


Kompetenznetz
Maligne Lymphome

Lymphom Kompetenz KOMPAKT



KML KONGRESSE

Expert:innen berichten zu
Lymphomen & Leukämien



EHA2024 HYBRID



Prof. Dr. med. Martin Dreyling
CCC | LMU Klinikum München

Mantelzell-Lymphom (MCL)

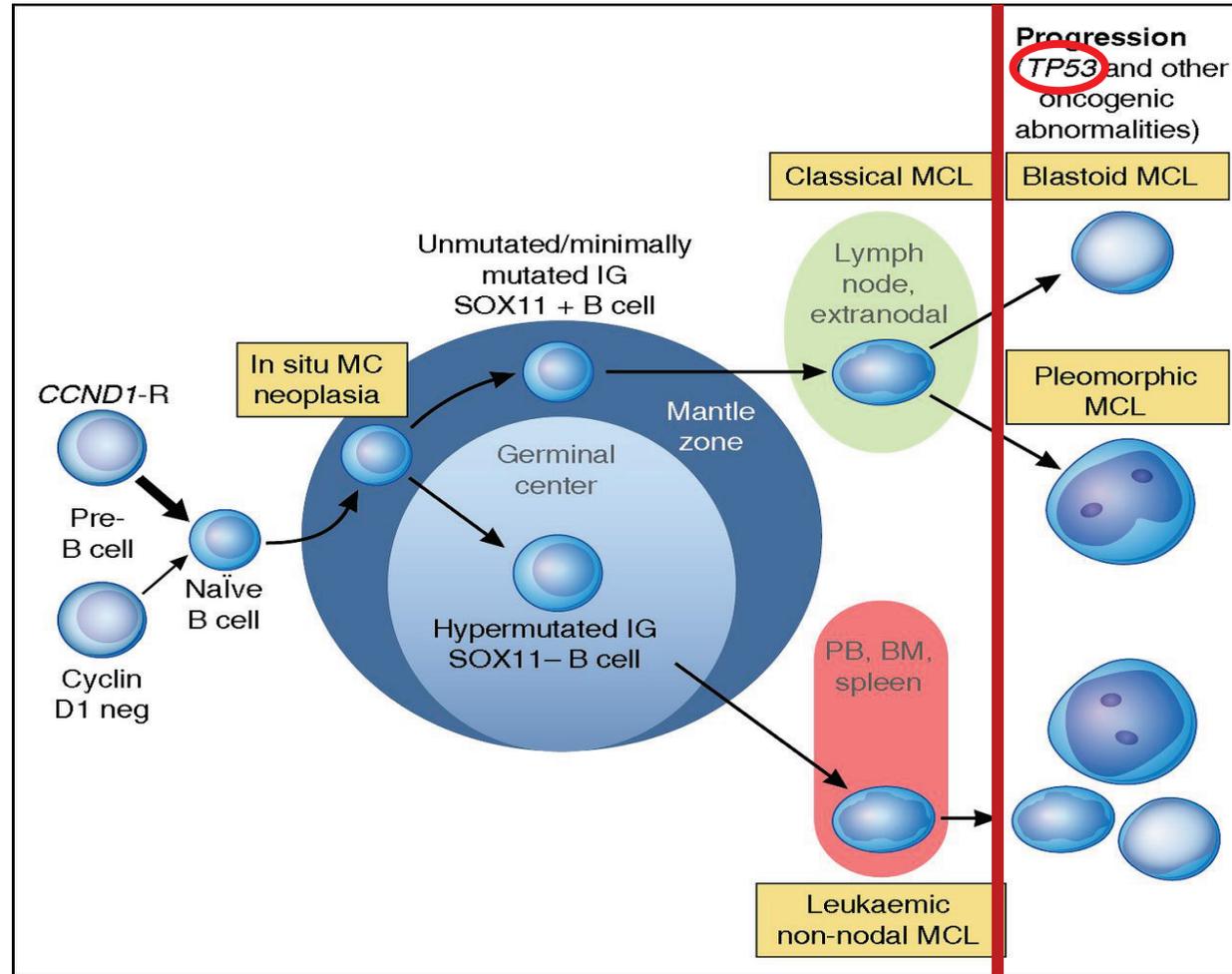
Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ASH2023 wird in Kooperation mit acht unterstützenden Firmen durchgeführt.
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Speakers Bureau	-
Speakers Honoraria	Astra Zeneca, Beigene, Gilead/Kite, Janssen, Lilly, Novartis, Roche
Scientific Advisory Board	Abbvie, Astra Zeneca, Beigene, BMS/Celgene, Gilead/Kite, Janssen, Lilly/Loxo, Novartis, Roche

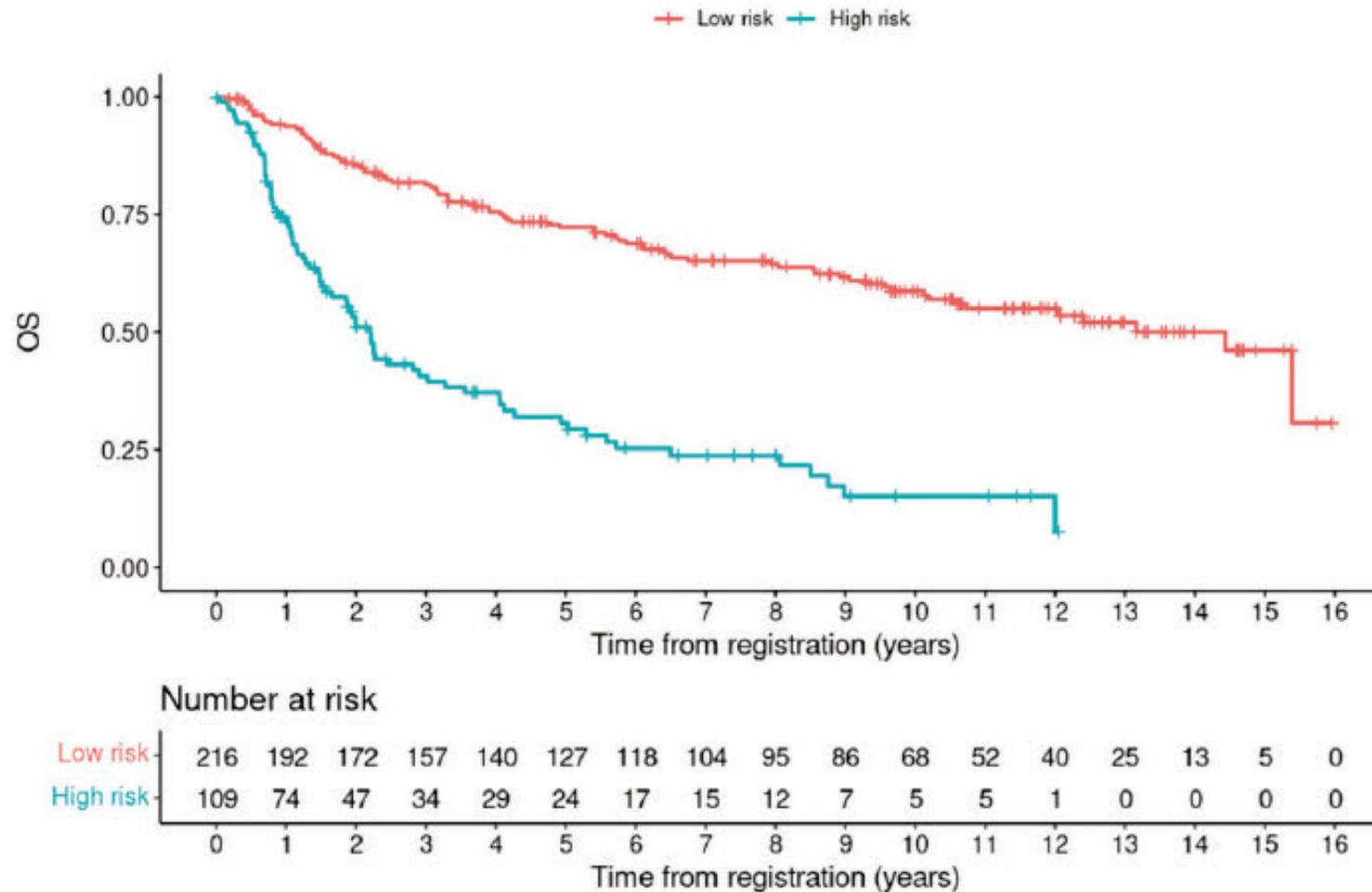
Mantelzell-Lymphom

Spektrum der Erkrankung



High risk Mantle cell lymphoma

Overall survival (n=465)



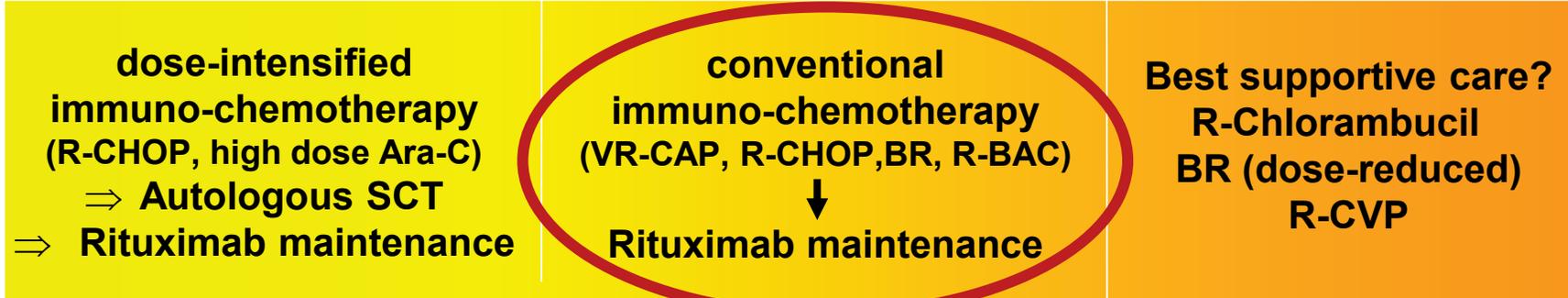
Mantle cell lymphoma

Therapeutic algorithm

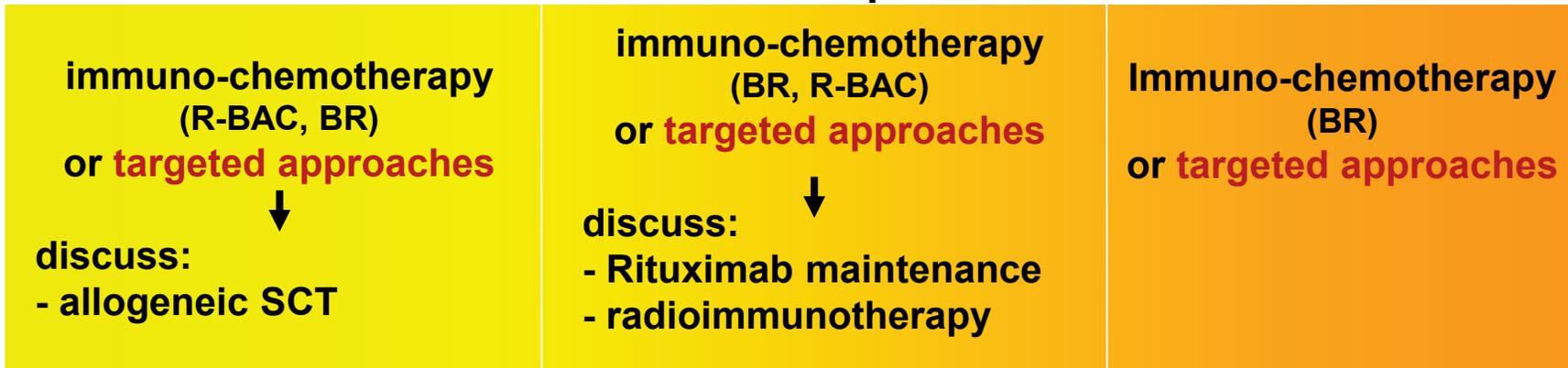
young patient (≤ 65)

elderly patient (>65)
First line treatment

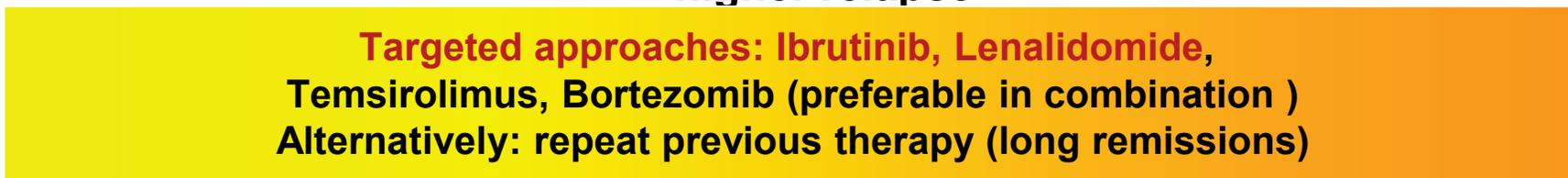
compromised patient



1. relapse



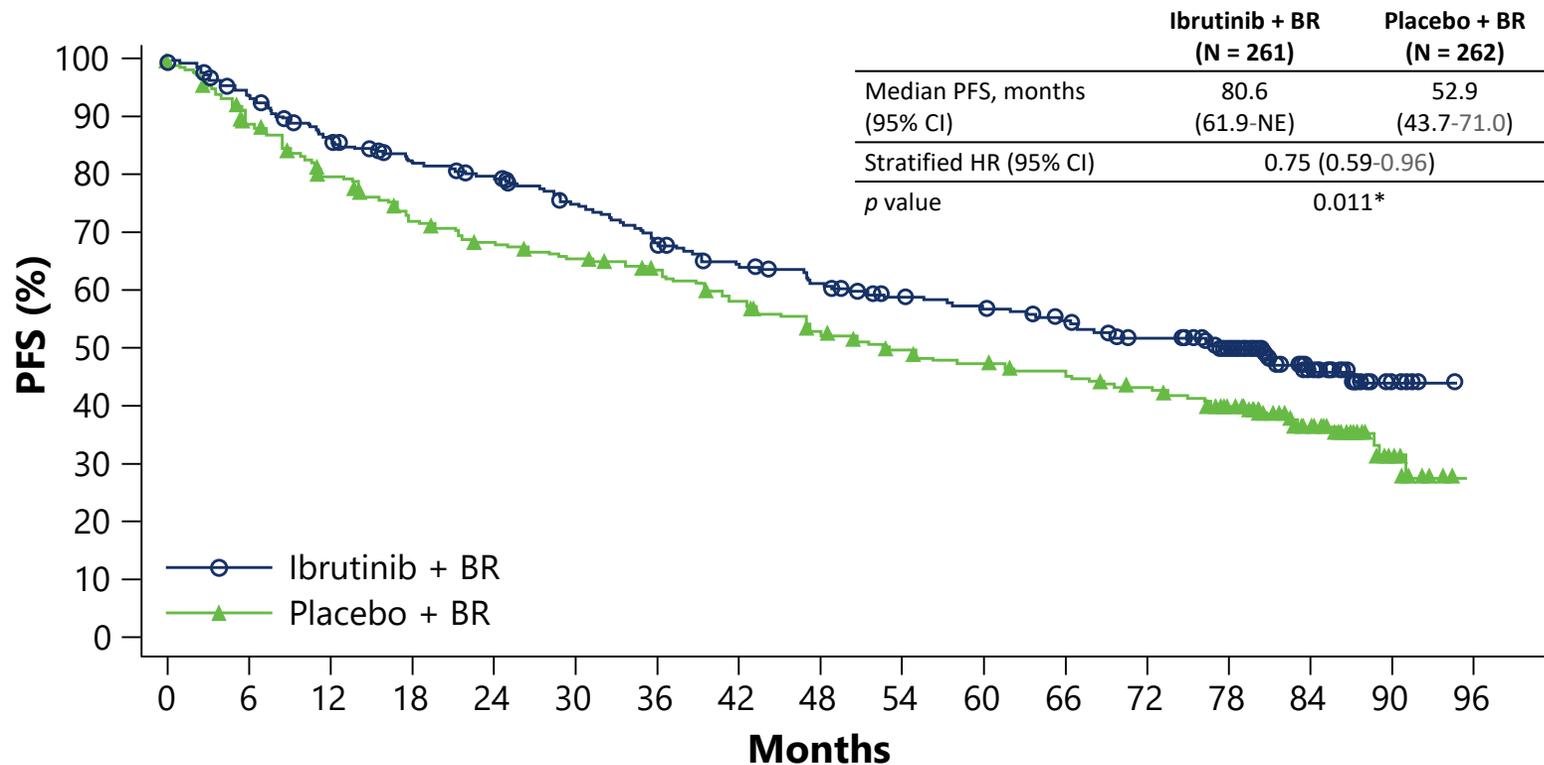
higher relapse



Mantle cell Lymphoma (older patients)

BR +/- Ibrutinib

Wang, NEJM 2022



Ibrutinib + BR and R maintenance achieved:

- Significant improvement in median PFS by 2.3 years (6.7 vs 4.4 years)
- 25% reduction in risk of PD or death

Patients at Risk

Ibrutinib + BR	261	228	207	191	182	167	152	139	130	120	115	106	95	78	39	11	0
Placebo + BR	262	226	199	177	166	158	148	135	119	109	103	98	90	78	41	11	0

Acalabrutinib plus bendamustine and rituximab in untreated mantle cell lymphoma (MCL): Results from the phase 3, double-blind, placebo-controlled ECHO trial

Michael Wang¹, Jiri Mayer², David Belada³, Yuqin Song⁴, Wojciech Jurczak⁵, Jonas Paludo⁶, Michael P. Chu⁷, Iryna Kryachok⁸, Laura Fogliatto⁹, Chan Cheah¹⁰, Marta Morawska^{11,12}, Juan-Manuel Sancho¹³, Yufu Li¹⁴, Caterina Patti¹⁵, Cecily Forsyth¹⁶, Jingyang Zhang¹⁷, Robin Lesley¹⁷, Safaa Ramadan¹⁸, Simon Rule¹⁸, Martin Dreyling¹⁹

¹MD Anderson Cancer Center, University of Texas, Houston, TX, USA; ²University Hospital Brno, Brno, Czech Republic; ³4th Department of Internal Medicine – Haematology, Charles University, Hospital and Faculty of Medicine, Hradec Králové, Czech Republic; ⁴Peking University Cancer Hospital & Institute, Beijing, China; ⁵Malopolskie Centrum Medyczne S.C, Krakow, Poland; ⁶Mayo Clinic, Rochester, MN, USA; ⁷Cross Cancer Institute, University of Alberta, Edmonton, Canada; ⁸National Cancer Institute, Kyiv, Ukraine; ⁹Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil; ¹⁰Sir Charles Gairdner Hospital, Nedlands, Australia; ¹¹Experimental Hematooncology Department, Medical University of Lublin, Lublin, Poland; ¹²Hematology Department, St. John's Cancer Center, Lublin, Poland; ¹³ICO-IJC-Hospital Germans Trias i Pujol, Badalona, Spain; ¹⁴Henan Cancer Hospital, Zheng Zhou, China; ¹⁵A.O.O.R. Villa Sofia Cervello, Palermo, Italy; ¹⁶Central Coast Haematology, North Gosford, Australia; ¹⁷AstraZeneca, South San Francisco, CA, USA; ¹⁸AstraZeneca, Cambridge, UK; ¹⁹Klinikum der Universitaet Munchen, Muenchen, Germany

Demographics and Baseline Characteristics

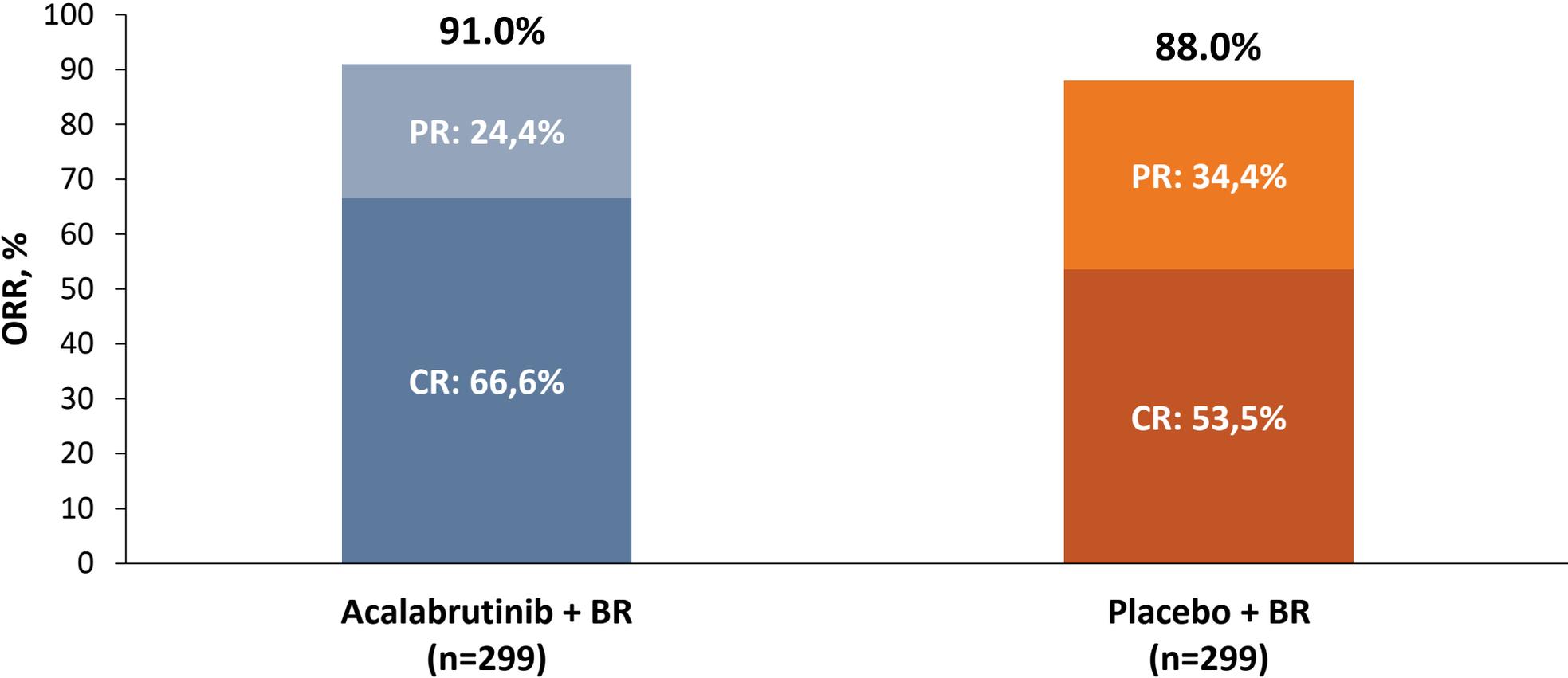
	Acalabrutinib + BR (n=299)	Placebo + BR (n=299)
Age, median (range), y	71 (65–85)	71 (65–86)
≥75 y, n (%)	84 (28.1)	77 (25.8)
Male, n (%)	214 (71.6)	209 (69.9)
ECOG PS, n (%)		
1	129 (43.1)	132 (44.1)
2	12 (4.0)	23 (7.7)
Tumor bulk ≥5 cm, n (%)	112 (37.5)	113 (37.8)
Blastoid/pleomorphic histology, n (%)	41 (13.7)	38 (12.7)
Simplified MIPI score, n (%)		
Low risk	99 (33.1)	101 (33.8)
Intermediate risk	128 (42.8)	125 (41.8)
High risk	72 (24.1)	73 (24.4)
Extranodal disease, n (%)	264 (88.3)	277 (92.6)
<i>TP53</i> status, n (%) ^a		
Mutated	22 (7.4)	29 (9.7)
Unmutated	97 (32.4)	83 (27.8)
Ki-67, n (%)		
<30%	133 (44.5)	126 (42.1)
≥30%	139 (46.5)	147 (49.2)

^aAll other patients in the acalabrutinib (n=180) and placebo (n=187) groups had unknown *TP53* mutation status.

BR, bendamustine + rituximab; ECOG PS, Eastern Cooperative Oncology Group performance status; MIPI, Mantle Cell Lymphoma International Prognostic Index.

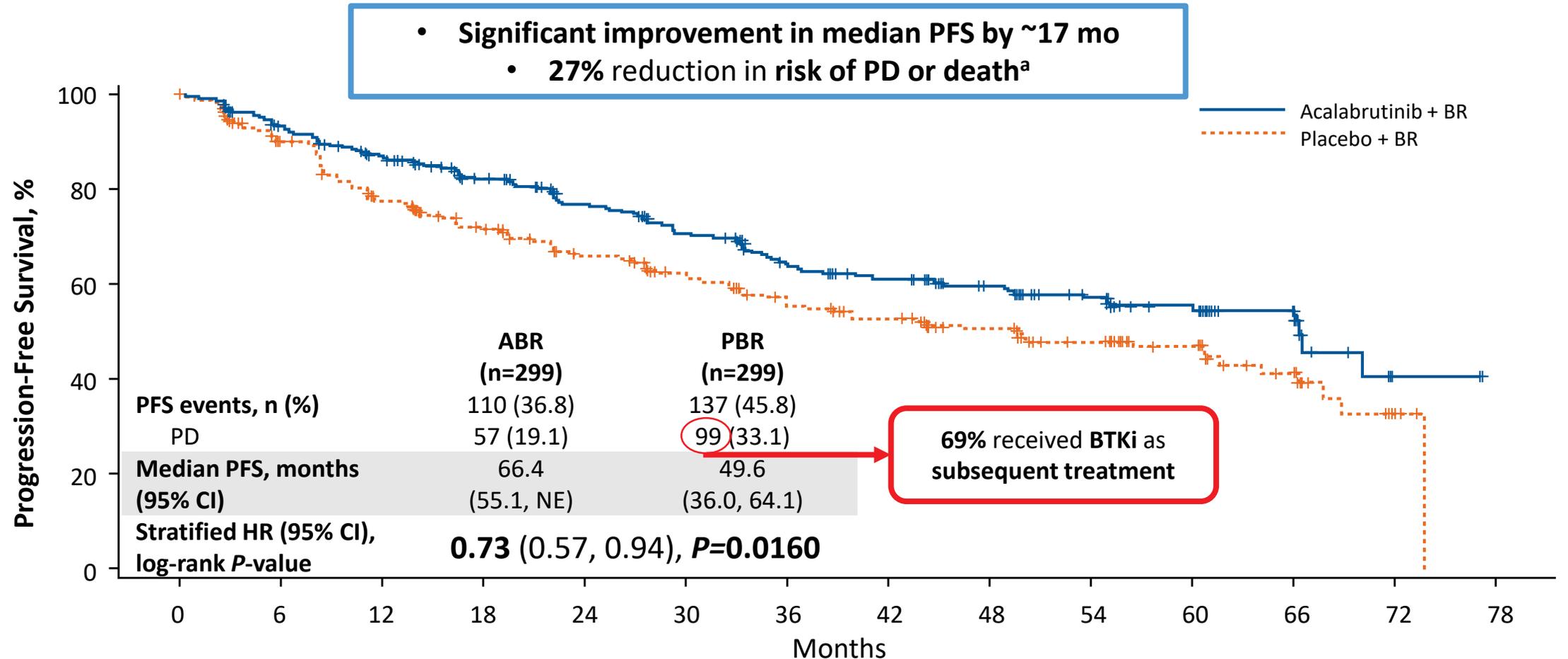
Best Overall Response and Complete Response Rates

- An additional 13% of patients achieved CR with acalabrutinib + BR



BR, bendamustine + rituximab; CI, confidence interval; CR, complete response; ORR, overall response rate; PR, partial response.

PFS (primary endpoint) Was Significantly Improved With Acalabrutinib + BR

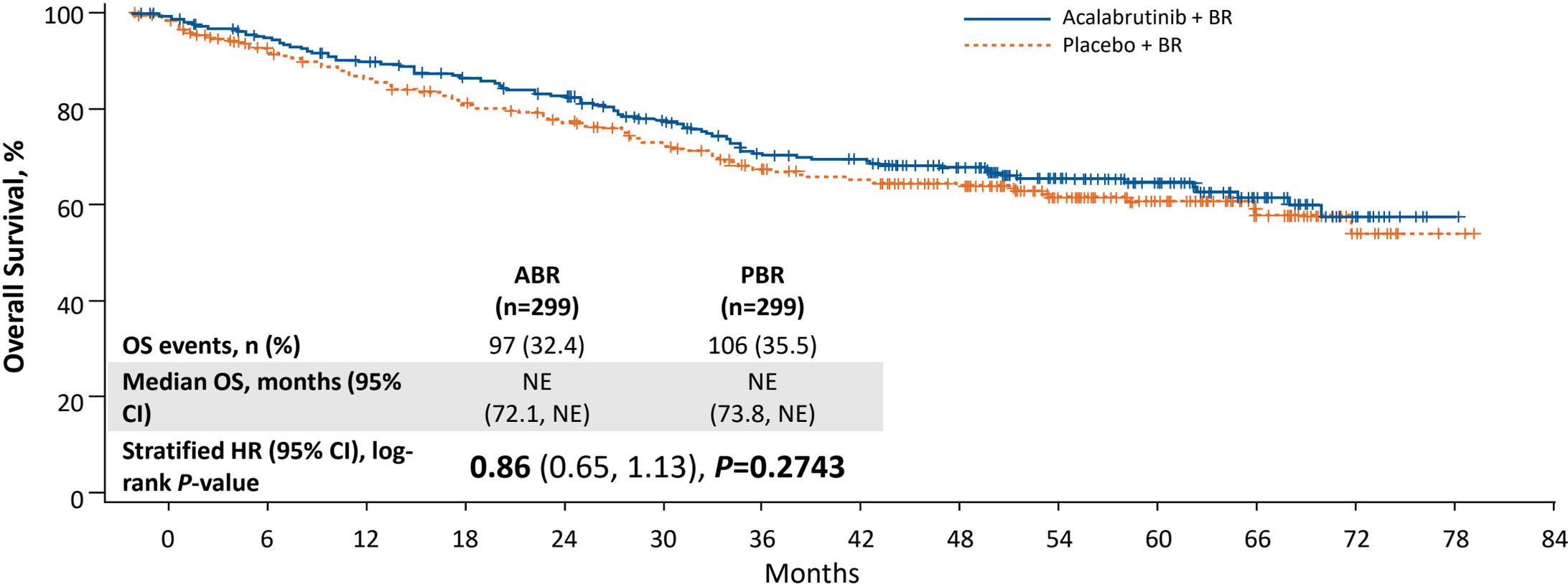


Number at risk	0	6	12	18	24	30	36	42	48	54	60	66	72	78
Acala + BR	299	258	232	205	182	156	136	122	98	73	53	34	2	0
Placebo + BR	299	243	204	181	159	142	118	102	84	63	44	25	4	0

^aAt a median follow-up of 45 months.

ABR, acalabrutinib + bendamustine + rituximab; BR, bendamustine + rituximab; BTKi, Bruton tyrosine kinase inhibitor; CI, confidence interval; HR, hazard ratio; NE, not estimable; PBR, placebo + bendamustine + rituximab; PD, progressive disease; PFS, progression-free survival.

Overall Survival Including Crossover



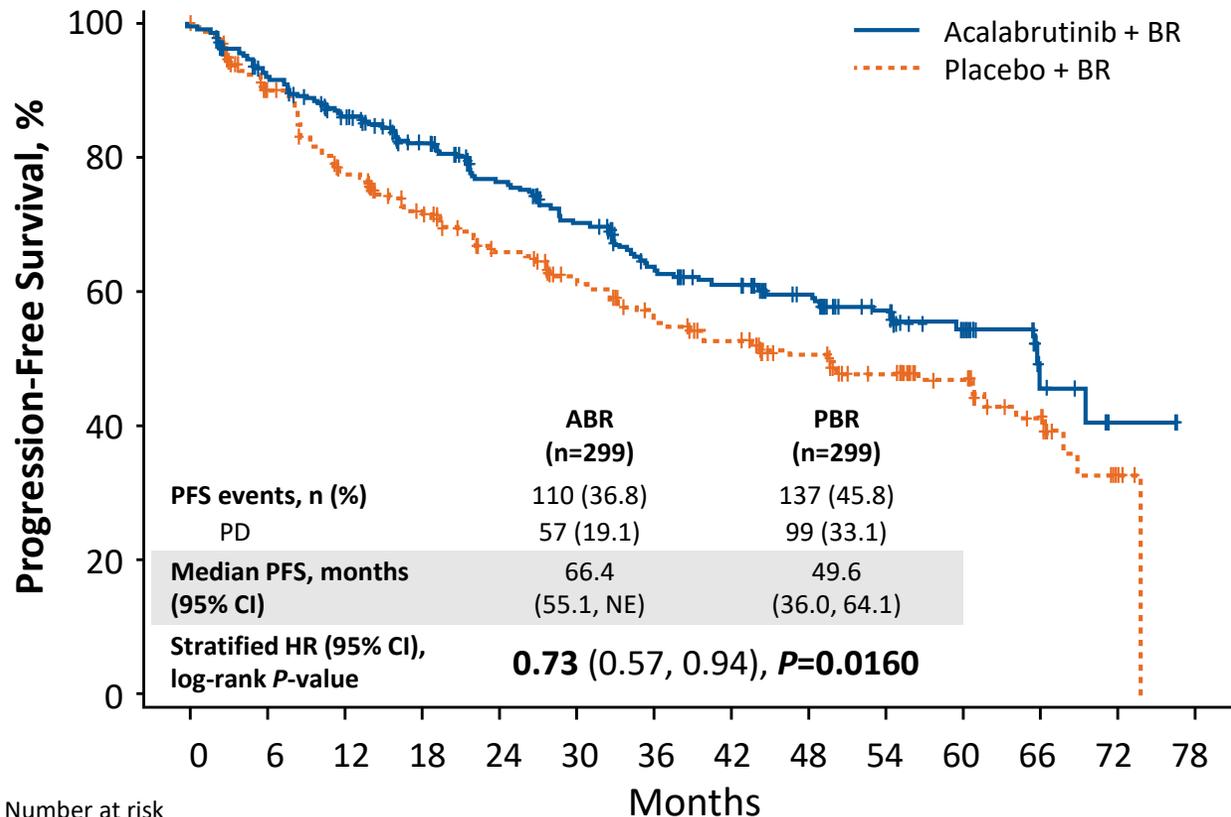
	ABR (n=299)	PBR (n=299)
OS events, n (%)	97 (32.4)	106 (35.5)
Median OS, months (95% CI)	NE (72.1, NE)	NE (73.8, NE)
Stratified HR (95% CI), log-rank P-value	0.86 (0.65, 1.13), P=0.2743	

Number at risk		0	6	12	18	24	30	36	42	48	54	60	66	72	78	84
Acala + BR	299	280	259	243	230	207	181	163	146	110	86	58	25	3	0	
Placebo + BR	299	268	247	229	215	193	175	157	141	108	78	51	21	3	0	

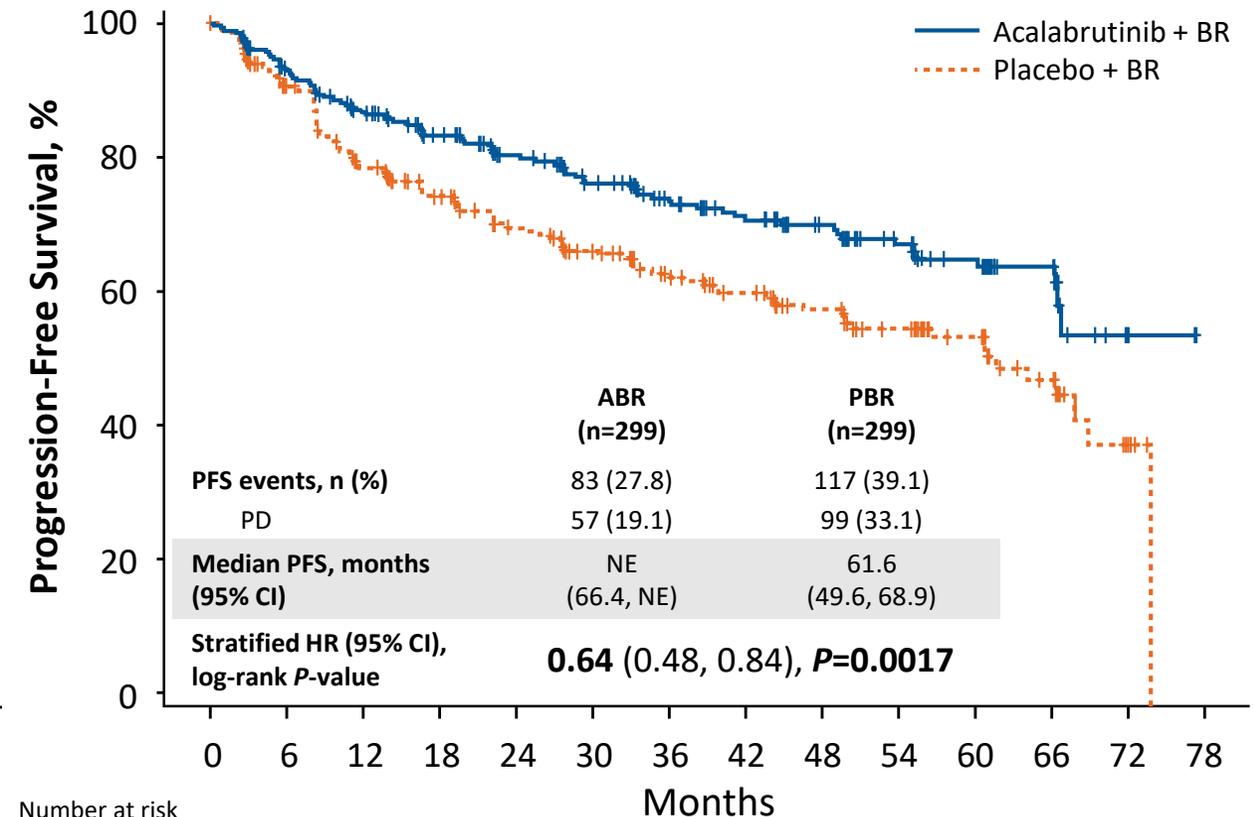
Median follow-up of 45 months.
 ABR, acalabrutinib + bendamustine + rituximab; BR, bendamustine + rituximab; CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival; PBR, placebo + bendamustine + rituximab.

PFS With and Without COVID-19 Deaths: Prespecified Sensitivity Analysis

Full analysis population



COVID-19 deaths censored



Number at risk		0	6	12	18	24	30	36	42	48	54	60	66	72	78
Acala + BR	299	258	232	205	182	156	136	122	98	73	53	34	2	0	
Placebo + BR	299	243	204	181	159	142	118	102	84	63	44	25	4	0	

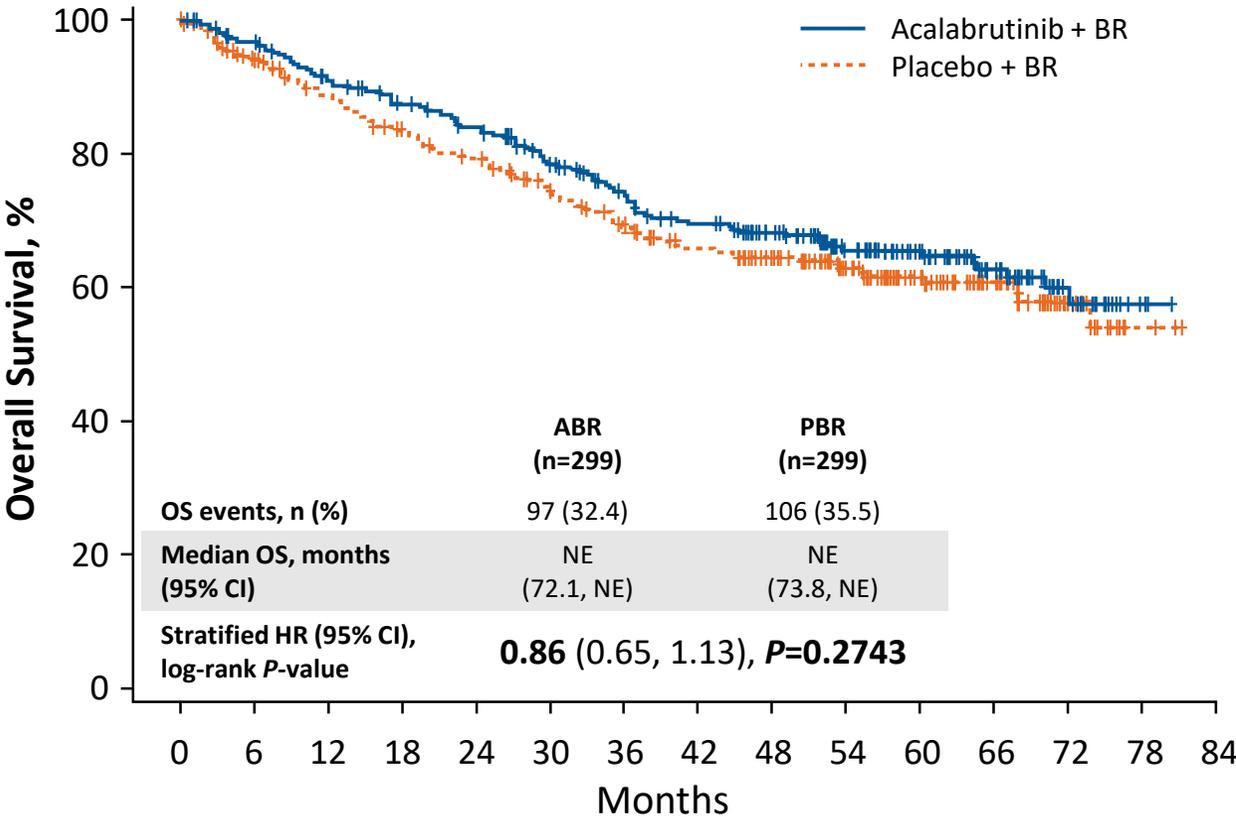
Number at risk		0	6	12	18	24	30	36	42	48	54	60	66	72	78
Acala + BR	299	258	232	205	182	156	136	122	98	73	53	34	2	0	
Placebo + BR	299	243	204	181	159	142	118	102	84	63	44	25	4	0	

36% risk reduction when censoring COVID-19 deaths

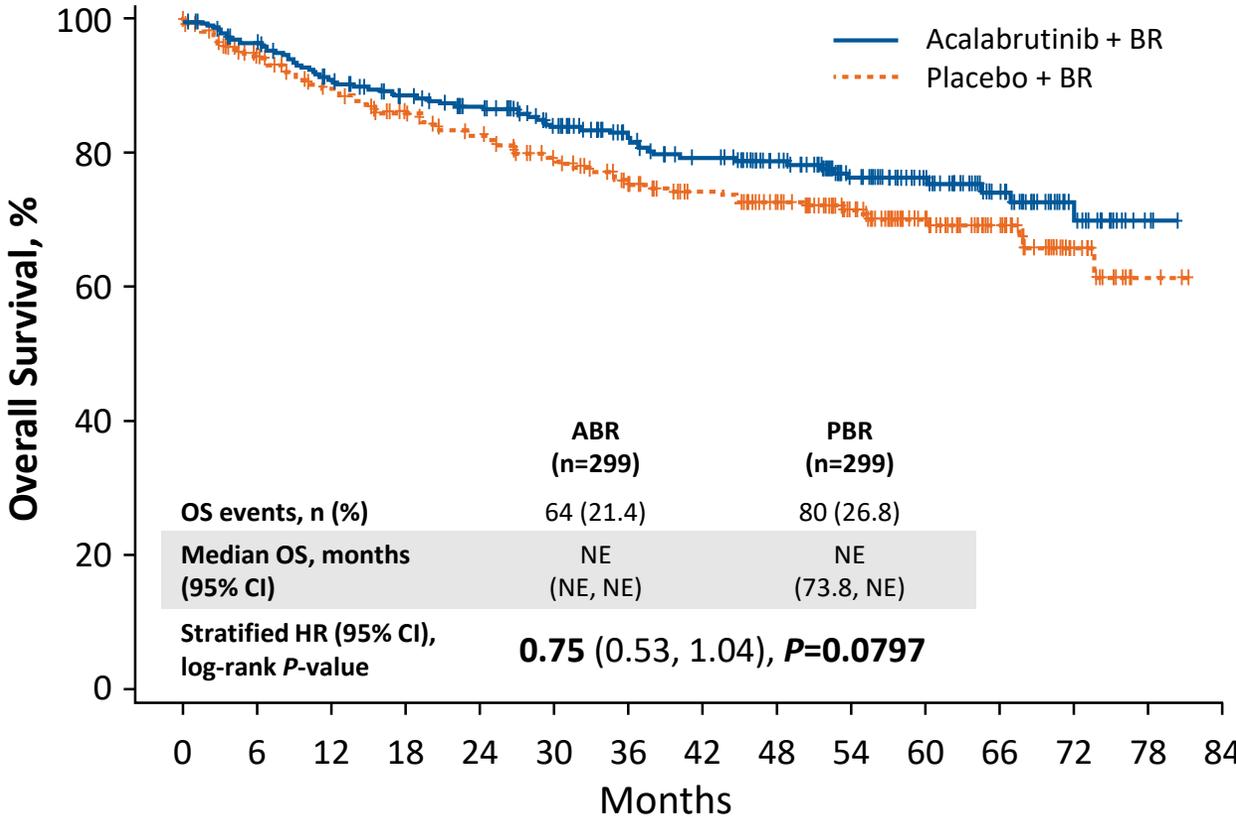
ABR, acalabrutinib + bendamustine + rituximab; BR, bendamustine + rituximab; CI, confidence interval; COVID-19, coronavirus disease 2019; HR, hazard ratio; NE, not estimable; PBR, placebo + bendamustine + rituximab; PFS, progression-free survival.

OS With and Without COVID-19 Deaths: Prespecified Sensitivity Analysis

Full analysis population (including crossover)



COVID-19 deaths censored



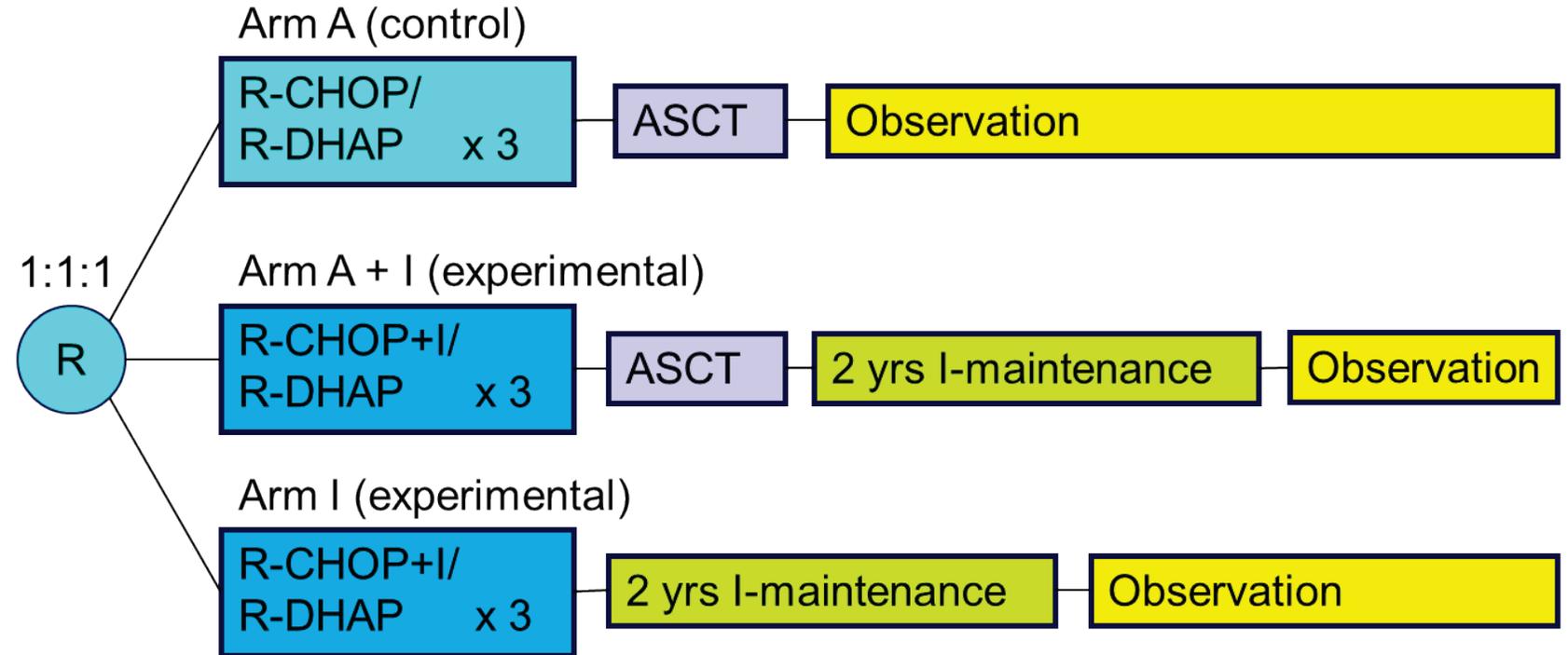
Number at risk	0	6	12	18	24	30	36	42	48	54	60	66	72	78	84	Number at risk	0	6	12	18	24	30	36	42	48	54	60	66	72	78	84
Acala + BR	299	280	259	243	230	207	181	163	146	110	86	58	25	3	0	Acala + BR	299	280	259	243	230	207	181	163	146	110	86	58	25	3	0
Placebo + BR	299	268	247	229	215	193	175	157	141	108	78	51	21	3	0	Placebo + BR	299	268	247	229	215	193	175	157	141	108	78	51	21	3	0

ABR, acalabrutinib + bendamustine + rituximab; CI, confidence interval; COVID-19, coronavirus disease 2019; HR, hazard ratio; NE, not estimable; OS, overall survival; PBR, placebo + bendamustine + rituximab.



TRIANGLE: Trial Design

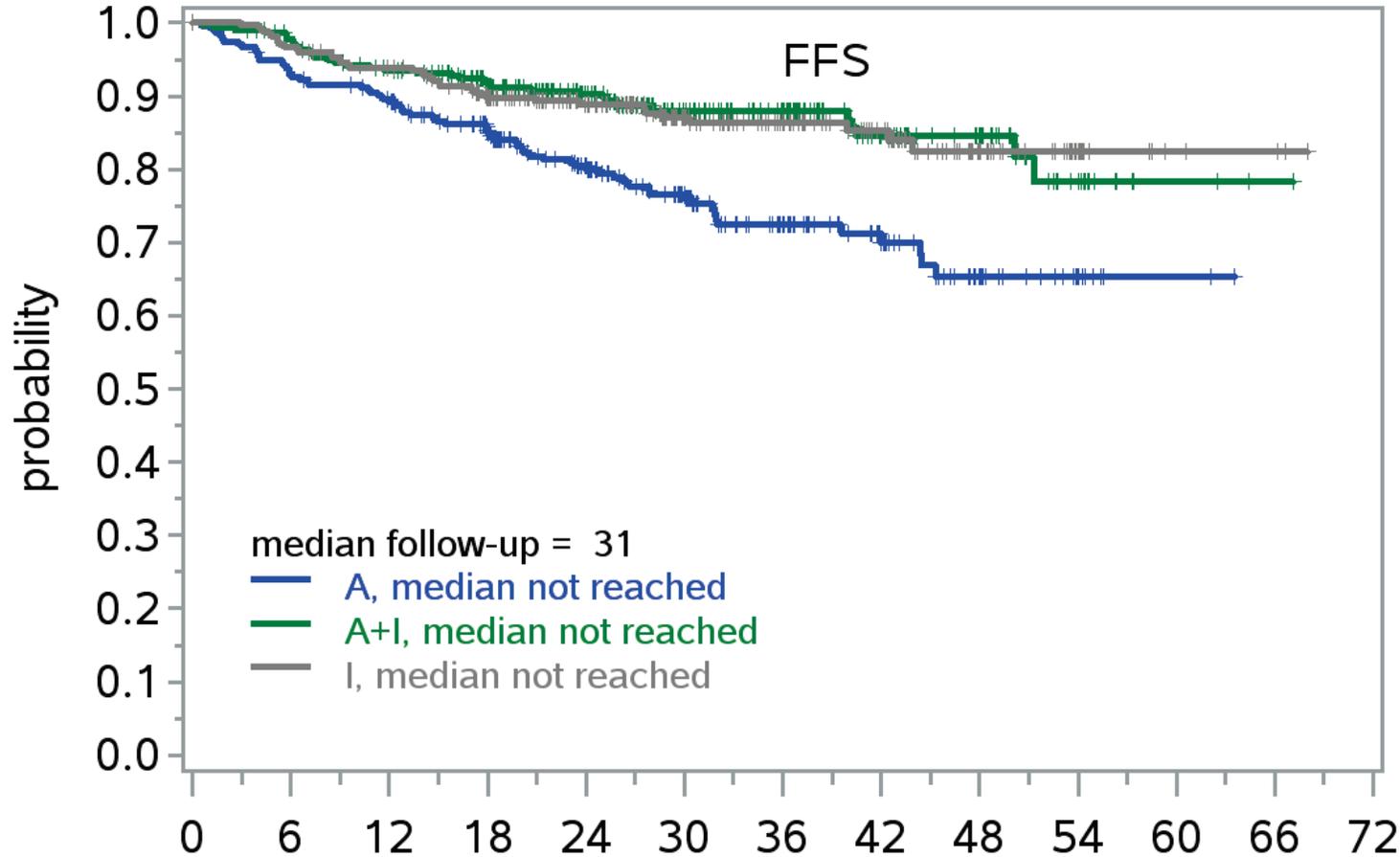
- MCL patients
- previously untreated
- stage II-IV
- younger than 66 years
- suitable for HA and ASCT
- ECOG 0-2
- Primary outcome: FFS
- Secondary outcomes:
 - Response rates
 - PFS, RD
 - OS
 - Safety



- R maintenance was added following national guidelines in all 3 trial arms
- Rituximab maintenance (without or with Ibrutinib) was started in 168 (58 %)/165 (57 %)/158 (54 %) of A/A+I/I randomized patients.



TRIANGLE: FFS Superiority of A+I vs. I ?



- Test A+I vs. I ongoing, no decision yet

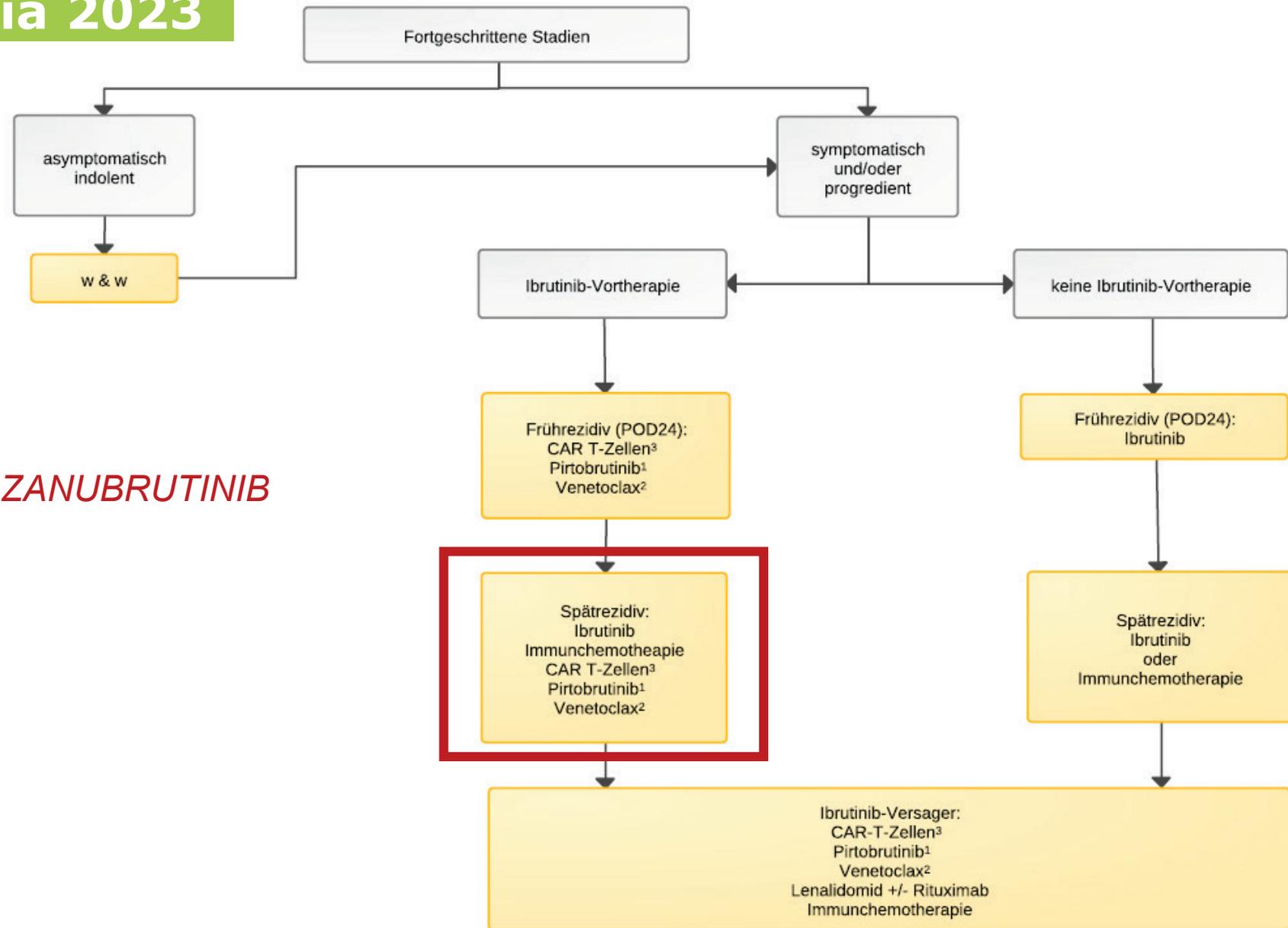
Next lymphoma treatment (among patients with first treatment failure)	A (n=68)		A+I (n=35)		I (n=37)	
Treatment with Ibrutinib	34	79%	4	24%	3	11%
Treatment without Ibrutinib	9	21%	13	76%	24	89%
No treatment	25		18		10	

	Numbers At Risk												
	months from randomisation												
	0	6	12	18	24	30	36	42	48	54	60	66	72
A	288	252	237	206	162	126	85	54	27	12	2	0	
A+I	292	270	253	226	184	137	109	65	40	17	3	1	
I	290	269	257	229	180	133	100	68	34	16	4	3	

A+I arm: IR-CHOP/R-DHAP+ASCT+I; I arm: IR-CHOP/R-DHAP+I. I: ibrutinib

Relapsed Mantle cell Lymphoma

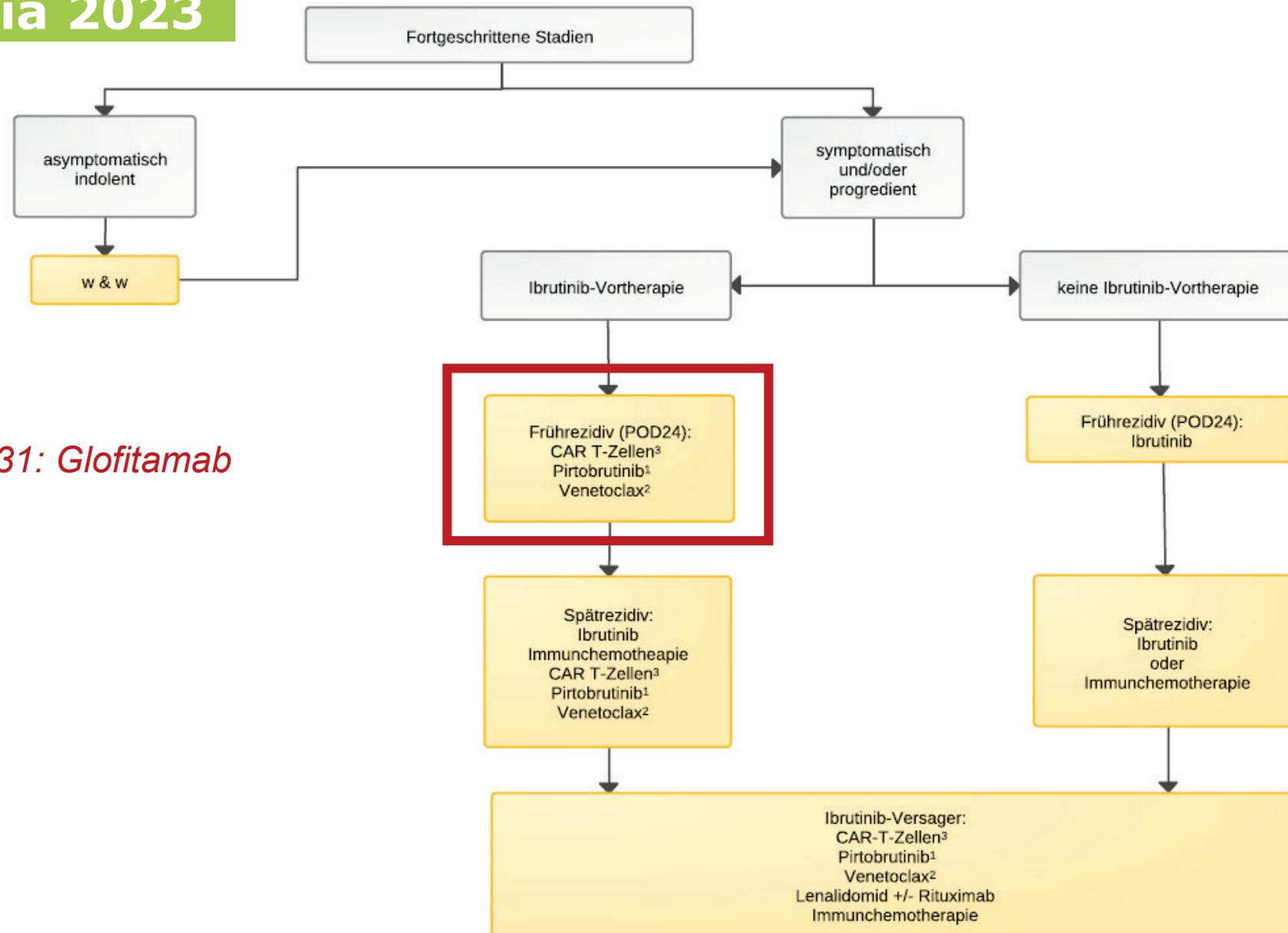
Onkopedia 2023



EHA 2024, P112:
SONROTOCLAX AND ZANUBRUTINIB

Relapsed Mantle cell Lymphoma

Onkopedia 2023



EHA 2024: S231: Glofitamab

Mantelzell-Lymphom

Take home messages EHA 2024

- Erstlinie: R-Chemo **+Ibrutinib**
- Rezidive: BTK-Inhibitor-**Kombination (Ibru/Ven)**
- **BTK-Versager:** CAR T-Zellen, (Pirtobrutinib), Venetoclax,
(Glofitamab)

Studientreffen 2022, Berlin



Die Kurzpräsentationen sind online unter

www.lymphome.de/eha2024

Für den Inhalt verantwortlich:

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