UNIKLINIK KÖLN

Follikuläre Lymphome

Sommersymposium 2021

Prof. Dr. Kai Hübel

Köln, 26. Juni 2021

Offenlegung möglicher Interessenskonflikte

Beratungs- bzw. Gutachtertätigkeit

Roche, Celgene/BMS, Servier, Sanofi, EUSA

Honorare

Roche, Celgene/BMS, Servier, Hexal, Sanofi, EUSA

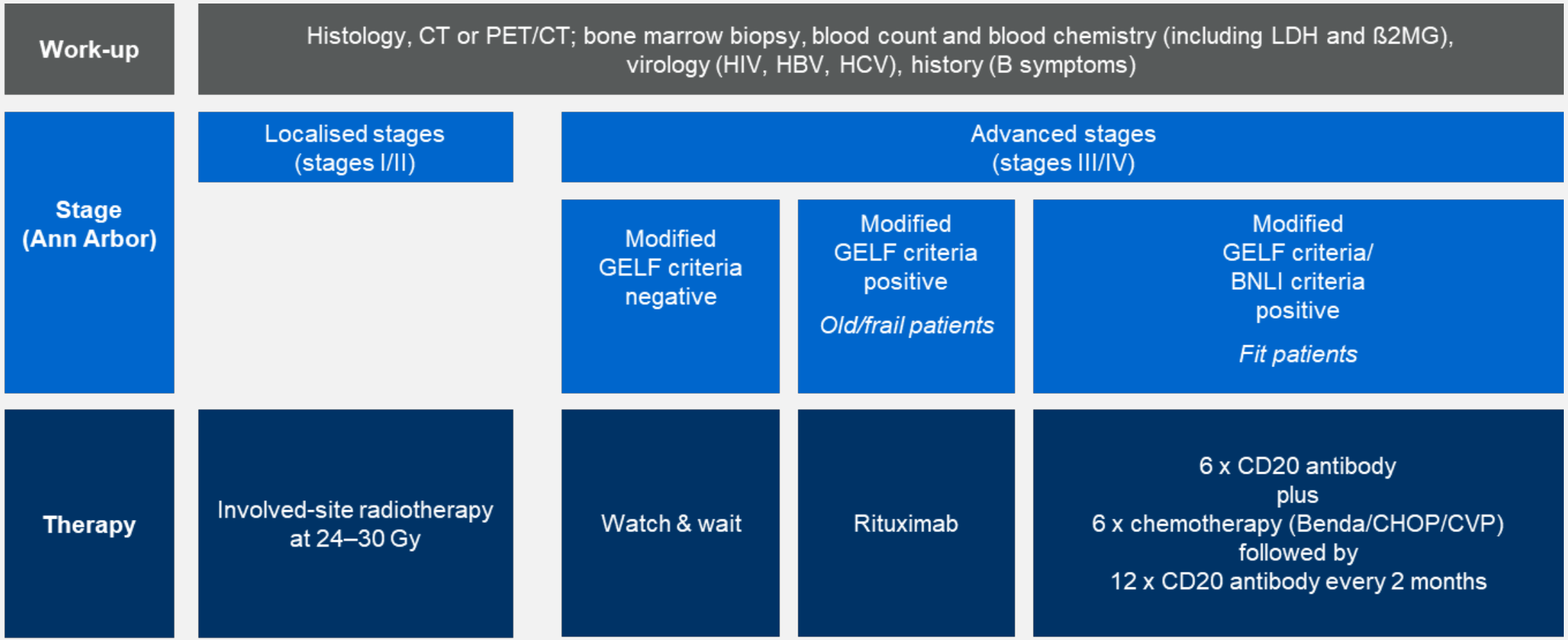
Finanzierung wissenschaftlicher Untersuchungen

Roche, Celgene, Servier, Hexal, Janssen

Andere finanzielle Beziehungen

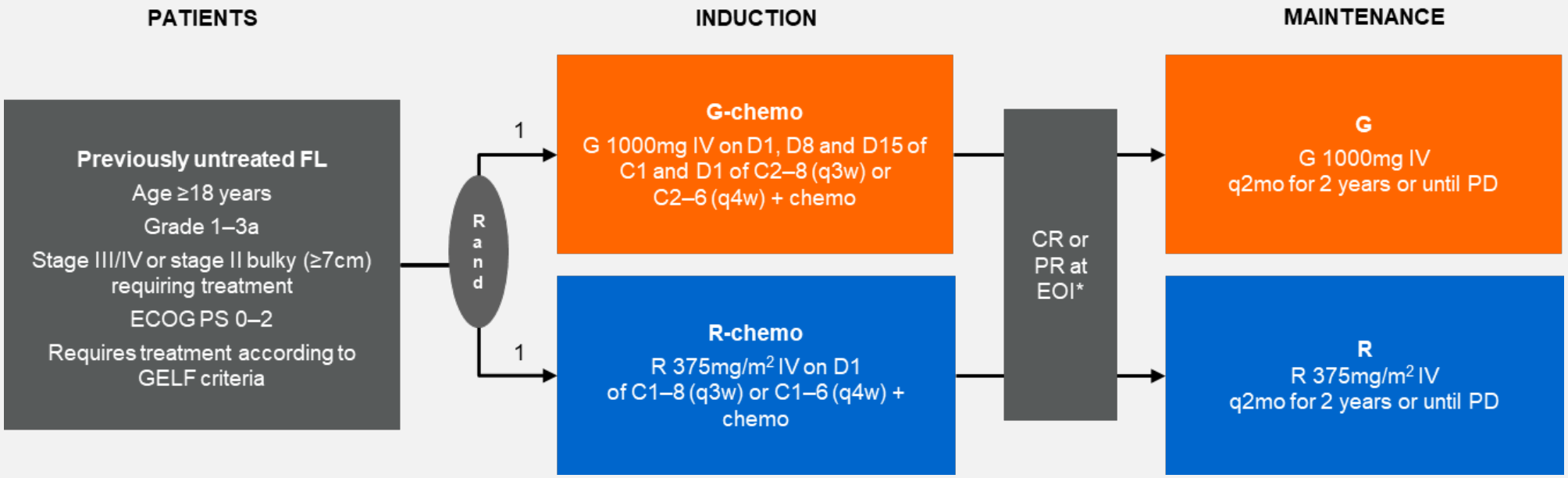
Reisekosten: Roche, Celgene, Servier, Hexal

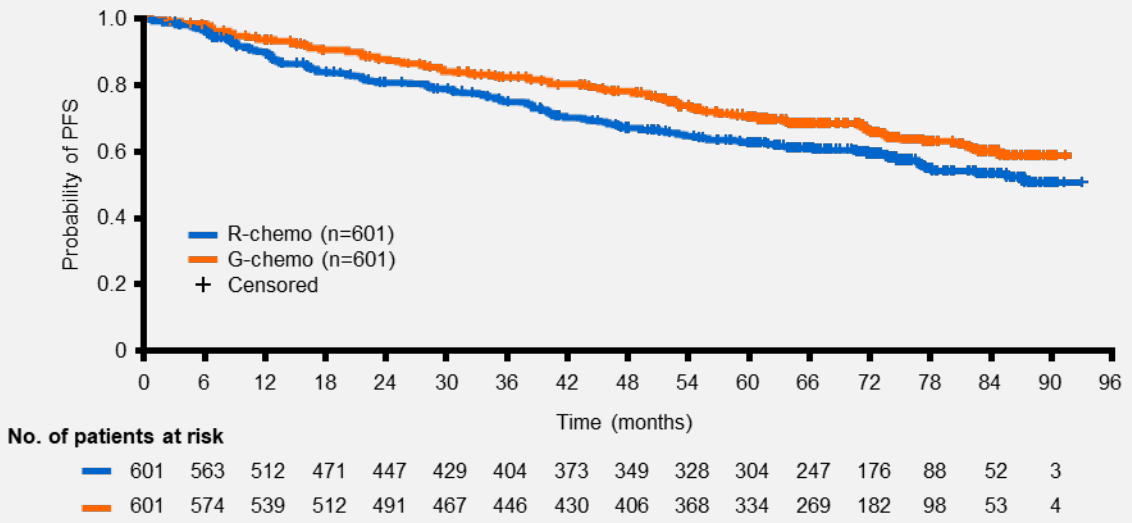
Erstlinientherapie des Follikulären Lymphoms



GELF, Groupe d'Etude des Lymphomes Folliculaires

GALLIUM-Studie





	G-chemo (n=601)	R-chemo (n=601)
Median PFS, months	NR	NR
5-year PFS, % (95% CI)	70.5 (66.4–74.1)	63.2 (59.0–67.1)
HR (95% CI), p-value	0.76 (0.62–0.92), p=0.0043	

Median follow-up: 76.5 months

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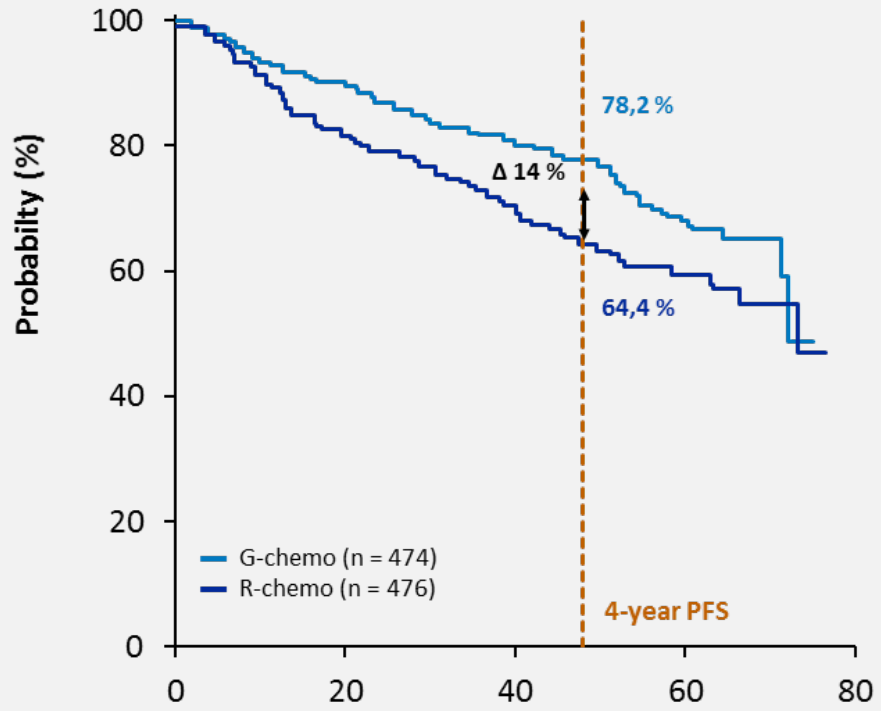
Townsend et al. EHA 2020

GALLIUM-Studie: PFS bei FLIPI ≥ 2



FLIPI ≥2	R-chemo, n=476*	G-chemo, n=474*
4-yr PFS, % (95% CI)	64.4 (59.9, 68.3)	78.2 (74.3, 82.1)
HR (95% CI)	**0.65** (0.52, 0.82)	

Median follow-up: 57.3 months

No. of patients at risk:

G-chemo	474	399	337	96	0
R-chemo	476	362	292	97	0

*Efficacy-evaluable population;
FLIPI, Follicular Lymphoma International Prognostic Index.

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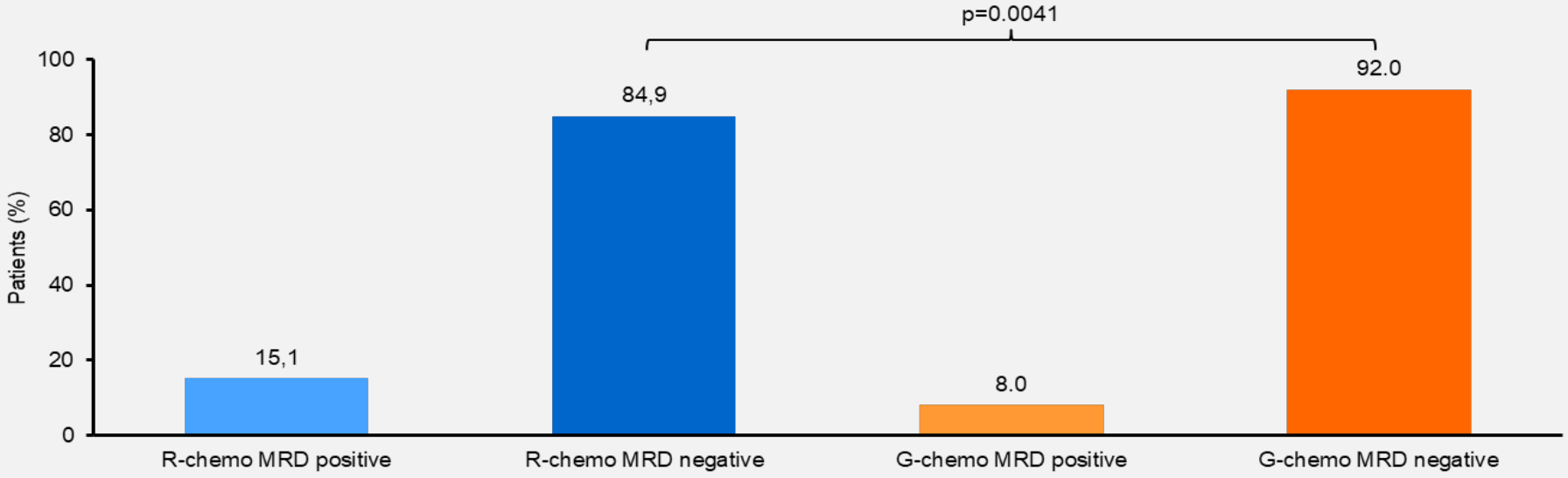
Launonen A et al. ICML 2019.

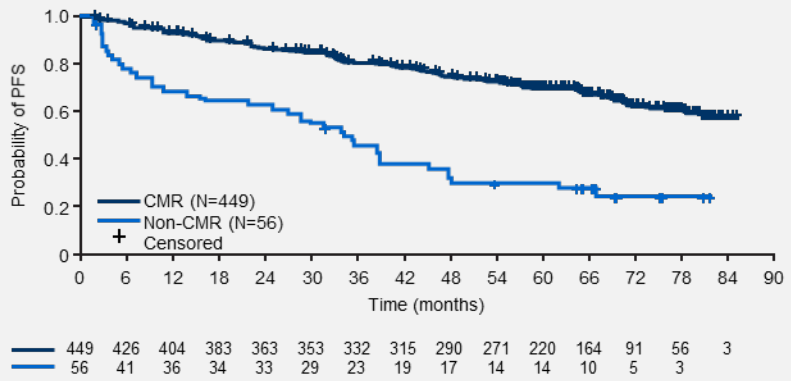
GALLIUM-Studie: MRD- und PET-Analysen

MRD response status in blood and bone marrow at EOI by treatment arm



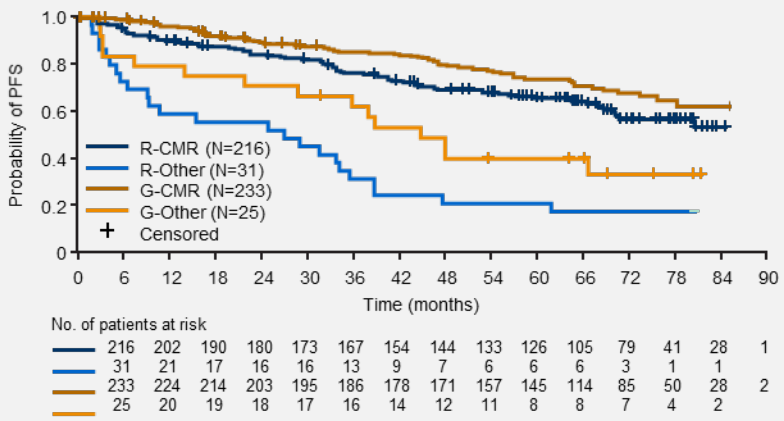
Pott et al. ASH 2016

INV-assessed PFS by EOI PET CMR status



CMR, complete metabolic response

INV-assessed PFS by EOI PET CMR status and treatment arm



Trotman et al. EHA 2020

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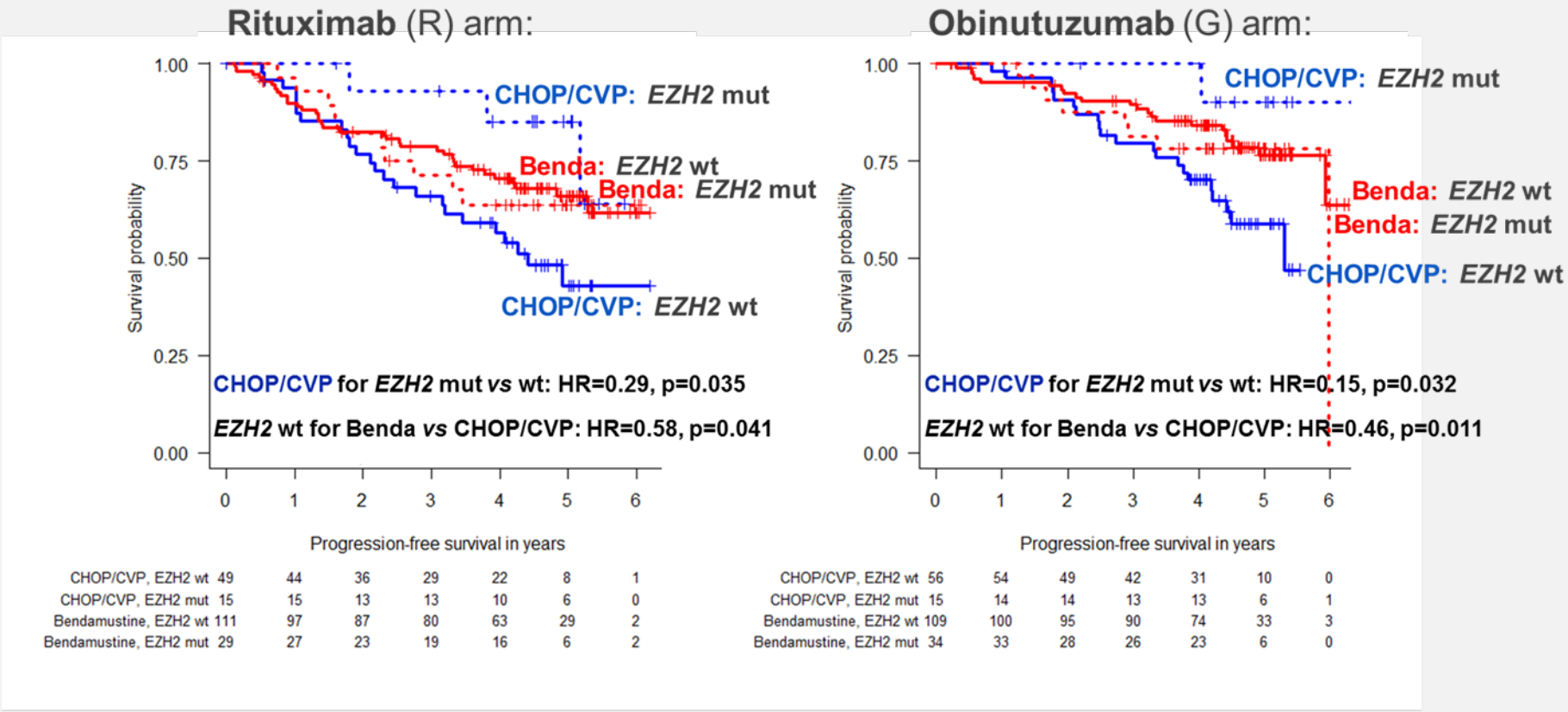
GALLIUM-Studie: EZH2-Mutation und Chemotherapie



Patienten mit *EZH2* Wildtyp profitieren von Bendamustin,
Patienten mit *EZH2* Mutation profitieren von CHOP/CVP.

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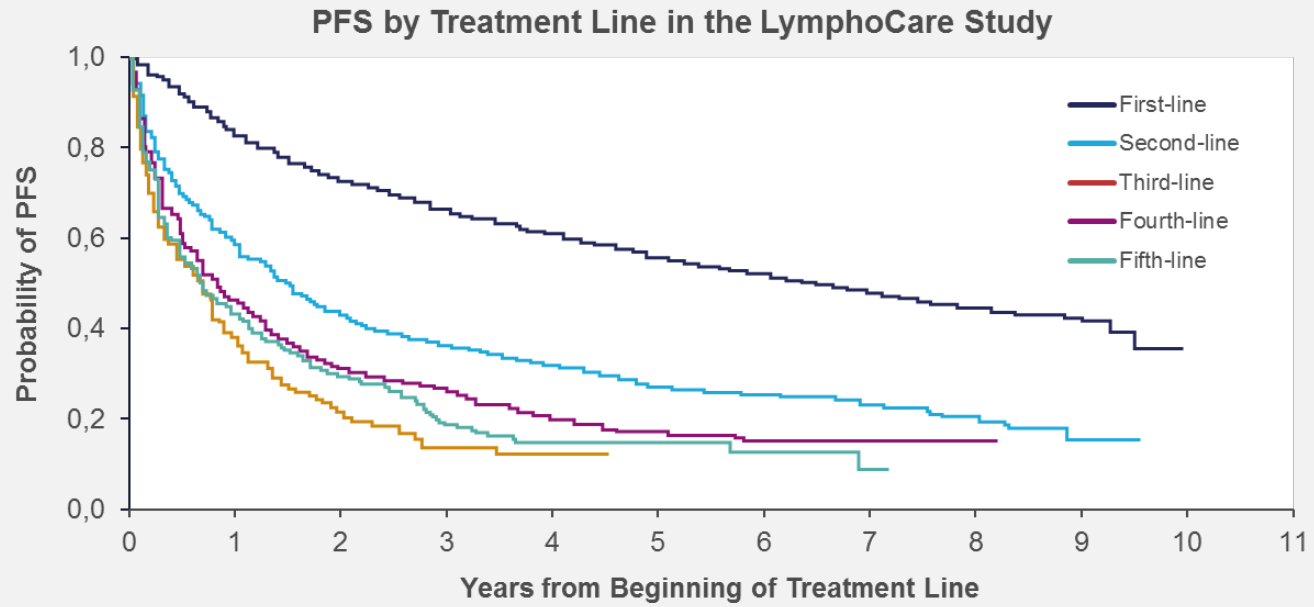
Jurinovic V et al., ASH 2019:122

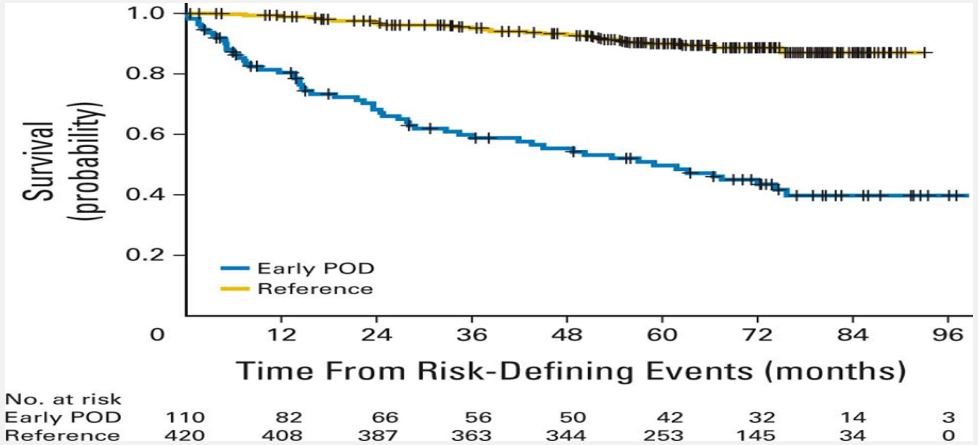
Rezidivtherapie des Follikulären Lymphoms



Treatment Line	Median PFS, months
First line (n=2429)	79.4
Second line (n=889)	18.0
Third line (n=438)	10.0
Fourth line (n=229)	8.3
Fifth line (n=123)	8.2

The relatively long survival for patients with FL is driven primarily by the duration of outcomes in 1L.

Based on data from a prospective US study of patients diagnosed with FL between March 2004 and March 2007 (n=2652)



POD24

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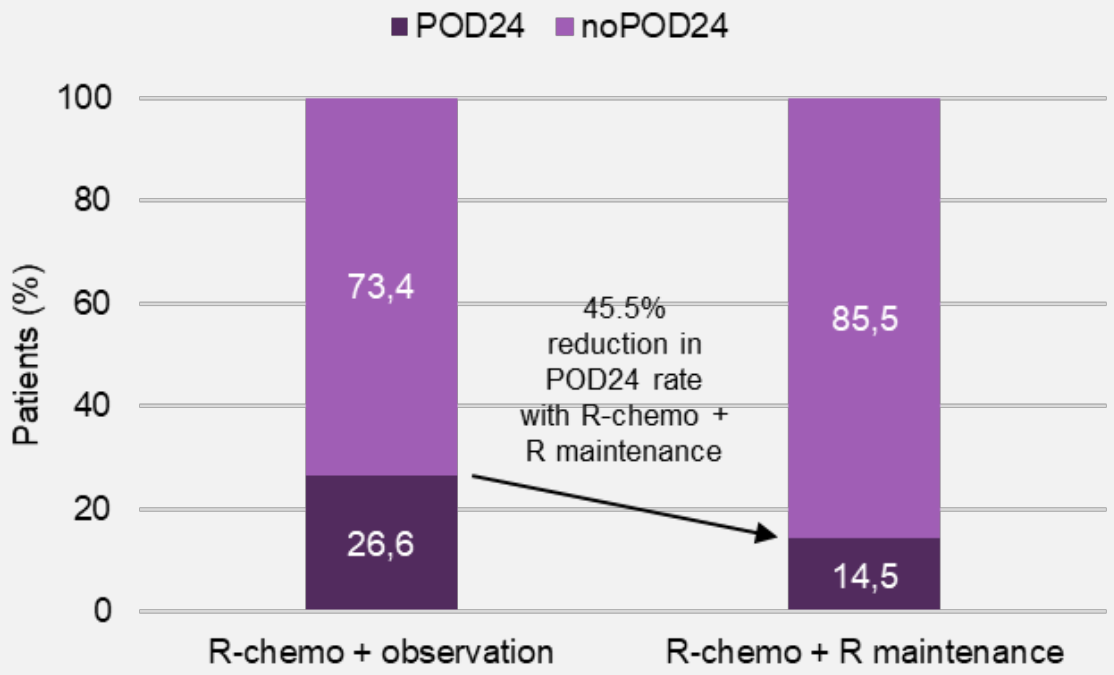
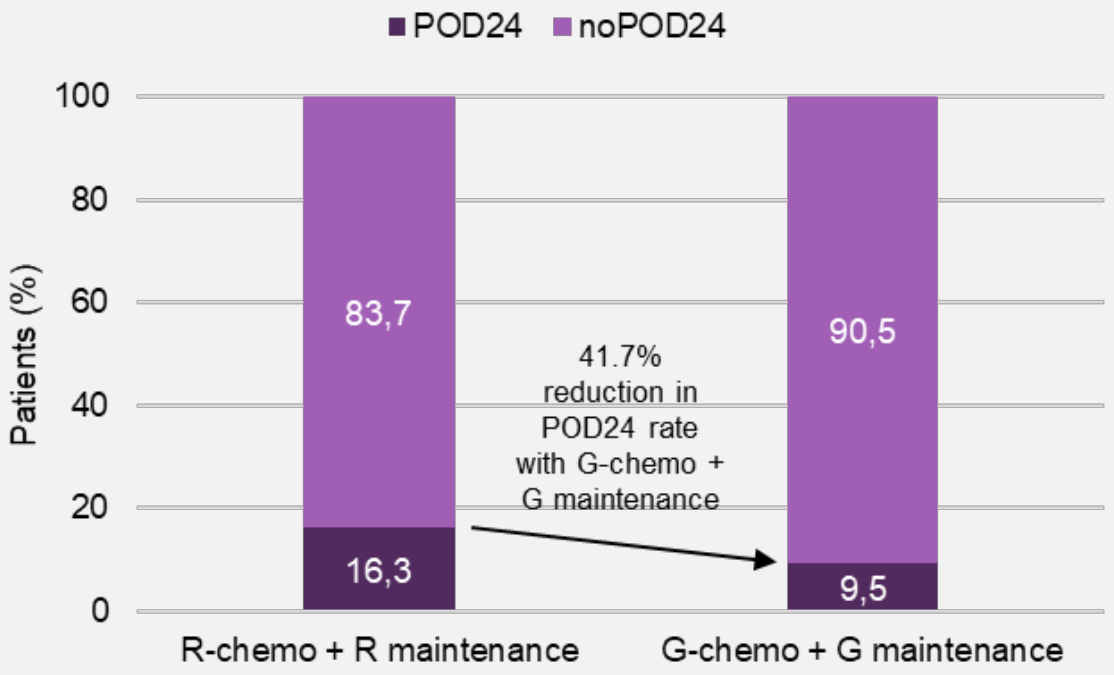
Link BK et al., Br J Hematol 2019, 184: 634ff; Rivas-Delgado A et al., Br J Hematol 2019, 184: 754ff, Casulo C et al., J Clin Oncol 2015;33:2516-2522

Einfluss der gewählten Behandlung auf POD24

Impact of treatment on rate of POD24 in PRIMA[1]

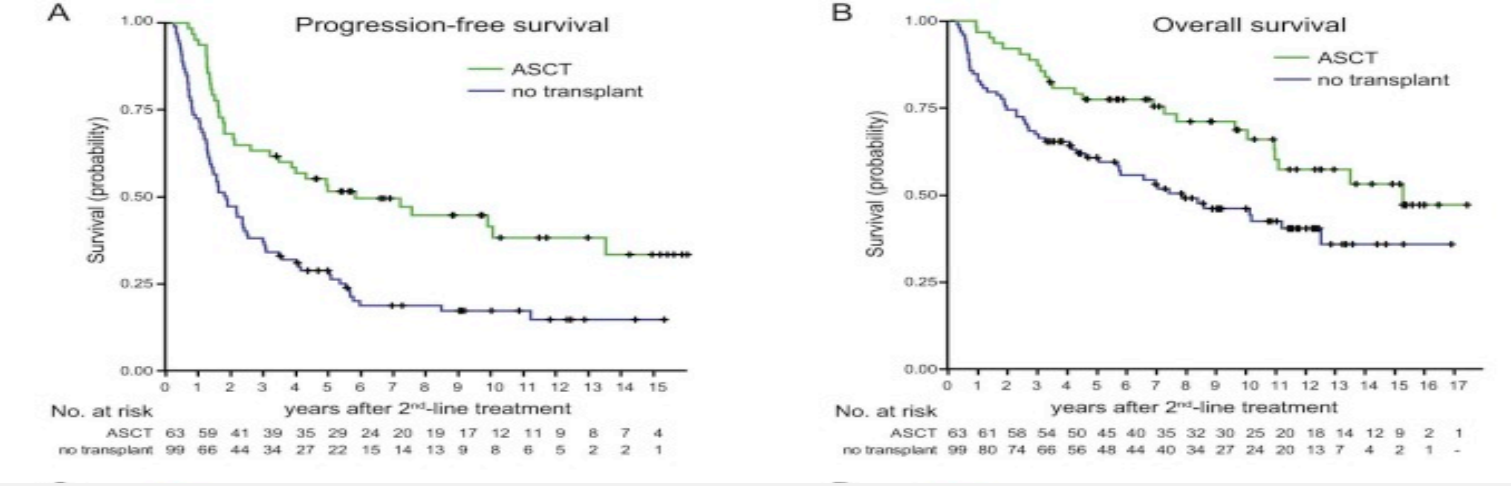


Impact of treatment on rate of POD24 in GALLIUM[2]

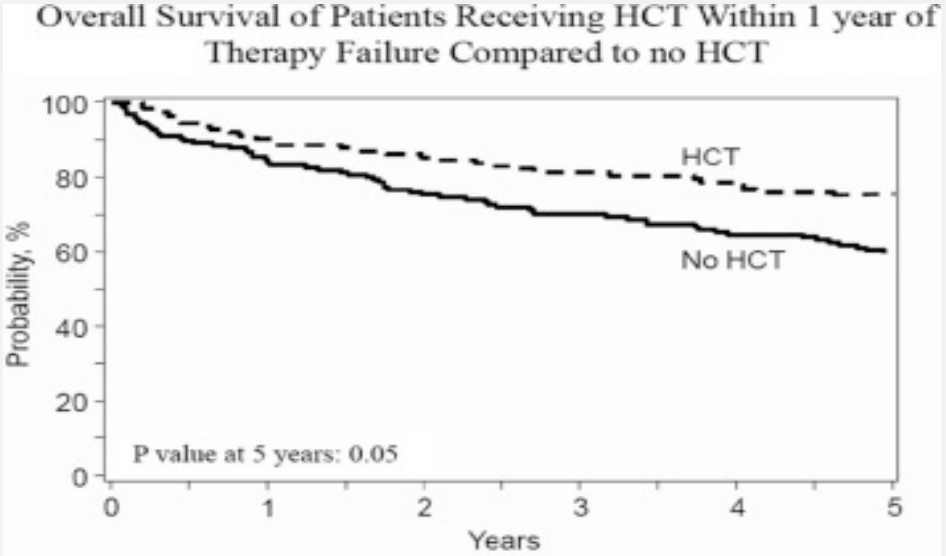


1. Bachy et al. Blood Adv 2021;5:1729–32
2. Seymour et al. Haematologica 2019;104:1202–8

Therapieoptionen beim Frührezidiv: Autologe Transplantation



Jurinovic V, BBMT 2018

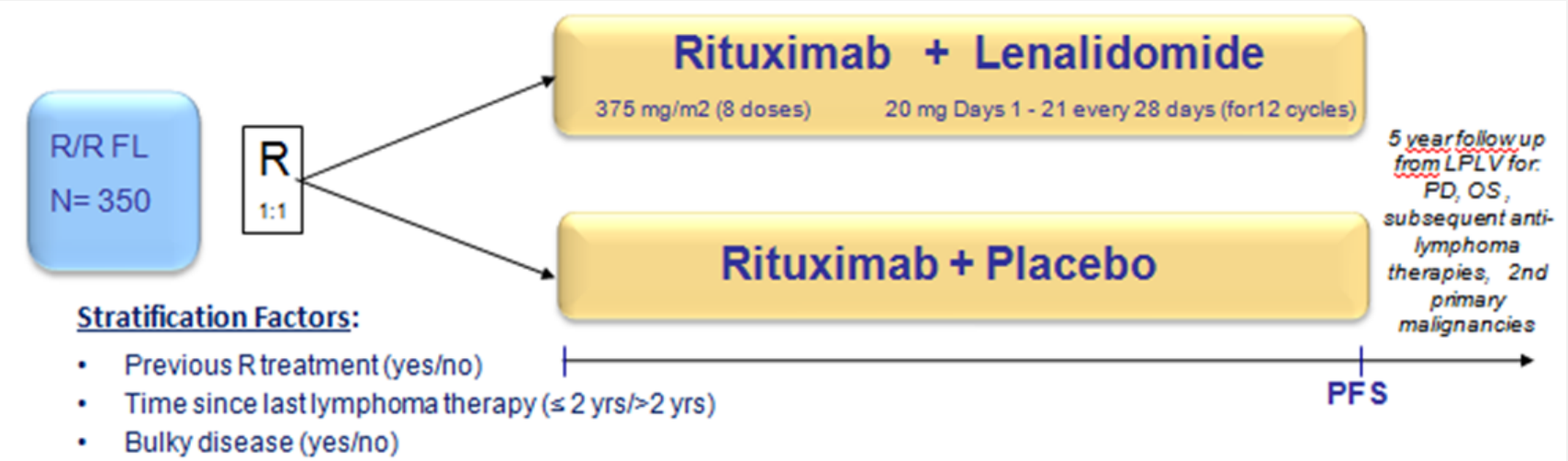


Casulo C, BBMT 2018

Die autologe Transplantation ist bei allen Patienten mit Rezidiv innerhalb von 24 Monaten nach der Erstlinie zu prüfen!

AUGMENT: R^2 vs R beim rezidvierten/refraktären FL

Phase III, doppel-blind, randomisiert



Primäres Zielkriterium: PFS

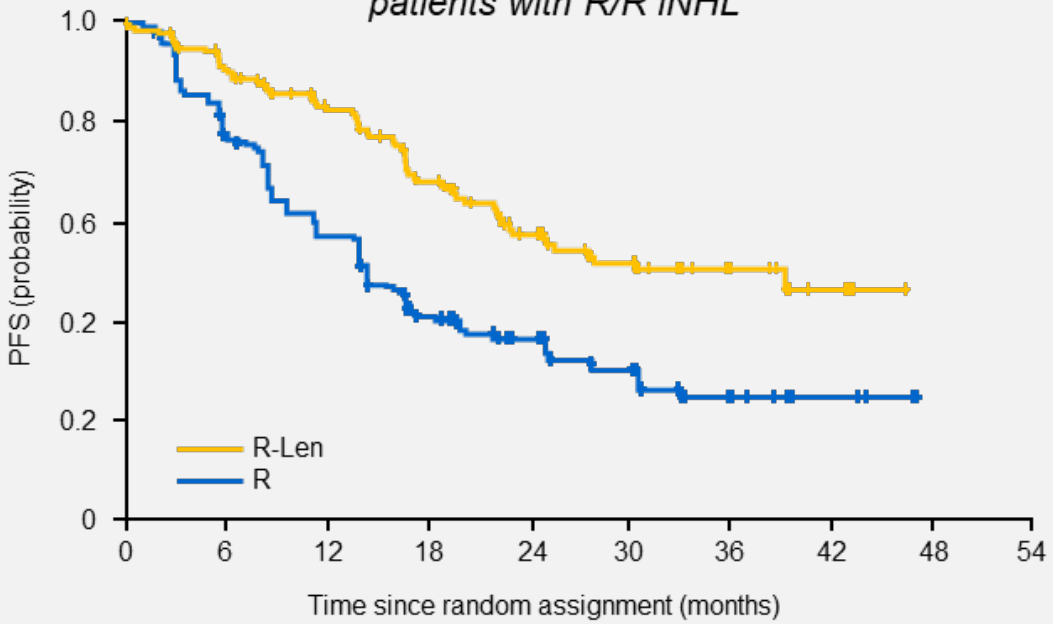
Medianes follow-up: 28,3 Mo

Leonard JP et al., J Clin Oncol 2019

AUGMENT: Effektivität

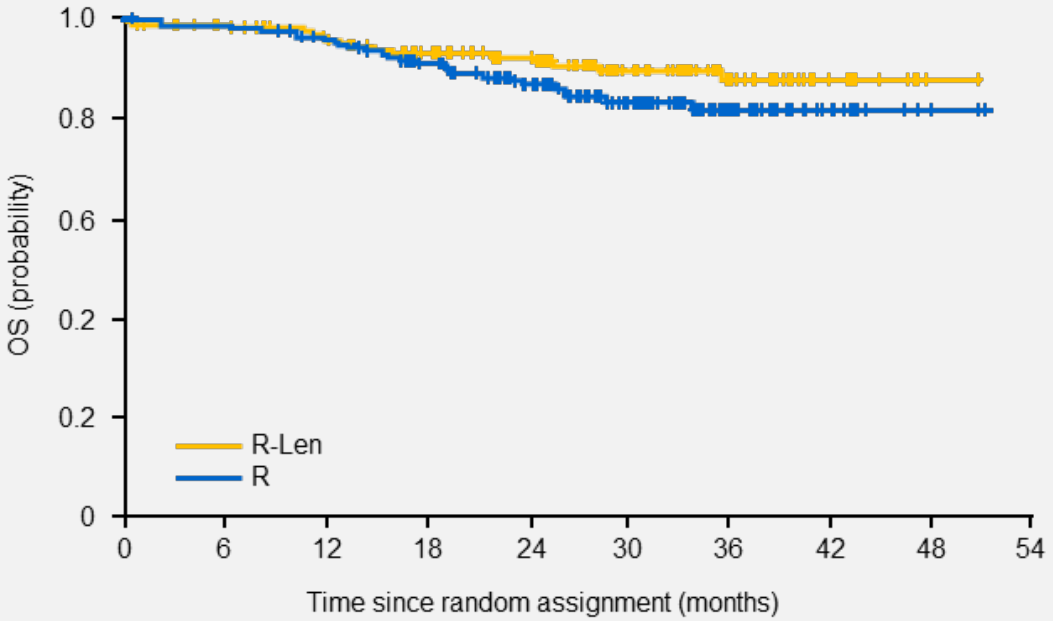
Randomised Phase III trial of R-Len vs R in 358 patients with R/R FL or MZL (NCT01938001)

KM estimates of IRC-assessed PFS (primary endpoint) among patients with R/R iNHL



	R-Len (n=178)	R (n=180)
Median PFS, months	39.4 (22.9–NR)	14.1 (11.4–16.7)
HR (95% CI), p-value	0.46 (0.34–0.62), p<0.0001	

KM estimates of OS among patients with R/R iNHL



	R-Len (n=178)	R (n=180)
Median OS, months	NR (NR–NR)	NR (NR–NR)
HR (95% CI)	0.61 (0.33–1.13)	

Leonard et al. J Clin Oncol 2019;37:1188–99

MAGNIFY

Randomised Phase III trial of R-Len maintenance vs R maintenance after R-Len induction in 393 patients with R/R FL, MZL or MCL (NCT01996865)

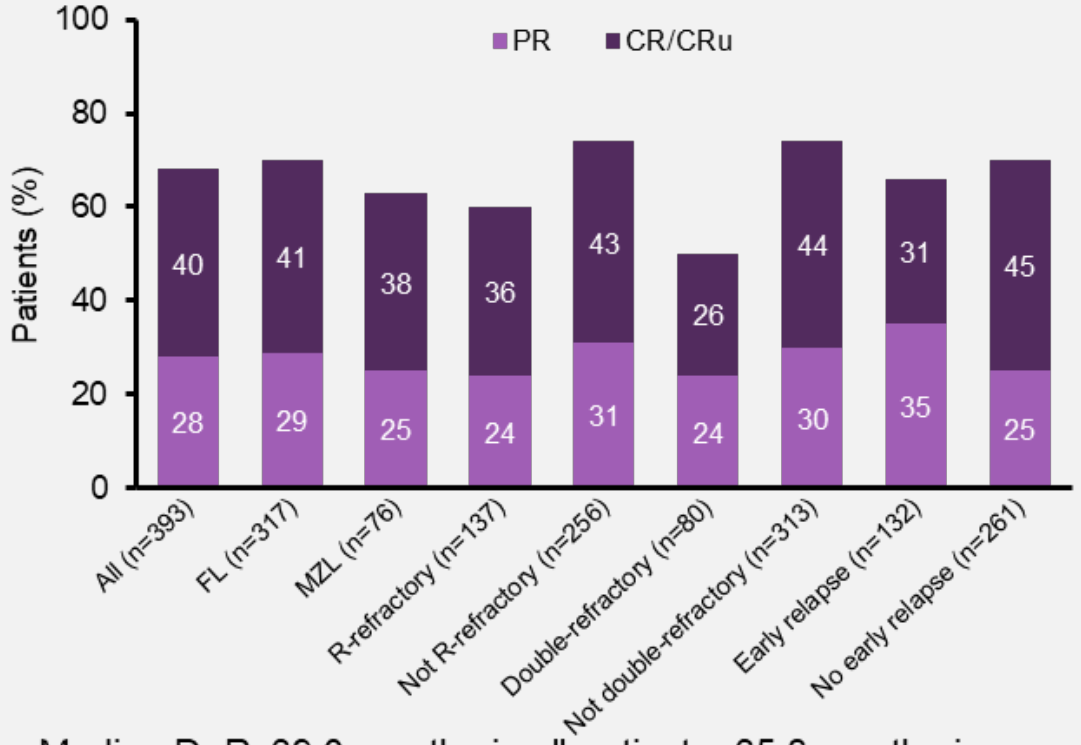
Common (≥5%) Gr 3–4 AEs during R-Len induction (n=391)

%	Gr 3–4
Any	68
Neutropenia	36
Leukopenia	7
Thrombocytopenia	6
Fatigue	5

- 372 patients (95%) had received prior R-containing regimens
- 137 patients (35%) were considered R-refractory
- 139 patients (35%) discontinued R-Len early (AEs: n=52, 13%; PD: n=45, 11%)

Median follow-up: 23.7 months (range: 0.6–57.8)

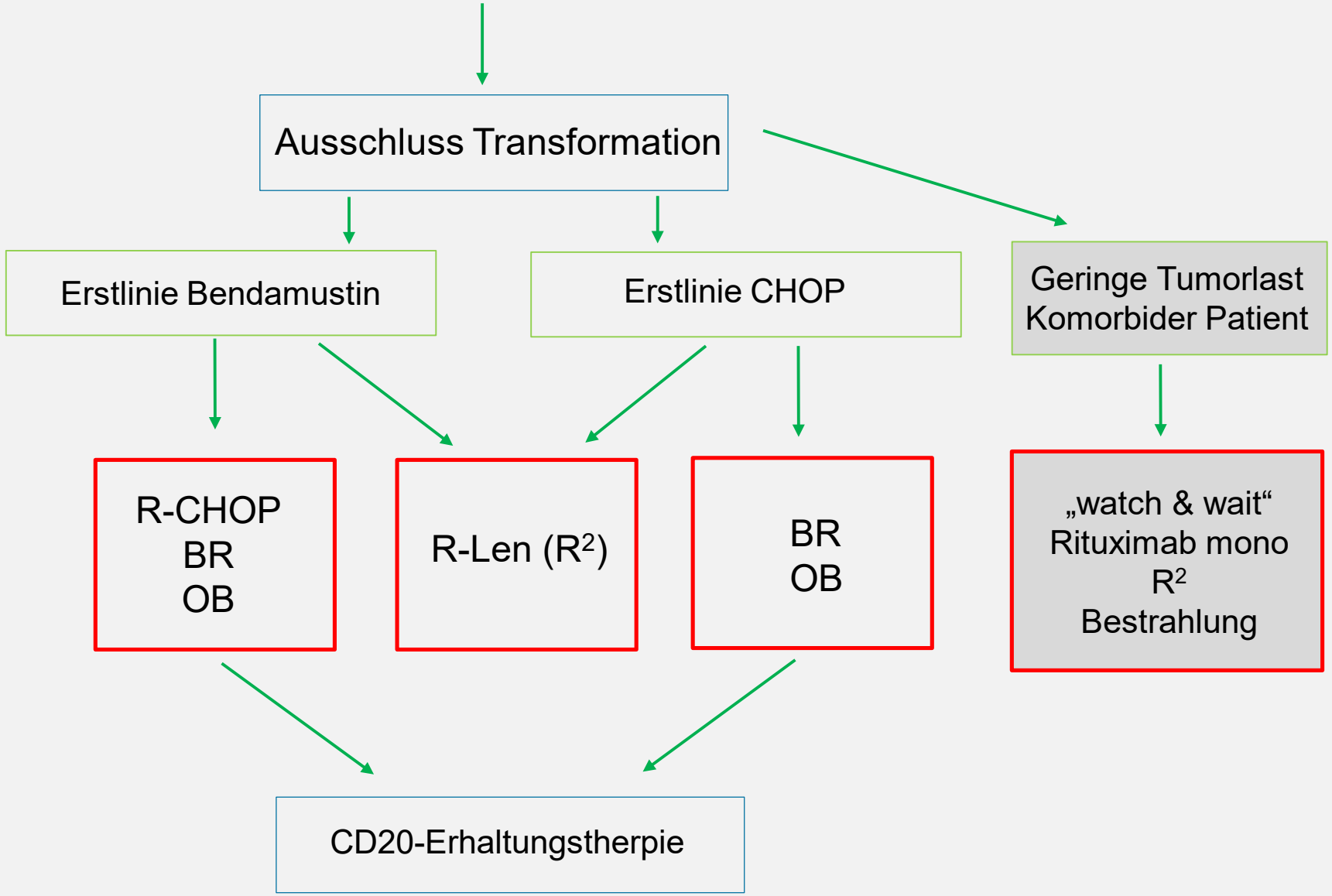
Response during R-Len induction (n=393)



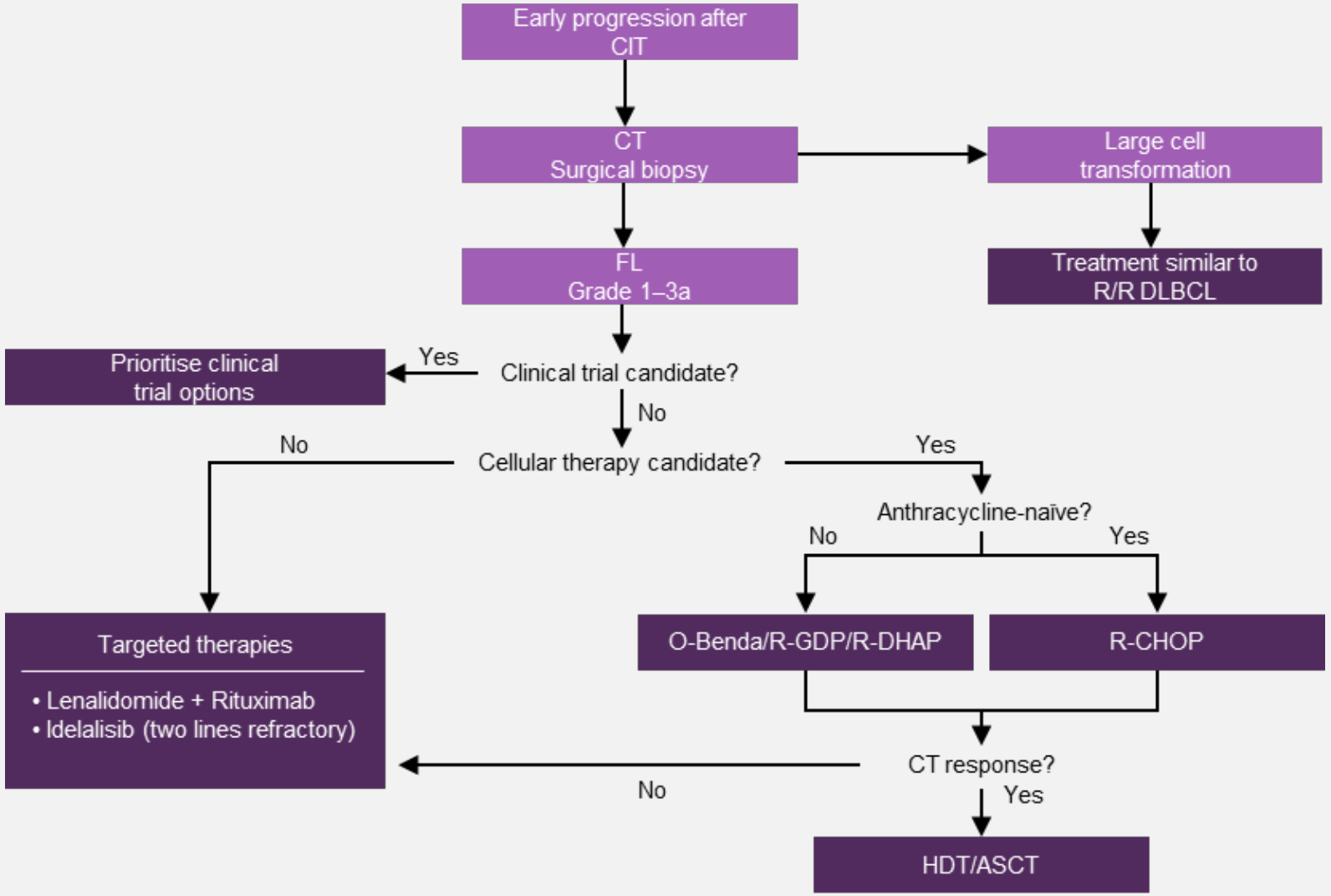
- Median DoR: 39.0 months in all patients, 35.8 months in R-refractory and NR in not R-refractory

Andorsky et al. ASCO 2020

Mögliches Therapiemanagement bei Spätrezidiven



Mögliches Therapiemanagement bei POD24



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In Anlehnung an Casulo and Barr. Blood 2019;133:1540–7

Ausblick

Tazemetostat

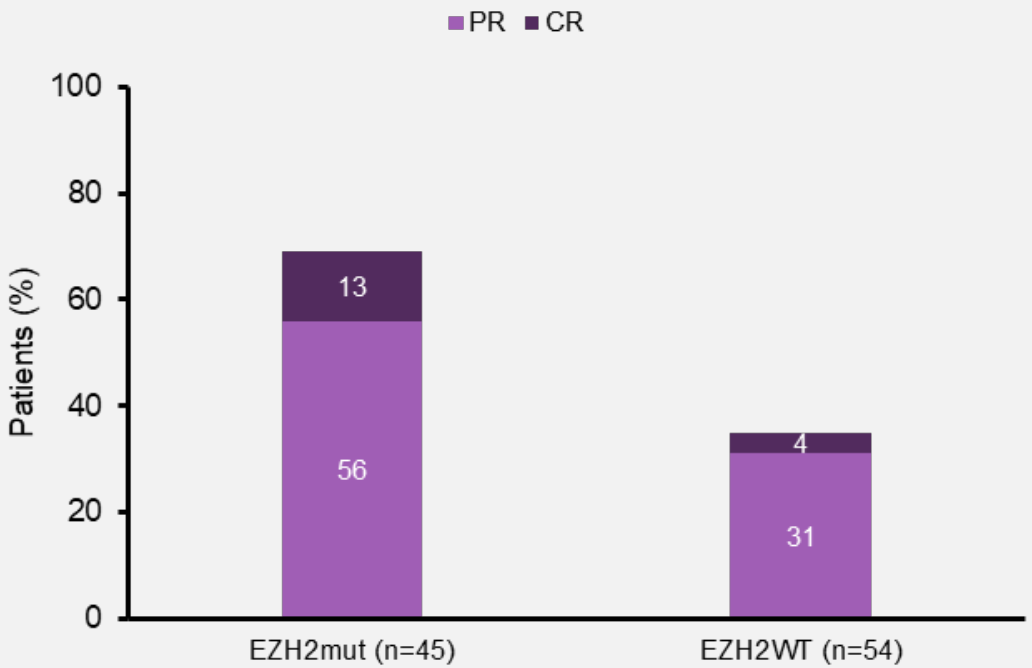
Single-arm Phase II trial of tazemetostat in 99 patients with R/R FL and ≥2 prior lines (NCT01897571)

AE summary in modified ITT population (n=99)

N (%)	Treatment-related
AE	80 (81)
Gr 3–5 AE*	
Thrombocytopenia	3 (3)
Neutropenia	3 (3)
Anaemia	2 (2)
SAE	4 (4)
Gr 5 (fatal) AE	0
AE leading to discontinuation of treatment	5 (5)

Median follow-up: 22.0 months in EZH2^{mut} cohort and 35.9 months in EZH2^{WT} cohort; *listed Gr 3–5 AEs are those with incidence ≥2%

IRC-assessed response in modified ITT population (n=99)



- Median DoR: 10.9 months in EZH2^{mut} and 13.0 months in EZH2^{WT}

Morschhauser et al. Lancet Oncol 2020;21:1433–42

Mosunetuzumab

Open-label Phase I/Ib dose-escalation and dose-expansion study of mosunetuzumab including 62 patients with R/R FL (NCT02500407)

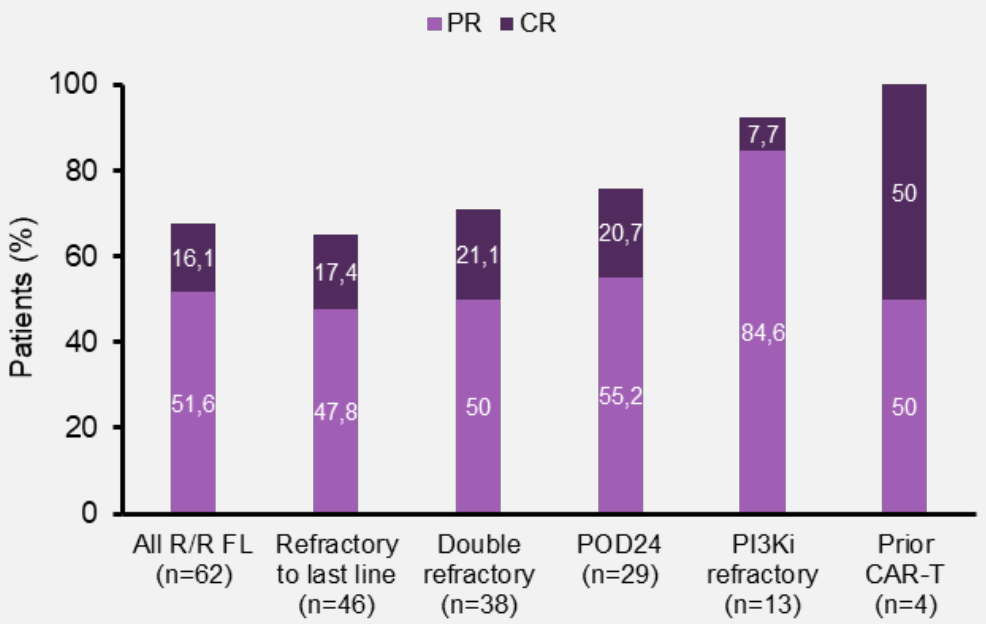
AE summary in R/R FL cohort (n=62)

	Any	Any related
AE	60 (96.8)	45 (72.6)
Gr 3–5 AE* Neutropenia Hypophosphataemia Anaemia	42 (67.7) 14 (22.6) 13 (21.0) 4 (6.5)	22 (35.5) 10 (15.1) 13 (21.0) 1 (1.6)
SAE	22 (35.5)	9 (14.5)
Gr 5 (fatal) AE	1 (1.6)	1 (1.6)†
AE leading to discontinuation of treatment	5 (8.1)	4 (6.5)‡

- 11/62 patients (17.7%) with CRS; all events (n=13) in C1 and Gr 1 or Gr 2

*Listed Gr 3–5 AEs are those with incidence ≥5%; †pneumonia; ‡pneumonia, neutropenia, arthritis and alanine aminotransferase increased

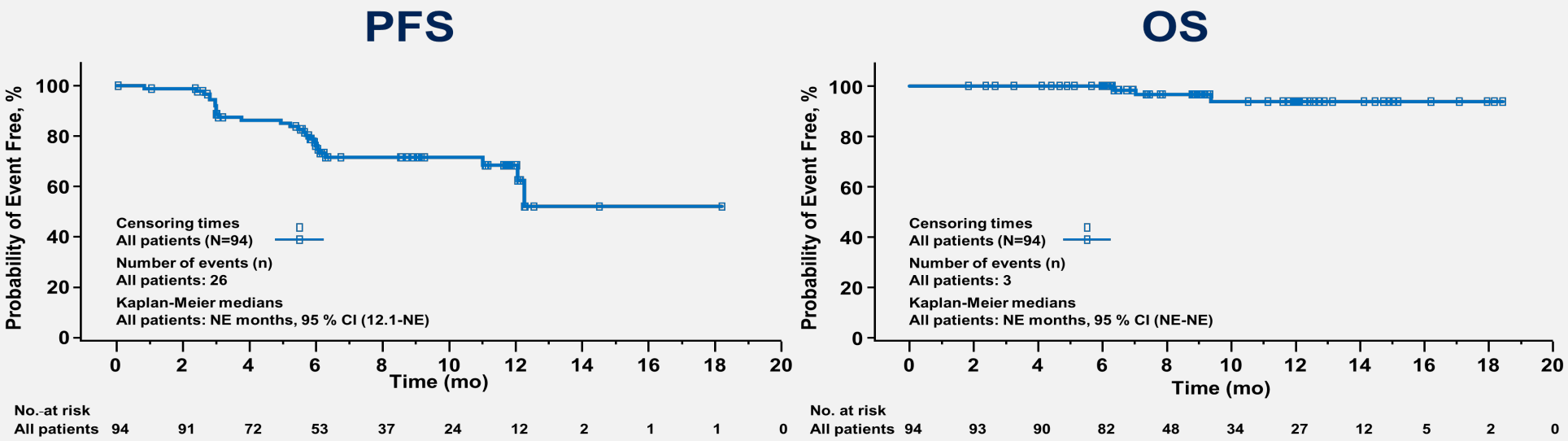
Response in R/R FL cohort (n=62)



- Median DoR: 20.4 months in all pts and 21.0 months in all CR pts

Assouline et al. ASH 2020

ELARA: Tisa-Cel beim r/r Follikulärem Lymphom



- Median PFS (95% CI, 12.1-NE) and OS (95% CI, NE-NE) were not reached
- 6-month PFS was 76% (95% CI, 65-84)

	Treated Patients N=97	
AESI (within 8 weeks of infusion)	**All grades, %**	**Grade ≥3, %**
Cytokine release syndrome[a,1]	48.5	**0**
Neurological adverse reactions	9.3	**1.0**
Infections	18.6	5.2
Tumor lysis syndrome	1.0	1.0
Prolonged depletion of B cells and/or agammaglobulinemia[b]	10.3	0
Hematologic disorders including cytopenias		
Neutropenia[c,d]	30.9	27.8
Anemia[c]	24.7	13.4
Thrombocytopenia[c]	16.5	9.3

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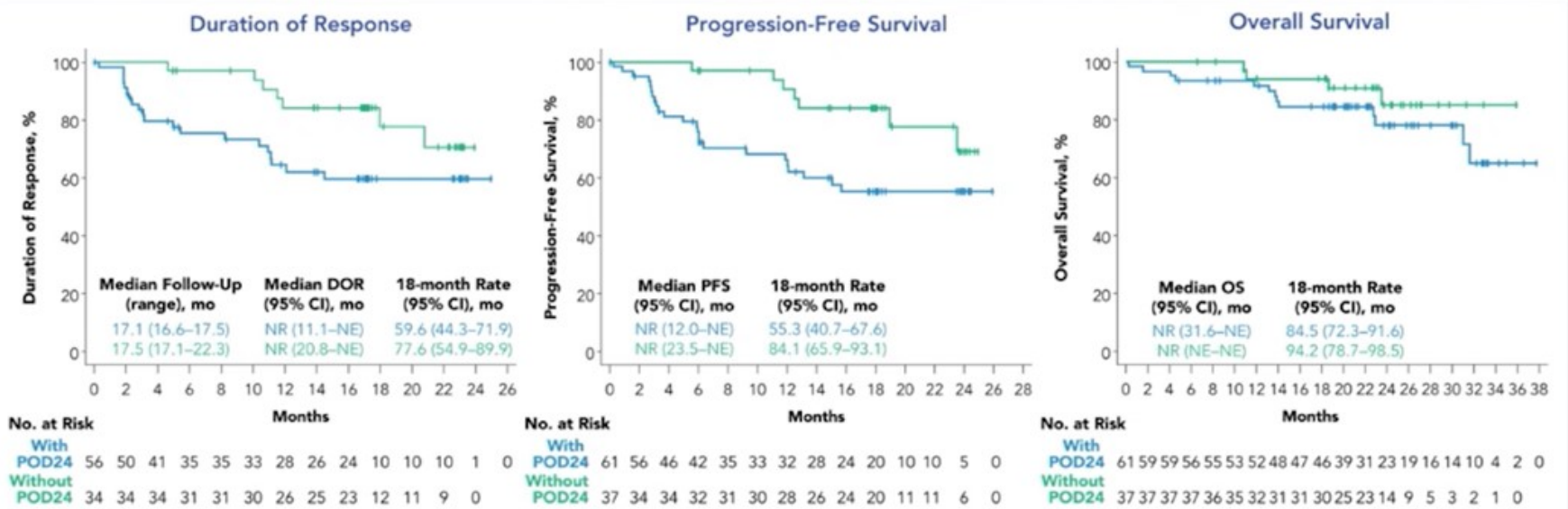
Schuster S.J.,et al, Abstract 7508, ASCO 2021

ZUMA-5: Axi-Cel beim r/r Follikulären Lymphom

Indolente Non-Hodgkin-Lymphome | Ergebnisse



- 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

EHA 2021: Jacobson, C.A. *et al.*, S213 OUTCOMES IN ZUMA-5 WITH AXICABTAGENE CILOLEUCEL IN PATIENTS WITH RELAPSED/REFRACTORY INDOLENT NON-HODGKIN LYMPHOMA WHO HAD THE HIGH-RISK FEATURE OF EARLY PROGRESSION AFTER FIRST CHEMOIMMUNOTHERAPY

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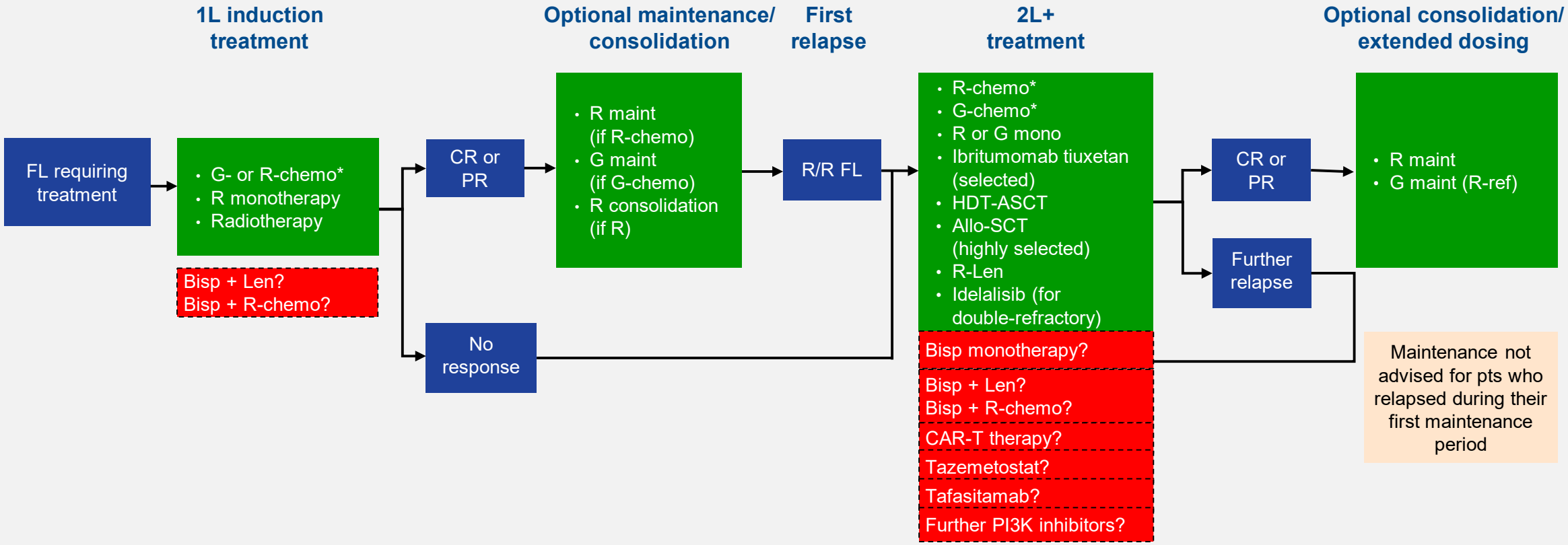
Jacobson C.A., et al., Abstract S213, EHA 2021

Wie werden neue Behandlungen die Therapielandschaft verändern?



Vielen Dank!