SESSIONE 2 CAR-T nel linfoma follicolare e mantellare

Moderatore: M. Di Ianni (Pescara)

Algoritmo di trattamento nel linfoma mantellare

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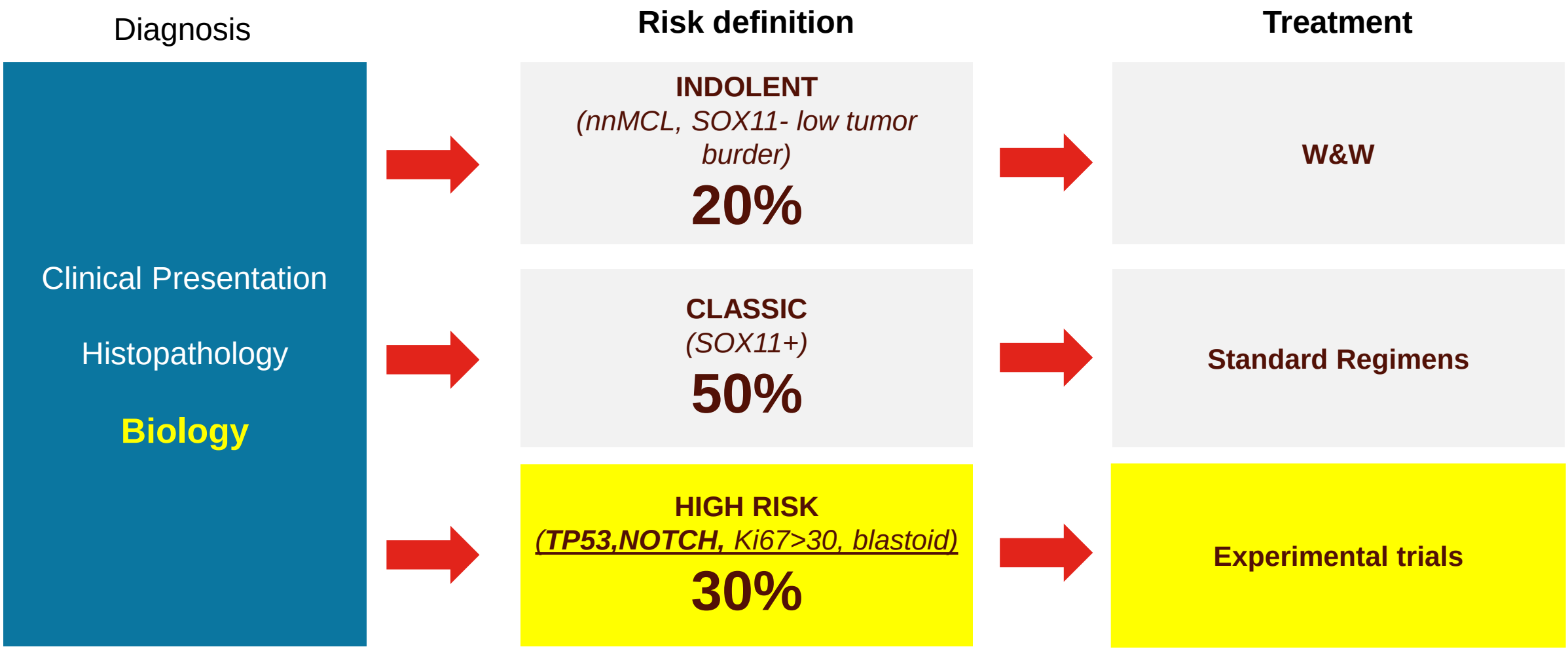
Maurizio Martelli

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Roche					X	X	
Gilead					X	X	
Novartis					X	X	
Takeda					X	X	
Abbvie					X	X	
Incyte	X				X	X	
Janssen					X	X	
BMS					X	X	
Beigene					X	X	
Eli Lilly					X	X	

New therapeutic approach in MCL



Courtesy of Carlo Visco

High risk features distribution

	Young (MCL-0208)	Nordic (MCL2-3)	Elderly (VR-BAC)
All patients	190	183	140
Ki67>30%	50 (28%)	68 (43%)	34 (24%)
TP53 mut	15 (8%)	20 (11%)	**28 (20%)**
TP53 del	**25 (13%)**	**29 (16%)**	19 (14%)
TP53 mut/del	**31 (17%)**	**37 (20%)**	**34 (24%)**
Blastoid	16 (8%)	**31 (17%)**	13 (9%)

Ferrero S et al, Haematologica 2020; Visco C et al, partial at ASH 2021; Eskelund et al, Blood 2017

Agenda

- First line therapy of younger / fit patients (is changing)
- First line therapy of elderly/ unfit patients
- Treatment in first relapse
- Treatment after BTKi failure

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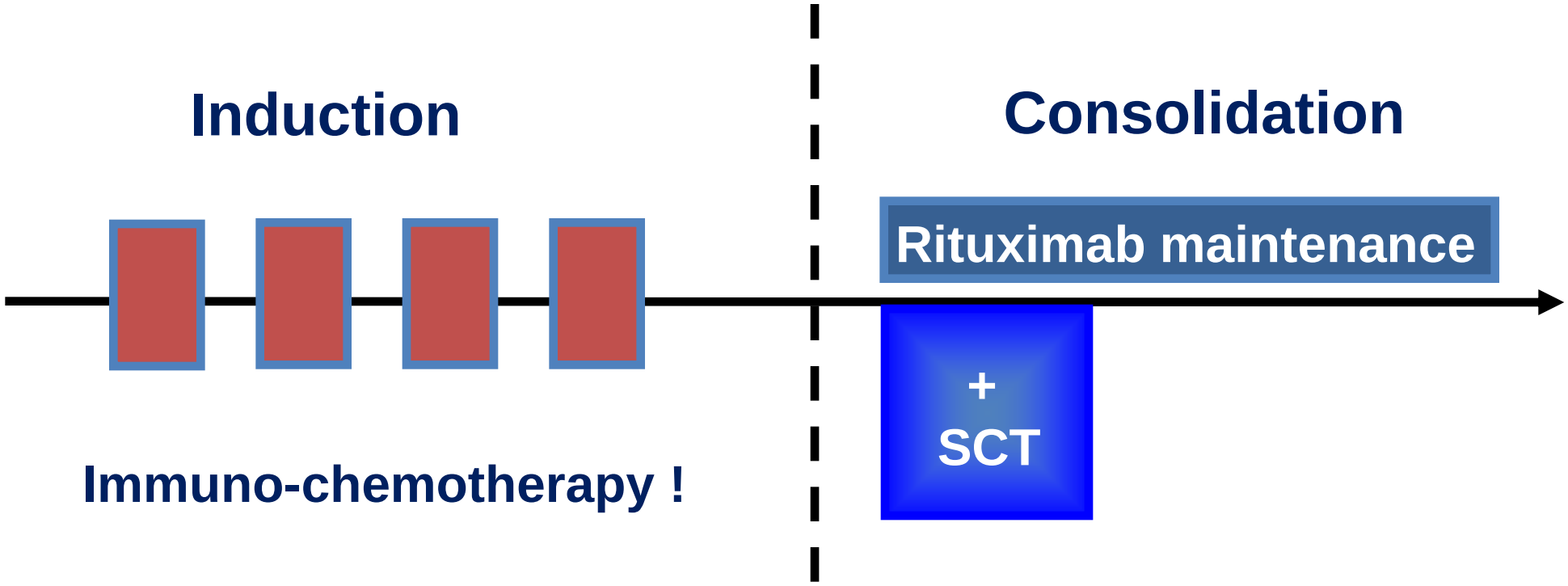
Current Treatment in Mantle Cell Lymphoma



Current Treatment in Mantle Cell Lymphoma

Preferred First-line Treatment Options

Aggressive Chemotherapy
R-DHAP (cisplatin, or oxaliplatin)
R-CHOP/R-DHAP (alternating)
NORDIC (maxi-CHOP/R + HD cytarabine)

→

Consolidation and Maintenance
HDT + ASCT → R maint for 3 yr

Preferred Second-line Treatment Options

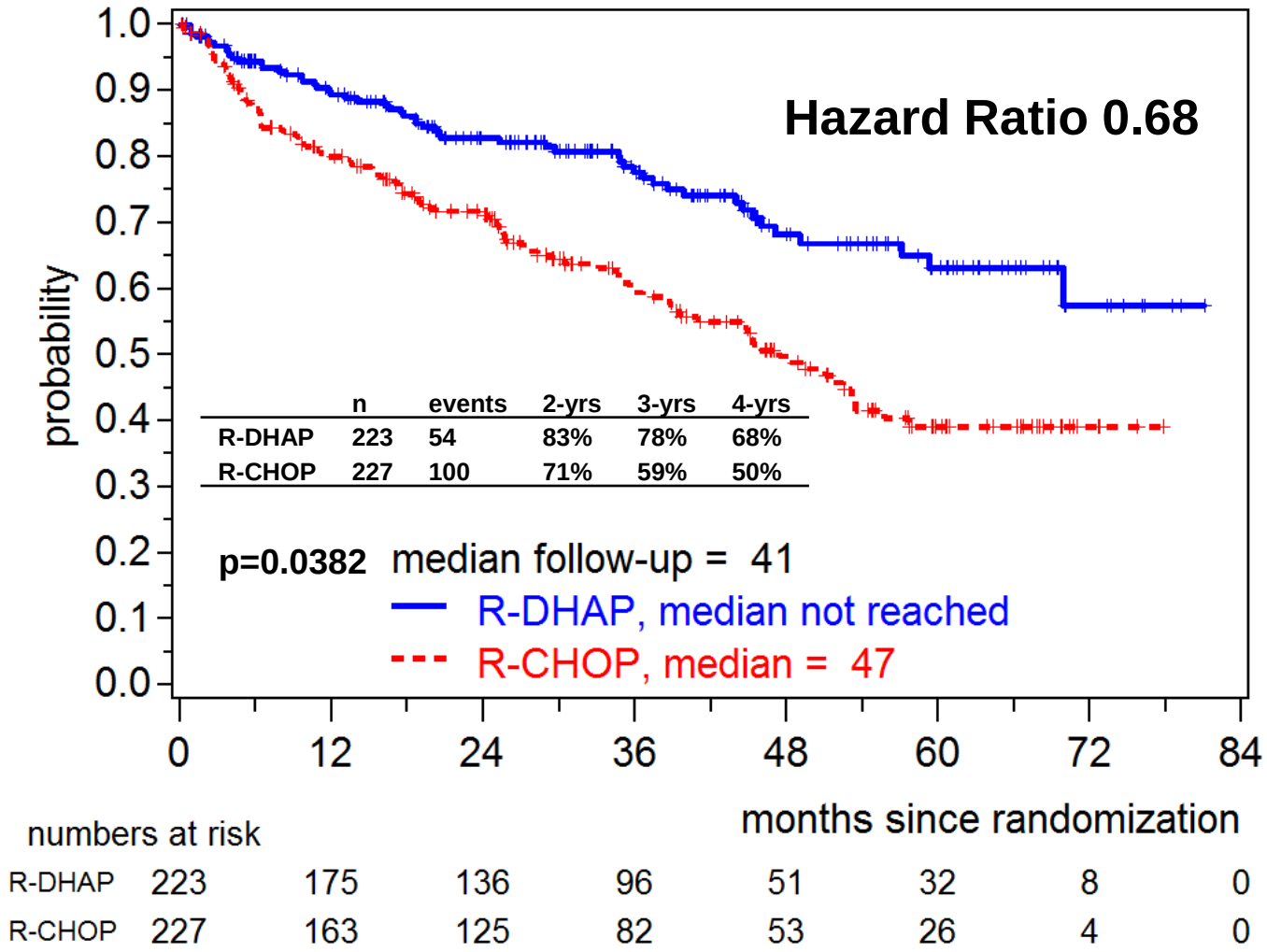
Third-line Treatment

Adattato da NCCN guidelines version 1.0 2024.

Intensive schemes including ASCT

MCL Network younger Trial

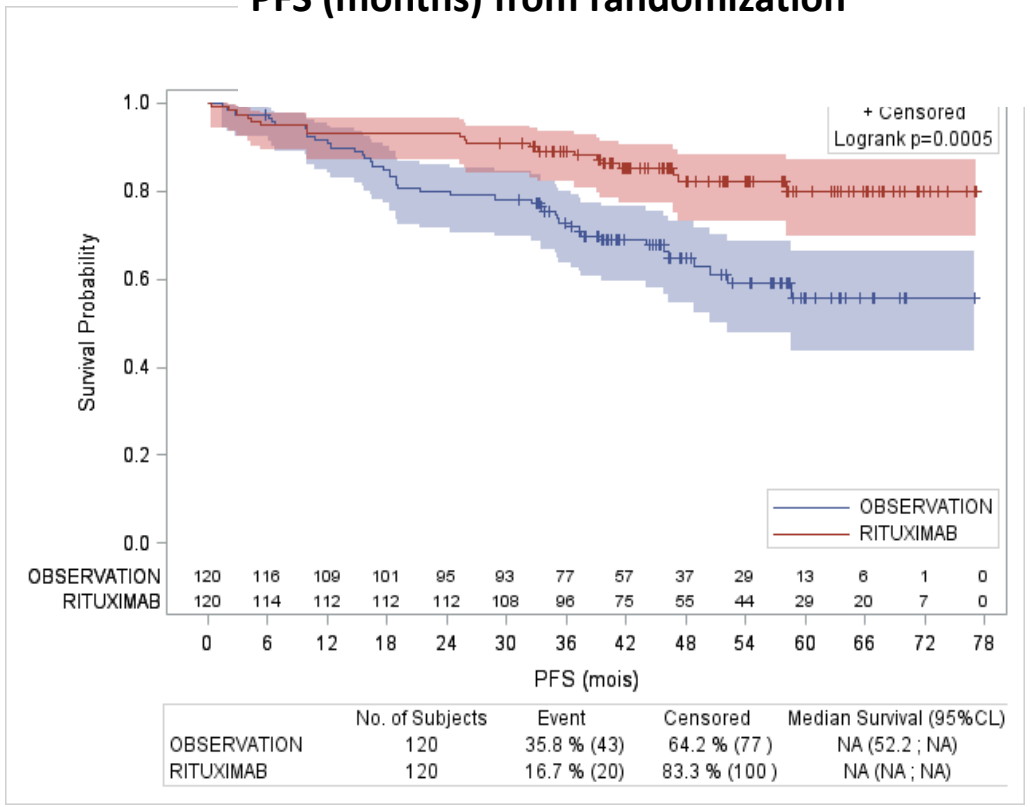
PFS



Hermine O, et al. Lancet Oncology 2013.

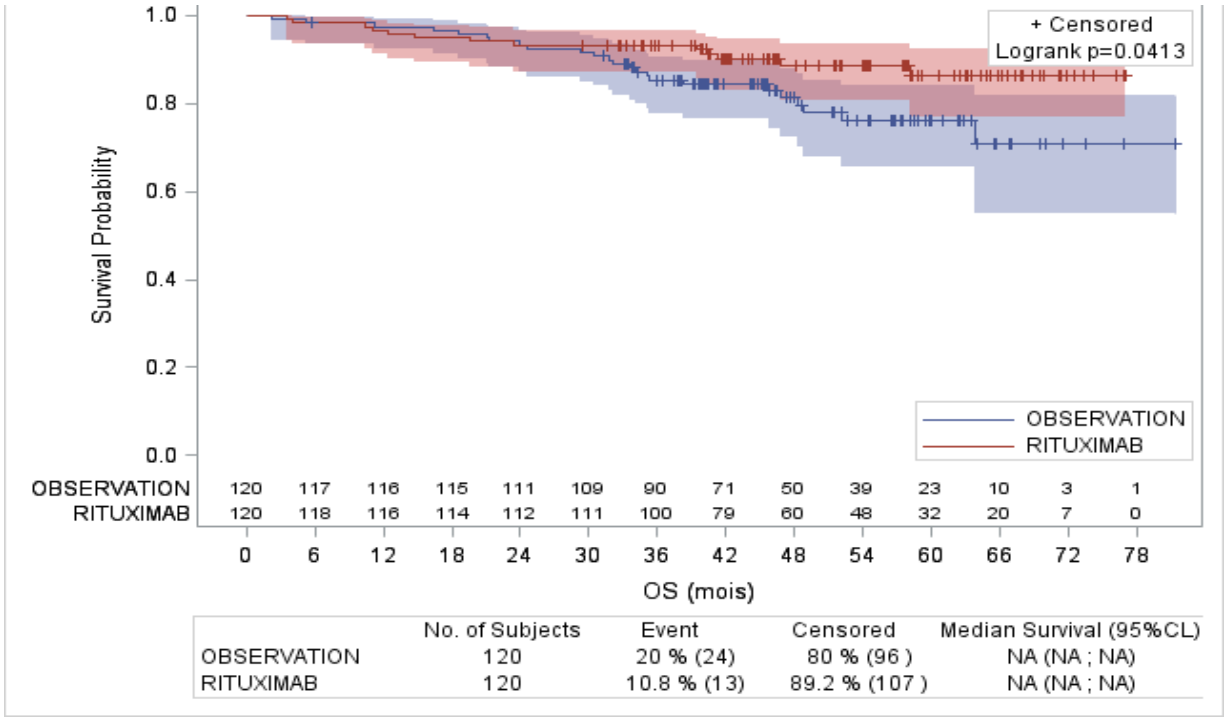
LyMa trial : survival from randomization

PFS (months) from randomization



	No. of Subjects	Event	Censored	Median Survival (95%CL)
OBSERVATION	120	35.8 % (43)	64.2 % (77)	NA (52.2 ; NA)
RITUXIMAB	120	16.7 % (20)	83.3 % (100)	NA (NA ; NA)

OS (months) from randomization



	No. of Subjects	Event	Censored	Median Survival (95%CL)
OBSERVATION	120	20 % (24)	80 % (96)	NA (NA ; NA)
RITUXIMAB	120	10.8 % (13)	89.2 % (107)	NA (NA ; NA)

mFU: 50.2m (46.4-54.2)

	PFS		
	Obs (95%CI)	**vs**	**Rituximab** (95%CI)
24m:	**79.8 %** (71.5-86.0)		**93.3 %** (87.1-96.6)
36m:	**72.8 %** (63.7-79.9)		**89.1 %** (82.0-93.5)
48m:	**64.6 %** (54.6-73.0)		**82.2 %** (73.2-88.4)

	OS		
	Obs (95%CI)	**vs**	**Rituximab** (95%CI)
24m:	**93.3 %** (87.0-96.6)		**93.3 %** (87.1-96.6)
36m:	**85.4 %** (77.5-90.7)		**93.3 %** (87.1-96.6)
48m:	**81.4 %** (72.3-87.7)		**88.7 %** (80.7-93.5)

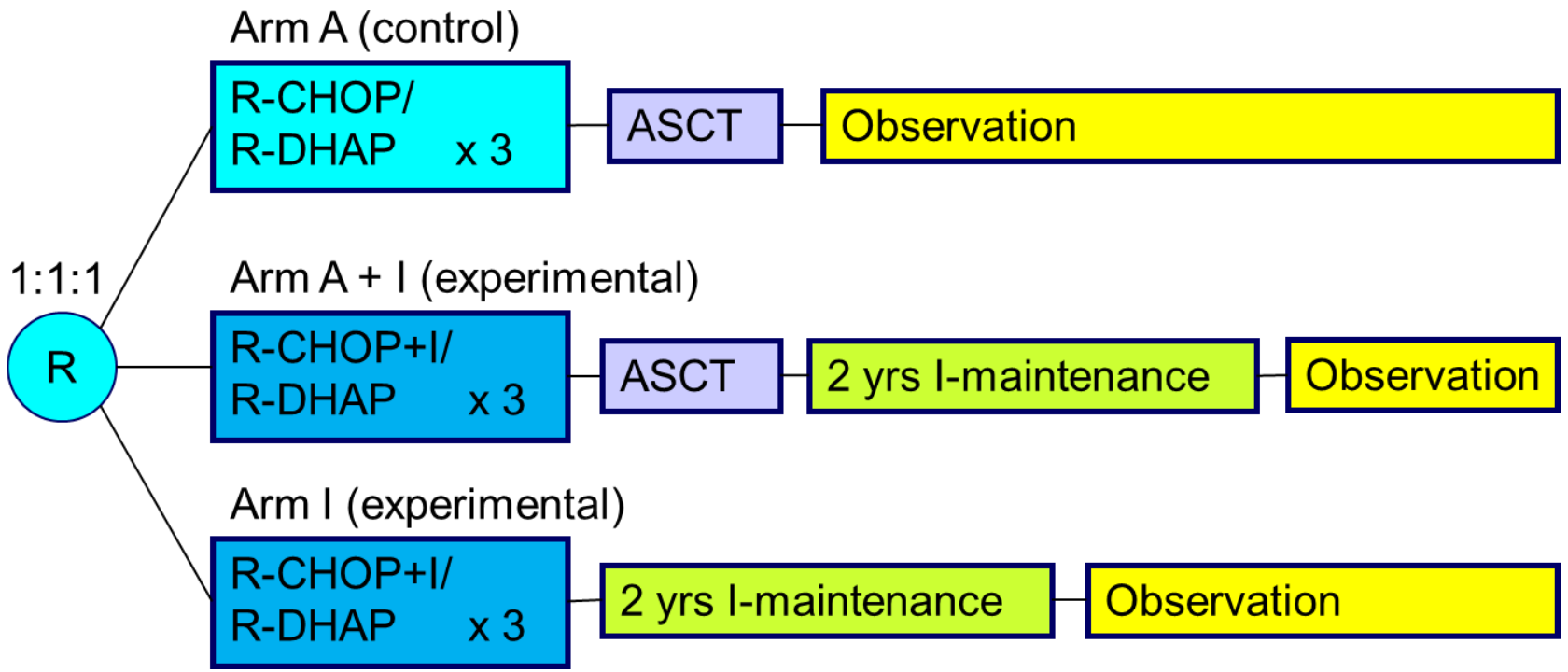
Le Gouill et al. N.Engl.Med 2017

TRIANGLE: Trial Design

- MCL patients
- previously untreated
- stage II-IV
- younger than 66 years
- suitable for HA and ASCT
- ECOG 0-2

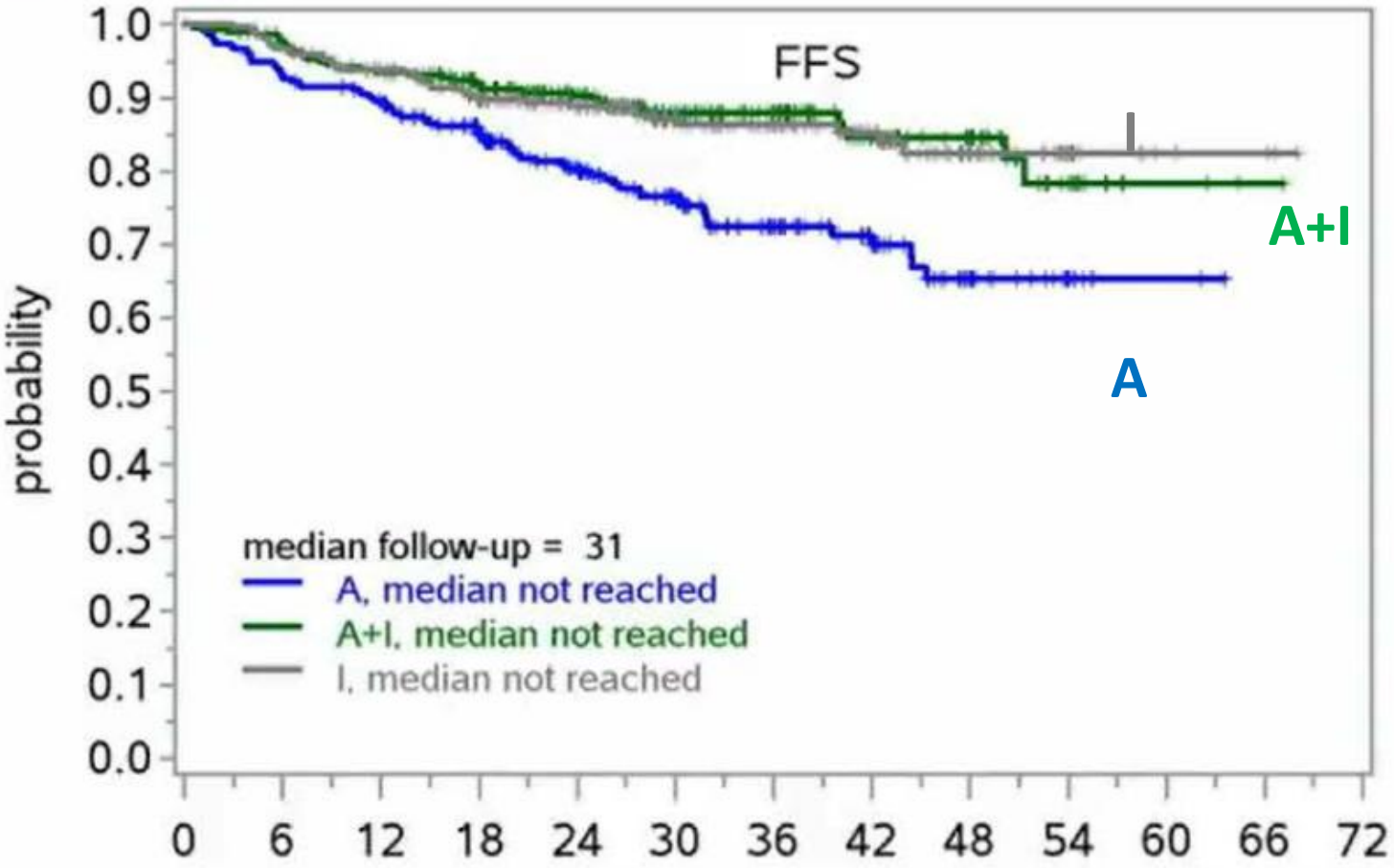
- Primary outcome: FFS

- 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 ?



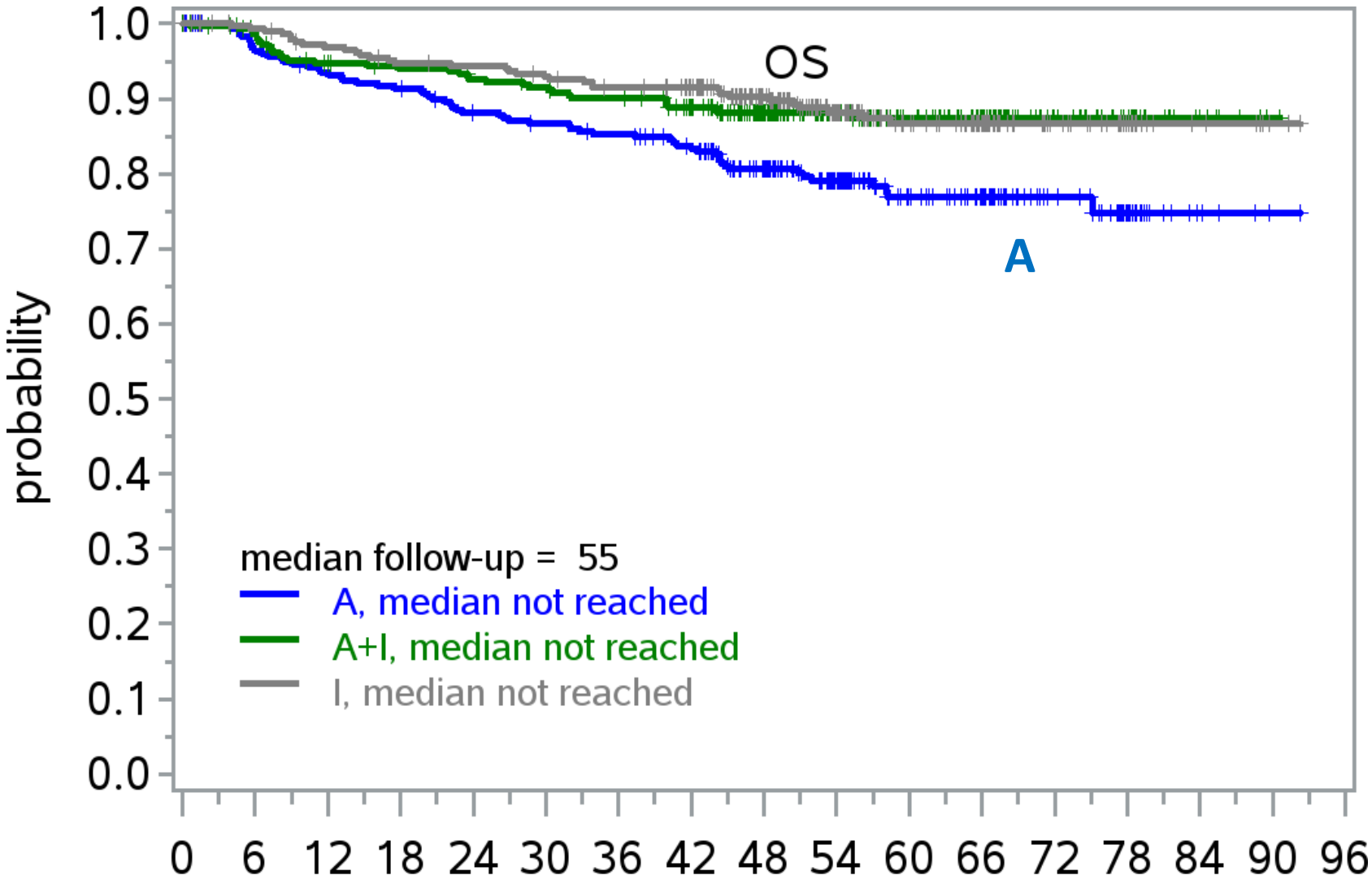
Numbers At Risk												
A	288	252	237	206	162	126	85	54	27	12	2	0
A+I	292	270	253	226	184	137	109	65	40	17	3	1
I	290	269	257	229	180	133	100	68	34	16	4	3

- 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	

Dreyling M et al, ASH 2022

TRIANGLE: Overall survival



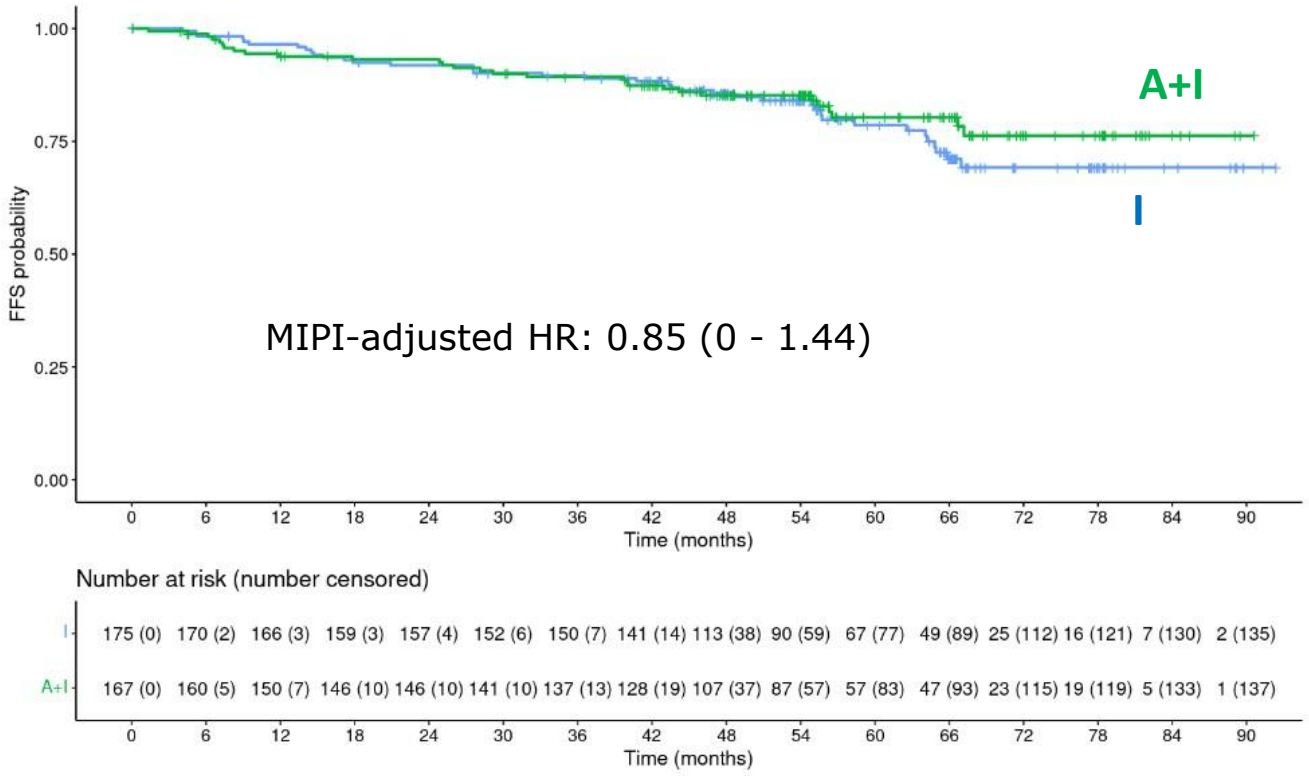
- 4-year OS:
  - A: 81%
    (MCL Younger exp.: 80%)
  - A+I: 88%
  - I: 90%

- two-sided test, (α = 5%):
  - A vs. I: p=0.0019, HR: 0.565
  - A vs. A+I: p=0.0036, HR I: 0.587
  - A+I vs. I: ongoing

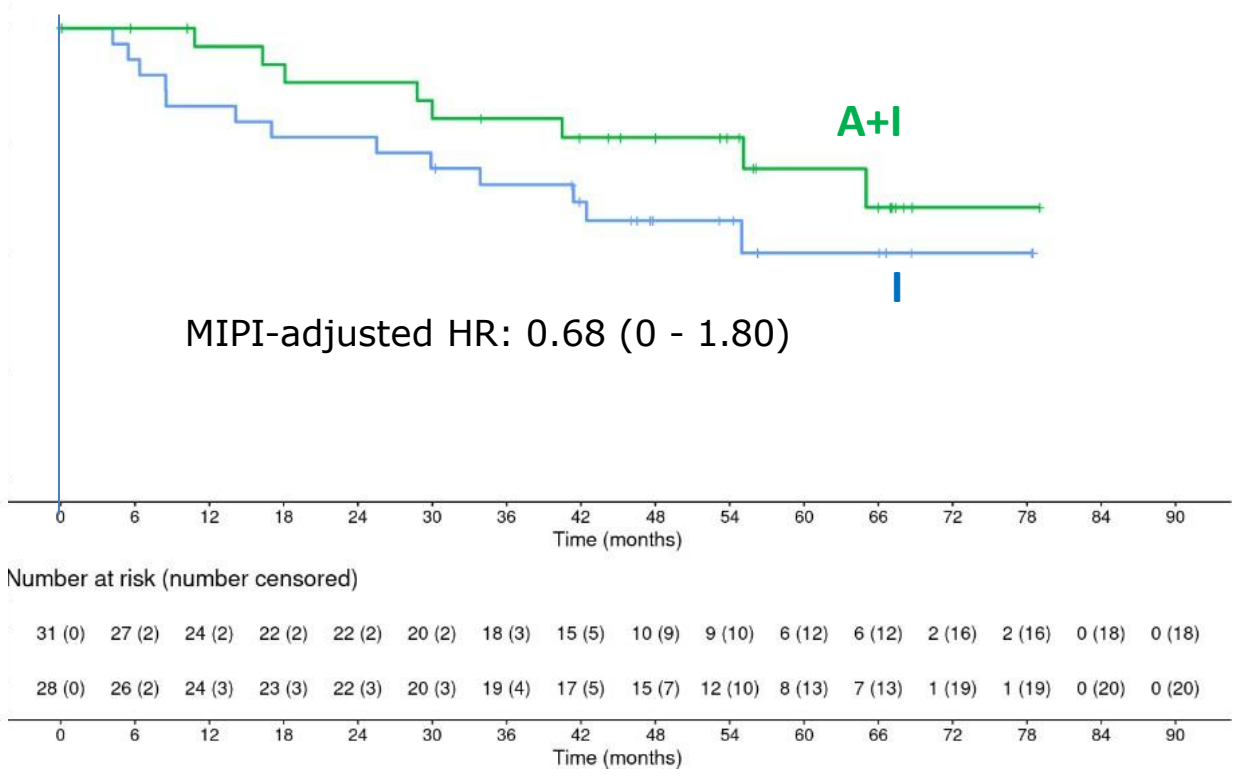
Dreyling M et al, ASH 2022

TRIANGLE: A+I vs. I (FFS) and p53 high expression

P53 low



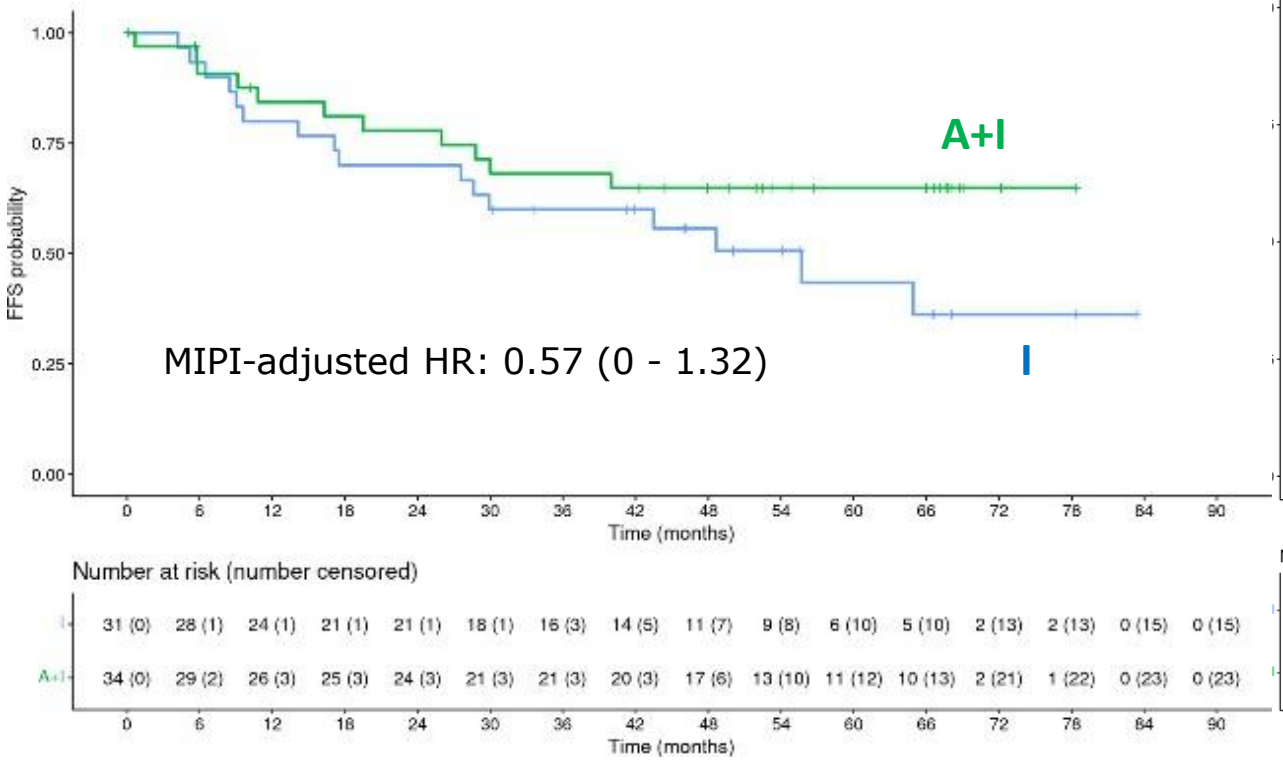
P53 high



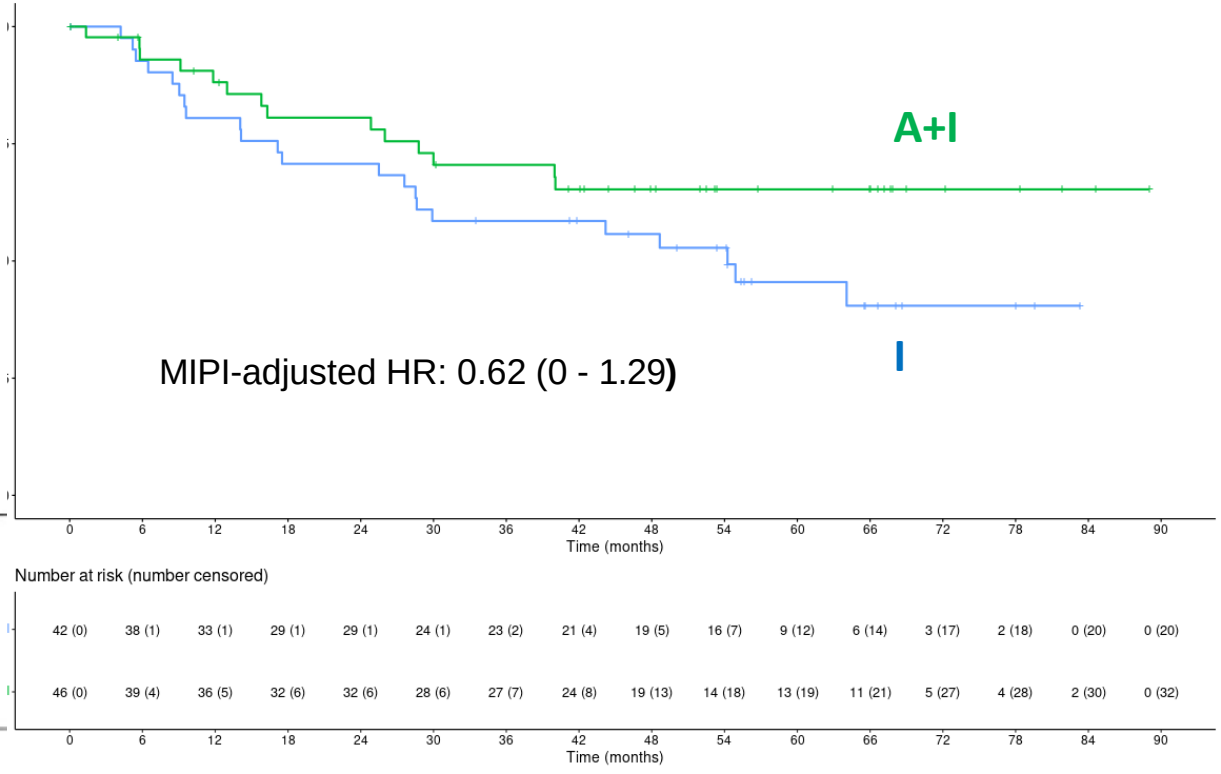
Dreyling M et al, ASH 2024

TRIANGLE: A+I vs. I (FFS) Ki-67 (50% cut-off) and citology blastoid

Citology Blastoid



Ki67 > 50%



Dreyling M et al, ASH 2024

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Less Aggressive Chemotherapy
BR
R-CHOP
RBAC

→ **Maintenance**
After R-CHOP: R maint until Progression.

Preferred Second-line Treatment Options

BTK inhibitor
- Ibrutinib

Third-line Treatment

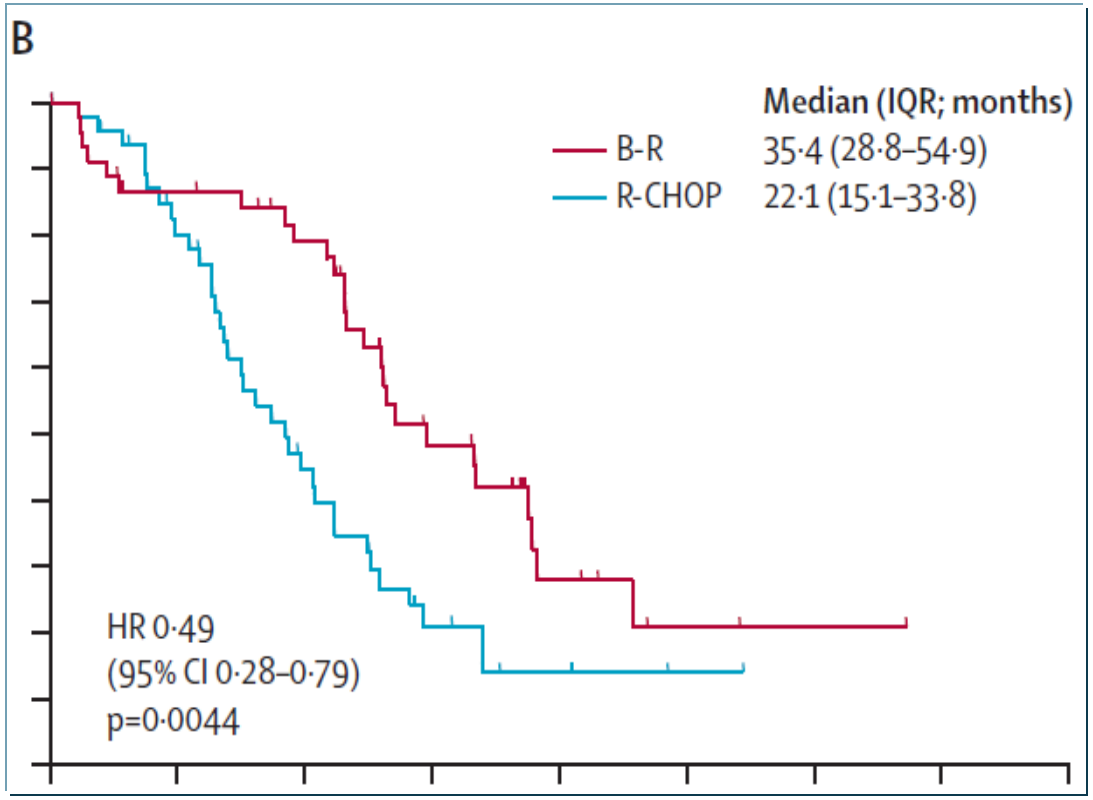
Brexucabtagene autoleucel (after chemoimmunotherapy and BTK inhibitor)

Pirtobrutinib

Adattato da NCCN guidelines version 1.0 2024.

Elderly MCL: Bendamustine-Rituximab (B-R) vs. R- CHOP

StiL NHL 1-2003



	B-R (n=261)	R-CHOP (n=253)	p value
Alopecia	0	245 (100%)*	<0·0001
Paresthesia	18 (7%)	73 (29%)	<0·0001
Stomatitis	16 (6%)	47 (19%)	<0·0001
Skin (erythema)	42 (16%)	23 (9%)	0·024
Skin (allergic reaction)	40 (15%)	15 (6%)	0·0006
Infectious episodes	96 (37%)	127 (50%)	0·0025
Sepsis	1 (<1%)	8 (3%)	0·019

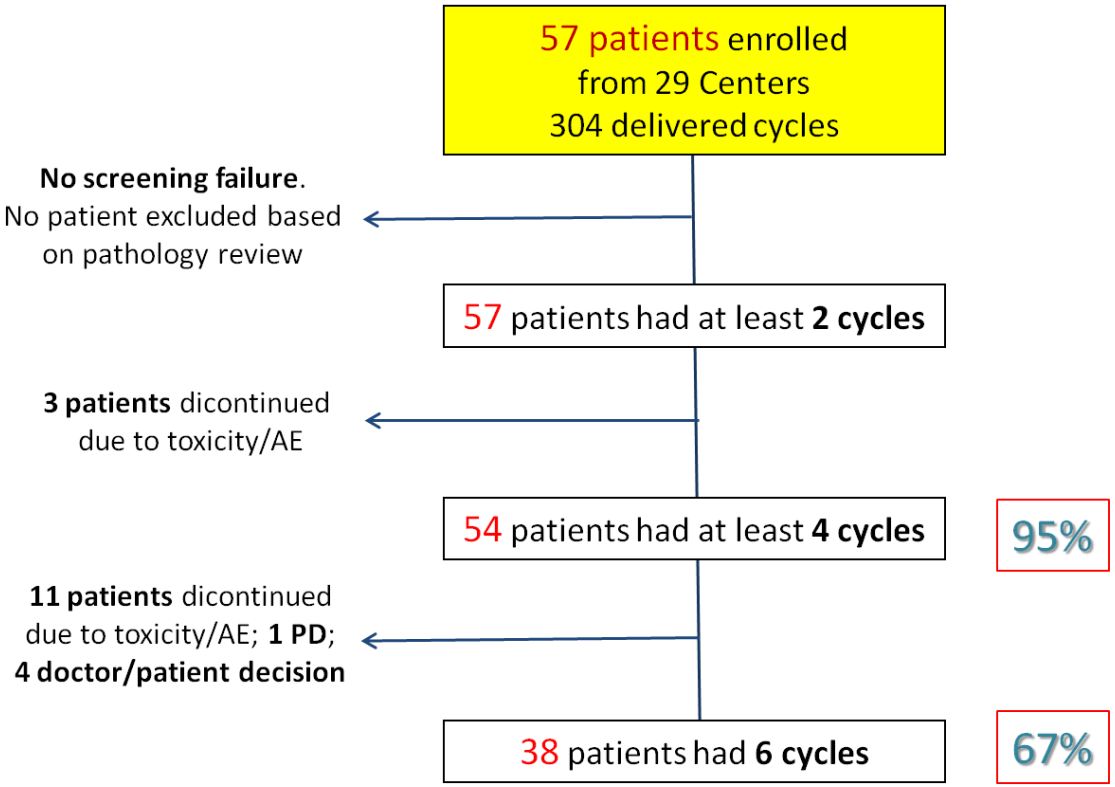
Rummel MJ et al. Lancet 2013;381:1203-10

FIL R-BAC 500 trial

✓ Patients' characteristics at inclusion

	Overall (57)	%
Age, years median (range)	71 (61-79)	
Gender male	43	75
Performance Status 0-1	54	94
AAS III-IV	52	91
MIPI risk category low intermediate high	9 23 25	16 40 44
BM involvement	36	63
Histology classical pleomorphic blastoid	43 8 6	75 14 11
Ki-67 (%) ≥30% median (range)	16 20 (5-85)	31

✓ Trial profile



Visco C. et al JCO 2017

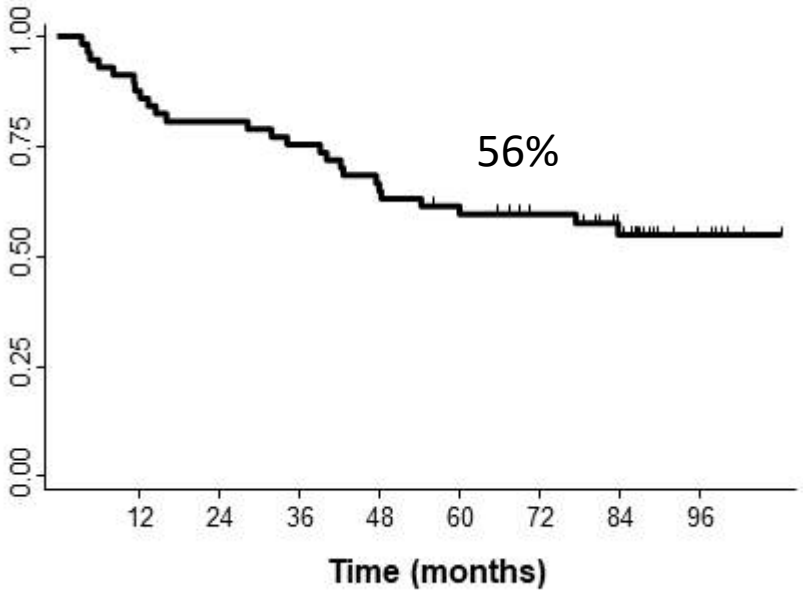
Rituximab Plus Bendamustine and Cytarabine (R-BAC) in Elderly Patients with Newly Diagnosed Mantle Cell Lymphoma: Long Term Follow-up and Mrd Results of a Phase 2 Study from the Fondazione Italiana Linfomi

FIL-RBAC500

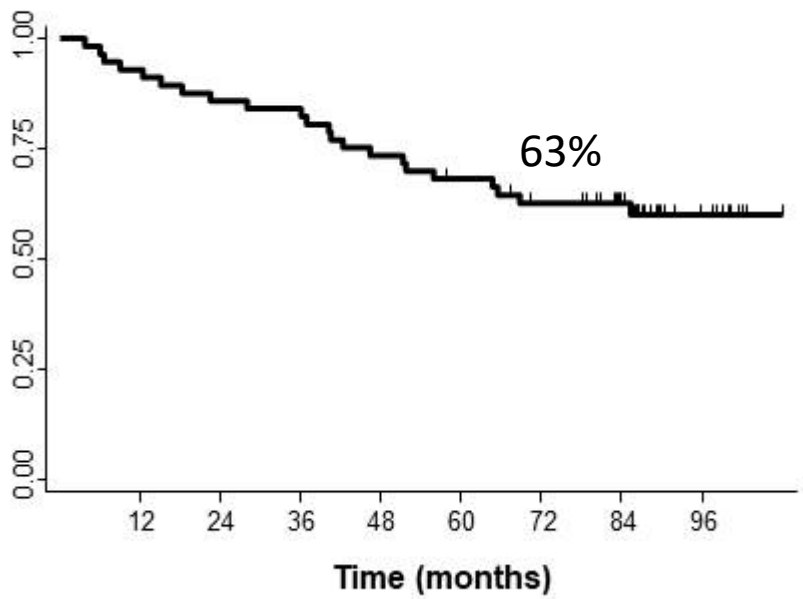
FONDAZIONE ITALIANA LINFOMI

- 7 years of median follow-up (86 months, range 57-107),
- median OS and PFS for all patients were not reached

7-yrs PFS



7-yrs OS



- Adverse predictive factors affecting PFS were blastoid morphology ($p<0.05$), elevated Ki67 $\geq$ 30% ($p<0.05$), and failure to achieve CR after 2 cycles ($p=0.03$).

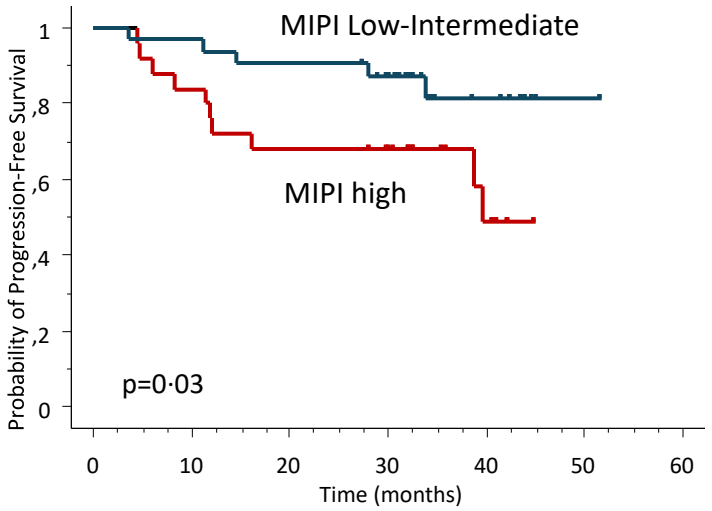
Tisi MC et al. Blood 2021 (384)

FIL R-BAC 500 trial Univariate analysis for PFS

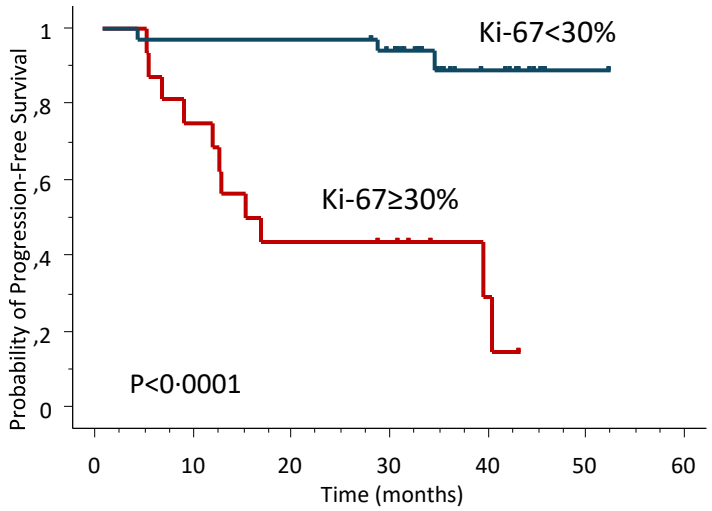
FIL-RBAC500

FONDAZIONE ITALIANA LINFOMI

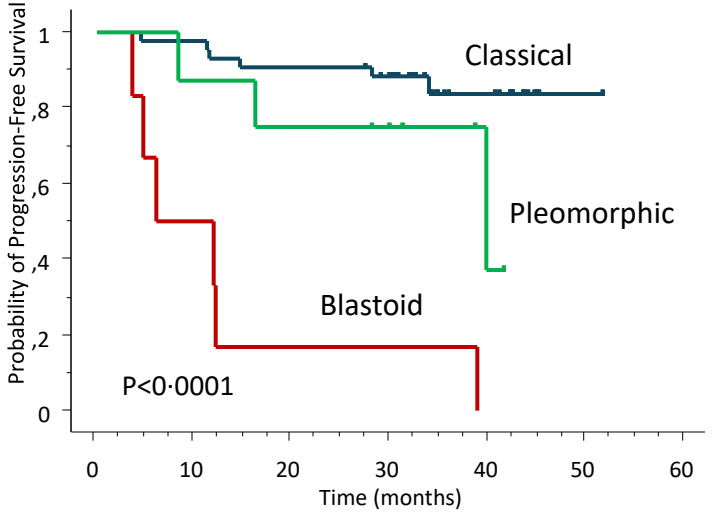
Grouping Variable: **MIPI**

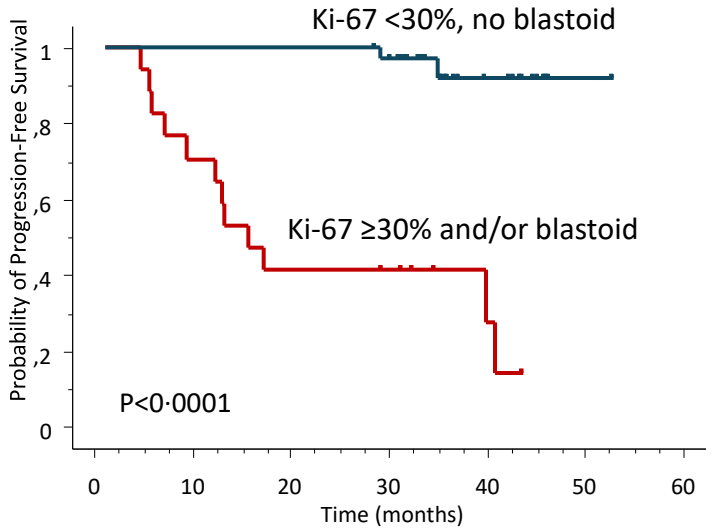


Grouping Variable: **Ki-67**



Grouping Variable: **Morphology**

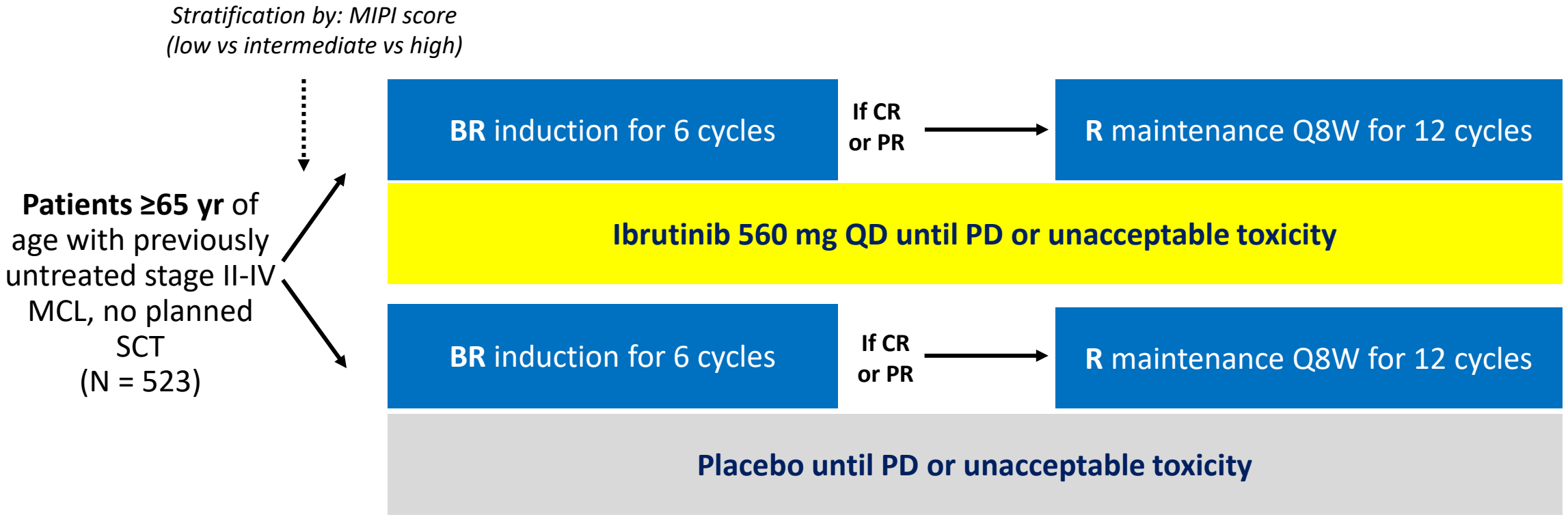




Visco C. et al JCO 2017

SHINE: A Randomized, Double-Blind, Phase 3 Study

- Multicenter, randomized, double-blind, placebo-controlled phase III trial

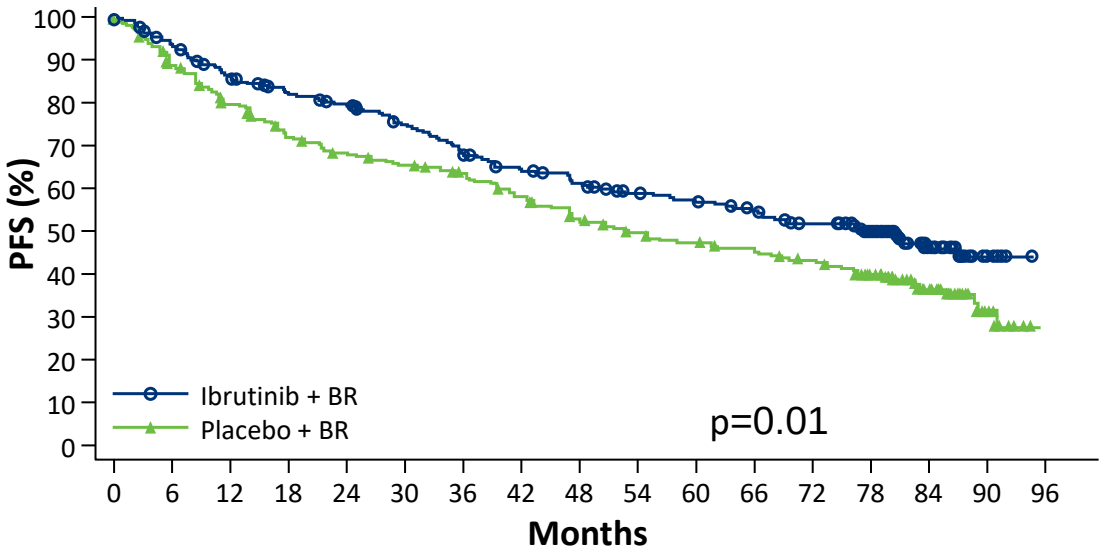


- **Primary endpoint:** investigator-assessed PFS (in ITT)
- **Key secondary endpoints:** ORR, time to next treatment, OS, safety

Wang M et al . NEJM. 2022;[Epub].

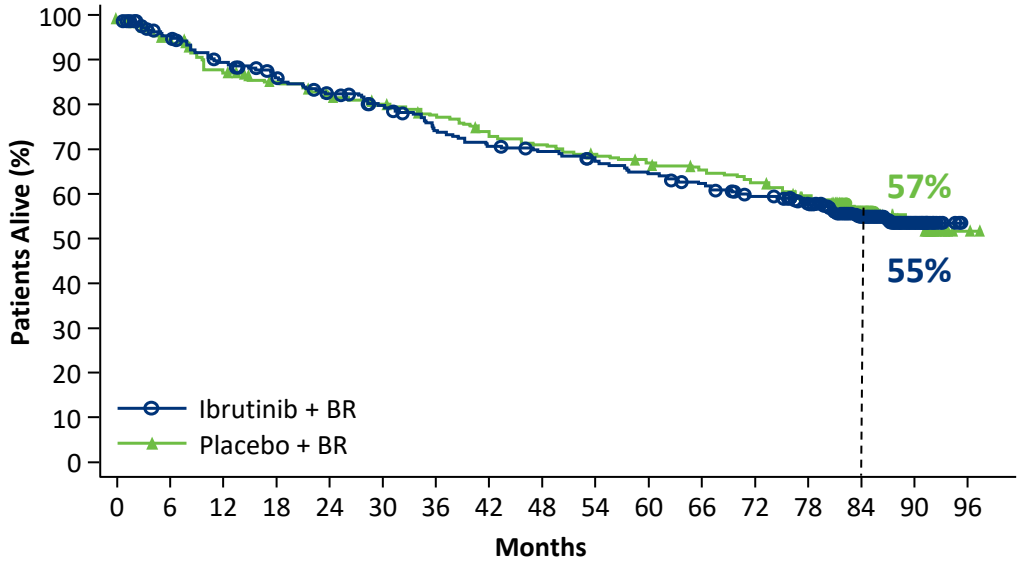
SHINE: A Randomized, Double-Blind, Phase 3 Study

Median PFS 6.7 vs 4.4 years



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

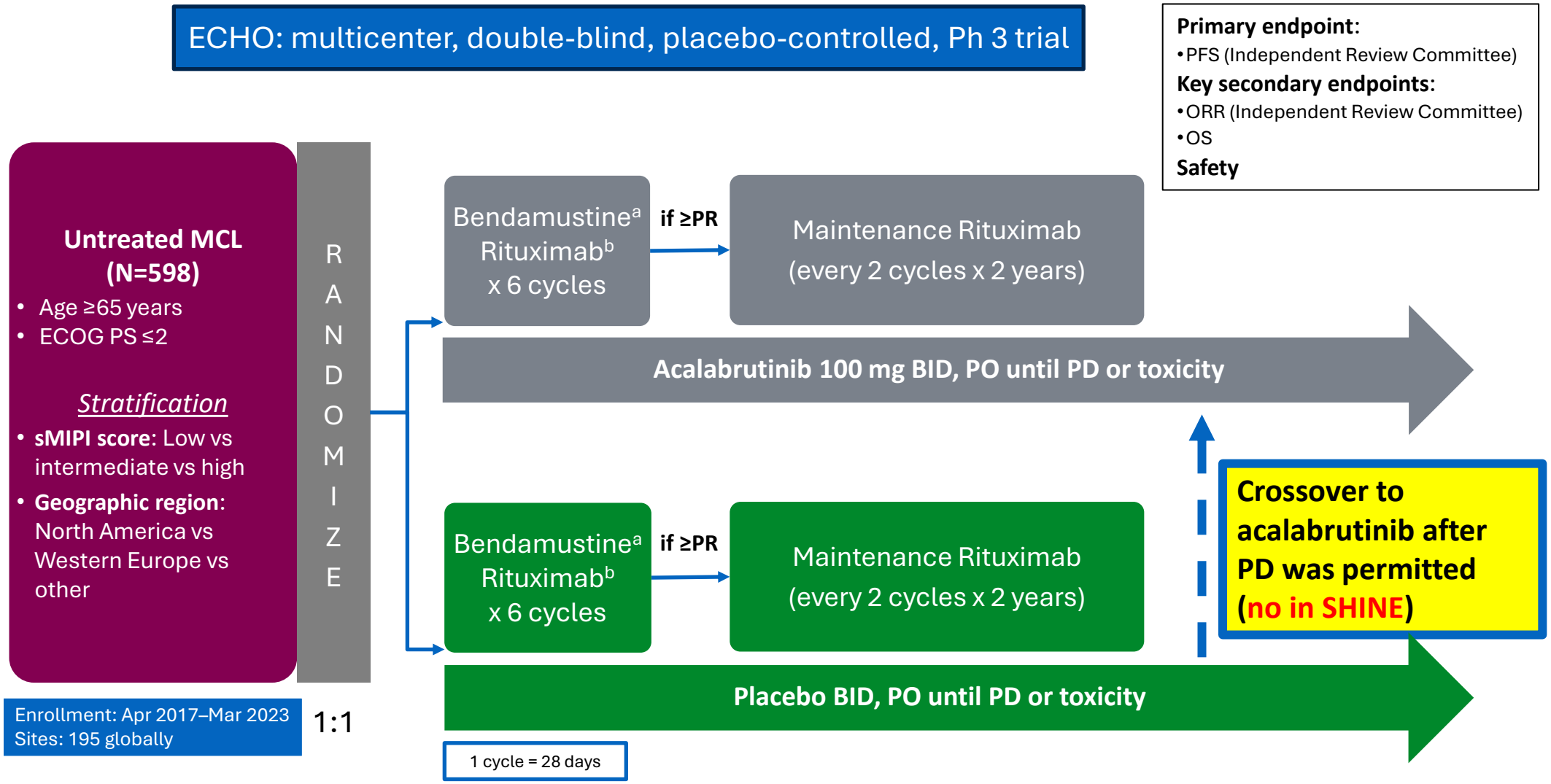


Patients at Risk

Ibrutinib + BR	261	239	221	208	197	187	171	163	158	152	145	138	128	118	70	25	0
Placebo + BR	262	244	223	212	203	197	188	177	171	165	159	154	147	137	90	31	2

Wang M et al . NEJM. 2022;[Epub].

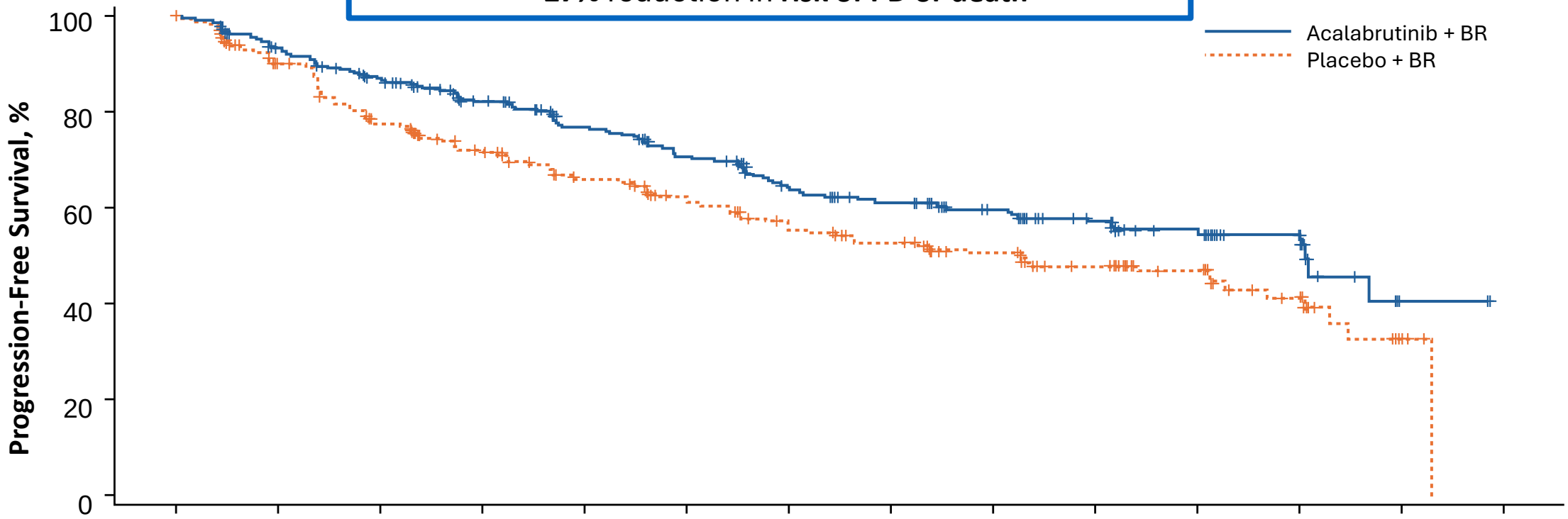
ECHO Phase III trial: statistically significant improvement in progression-free survival in 1st-line elderly MCL



Wang et al. EHA 2024 and ASH 2024

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

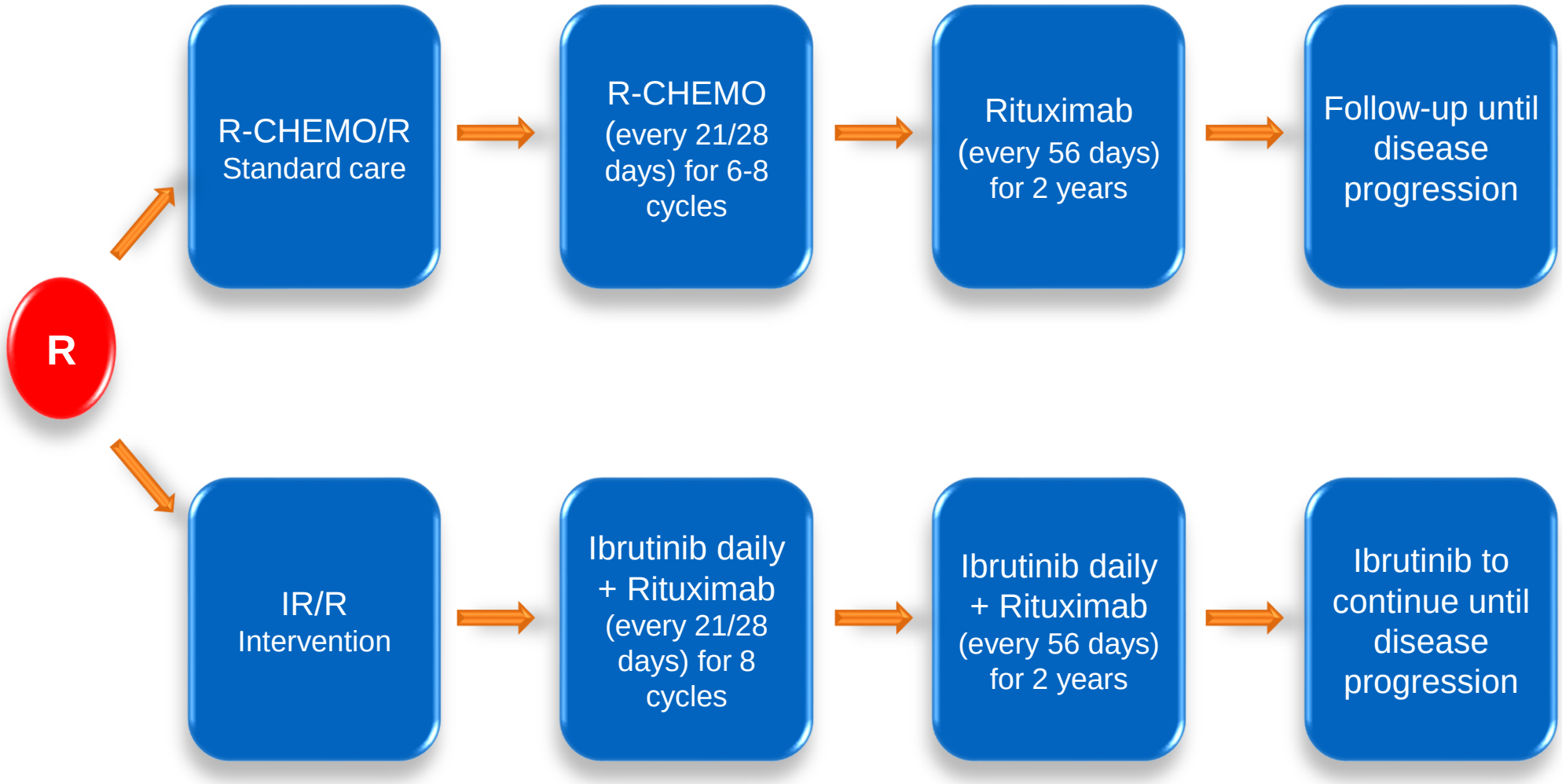
- **Significant improvement in median PFS by ~17 mo**
- **27%** reduction in **risk of PD or death[a]**



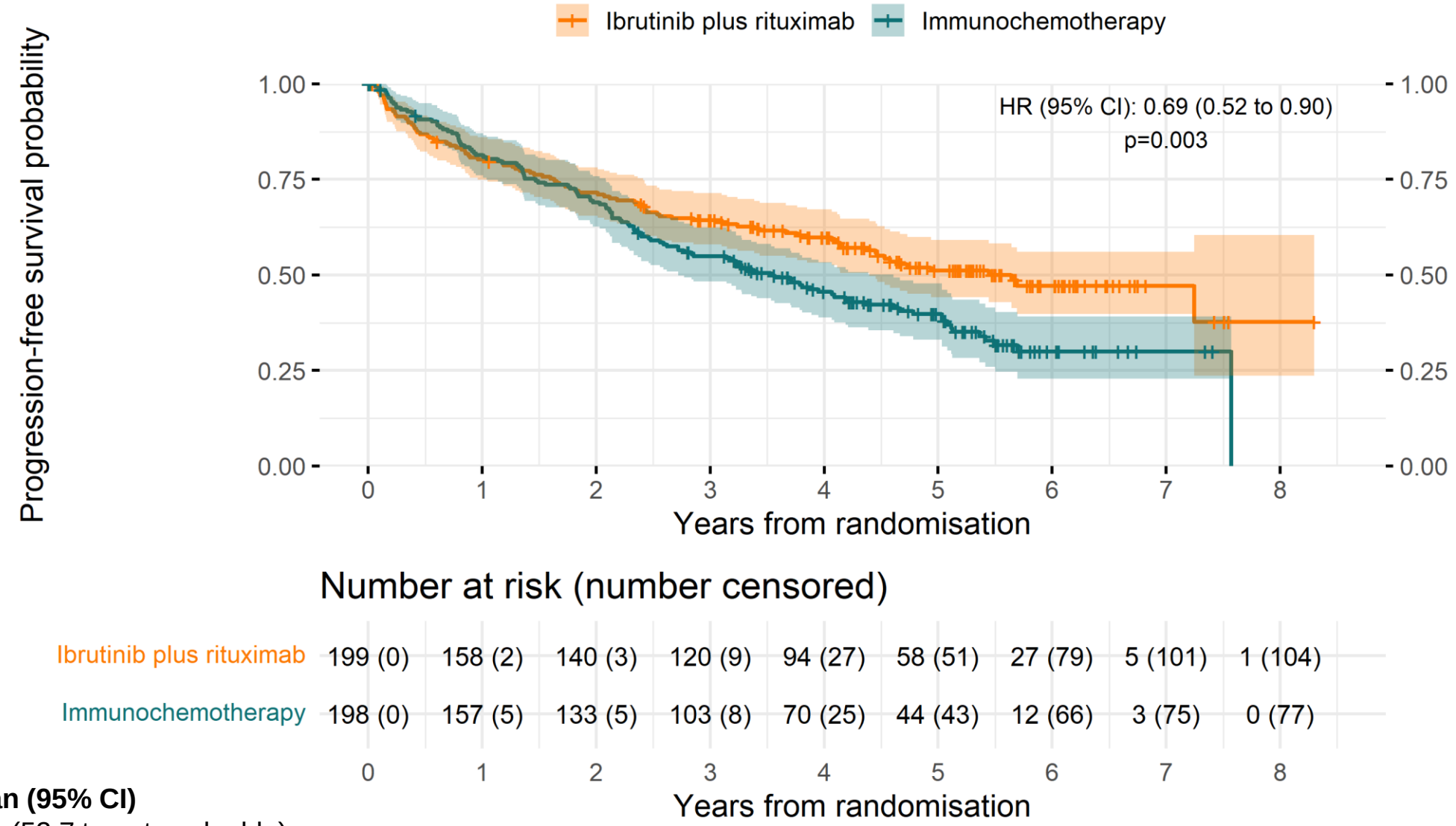
Median PFS, months	66.4	49.6
(95% CI)	(55.1, NE)	(36.0, 64.1)
Stratified HR (95% CI), log-rank *P*-value	**0.73** (0.57, 0.94), ***P*=0.0160**	

Wang et al. EHA 2024 and ASH 2024

Elderly mantle cell lymphoma ENRICH – NCRI multicentre Randomised open label phase II/III trial



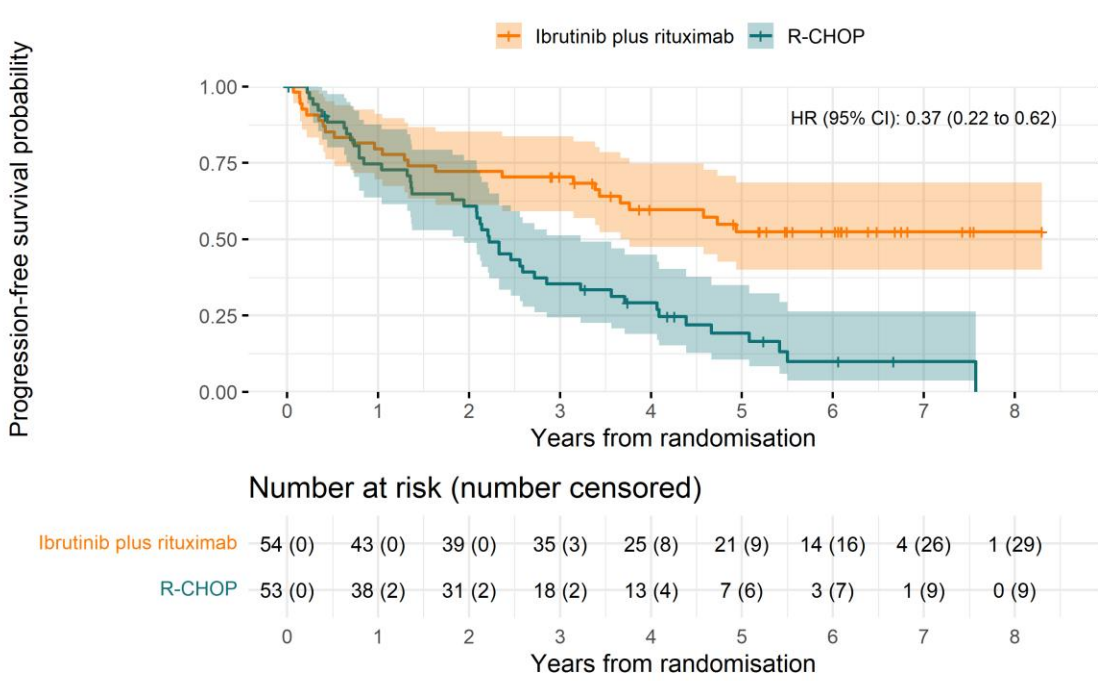
Progression-free survival

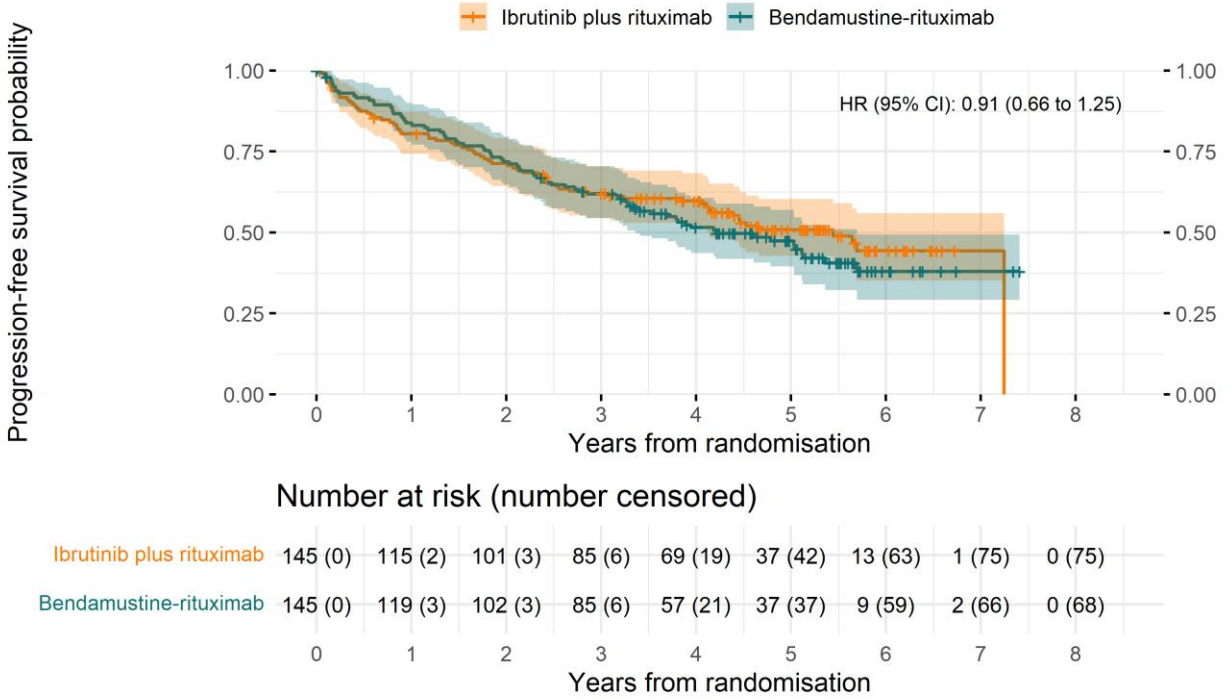


PFS median (95% CI)
IR: 65.3 mo (52.7 to not evaluable)
R-chemo: 42.4 mo (32.7 to 55.3)

Lewis D.J.et al ASH 2024

PFS for R-CHOP and BR choice





5-year PFS (95% CI)
IR: 52.4% (40.0% to 68.6%)
R-CHOP: 19.2% (10.6% to 35.1%)

5-year PFS (95% CI)
IR: 50.8% (42.8% to 60.4%)
BR: 47.4% (39.5% to 56.9%)

Lewis D.J.et al ASH 2024

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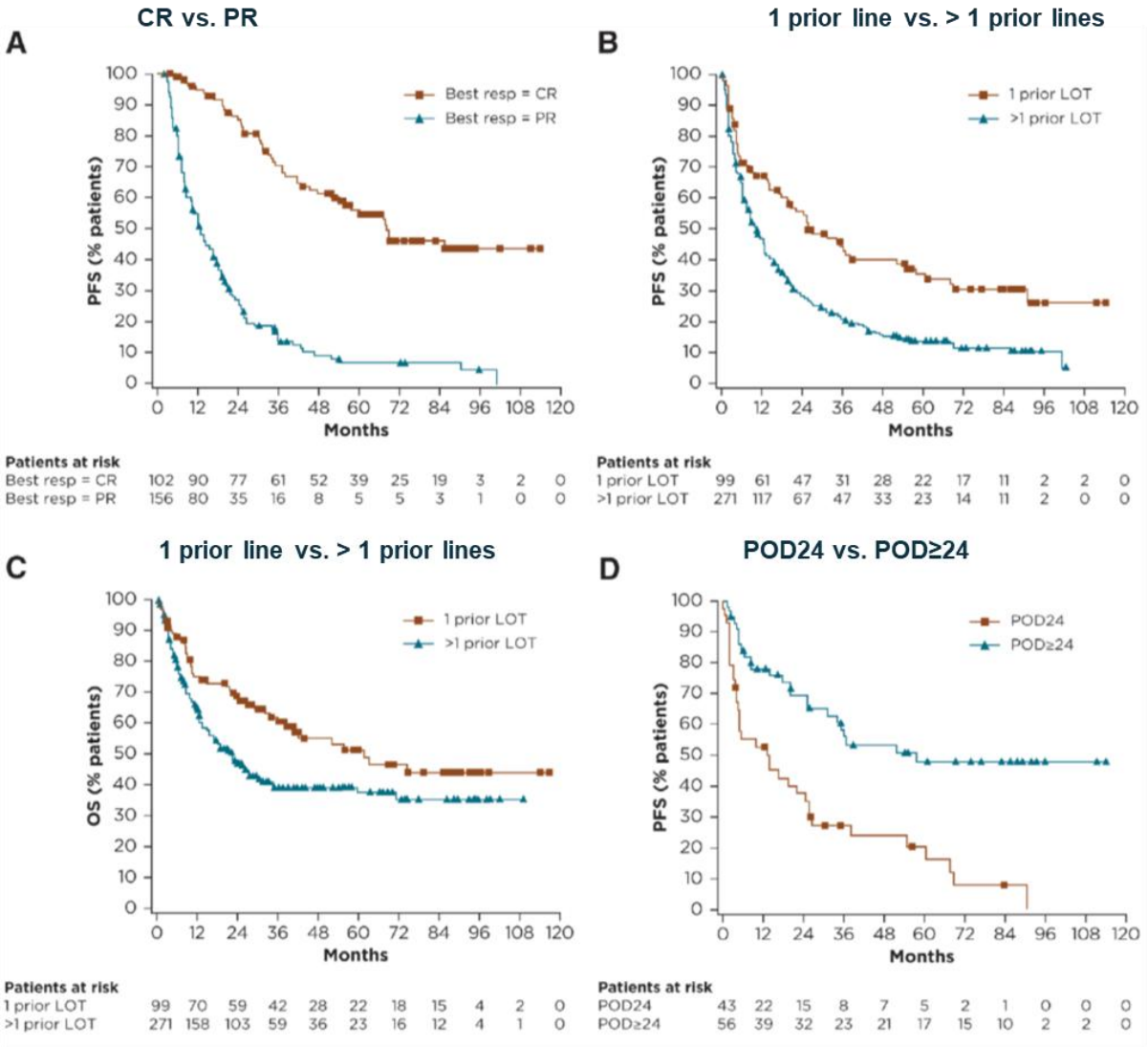
Brexucabtagene autoleucel (after chemoimmunotherapy and BTK inhibitor)

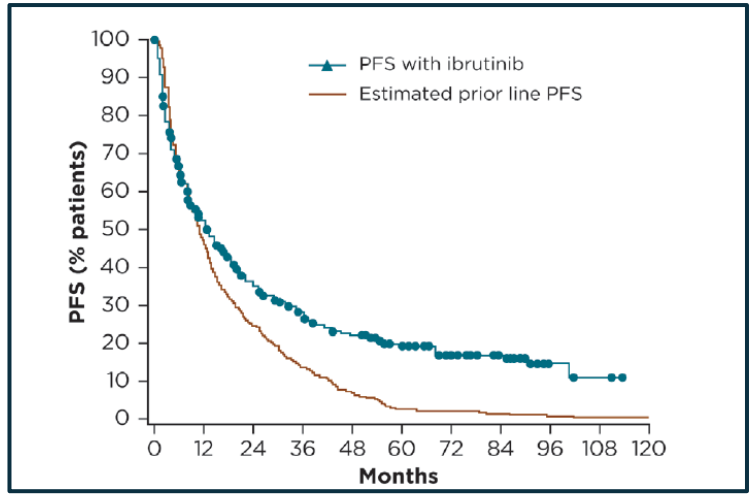
Pirtobrutinib

Adattato da NCCN guidelines version 1.0 2024.

Ibrutinib in RR-MCL: PFS and OS by status after first line of therapy



- Pooled analysis of ibrutinib treatment in **R/R MCL (3 trials; 370 pts)** @ FU of ~10 years [PCYC-1104, SPARK, RAY]
- Single-agent ibrutinib mitigates the historical trend of successive decline in PFS with each line of CIT regardless of age and prior LOT
- Patients achieving PFS > prior regimen:
  - low-risk sMIPI
  - non-bulky disease
  - non-blastoid histology
  - wild-type TP53



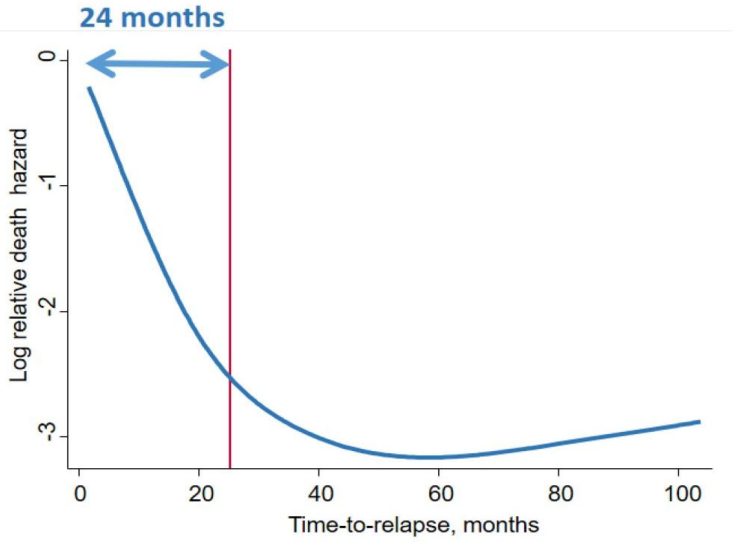
Dreyling M. et al. Hemasphere. 2022

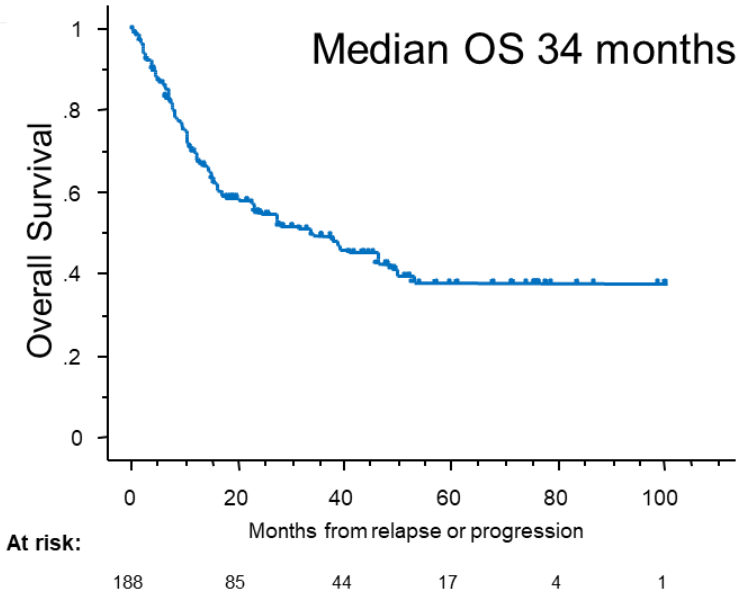
Time to progression of MCL after HDAC-based regimens defines patients at high risk

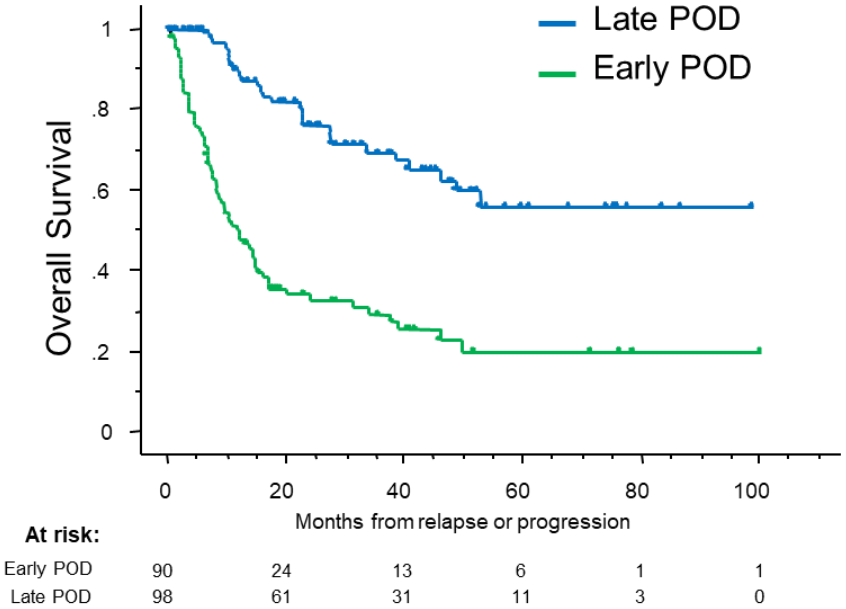
FONDAZIONE ITALIANA LINFOMI

Early POD definition

Trend in the risk of death*



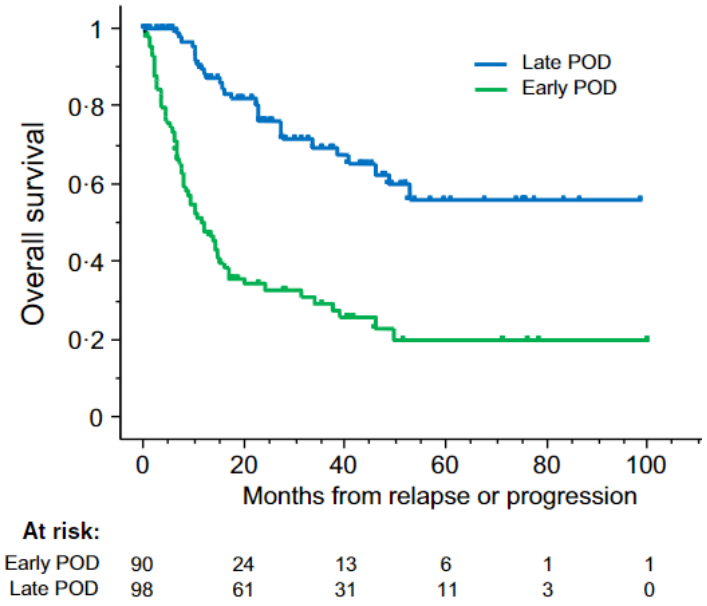




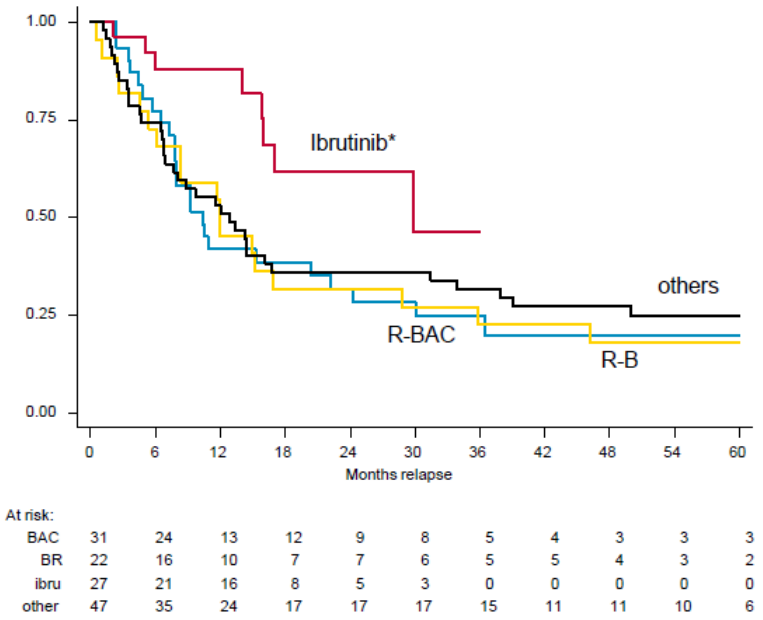
POD within 2 years of diagnosis identifies a population of patients who have remarkably poor outcomes

Visco C, BJH 2019

Standard of care for first relapse: Time to POD



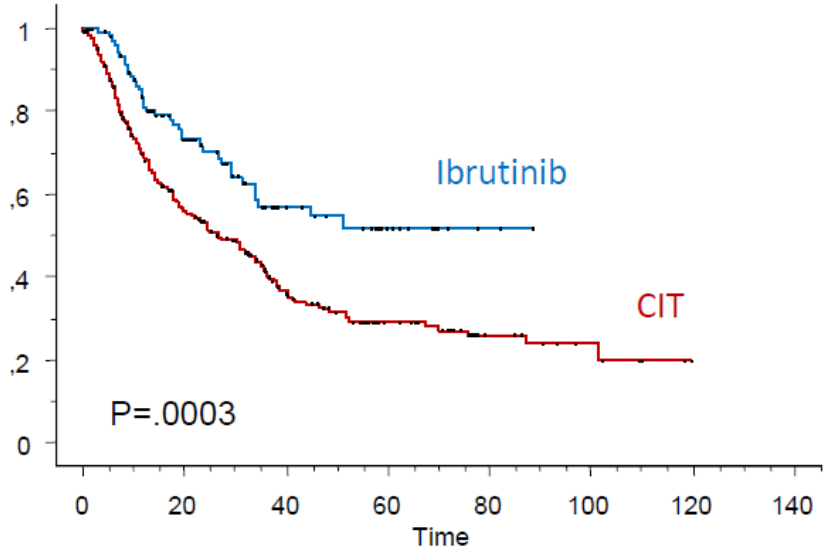
Early POD



*Ibru vs R-B and R-BAC (P=0.02); vs others (P=0.03)

PFS-2

Late POD



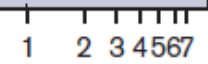
Median 26 months for CIT;
NR for Ibrutinib

Visco C et al, BJH 2019; Visco C et al, Leukemia 2020; Malinverni C et al, Blood 2024

Estimating duration of benefit from second line BTK inhibitors in patients with RR-MCL

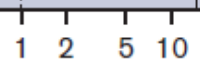
A PFS-2

Variable		N	Hazard ratio	P
POD	POD>24	79	Reference	
	POD6–24	51	2.19 (1.47, 3.28)	<.001
	POD6	30	4.82 (3.04, 7.65)	<.001
KI67	<30%	92	Reference	
	>=30%	68	1.47 (1.11, 1.94)	.007
MIPI	Low	49	Reference	
	Intermediate or High	111	1.18 (0.81, 1.72)	.384

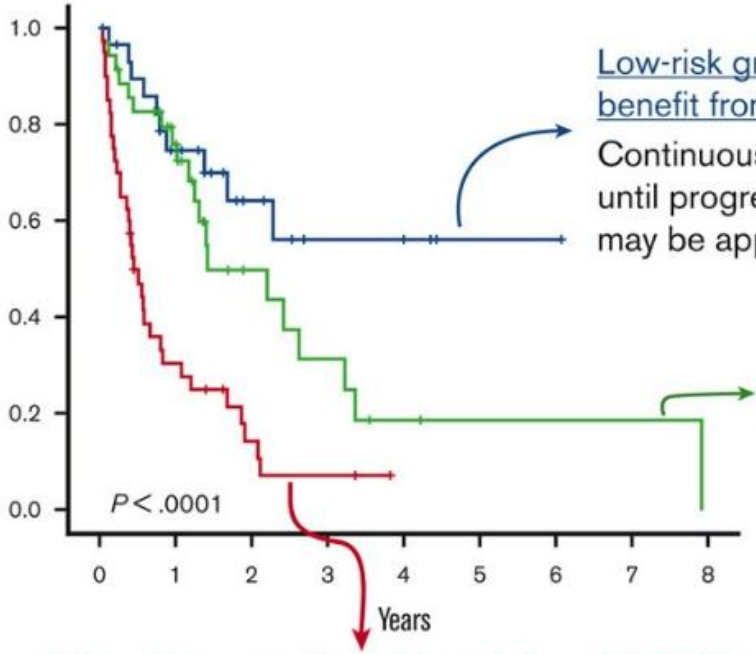


B OS-2

Variable		N	Hazard ratio	P
POD	POD>24	79	Reference	
	POD6–24	51	2.88 (1.20, 6.93)	.02
	POD6	30	5.24 (2.29, 12.00)	<.001
KI67	<30%	92	Reference	
	>=30%	68	1.43 (1.06, 1.93)	.02
MIPI	Low	49	Reference	
	Intermediate or High	111	0.93 (0.76, 1.15)	.51



The MCL BTKi MIPI categorizes these results into three clinically relevant PFS2 subgroups (also in QxMD).



Low-risk group: sustained benefit from 2L BTKi

Continuous BTKi monotherapy until progression or toxicity may be appropriate

Intermediate-risk group:

Either approach is reasonable

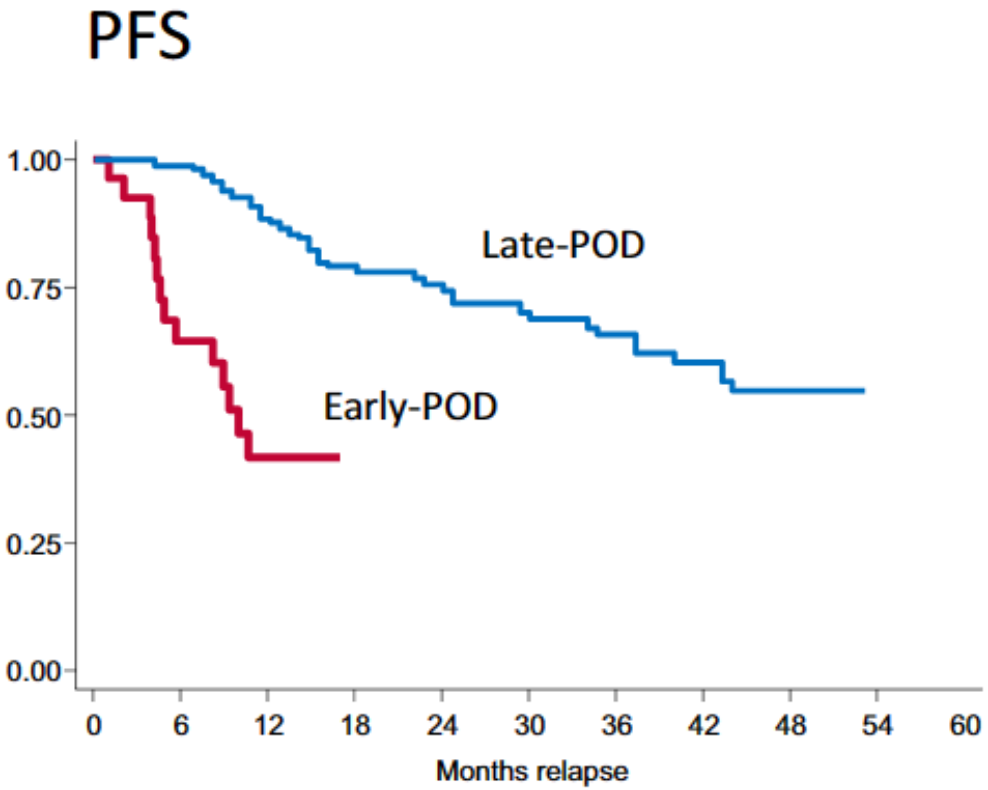
High-risk group: limited benefit from 2L BTKi

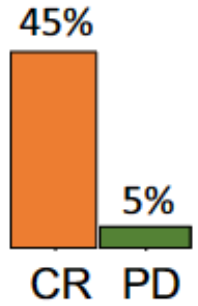
Would benefit from alternatives to continuous BTKi monotherapy

- Early CAR T-cell therapy
- Early Allogeneic SCT
- Novel agents as standalone therapy or together with BTKi

Villa D, et al. Blood Adv. 2023; 7, 4576

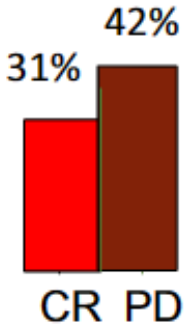
Ibrutinib at first relapse and CarT





Late-POD

Standard approach during BTKi
Refer to CAR-T centre if suboptimal response or high-risk features (i.e. TP53 mutation)



Early-POD

Refer to CAR-T centre at start of therapy
Close clinical monitoring
Restage 8-12 weeks

Patient identification at first relapse (before starting 2L): High risk patients

- Blastoid/pleomorfic morphology
- TP53 mut (including high expression of p53 with immunohistochemistry)
- Ki 67 > 50%
- Bulky > 5 cm
- POD24
- sMIPI high score

Visco, BJH 2023; Eyre BJH 2023

Agenda

- First line therapy of younger / fit patients (is changing)
- First line therapy of elderly/ unfit patients
- Treatment in first relapse
- Treatment after BTKi failure

Current Treatment in Mantle Cell Lymphoma

Preferred First-line Treatment Options

Aggressive Chemotherapy
R-DHAP (cisplatin, or oxaliplatin)
R-CHOP/R-DHAP (alternating)
NORDIC (maxi-CHOP/R + HD cytarabine)

→ **Consolidation and Maintenance**
HDT + ASCT → R maint for 3 yr

Less Aggressive Chemotherapy
BR
R-CHOP
RBAC

→ **Maintenance**
After R-CHOP: R maint until Progression.

Preferred Second-line Treatment Options

BTK inhibitor
- Ibrutinib

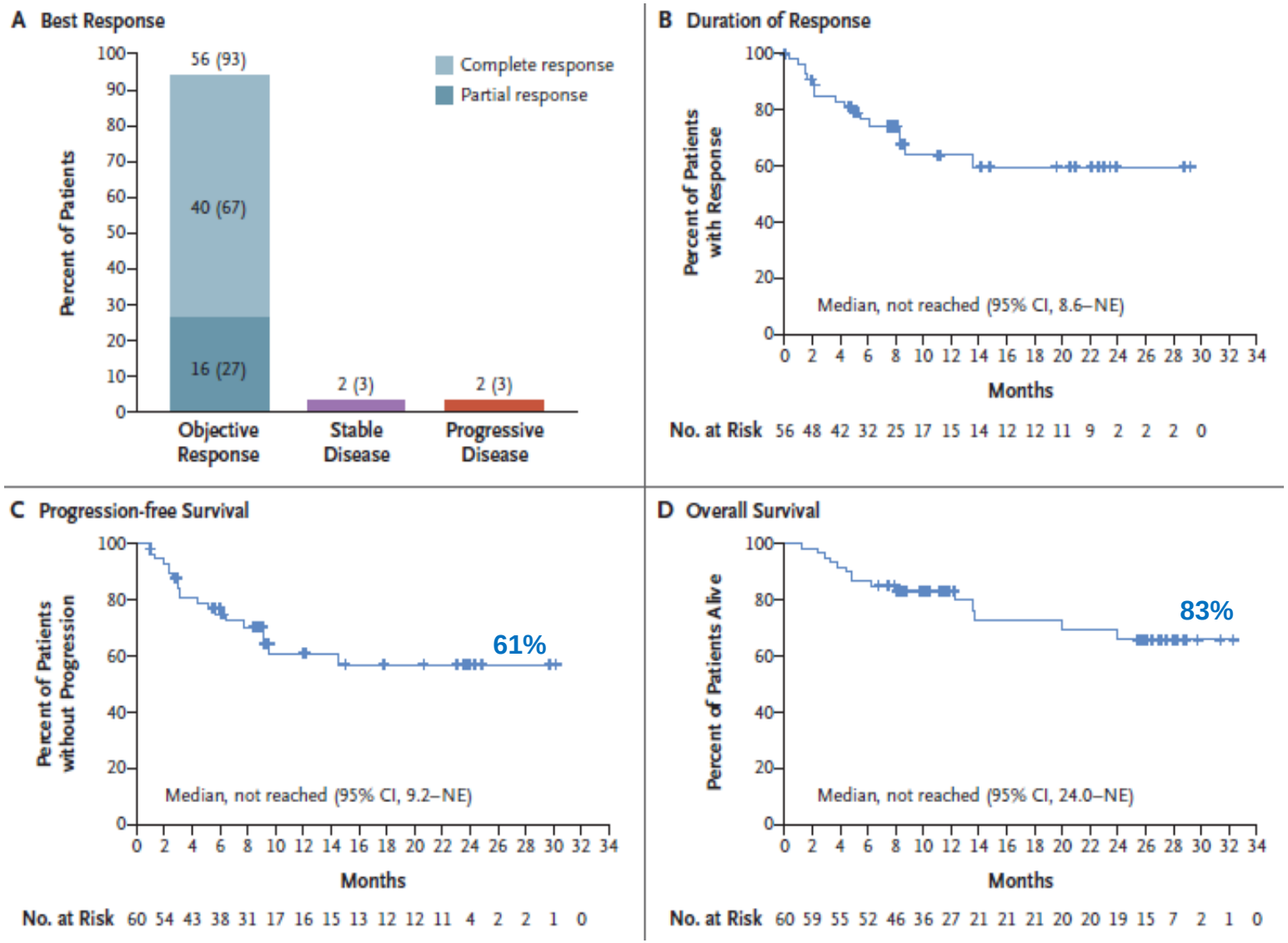
Third-line Treatment

Brexucabtagene autoleucel (after chemoimmunotherapy and BTK inhibitor)

Pirtobrutinib

Adattato da NCCN guidelines version 1.0 2024.

MCL ZUMA 2: phase 2 study



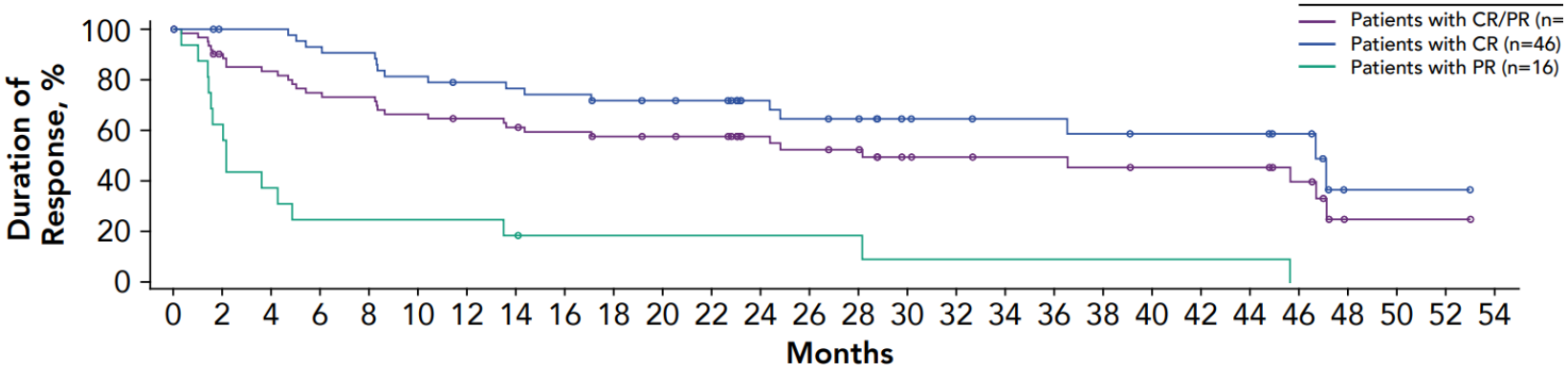
Median follow up: 12.3 months

74 patients enrolled

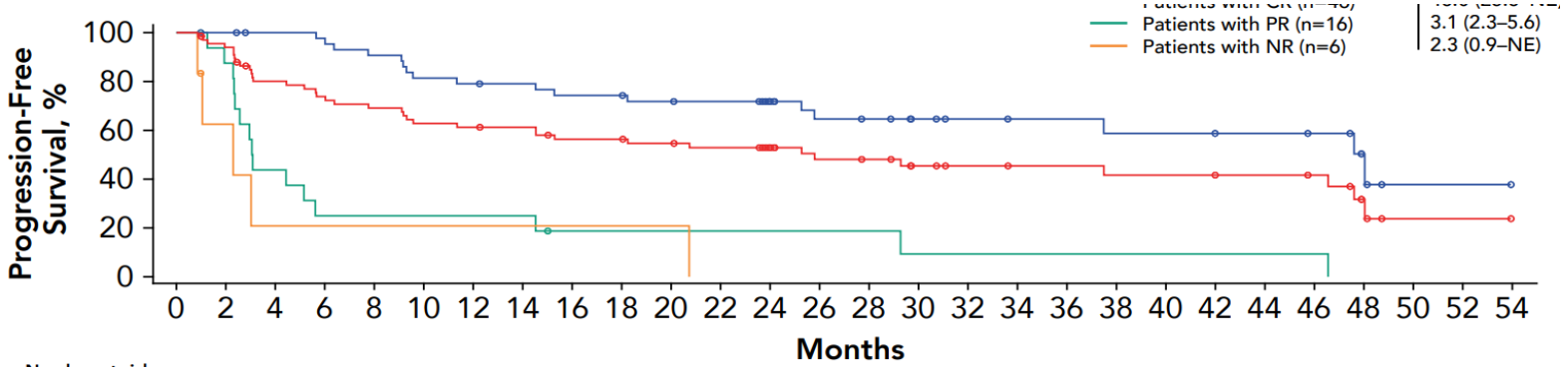
Wang M, et al. N Engl J Med 2020

Three-Year Follow-up of Outcomes With KTE-X19 in Patients with R/R MCL in ZUMA-2

DOR

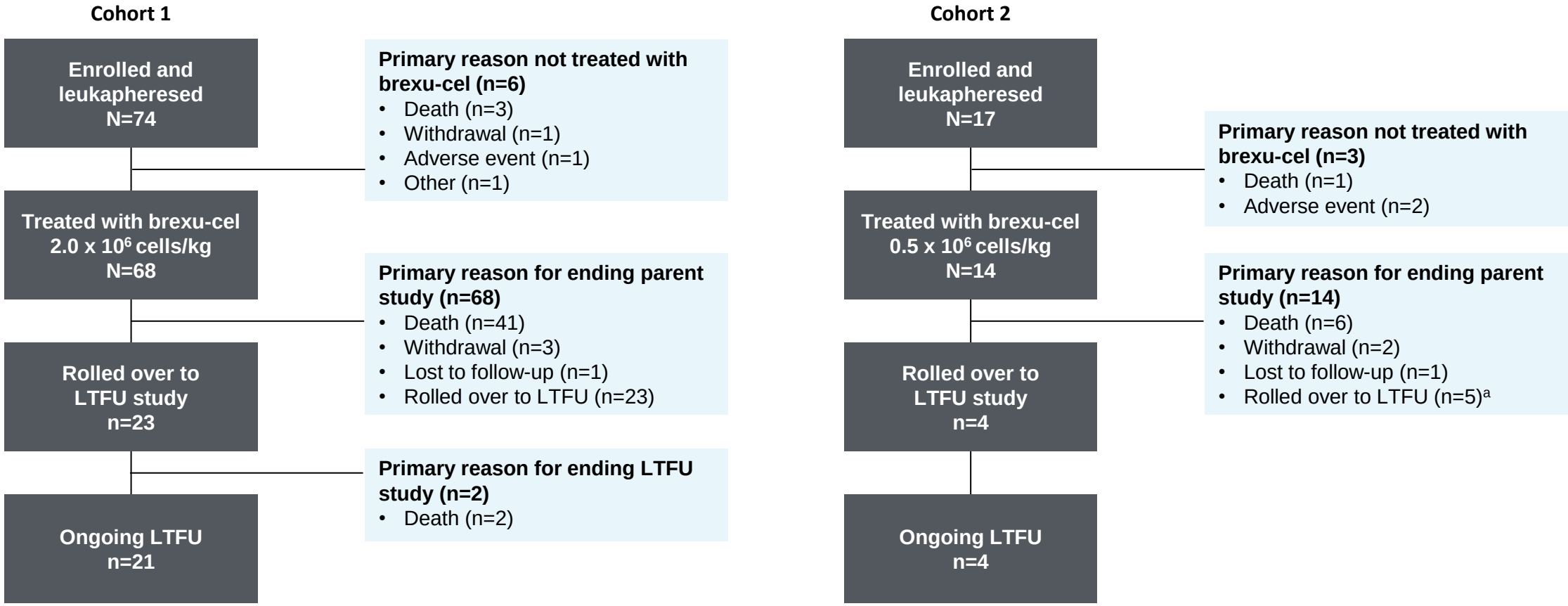


PFS



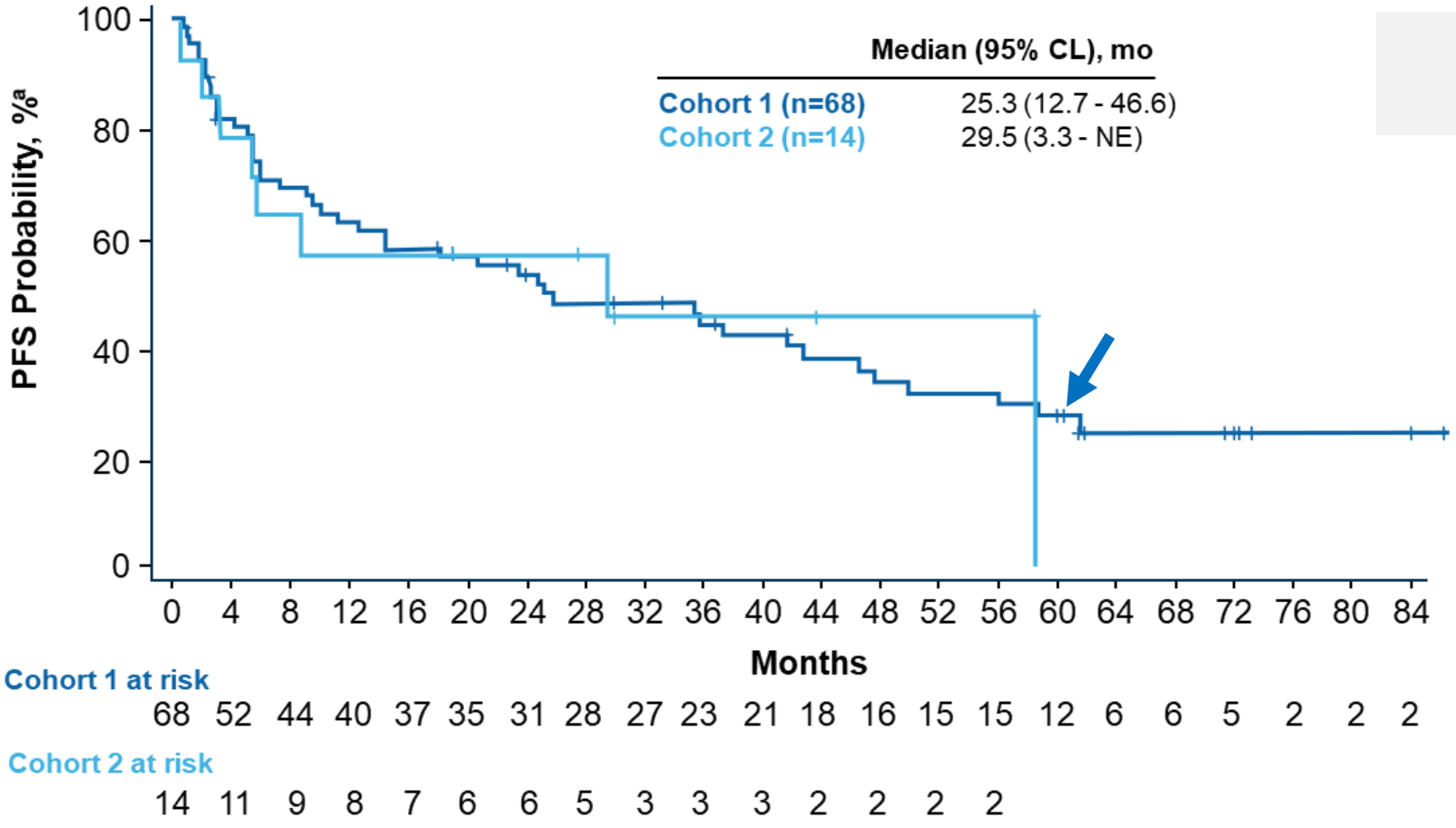
. Wang M, et al. J Clin Oncol 2022;

Patient disposition for ZUMA-2 Cohorts 1 and 2: follow up 5-years



Wang M et al, ASH 2024

Patient disposition for ZUMA-2 Cohorts 1 and 2: follow up 5-years



ORR 93%
CR rate 64%

Median age 65
(38-79)

Median follow-up of 5 years

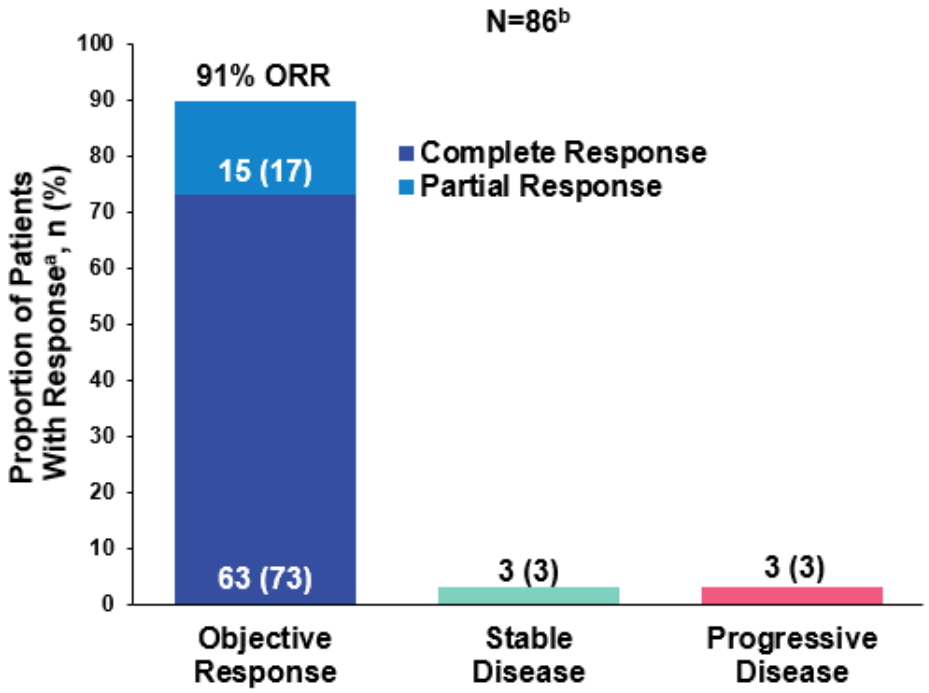
Late-onset toxicities were infrequent; only 3% of treatment-emergent adverse events of interest in ZUMA-2 occurred during this longer follow-up.

Wang M et al, ASH 2024

Patient disposition and response for ZUMA-2 Cohorts 3

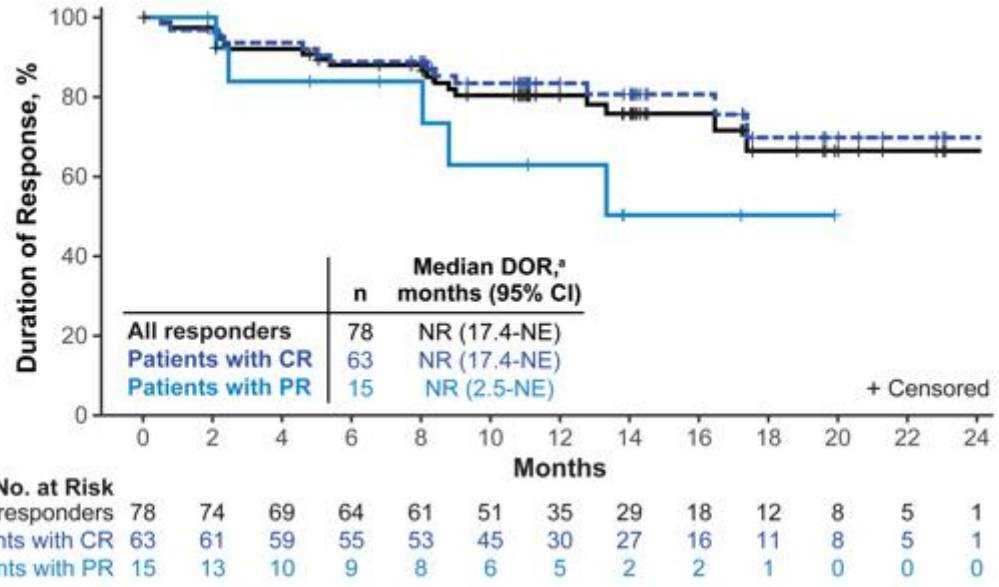
BTKI naive

Characteristic[a]	Cohort 3 (N=86)
Median age (range), years	64 (40-82)
Male, n (%)	67 (78)
ECOG PS of 1, n (%)	27 (31)
Intermediate and high simplified MIPI, n (%)	63 (73)
TP53 IHC by central laboratory performed,[b] n (%)	59 (69)
TP53 ≥50%, n (%)	7 (8)
TP53 mutation status by local laboratory performed,[c] n (%)	33 (38)
Yes	15 (17)
No	18 (21)
Ki-67 IHC by central laboratory performed,[b] n (%)	59 (69)
Ki-67 ≥30%	40 (47)
Ki-67 ≥50%	18 (21)
LDH relative to upper limit, n (%)	
LDH >ULN	49 (57)
Median tumor burden (SPD) by central read (mm^2),[d] (range)	1734 (204-31,212)
Extranodal disease, n (%)	45 (52)
Bone marrow involvement from diagnosis history, n (%)	34 (40)

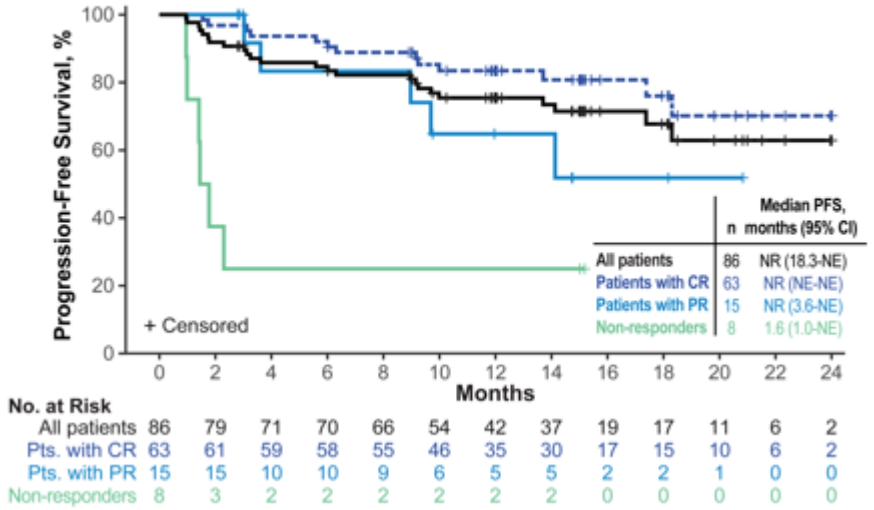


Wang M et al, ASH 2024

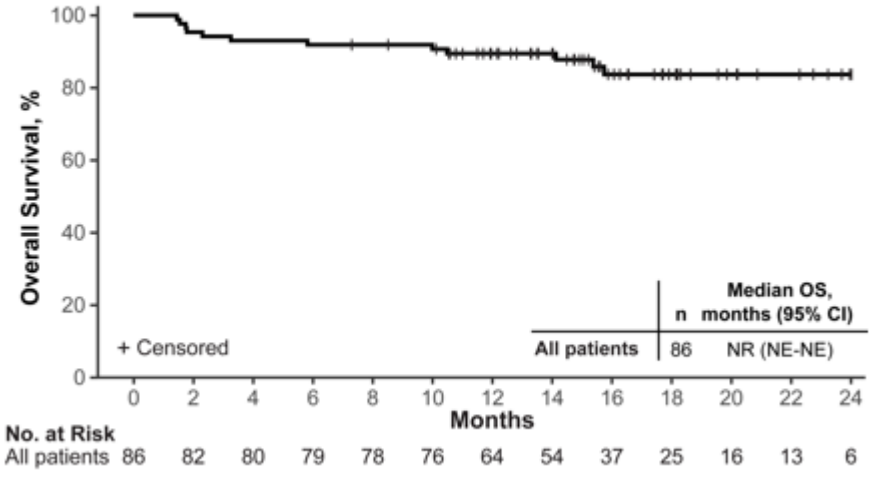
Patient disposition for ZUMA-2 Cohorts 3: survival curves



Progression-Free Survival[a]



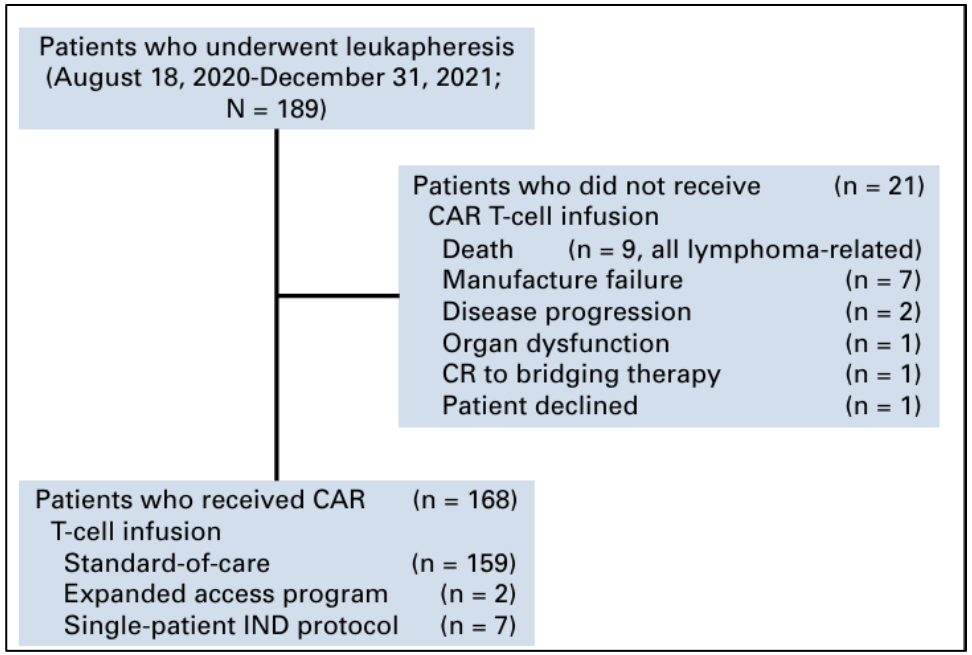
Overall Survival

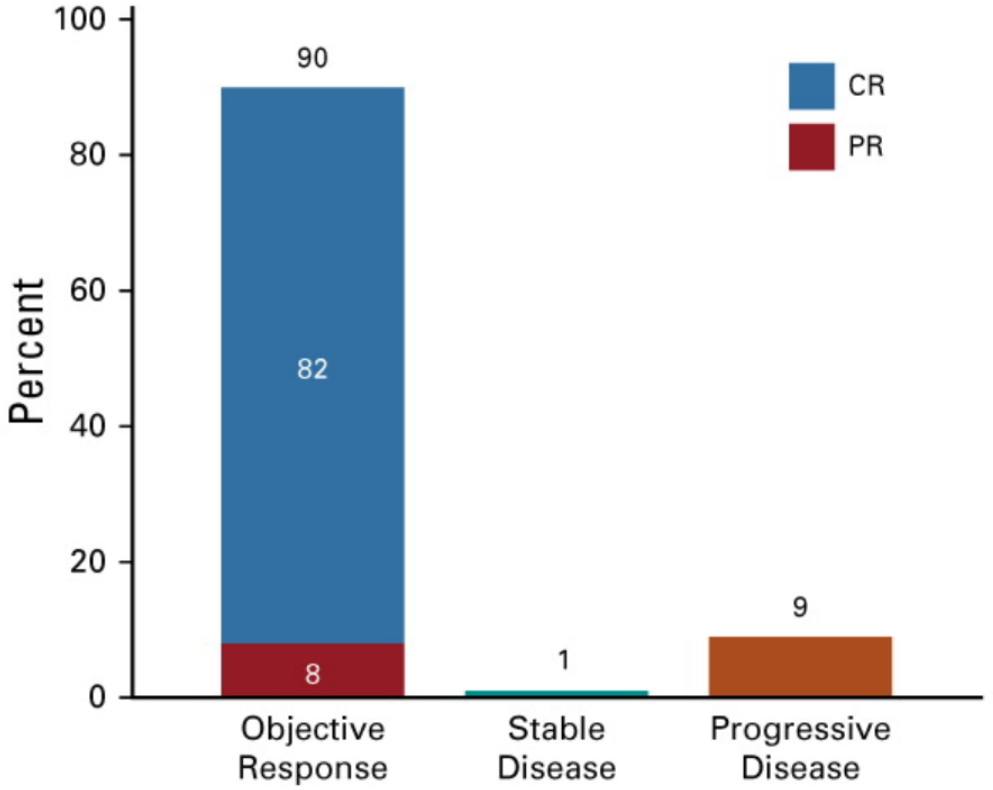


Wang M et al, ASH 2024

Brexu-cel for R/R MCL in Standard of Care Practice: results from the US consortium

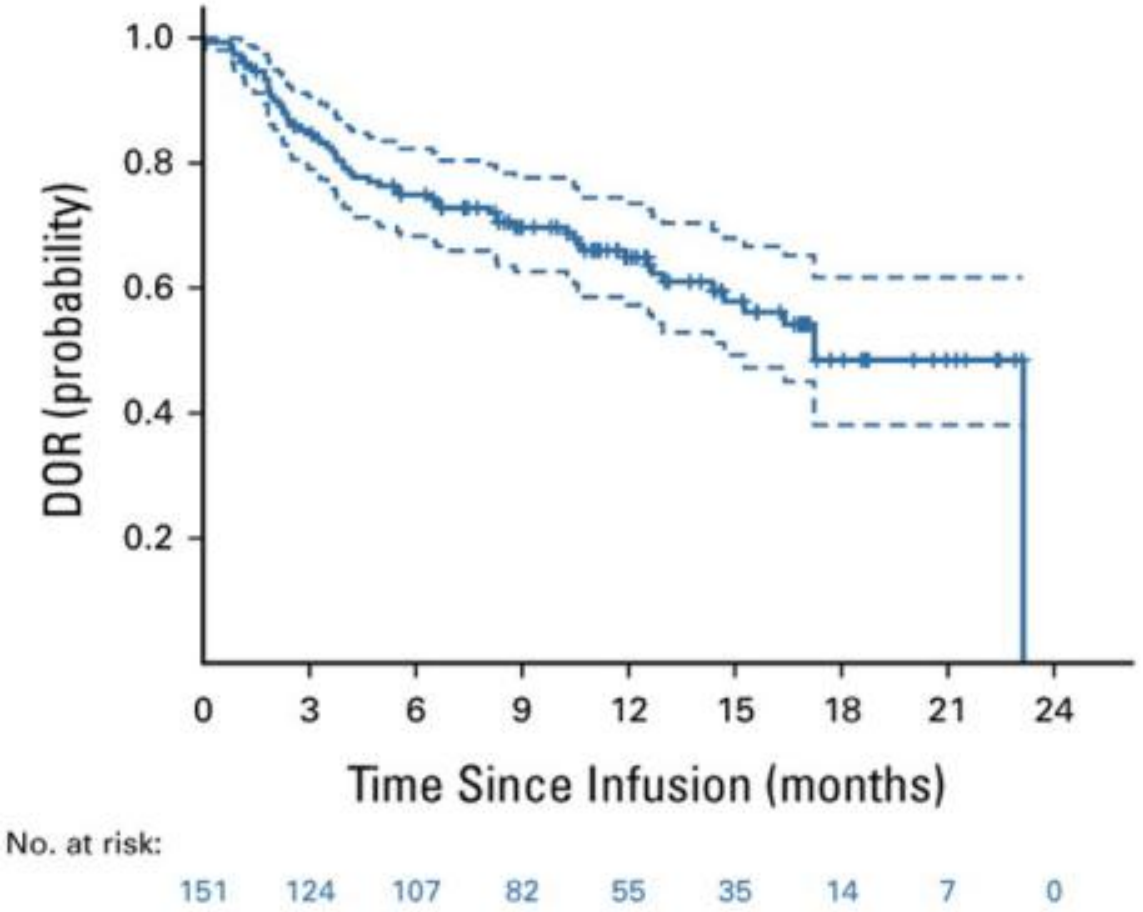
US Lymphoma CAR T Consortium: retrospective, multicenter study in patients receiving KTE-X19 (n= 189)

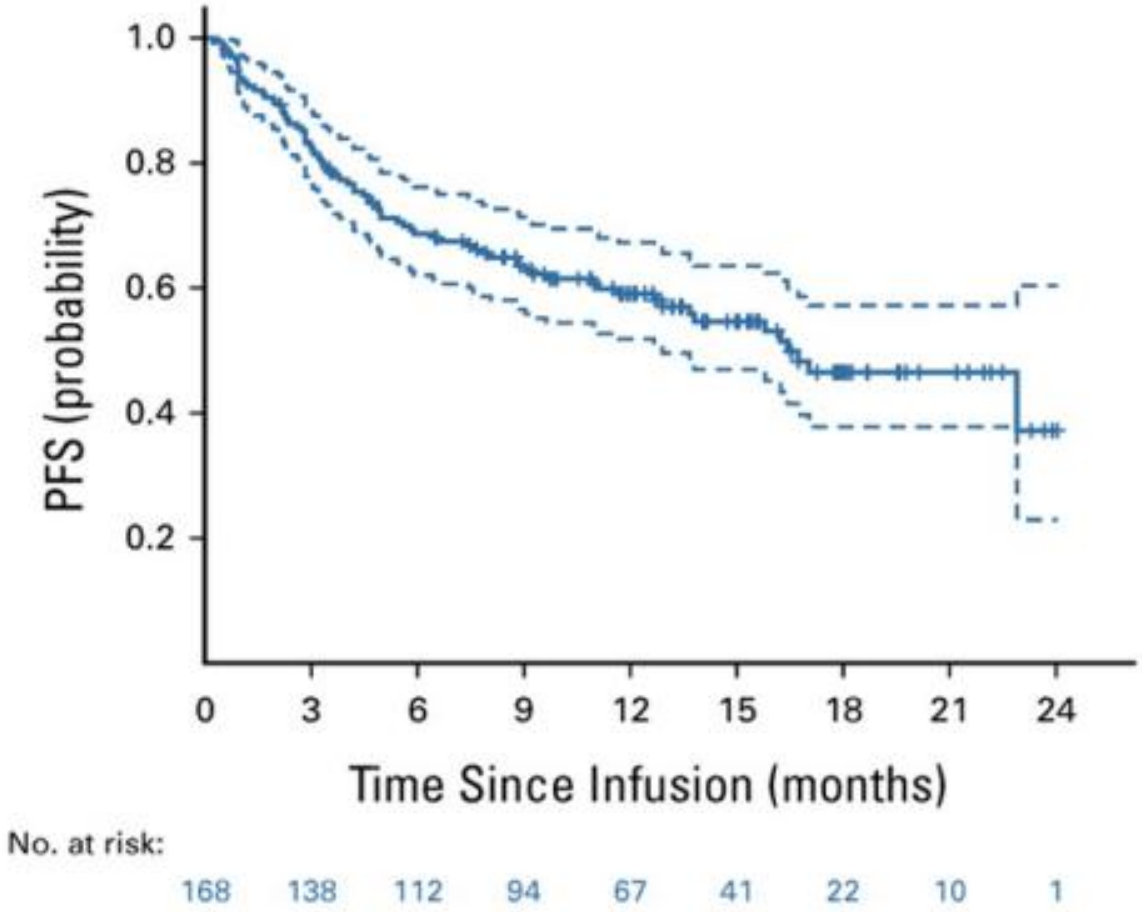




Wang Y, et al. JCO 2023

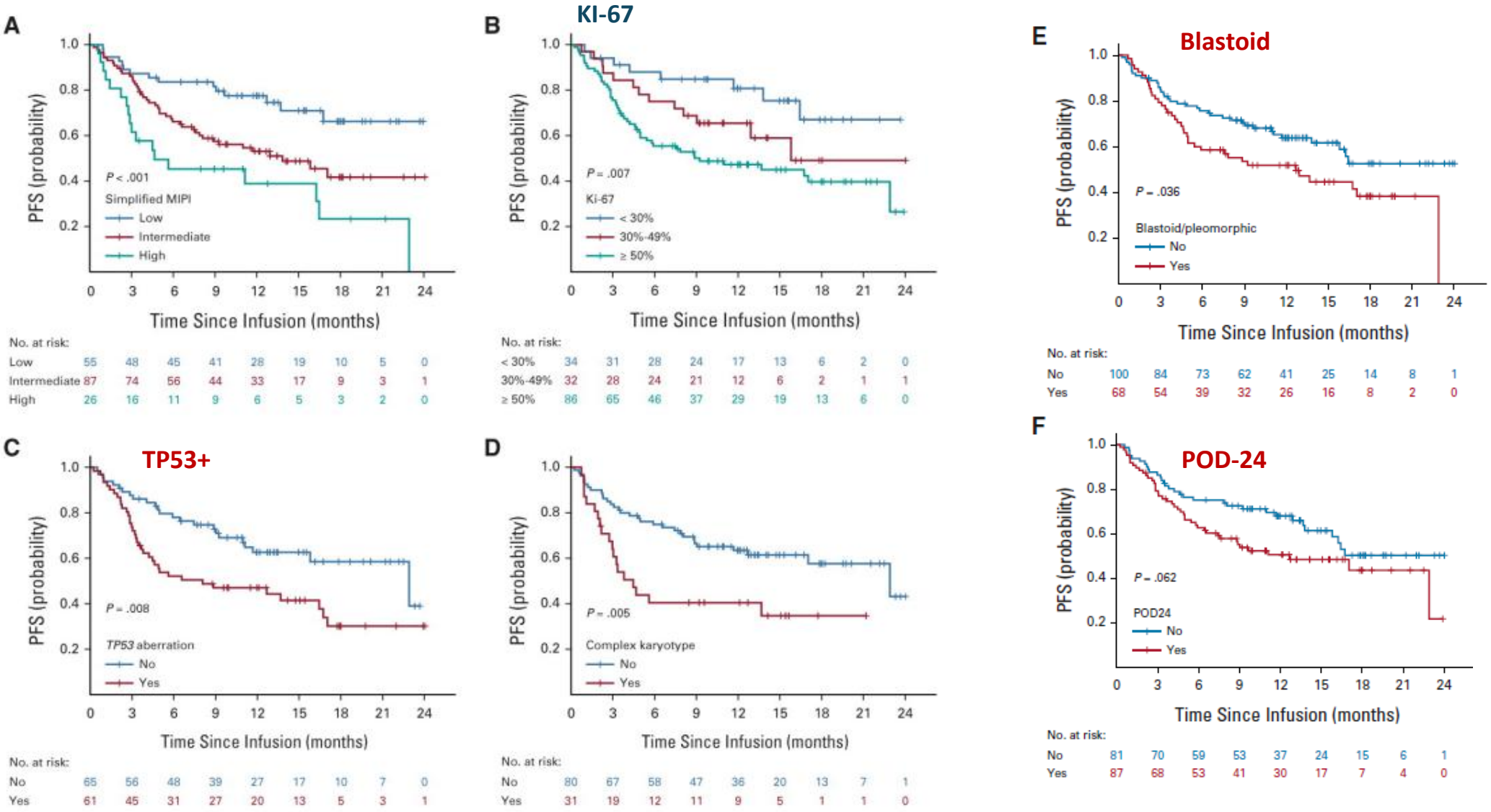
Brexu-cel for R/R MCL in Standard of Care Practice





Wang Y, et al. JCO 2023

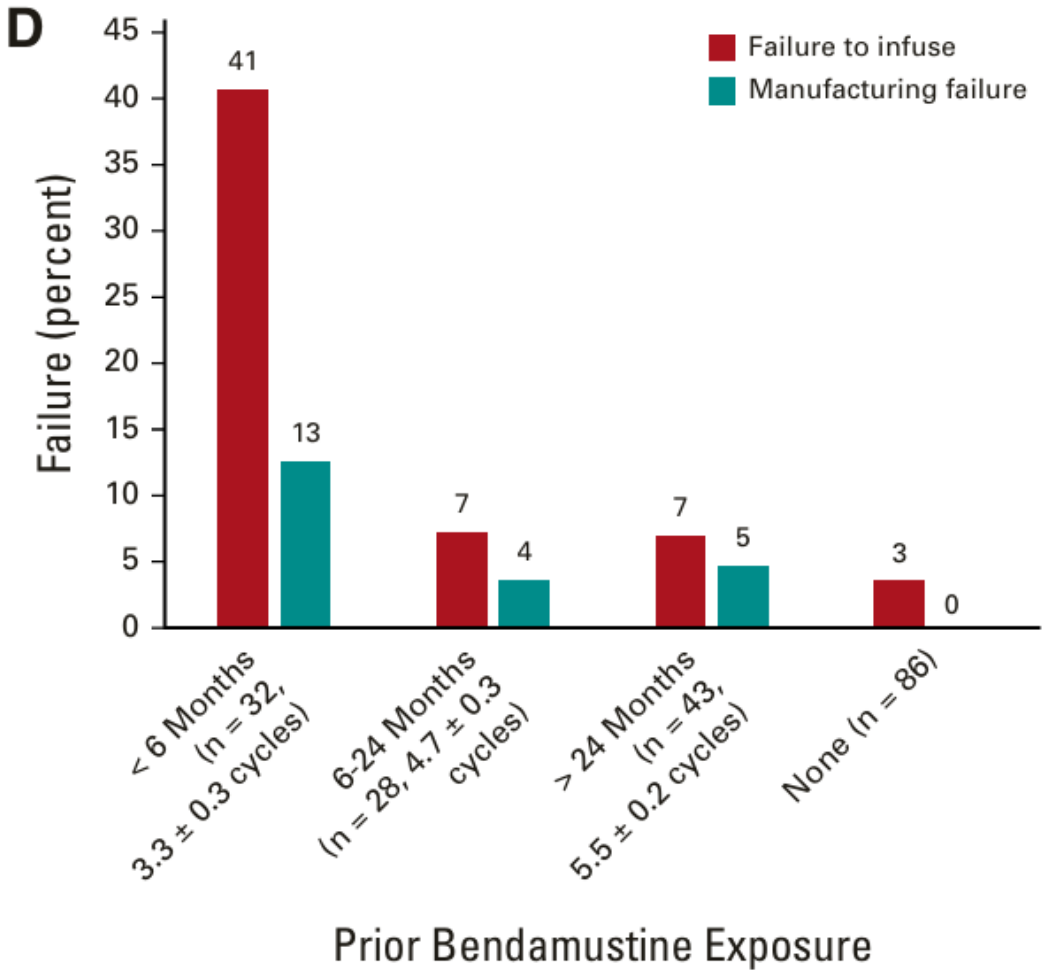
Brexu-cel for R/R MCL in Standard-of-Care Practice

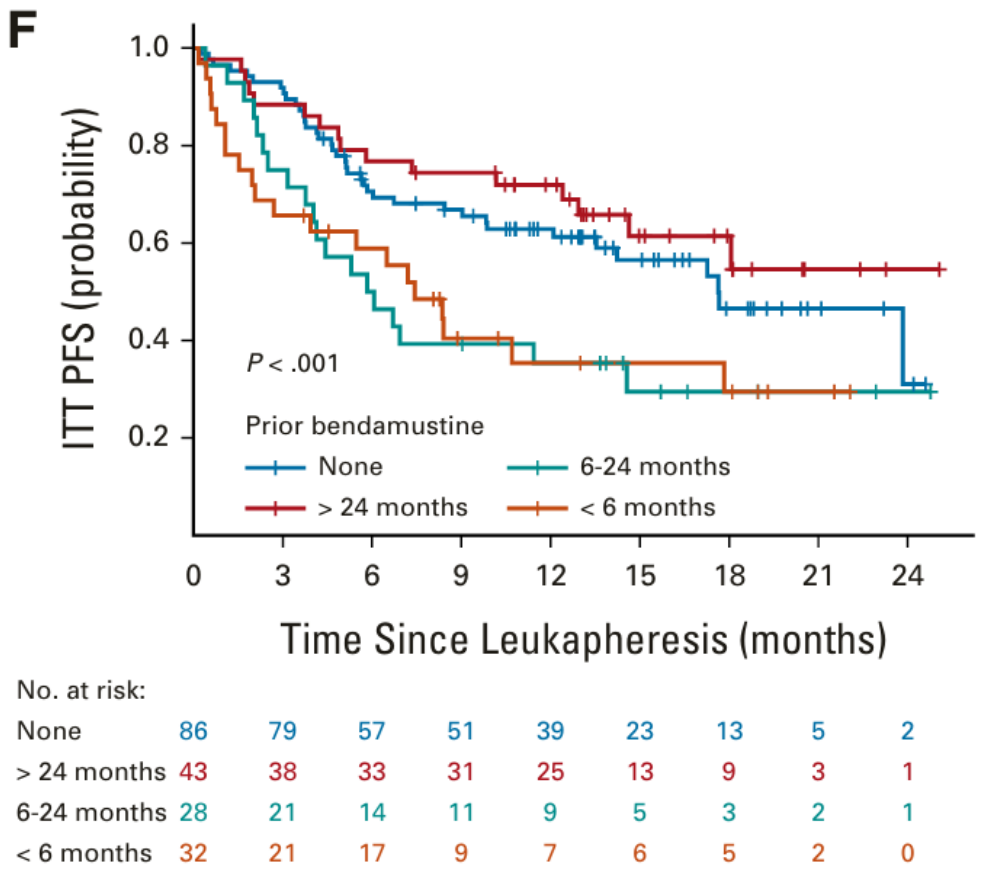


Wang Y, et al. JCO 2023

Prior Bendamustine exposure and outcomes

103/189 patients received prior bendamustine





No. at risk:

None	86	79	57	51	39	23	13	5	2
> 24 months	43	38	33	31	25	13	9	3	1
6-24 months	28	21	14	11	9	5	3	2	1
< 6 months	32	21	17	9	7	6	5	2	0

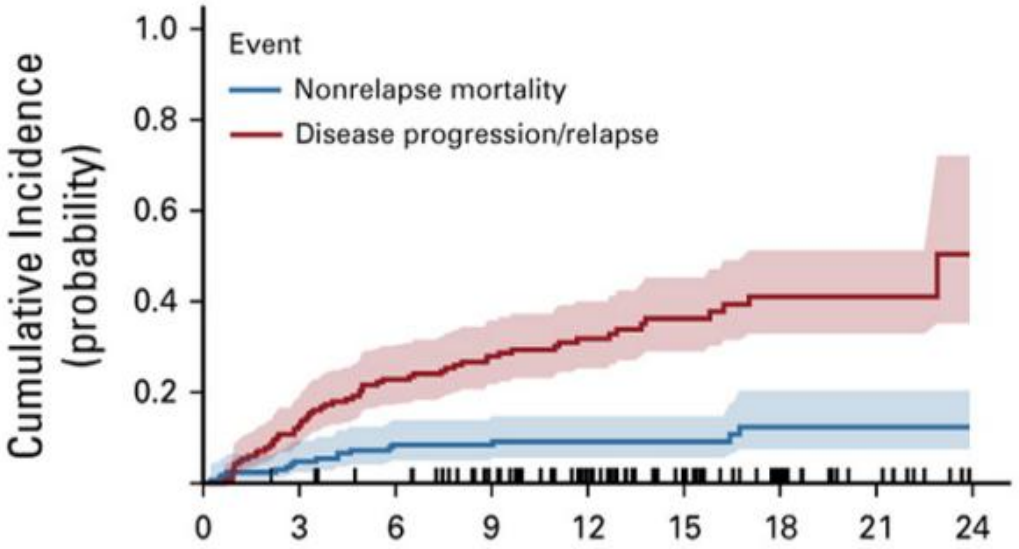
Wang Y, et al. JCO 2023

Short term and long term toxicity

- The incidences of CRS and ICANS were comparable to those reported in ZUMA-2.
- Tocilizumab and corticosteroids use appeared to be more frequent in this Consortium study cohort

	CRS, n (%)	ICANS, n (%)	ZUMA-2 CRS (%)	ZUMA-2 NE (%)
Total	86 (91%)	57 (60%)	91%	63%
Max Grade*				
1-2	78 (82%)	24 (25%)	76%	32%
3-4	8 (8%)	33 (35%)	15%	31%
Days to onset	4 (0-11)	6 (1-15)	2 (1-13)	7
Days to max Grade	5 (0-7)	7 (3-15)	-	-
Duration	5 (1-33+)	6 (2-144+)	11	12

- **The non relapse mortality was 9.1% at 1 year**, primarily because of infections.



Wang Y, et al. JCO 2023

Brexucabtagene Autoleucel for R/R MCL in Standard-of-Care Practice

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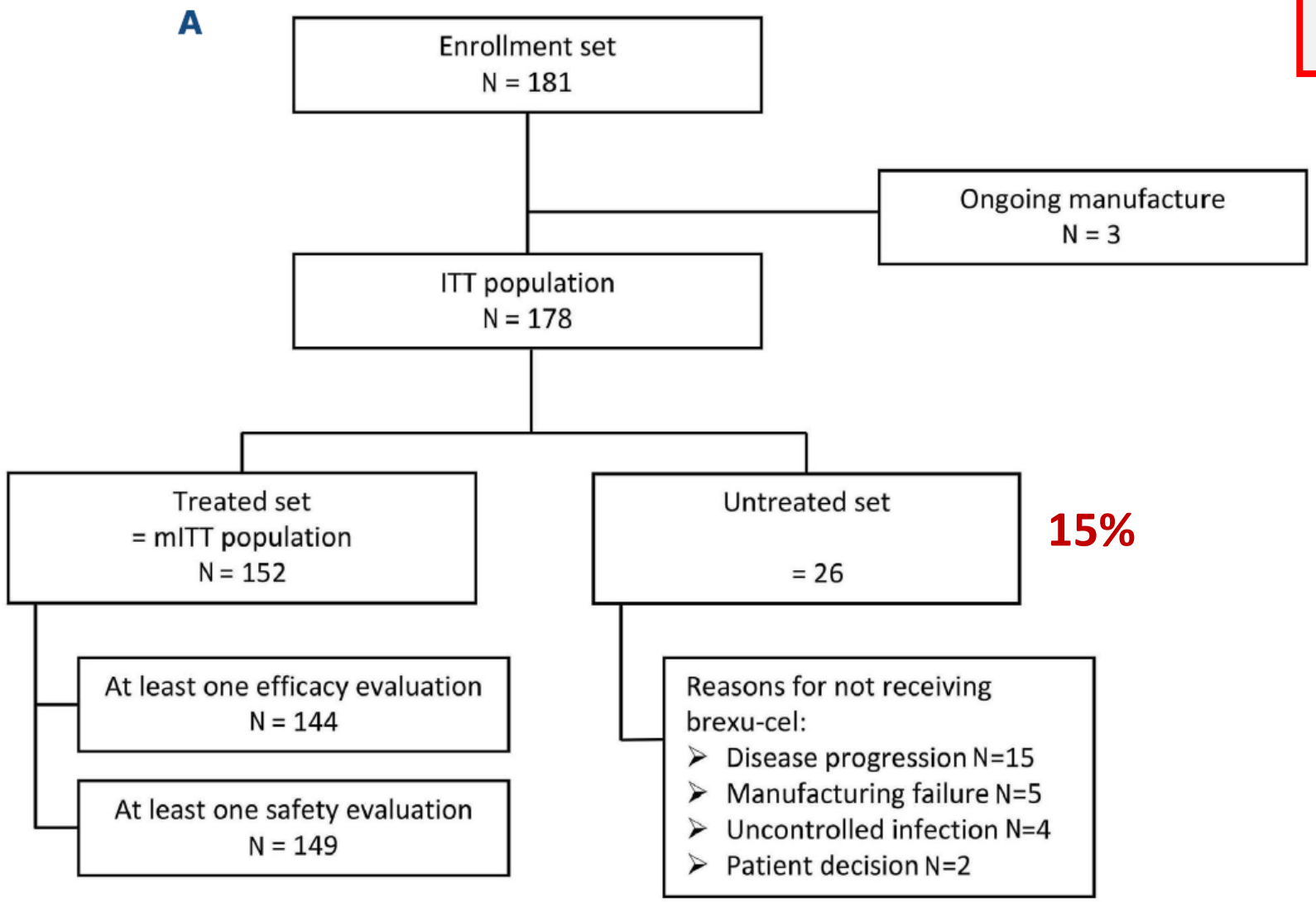

Herbaux C et al, Haematologica 2024

Brexucabtagene Autoleucel for R/R MCL in Standard-of-Care Practice

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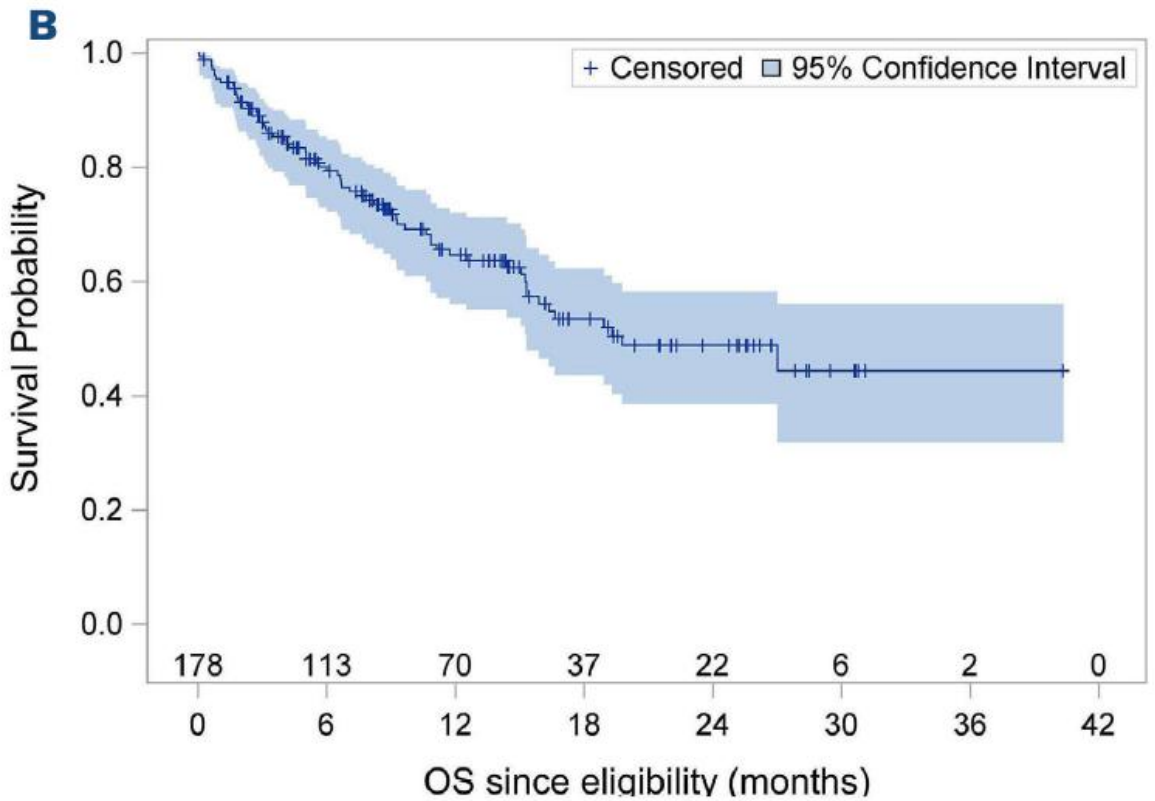
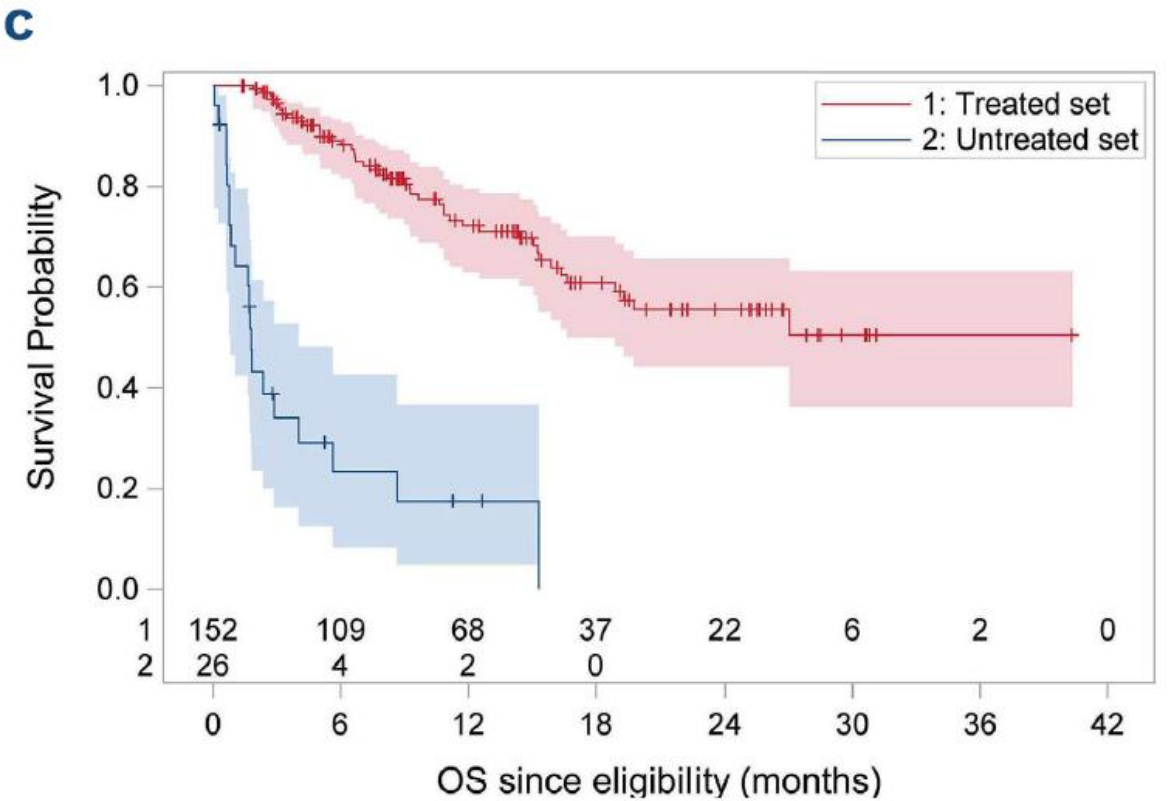


Subjects	Event	Censored	Median Survival (95%CI)
178	36.5 % (65)	63.5 % (113)	19.8 (15.3 - NA)



	Subjects	Event	Censored	Median Survival (95% CI)
Treated set	152	29.6 % (45)	70.4 % (107)	Not reached (18.9 - NA)
Untreated set	26	76.9 % (20)	23.1 % (6)	1.8 (0.9 - 4)

Herbaux C et al, Haematologica 2024

DOI: 10.1111/bjh.19961

ORIGINAL PAPER
Transplantation and Cellular Therapy

Brexucabtagene autoleucel in-vivo expansion and BTKi refractoriness have a negative influence on progression-free survival in mantle cell lymphoma: Results from CART-SIE study

Federico Stella[1,2] | Annalisa Chiappella[2] | Martina Magni[2] | Francesca Bonifazi[3] | Chiara De Philippis[4] | Maurizio Musso[5] | Ilaria Cutini[6] | Silva Ljevar[7] | Anna Maria Barbui[8] | Mirko Farina[9] | Massimo Martino[10] | Massimo Massaia[11] | Giovanni Grillo[12] | Piera Angelillo[13] | Barbara Botto[14] | Francesca Patriarca[15] | Mauro Krampera[16] | Luca Arcaini[17,18] | Maria Chiara Tisi[19] | Pierluigi Zinzani[3] | Federica Sorà[20] | Stefania Bramanti[4] | Martina Pennisi[2] | Cristiana Carniti[2] | Paolo Corradini[1,2]

Società Italiana di Ematologia

CART-SIE

PI: Prof Paolo Corradini

Participants: all Italian qualified centers for CAR-T treatment

Aim of this analysis was to evaluate efficacy and safety outcomes of patients with R/R MCL treated with brexu-cel

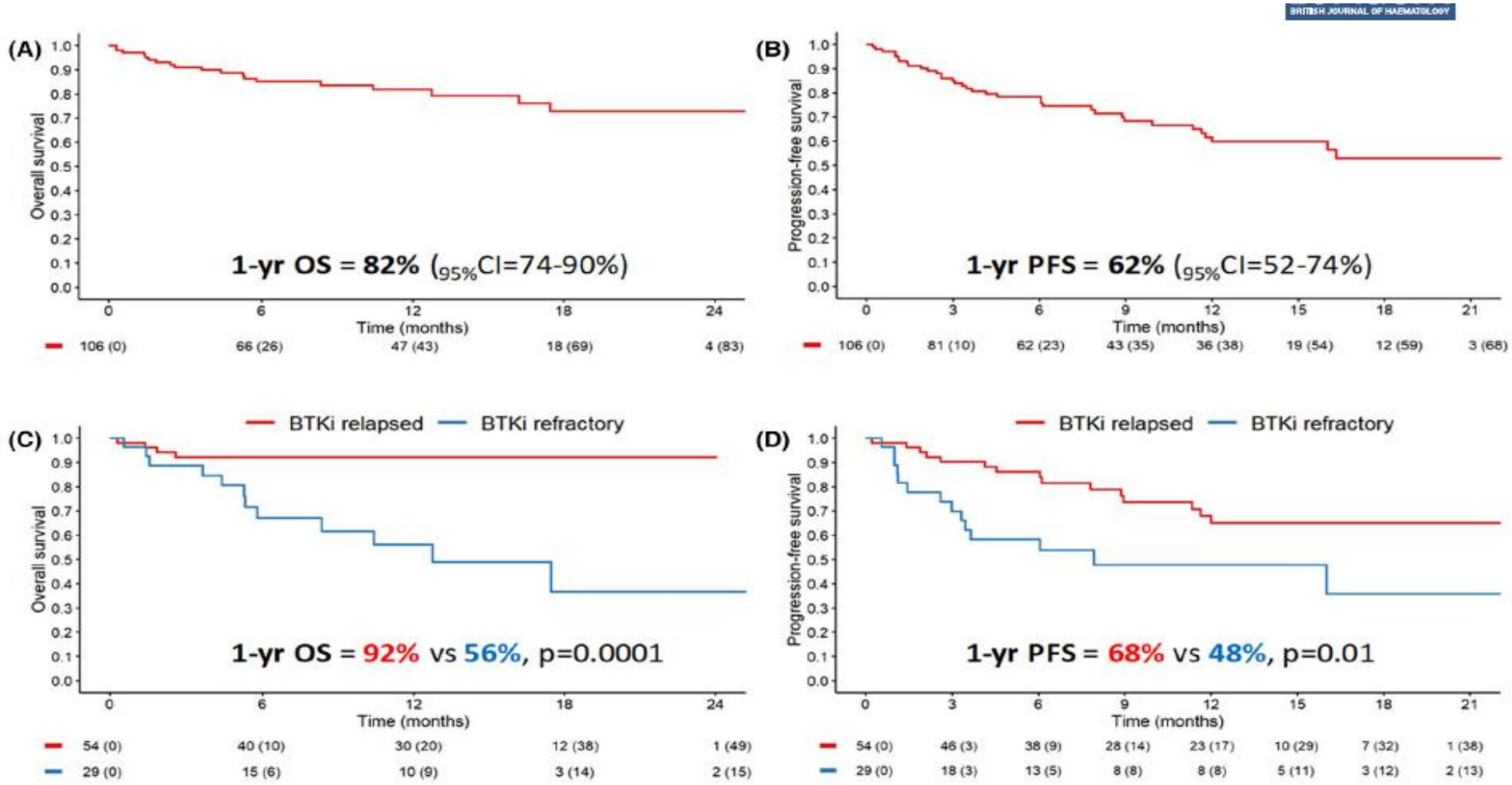
March 2019 – July 2024: 106 MCL

Stella F. et al, B.J.Hematology 2024

Brexucabtagene autocell in real word : PFS and OS

CART-SIE

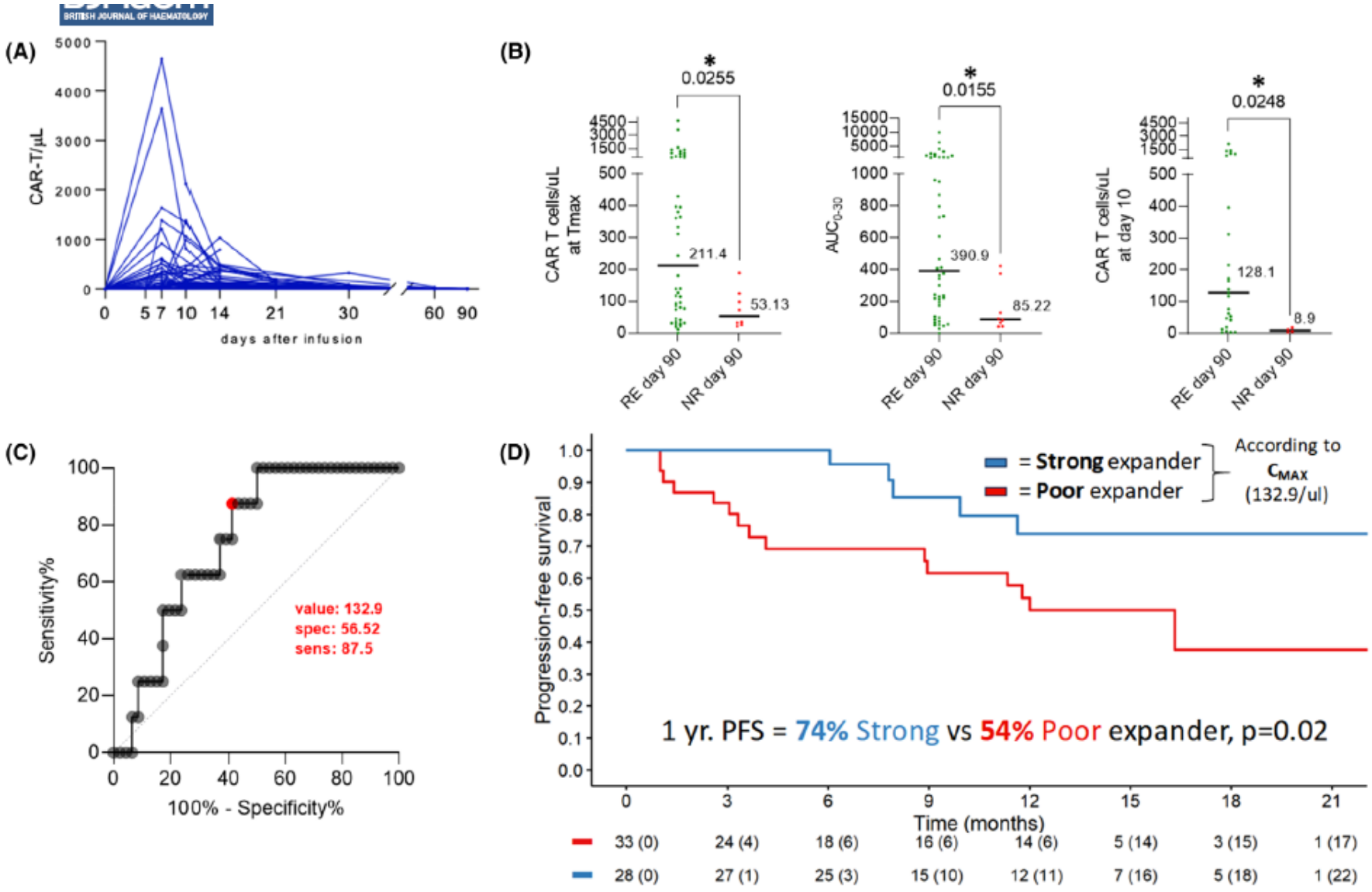
Responser day + 90: ORR 77%, CR 70%



Median follow-up: 12.07 months (IQR: 5.95, 17.86

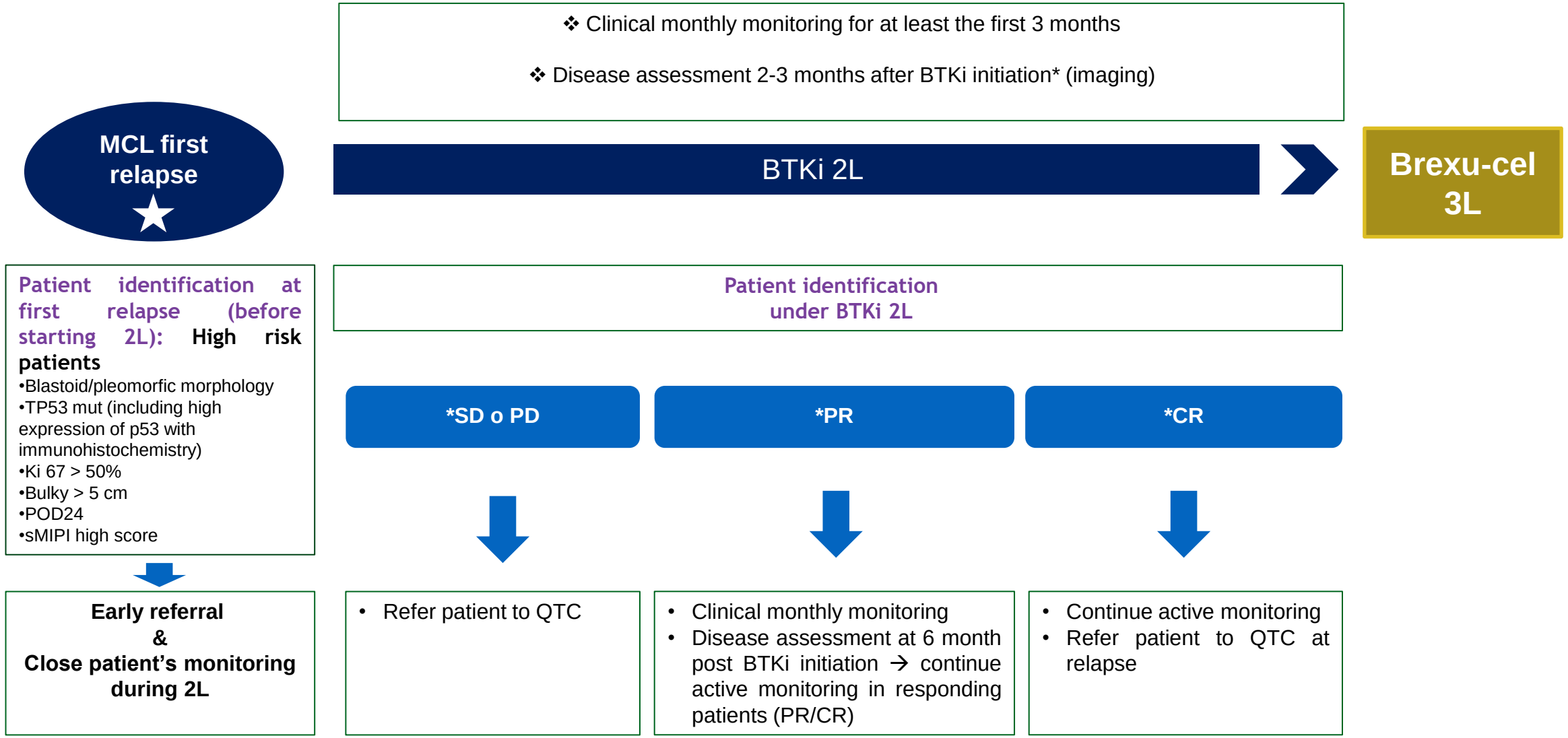
Stella F. et al, B.J.Hematology 2024

In vivo Brexu-cell exspansion



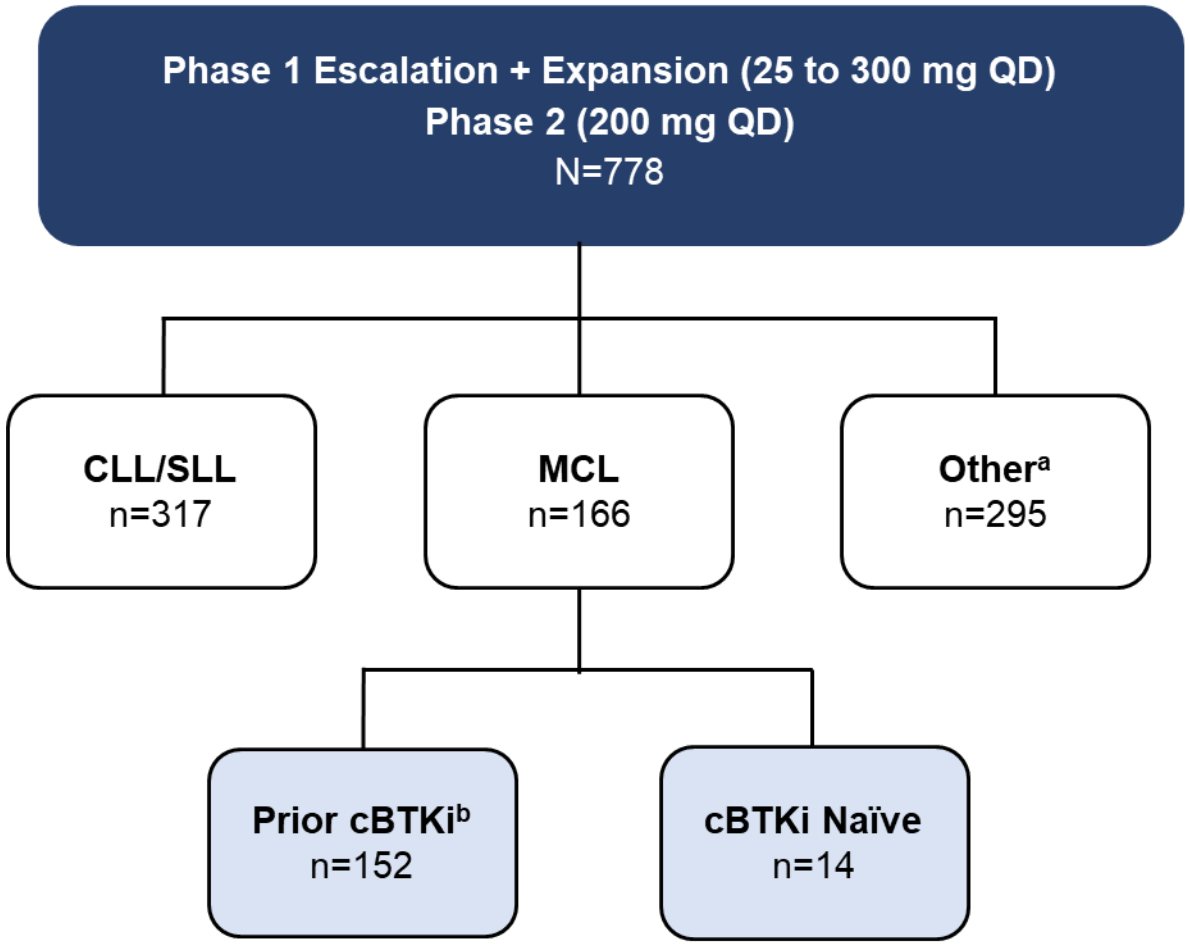
Stella F. et al, B.J.Hematology 2024

Patient journey for MCL



Eyre T.A. et al. Br J Haematol 2024; 204:108-126

Pirtobrutinib Phase 1/2 BRUIN Study: Design, Eligibility and Enrollment



Phase 1 3+3 design

- 28-day cycles
- Intra-patient dose escalation allowed
- Cohort expansion permitted at doses deemed safe

Eligibility

- Age ≥18
- ECOG 0-2
- Active disease and in need of treatment
- Previously treated

Key endpoints

- Safety/tolerability
- Determine MTD and RP2D
- Pharmacokinetics
- Efficacy (ORR according to Lugano criteria, DoR, PFS, and OS)

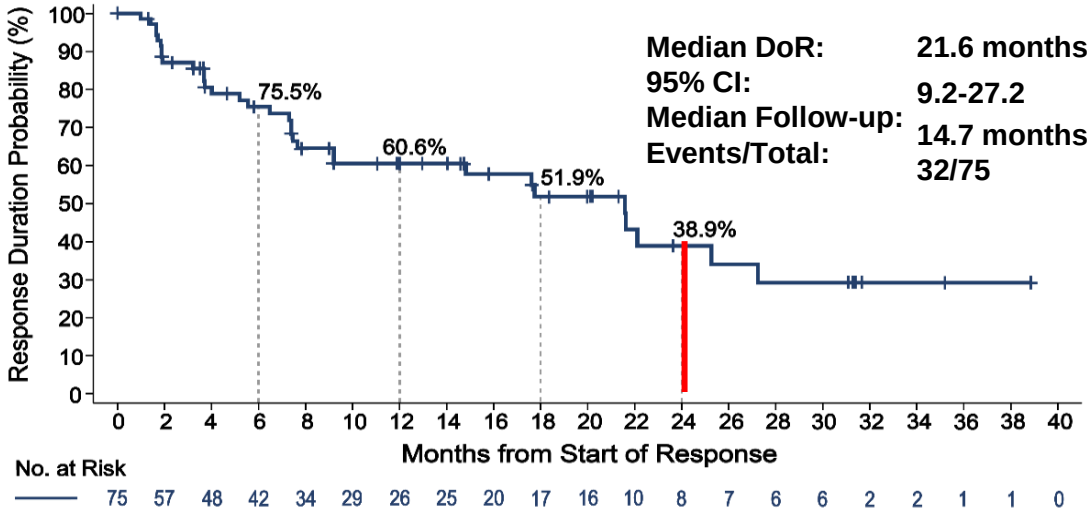
Data cutoff of 05 May 2023 (NCT03740529). [a]Other includes DLBCL, WM, FL, MZL, Richter transformation, B-PLL, Hairy Cell Leukemia, PCNSL, and other transformations. [b]Prior cBTKi includes Primary Analysis Set (PAS) n=90 and Supplemental Cohort n=62. The PAS comprised the first 90 patients enrolled and served as the primary efficacy population for regulatory interactions and met the following criteria:; had measurable disease, had received a prior cBTKi containing regimen, had no known central nervous system involvement. Updated data from the PAS90 population can be found in supplemental via QR code.

Cohen et al.; ASH 2023

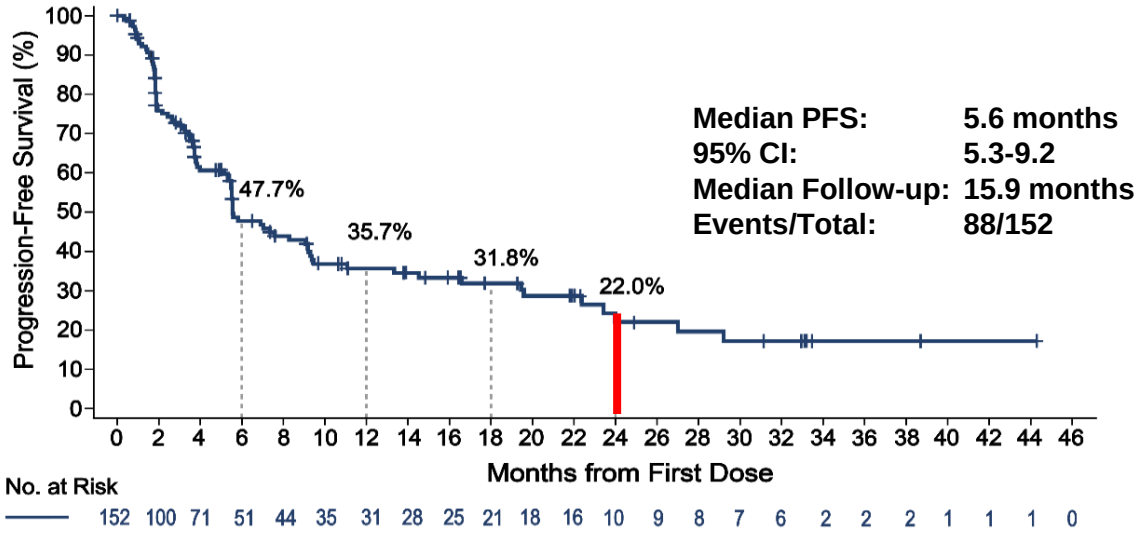
Pirtobrutinib phase 1/2 BRUIN Study: outcomes in Prior cBTKi pts with MCL

Prior cBTKi	n=152
ORR[b] % (95% CI)	49.3 (41.1-57.6)
Best Response, n (%)	
CR	24 (15.8)
PR	51 (33.6)

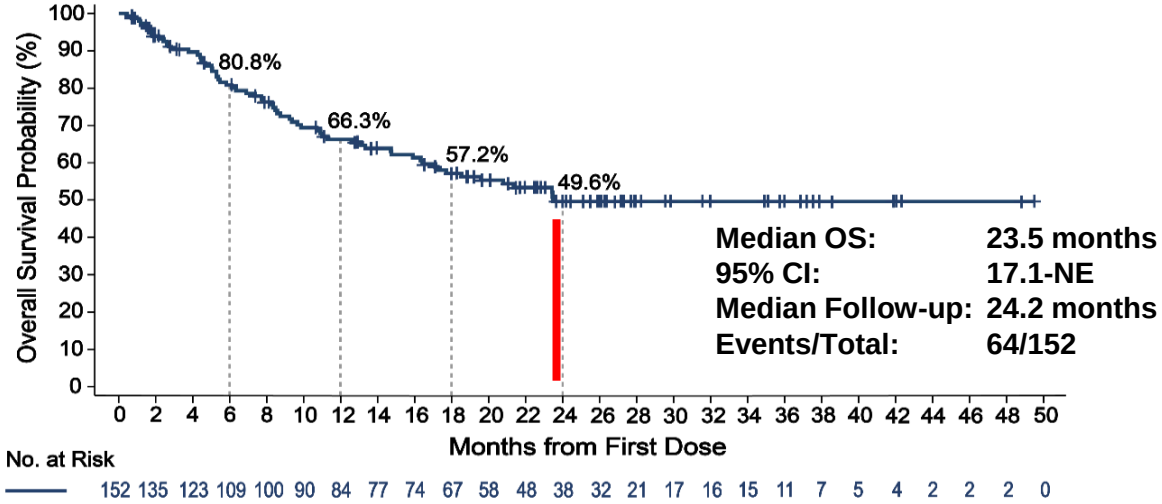
Duration of Response



Progression-Free Survival



Overall Survival



Cohen et al.; ASH 2023

Glofitamab RR-MCL : step-up dosing: baseline characteristics by prior BTKi

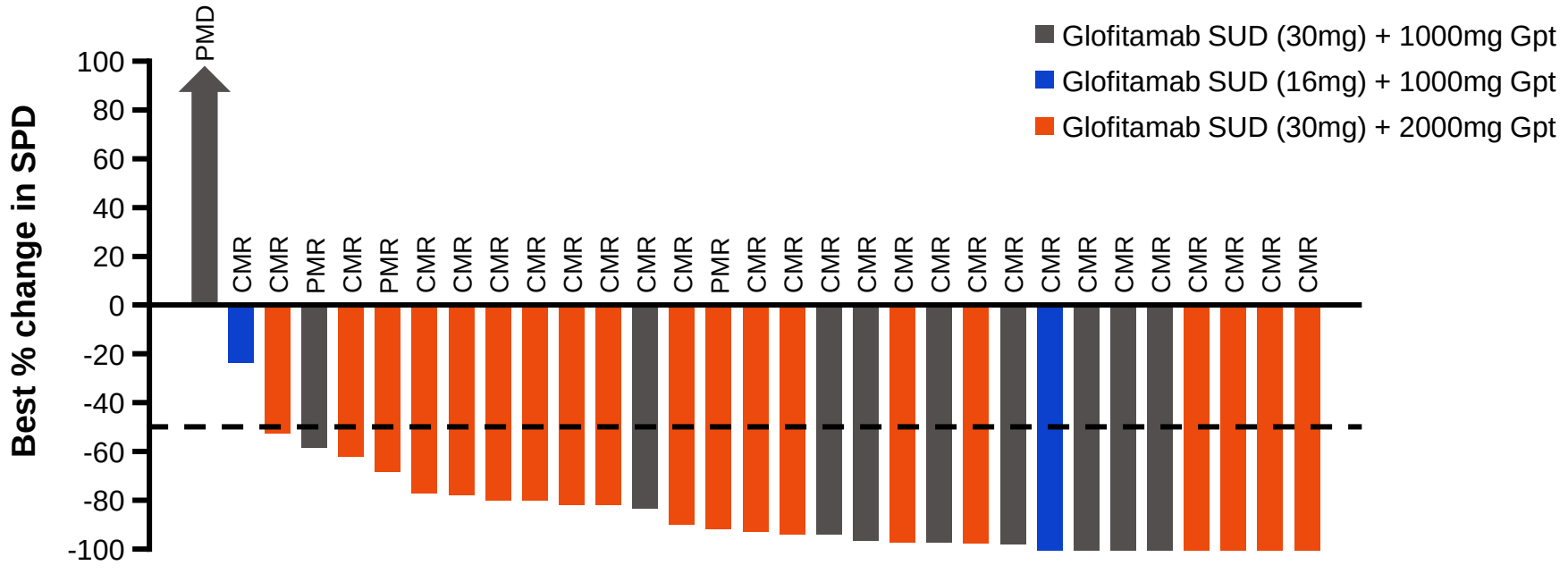
n (%) of patients unless stated		Prior BTKi (n=31)*	BTKi naïve (n=29)*	All patients (N=60)*
Median age, years (range)		70.0 (41–84)	72.0 (52–86)	72.0 (41–86)
Male		23 (74.2)	21 (72.4)	44 (73.3)
Ann Arbor stage III/IV		28 (90.3)	24 (82.8)	52 (86.7)
MCL IPI score ≥6		7 (22.6)	8 (27.5)	15 (25.0)
Median no. of prior lines (range)		3.0 (1–5)	2.0 (1–4)	2.0 (1–5)
Median time since last prior therapy to first study treatment, months (range)		1.3 (0.1–53.2)	7.4 (1.1–132.5)	2.4 (0.1–132.5)
Median time since last anti-CD20 therapy to first study treatment, months (range)		15.1 (0.7–159.0)	25.1 (1.4–132.5)	16.3 (0.7–159.0)
Refractory status	Refractory to any prior therapy	30 (96.8)	20 (69.0)	50 (83.3)
	Refractory to 1L therapy	17 (54.8)	14 (48.3)	31 (51.7)
	Refractory to last prior therapy	27 (87.1)	17 (58.6)	44 (73.3)

A higher proportion of patients with prior BTKi therapy were refractory to their last prior therapy compared with BTKi-naïve patients

1. Philips T, et al. ASH 2021; oral presentation (abstract #130).
2. Philips T, et al. ASH 2022; oral presentation (abstract #74).

Glofitamab step-up dosing: Antitumor activity

Best percentage change from baseline SPD* (CCOD: March 14, 2022)

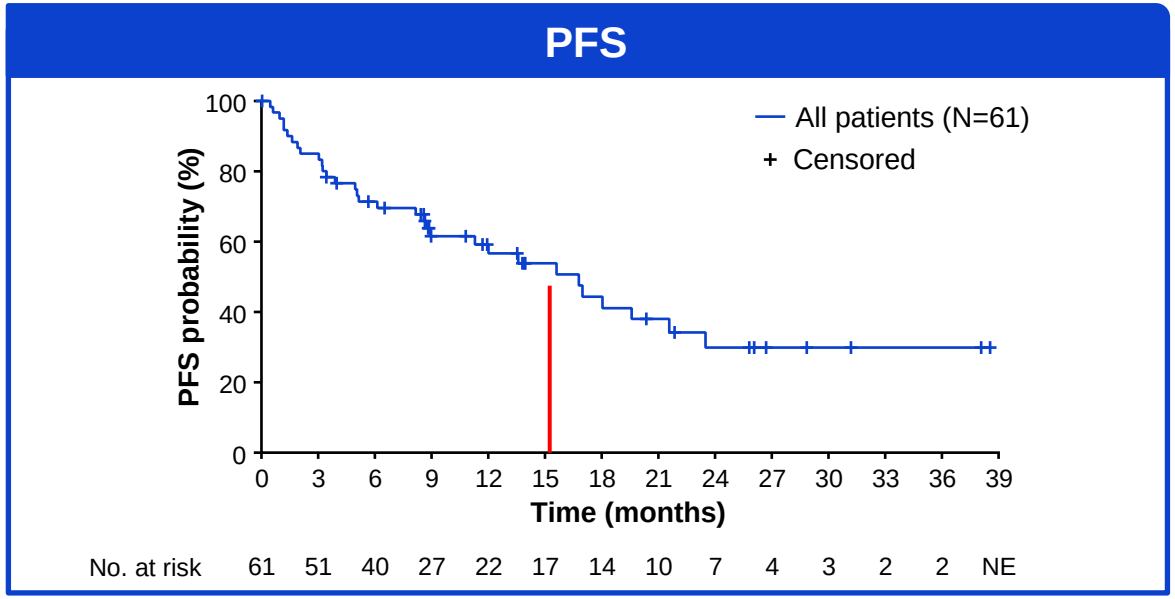


- **All glofitamab regimens investigated showed activity in R/R MCL**

Philips T, et al. ASH 2022; oral presentation (abstract #74).

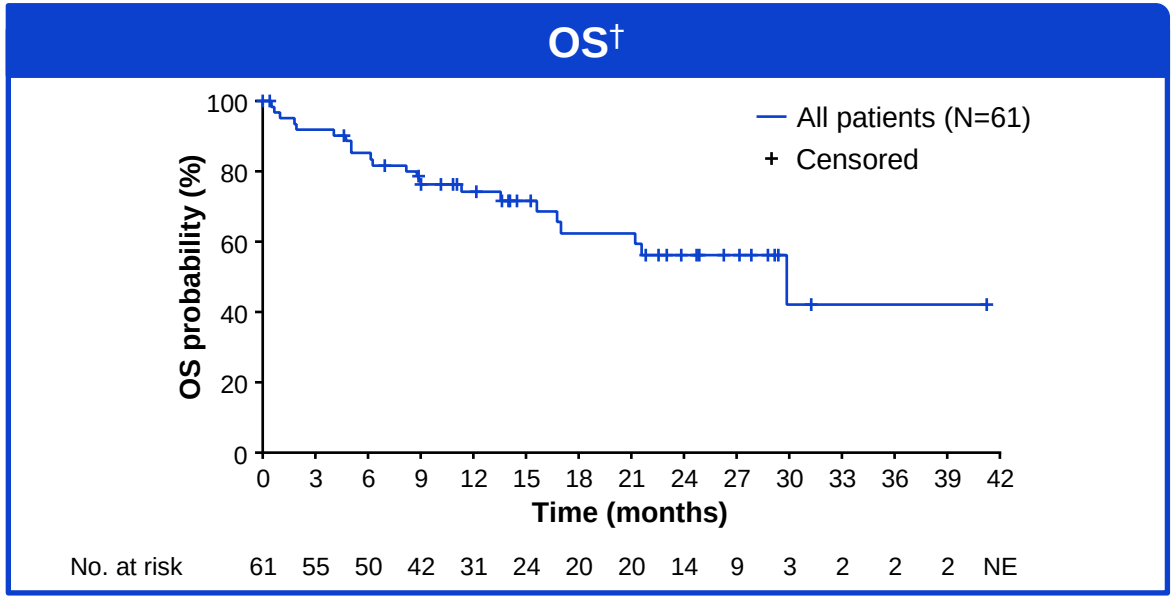
Glofitamab step-up dosing: Time-to-event endpoints

PFS



	Prior BTKi n=32*	All patients N=61*
Median PFS follow-up, months (95% CI)	26.1 (13.5–31.2)	19.6 (11.9–26.1)
Median PFS, months (95% CI)	8.6 (3.4–15.6)	**16.8 (8.9–21.6)**
15-month PFS rate, % (95% CI)	33.0 (14.8–51.1)	54.0 (40.1–67.8)

OS†



	Prior BTKi n=32*	All patients N=61*
Median OS follow-up, months (95% CI)	24.7 (13.6–28.8)	21.8 (14.0–24.9)
Median OS, months (95% CI)	21.2 (9.0–NE)	**29.9 (17.0–NE)**
15-month OS rate, % (95% CI)	55.0 (36.5–73.6)	71.4 (59.3–83.5)

- **Clinically significant PFS and OS at 15 months were achieved with fixed-duration glofitamab**

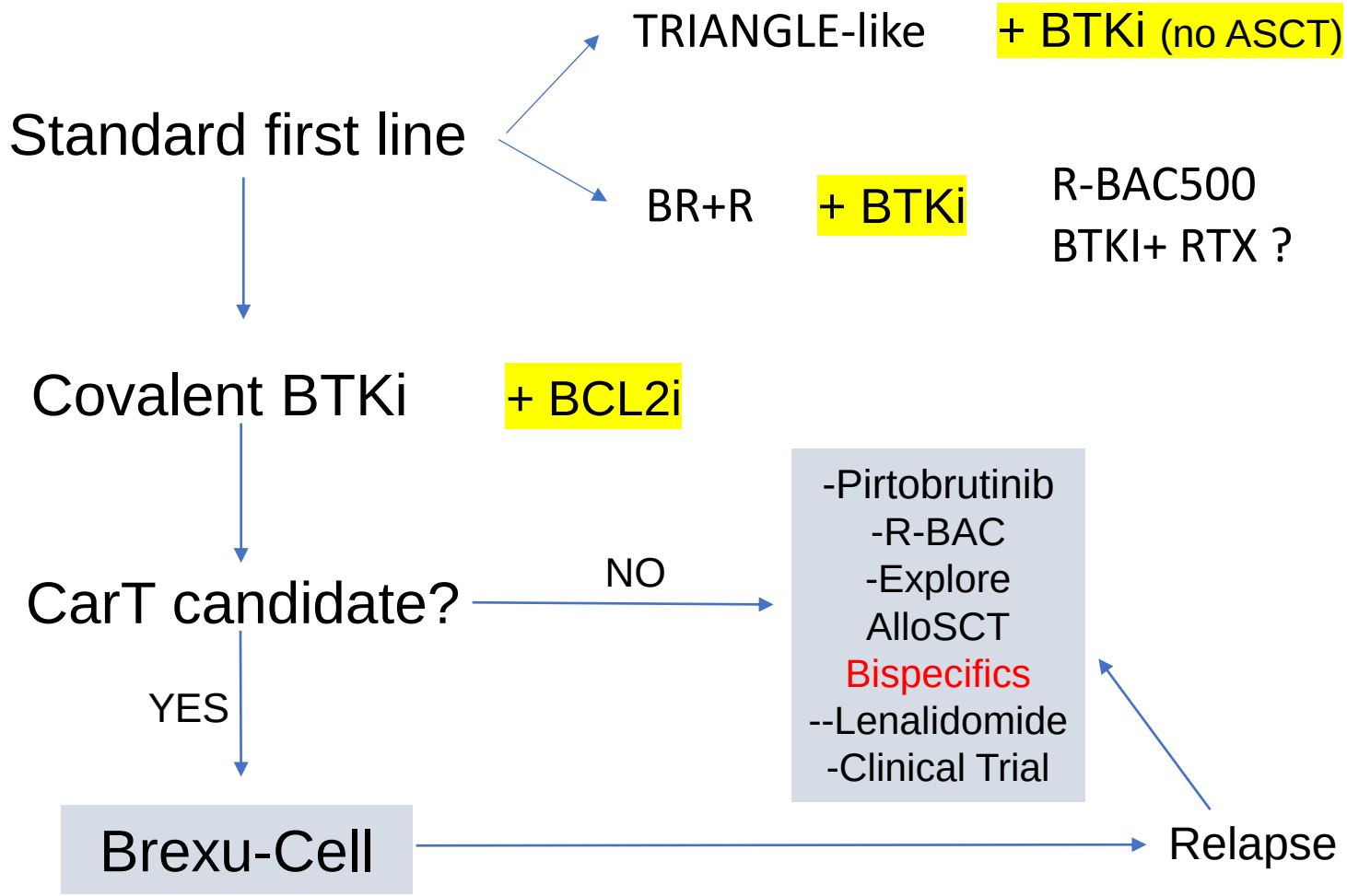
Philips T, et al. J Clin Oncol October 4, 2024

Treatment algorithm

Upfront

First relapse

Second relapse or further



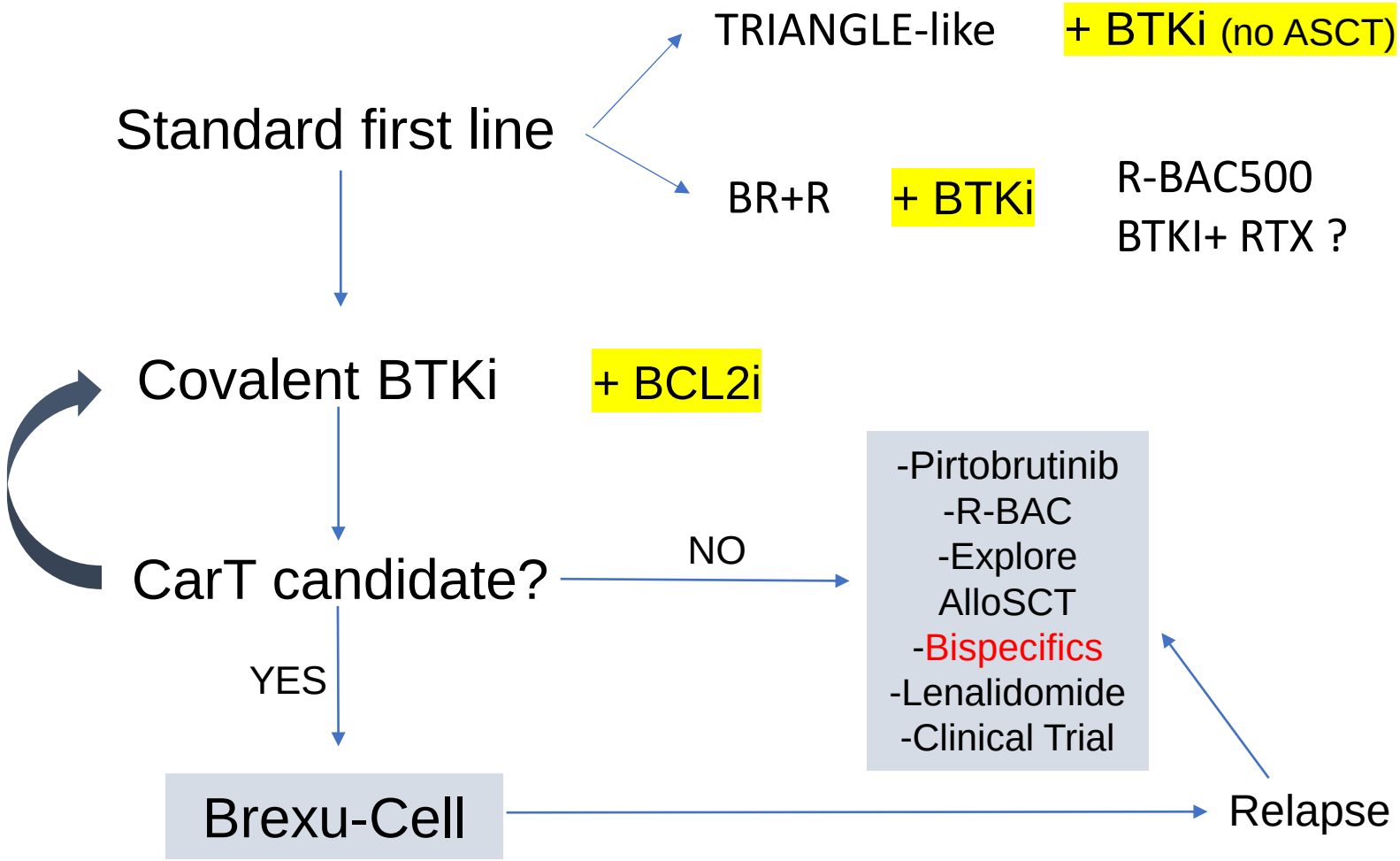
Courtesy of Carlo Visco

Treatment algorithm

Upfront

First relapse

Second relapse or further



Courtesy of Carlo Visco

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SISTEMA SANITARIO REGIONALE
AZIENDA OSPEDALIERO-UNIVERSITARIA
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FONDAZIONE
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LINFOMI

Gruppo per la terapia dei linfomi non Hodgkin
Ematologia Sapienza Roma

Grazie!

… a voi tutti per l'attenzione