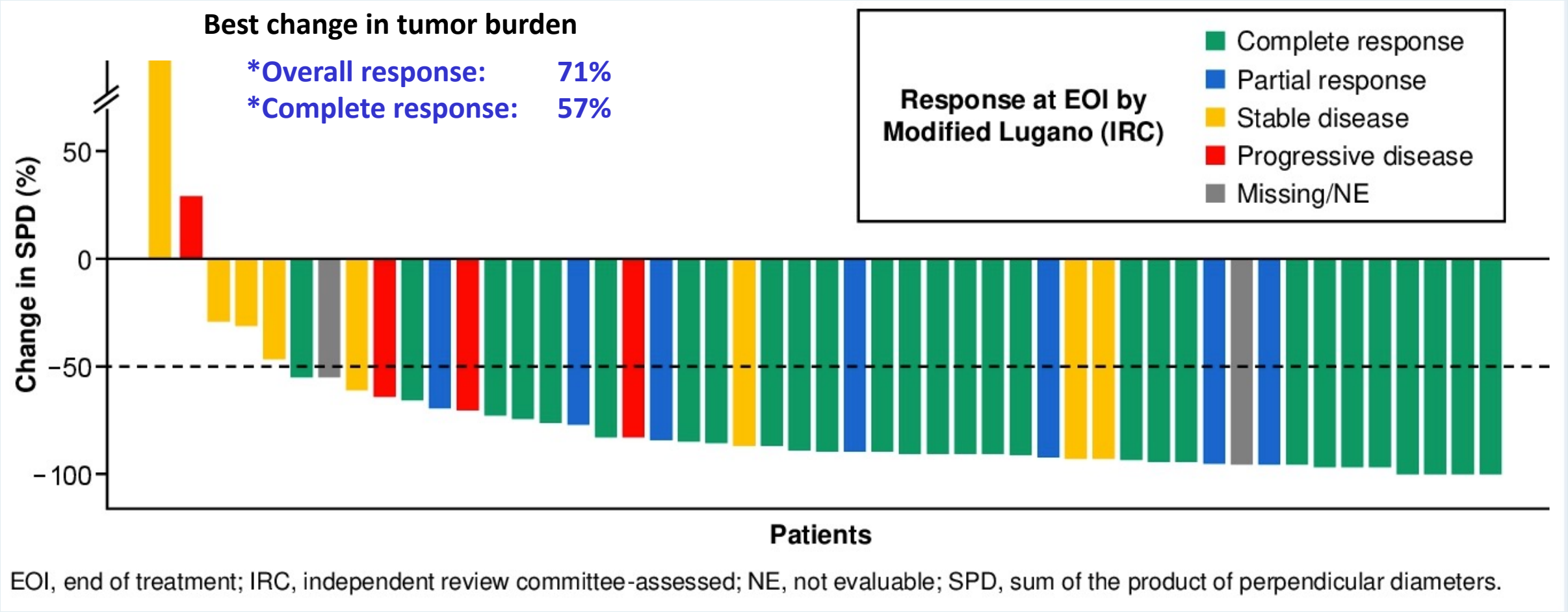
Adverse Events

Event	All Grades	Grade ≥ 3	
Upper respiratory infection	9 (16.1%)	0	(0%)
Tumor lysis syndrome[2]	8 (14.3%)	8	(14.3%)
Abdominal Pain	8 (14.3%)	1	(1.8%)
Alkaline Phosphatase increase	7 (12.5%)	0	(0%)
Dysgeusia	7 (12.5%)	0	(0%)
Dyspepsia	7 (12.5%)	0	(0%)
Pyrexia	7 (12.5%)	0	(0%)
Overall Adverse Events Gr ≥ 3		47	(83.9%)
Serious Adverse Events		31	(55.4%)

Portell CA et al. ASH 2021;Abstract 814.

Courtesy of John P Leonard, MD

Phase Ib/II Study of Polatuzumab Vedotin + Obinutuzumab + Venetoclax for R/R Follicular Lymphoma: *Response*



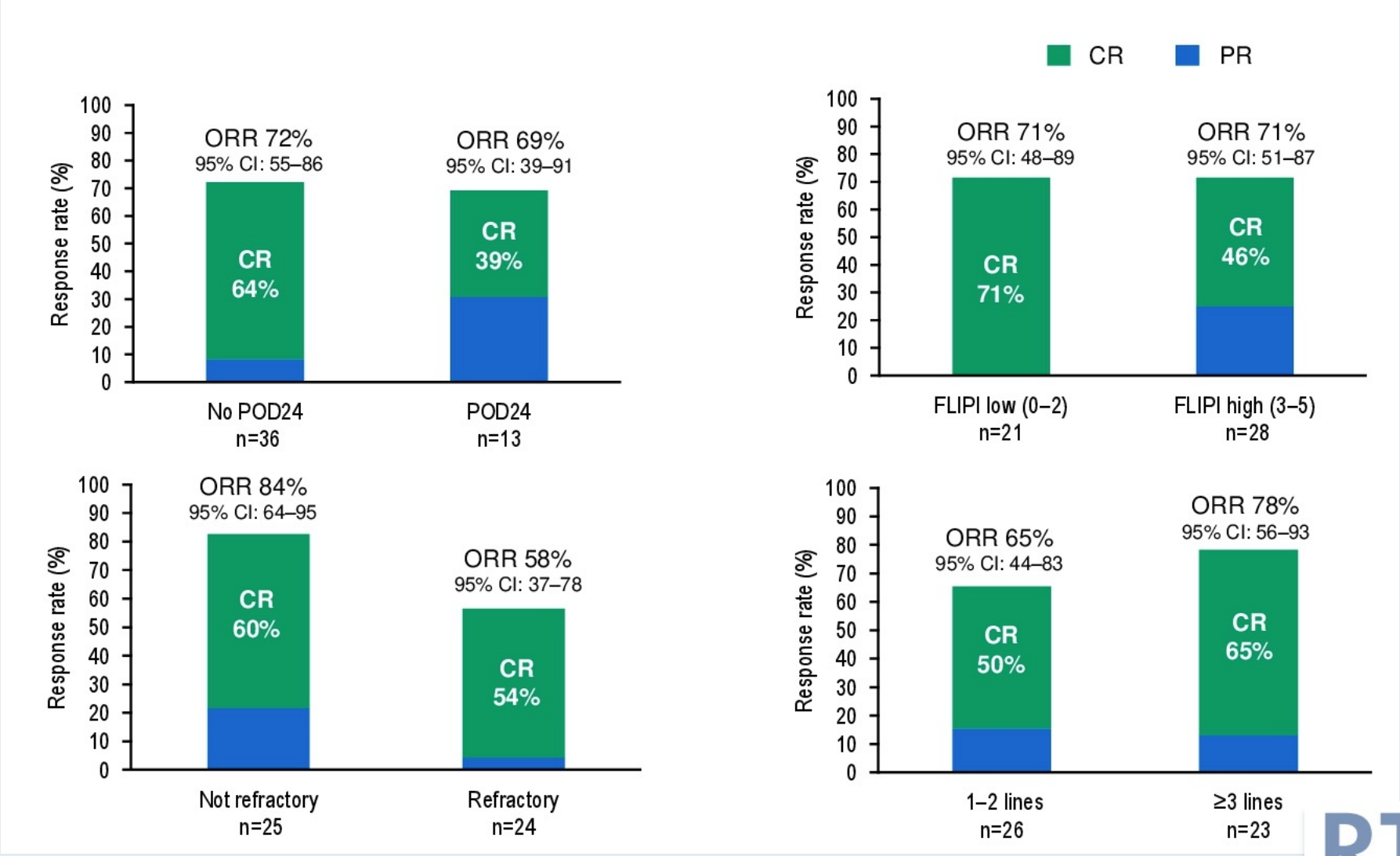
EOI, end of treatment; IRC, independent review committee-assessed; NE, not evaluable; SPD, sum of the product of perpendicular diameters.

*Modified Lugano 2014 response by IRC

Bannerji R et al. ASCO 2021;Abstract 7534.

Courtesy of John P Leonard, MD

Polatuzumab Vedotin + Obinutuzumab + Venetoclax: *Response Rates at EOI by Subgroup*



Bannerji R et al. ASCO 2021;Abstract 7534.

Courtesy of John P Leonard, MD

Polatuzumab Vedotin + Obinutuzumab + Venetoclax: *Adverse Events*

AE, n (%)	Safety-evaluable (N=74)	
	All grade	Grade 3–4
Hematologic AEs		
Neutropenia	31 (42)	29 (39)
Thrombocytopenia	23 (31)	14 (19)
Non-hematologic AEs		
Infections*	48 (65)	12 (16)
Diarrhea	41 (55)	4 (5)
Nausea	35 (47)	3 (4)
Peripheral neuropathy†‡	33 (45)	0
Fatigue	28 (38)	1 (1)
Infusion-related reaction	25 (34)	3 (4)

AEs to monitor, n (%)	Safety-evaluable (N=74)	
Peripheral neuropathy†‡	All grade	33 (45)
	Grade 2	13 (18)
	Grade 3	0
	Led to dose reduction	4 (5)
AESIs, n (%)		
Tumor lysis syndrome§		2 (3)
Second malignancies†		6 (8)
Squamous cell carcinoma		3 (4)
Intraocular melanoma		1 (1)
Myelodysplastic syndrome		1 (1)
Skin cancer		1 (1)

Bannerji R et al. ASCO 2021;Abstract 7534.

Courtesy of John P Leonard, MD

Phase Ib/II Study of Obinutuzumab + Atezolizumab + Lenalidomide for R/R FL (N = 32): *Efficacy*

Efficacy endpoints	PET-CT (modified Lugano 2014)	CT-MRI (Lugano 2014)
Overall response rate	78.1%	81.3%
CR rate	71.9%	31.3%
CR rate (double-refractory)	67.0%	Not reported
CR rate (POD24)	50.0%	Not reported
PR rate	6.3%	50.0%
SD rate	6.3%	3.1%
PD rate	9.4%	12.5%
36-month PFS	68.4%	
36-month OS	90.0%	

Morschhauser F et al. *Blood Cancer J* 2021;11(8):147.

Courtesy of John P Leonard, MD

Obinutuzumab + Atezolizumab + Lenalidomide for R/R FL: *Summary of Adverse Events*

Patient, *n* (%)	G-atezo-len 15 mg (*n* = 4)	G-atezo-len 20 mg (*n* = 34)	All patients (*N* = 38)
Any AE	4 (100.0)	34 (100.0)	38 (100.0)
Grade 3–5 AE	4 (100.0)	28 (82.4)	32 (84.2)
Grade 5 (fatal) AE[a]	0	2 (5.9)	2 (5.3)
Serious AE	2 (50.0)	16 (47.1)	18 (47.4)
AE leading to discontinuation of any study drug[b]	1 (25.0)	10 (29.4)	11 (28.9)
AE leading to study discontinuation[c]	0	2 (5.9)	2 (5.3)
AE leading to dose interruption of any treatment	4 (100.0)	30 (88.2)	34 (89.5)

Morschhauser F et al. Blood Cancer J 2021;11(8):147.

Courtesy of John P Leonard, MD

Meet The Professor

Optimizing the Management of Metastatic Castration-Resistant Prostate Cancer

Wednesday, January 5, 2022
12:30 PM - 1:30 PM ET

Faculty

Prof Karim Fizazi, MD, PhD

Moderator

Neil Love, MD

RTP
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TO PRACTICE

Thank you for joining us!

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

RTP Year in Review 2022