9th POSTGRADUATE
Lymphoma
Conference

Novel Agents in Follicular Lymphoma

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Bethesda, MD

Florence,
March 20-21, 2025

Hotel Brunelleschi

President:
P.L. Zinzani

Disclosures

Disclosures of Bruce Cheson

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Regeneron						X	
AstraZeneca						X	
Beigene						X	
Lilly					x	X	

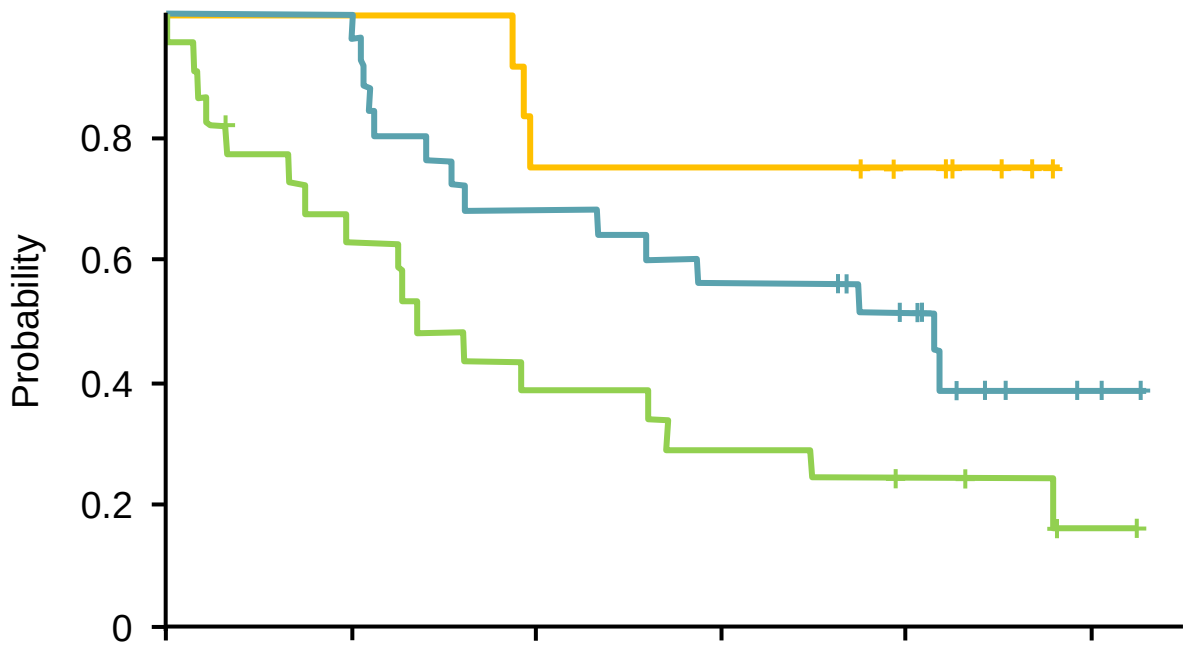
CALGB-50402:Galiximab+Rituximab in Previously Untreated FL

FLIPI Score	ORR (p=0.059)	CR (p=0.03)
0-1	11 (92%)	9 (75%)
2	20 (80%)	12 (48%)
3-5	12 (55%)	6 (27%)

- ORR not associated with stage, sex, bulky disease, marrow involvement, or age > 60

Czuczman et al, Ann Oncol, 23:2356, 2012

Progression-free survival by FLIPI score

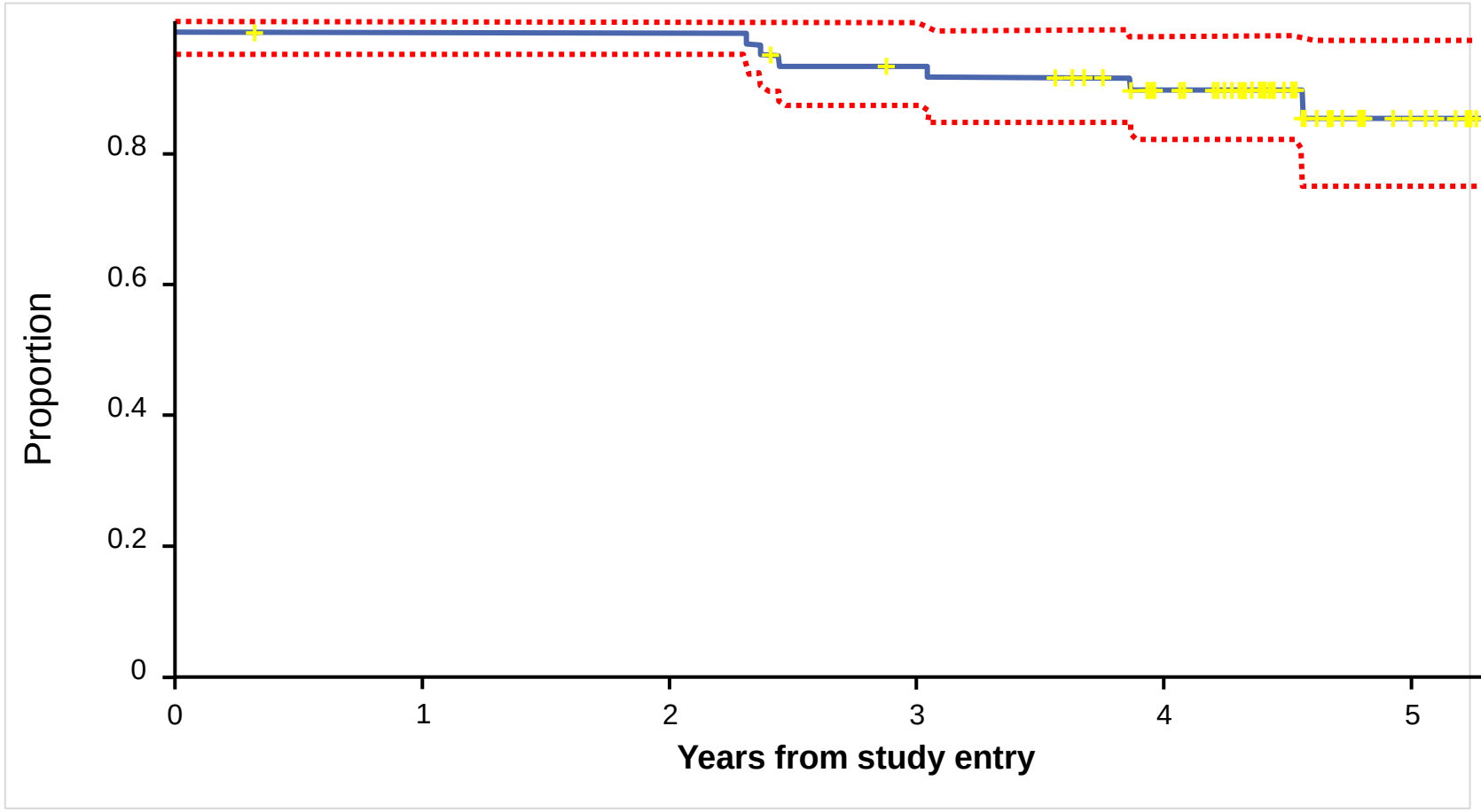


	N	Events	Chi-square	P value
Low	12	3	11.45	
Intermediate	25	14		0.0033
High	22	17		

(Med f/u 4.3 y)

Czuczman et al, Ann Oncol, 23:2356, 2012

Overall survival of 61 assessable patients over a median follow-up time of 4.3 years



N	Events
61	7

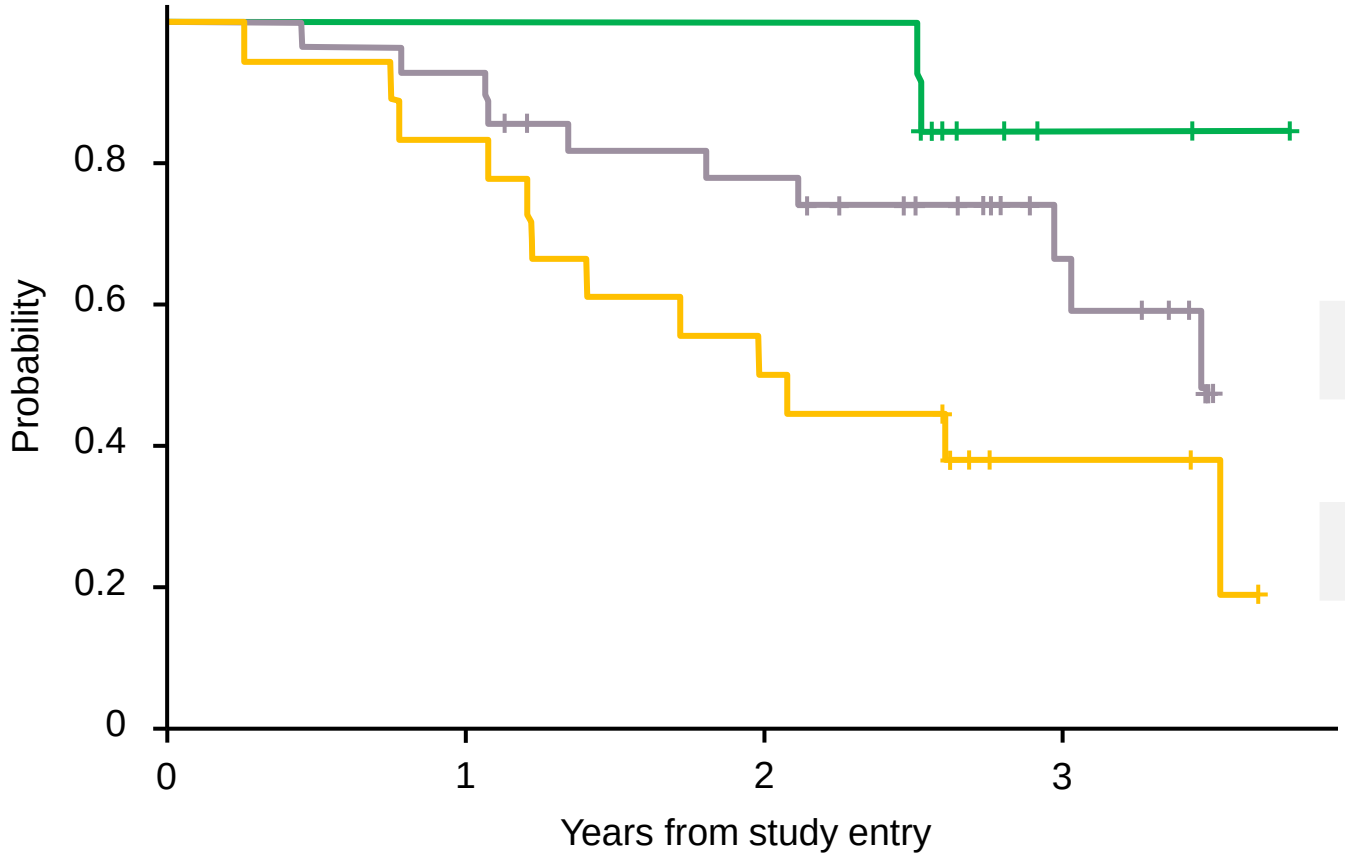
Czuczman M S et al. Ann Oncol 2012;23:2356-2362

CALGB-50701

- **Epratuzumab + rituximab**
- **59 evaluable pts**
- **Fifty-five of the 59 eligible pts completed all therapy**
- **ORR 86.5%**
  - 25 CRs (42.4%)
  - 27 PRs (45.8%)
  - 6 had stable disease (10.2%)
- **Median time to CR was 9.2 months**
- **21 pts progressed** (4 after CR, 13 after PR; 4 after stable disease)

Grant et al, Cancer, 119:3757, 2013

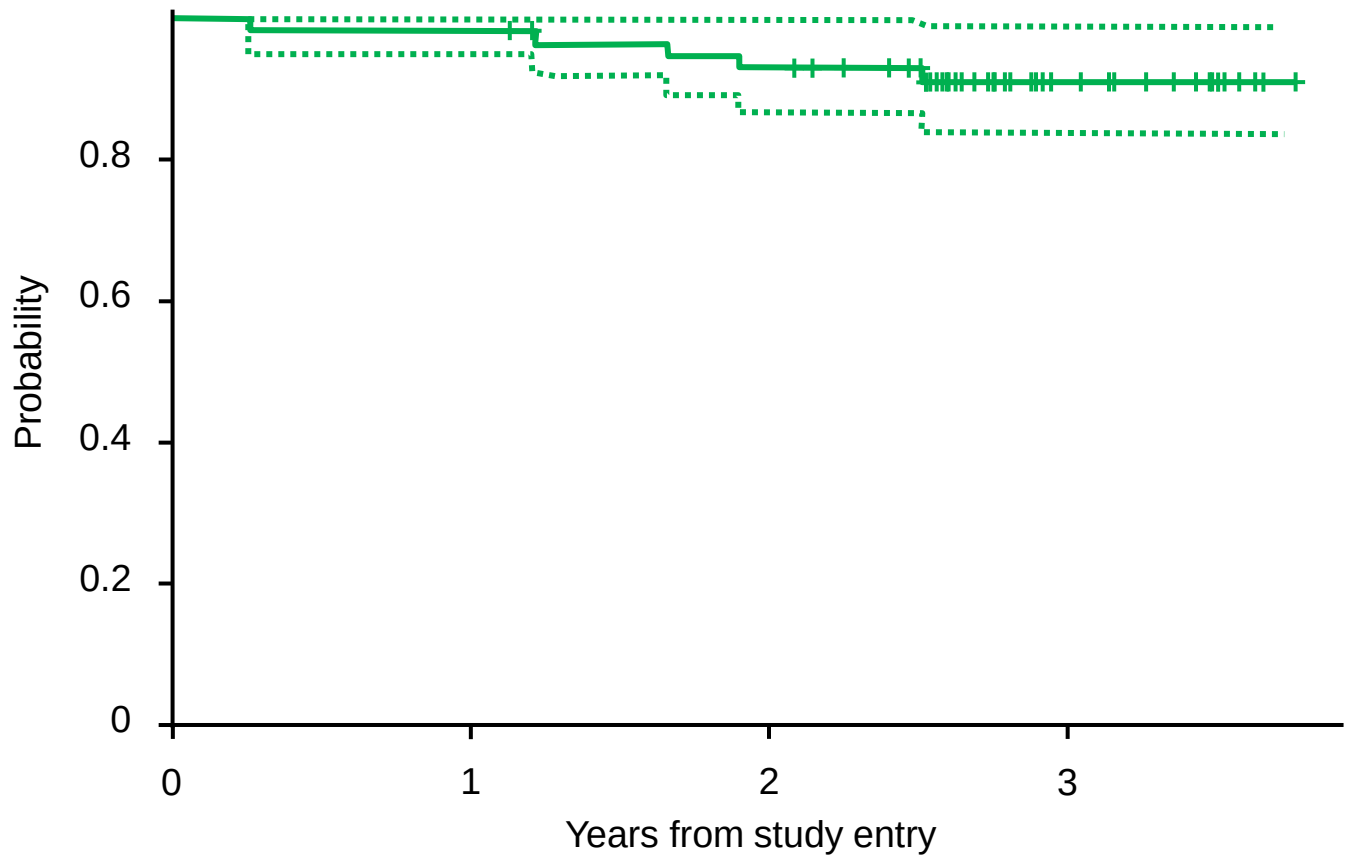
Progression-free survival by FLIPI risk group



	N	Events	Chi-square	P value
Low	13	2	7.68	
Intermediate	28	10		0.0215
High	18	12		

Grant et al, Cancer. 2013;119:3797-804

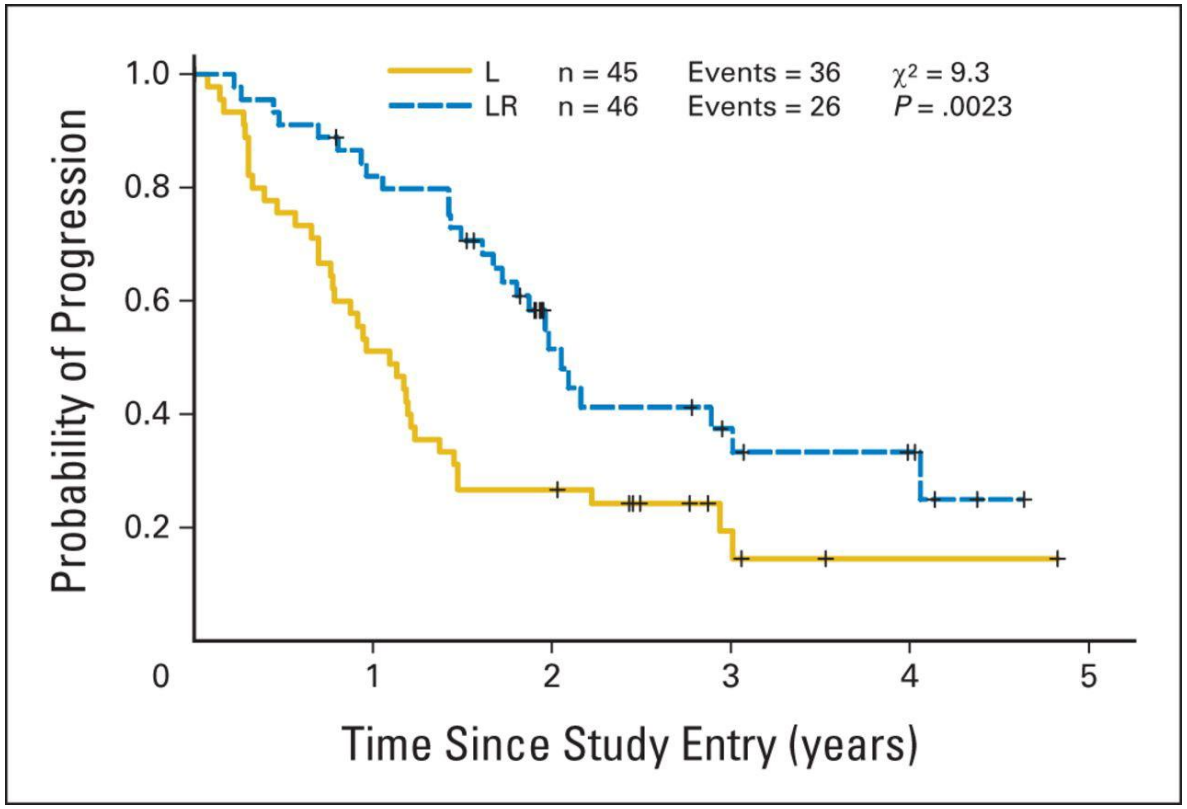
CALGB 50701:Overall Survival

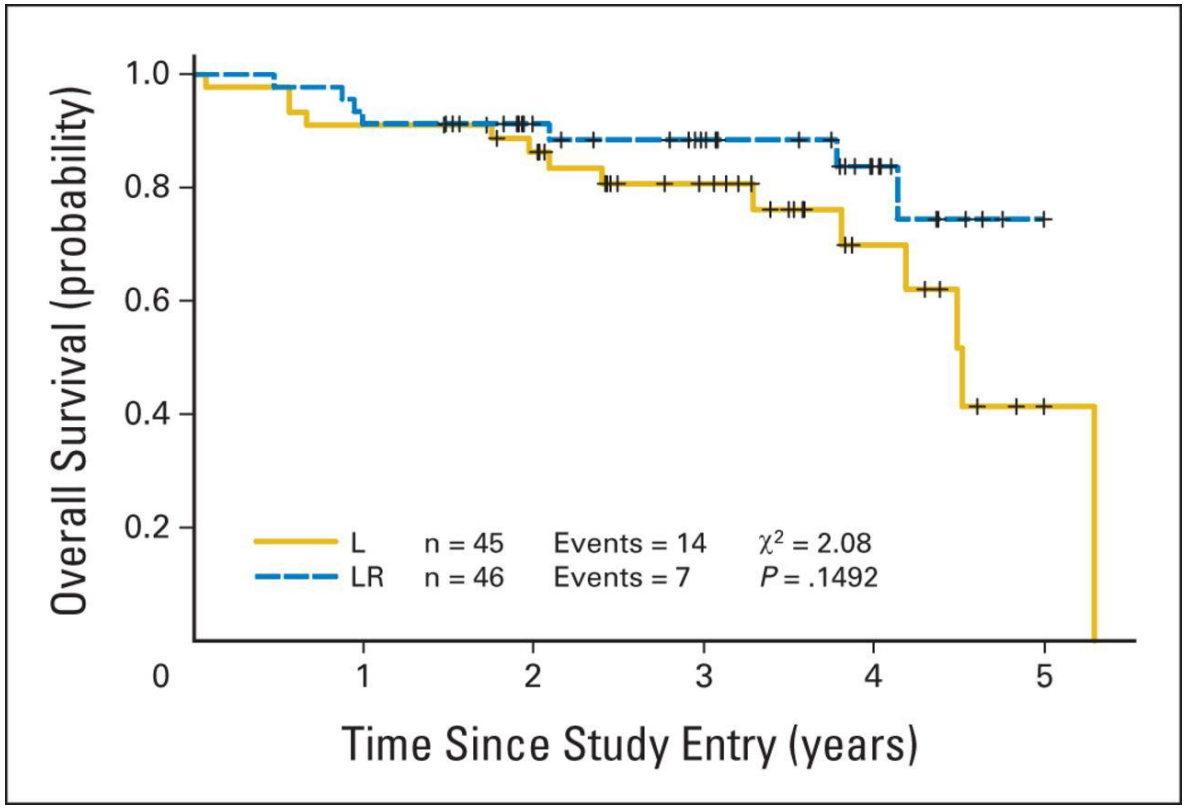


N	Events
59	5

Grant et al, Cancer. 2013;119:3797-804

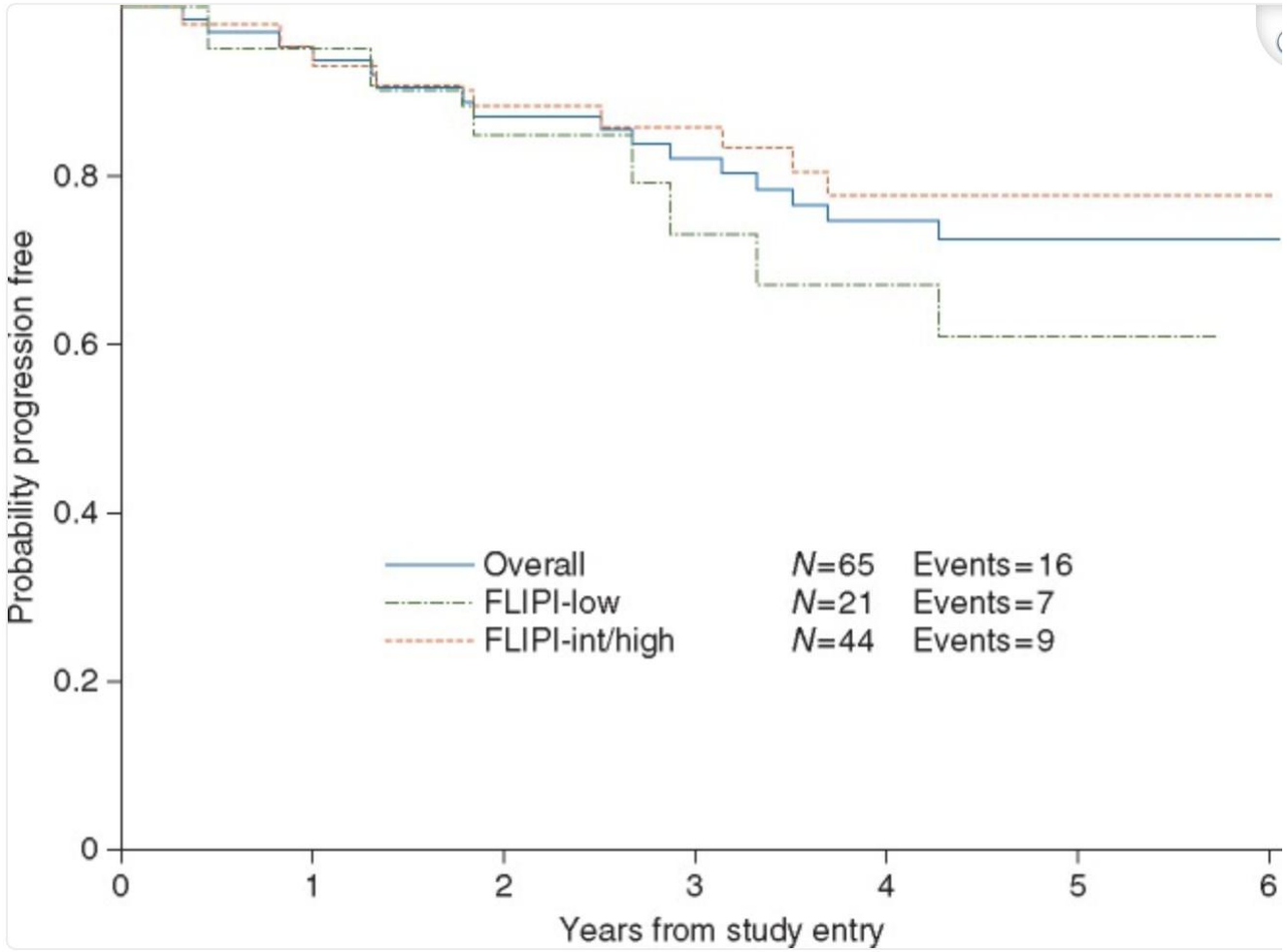
CALGB (Alliance 50401) in Relapsed FL: R^2 vs L





Leonard JP…Cheson BD, JCO 33:3635, 2015

R^2 As Initial Treatment of FL



Martin P ….Cheson BD, Ann Oncol 28:2806, 2017

ROSEWOOD: Study Design

Stratification by geographic region, number of prior lines, rituximab refractory status

Adults with grade 1-3a R/R FL previously treated with ≥2 prior regimens, including an anti-CD20 antibody and appropriate alkylator-based combination therapy; no prior BTK inhibitor; ECOG PS 0-2
(N = 217)

Zanubrutinib + Obinutuzumab*
(n = 145)

Obinutuzumab*
(n = 72)

Treated until disease progression or unacceptable toxicity†

*Zanubrutinib dosed at 160 mg PO BID. Obinutuzumab dosed at 1000 mg IV on Days 1, 8, and 15 of Cycle 1; Day 1 of cycles 2-6 and then Q8W up to a maximum of 20 doses. †Patients assigned to obinutuzumab with centrally confirmed PD or no response at 12 mo could crossover to receive combination therapy.

- **Primary endpoint:** ICR-assessed ORR according to Lugano classification
- **Key secondary endpoints:** investigator-assessed ORR, CR, DoR, PFS, OS, safety

Zinzani et al, JCO 41:5107, 2023

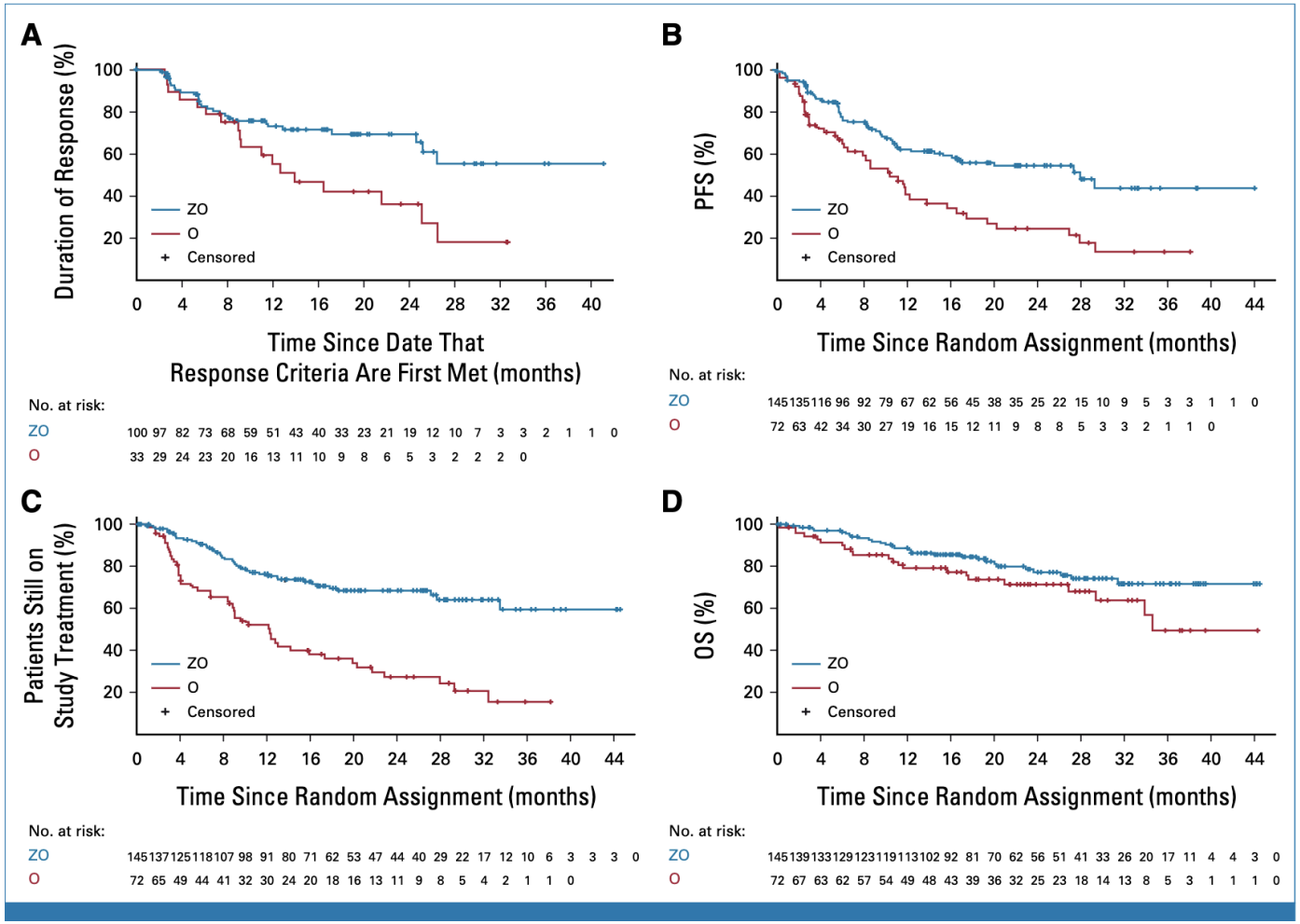
ROSEWOOD: Patient Outcomes

End Point	ZO (n = 145)	O (n = 72)	HR (95% CI)	Two-Sided *P* Value
ORR by ICR, % (95% CI)	69 (61 to 76)	46 (34 to 58)	—	.001
CR, No. (%)	57 (39)	14 (19)	—	.004
PR, No. (%)	43 (30)	19 (26)	—	—
DOR by ICR, months, median (95% CI)	NE (25.3 to NE)	14.0 (9.2 to 25.1)	—	—
18-month rate, %	69 (58 to 78)	42 (23 to 60)	—	—
Duration of CR by ICR, months, median (95% CI)	NE (26.5 to NE)	26.5 (2.7 to NE)	—	—
18-month rate, % (95% CI)	87 (74 to 94)	51 (21 to 75)	—	—
PFS by ICR, months, median (95% CI)	28.0 (16.1 to NE)	10.4 (6.5 to 13.8)	0.50 (0.33 to 0.75)	<.001
Median TTNT, months	NE (33.4 to NE)	12.2 (8.5 to 17.3)	0.34 (0.22 to 0.52)	<.001
Median OS, months (95% CI)	NE (NE to NE)	34.6 (29.3 to NE)	0.62 (0.35 to 1.07)	.085
24-month rate, % (95% CI)	77 (68 to 84)	71 (58 to 81)	—	—

Abbreviations: CR, complete response; DOR, duration of response; HR, hazard ratio; ICR, independent central review; NE, not estimable; O, obinutuzumab; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; TTNT, time to next treatment; ZO, zanubrutinib plus obinutuzumab.

Zinzani et al, JCO 41:5107, 2023

ROSEWOOD: Patient Outcomes



Zinzani et al, JCO 41:5107, 2023

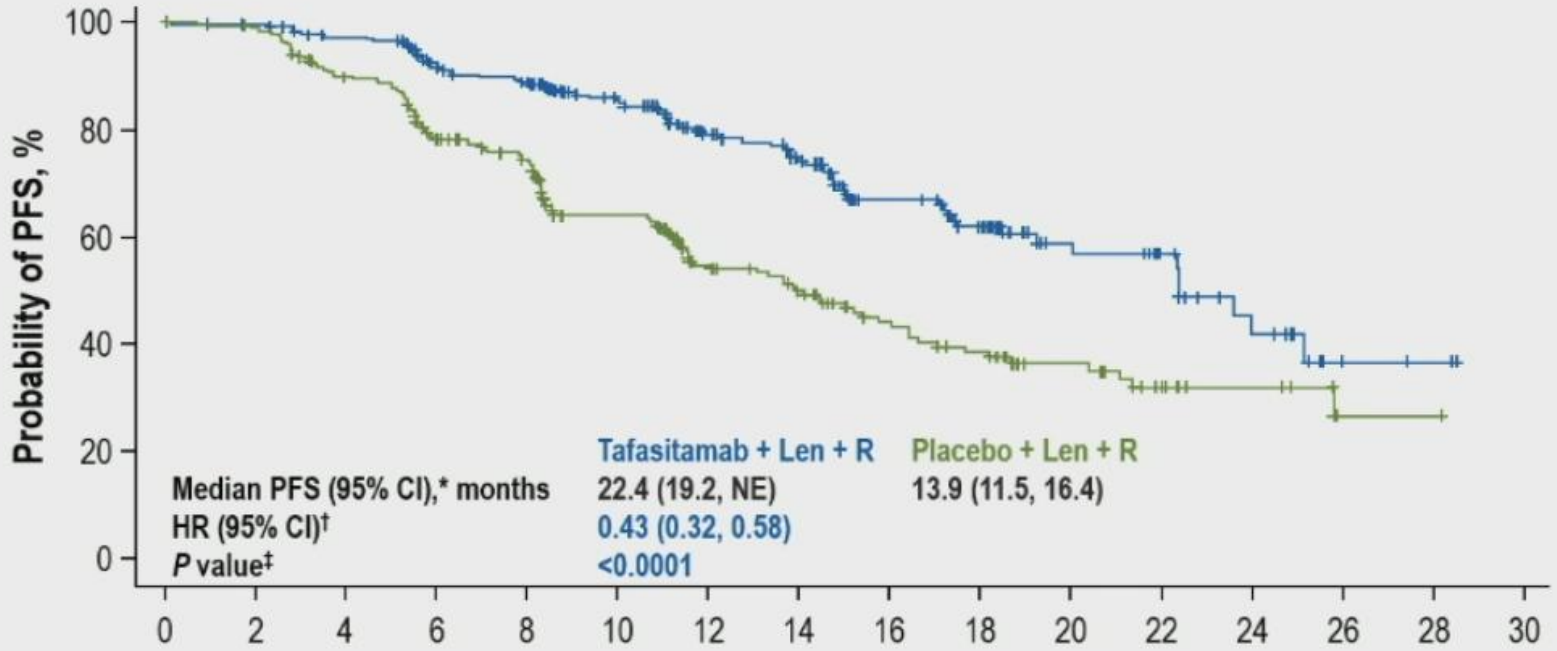
Tafasitamab Plus Lenalidomide and Rituximab for Relapsed or Refractory Follicular Lymphoma: Results From a Phase 3 Study (inMIND)

Laurie H. Sehn,[1] Stefano Luminari,[2,3] Christian W. Scholz,[4] Kai Hübel,[5] Antonio Salar,[6] Shankara Paneesha,[7,8] Björn E. Wahlin,[9] Panayiotis Panayiotidis,[10] Hui Peng Lee,[11] Ana Jimenez Ubieto,[12] Juan-Manuel Sancho,[13] Tae Min Kim,[14] Eva Domingo Domenech,[15] Takahiro Kumode,[16] Christina Poh,[17] Catherine Thieblemont,[18] Dries Deeren,[19] Edwin de Wit,[20] Michael Arbushites,[21] Marie-Laure Casadebaig[20] and Marek Trneny[22]

[1]BC Cancer Centre for Lymphoid Cancer and The University of British Columbia, Vancouver, BC, Canada; [2]Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy; [3]Surgical, Medical and Dental Department of Morphological Sciences related to Transplant, Oncology and Regenerative Medicine, University of Modena and Reggio Emilia, Reggio Emilia, Italy; [4]Vivantes Klinikum Am Urban, Berlin, Germany; [5]University of Cologne and Faculty of Medicine and University Hospital of Cologne, Cologne, Germany; [6]Hospital del Mar-IMIM, Barcelona, Spain; [7]University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; [8]University of Birmingham, Birmingham, UK; [9]Karolinska University Hospital, Stockholm, Sweden; [10]National and Kapodistrian University of Athens Medical School, General Hospital LAIKO, Athens, Greece; [11]Flinders Medical Centre, Adelaide, South Australia, Australia; [12]Servicio de Hematología, Hospital 12 de Octubre, Madrid, Spain; [13]ICO-IJC-Hospital Germans Trias i Pujol, Badalona, Universitat Autònoma de Barcelona, Barcelona, Spain; [14]Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Republic of Korea; [15]Institut Català d'Oncologia, Hospital Duran I Reynals, IDIBELL, Barcelona, Spain; [16]Kindai University, Osaka, Japan; [17]Fred Hutchinson Cancer Center/University of Washington, Seattle, WA, USA; [18]Saint-Paris Cité Université; Assistance Publique-Hôpitaux de Paris, Saint-Hospital, Paris, France; [19]AZ Delta General Hospital, Roeselare, Belgium; [20]Incyte International Biosciences Sàrl, Morges, Switzerland; [21]Incyte Corporation, Wilmington, DE, USA; [22]First Faculty of Medicine, Charles University, Prague, Czech Republic

Presented at the 66th ASH Annual Meeting & Exposition • San Diego, CA, USA • December 7-10, 2024 (Abstract #LBA-1)

Primary Endpoint: PFS by Investigator Assessment



Median follow-up time: 14.1 months

No. at Risk

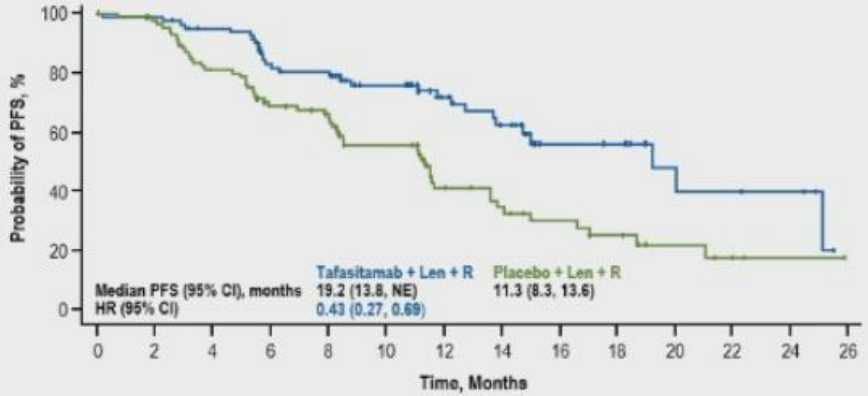
Tafasitamab + Len + R	273	261	250	212	200	164	119	103	71	57	30	22	12	3	2	0
Placebo + Len + R	275	265	235	192	173	126	82	70	48	40	26	16	10	2	2	0

Significant improvement in PFS was observed with tafasitamab

ITT population. *Estimated using Kaplan-Meier method. †Estimated using a stratified Cox proportional hazard model. ‡Stratified log-rank test with a 2-sided significance level of 5%. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; PFS, progression-free survival; R, rituximab.

PFS by POD24 Status and Refractoriness to Anti-CD20

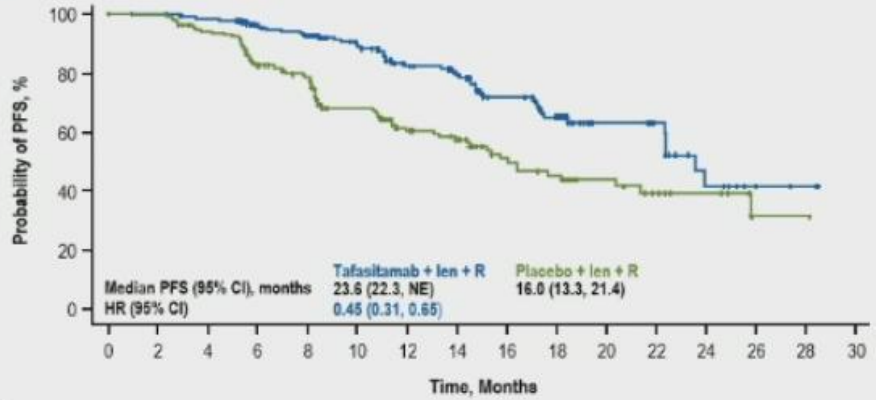
POD24: Yes



No. at Risk

Tafasitamab + Len + R	85	81	75	60	57	46	32	25	13	12	6	5	4	0
Placebo + Len + R	88	83	67	52	46	35	21	16	12	9	5	2	1	0

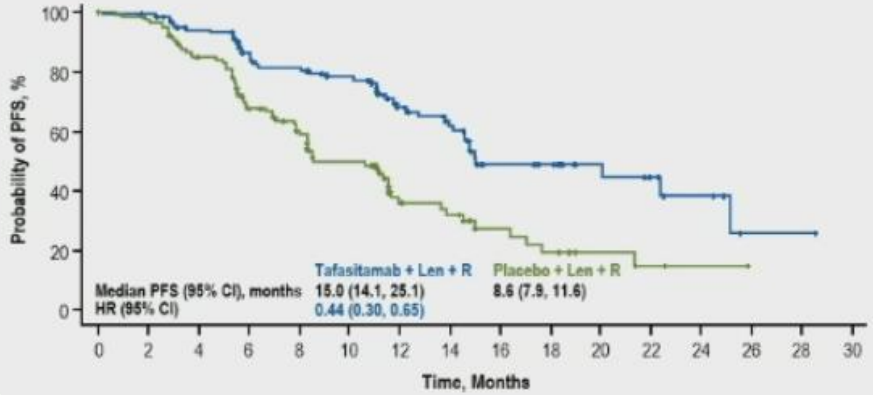
POD24: No



No. at Risk

Tafasitamab + Len + R	188	180	175	152	143	118	87	78	58	45	24	17	8	3	2	0
Placebo + Len + R	187	182	168	140	127	91	61	54	36	31	21	14	9	2	2	0

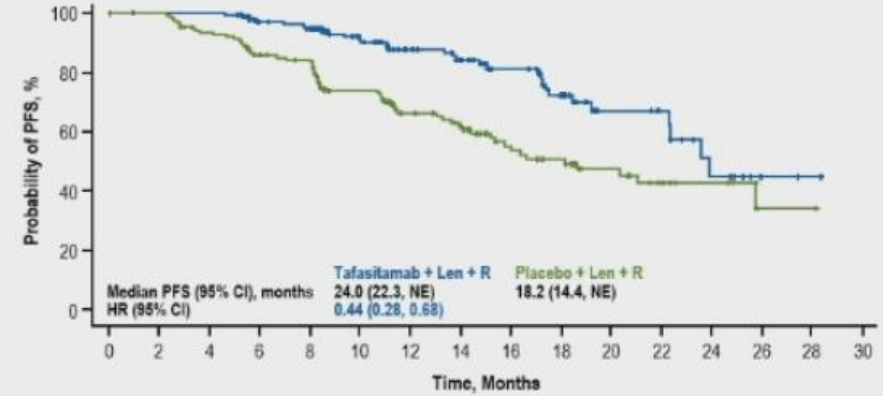
Anti-CD20 Refractory: Yes



No. at Risk

Tafasitamab + Len + R	118	113	102	86	80	71	46	38	21	19	11	8	5	1	1	0
Placebo + Len + R	115	108	91	66	54	41	20	16	10	7	4	2	1	0	0	0

Anti-CD20 Refractory: No

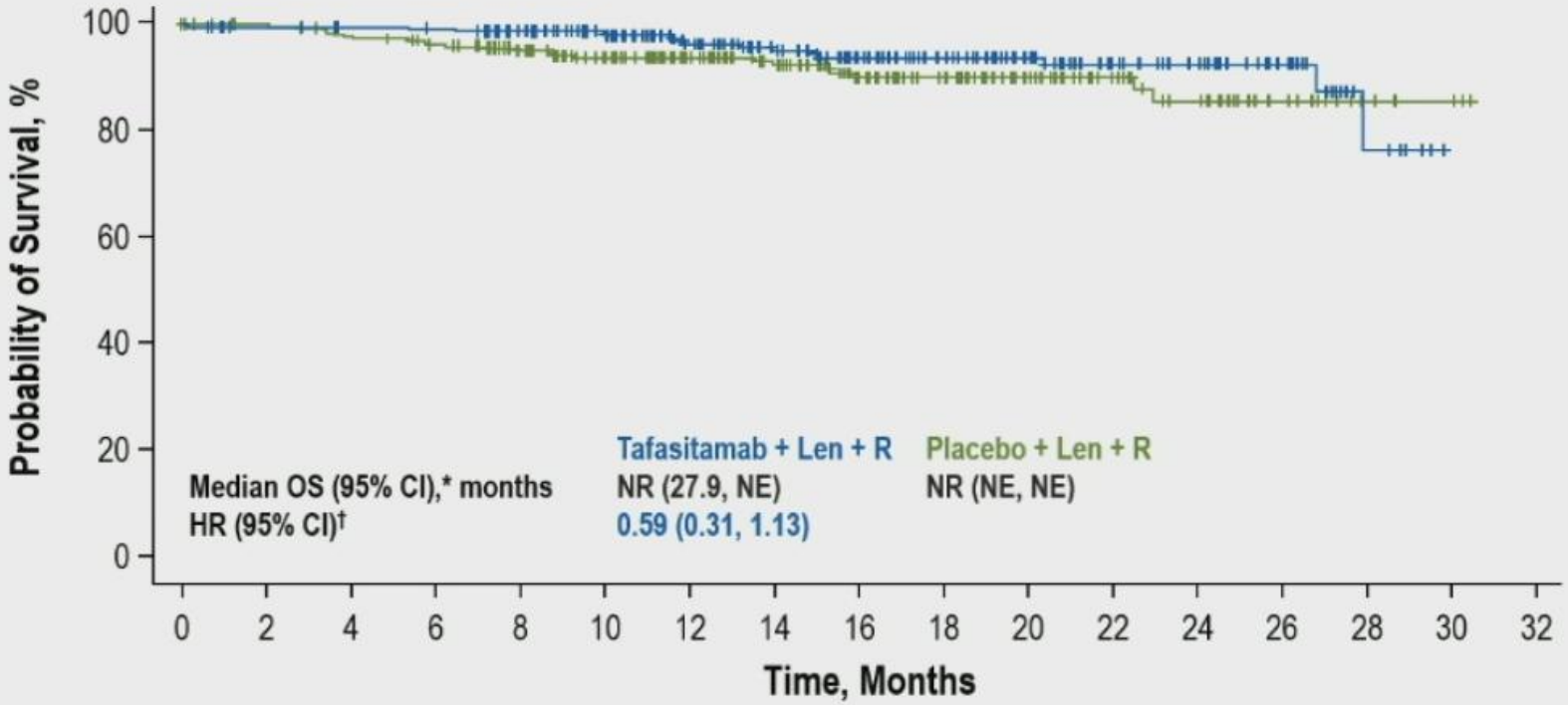


No. at Risk

Tafasitamab + Len + R	155	148	148	126	120	93	73	65	50	38	19	14	7	2	1	0
Placebo + Len + R	160	157	144	126	119	85	62	54	38	33	22	14	9	2	2	0

ITT population. Subgroup analyses are based on stratification factor. Analysis by investigator assessment. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; PFS, progression-free survival; POD24, progression of disease within 24 months of initial diagnosis; R, rituximab.

Overall Survival



No. at Risk																	
Tafasitamab + Len + R	273	266	263	261	240	216	178	149	124	103	80	53	42	26	7	0	0
Placebo + Len + R	275	268	260	252	230	203	164	138	108	90	66	46	34	15	6	3	0

- OS was tested only for futility at the time of the primary analysis
- After a median follow-up of 15.3 months, the futility threshold was not crossed and a positive trend was observed

ITT population. Analysis by investigator assessment. *Estimated using Kaplan-Meier method. †Estimated using a stratified Cox proportional hazard model. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; NR, not reached; OS, overall survival; R, rituximab.

Loncastuximab tesirine with rituximab induces robust and durable complete metabolic responses in high-risk relapsed/refractory follicular lymphoma

Juan Alderuccio, Alvaro Alencar, Jonathan H. Schatz, Russ A. Kuker, David Sicre, Georgios Pongas, Isildinha M. Reis, Jay Spiegel, Laura Medina Andara, Lazaros J. Lekakis, Joseph S. Gyedu, Jose Sandoval-Sus, Amer Beitinjaneh, Michele Stanchina, Asaad Trabolsi, Izidore S. Lossos, Joseph D. Rosenblatt, David Lessen, Craig H. Moskowitz

American Society of Hematology 2024, Abstract 337

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

NCI Designated Cancer Center

@SylvesterCancer

Prior Treatment Characteristics

	n = 39	%
Refractory to last therapy	20	51
Relapsed FL	19	49
Median no, of prior lines, n (range)	1 (1-6)	
≥3 lines of therapy	11	28
Prior frontline regimens		
• **R-CHOP**	22	56
• **Bendamustine with rituximab**	10	26
• **Rituximab**	6	15
• **Fludarabine, mitoxantrone, dexamethasone with rituximab**	1	3

TEAEs

	Most Common (≥10% Overall) Treatment-Emergent Adverse Events							
	Adverse event	Grade 1-2, n	%	Grade 3, n	%	Grade 4, n	%	Any grade, n	%
Hematological TEAEs	Neutropenia	10	25.6	4	10.3	1	2.6	15	38.5
	Anemia	14	35.9					14	35.9
	Lymphopenia	5	12.8	5	12.8	3	7.7	13	33.3
	Thrombocytopenia	9	23.1					9	23.1
Non-hematological TEAEs	Hyperglycemia	16	41	1	2.6			17	43.6
	Increased ALP	16	41					16	41
	Increased ALT	14	35.9	1	2.6			15	38.5
	Fatigue	15	38.5	1	3.1			15	38.5
	Increased AST	15	38.5					15	38.5
	Rash maculo-papular	14	35.9					14	35.9
	Localized edema	5	12.8	1	2.6			6	15.4
	Photosensitivity	6	15.4					6	15.4
	Generalized edema	5	12.8	1	2.6			6	15.4
	Diarrhea	6	15.4					6	15.4
	Pleural effusion	5	12.8					5	12.8
	Dyspnea	4	10.3	1	2.6			5	12.8

Post-hoc Efficacy Analyses

	n	Best ORR	Best CR rate
POD24*	20	100%	85%
High risk FLIPI score	24	96%	67%
Prior transformed FL	11	100%	73%
Rituximab with an alkylating agent	32	100%	75%

**Previously treated with rituximab and an alkylating agent*

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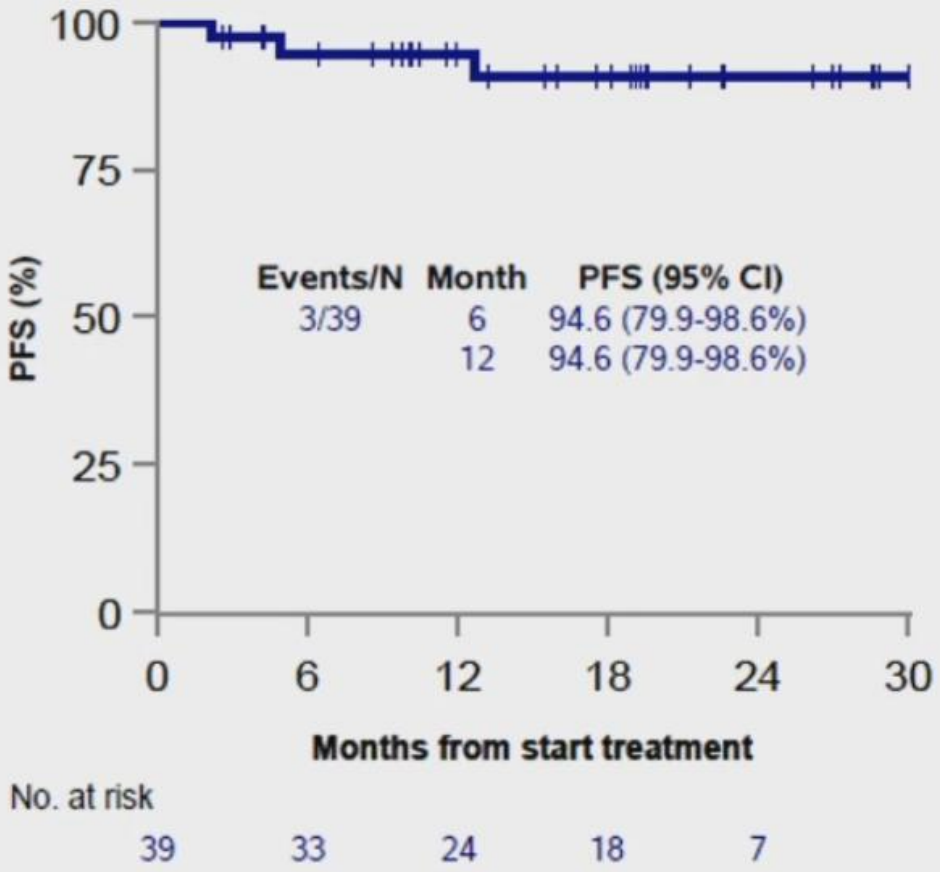
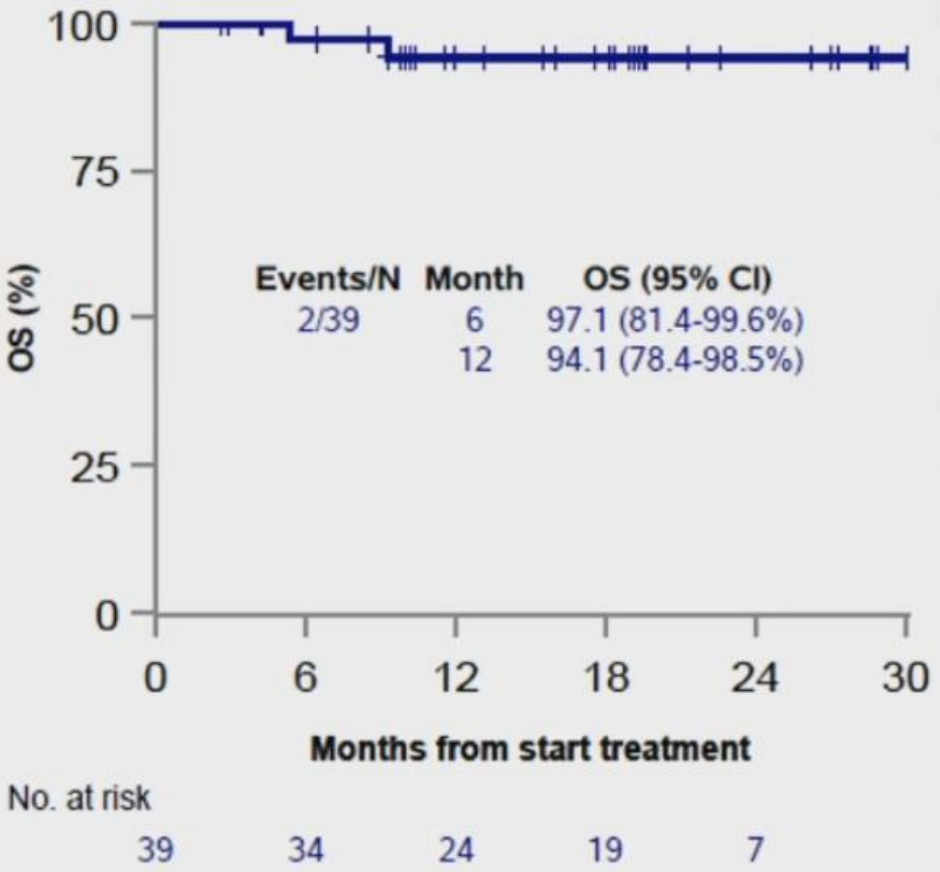
UNIVERSITY OF MIAMI HEALTH SYSTEM

Time-to-Event Endpoints





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Fixed-Duration Epcoritamab + R^2 Drives Deep and Durable Responses in Patients with Relapsed or Refractory Follicular Lymphoma: 2-Year Follow-Up from Arm 2 of the EPCORE NHL-2 Trial

Lorenzo Falchi, MD,[1] Anna Sureda, MD, PhD,[2] Sirpa Leppä, MD, PhD,[3] Joost S.P. Vermaat, MD, PhD,[4] Marcel Nijland, MD, PhD,[5] Jacob Haaber Christensen, MD, PhD,[6] Sven de Vos, MD, PhD,[7] Harald Holte, MD, PhD,[8] Reid W. Merryman, MD,[9] Pieternella J. Lugtenburg, MD, PhD,[10] Pau Abrisqueta, MD, PhD,[11] Kim M. Linton, MBChB, PhD,[12] Gauri Sunkersett, DO,[13] Christopher Morehouse, MS,[14] Andrew J. Steele, PhD,[14] Jennifer Marek,[14] Liwei Wang, PhD,[14] Daniela Hoehn, MD, PhD,[14] Martin Hutchings, MD, PhD,[15] David Belada, MD, PhD[16]

[1]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Clinical Hematology Department, Institut Català d'Oncologia – L'Hospitalet, IDIBELL, Universitat de Barcelona, Barcelona, Spain; [3]University of Helsinki and Helsinki University Hospital Comprehensive Cancer Center, Helsinki, Finland; [4]Leiden University Medical Center, Leiden, Netherlands; [5]University Medical Center Groningen and University of Groningen, Groningen, Netherlands; [6]Odense University Hospital, Odense, Denmark; [7]Ronald Reagan University of California Los Angeles Medical Center, Los Angeles, CA, USA; [8]Oslo University Hospital and KG Jebsen Center for B-cell Malignancies, Oslo, Norway; [9]Dana-Farber Cancer Institute, Boston, MA, USA; [10]On behalf of the Lunenburg Lymphoma Phase I/II Consortium-HOVON/LLPC, Erasmus MC Cancer Institute, University Medical Center, Department of Hematology, Rotterdam, Netherlands; [11]Hospital Universitario Vall d'Hebron, Barcelona, Spain; [12]The Christie NHS Foundation Trust, Manchester Cancer Research Centre, and Division of Cancer Sciences, University of Manchester, Manchester, UK; [13]AbbVie, North Chicago, IL, USA; [14]Genmab, Plainsboro, NJ, USA; [15]Rigshospitalet and University of Copenhagen, Copenhagen, Denmark; [16]4th Department of Internal Medicine – Hematology, University Hospital and Faculty of Medicine, Hradec Králové, Czech Republic

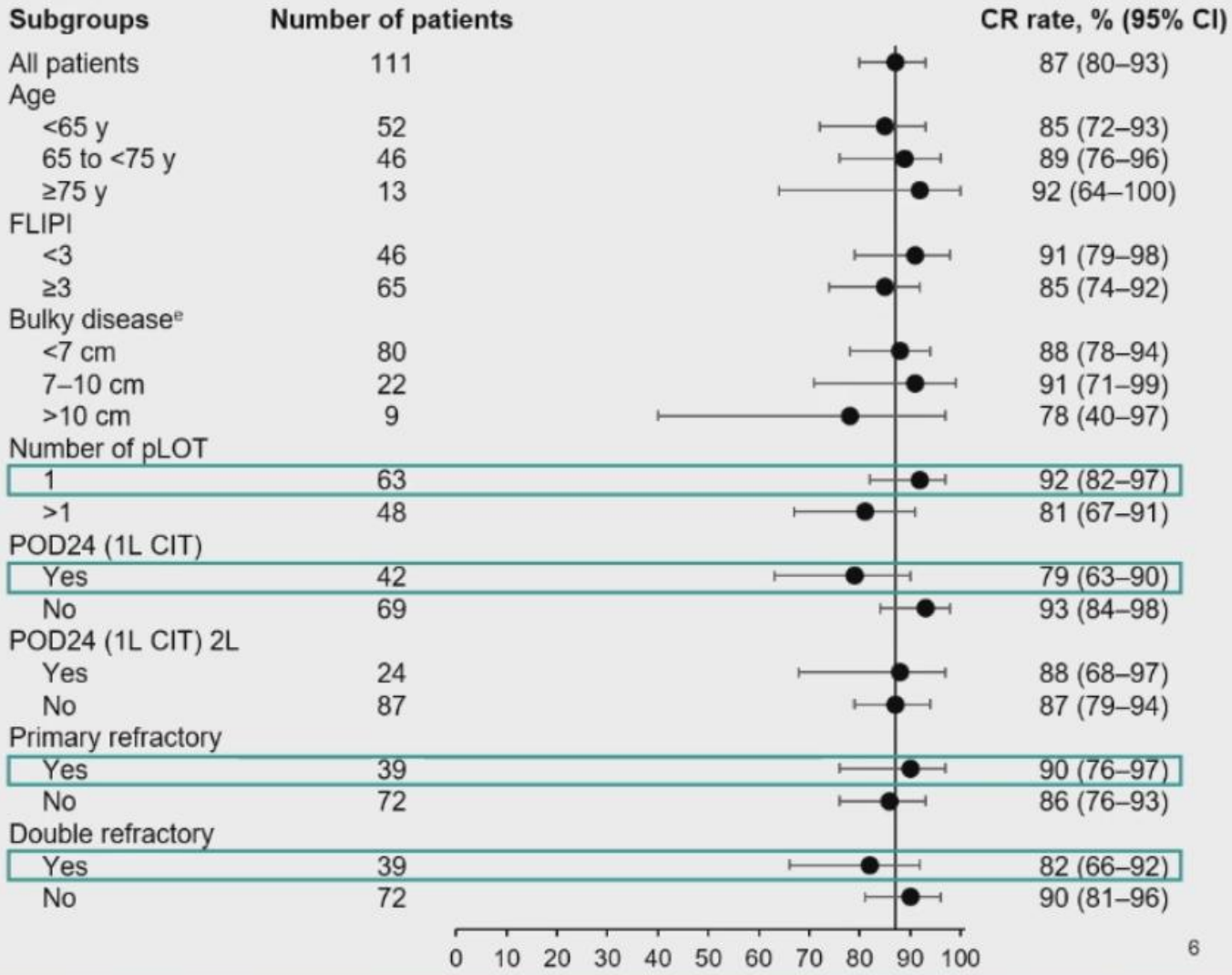
Presented at the American Society of Hematology Annual Meeting; December 7–10, 2024; San Diego, CA, USA

Deep Responses Regardless of High-Risk Features

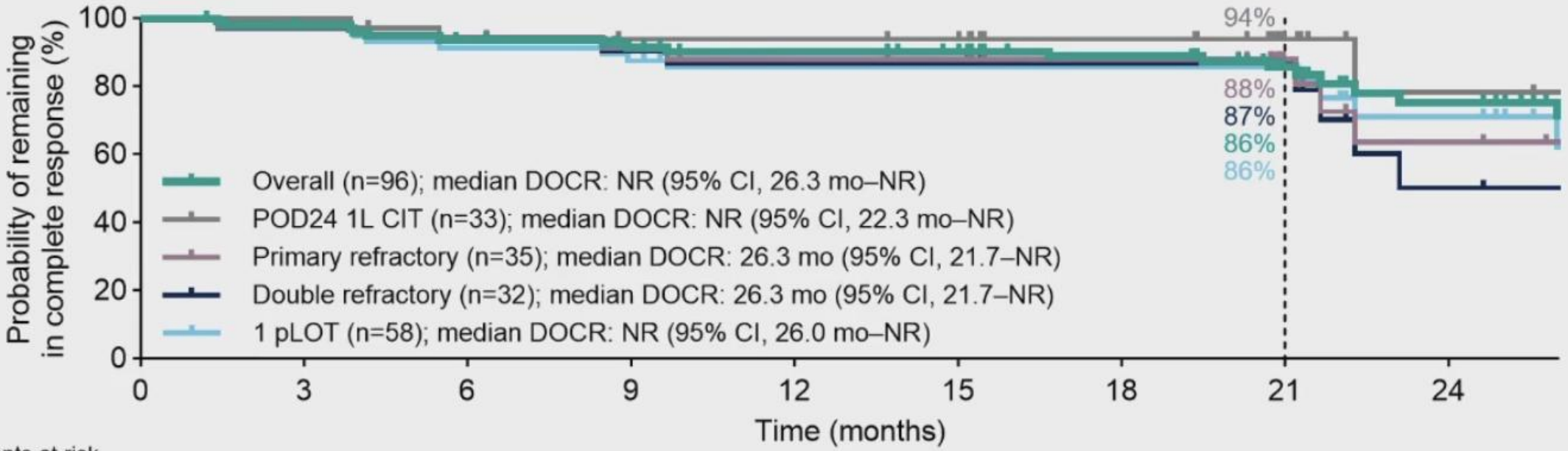
Best Response, n (%)[a]	N=111
Overall response	107 (96)
Complete response	97 (87)
Partial response	10 (9)
Progressive disease	2 (2)

MRD Negativity, n/n (%)	MRD Evaluable
MRD negativity at any time[b]	66/75 (88)
MRD negative and complete response[c]	63/68 (93)
MRD negativity in high-risk subgroups[d]	
POD24 (1L CIT)	26/30 (87)
Primary refractory	25/28 (89)
Double refractory	23/27 (85)

[a]Two patients were not evaluable for response. [b]MRD negative at any time point with an assay cutoff of 10^{-6} (PBMC assay; clonoSEQ). [c]One patient became MRD positive at a subsequent assessment (C5D1); patient later experienced radiographic PD. [d]Patients could be counted in ≥1 high-risk subgroup. [e]Bulky disease per investigator.



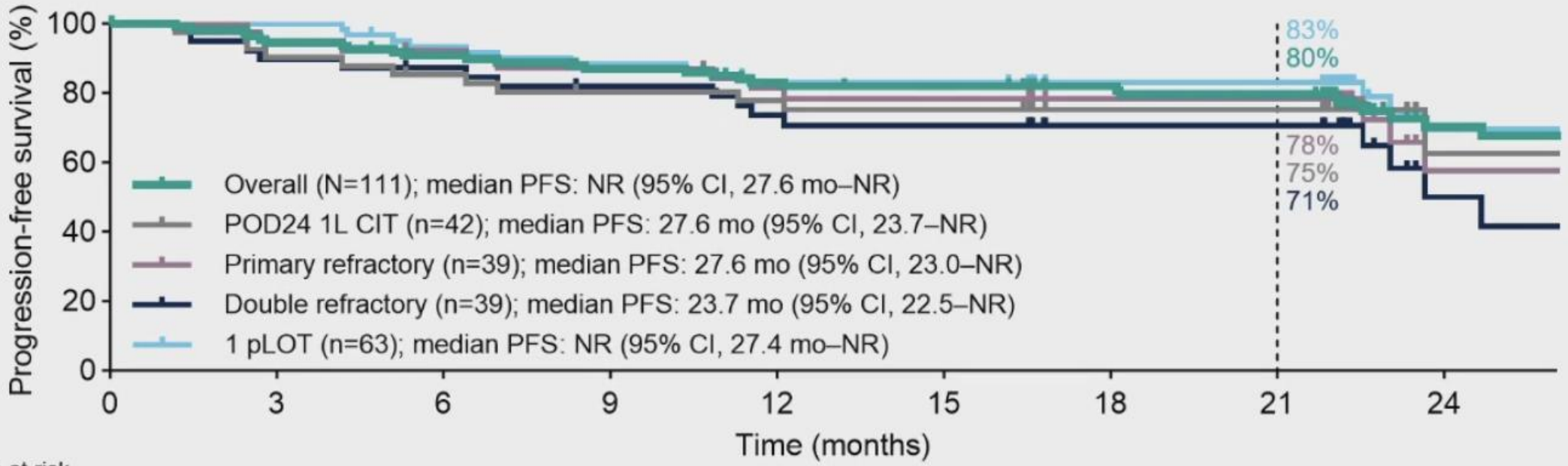
Durable Complete Responses Across High-Risk Subgroups



Patients at risk									
Overall	96	92	85	79	75	72	63	37	27
POD24 1L CIT	33	33	30	28	28	27	21	10	5
Primary refractory	35	34	32	28	26	25	22	12	7
Double refractory	32	31	29	26	24	23	18	11	5
1 pLOT	58	56	51	46	42	39	36	20	13

Data cutoff: May 15, 2024. Median follow-up for DOCR: 20.9 months

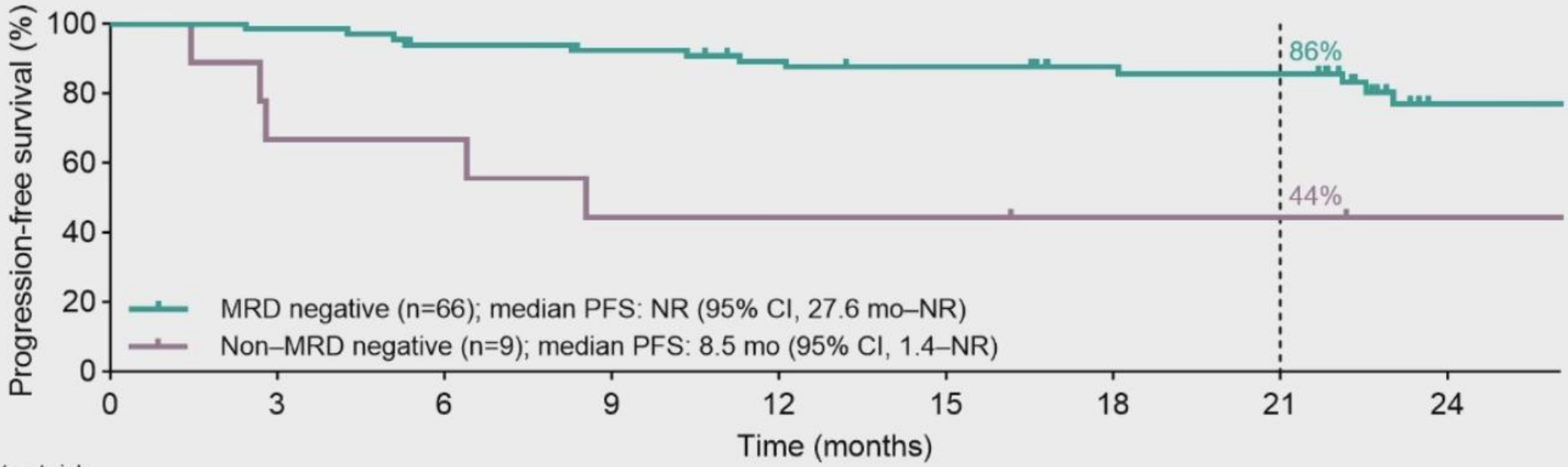
PFS Observed in Most Patients, Highest With 1 pLOT



Patients at risk									
Overall	111	102	95	90	82	80	68	66	29
POD24 1L CIT	42	37	34	31	30	29	21	21	5
Primary refractory	39	37	35	32	28	27	22	22	7
Double refractory	39	35	33	30	26	25	18	18	6
1 pLOT	63	61	55	52	45	45	38	38	13

Data cutoff: May 15, 2024. PFS is among the full analysis population. Median follow-up for PFS: 22.3 months.

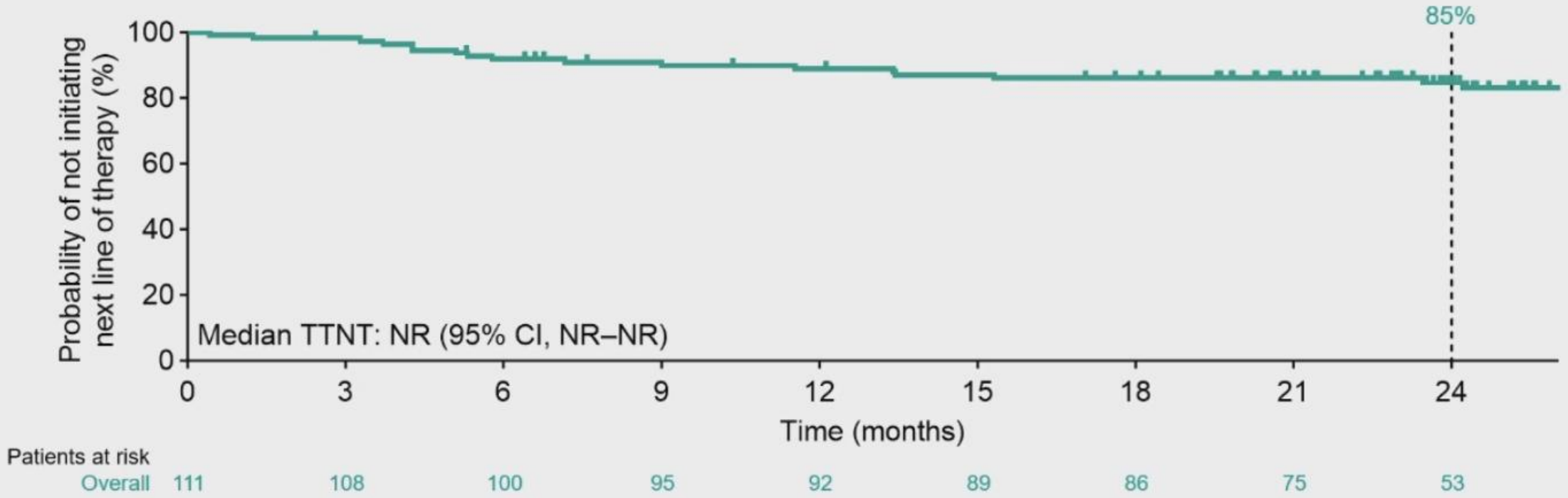
MRD Negativity Associated With Improved PFS



Patients at risk									
MRD negative	66	65	61	59	55	53	44	43	20
Non–MRD negative	9	6	6	4	4	4	3	3	2

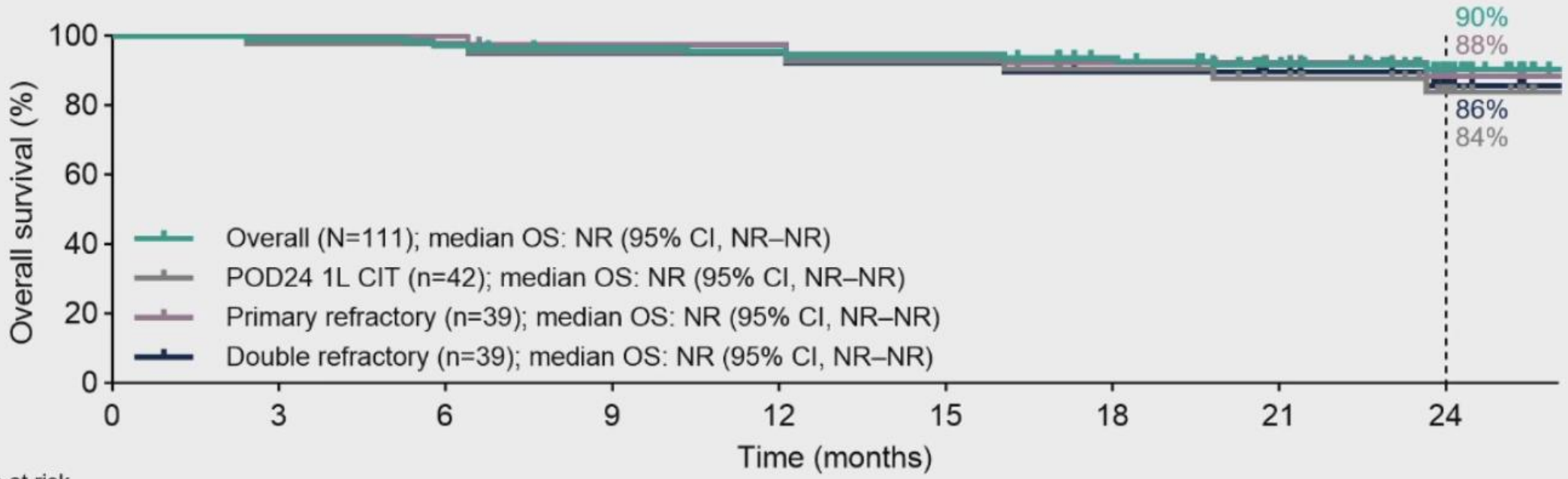
Data cutoff: May 15, 2024. PFS is among 75 MRD-evaluable patients. MRD negative at any time point with an assay cutoff of 10^{-6} (PBMC assay; clonoSEQ). Median follow-up for PFS for the full analysis population: 22.3 months. Percentages are Kaplan–Meier estimates.

Next Therapy Not Initiated for Most Patients by 2 Years



Data cutoff: May 15, 2024. TTNT is among the full analysis population. Median follow-up for TTNT: 24.7 months. Percentages are Kaplan–Meier estimates.

Most Patients Remained Alive at 2 Years



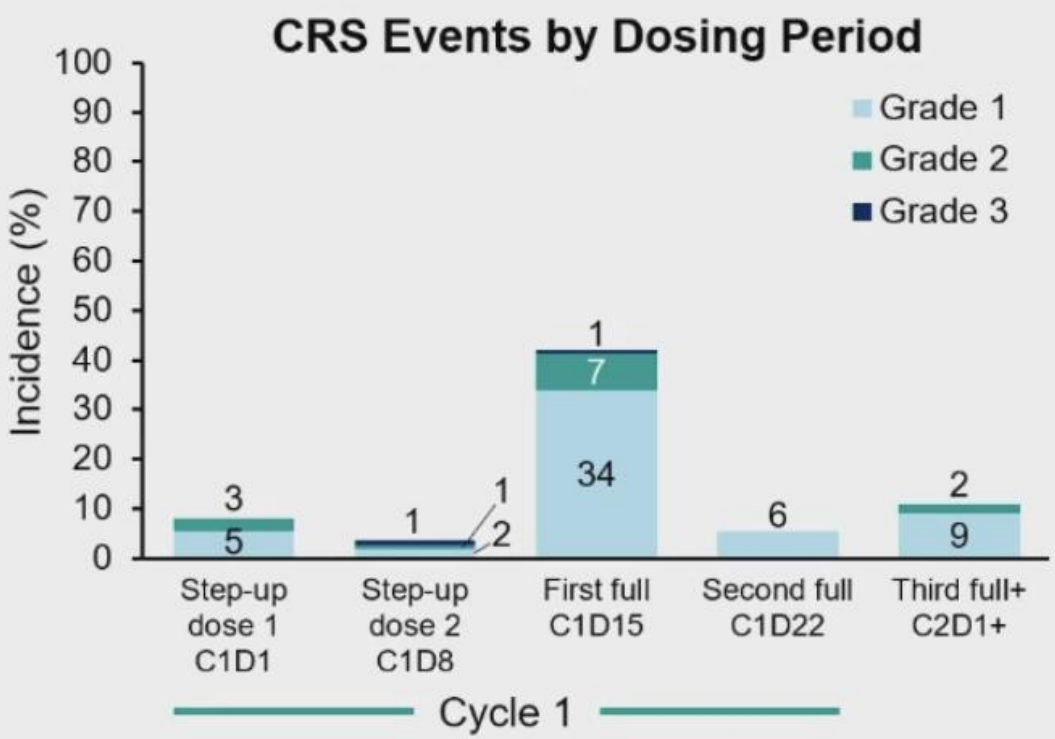
Patients at risk									
Overall	111	110	108	104	103	102	96	83	62
POD24 1L CIT	42	41	41	39	39	38	34	29	19
Primary refractory	39	39	39	37	37	36	32	29	20
Double refractory	39	39	38	36	36	35	30	25	18

Data cutoff: May 15, 2024. OS is among the full analysis population. Median follow-up: 25.3 months (range, 2.4+ to 34.1). Percentages are Kaplan–Meier estimates.

Primarily Low-Grade CRS and ICANS With 2 Step-Up Doses; Timing of CRS Was Predictable

	N=111
CRS, n (%)[a]	57 (51)
Grade 1	42 (38)
Grade 2	13 (12)
Grade 3	2 (2)
Median time to onset after first full dose, d (range)	2 (1–9)
CRS resolution, n/n (%)	57/57 (100)
Median time to resolution, d (range)[b]	2 (1–23)
Treated with tocilizumab, n (%)	14 (13)
Leading to epcoritamab discontinuation, n (%)	**0**

- A grade 1 ICANS event occurred; the event resolved in 7 days without treatment and did not lead to treatment discontinuation



[a]Graded by Lee et al 2019 criteria.[1] [b]Median is Kaplan–Meier estimate based on longest CRS duration in patients with CRS. **1.** Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-38.

Abstract #340

Single-Agent Mosunetuzumab Produces High Complete Response Rates in Patients with Newly Diagnosed Follicular Lymphoma: Primary Analysis of the MITHIC-FL1 Trial

Lorenzo Falchi, MD,[1] Michelle Okwali, MPH,[1] Alexandra Lopes Ferreira, BS,[1] Paul Hamlin, MD,[1] Jennifer Lue, MD,[1] Paola Ghione, MD,[1] Colette Owens, MD,[1] Pallawi Torka, MD,[1] Anita Kumar, MD,[1] Raphael Steiner, MD,[1] Zachary Epstein-Peterson, MD,[1] M. Lia Palomba, MD,[1] Robert Stuver, MD,[1] Ariela Noy, MD,[1] Anastasia Martinova, RN,[1] Lauren Wood, RN,[1] Clare Grieve, MPH,[1] Walter Ramos Amador, MPH, MS,[1] Santosha Vardhana, MD, PhD,[1] Andrew D. Zelenetz, MD, PhD,[1] Lori A. Leslie, MD,[2] Joseph L. Roswarski, MD,[3] Kieron Dunleavy, MD,[3] Andre Goy, MD, MS,[2] Gilles Salles, MD, PhD[1]

[1]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY; [2]Lymphoma Division, John Theurer Cancer Center, Hackensack, NJ; [3]Lymphoma, Hematologic Malignancies Division, Lombardi Comprehensive Cancer Center, Washington, DC

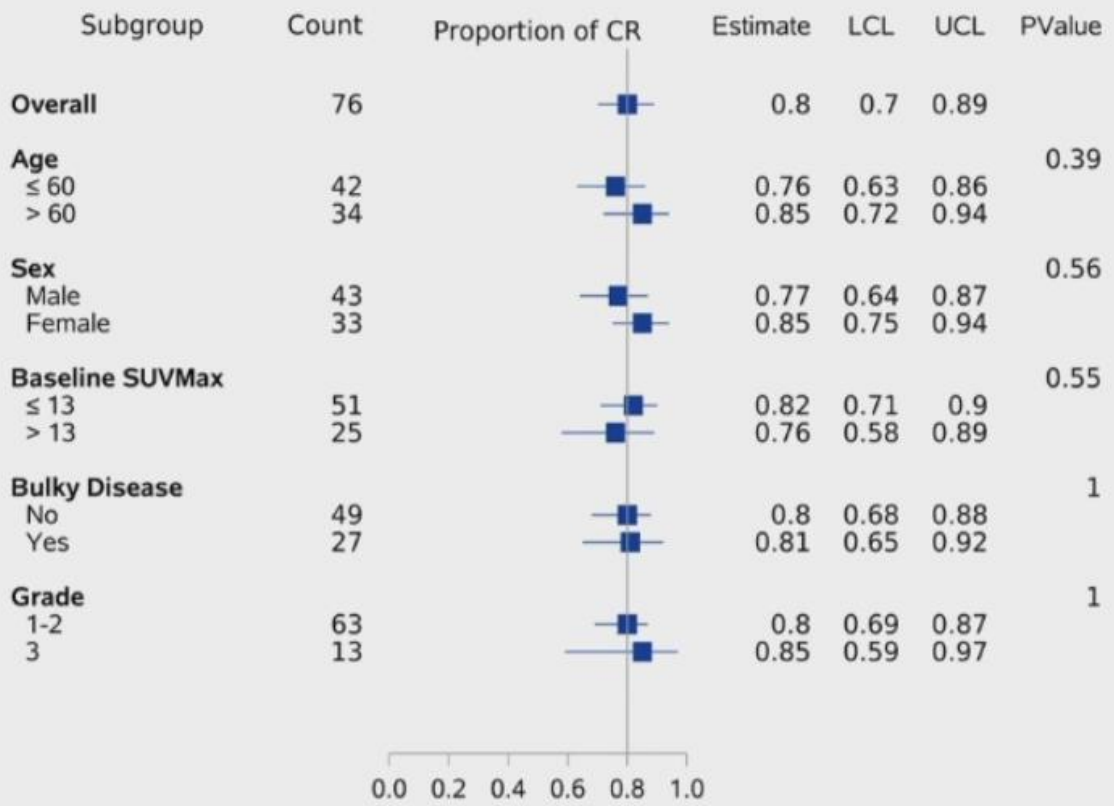
Memorial Sloan Kettering Cancer Center

Presented at the 66th American Society of Hematology Annual Meeting and Exposition; December 9–12, 2024; San Diego, CA

SC mosun in 1L FL

Complete response rates were consistently high

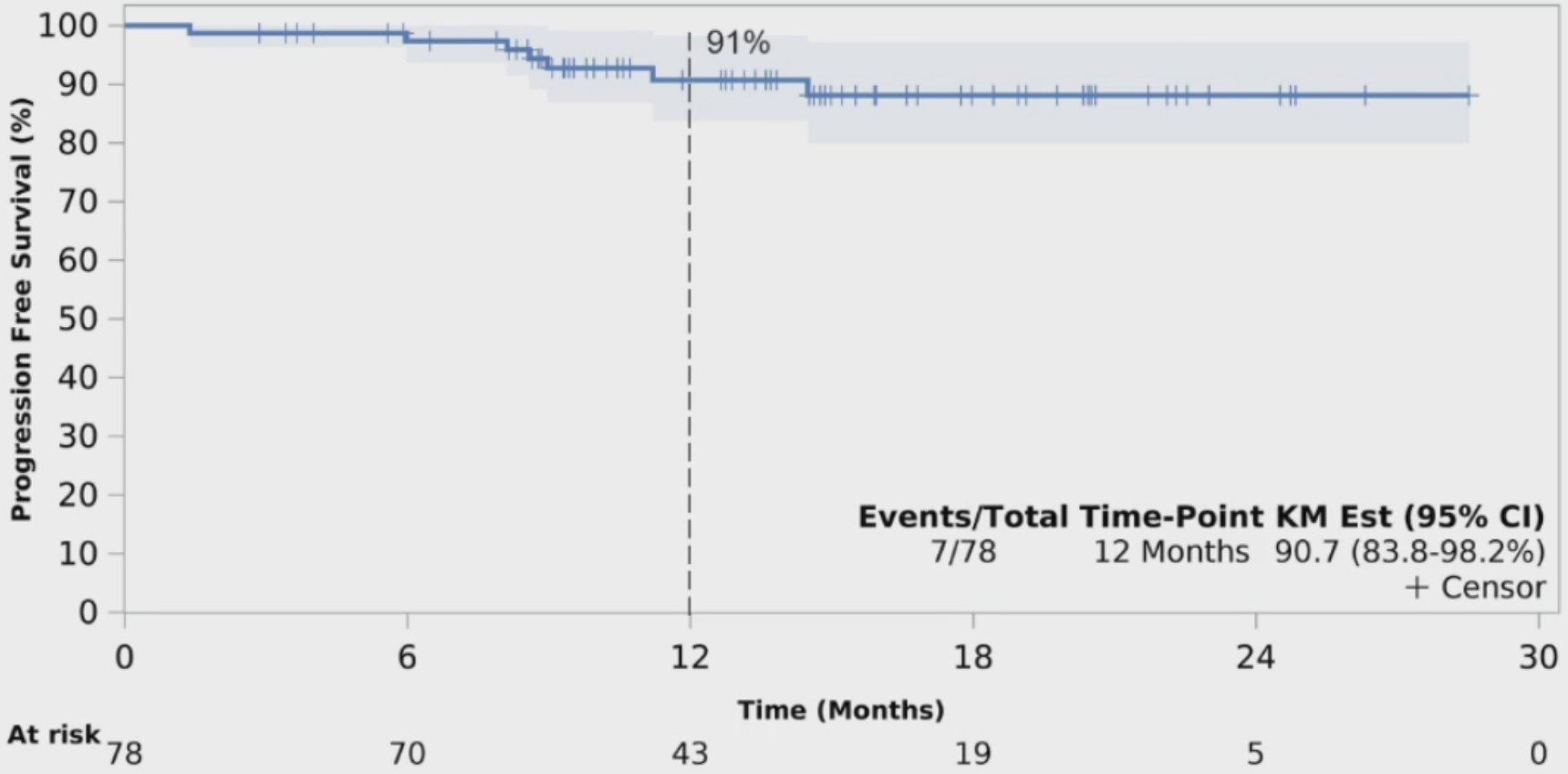
Response type	Response evaluable (N=76)	Intention-to-treat (N=78)
Overall response	**96%**	94%
Complete response	**80%**	78%
Partial response	16%	15%
Stable disease	3%	3%
Progressive disease	1%	1%
Non-evaluable	n/a	3%



Data cutoff: November 1, 2024; response assessed per the 2014 Lugano criteria and integrated with the 2016 LYRIC criteria; evaluable = patients who received at least one dose of study drug and underwent at least one response assessment;

SC mosun in 1L FL

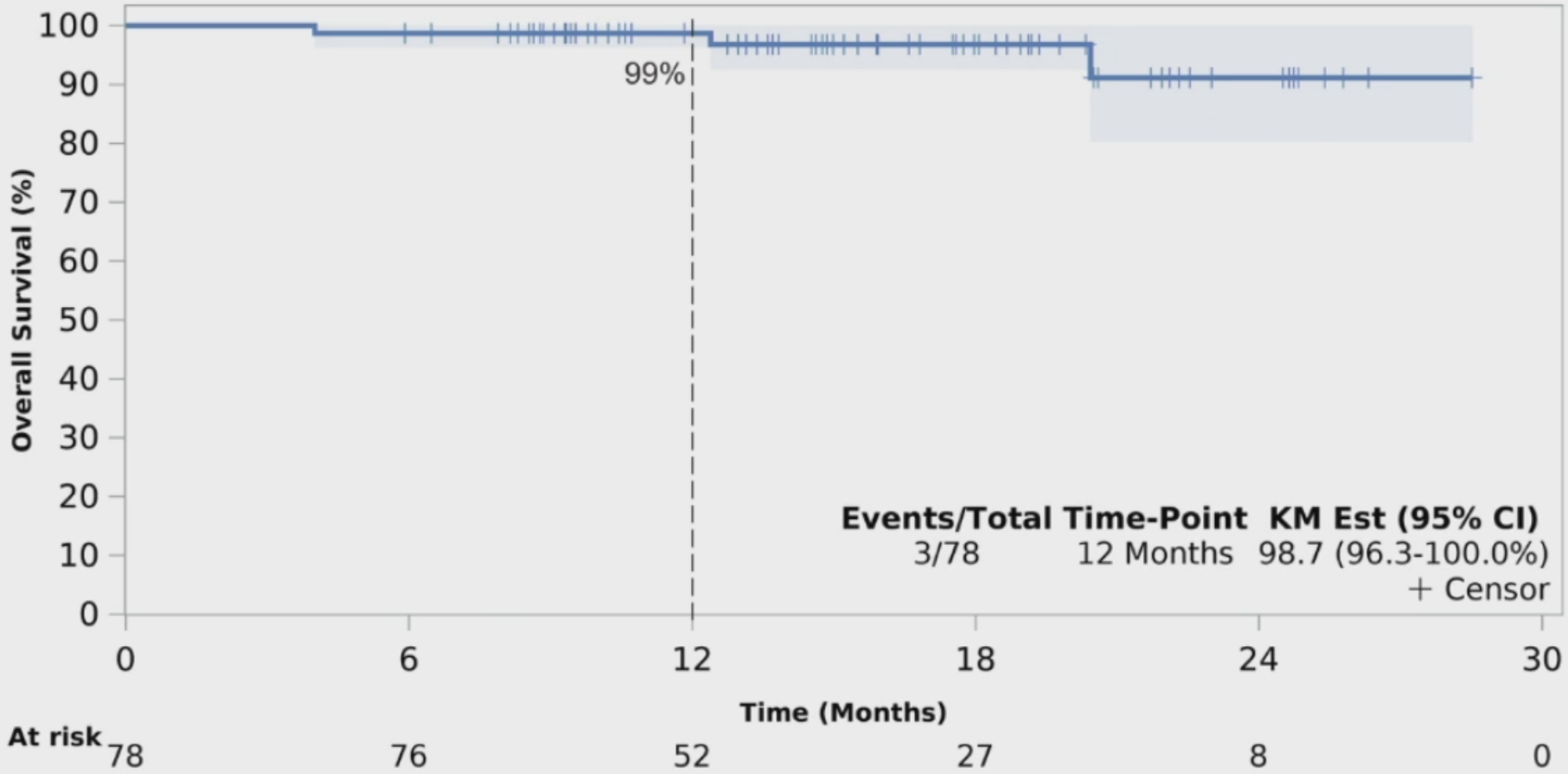
Progression Free Survival



- **An estimated 91% of patients remained progression-free at 1 year**
- 7 patients progressed:
  - 3 patients had CD20- POD with FL histology
  - 3 patients had transformation to CD20+ DLBCL (one 6 weeks after study entry); after chemoimmunotherapy all achieved CR

SC mosun in 1L FL

Overall Survival



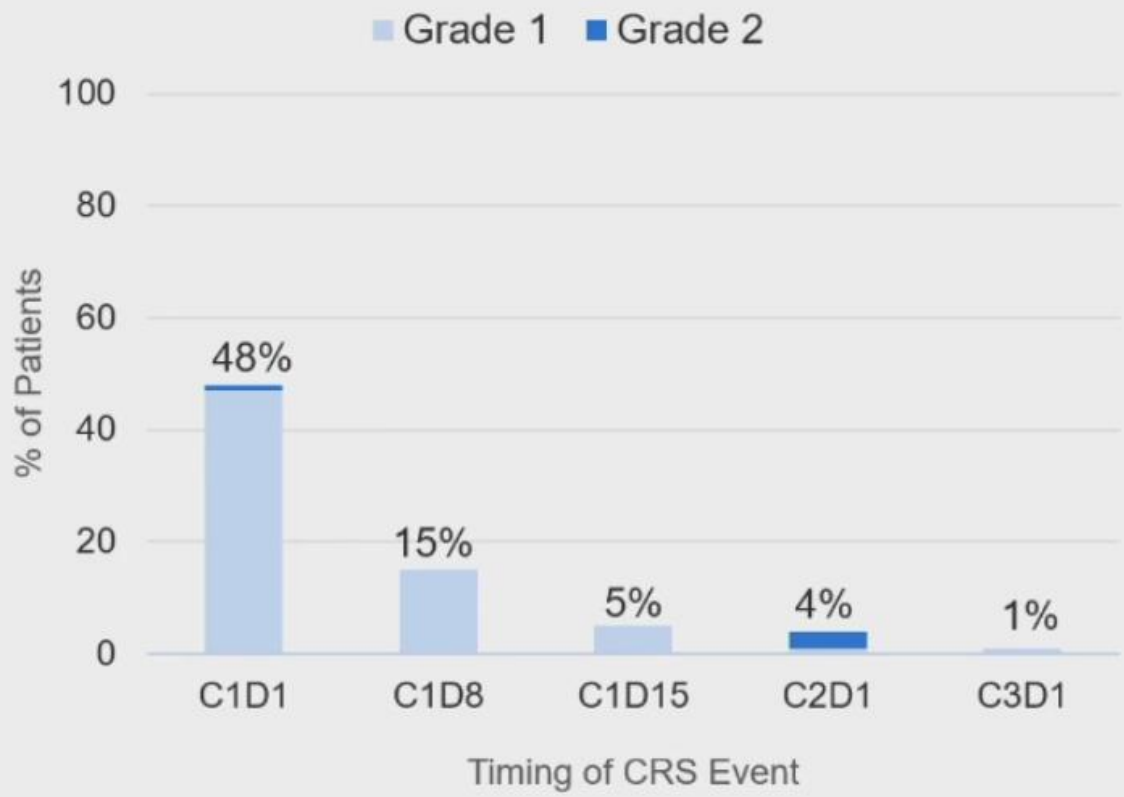
One patient died while on study from complications of COVID-19 pneumonia at 4 months Two patients died having been off study: one from a second cancer and one from sudden cardiac death at 12 months and 20 months, respectively

SC mosun in 1L FL

Cytokine release syndrome: Mild and managed outpatient

CRS*	All patients (N=78)
Incidence	42 (54%)
Grade 1	40 (51%)
Grade 2	2 (3%)
n. unique CRS episodes	59
Median time to onset, h (range)	
1st episode	24 (3 – 91)
2nd episode	44 (19 – 312)
3rd episode	80 (76 – 83)
Resolved	59 (100.0%)
Median time to resolution, h (range)	22 (2 – 264)
Corticosteroid use	12 (20%)
Tocilizumab use	3 (5%)
CRS leading to hospitalization	4 (7%)
CRS leading to SAE	4 (7%)

*Graded per Lee et al. Biol Blood Marrow Transplant 2019 Apr;25(4):625-638



P341

Escalating Doses of AZD0486, a Novel CD19xCD3 T-cell Engager, Result in High Complete Remissions with Rapid Clearance of Minimal Residual Disease in Patients with Relapsed/Refractory Follicular Lymphoma

Jing-Zhou Hou,[1] Ranjit Nair,[2] Ryan Jacobs,[3] Tae Min Kim,[4] Seok-Goo Cho,[5] Dai Maruyama,[6] Sumana Devata,[7] Yazeed Sawalha,[8] Dok Hyun Yoon,[9] Constantine S. Tam,[10] Koji Izutsu,[11] Matthew Matasar,[12] Don Stevens,[13] Aravind Ramakrishnan,[14] Denise Brennan,[15] Xu Zhu,[15] Robin Lesley,[16] Yasuhiro Oki,[16] David Sermer,[17] Sameh Gaballa[18]

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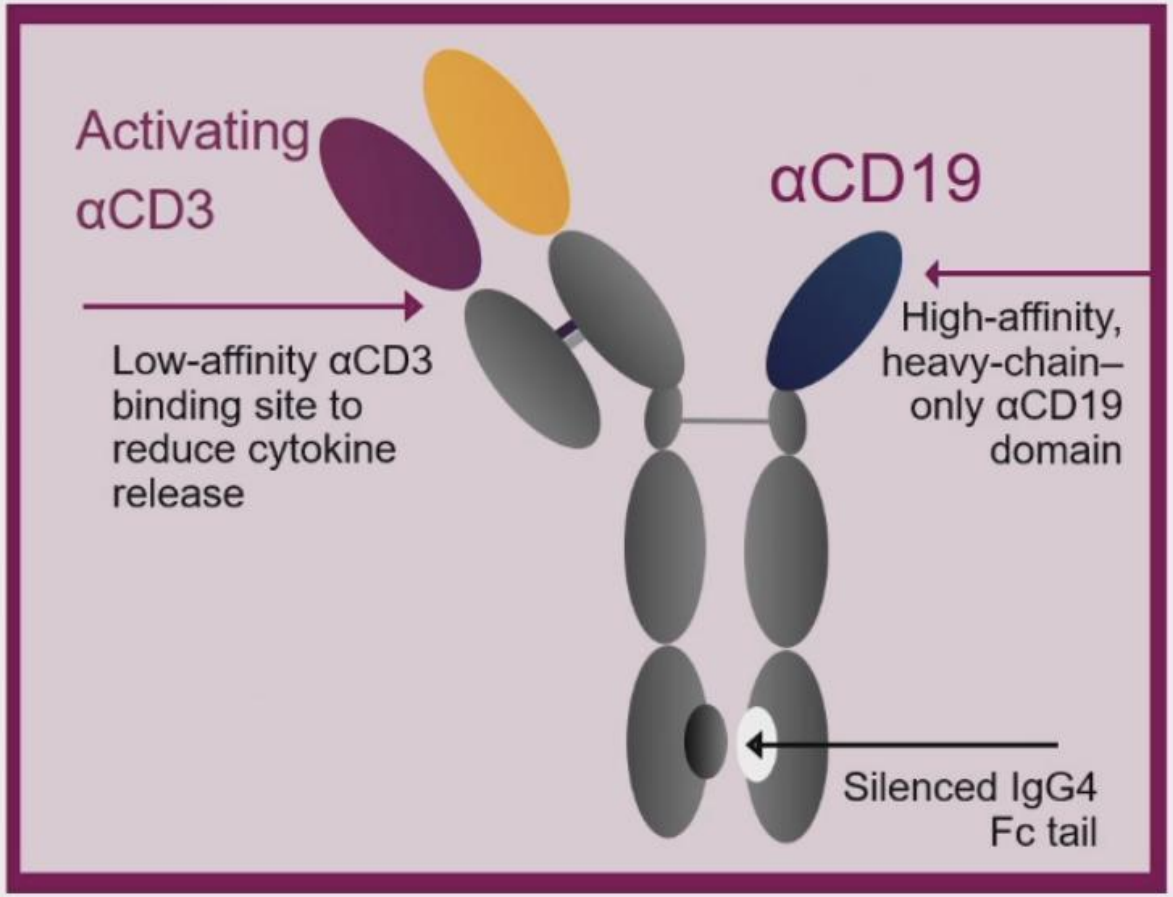
Introduction

- AZD0486 is an IgG4 fully human CD19xCD3 bispecific T-cell engager (TCE), with a half-life of 8–12 days[1-3]
- Two step-up dosing (C1D1: 0.27 mg; C1D8: 1 mg; C1D15: target dose) enabled administration of the drug to achieve therapeutic target dose[4,5]
- Here, we present updated efficacy, safety, and PK/PD data of AZD0486 in patients with R/R FL

AZD0486 Structure



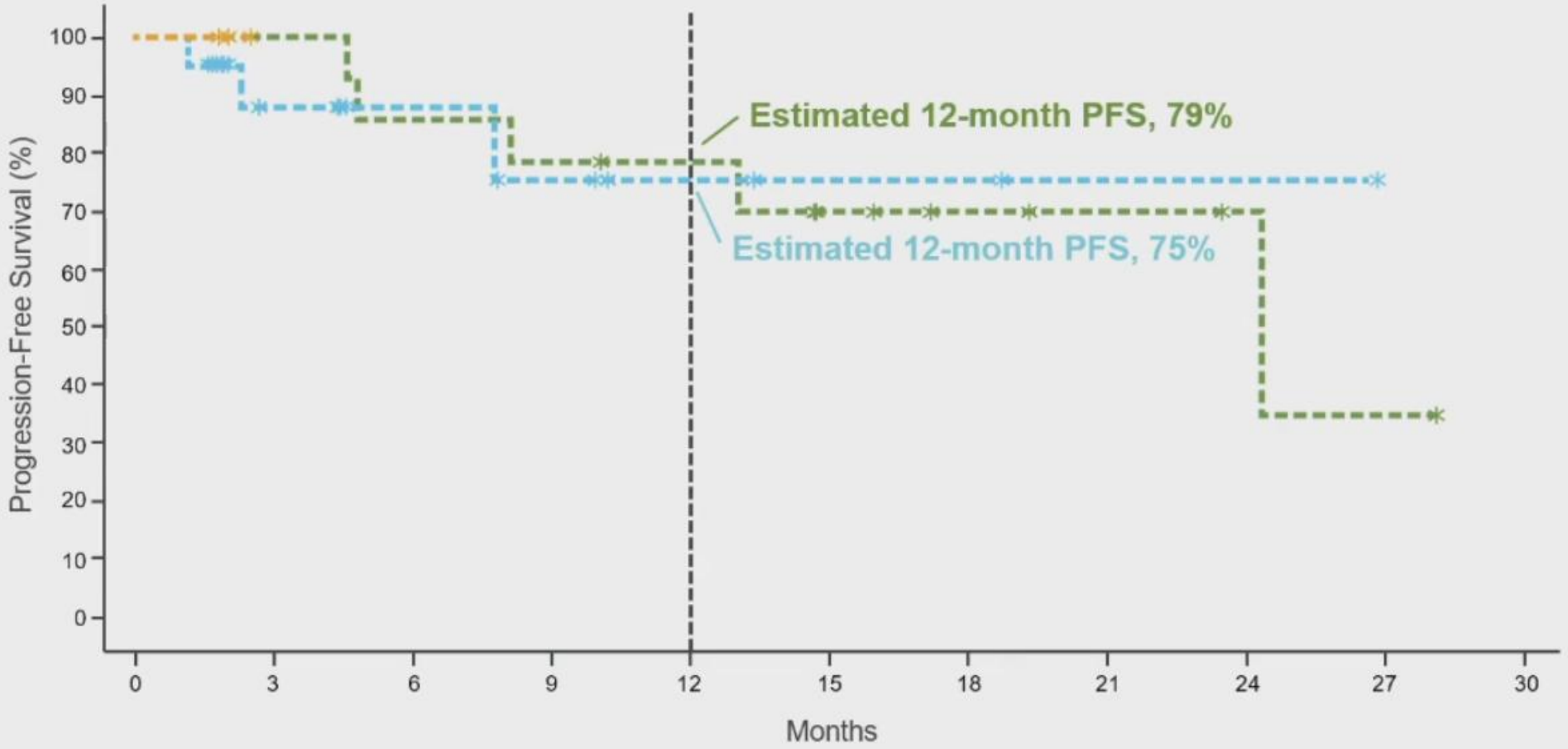
1. Malik-Chaudhry HK, et al. *MAbs*. 2021;313:1890411. **2.** Trinklein ND, et al. *MAbs*. 2019;11:639-52. **3.** Hou JZ, et al. *Blood*. 2022;140(Suppl 1):1474-5. **4.** Gaballa S, et al. *Blood*. 2023(suppl 1):1662. **5.** Devata S, et al. *HemaSphere*. 2024;8(Suppl 1):2059-2060.

High Response Rates Overall and in High-Risk Populations

Patients	N	ORR	CR rate
All TD ≥2.4 mg	41	95%	85%
Baseline and Disease Characteristics			
POD24	14	100%	100%
Bulky disease	9	78%	56%
CD20 negative disease	6	100%	83%
Refractory disease	6	83%	83%
Prior Therapies			
CD20 TCE	4	75%	75%
CD19 CAR-T	6	83%	67%
Lenalidomide	14[a]	93%	93%

[a]One patient died prior to response assessment.

Progression-Free Survival by Target Dose



No. at risk											
2.4 mg	14	14	12	11	9	6	4	3	2	1	0
7.2 mg	21	11	7	5	3	2	2	1	1	0	
15 mg	5	0									

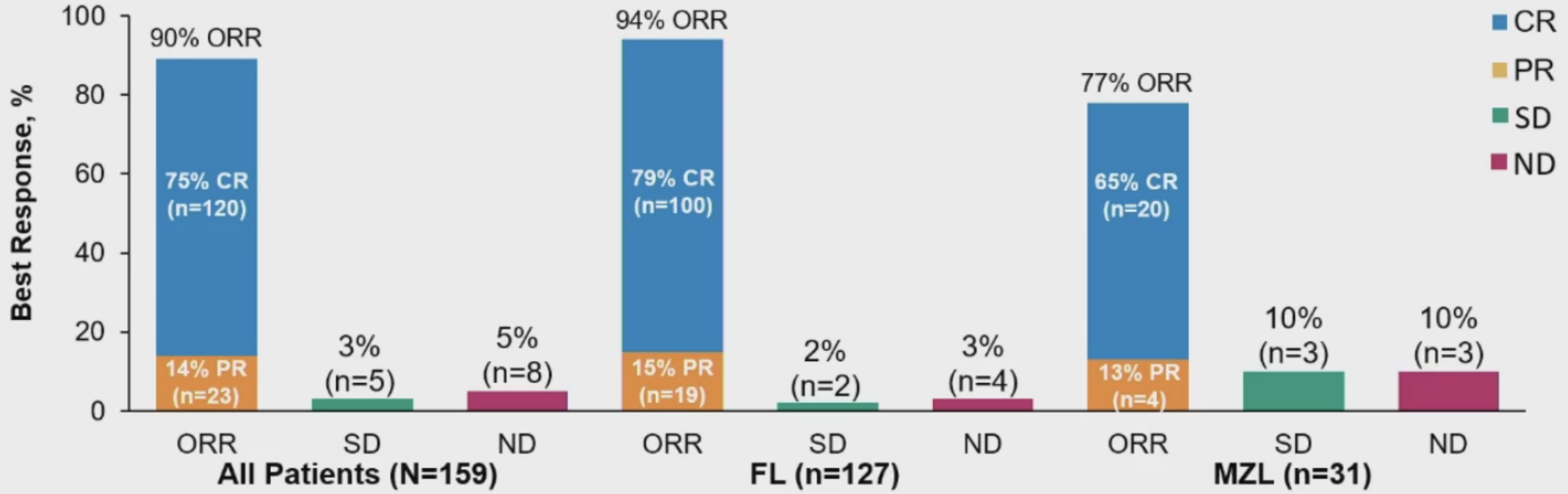
5-Year Follow-Up Analysis From ZUMA-5: A Phase 2 Trial of Axicabtagene Ciloleucel in Patients With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

Sattva Neelapu, MD[1*]; Julio Chavez, MD[2*]; Alison R. Sehgal, MD[3]; Narendranath Epperla, MD, MS[4]; Matthew Ulrickson, MD[5]; Emmanuel Bachy, MD, PhD[6]; Pashna N. Munshi, MD[7]; Carla Casulo, MD[8]; David G. Maloney, MD, PhD[9]; Sven de Vos, MD, PhD[10]; Ran Reshef, MD[11]; Lori Leslie, MD[12]; Olalekan O. Oluwole, MD, MPH, MBBS[13]; Ibrahim Yakoub-Agha, MD, PhD[14]; Rashmi Khanal, MD[15]; Joseph D. Rosenblatt, MD[16]; Jacob Wulff, DrPH[17]; Rhine Shen, PhD[17]; Wangshu Zhang, PhD[17]; Soumya Poddar, PhD[17]; Harry Miao MD, PhD[17]; Olga Nikolajeva, MD[17]; and Caron A. Jacobson, MD[18]

*These authors contributed equally

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Moffitt Cancer Center, Tampa, FL, USA; [3]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [4]The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [5]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [6]Centre Hospitalier Lyon Sud, Pierre-Bénite, France; [7]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; [8]University of Rochester Medical Center - Wilmot Cancer Center, Rochester, NY, USA; [9]Fred Hutchinson Cancer Center, Seattle, WA, USA; [10]Ronald Reagan University of California Los Angeles Medical Center, Santa Monica, CA, USA; [11]Columbia University Herbert Irving Comprehensive Cancer Center, New York City, NY, USA; [12]John Theurer Cancer Center, Hackensack, NJ, USA; [13]Vanderbilt University Medical Center, Nashville, TN, USA; [14]CHU de Lille, Univ Lille, INSERM U1286, Infinite, 59000 Lille, France; [15]Fox Chase Cancer Center, Philadelphia, PA, USA; [16]University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA; [17]Kite, a Gilead Company, Santa Monica, CA, USA; and [18]Dana-Farber Cancer Institute, Boston, MA, USA

Overall Response and Complete Response Rates



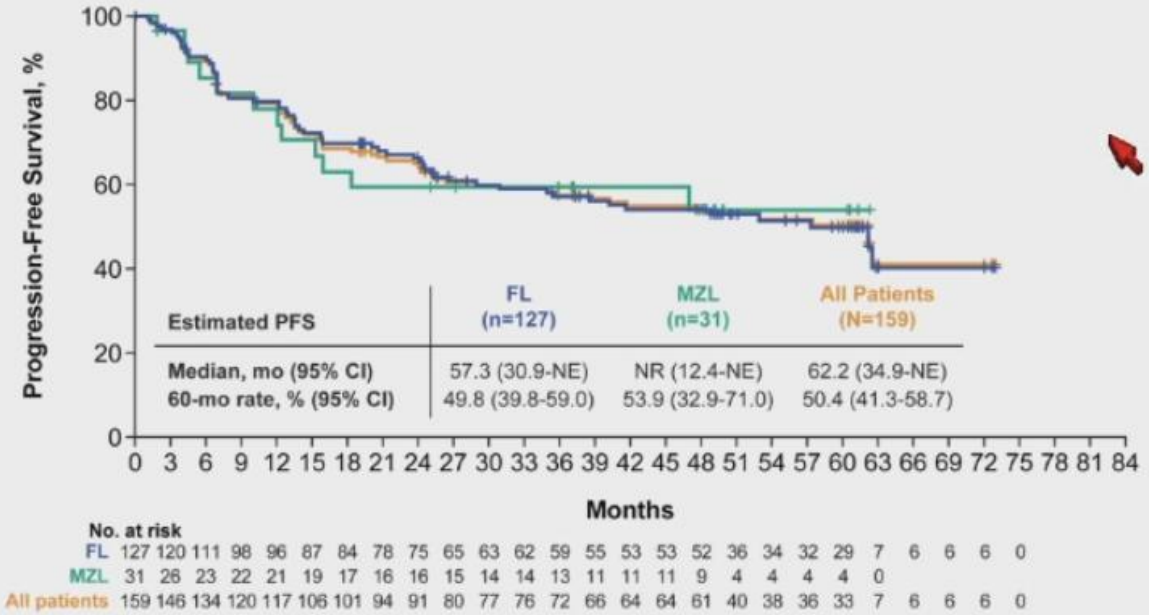
- Median follow-up from leukapheresis in enrolled patients with iNHL (N=159) was 64.6 months (range, 32.3-81.4)
  - In FL (n=127), median follow-up was 65.7 months (range, 56.7-81.4)
  - In MZL (n=31), median follow-up was 55.8 months (range, 32.3-76.4)
- Response remained consistent with prior analyses[1]

1. Neelapu S, et al. *Blood.* 2023;142(Suppl 1):4868.

CR, complete response; FL, follicular lymphoma; iNHL, indolent non-Hodgkin lymphoma; MZL, marginal zone lymphoma; ND, not done; ORR, overall response rate; PR, partial response; SD, stable disease.

PFS and Cumulative Incidence of Progression and Lymphoma-Specific Death

Progression-Free Survival[a]



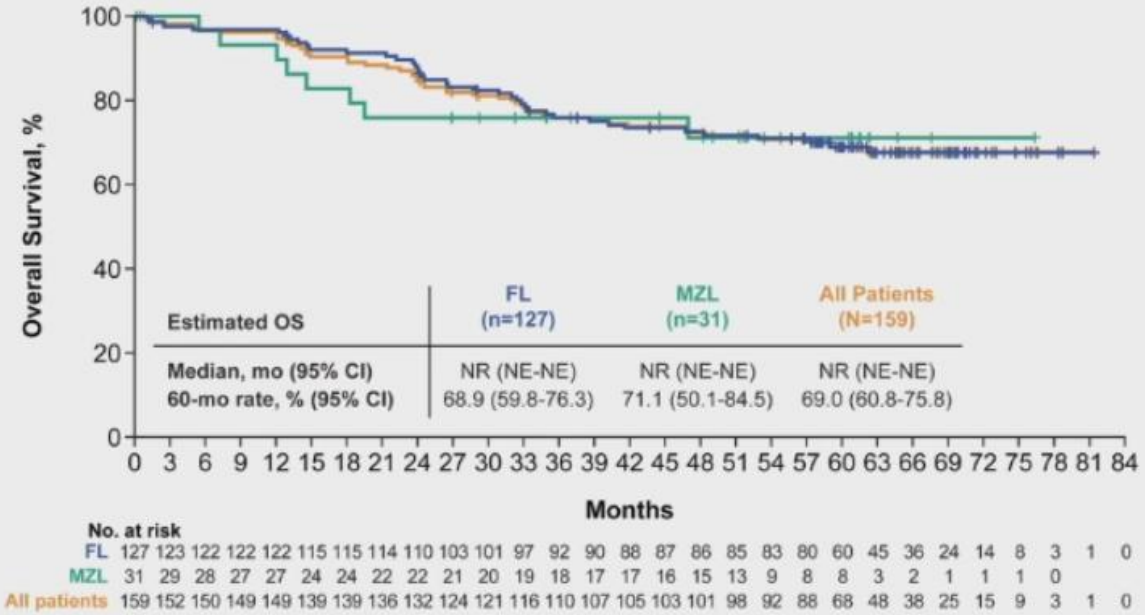
Cumulative Incidence of Progression and Lymphoma-Specific Death in FL[a,b]

- Median PFS was 62.2 months; the 60-month PFS rate was 50.4%
  - 60-month PFS rates in patients with FL were consistent regardless of high-risk factors, including POD24
  - In those with a CR, the 60-month PFS rate was 61.9%; in those with PR, the rate was 9.1%
- Among patients with FL, the 60-month rate of progression or lymphoma-specific death was 35.1%

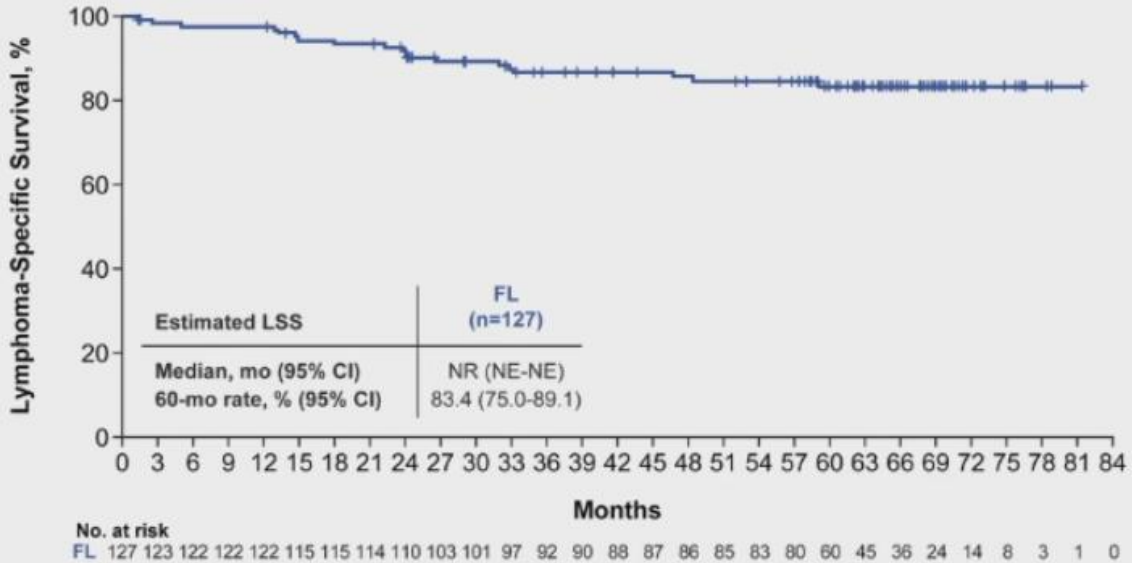
[a] Progression events were determined by the investigator. [b] Death due to lymphoma included death due to disease progression or determined to be disease related. Death due to study treatment complications included death determined to be related to axi-cel or lymphodepleting chemotherapy. These were analyzed per investigator assessment.
Axi-cel, axicabtagene ciloleucel; CR, complete response; FL, follicular lymphoma; MZL, marginal zone lymphoma; NE, not estimable; NR, not reached; PFS, progression-free survival; POD24, progression <2 years from initiating first anti-CD20–containing chemoimmunotherapy; PR, partial response.

OS and Lymphoma-Specific Survival

Overall Survival



Lymphoma-Specific Survival[a]



- Median lymphoma-specific survival in FL was not reached (95% CI, NE-NE), with 83.4% of patients achieving the 60-month landmark

[a] Death due to lymphoma included death due to disease progression or determined to be disease related. Death due to study treatment complications included death determined to be related to axi-cel or lymphodepleting chemotherapy. These were analyzed per investigator assessment. Deaths not related to lymphoma or study treatment were censored.
Axi-cel, axicabtagene ciloleucel; FL, follicular lymphoma; LSS, lymphoma-specific survival; MZL, marginal zone lymphoma; NE, not estimable; NR, not reached; OS, overall survival.

Conclusions

- Novel therapeutic agents are available for R/R as well as front-line FL
- Combinations will likely improve outcomes even further
- Combinations should be based on scientific rationale
- Careful selection of patients for specific therapies
- ctDNA/MRD is essential
  - Predicting outcome
  - Assessing response
  - Monitoring response
- Increase likelihood of cure

Keep Rocking On!!