Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

18th ICML LUGANO

17. – 21. Juni 2025

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Prof. Dr. med. Lena Illert
TUM Klinikum Rechts der Isar

Follikuläres Lymphom (FL)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ICML 2025 LUGANO, Italien wird in Kooperation mit fünf unterstützenden Firmen durchgeführt.
Meine persönlichen Disclosures betreffen:

Anstellungsverhältnis, Führungsposition	Professorin TU München
Beratungs-/ Gutachtertätigkeit	Illumina, Janssen, Roche, Takeda, Incyte, SOBI, BMS, Beigene
Besitz von Geschäftsanteilen, Aktien oder Fonds	n.a.
Patent, Urheberrecht, Verkaufslizenz	n.a.
Honorare	ONKOupdate, ASH Today, Onkowissen, Abbvie, Takeda, Roche, Janssen, AstraZeneca, Beigene
Finanzierung wissenschaftlicher Untersuchungen	Prof. Illert leitet die DKTK geförderte, akademische SORATRAM-Phas I/II Studie, dessen Sponsor das Uniklinikum Freiburg ist; Sorafenib wird hierfür freundlicherweise von Bayer zur Verfügung gestellt.
Andere finanzielle Beziehungen	Travel support: Janssen, Takeda, AstraZeneca, Beigene
Immaterielle Interessenkonflikte	n.a.

Kapitel 1

Erstlinie

Follikuläres Lymphom im frühen Stadium:

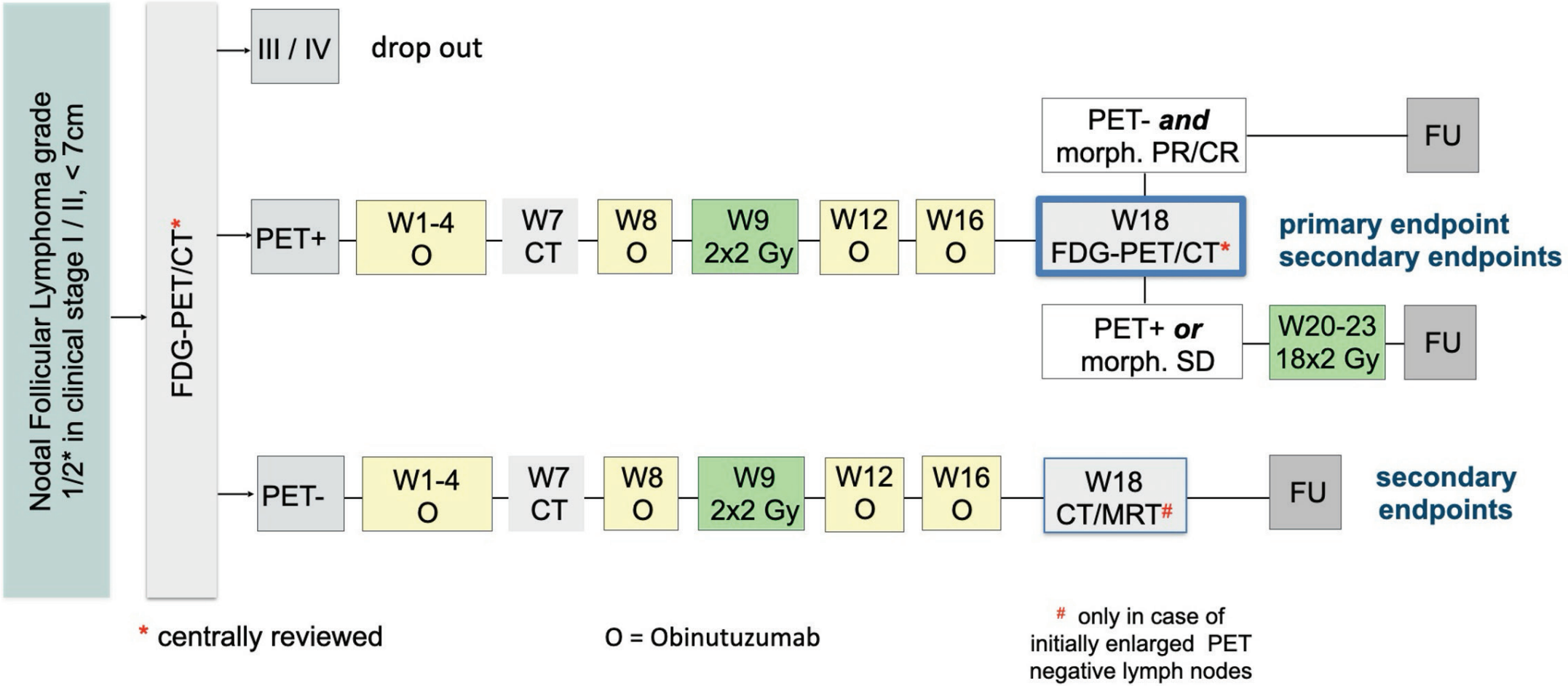
- Wieviel Strahlentherapie brauchen wir für eine Kuration?

High PFS with low infield recurrences after low dose radiotherapy and Obinutuzumab in early stage nodal follicular lymphoma: final results of the GAZAI study (GLA 2018-3)

Abstract # 110

Klaus Herfarth et al.

GAZAI Studiendesign



Primärer Endpunkt: Metabolische CR in Woche 18 in Patienten mit PET+ Lymphom

GAZAI Response Rate

metabolic

	w 18	DS
CR	**46 (87 %)**	1/2

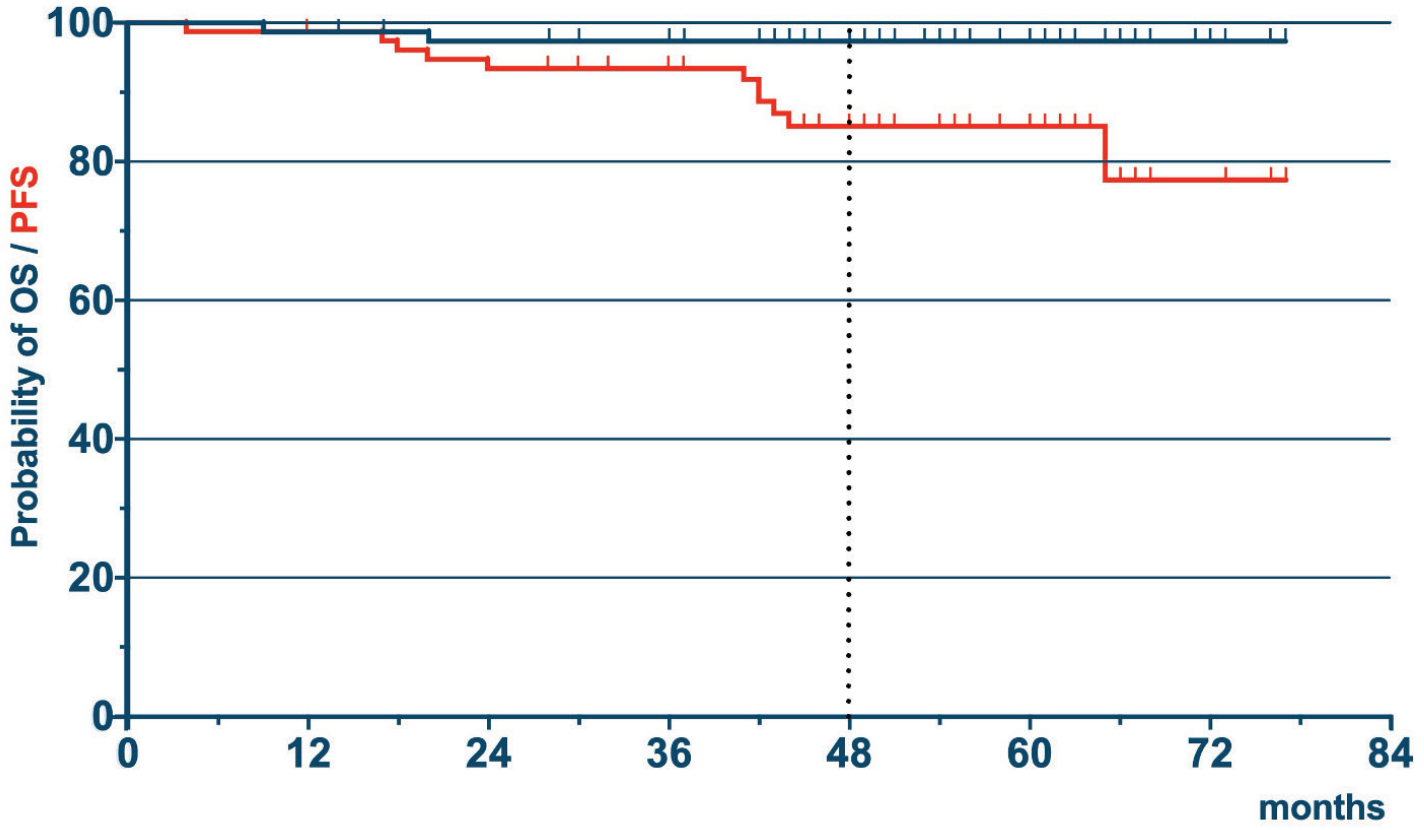
morphologic

	w 18
CR/CRu	**49 (91 %)**

Herfarth et al. ICML 2023

3 / 6 patients with mPR received Salvage RT

GAZAI Overall Survival and Progression Free Survival



- Median f/u 49 months
- OS (4 yrs) 97%
- PFS (4 yrs) 85%
- 10 recurrences after median 41 months

median follow-up of 49 months

GAZAI Recurrences

- Relation to RT volume

inside	i/o	outside
1	2*	7

- initial stage

Io	I	II
0 / 24	4 / 24	6 / 30

* 1 patient with salvage RT in week 22-24

GAZAI Zusammenfassung

- Hohes progressionsfreies Überleben (PFS) und niedriger Rate an Rezidiven im Bestrahlungsfeld nach low-dose Radiotherapie und Obinutuzumab bei nodal begrenztem follikulären Lymphom im limitierten Stadium

- Aktuell rekrutiert die Phase III FORTplus Studie an vielen Zentren (Nicht- Überlegenheit 2x2 Gy + Obi vs. 12x2 Gy + Ritux)

Kapitel 2

Erstlinie – fortgeschrittene Stadien

Chemo-frei - *Ready for Prime Time* ?

Mosunetuzumab (mosun) Produces Durable Benefit in Patients (pts) with Newly Diagnosed Follicular Lymphoma (FL): Extended Follow up of the MITHIC-FL1 Trial.

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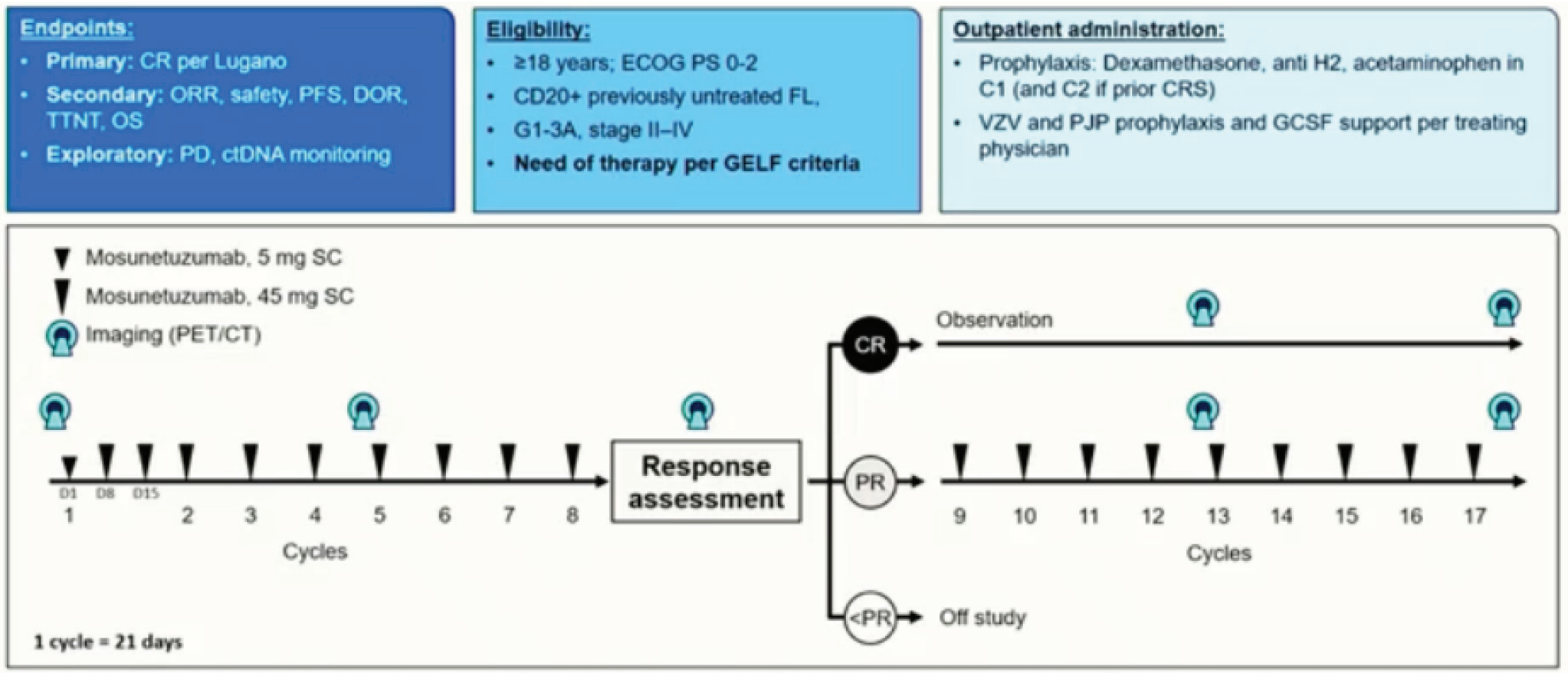
Lorenzo Falchi, New York, NY, US

MITHIC-FL1 Trial: Studiendesign

Mosunetuxumab s.c. Monotherapie 1st Line FL



n = 78 Pat eingeschlossen; 76 Pat. auswertbar für Effektivität

Time-limited concept bei CR

Median Follow up 16.7 Monate

MITHIC-FL1 Trial: Patienten-Characteristica

Mosunetuxumab s.c. Monotherapie 1st Line FL

Characteristic	All patients (N=78)
Median age, y (range)	59 (26 - 83)
Female, n (%)	34 (44%)
Race, n (%)	
White	60 (77%)
Asian	10 (13%)
Black	2 (3%)
Unknown	6 (8%)
Ethnicity, n (%)	
Non-Hispanic	70 (89%)
Unknown	5 (6%)
ECOG Status, n (%)	
0	62 (79%)
1	16 (21%)
Elevated LDH, n (%)	9 (12%)
Median SUV_{max} (range)	11.6 (3.7 - 41.1*)

Characteristic	All patients (N=78)
Grade, n (%)	
1-2	63 (81%)
3A	15 (19%)
Stage, n (%)	
II	7 (9%)
III	13 (17%)
IV	58 (74%)
FLIPI, n (%)	
0-2	58 (74%)
3-4	20 (26%)
GELF criteria, n (%)	
≥3 lymph nodes of ≥3 cm	48 (62%)
≥7 cm tumor mass	29 (37%)
Mass-related symptoms	44 (56%)
B Symptoms, n (%)	19 (24%)
Other¶	7 (9%)

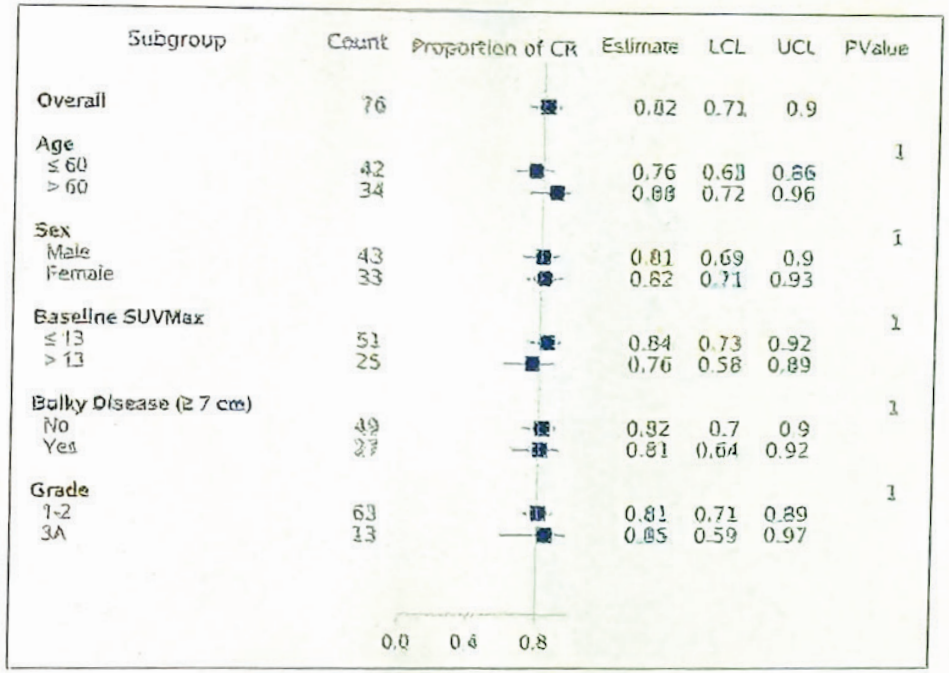
* DLBCL diagnosed 6 weeks after treatment initiation on a left axillary lymph node with baseline SUV 41 not previously biopsied; LDH, lactate dehydrogenase; FLIPI, follicular lymphoma international prognostic index; ¶ Serosal effusions in 3 (4%); splenomegaly in 2 (3%); cytopenias in 2 (3%); end-organ damage in 1 (1%)

MITHIC-FL1 Trial: Results Response Rates

Mosunetuxumab s.c. Monotherapie 1st Line FL

Responses Were Deep and Consistent Across Key Subgroups

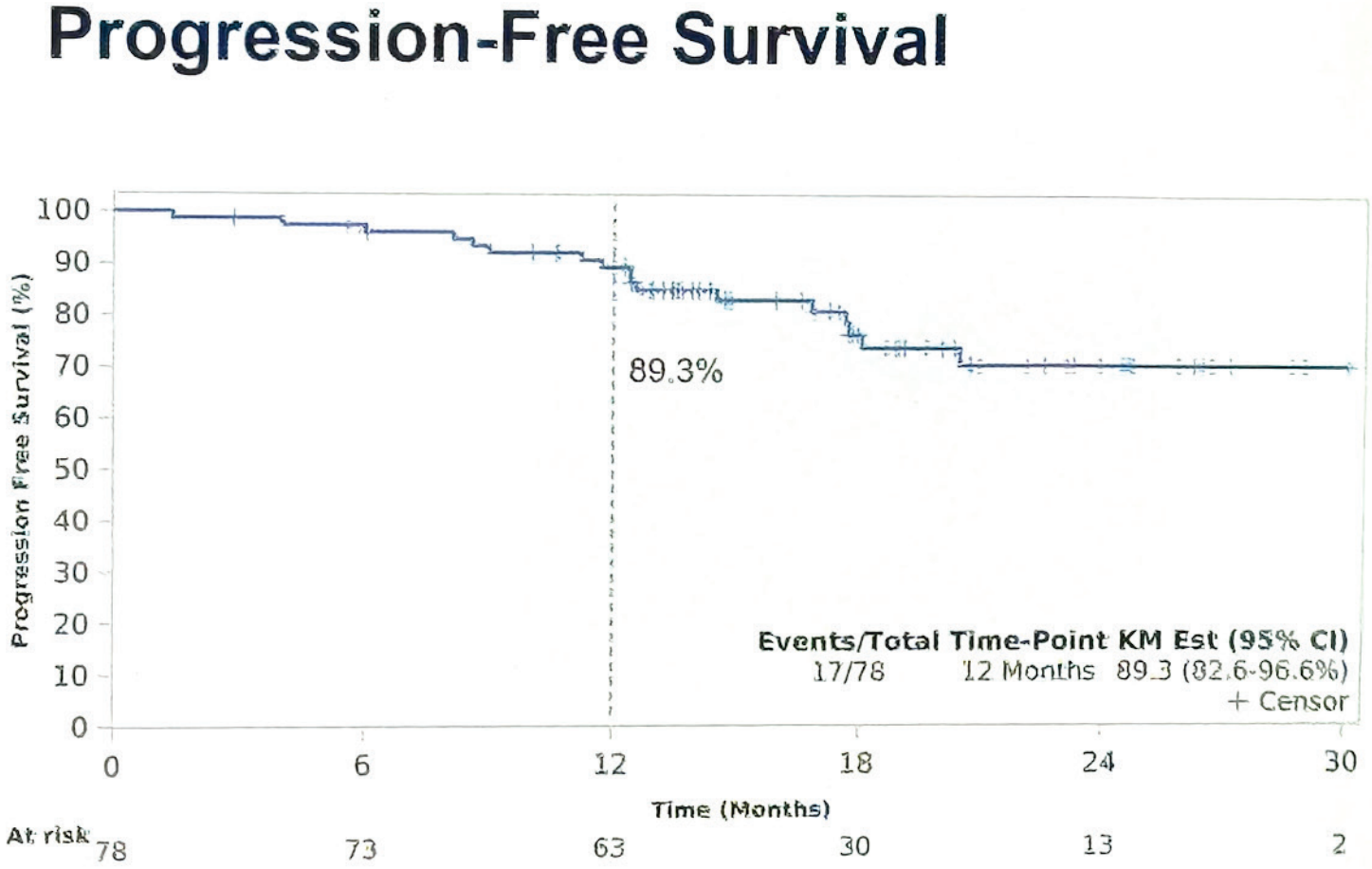
Response type	Response evaluable (N=76)	Intention-to-treat (N=78)
Overall response	95%	92%
Complete response*	82%	79%
Partial response	13%	13%
Stable disease	3%	3%
Progressive disease	3%	3%
Non-evaluable	n/a	3%



Intention-to-treat group includes all patients who received at least one dose of mosunetuzumab. Response evaluable population includes all patients who had at least one radiographic response evaluation. *One patient's end-of-treatment response adjudication was updated from a partial response to a complete response after biopsy of the only persistent FDG-avid lesion after treatment demonstrated Schwannoma; this patient received a total of 17 mosunetuzumab cycles

MITHIC-FL1 Trial Results – Progression free survival

Mosunetuxumab s.c. Monotherapie 1st Line FL



- 13 Patients experienced PD:
  - 7 are on observation
  - 2 received radiation to a single site of PD
  - 4 had transformation and were treated with R-CHOP (all in continued CR)
- CD20 status by IHC at PD:
  - 6 CD20+
  - 3 CD20-
  - 2 not biopsied

Median Follow up 16.7 Monate

Bispezifische Antikörper in der Erstlinie FL

Aktuell rekrutiert die Phase III **MorningLyte** Studie an vielen Zentren in Deutschland (Mosunetuzumab + Lenalidomid vs. Immun-Chemotherapie)

Kapitel 3

Zweitlinie

Practise Changing Results !

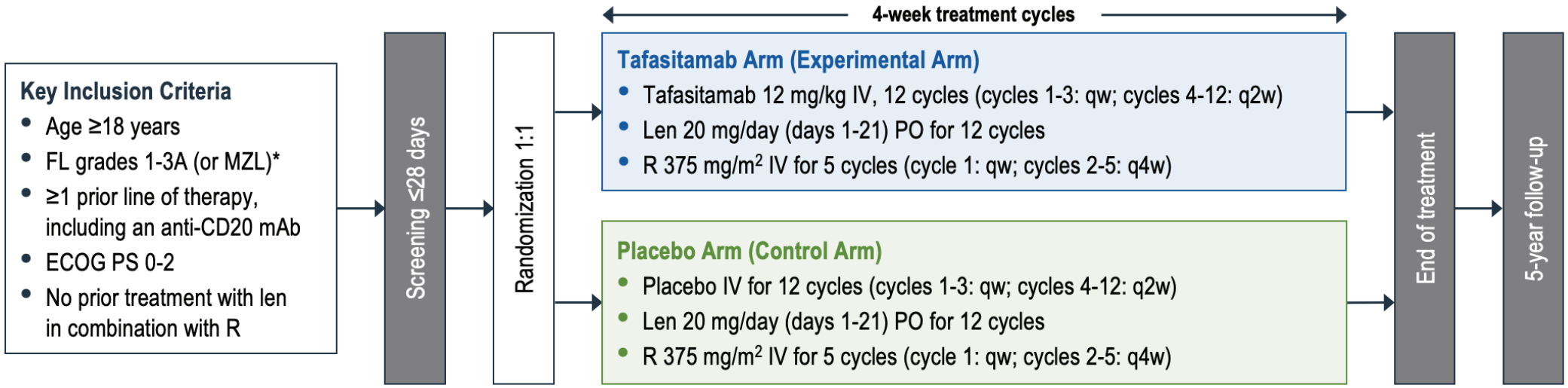
Outcomes From the Phase 3 inMIND Study of Tafasitamab (Tafa) Plus Lenalidomide (Len) and Rituximab (R) for Patients With Relapsed/Refractory Follicular Lymphoma (R/R FL)

 # 28

Laurie H Sehn, Vancouver, BC, CA

inMIND Trial: Studiendesign

Phase 3, Double-Blind, Placebo-Controlled, International, Multicenter Randomized Study



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, QoL, MRD
- **Exploratory:** TTNT, B-cell recovery, Ig levels, CD19 expression

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

inMIND Trial: Baseline Characteristics

Tafa + Ritux + Lenalodomide in R/R FL

Variable	Tafasitamab + Len + R (n=273)	Placebo + Len + R (n=275)	Total (N=548)
Median age, years (range)	64.0 (36, 88)	64.0 (31, 85)	64.0 (31, 88)
≥75, n (%)	54 (19.8)	54 (19.6)	108 (19.7)
Male sex, n (%)	150 (54.9)	149 (54.2)	299 (54.6)
Median time since initial diagnosis of FL, years (range)	5.2 (0, 34)	5.5 (1, 33)	5.3 (0, 34)
ECOG PS at screening, n (%)			
0	181 (66.3)	192 (69.8)	373 (68.1)
1-2	92 (33.7)	83 (30.2)	175 (31.9)
Bone marrow involvement, n (%)			
Yes	88 (32.2)	91 (33.1)	179 (32.7)
No	169 (61.9)	162 (58.9)	331 (60.4)
Unknown/Missing	16 (5.9)	22 (8.0)	38 (6.9)
Ann Arbor stage, n (%)			
I or II	52 (19.0)	50 (18.2)	102 (18.6)
III or IV	221 (81.0)	225 (81.8)	446 (81.4)
FL grade, n (%)			
1 or 2	203 (74.4)	203 (73.8)	406 (74.1)
3A	67 (24.5)	71 (25.8)	138 (25.2)
B symptoms, n (%)	63 (23.1)	67 (24.4)	130 (23.7)
FLIPI score, n (%)			
0-1	57 (20.9)	57 (20.7)	114 (20.8)
2	79 (28.9)	67 (24.4)	146 (26.6)
3-5	137 (50.2)	150 (54.5)	287 (52.4)
GELF criteria, n (%)	222 (81.3)	232 (84.4)	454 (82.8)
FL diagnosis confirmed by central pathology, n (%)	256 (93.8)	251 (90.5)	507 (92.2)

ITT population. ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; FLIPI, Follicular Lymphoma International Prognostic Index; GELF, Groupe d'Etude des Lymphomes Folliculaires; ITT, intent-to-treat; Len, lenalidomide; R, rituximab.

inMIND Trial: Treatment History

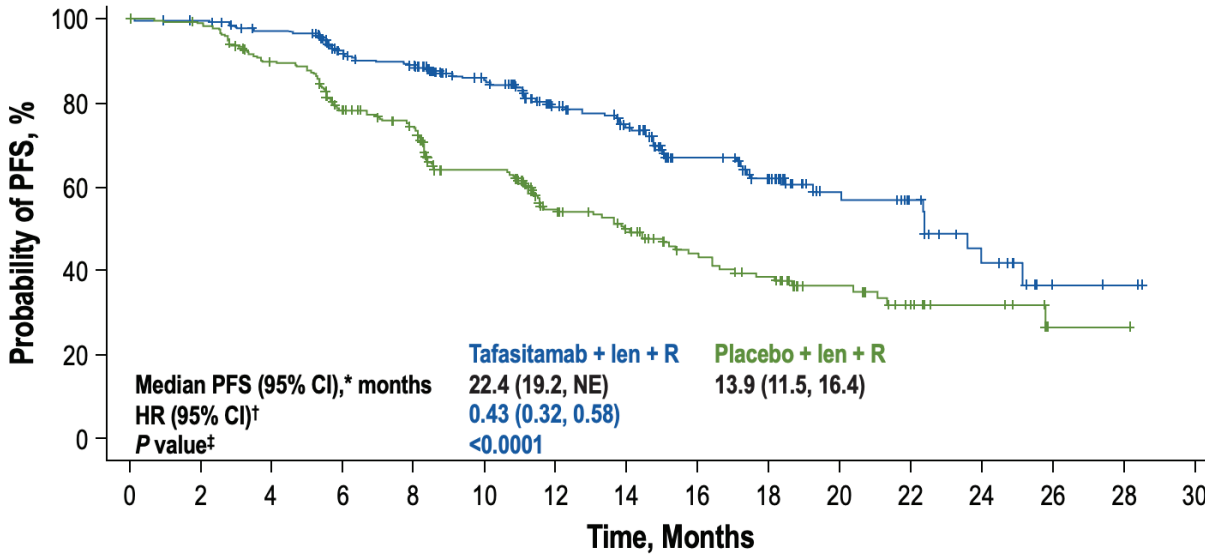
Tafa + Ritux + Lenalodomide in R/R FL

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)
Number of prior lines of therapy, n (%)			
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)
Prior systemic anti-cancer treatment regimens, n (%)			
Anthracyclines	161 (59.0)	167 (60.7)	328 (59.9)
Anti-CD20 plus CHOP	151 (55.3)	161 (58.5)	312 (56.9)
Bendamustine alone or in combination	114 (41.8)	101 (36.7)	215 (39.2)
Anti-CD20 monotherapy	54 (19.8)	51 (18.5)	105 (19.2)
Anti-CD20 plus CVP	30 (11.0)	43 (15.6)	73 (13.3)
Chemotherapy plus ASCT	19 (7.0)	23 (8.4)	42 (7.7)
Time since last anti-lymphoma 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)
Relapsed/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)

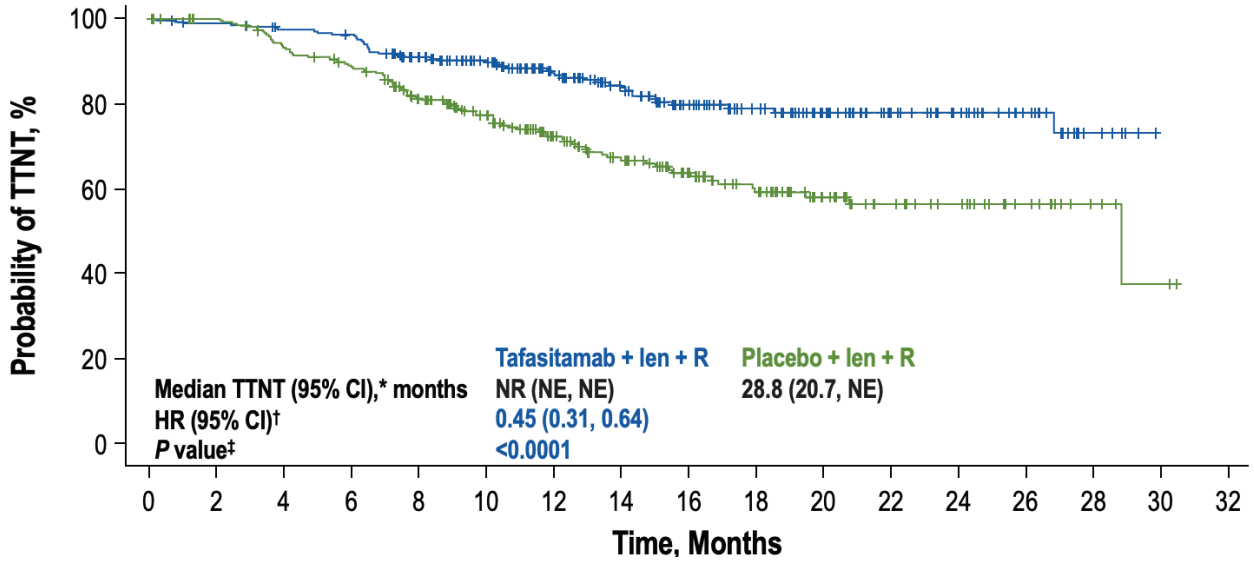
inMIND Trial: PFS und TTNT

Tafa + Ritux + Lenalodomide in R/R FL

Progression Free Survival

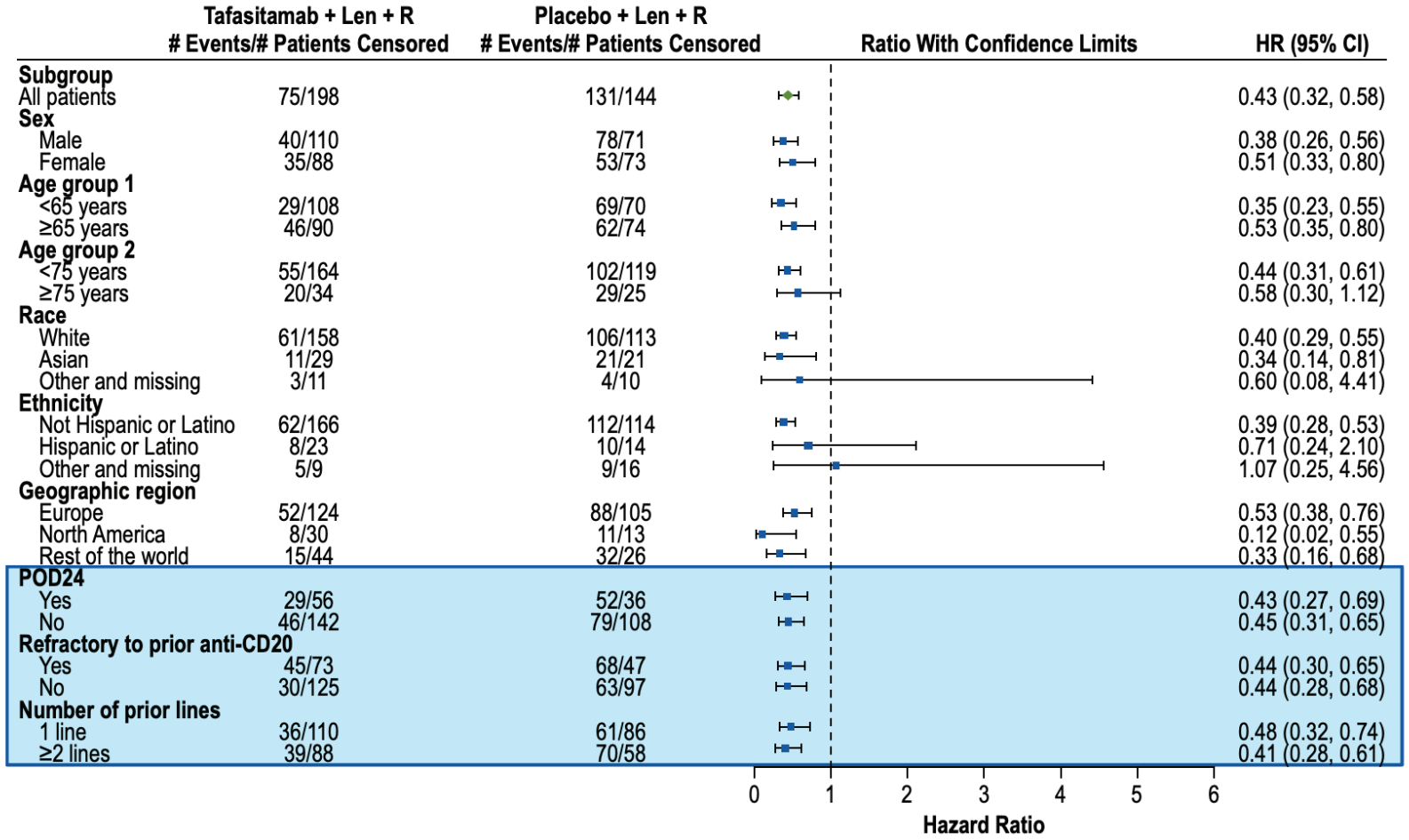


Time to next treatment



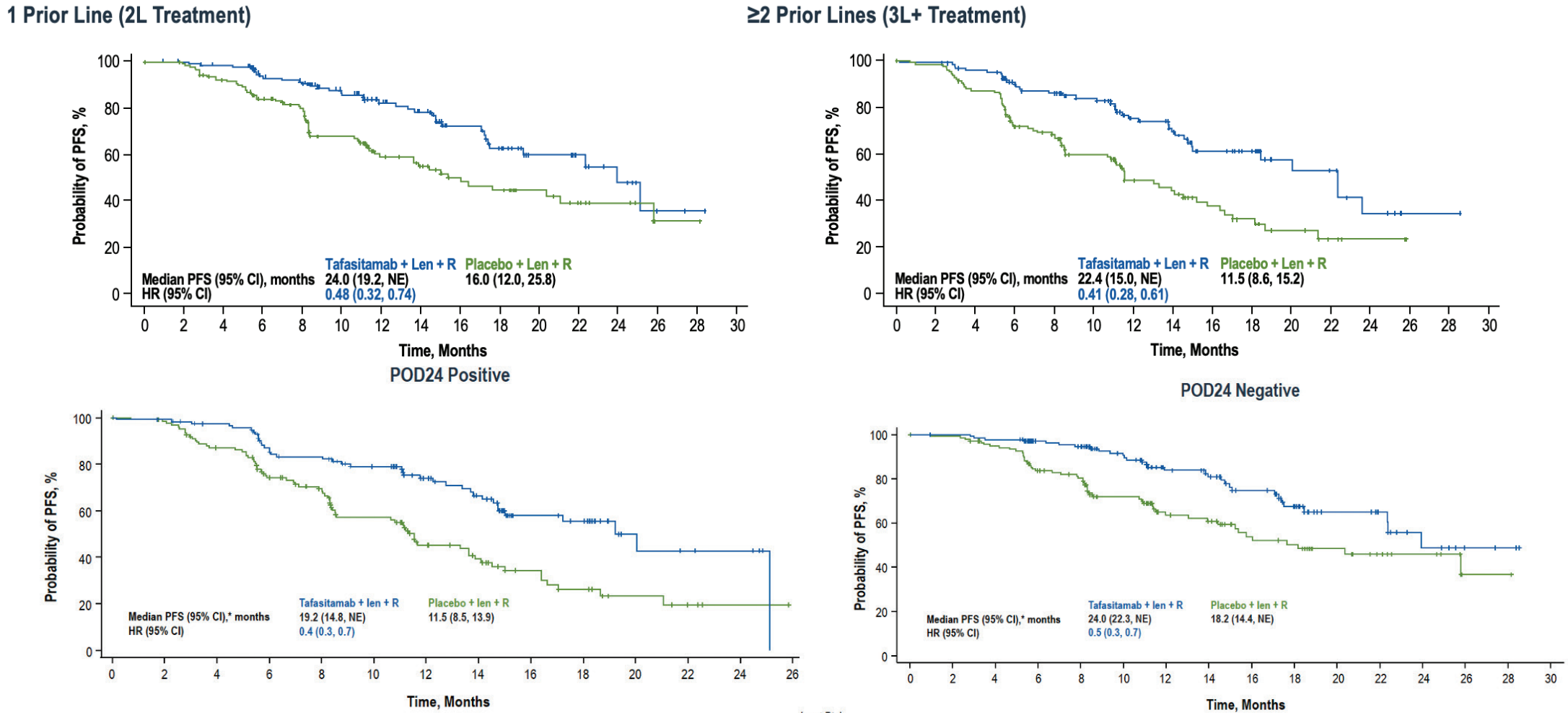
inMIND Trial: Prespecified Subgroup Analysis of PFS

Tafa + Ritux + Lenalodomide in R/R FL



inMIND Trial: Prespecified Subgroup Analysis of PFS

Tafa + Ritux + Lenalodomide in R/R FL



POD24 (defined as progression within start of initial treatment)

inMIND Trial: Transformation and CD19 Expression

Tafa + Ritux + Lenalodomide in R/R FL

Histological Transformation

Variable	Tafasitamab + Len + R (n=273)	Placebo + Len + R (n=275)
Patients with transformation into more aggressive histology,* n (%)	0 (0.0)	9 (3.3)
Rate of transformation into more aggressive histology (95% CI)	0.0 (0.0, 1.3)	3.3 (1.5, 6.1)
Median time to transformation (95% CI)†	NR (NE, NE)	NR (NE, NE)

CD19 Expression at End of Treatment or Follow-Up

Sample	Tafasitamab + Len + R (n=273)	Placebo + Len + R (n=275)
Total samples,* n	13	19
Lymphoma detected, n	8	16
CD19 positive,† n/N	7/8	16/16

23 out of 24 post-treatment samples where lymphoma was detected remained CD19-positive

- 1 sample from a patient who received tafasitamab + len + R and achieved a PR was CD19 negative (this patient had 80% CD19-negative tumour cells at screening)

inMIND Trial: Summary

Tafa + Ritux + Lenalodomide in R/R FL

- Practise-Changing nach Zulassung für R/R FL Patienten (nach Zulassung)
- Aktuell keine Hinweise für CD19 Loss nach Tafasitamab-Behandlung

Kapitel 4

Drittline

Update zelluläre Therapien - Long Term Remission

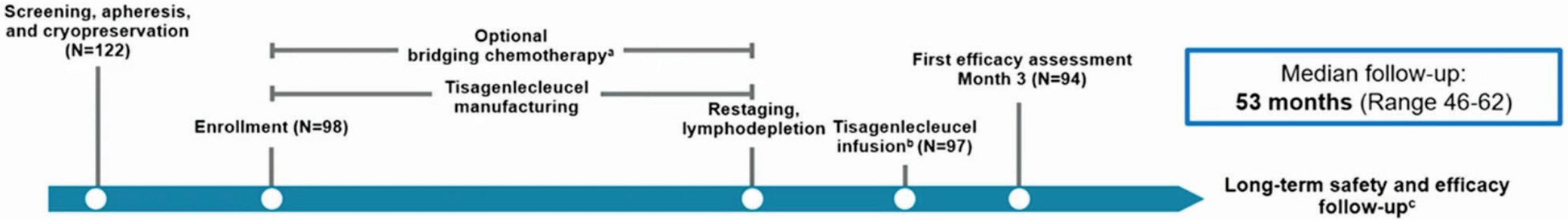
Phase 2 ELARA Trial 4-year Update: Clinical Outcomes of Tisagenlecleucel in Patients (pts) With High-Risk Relapsed/Refractory Follicular Lymphoma (r/r FL)

 # 138

Catherine Thieblemont, Paris, FR

ELARA Trial 4-year Update: Study Design

Tisagenlecleucel in R/R FL Patien*innen



Key eligibility criteria	Study treatment	End points
• ≥18 years of age • FL grade 1, 2, or 3A • Relapsed/refractory disease[d] • No evidence of histological transformation/FL3B • No prior anti-CD19 therapy or allogeneic HSCT	Tisagenlecleucel dose range (single IV infusion) was $0.6\text{-}6\times10^8$ CAR-positive viable T cells	**Primary:** CRR by IRC **Secondary:** ORR, DOR, PFS, OS, safety, cellular kinetics

- Bridging therapy was allowed and was followed by disease re-evaluation before tisagenlecleucel infusion
- Cellular kinetics were determined by measurement of transgene levels by qPCR
- MRD levels were determined via clonoSEQ® next-generation sequencing assay performed at Adaptive Biotechnologies (Seattle, WA, USA)

ELARA Trial 4-year Update: Patients Characteristics

Tisagenlecleucel in R/R FL Patien*innen

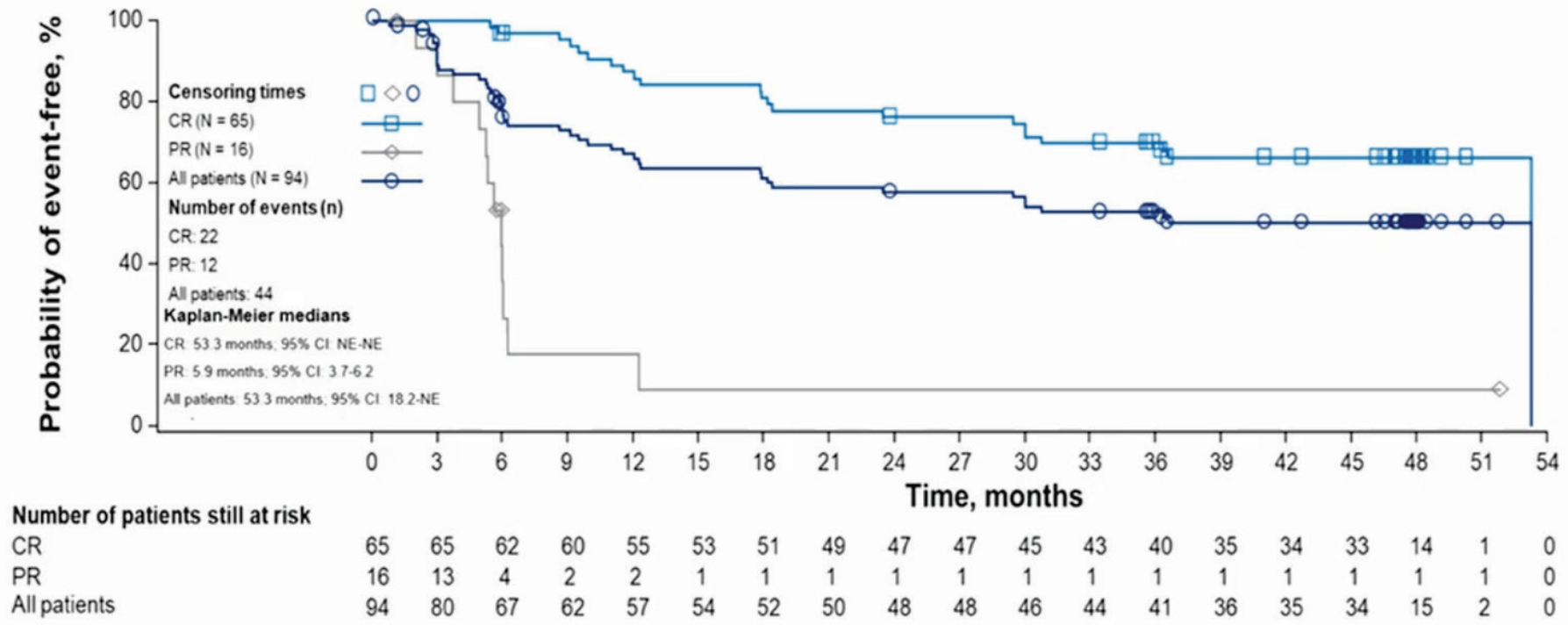
	Infused set (N = 97) n (%)
Median age (range), years	57.0 (29-73)
18 to <65 years	73 (75)
≥65 years	24 (25)
ECOG PS ≥1 prior to infusion	42 (43)
Stage at study entry III-IV	83 (86)
Bone marrow involvement	37 (38)
Bulky disease[a]	63 (65)
FLIPI high at study entry (≥3)	58 (60)
Median no. of prior therapies (range)	4 (2-13)
POD24[b]	61 (63)
Refractory disease to last line of therapy	76 (78)
Refractory to ≥2 regimens	69 (71)
Double refractory: anti-CD20 mAb + alkylating agent	66 (68)
Refractory to PI3K inhibitors	14 (14)
Prior autologous HCT	35 (36)

- Key patient subgroups at high risk among efficacy-evaluable patients (N = 94):
  - Disease refractory to ≥2 prior regimens: 72%
  - Bulky disease (>7 cm or at least 3 lesions >3 cm): 66%
  - POD24 from first anti-CD20 mAb-containing therapy: 65%
  - High FLIPI (≥3): 61%
  - High tumor burden (TMTV >510 mL[1,2]): 21%

Median Follow up 53 months

ELARA Trial 4-year Update: 48 months Progression free Survival

Tisagenlecleucel in R/R FL Patien*innen



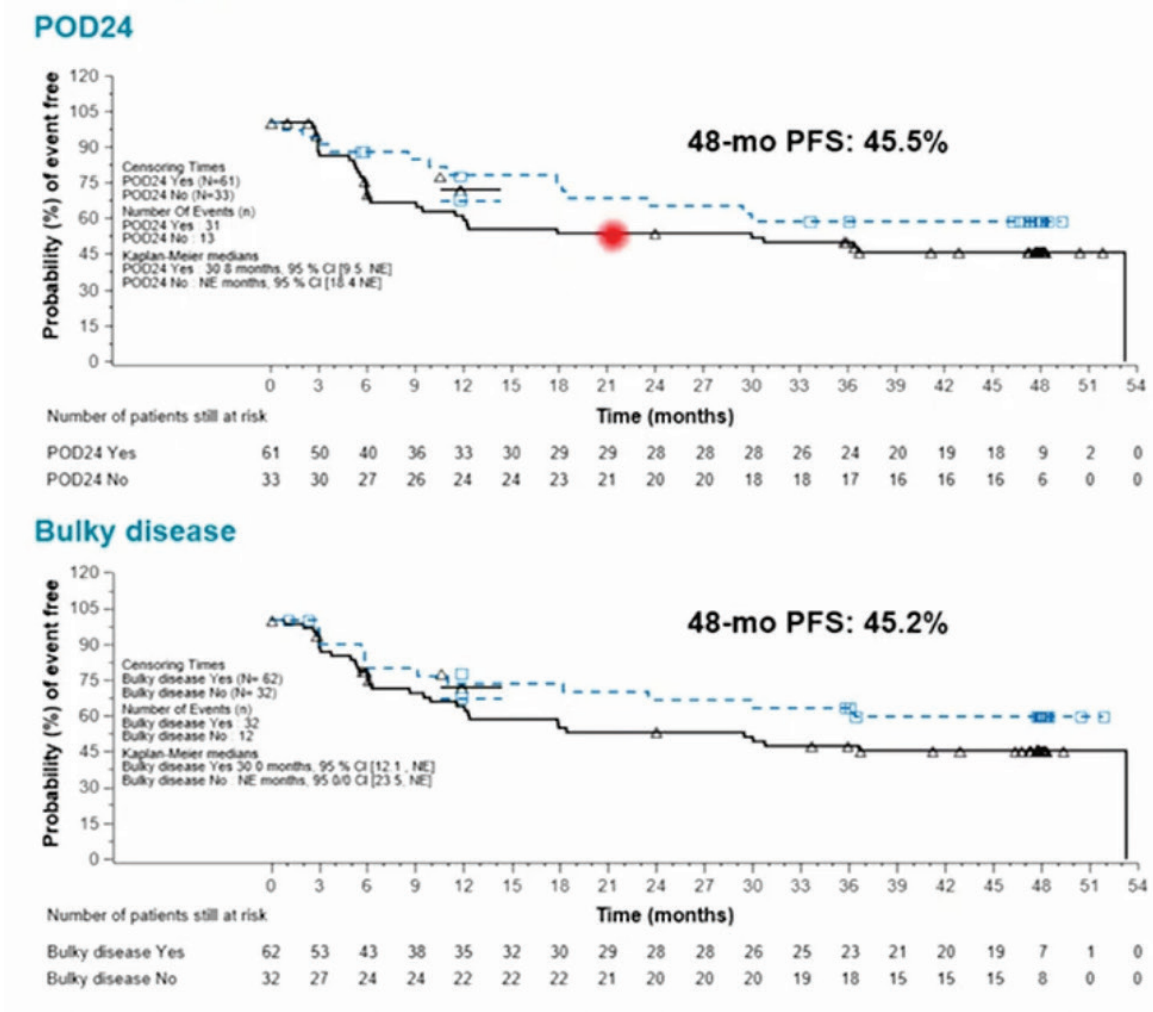
	48-mo PFS, %
In all patients	50.2
In patients with BOR of CR	66.1

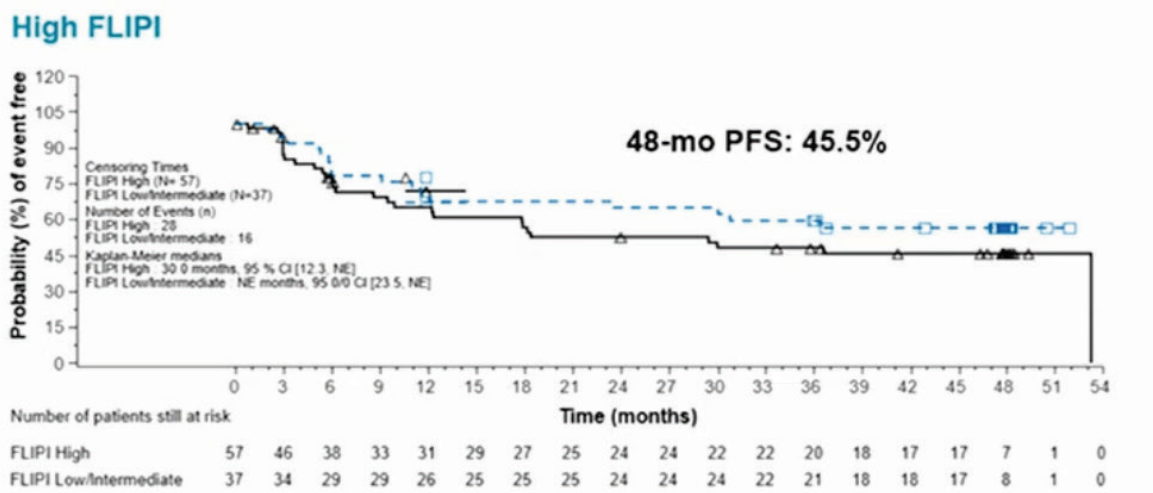
- High response rate reported anytime post-infusion (CR: 69.1%)[1]

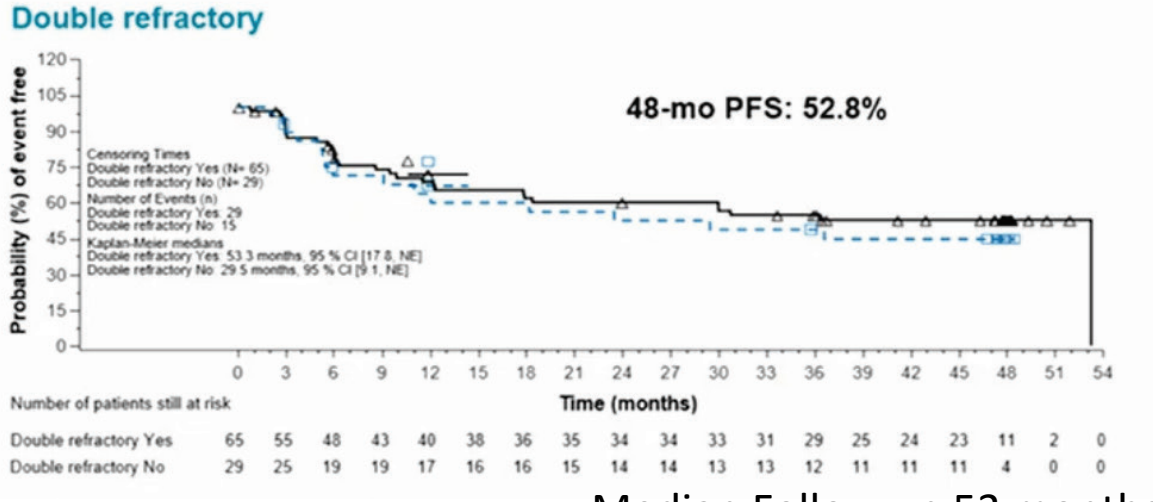
Median Follow up 53 months

ELARA Trial 4-year Update: 48- months Progression Free Survival in high-risk Patient population

Tisagenlecleucel in R/R FL Patien*innen







Median Follow up 53 months

- Eine mit **2x2 Gy** deutlich reduzierte Strahlendosis plus Obinutuzumab zeigt eine **hohe Effektivität** in den frühen Stadien des FL **mit hohem progressionsfreiem Überleben (PFS)** und **niedriger Rate an Rezidiven im Bestrahlungsfeld**
- **Bispezifische AKs** zeigen vielversprechende Daten in der **Erstlinie**, Studienkonzepte sind in Deutschland (u.a**. *MorningLyte*** in Kombination mit Lenalidomid erhältlich)
- **Tafasitamab, Lenalidomid und Rituximab** wird einen neuen Standard in der **Zweitlinie des FL** definieren. CD19 scheint nach Tafasitamab-Therapie vorhanden zu bleiben.
- Die Langzeitdaten zu **Tisagenlecleucel** zeigen ein dauerhaftes **Ansprechen bei 50% der Patienten** mit mehrfach rezidiviertem FL (auch in high-risk Subgruppen)

Alle Kurzpräsentationen sind online unter

www.lymphome.de/icml2025

Für den Inhalt verantwortlich:

Prof. Dr. med. Lena Illert

TUM Klinikum Rechts der Isar

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Expert:innen berichten zu Lymphomen & Leukämien

Kompetenznetz Maligne Lymphome

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