Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

66th ASH Meeting 2024

San Diego & virtuell

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Expert:innen berichten zu Lymphomen & Leukämien

Prof. Dr. med. Kai Hübel
Uniklinik Köln

Follikuläre Lymphome (FL)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ASH2024 wird in Kooperation mit sieben unterstützenden Firmen durchgeführt.
Meine persönlichen Disclosures betreffen:

Anstellungsverhältnis, Führungsposition	Oberarzt, Uniklinik Köln
Beratungs-/ Gutachtertätigkeit	Roche, BMS, Incyte, Recordati, AbbVie, Novartis, Gilead, Miltenyi Biotec, BeiGene, Sandoz
Besitz von Geschäftsanteilen, Aktien oder Fonds	entfällt
Patent, Urheberrecht, Verkaufslizenz	entfällt
Honorare	Roche, Incyte, Recordati, Sandoz, Novartis, BeiGene, AbbVie
Finanzierung wissenschaftlicher Untersuchungen	Roche, Gilead, Incyte
Andere finanzielle Beziehungen	entfällt
Immaterielle Interessenkonflikte	entfällt

Kapitel 1

Die aktuelle Diskussion im Rezidiv: Bispezifische Antikörper oder CAR-T-Zellen?

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

Abstract #342

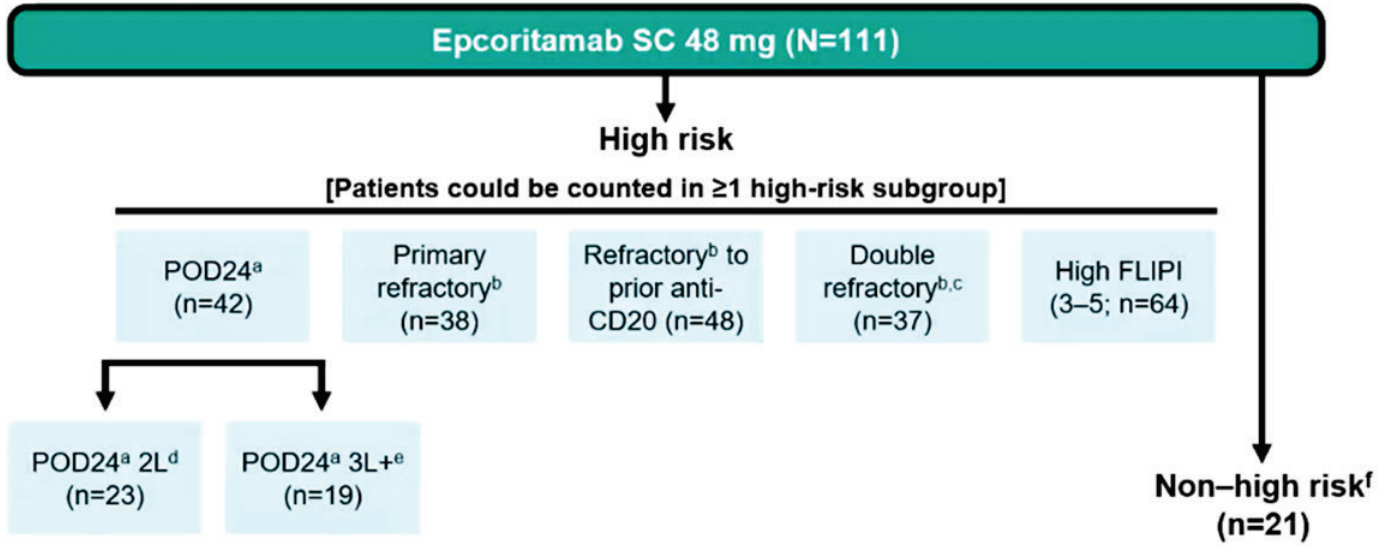
Lorenzo Falchi et al.

Studienüberblick

N=111

Key inclusion criteria

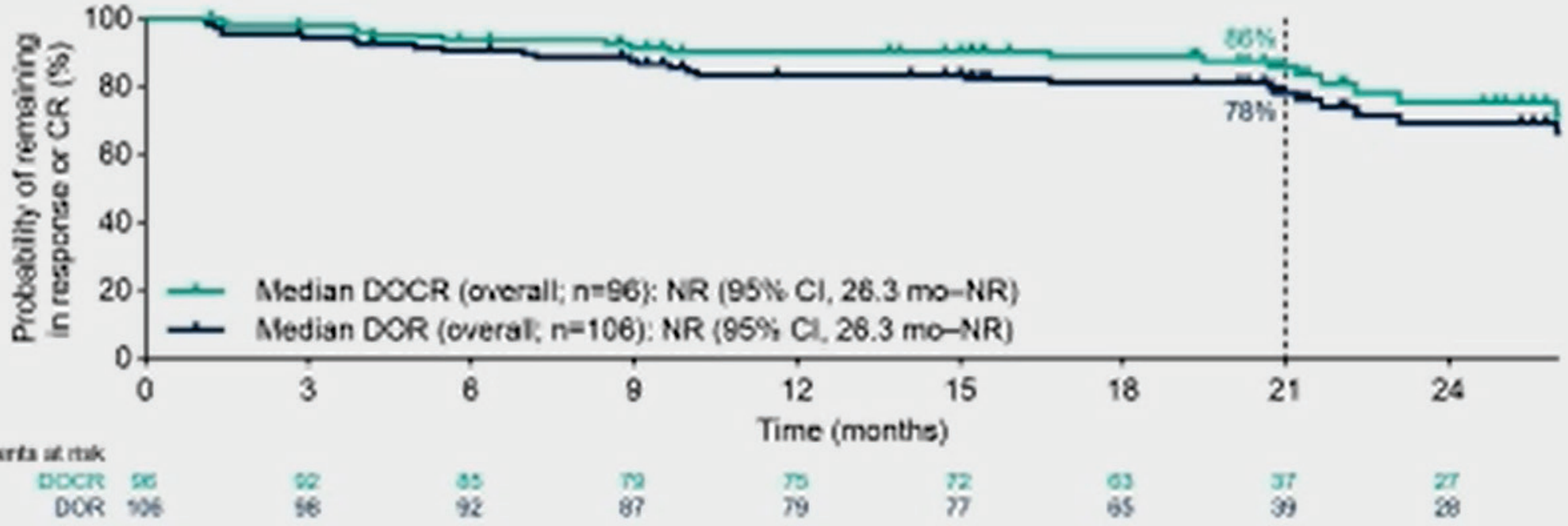
- R/R CD20⁺ FL
  - Grade 1, 2, or 3A
  - Stage II–IV
- Need for treatment based on symptoms or disease burden, as determined by GELF criteria[1]
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function



[a]POD24: Progression within 2 y of initiating first-line treatment that included chemoimmunotherapy. [b]Refractory: No response or relapse within 6 mo after therapy. [c]Double refractory: Refractory to both anti-CD20 and an alkylating agent. [d]Patients received epcoritamab SC in second line. [e]Patients received epcoritamab SC in third line or beyond. [f]Non–high risk: Patients who do not meet criteria for any of the predefined high-risk factors (eg, POD24, primary refractory, refractory to prior anti-CD20, double refractory, and high FLIPI). [g]Tumor response was evaluated by PET-CT obtained at 6, 12, 18, 24, 36, and 48 wk, and every 24 wk thereafter, until disease progression. **1.** Brice P, et al. *J Clin Oncol*. 1997;15:1110-7.

DOR

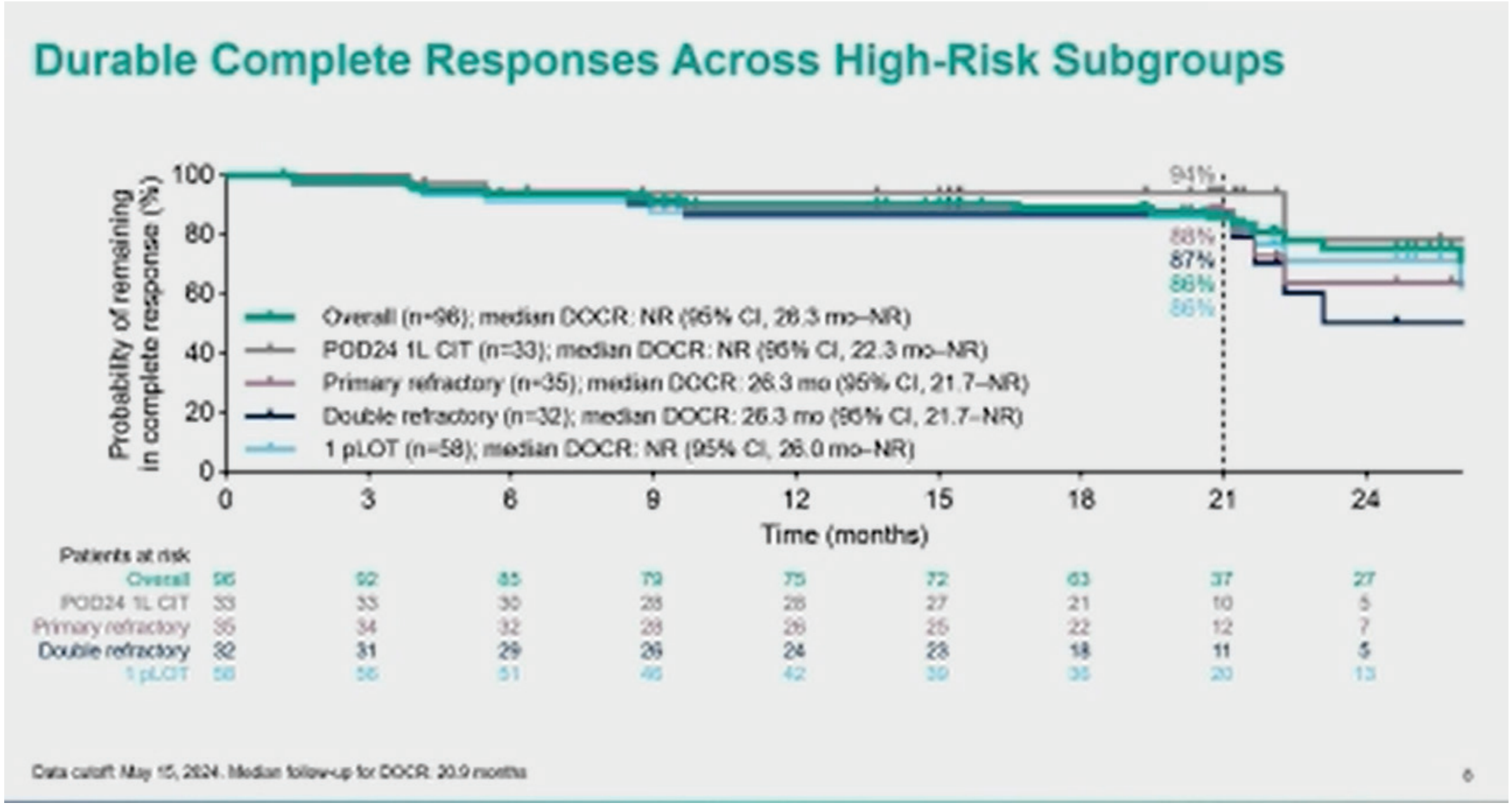
Durable Responses



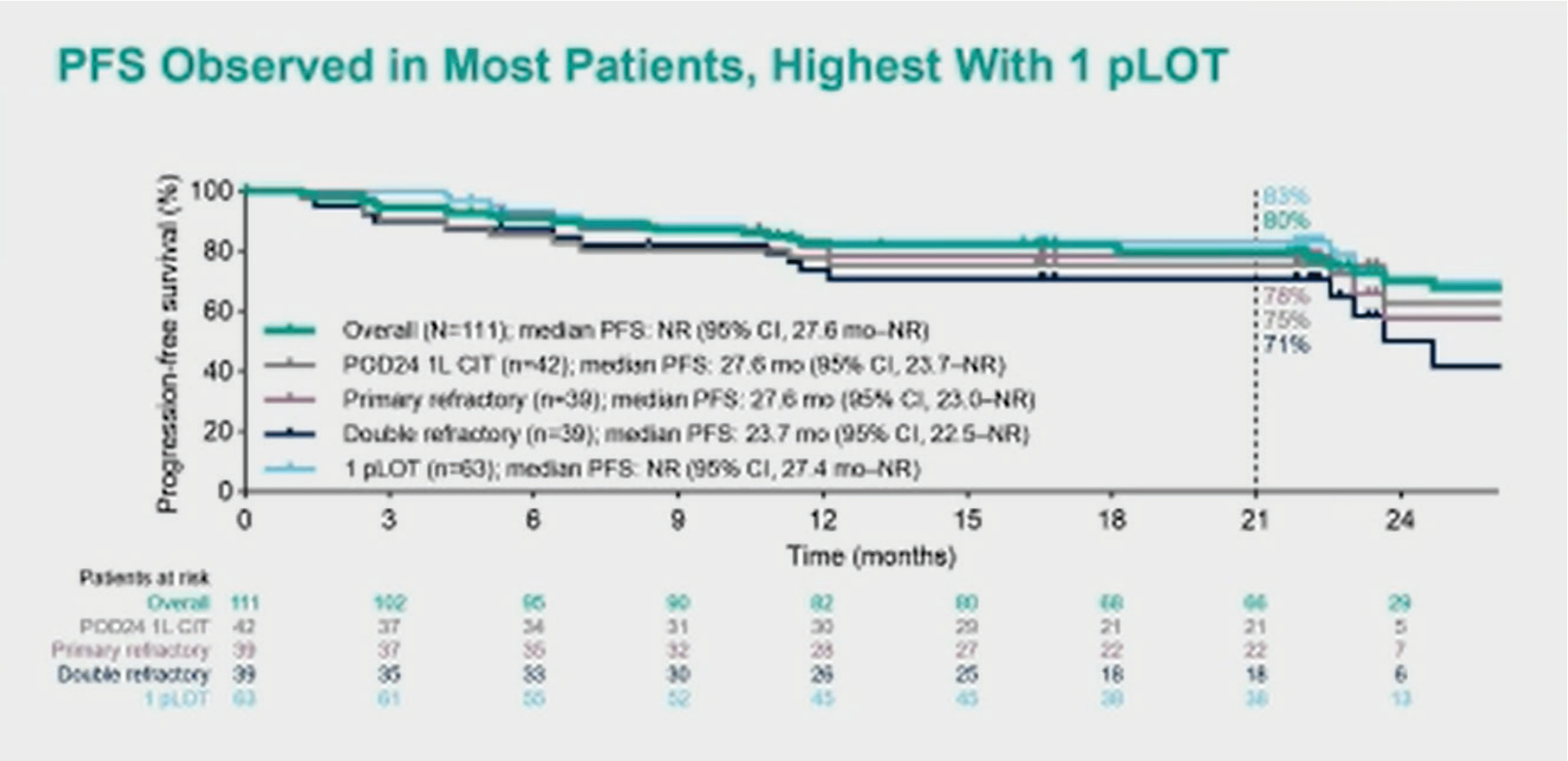
- 93% (37/40) of patients with CR who completed treatment per protocol remained in CR[a]
- 81% (25/31) of patients with CR who discontinued epcoritamab treatment early due to reasons other than PD remained in CR[b]

Data cutoff: May 15, 2024. Response-evaluable population. Median follow-up for DOR/DOCR: 21.0/23.9 months.
[a]17 of the 19 patients with CR at end of treatment and response evaluations after end of treatment (89%) remained in CR. [b]Median epcoritamab treatment duration: ~1 year.

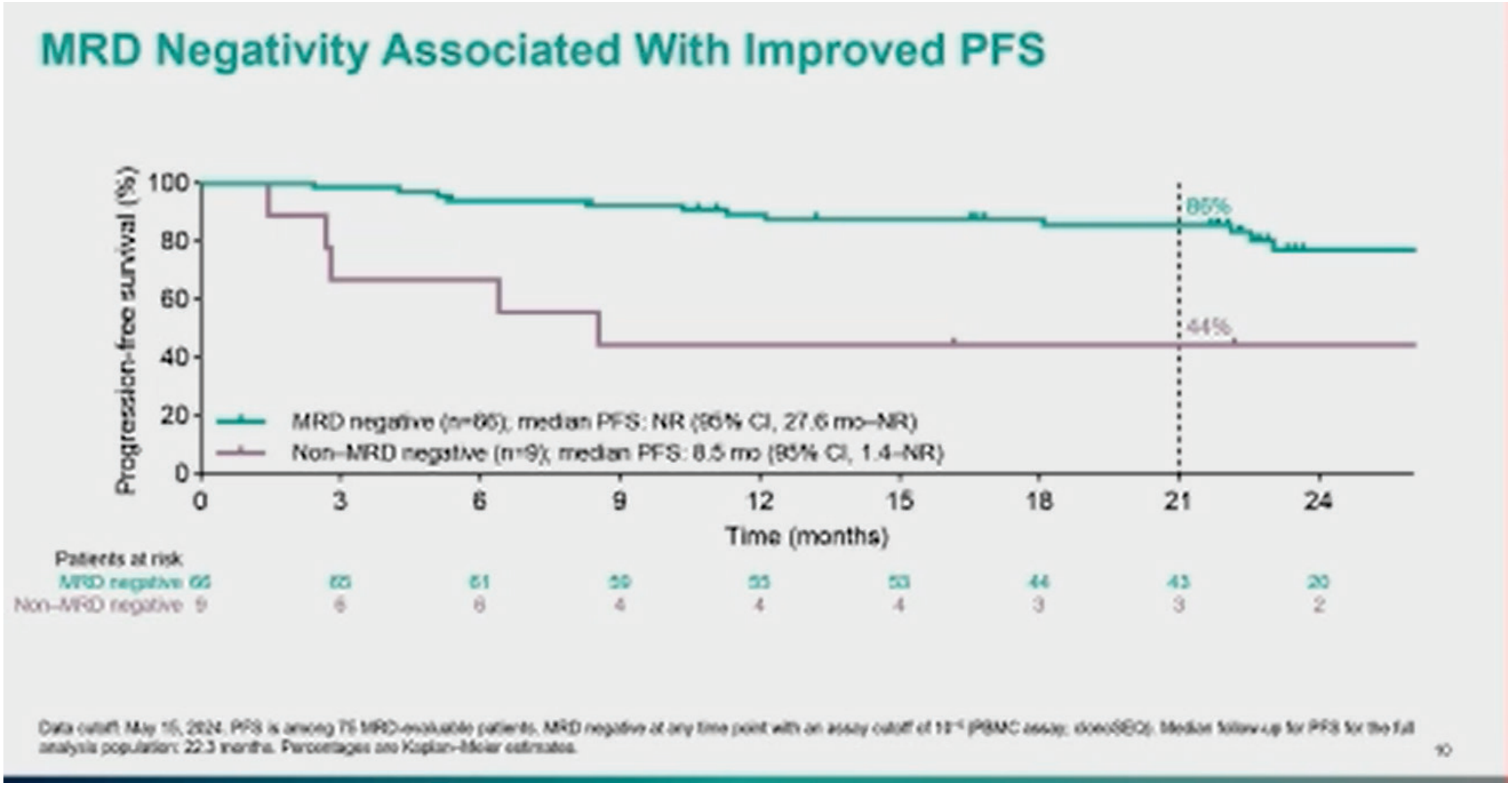
DOR in Risikogruppen



PFS


PFS Observed in Most Patients, Highest With 1 pLOT
Progression-free survival (%)
100
80
60
40
20
0
0
3
6
9
12
15
18
21
24
Time (months)
Overall (N=111); median PFS: NR (95% CI, 27.6 mo–NR)
PCD24 1L CIT (n=42); median PFS: 27.6 mo (95% CI, 23.7–NR)
Primary refractory (n=39); median PFS: 27.6 mo (95% CI, 23.0–NR)
Double refractory (n=39); median PFS: 23.7 mo (95% CI, 22.5–NR)
1 pLOT (n=63); median PFS: NR (95% CI, 27.4 mo–NR)
83%
80%
78%
75%
71%
Patients at risk
Overall 111 102 95 90 82 80 68 64 29
PCD24 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 36 13

MRD


MRD Negativity Associated With Improved PFS
Progression-free survival (%)
100
80
60
40
20
0
0
3
6
9
12
15
18
21
24
Time (months)
85%
44%
MRD negative (n=66); median PFS: NR (95% CI, 27.6 mo–NR)
Non-MRD negative (n=9); median PFS: 8.5 mo (95% CI, 1.4–NR)
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 10⁻⁵ (PBMC assay; clonoSEQ). Median follow-up for PFS for the full analysis population: 22.3 months. Percentages are Kaplan-Meier estimates.
10

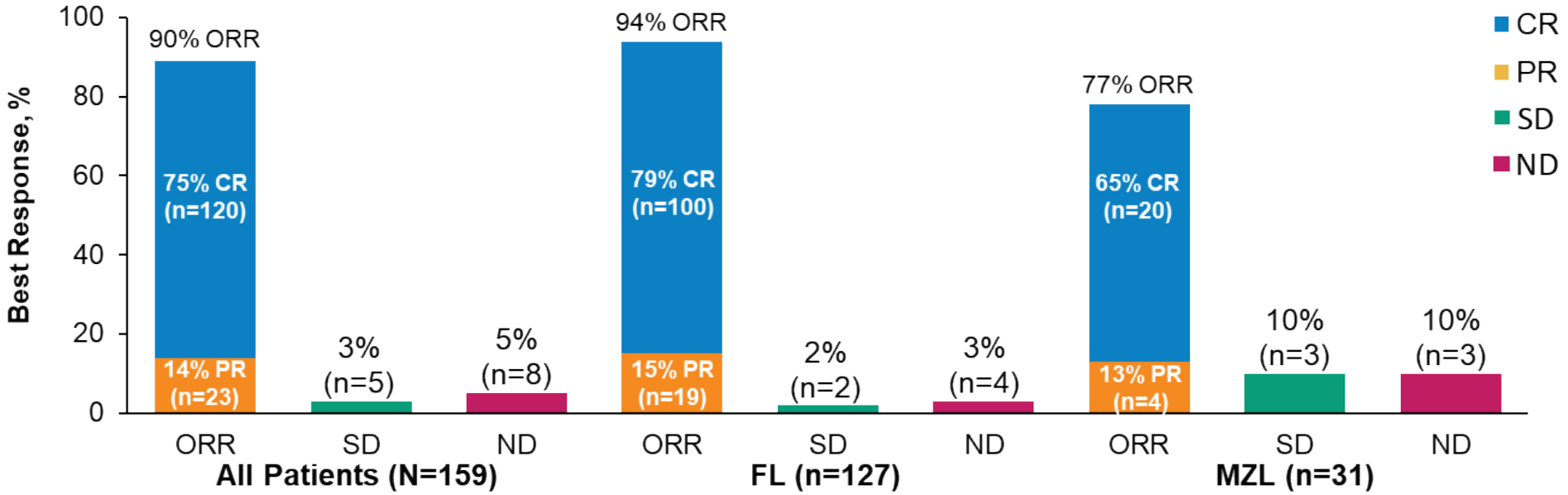
5-Year Follow-up Analysis from ZUMA-5: A Phase 2 Trial of Axicabtagene Ciloleucel (Axi-Cel) in Patients with Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

Abstract #864

Sattva S. Neelapu et al.

Ansprechraten

N=159



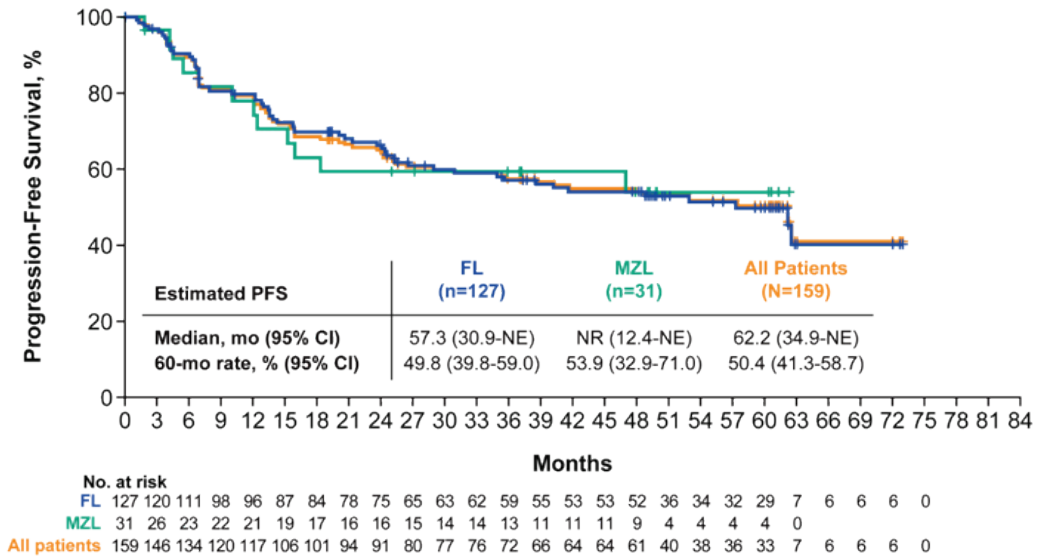
- Median follow-up from leukapheresis in enrolled patients with iNHL (N=159) was 64.6 months (range, 32.3-81.4)
  - In FL (n=127), median follow-up was 65.7 months (range, 56.7-81.4)
  - In MZL (n=31), median follow-up was 55.8 months (range, 32.3-76.4)
- Response remained consistent with prior analyses[1]

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

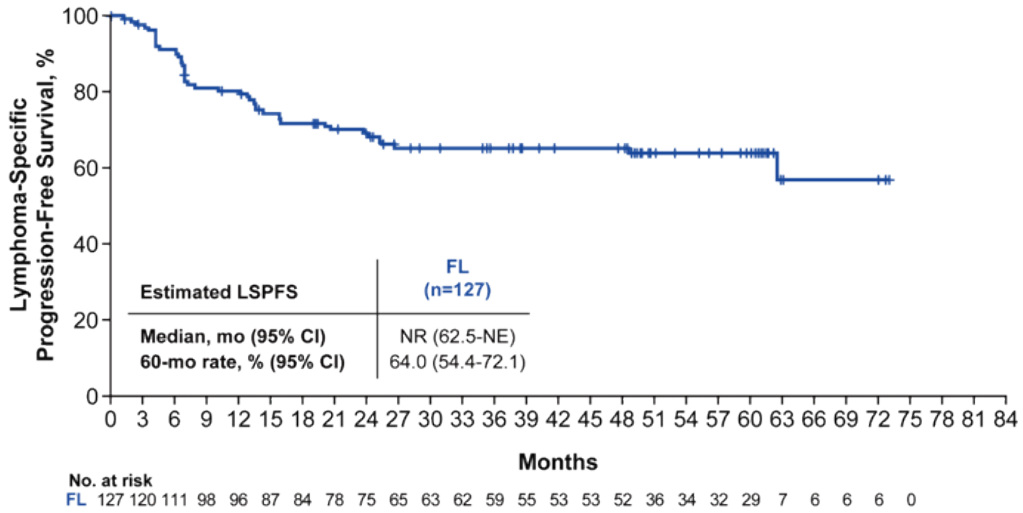
CR, complete response; FL, follicular lymphoma; iNHL, indolent non-Hodgkin lymphoma; MZL, marginal zone lymphoma; ND, not done; ORR, overall response rate; PR, partial response; SD, stable disease.

PFS und Lymphom-spezifisches PFS

Progression-Free Survival[a]



Lymphoma-Specific Progression-Free Survival[a,b]

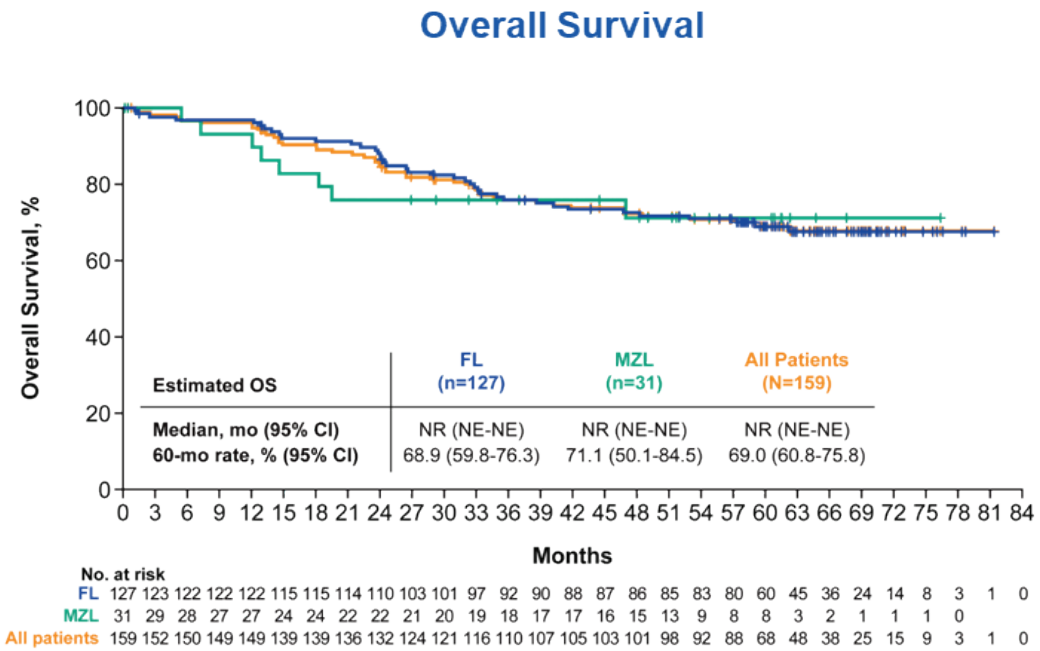


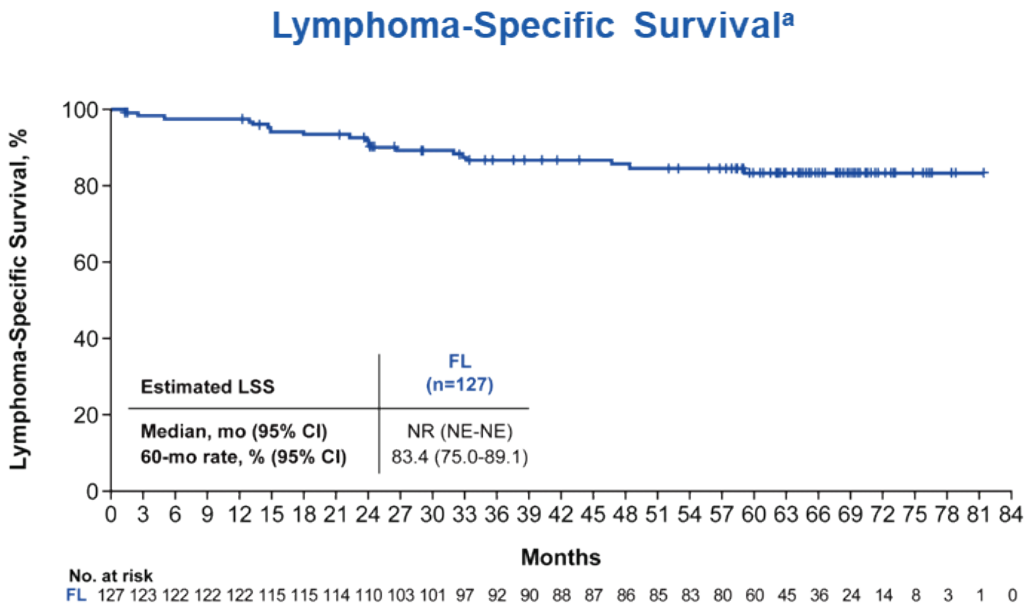
- Median lymphoma-specific PFS in FL was not reached (95% CI, 62.5-NE), with 64.0% of patients achieving the 60-month landmark
  - Only 4 patients progressed >24 months post-leukapheresis; 2 patients progressed >30 months post-leukapheresis

[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. Deaths not related to lymphoma or study treatment were censored.

Axi-cel, axicabtagene ciloleucel; FL, follicular lymphoma; LSPFS, lymphoma-specific progression-free survival; MZL, marginal zone lymphoma; NE, not estimable; NR, not reached; PFS, progression-free survival.

OS und Lymphom-spezifisches OS





- 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.

Toxizitäten im Verlauf und Todesfälle

Following the 4-year analysis[1]:

- 3 new events not related to axi-cel were reported, including Grade 3 prostate cancer, Grade 1 bladder cancer, and Grade 4 myelodysplastic syndrome
- 1 patient died due to pneumonia (not related to axi-cel)
  - No patients died of disease progression following the previous analysis

n, (%)	All Patients N=152	Years Post–Axi-Cel Infusion					
		0-1	1-2	2-3	3-4	4-5	>5
Patients who died	46 (30)	10 (7)	15 (10)	11 (7)	6 (4)	3 (2)	1 (1)
Relapse mortalities							
Progressive disease	14 (9)	5 (3)	5 (3)	2 (1)	1 (1)	1 (1)	0
Non-PD after PD	9 (6)	1 (1)	3 (2)	4 (3)	1 (1)	0	0
Non-relapse mortalities							
Secondary malignancy[a]	6 (4)	1 (1)	2 (1)	1 (1)	2 (1)	0	0
Cardiac-related	3 (2)	0	1 (1)	0	1 (1)	0	1 (1)
Infection-related[b]	11 (7)	2 (1)	2 (1)	4 (3)	1 (1)	2 (1)	0
Other[c]	3 (2)	1 (1)	2 (1)	0	0	0	0

[a] No secondary malignancy was of T-cell origin. [b] Three of the infection-related deaths were related to COVID-19.
[c] Two deaths were due to unknown causes and 1 was due to CRS and multi-organ failure.
Axi-cel, axicabtagene ciloleucel; CRS, cytokine release syndrome; PD, progressive disease.

Kapitel 2

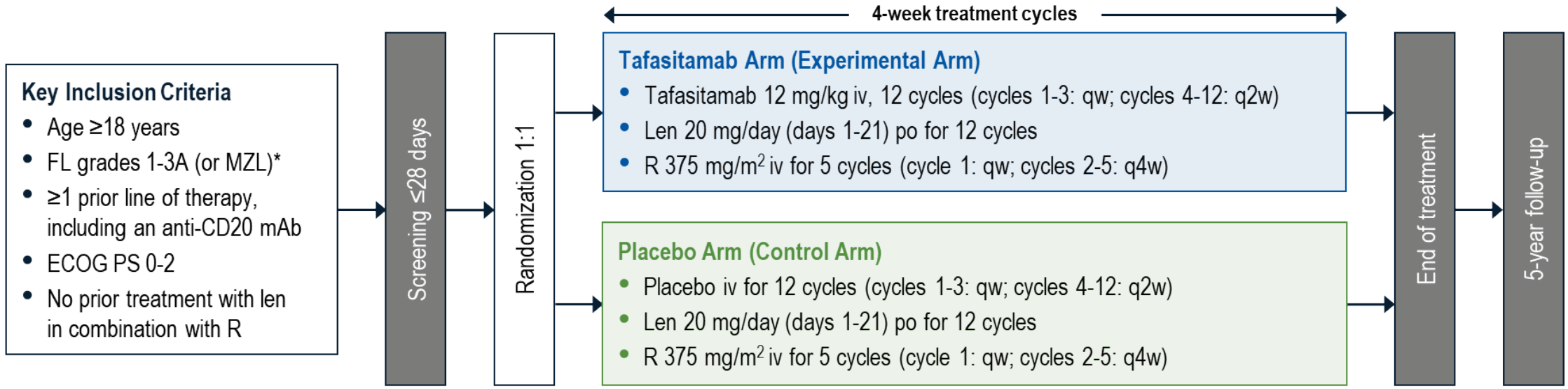
Neue Substanzen

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

Abstract #LBA-1

Laurie H. Sehn et al.

Studiendesign



Stratification Factors (Patients With FL)

- POD24
- Refractoriness to prior anti-CD20 mAb therapy
- Number of prior lines of therapy (1 or ≥2)

Study Endpoints in FL Population (Investigator Assessed Unless Specified)

- **Primary study endpoint:** **PFS**
- **Key secondary:** PET-CR rate in the FDG-avid population, OS
- **Select other secondary:** PFS by IRC, ORR, DOR, safety
- **Exploratory:** TTNT

- Powered to assess PFS in the FL population, triggered when 174 investigator-assessed events occurred
- OS analysis planned after 5 years of follow-up

*Limited number of patients with MZL were enrolled but the study was not powered for this population; data for patients with MZL will be presented separately.
DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; FL, follicular lymphoma; IRC, independent review committee; iv, intravenous; len, lenalidomide; mAb, monoclonal antibody; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PET-CR, positron emission tomography-complete response; PFS, progression-free survival; po, orally; POD24, disease progression within 24 months of initial diagnosis; TTNT, time to next treatment; qw, weekly; q2w, every 2 weeks; q4w, every 4 weeks; R, rituximab.

Bisheriger Therapieverlauf

Variable	Tafasitamab + Len + R (n=273)	Placebo + Len + R (n=275)	Total (N=548)
Median number of prior lines of therapy (range)	1.0 (1, 7)	1.0 (1, 10)	1.0 (1, 10)
1	147 (53.8)	153 (55.6)	300 (54.7)
2	66 (24.2)	71 (25.8)	137 (25.0)
3	39 (14.3)	30 (10.9)	69 (12.6)
≥4	21 (7.7)	21 (7.6)	42 (7.7)
Time since last antilymphoma therapy, n (%)			
≤2 years	147 (53.8)	157 (57.1)	304 (55.5)
>2 years	126 (46.2)	118 (42.9)	244 (44.5)
POD24, n (%)	85 (31.1)	88 (32.0)	173 (31.6)
Relapse/refractory status to last therapy, n (%)			
Relapsed	148 (54.2)	164 (59.6)	312 (56.9)
Refractory	112 (41.0)	97 (35.2)	209 (38.1)
Undetermined	13 (4.8)	14 (5.1)	27 (4.9)
Refractory to prior anti-CD20 therapy, n (%)	118 (43.2)	115 (41.8)	233 (42.5)

ITT population.
ITT, intent-to-treat; len, lenalidomide; POD24, disease progression within 24 months of initial diagnosis; R, rituximab.

Ansprechraten

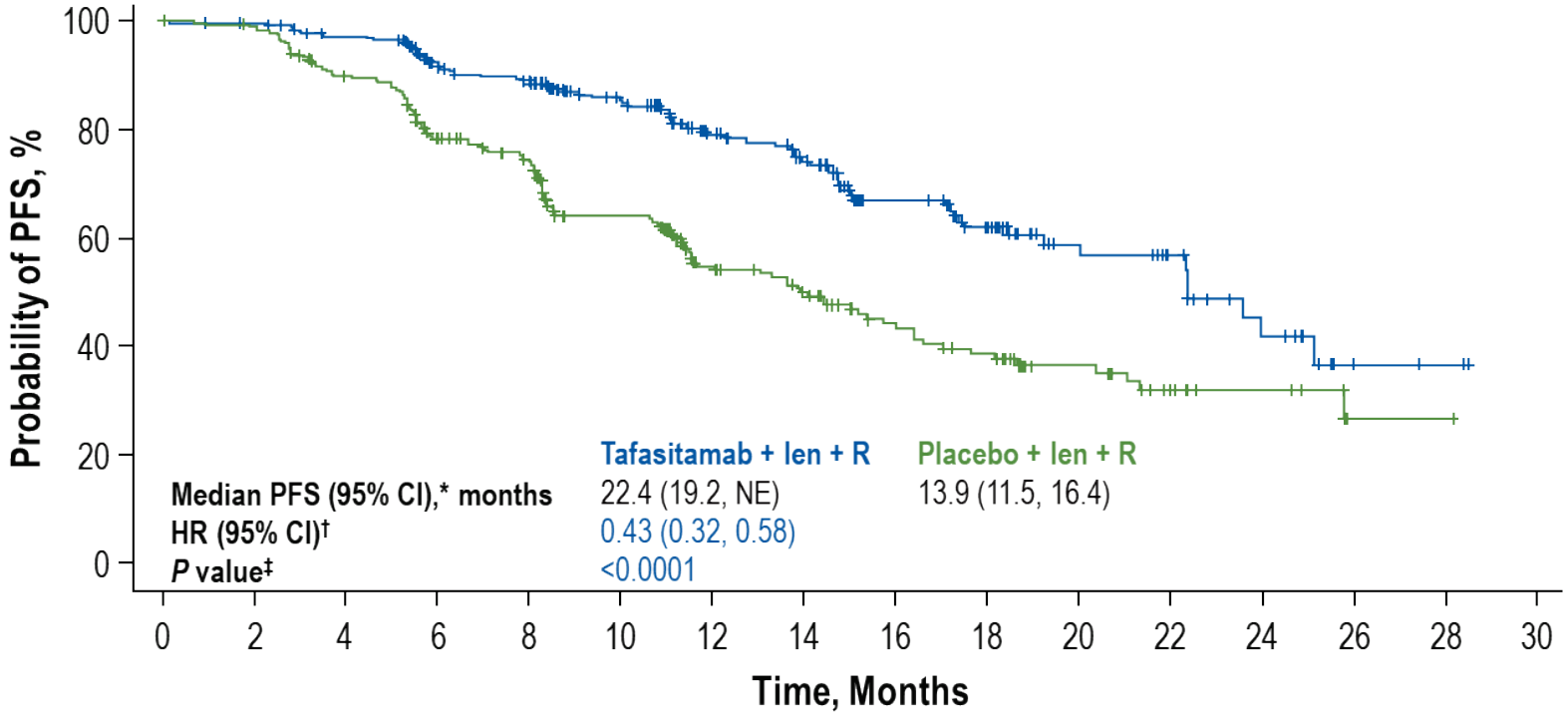
PET-CR (FDG-Avid Population)	Tafasitamab + Len + R	Placebo + Len + R
Patients with FDG-avid disease at baseline	251	254
Patients with postbaseline PET assessments, n (%)*	201/251 (80.1)	205/254 (80.7)
Best metabolic response based on PET, n (%)†		
CMR	124 (49.4)	101 (39.8)
PMR	37 (14.7)	39 (15.4)
NMR/SD	19 (7.6)	12 (4.7)
PMD	19 (7.6)	51 (20.1)
Not done	50 (19.9)	46 (19.3)
PET-CR rate, % (95% CI)	49.4 (43.1, 55.8)	39.8 (33.7, 46.1)
Odds ratio (95% CI)	1.5 (1.04, 2.13)	
Nominal *P* value	0.0286	

ORR (ITT Population)	Tafasitamab + Len + R	Placebo + Len + R
Patients, n	273	275
Best overall response, n (%)‡		
CR	142 (52.0)	112 (40.7)
PR	86 (31.5)	87 (31.6)
SD	28 (10.3)	46 (16.7)
PD	7 (2.6)	20 (7.3)
NE	2 (0.7)	0
Not done	8 (2.9)	10 (3.6)
ORR, % (95% CI)	83.5 (78.6, 87.7)	72.4 (66.7, 77.6)
Odds ratio (95% CI)	2.0 (1.30, 3.02)	
Nominal *P* value	0.0014	

Significant improvement in PET-CR rate and ORR was observed with tafasitamab

Analysis by investigator assessment.
*Calculated based on patients with a positive PET scan at baseline, defined as having a Deauville score of 4 or 5 at baseline. †Two patients (0.8%) in both arms had PET after confirmed PD or new antilymphoma treatment initiation. ‡Per Lugano 2014 classification.
CI, confidence interval; CMR, complete metabolic response; CR, complete response; FDG, fluorodeoxyglucose; ITT, intent-to-treat; len, lenalidomide; NE, not evaluable; NMR, nonmetabolic response; ORR, overall response rate; PD, progressive disease; PET, positron emission tomography; PET-CR, positron emission tomography-complete response; PMD, progressive metabolic disease; PMR, partial metabolic response; PR, partial response; R, rituximab; SD, stable disease.

Primärer Endpunkt PFS

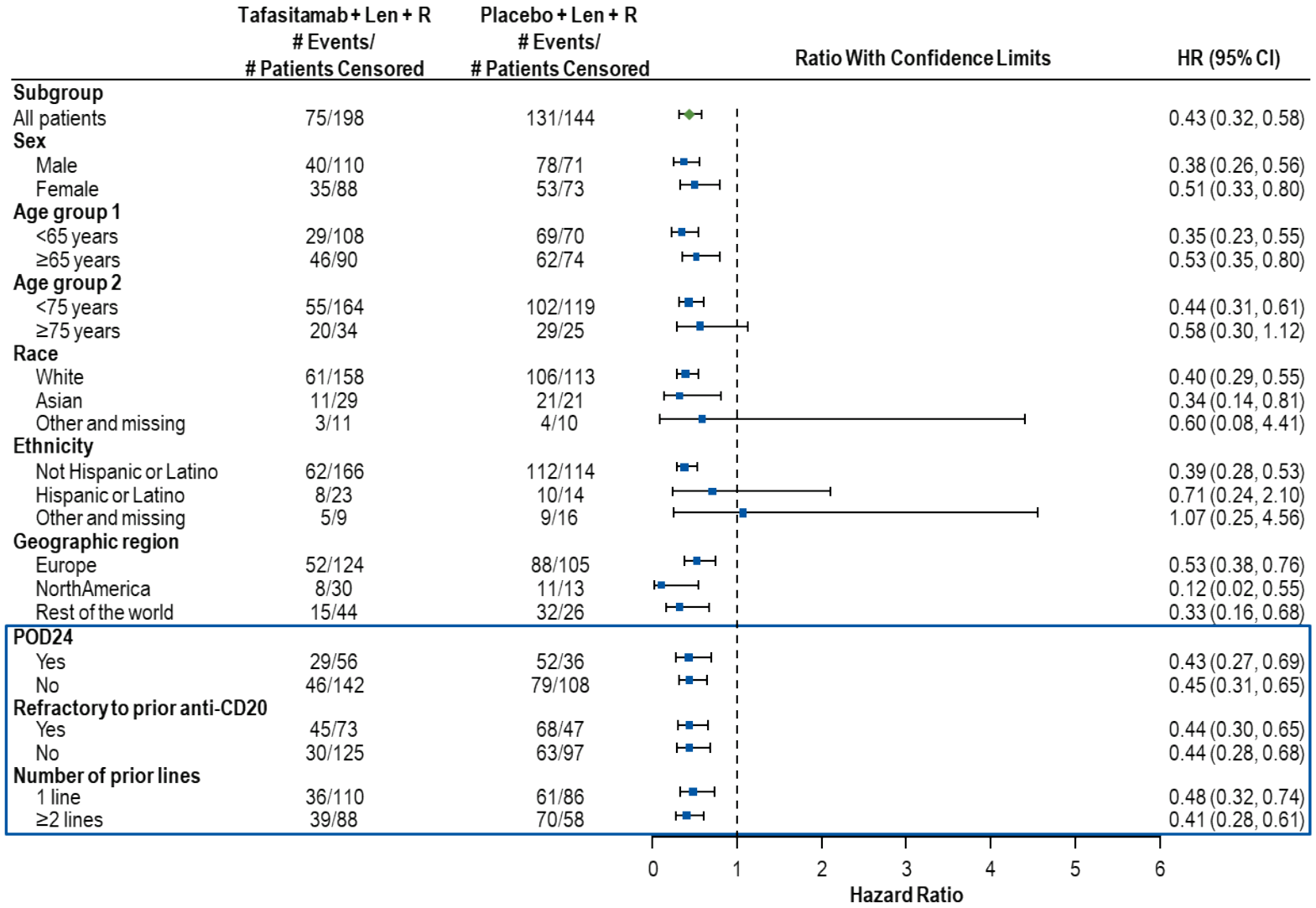


No. at Risk																
Tafasitamab + len + R	273	261	250	212	200	164	119	103	71	57	30	22	12	3	2	0
Placebo + len + R	275	265	235	192	173	126	82	70	48	40	26	16	10	2	2	0

Significant improvement in PFS was observed with tafasitamab

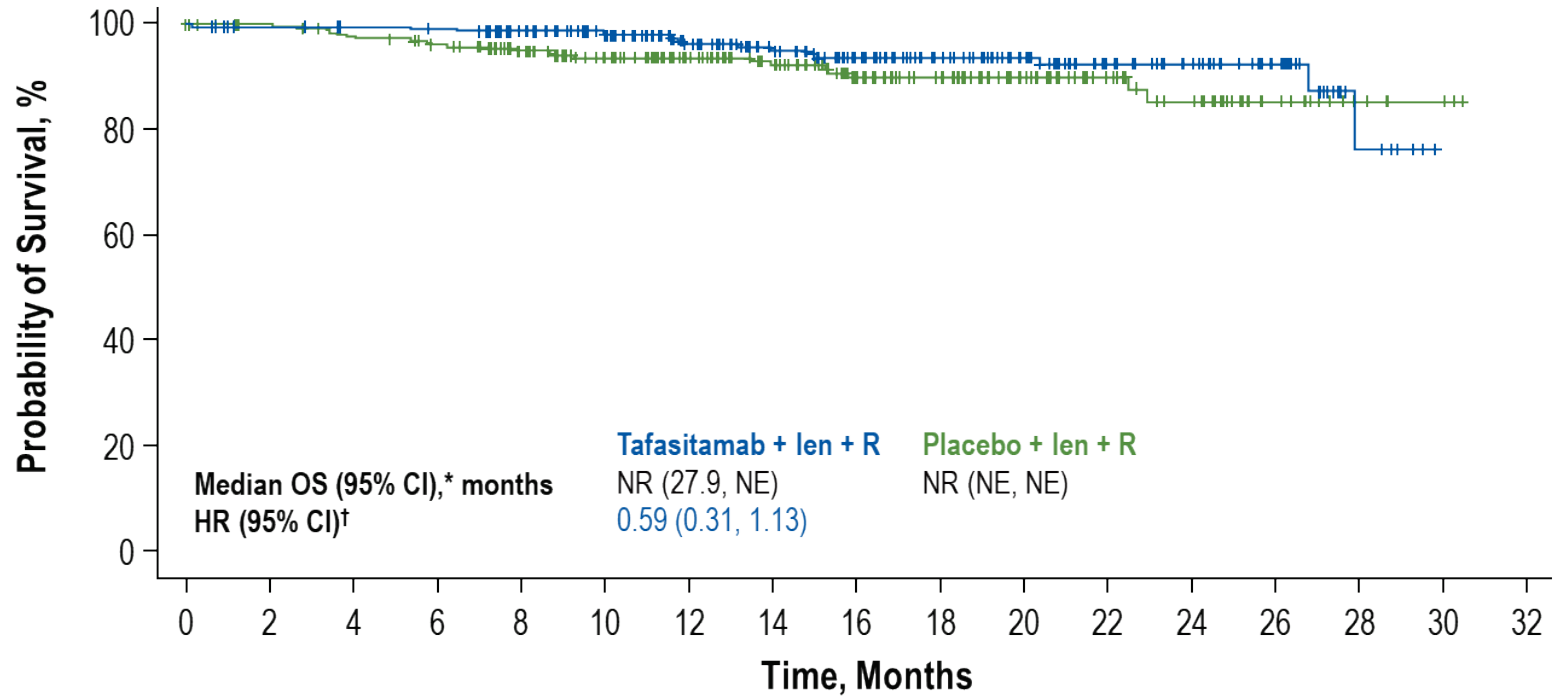
ITT population.
*Estimated using Kaplan-Meier method. †Estimated using a stratified Cox proportional hazard model. ‡Stratified log-rank test with a 1-sided significance level of 2.5%.
CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; len, lenalidomide; NE, not evaluable; PFS, progression-free survival; R, rituximab.

PFS-Subgruppenanalyse



ITT population. Analysis by investigator assessment.
CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; len, lenalidomide; PFS, progression-free survival; POD24, progression of disease within 24 months; R, rituximab.

OS



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.

Toxizitäten

Grade 3 or 4 TEAEs (≥5% in Any Group)

Preferred Term	Tafasitamab + Len + R (n=274)*	Placebo + Len + R (n=272)†	Total (n=546)
Neutropenia	109 (39.8)	102 (37.5)	211 (38.6)
Pneumonia	23 (8.4)	14 (5.1)	37 (6.8)
Thrombocytopenia	17 (6.2)	20 (7.4)	37 (6.8)
COVID-19	16 (5.8)	6 (2.2)	22 (4.0)
Neutrophil count decreased	16 (5.8)	18 (6.6)	34 (6.2)
COVID-19 pneumonia	13 (4.7)	3 (1.1)	16 (2.9)

- Dose interruptions or discontinuations due to TEAEs were similar between tafasitamab and placebo arms, n (%):
  - Dose delay or interruption due to TEAEs: 203 (74%) vs 190 (70%)
  - Discontinued study treatment due to TEAEs: 30 (11%) vs 18 (7%)
- Len discontinuations due to TEAEs were similar between tafasitamab and placebo arms, n (%):
  - 39 (14%) vs 31 (11%)
- Len dose reductions were similar between tafasitamab and placebo arms, n (%):
  - 1 dose reduction: 53 (19%) vs 44 (16%)
  - 2 dose reductions: 23 (8%) vs 14 (5%)
  - ≥3 dose reductions: 9 (3%) vs 9 (3%)

Safety population.
*One patient randomized to the placebo + len + R group is included in the tafasitamab + len + R safety population because the patient erroneously received tafasitamab.
†Three patients randomized to the placebo + len + R group are not included in the safety population because they erroneously received tafasitamab (n=1), or did not receive any study treatment due to confirmation of R hypersensitivity (n=1), or the patient withdrew from the study (n=1).
COVID-19, coronavirus disease 2019; len, lenalidomide; R, rituximab; TEAE, treatment-emergent adverse event.

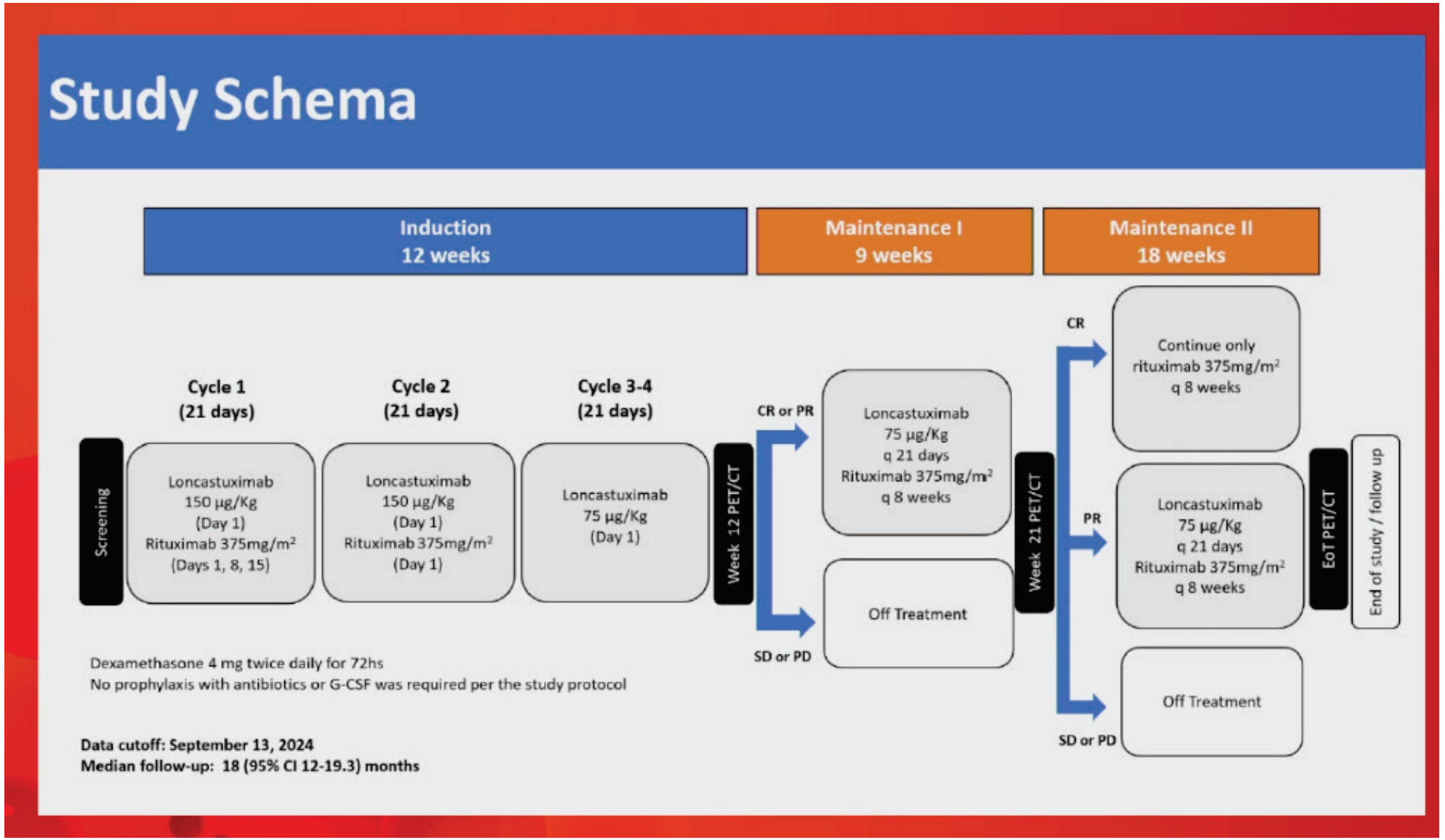
Loncastuximab Tesirine with Rituximab Induces Robust and Durable Complete Metabolic Responses in High-Risk Relapsed/Refractory Follicular Lymphoma

Abstract #337

Juan Pablo Alderuccio et al.

Studiendesign

N=39



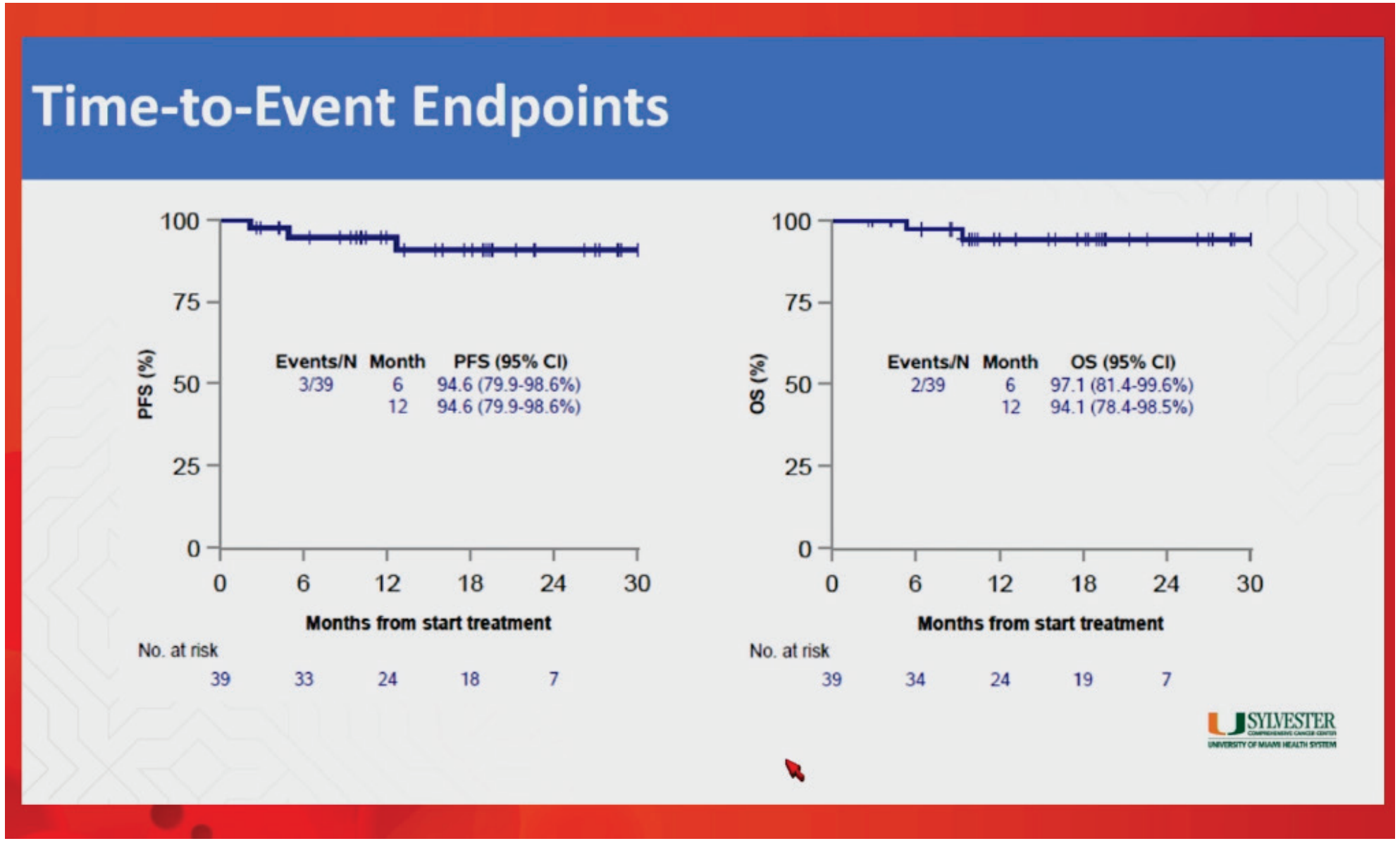
Ansprechen in Risikogruppen

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*

PFS und OS


Time-to-Event Endpoints
PFS (%)
100
75
50
25
0
Events/N Month PFS (95% CI)
3/39 6 94.6 (79.9-98.6%)
12 94.6 (79.9-98.6%)
0 6 12 18 24 30
Months from start treatment
No. at risk
39 33 24 18 7
OS (%)
100
75
50
25
0
Events/N Month OS (95% CI)
2/39 6 97.1 (81.4-99.6%)
12 94.1 (78.4-98.5%)
0 6 12 18 24 30
Months from start treatment
No. at risk
39 34 24 19 7
SYLVESTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

Toxizitäten

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

Zusammenfassung | Take-Home-Messages

- Der CD3xCD20 bispezifische Antikörper Epcoritamab erreicht in der Kombination mit R^2 ein tiefes und anhaltendes Ansprechen und hat das Potential, im Therapiealgorithmus des FL weiter nach vorne zu rücken.

- Die Langzeitdaten zu Axi-Cel belegen ein dauerhaftes Ansprechen bei >50% der Patienten mit mehrfach rezidiviertem FL.

- Die Kombination von Tafasitamab plus R^2 verringert das PFS-Risiko gegenüber R^2 um 57% und kann einen neuen Therapiestandard im r/r FL definieren.

- Erste Daten zu Loncastuximab tesirin plus Rituximab beim r/r FL deuten auf eine vielversprechende Aktivität bei guter Verträglichkeit hin.

Die Kurzpräsentationen sind online unter

www.lymphome.de/ash2024

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