



65th ASH Meeting 2023
San Diego & virtuell

Lymphom
Kompetenz
KOMPAKT



KML KONGRESSE

Expert:innen berichten zu
Lymphomen & Leukämien



Prof. Dr. med. Kai Hübel
Uniklinik Köln

Follikuläre Lymphome (FL)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ASH2023 wird in Kooperation mit acht unterstützenden Firmen durchgeführt.

Meine persönlichen Disclosures betreffen:

Anstellungsverhältnis, Führungsposition	Oberarzt, Uniklinik Köln
Beratungs-/ Gutachtertätigkeit	Roche, BMS, Incyte, Recordati, AbbVie, Novartis, Gilead, Miltenyi Biotec, BeiGene
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, Sandoz
Andere finanzielle Beziehungen	entfällt
Immaterielle Interessenkonflikte	entfällt

Kapitel 1

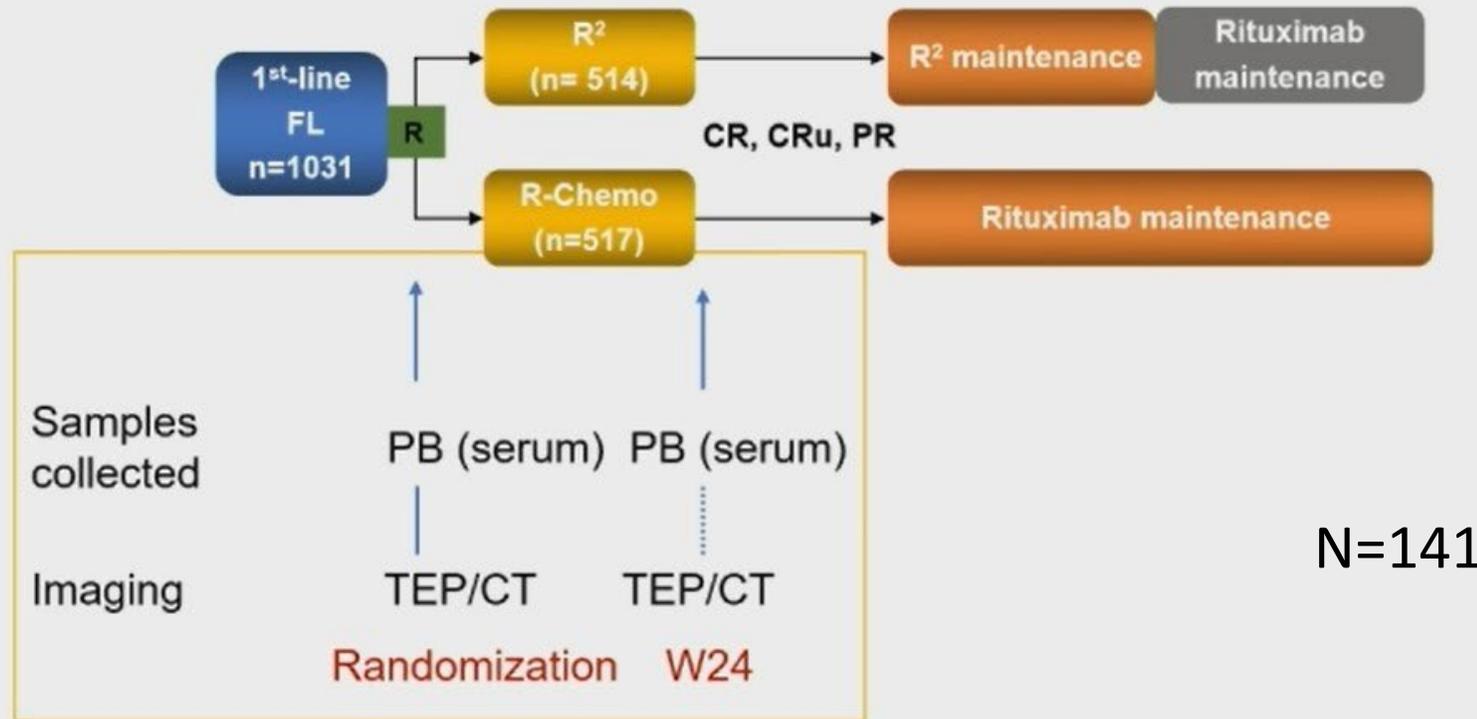
Wie können wir den Verlauf eines Patienten mit FL besser prognostizieren?

Combining PET/CT and ctDNA Assessments at 6 Months from Induction Treatment Better Predicts Outcome in Previously Untreated Patients with Follicular Lymphoma: A Relevance Ancillary Lysa Study

Abstract #170

Alexis Claudel et al.

Design und Methoden (RELEVANCE-Studie)

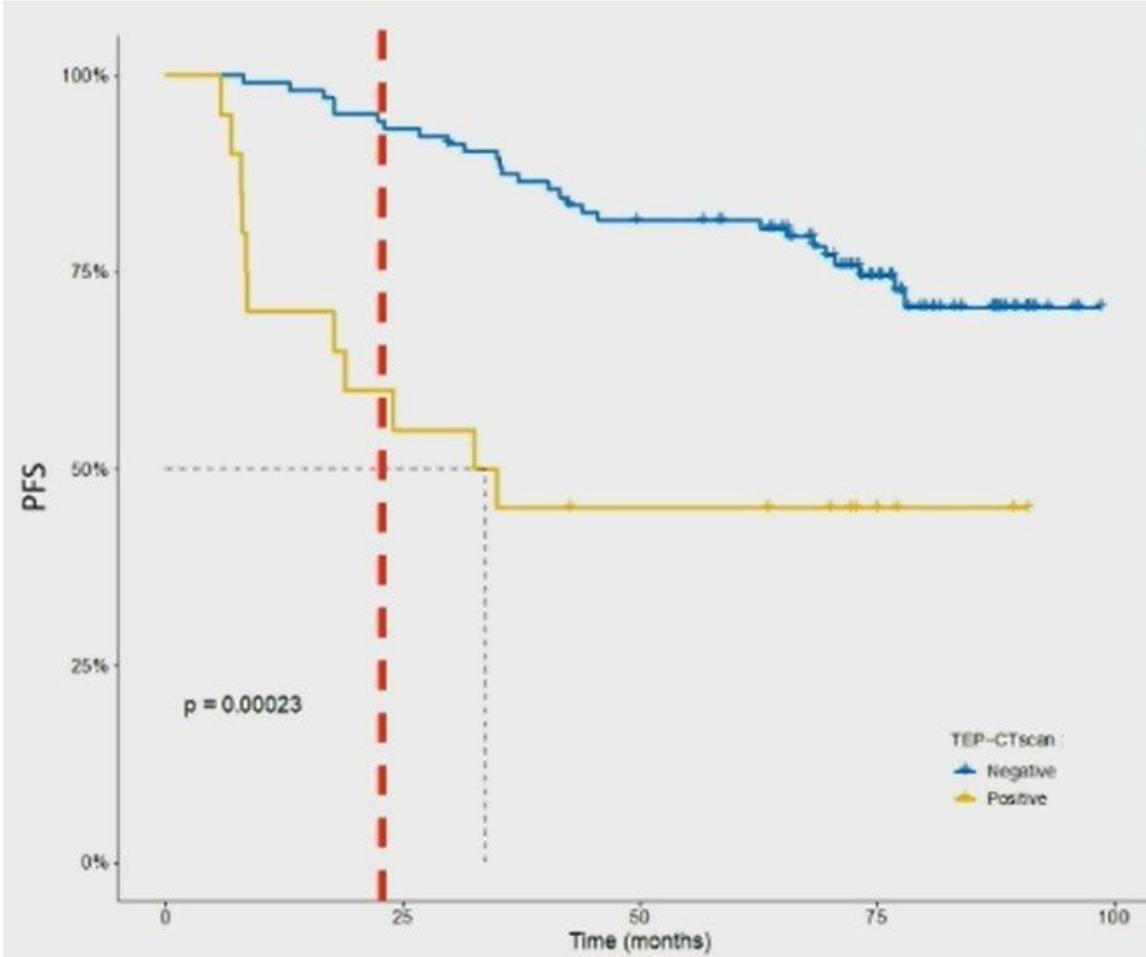


12/08/2023

Alexis Claudel - 2023 ASH Meeting, San Diego

Morschhauser et al,
NEJM 2018

PFS: PET/CT positiv vs PET/CT negativ



At risk	0	25	35	50	75	100
— Negative	104	97	82	47	0	0
— Positive	20	11	8	4	0	0

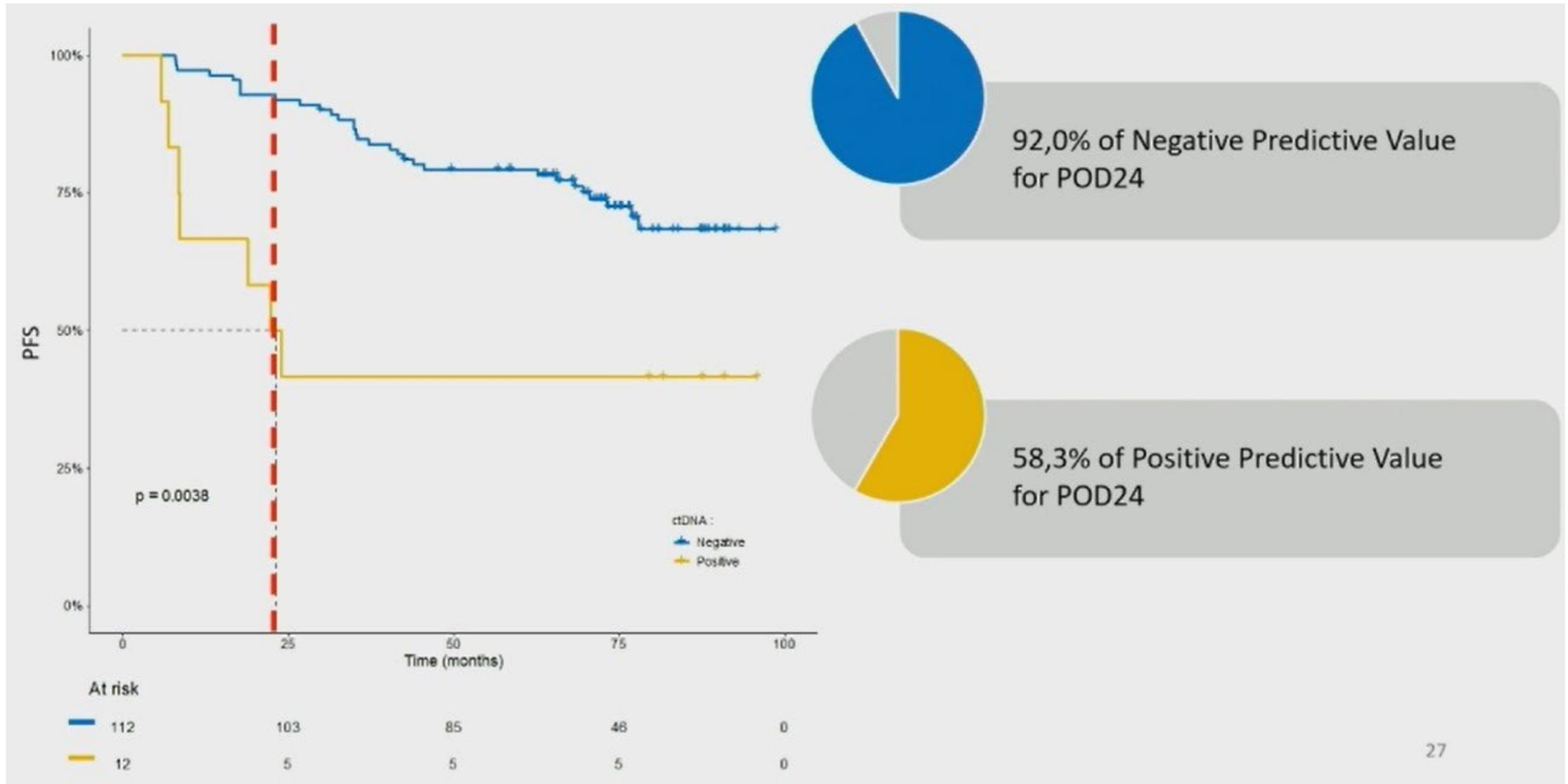


93,3% of Negative Predictive Value for POD24

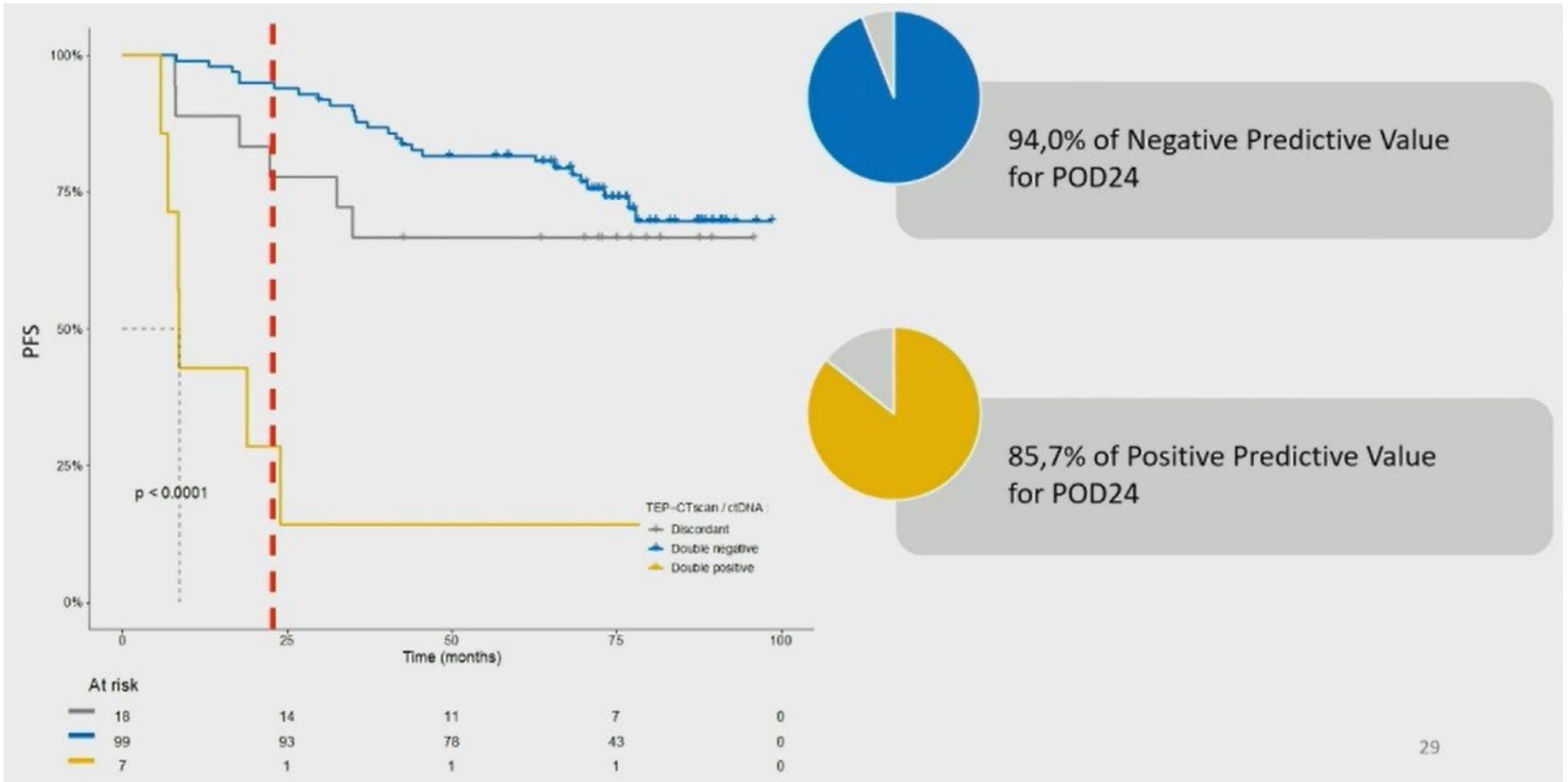


45,0% of Positive Predictive Value for POD24

PFS: ctDNA positiv vs ctDNA negativ



PFS: PET/CT kombiniert mit ctDNA



Kapitel 2

Bispezifische Antikörper beim FL

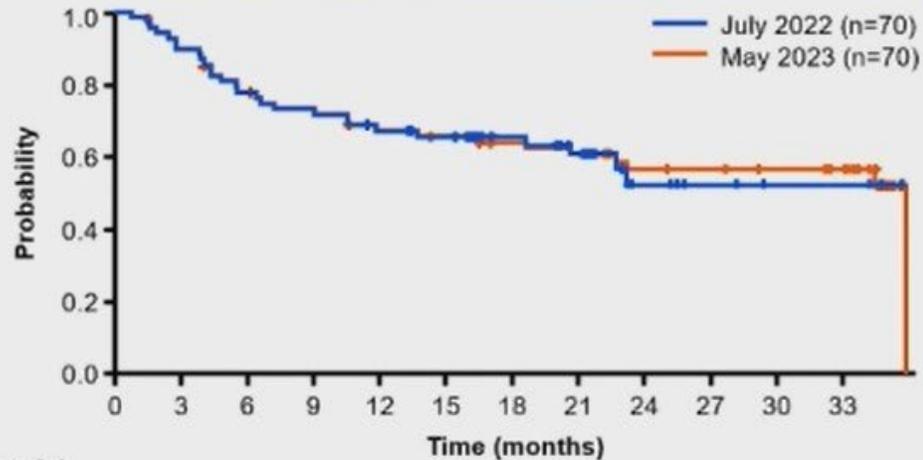
Mosunetuzumab Monotherapy Continues to Demonstrate Durable Responses in Patients with Relapsed and/or Refractory Follicular Lymphoma after ≥ 2 Prior Therapies: 3-Year Follow-up from a Pivotal Phase II Study

Abstract #603

Stephen J. Schuster et al.

Dauer des Ansprechens

DOR (July 2022 vs May 2023 data cut-off)

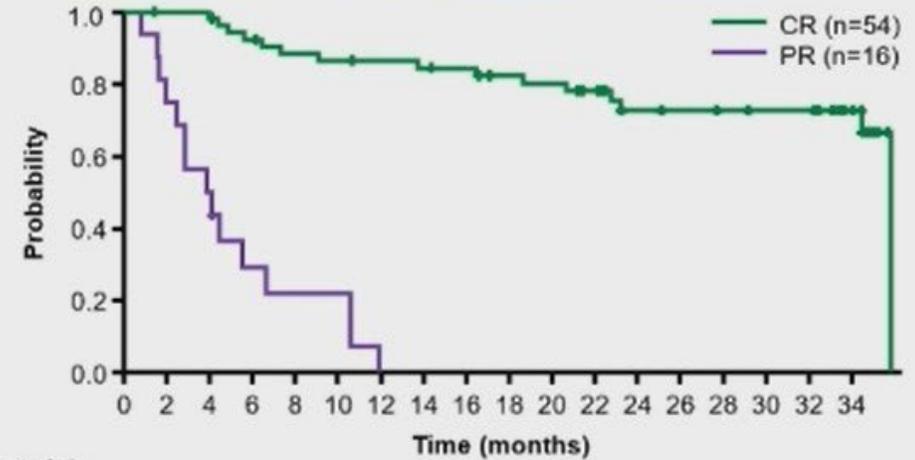


Patients at risk		Time (months)											
July 2022	70	62	52	48	42	38	30	25	9	5	3	3	
May 2023	70	62	52	48	43	41	38	36	26	25	23	21	

n=70

Median DOR, months (95% CI)*	35.9 (20.7–NE)
30-month DOR rate, % (95% CI)†	56.6% (44.2–68.9)

DOR for CR vs PR (May 2023 data cut-off)



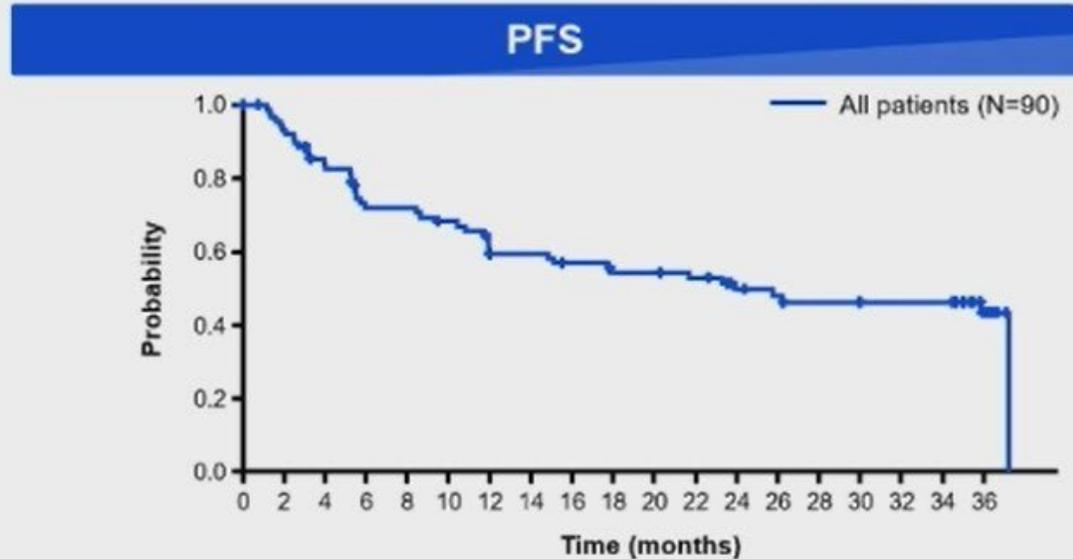
Patients at risk		Time (months)																
CR	54	53	52	48	45	44	43	42	41	38	37	34	26	25	24	23	23	15
PR	16	12	8	4	3	3	NE											

Median DOR in patients with CR, months (95% CI); n=54*	35.9 (NE–NE)
Median DOR in patients with PR, months (95% CI); n=16*	4.0 (2.5–6.7)

72.7% (95% CI: 60.8–86.8) of patients with a CR are estimated to remain alive and progression-free 30 months after their first response

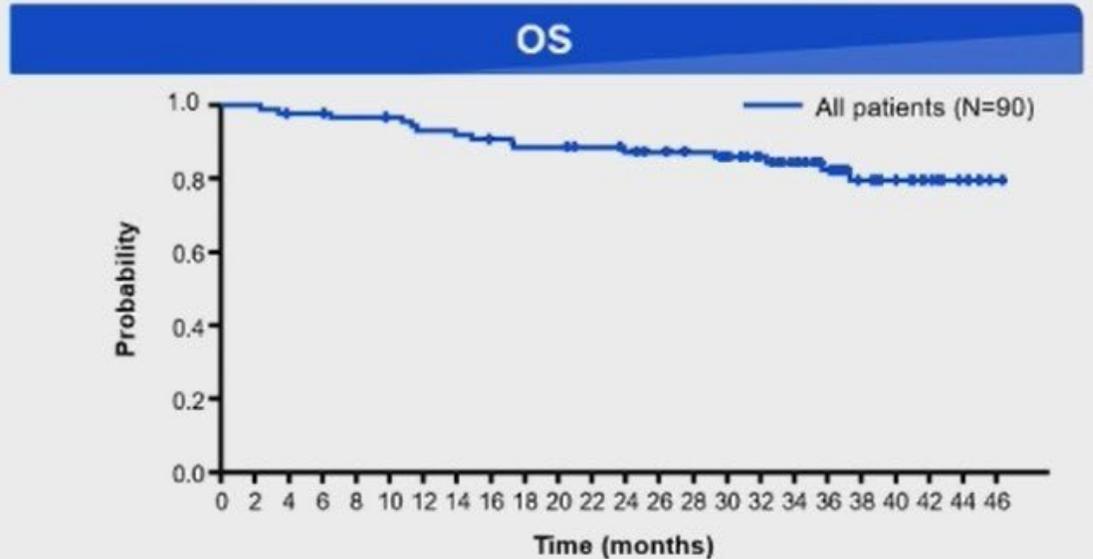
*Responders per INV assessment. †36-month DOR data are not available as this analysis was conducted from the first response assessment, therefore the landmark analysis is shorter for the duration outputs.

PFS und OS



Patients at risk 90 81 72 60 59 55 47 46 43 40 40 38 30 27 25 25 24 24 13

N=90	
Median PFS, months (95% CI)	24.0 (12.0–NE)
36-month PFS, months (95% CI)	43.2% (31.3–55.2)



Patients at risk 90 89 87 86 85 84 81 80 78 76 76 74 72 70 68 62 56 51 39 26 21 14 8 1

N=90	
Median OS, months (95% CI)	NR (NE–NE)
36-month OS, months (95% CI)	82.4% (73.8–91.0)

Robust and stable progression-free and overall survival rates at 3 years

OS, overall survival; PFS, progression-free survival.

Folgetherapien

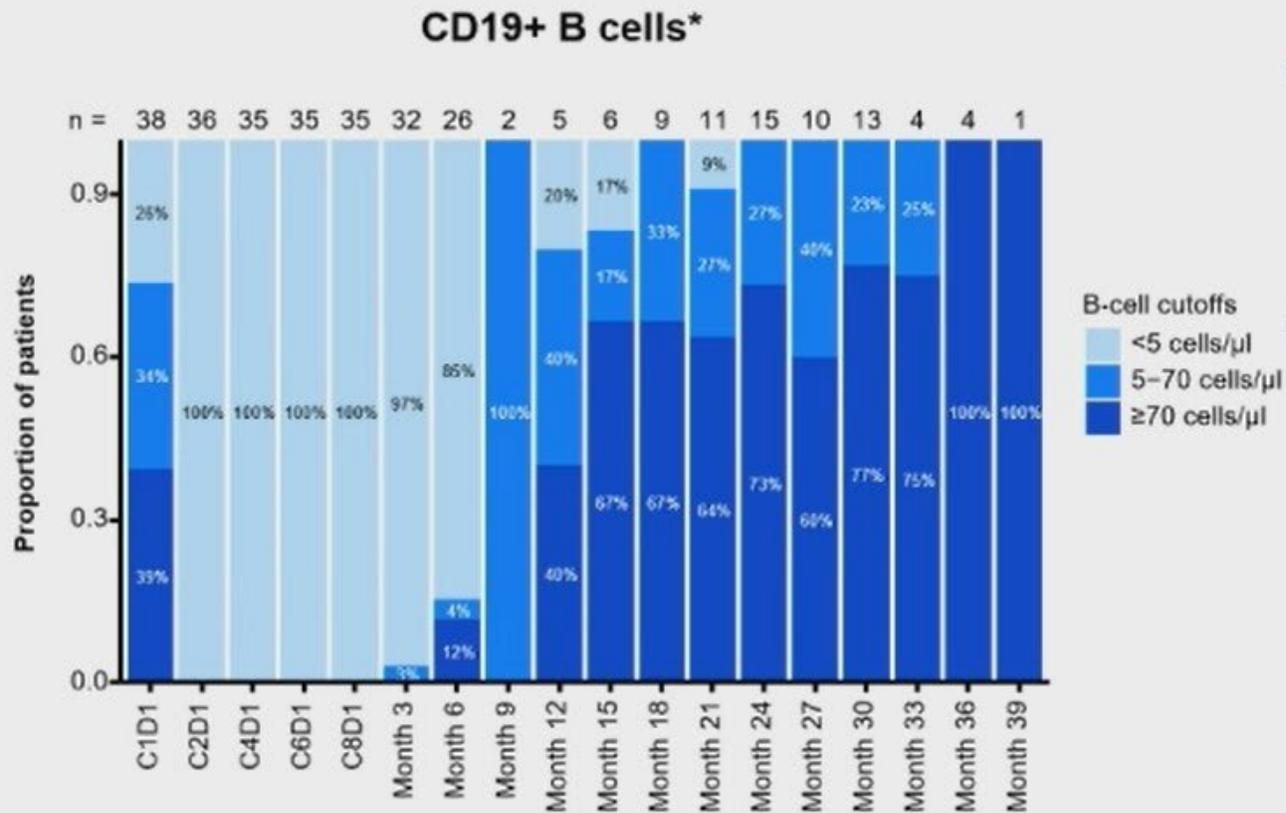
n, unless stated	N=90
Median TTNT, months (95% CI)	37.3 (18.0–NE)
Any new anti-lymphoma therapy	36 (40%)
New systemic treatments	35 (39%)
Chemo +/- immunotherapy	20 (22%)
PI3K inhibitors +/- immunotherapy	10 (11%)
CAR T-cell therapy	9 (10%)
BTK inhibitors +/- venetoclax	5 (6%)
Lenalidomide +/- immunotherapy	4 (4%)
Radiotherapy	9 (10%)
Excision of tumor	2 (2%)
Allogeneic stem cell transplant	2 (2%)
Autologous stem cell transplant	2 (2%)

5 patients received mosunetuzumab retreatment

Response to mosunetuzumab retreatment; n	n=5
CR	3 (60%)
PR	0
SD	2 (40%)
PD	0

BTK, Bruton tyrosine kinase; CAR, chimeric antigen receptor; chemo, chemotherapy; PD, progressive disease; PI3K, phosphoinositide 3-kinase; TTNT, time to next therapy or death.

B-Zell-Depletion und –Erholung



- Peripheral blood B-cell depletion following treatment with mosunetuzumab occurred rapidly by the initiation of C2 dosing in all patients (n=74)
- Time-to-event analysis in patients with end-of-treatment (C8) and follow-up samples (n=38) was performed to assess B-cell recovery
 - Median time to recovery to quantitative levels was 18.4 months (95% CI: 12.8–25.0)
 - Median time to recover to the lower level of normal was 25.1 months (95% CI: 19.0–NE)

*CD19+ B cells were monitored by flow cytometry at C1, C2, C4, and C8, and every 3 months during follow-up or until progression or next lymphoma treatment. The lower limit of quantitation was 5 cells/μl and the lower limit of normal was 70 cells/μl. Depletion was analyzed in all patients with a pre-dose and at least one on-treatment sample. Recovery was analyzed in patients with a CR and at least one follow-up sample.

Übersicht: CD20xCD3 bispezifische AK beim r/r FL

	Odronextamab	Mosunetuzumab	Epcoritamab
Quelle	Villasboas et al., ASH 2023	Schuster et al., ASH 2023	Linton et al., ASH 2023
medianes F/u	26,6 month	37,4 month	17,4 month
Anzahl pts med. Vortherapie	128 3 (2 - 13)	90 3 (2 - 10)	128 3 (2 - 9)
refr. to last treatment / POD24	73% / 50%	69% / 52%	69% / 42%
ORR / CRR	80% / 72%	78% / 60%	82% / 63%
mDOR / 2y-DOCR-rate	21,7 month 48%	36 month 63%	NR N/A
PFS / OS	mPFS 20,7 month (17-26) 3y-OS-r: 63%	mPFS: 24 month (12-NR) 3y-OS-r: 82,4% (74-91)	mPFS: 15,4 month NR
ICANS / AEs ≥ Grad 3 CRS / CRS ≥ Grad 3	1% / 78% (ICML 2023) 55% / 1%	4% / 70% 44% / 2%	6% / NA 67% / 2%
related Th.abbruch: AE	11,5% (ICML 2023)	4%	19%
Angaben zu Infektionen Angaben zu fatalen TEAEs	≥ Grad 3: 36%, Grad 5: 10% 2 pts	serious: 17%, Grad 3/4: 14%* 0	treatm-related: 40% COVID-19 13 pts (10%)

Kapitel 3

CAR-T-Zellen beim FL

Real-Word Experience of CAR T-Cells in Patients with Relapsed/Refractory Follicular Lymphoma : A Descart Registry Analysis from the Lysa

Abstract #296

Loic Ysebaert et al.

Patienten-Charakteristik

	Patient population N=70	
Sex Male	46	(65.7%)
Age (years)*		
Median (min ; max)	62 (34 ; 79)	
ECOG*		
0-1	57	(93.4%)
>=2	4	(6.6%)
Missing	9	
LDH > Normal*		
No	40	(63.5%)
Yes	23	(36.5%)
Missing	7	
Bulky disease (>5cm)		
No	53	(77.9%)
Yes	15	(22.1%)
Missing	2	
Nb or prior lines of therapy		
Median (min ; max)	3 (2;9)	
Prior treatment	70	(100.0%)
Bendamustine	31	(44.3%)
Lenalidomide	33	(47.1%)
Bispecific anti-CD3 anti-CD20	9	(12.9%)
Prior autologous transplant	31	(44.3%)

Bridging therapy	41	(58.6%)
Lenalidomide	15	(21.4%)
(Immuno)-chemotherapy	22	(31.4%)
Other	4	(5.7%)
Disease status before CAR-T infusion		
Complete Response	5	(12.2%)
Partial Response	13	(31.7%)
Stable Disease	6	(14.6%)
Progressive Disease	16	(39.0%)
Missing	1	(2.4%)
POD24		
Yes	44	(62.9%)
Time from leukapheresis to infusion, Median (IQR) in days	41	37-55

*assessed at CAR T infusion

Tisa-Cel: n=62

Axi-Cel: n=8

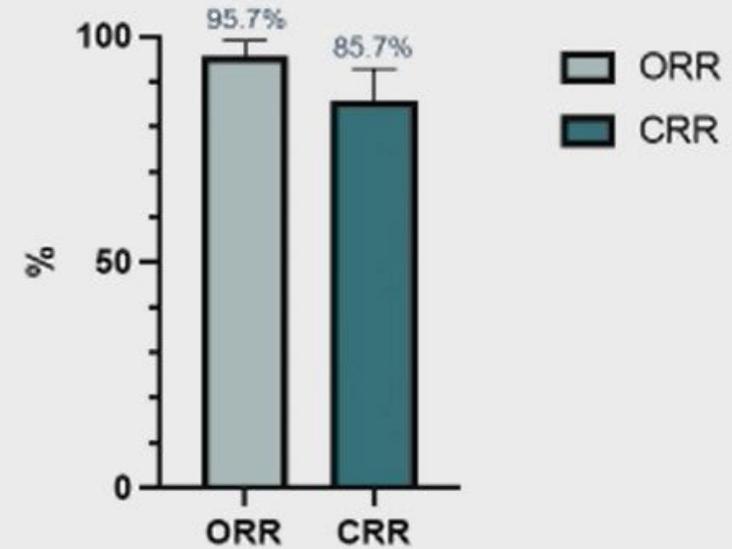
Bachy et al. ASH 2023, Abstract #296

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Ansprechen

	Patient population	
	N=70	
Best ORR*		
Best ORR (CR/PR)	67	(95.7%)
95% CI	[88.0% ; 99.1%]	
Best CRR*		
Best CRR	60	(85.7%)
95% CI	[75.3% ; 92.9%]	

*defined as the best response according to the Lugano 2024 classification at 1, 3 or 6 months
Abbreviations: ORR, overall response rate; CRR, complete response rate; CR, complete response; PR, partial response.

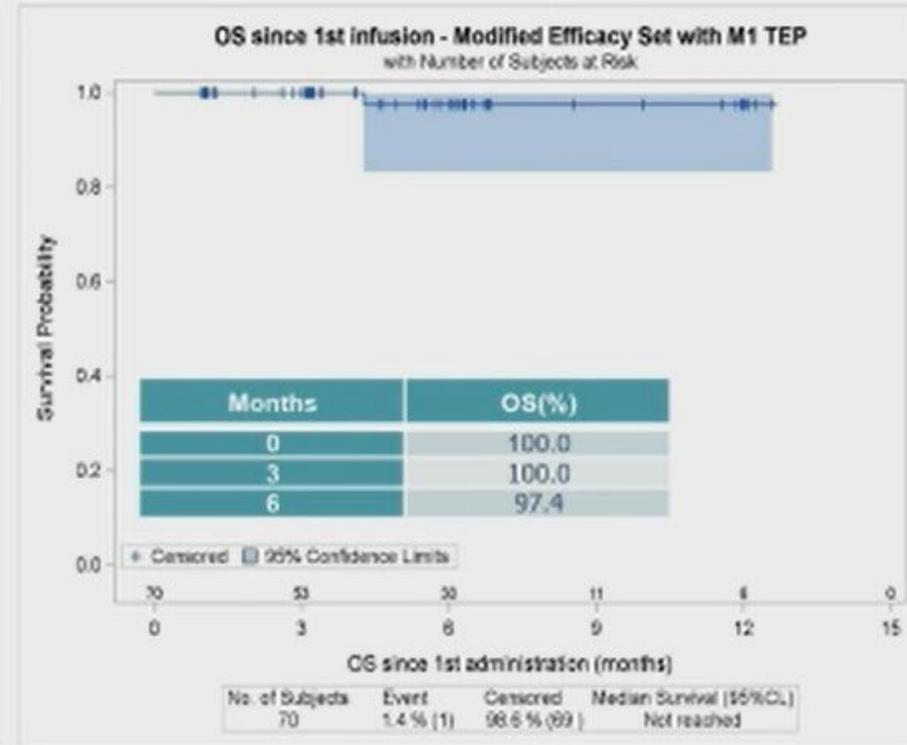
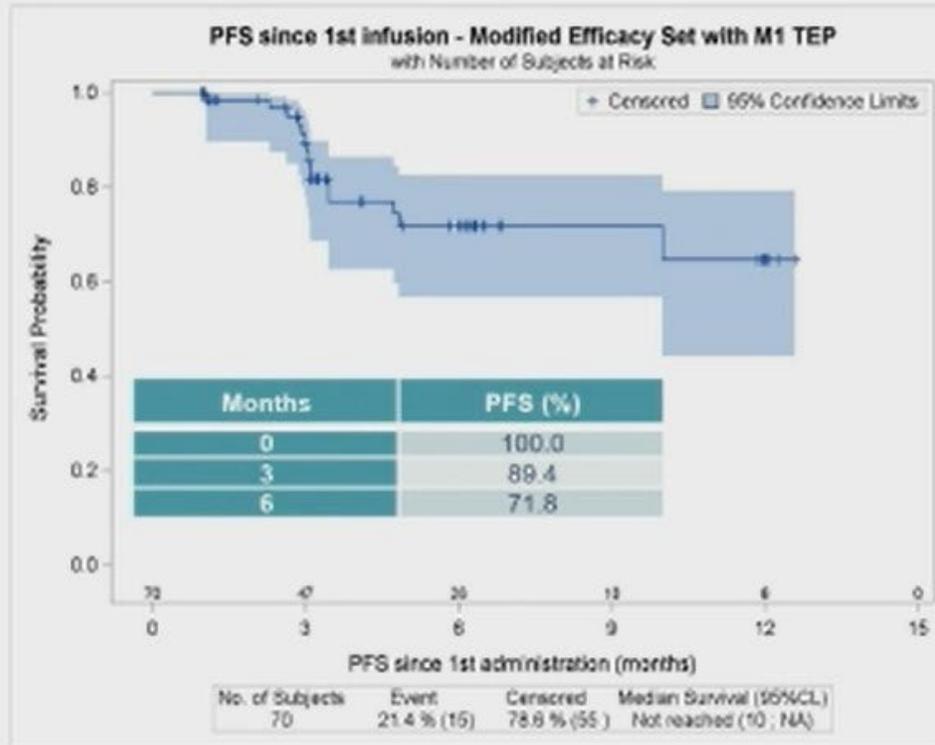


Bachy et al. ASH 2023, Abstract #296

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PFS und OS

	Median	Min	Max
FU (mos.)	5.4	1.0	12.6



Bachy et al. ASH 2023, Abstract #296

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	Patient population	
	N=70	
Cytokine release syndrome		
Any	52	(74.3%)
Grade 1-2	51	(72.9%)
Grade 3-4	1	(1.4%)
Neurotoxicity		
Any	19	(27.1%)
Grade 1-2	16	(22.9%)
Grade 3-4	3	(4.3%)
Macrophage Activation Syndrome (MAS) (any grade)	0	(0.0%)
Persistent grade ≥ 3 cytopenia (>1 month)		
Anemia	6	(8.6%)
Thrombocytopenia	13	(18.6%)
Neutropenia	35	(50.0%)

Bachy et al. ASH 2023, Abstract #296

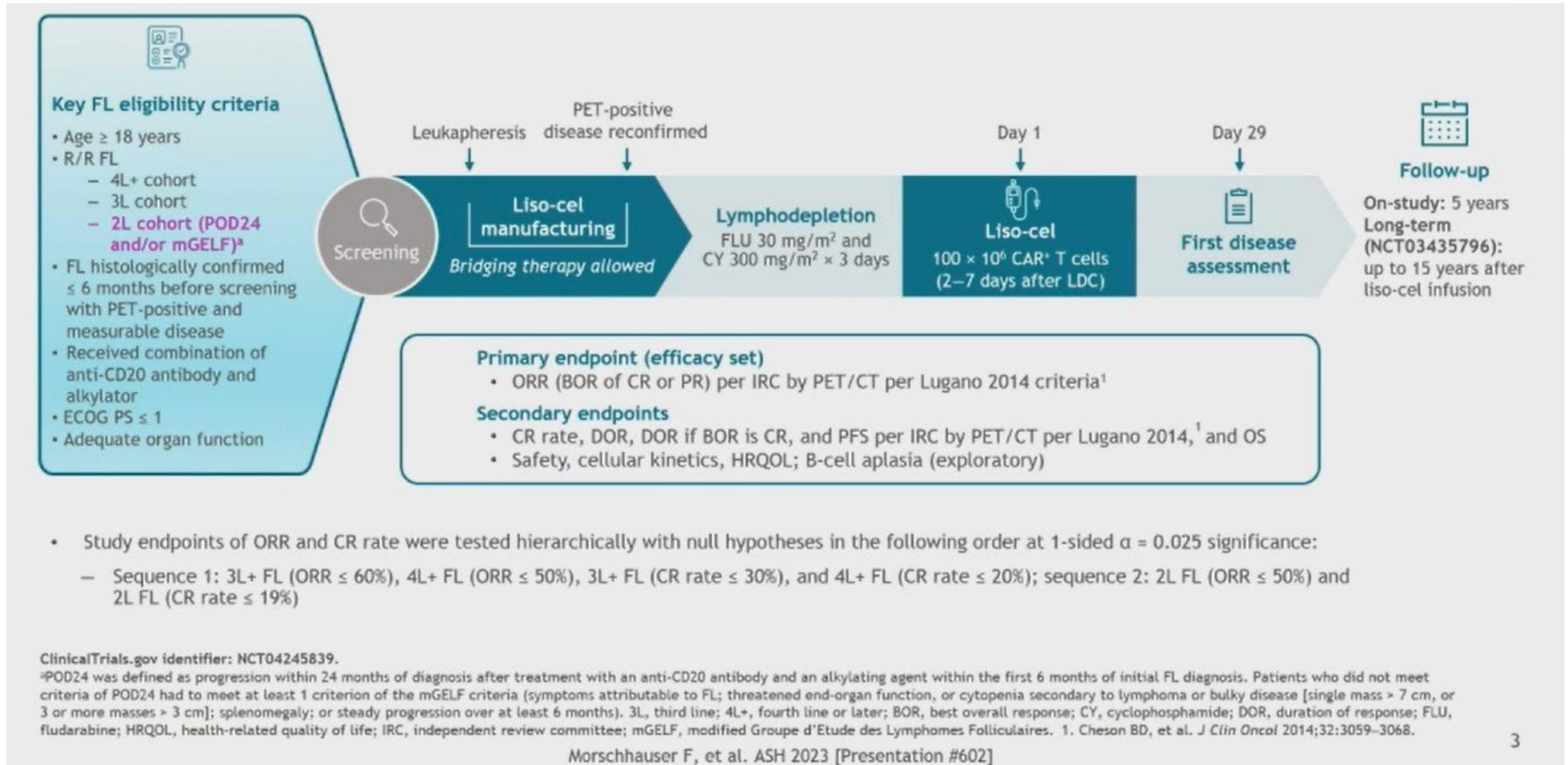
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Phase 2 Study Primary Analysis of Lisocabtagene Maraleucel as Second-Line Therapy in Patients with High-Risk Relapsed or Refractory Follicular Lymphoma

Abstract #602

Franck Morschhauser et al.

TRANSCEND FL-Studie: Design



TRANSCEND FL-Studie: Patienten-Charakteristik

	2L FL (n = 23)	3L+ FL (n = 107)
Median (range) age, y	53 (34–69)	62 (23–80)
Male, n (%)	17 (74)	66 (62)
FL grade 1 or 2 / 3a at screening, ^a n (%)	17 (74) / 6 (26)	81 (76) / 25 (23)
Ann Arbor stage at screening, n (%)		
Stage I/II	6 (26)	12 (11)
Stage III/IV	17 (74)	95 (89)
FL International Prognostic Index at screening, n (%)		
Low risk (0–1) / intermediate risk (2)	11 (48) / 4 (17)	12 (11) / 34 (32)
High risk (3–5)	8 (35)	61 (57)
LDH > ULN before lymphodepletion, n (%)	6 (26)	47 (44)
Met mGELF criteria at most recent relapse, n (%)	16 (70)	57 (53)
Symptoms attributable to FL	6 (26)	13 (12)
Threatened end-organ function/cytopenia secondary to lymphoma/bulky disease	7 (30)	24 (22)
Splenomegaly	0	4 (4)
Steady progression over at least 6 months	3 (13)	16 (15)
Median (range) prior lines of systemic therapy	1 (1–1)	3 (2–10)
Prior HSCT, n (%)	0	33 (31)
Received prior rituximab and lenalidomide, n (%)	0	23 (21)
Refractory to last systemic therapy, ^b n (%)	15 (65)	72 (67)
Double refractory (anti-CD20 and alkylator), ^c n (%)	11 (48)	69 (64)
POD24 from initial immunochemotherapy, n (%)	15 (65)	58 (54)
POD24 from diagnosis, n (%)	12 (52)	46 (43)
Received bridging therapy, n (%)	5 (22)	44 (41)

^aOne patient with 3L+ FL had unknown grade of FL at screening; ^bDefined as progression or stable disease while on last line of therapy or within 6 months of completing the last line of therapy; ^cPatients whose disease was refractory to both an anti-CD20 antibody and an alkylating agent or refractory to anti-CD20 maintenance therapy.

Morschhauser F, et al. ASH 2023 [Presentation #602]

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TRANSCEND FL-Studie: Therapieansprechen

2L FL efficacy set (n = 23)



Primary and key secondary endpoints were met

All null hypotheses were rejected

ORR was 96%, with all responders achieving CR

In patients with 3L+ FL¹

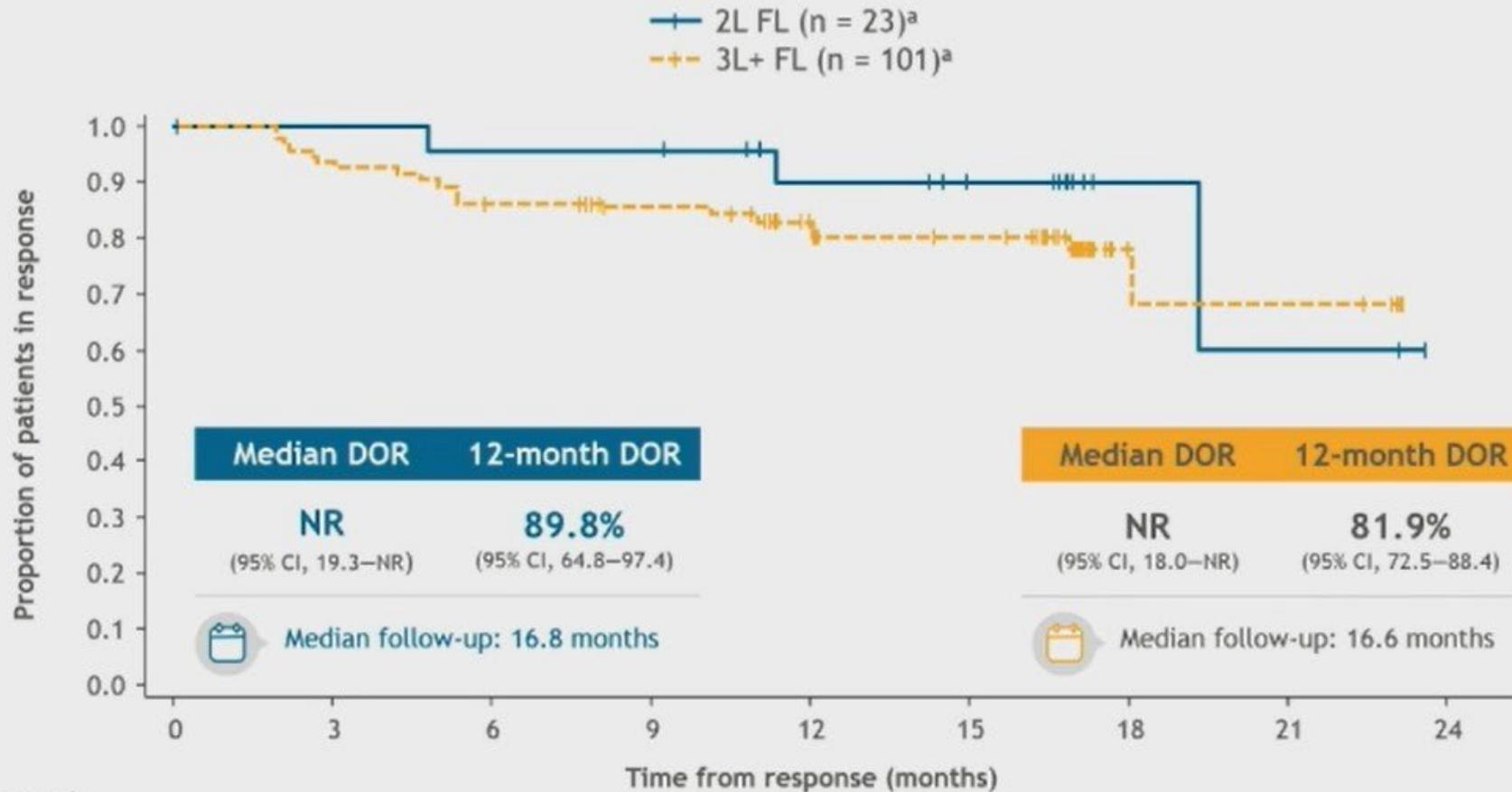
- ORR = 97%
- CR rate = 94%

^aOne-sided P value (H_0 of ORR \leq 50%; H_0 of CR rate \leq 19%).

H_0 , null hypothesis; SD, stable disease.

1. Morschhauser F, et al. *Hematol Oncol* 2023;41(suppl 2):877–880.

TRANSCEND FL-Studie: Dauer des Ansprechens



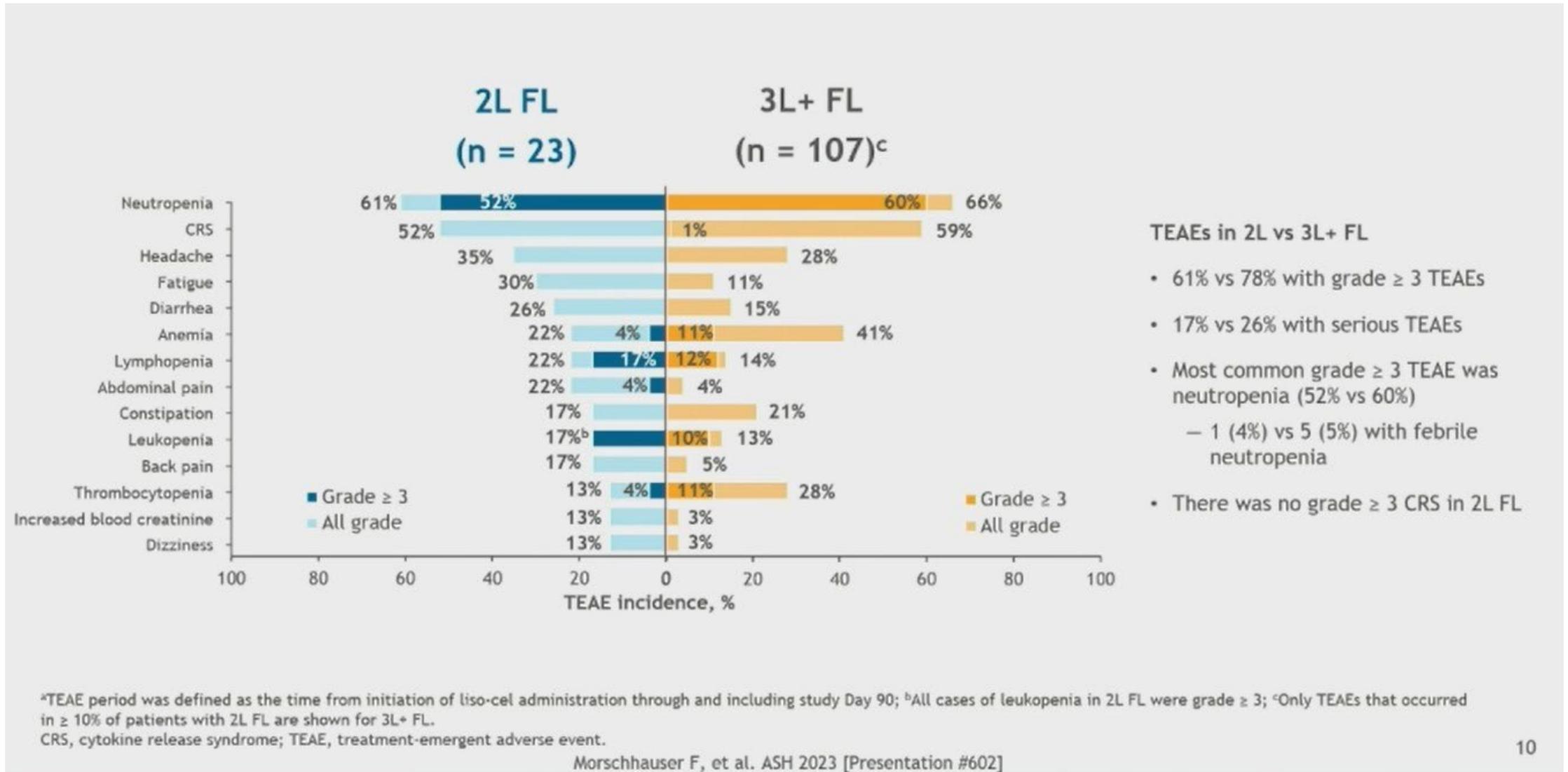
No. at risk (censored)

	0	3	6	9	12	15	18	21	24
2L FL	22 (0)	22 (0)	21 (0)	21 (0)	16 (4)	13 (3)	3 (10)	2 (0)	0 (2)
3L+ FL	98 (0)	91 (1)	83 (1)	77 (5)	62 (12)	49 (12)	8 (40)	7 (0)	0 (7)

^aTwenty-two of the 23 patients with 2L FL were responders; 98 of the 101 patients with 3L+ FL were responders.
 NR, not reached.

Morschhauser F, et al. ASH 2023 [Presentation #602]

TRANSCEND FL-Studie: Nebenwirkungen



Zusammenfassung | Take-Home-Messages

- Die Kombination aus PET/CT-Ergebnissen und Bestimmung der ctDNA kann wichtige Informationen zur Prognose der Patienten liefern, insbesondere hinsichtlich POD24.
- Die 3-Jahres-Daten zu Mosunetuzumab bestätigen die initialen Studienergebnisse.
- Im Vergleich verschiedener bispezifischer Antikörper deuten sich Unterschiede z.B. im PFS oder der Abbruchrate an.
- Erste „real-world-Daten“ zu Tisa-Cel und Axi-Cel bestätigen die Ergebnisse der Zulassungsstudien.
- In einer Phase-II-Studie zeigt Liso-Cel eine gute Effektivität bei Risiko-Patienten in der Zweitlinie.

Die Kurzpräsentationen sind online unter

www.lymphome.de/ash2023

Für den Inhalt verantwortlich:

Prof. Dr. med. Kai Hübel

Uniklinik Köln

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