



RELAPSED MANTLE CELL LYMPHOMA: CAR-T, PIPTOBRUTINIB, AND NOVEL THERAPIES

ALEX F. HERRERA, MD

Chief, Division of Lymphoma
Professor, Department of Hematology and Hematopoietic Cell Transplantation
Director, Toni Stephenson Lymphoma Center
City of Hope
Duarte, California, USA

Disclosures



Bristol Myers Squibb – research funding, consultancy

Genentech – research funding, consultancy

Merck – research funding, consultancy

Pfizer- research funding, consultancy

KiTE Pharma/Gilead - consultancy

AstraZeneca –consultancy

ADC Therapeutics –consultancy

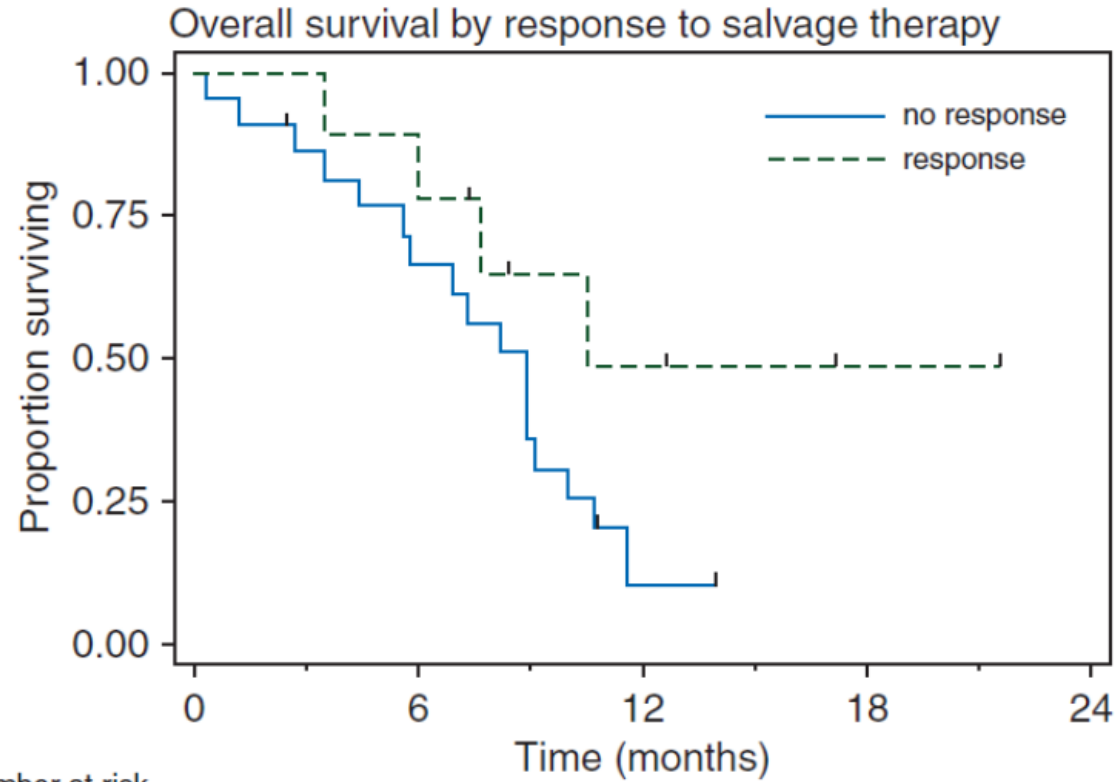
Genmab – consultancy

Allogene Therapeutics – consultancy

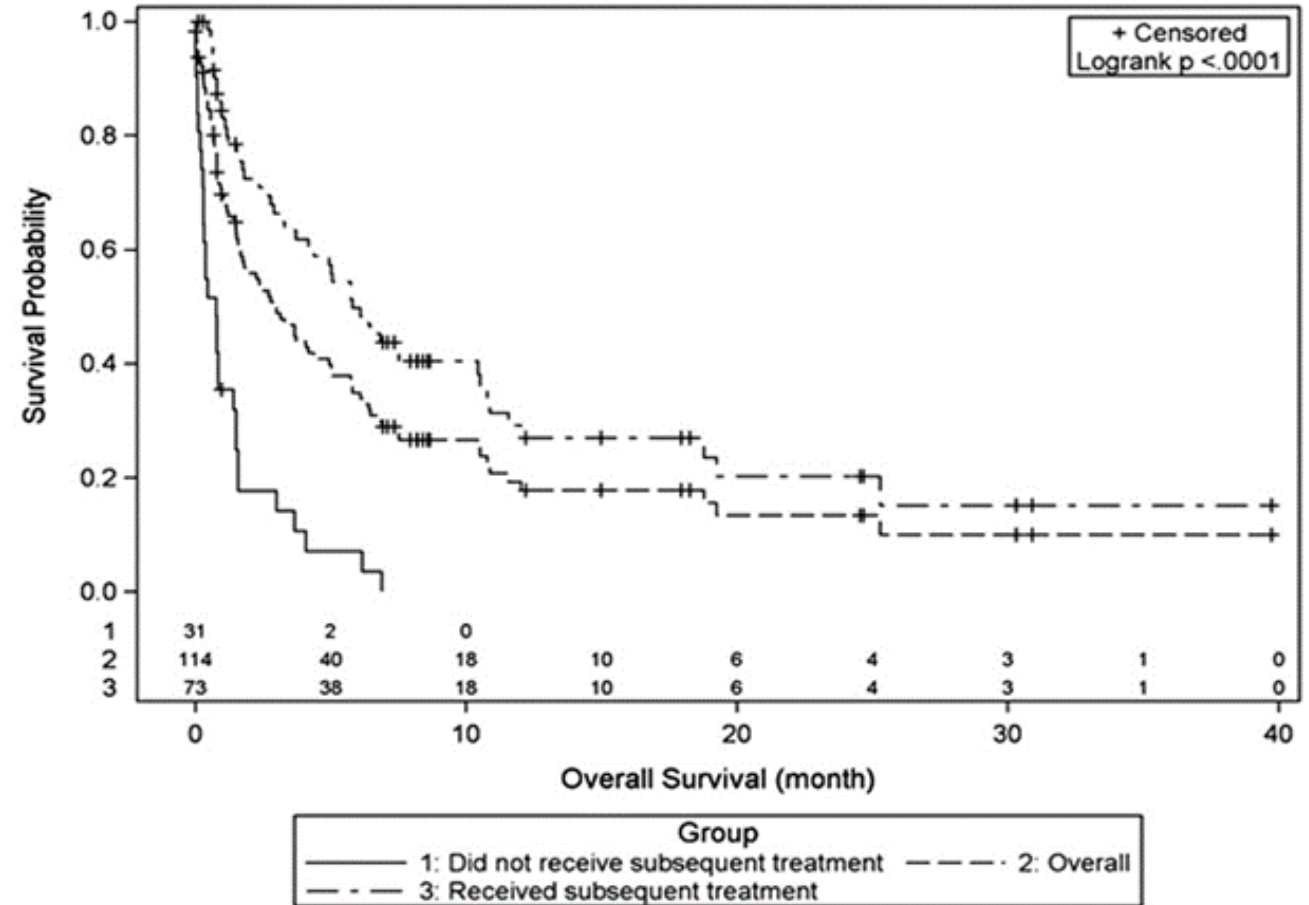
Eli Lilly and Company – consultancy

Incyte - consultancy

Relapsed/Refractory MCL: Dismal Outcomes after BTK inhibition failure



Number at risk	0	6	12	18	24
no response	22	13	1	0	0
response	9	8	3	1	0



Pirtobrutinib mechanism of action



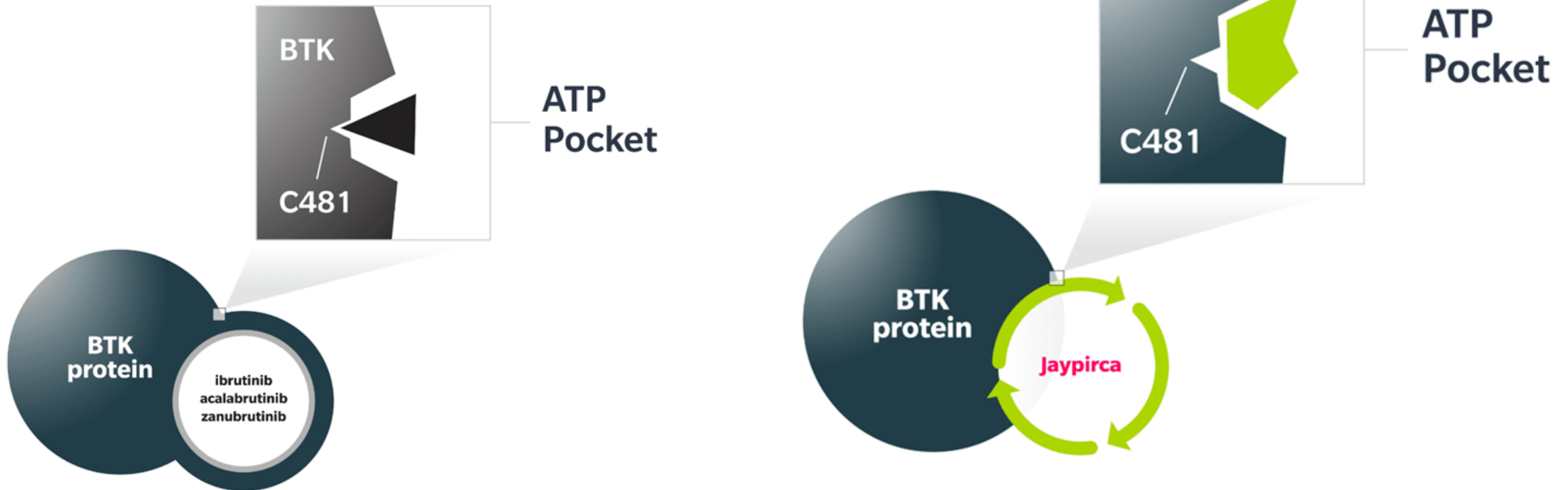
Jaypirca can **continue to leverage the BTK pathway**^{1,2}

IN PRECLINICAL STUDIES:
Covalent binding³

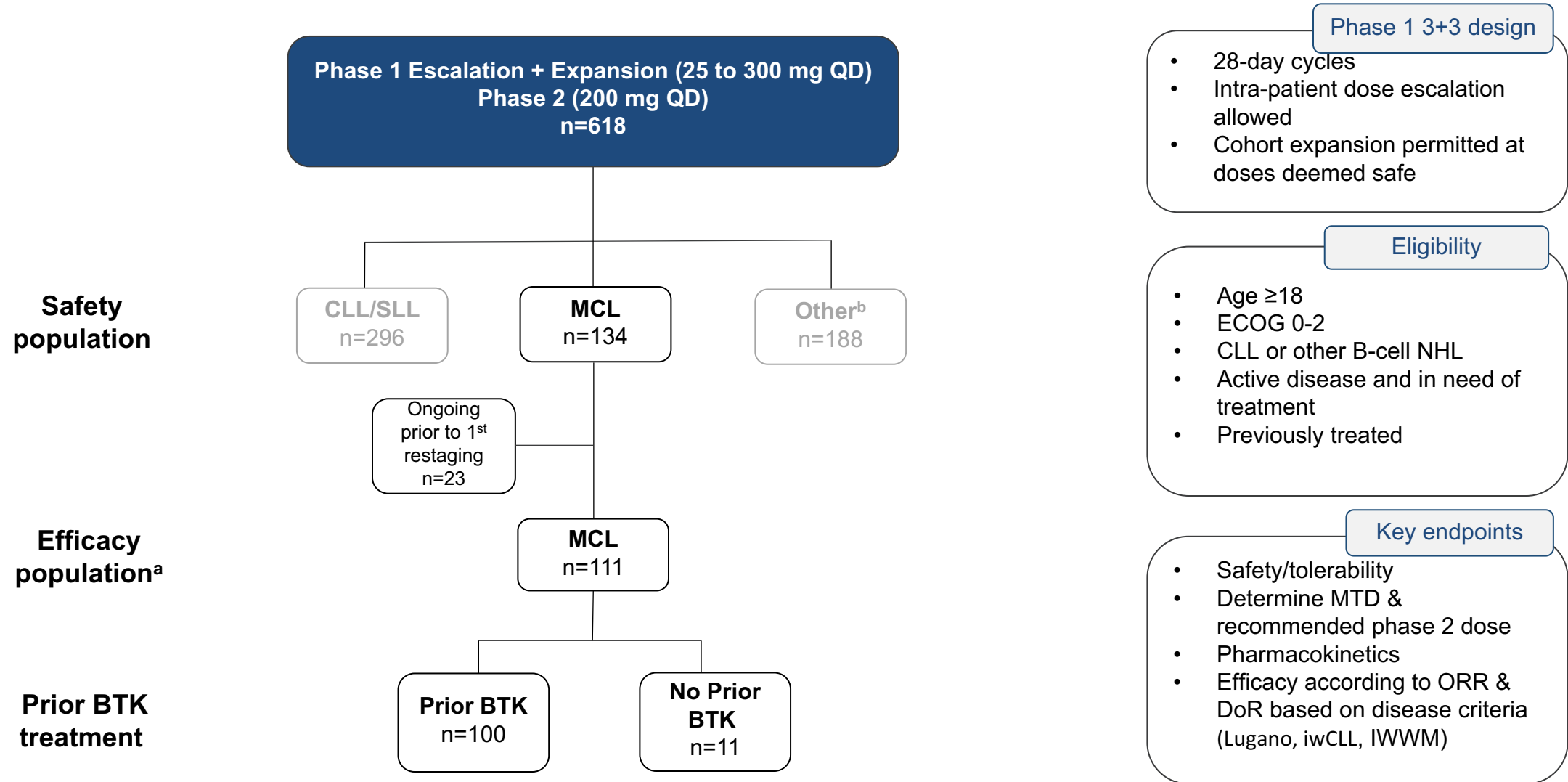
All other approved BTK inhibitors bind to the ATP binding site and form a covalent bond with C481^{3†}

Pirtobrutinib: reversible binding¹

Pirtobrutinib binds reversibly to the BTK protein in the ATP pocket and does not depend on C481^{1†}



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

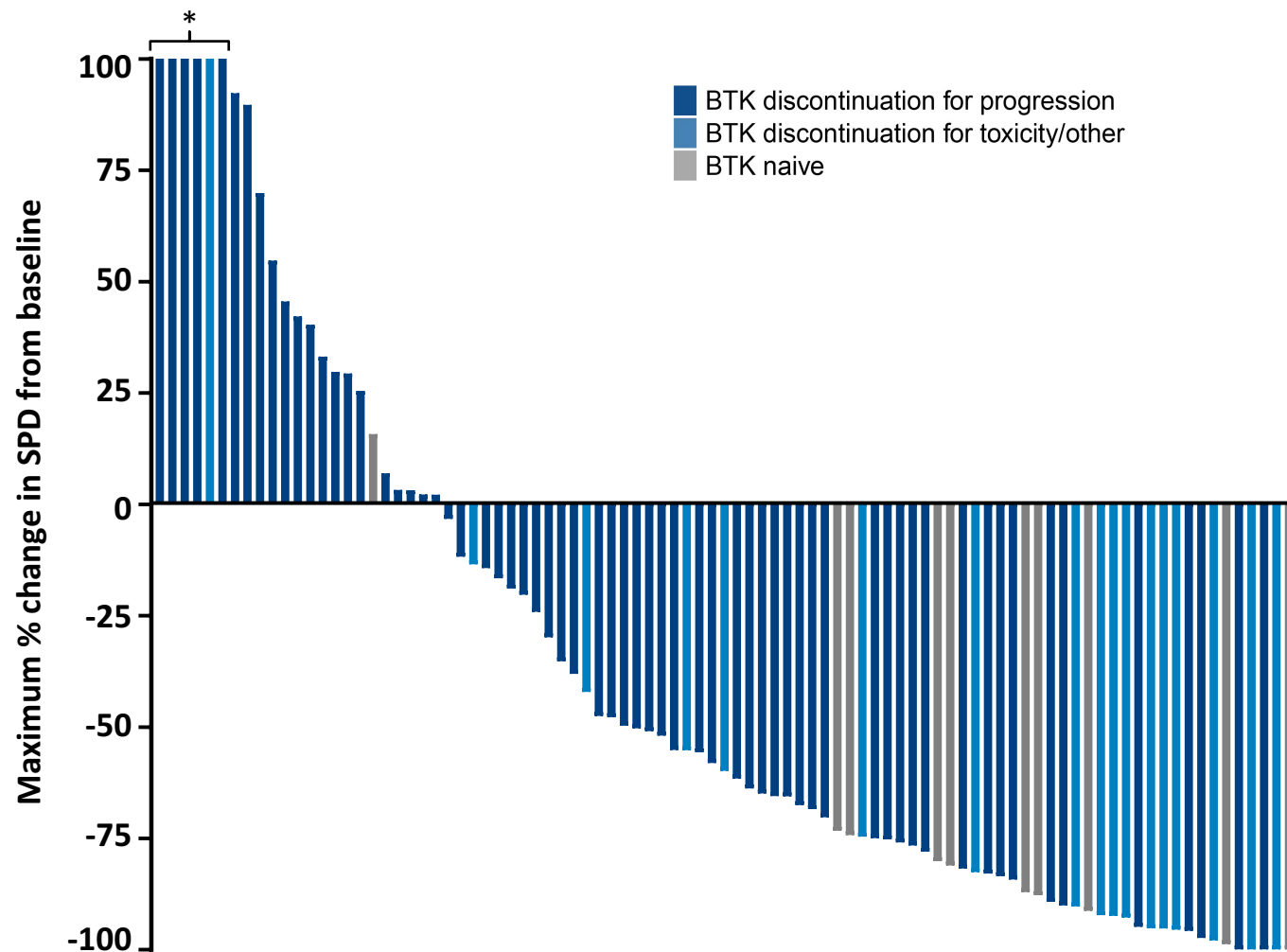


Pirtobrutinib: Patient Characteristics

Characteristics	MCL (n=134)
Median age (range), years	70 (46, 88)
Female / Male, n (%)	30 (22) / 104 (78)
Histology	
Classic	108 (81)
Pleomorphic/Blastoid	26 (19)
ECOG PS, n (%)	
0	82 (61)
1	50 (37)
2	2 (2)
Median number prior lines of systemic therapy (range)	3 (1, 9)
Prior therapy, n (%)	
BTK inhibitor	120 (90)
Anti-CD20 antibody	130 (97)
Chemotherapy	122 (91)
Stem cell transplant ^b	30 (22)
IMiD	23 (17)
BCL2 inhibitor	20 (15)
Proteasome inhibitor	17 (13)
CAR-T	7 (5)
PI3K inhibitor	5 (4)
Reason discontinued prior BTKi ^a	
Progressive disease	100 (83)
Toxicity/Other	20 (17)

Data cutoff date of 16 July 2021. Total % may be different than the sum of the individual components due to rounding. ^aCalculated as percent of patients who received prior BTK inhibitor. ^b3 patients had both auto and allo stem cell transplants.

Pirtobrutinib Efficacy in Mantle Cell Lymphoma



BTK Pre-Treated MCL Patients^a		n=100
Overall Response Rate^b, % (95% CI)	51% (41-61)	
Best Response		
CR, n (%)	25 (25)	
PR, n (%)	26 (26)	
SD, n (%)	16 (16)	
BTK Naive MCL Patients^a		n=11
Overall Response Rate^b, % (95% CI)	82% (48-98)	
Best Response		
CR, n (%)	2 (18)	
PR, n (%)	7 (64)	
SD, n (%)	1 (9)	

Efficacy also seen in patients with prior:

- Stem cell transplant (n=28): ORR 64% (95% CI: 44-81)
- CAR-T therapy (n=6): ORR 50% (95% CI: 12-88)

Data cutoff date of 16 July 2021. Data for 20 MCL patients are not shown in the waterfall plot due to no measurable target lesions identified by CT at baseline, discontinuation prior to first response assessment, or lack of adequate imaging in follow-up. *Indicates patients with >100% increase in SPD. ^aEfficacy evaluable patients are those who had at least one post-baseline response assessment or had discontinued treatment prior to first post-baseline response assessment. ^bORR includes patients with a best response of CR and PR. Response status per Lugano 2014 criteria based on investigator assessment. Total % may be different than the sum of the individual components due to rounding.

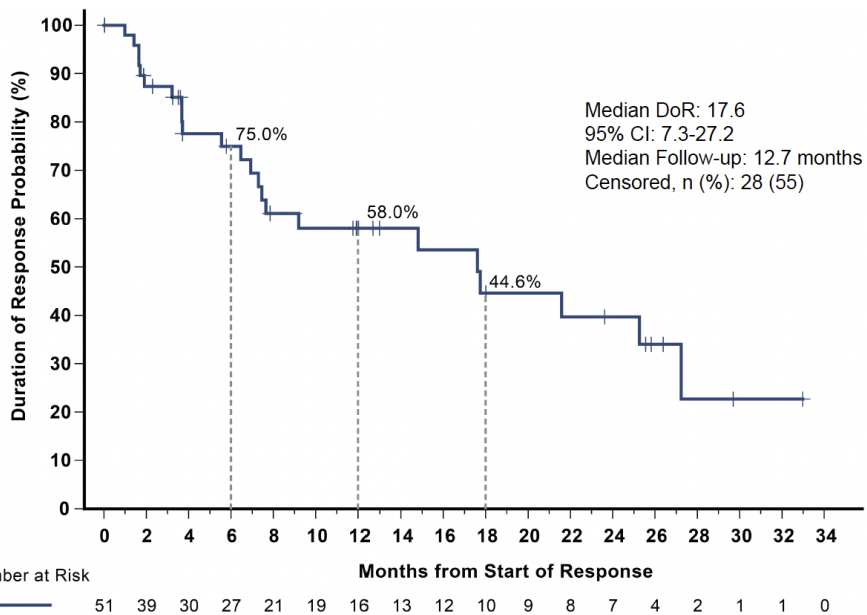
Pirtobrutinib: Responses in Prior BTKi Exposed



	N	ORR	mPFS	mOS	mDOR	1y DOR	1y PFS
BTK progressed	74	50%	5.5 m	23.4 m	14.8m	-	-
BTK intolerant	12	92%	NR	NR	NR	78.8%	82.5%

Updated Results and Subgroup Analysis From the BRUIN Phase 1/2 Study of Pirtobrutinib in Patients With R/R MCL: DOR, PFS, and OS

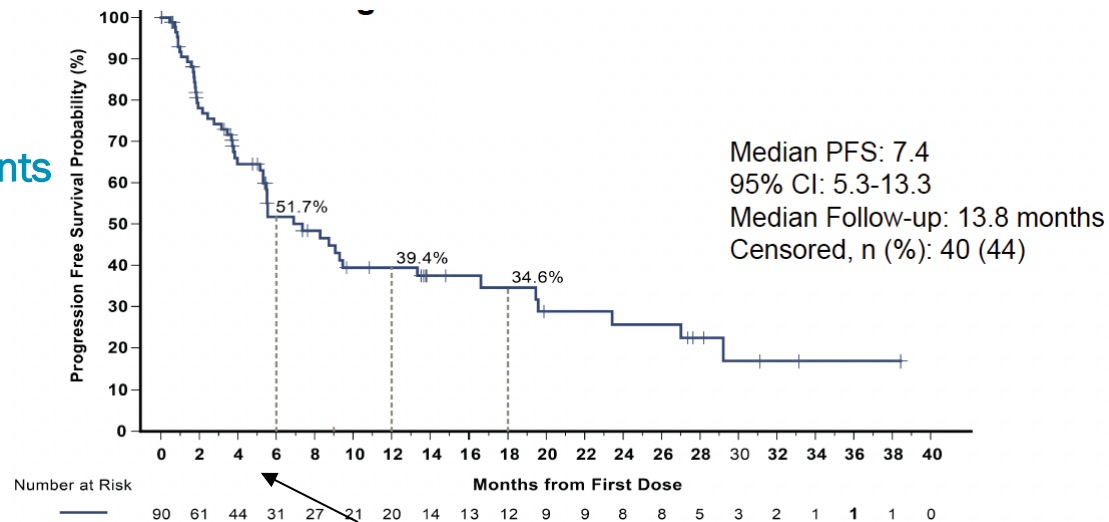
DOR in Prior cBTKi Patients



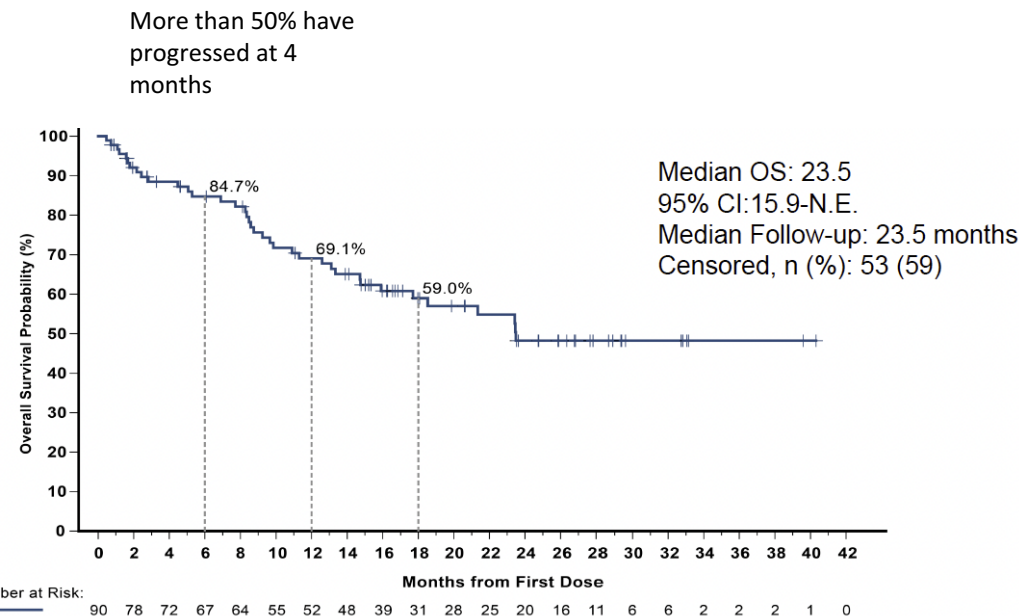
Majority have lost response, and most of the 21 would be those on pirta due to intolerance as those patients DOR is NR

- Median DOR, PFS, and OS were not reached in the cBTKi-naïve cohort
- 18-month rates (95% CI)
 - DOR: 100% (100)
 - PFS: 92.3% (56.6-98.9)
 - OS: 92.3% (56.6-98.9)

PFS in Prior cBTKi Patients



OS in Prior cBTKi Patients



More than 50% have progressed at 4 months

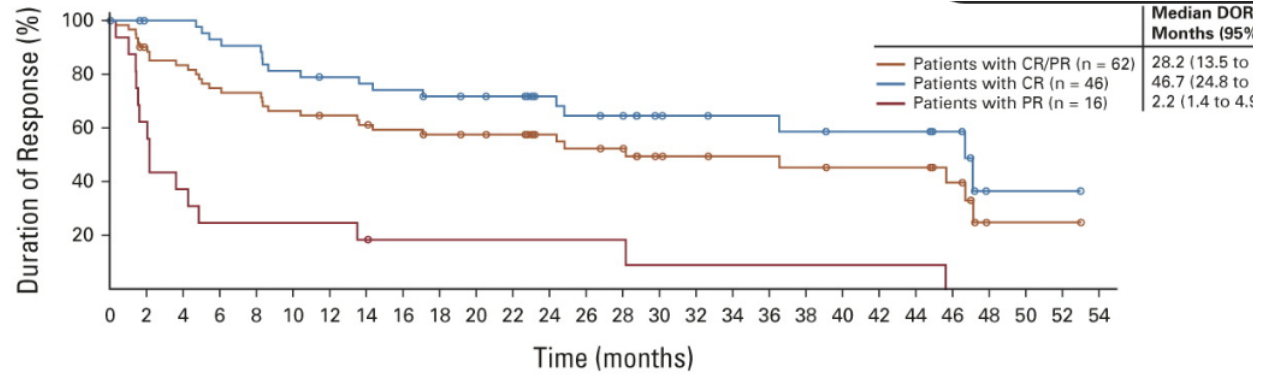
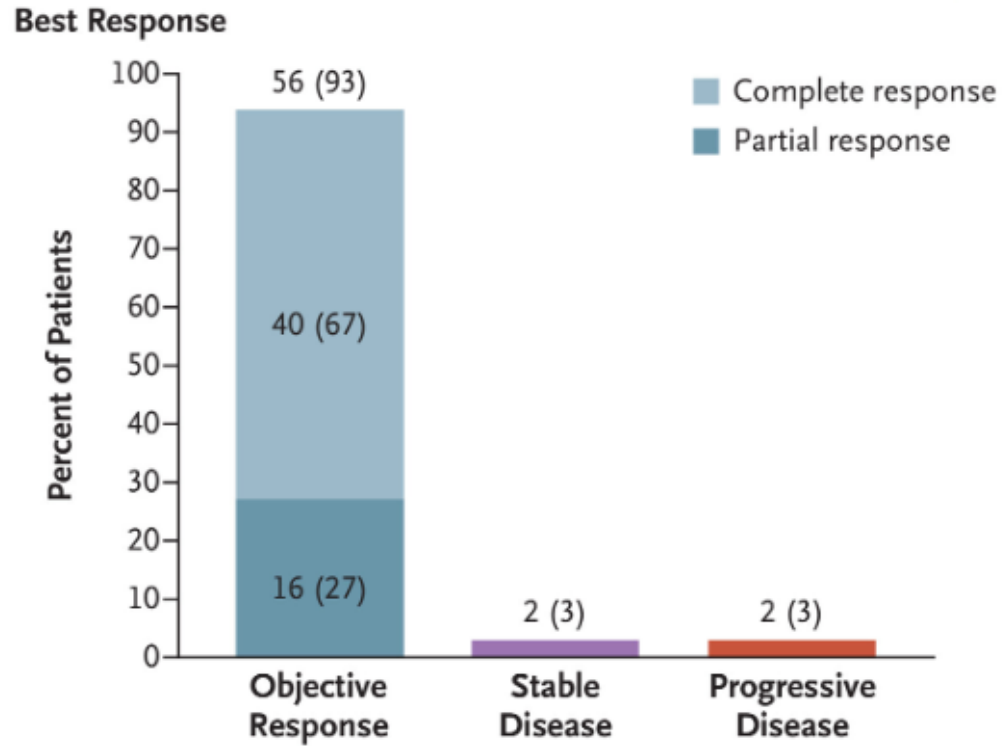
Updated Results and Subgroup Analysis From the BRUIN Phase 1/2 Study of Pirtobrutinib in Patients With R/R MCL: Safety and Summary

AEs for Patients With MCL (n=166), %		TEAEs (≥15%)		TRAEs	
		Any Grade	Grade ≥3	Any Grade	Grade ≥3
Fatigue		31.3	3.0	21.1	2.4
Diarrhea		22.3	0.0	12.0	0.0
Dyspnea		16.3	1.2	9.0	0.6
AEs of special interest	Bruising	16.3	0.0	11.4	0.0
	Rash	8.4	0.6	5.4	0.0
	Arthralgia	9.0	1.2	2.4	0.0
	Hemorrhage/hematoma	10.2	2.4	4.2	0.6
	Hypertension	3.6	0.0	1.8	0.0
	Afib/flutter	3.6	1.8	0.6	0.0

- Median time on treatment for the MCL population: 5 months
- Discontinuations due to TRAEs: 3% (n=5)
- Dose reductions due to TRAEs: 6% (n=10)

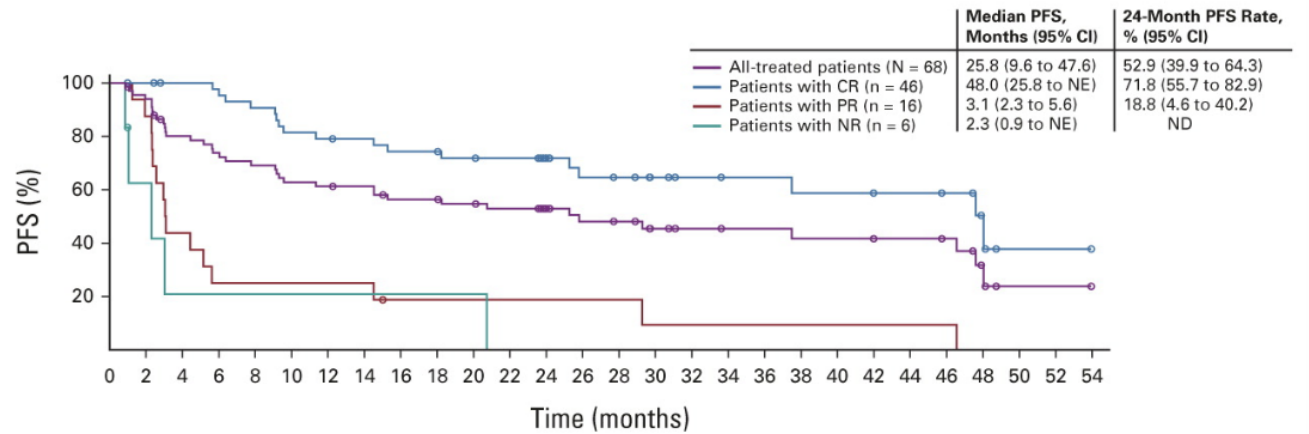
Shah NN, et al. ASCO 2023. Abstract 7514. Jurczak J, et al. EHA 2023. Abstract P1087. Cheah CY, et al. ICML 2023. Abstract 102.

Brexu-cel Efficacy



risk:

s with CR/PR	62	53	49	44	43	39	37	35	33	31	30	29	22	20	19	14	13	12	12	11	10	10	10	7	1	1	1	0
s with CR	46	43	43	40	39	35	33	32	31	29	28	27	20	18	17	13	12	11	11	10	9	9	9	7	1	1	1	0
s with PR	16	10	6	4	4	4	4	3	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	0	0	0	0	0



No. at risk:

All-treated patients	68	62	51	47	44	40	39	38	34	34	32	30	24	20	19	15	13	12	12	11	11	10	10	9	4	1	1	0
Patients with CR	46	45	43	42	39	35	34	33	31	31	29	28	22	18	17	14	12	11	11	10	10	9	9	8	4	1	1	0
Patients with PR	16	14	7	4	4	4	4	4	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	0	0	0	0
Patients with NR	6	3	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Brexu-cel: High Rates of CRS and ICANS

- No Grade 5 CRS occurred

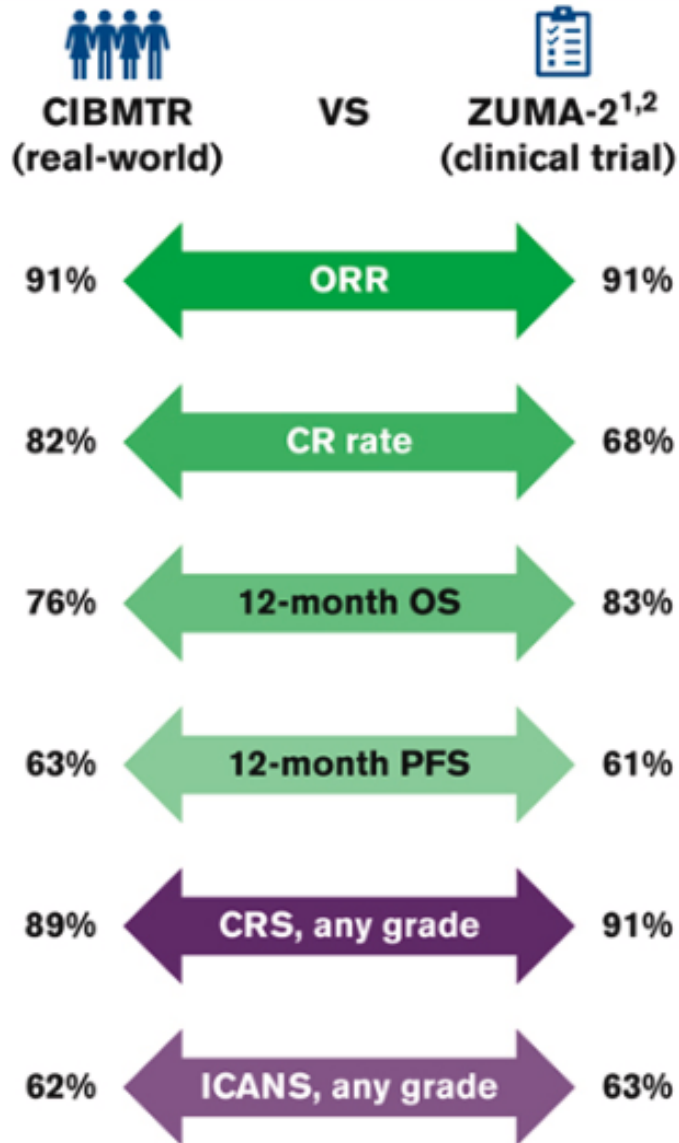
Parameter	N = 68
CRS, n (%) ^a	
Any grade	62 (91)
Grade ≥ 3	10 (15)
Most common any grade symptoms of CRS, n (%)	
Pyrexia	62 (91)
Hypotension	35 (51)
Hypoxia	23 (34)
AE management, n (%)	
Tocilizumab	40 (59)
Corticosteroids	15 (22)
Median time to onset (range), days	2 (1 – 13)
Median duration of events, days	11
Patients with resolved events, n (%)	62/62 (100)

Parameter	N = 68
Neurologic events, n (%) ^a	
Any grade	43 (63)
Grade ≥ 3	21 (31)
Most common any grade symptoms, n (%)	
Tremor	24 (35)
Encephalopathy	21 (31)
Confusional state	14 (21)
AE management, n (%)	
Tocilizumab	18 (26)
Corticosteroids	26 (38)
Median time to onset (range), days	7 (1 – 32)
Median duration of events, days	12
Patients with resolved events, n (%)	37/43 (86) ^b

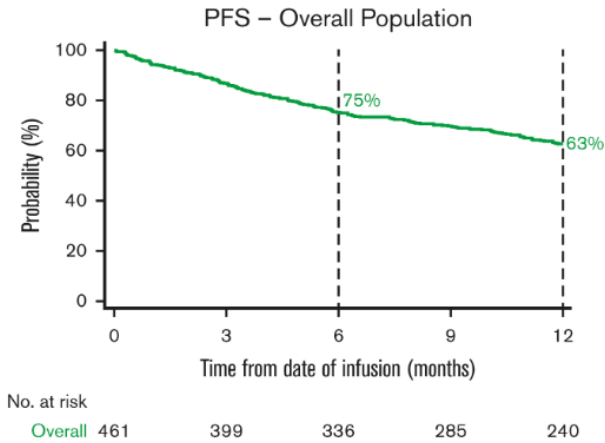
Wang M et al, KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. N Engl J Med. 2020 Apr 2;382(14):1331-1342. doi: 10.1056/NEJMoa1914347. PMID: 32242358; PMCID: PMC7731441.

Wang M et al NEJM 2020; Wang M et al. JCO 2022

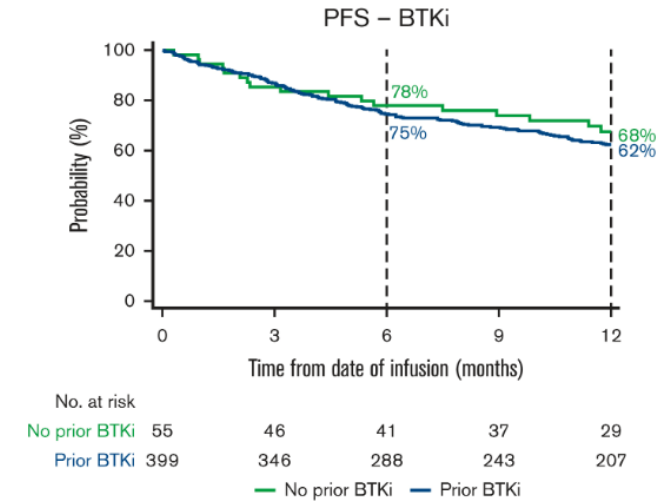
RWE confirms Zuma-2 safety and efficacy including subgroups



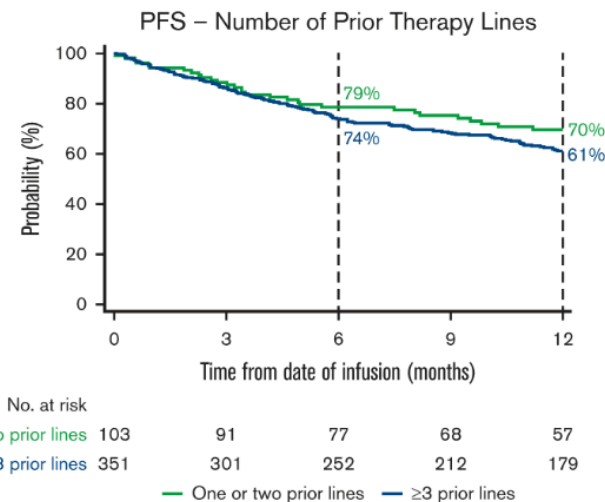
A



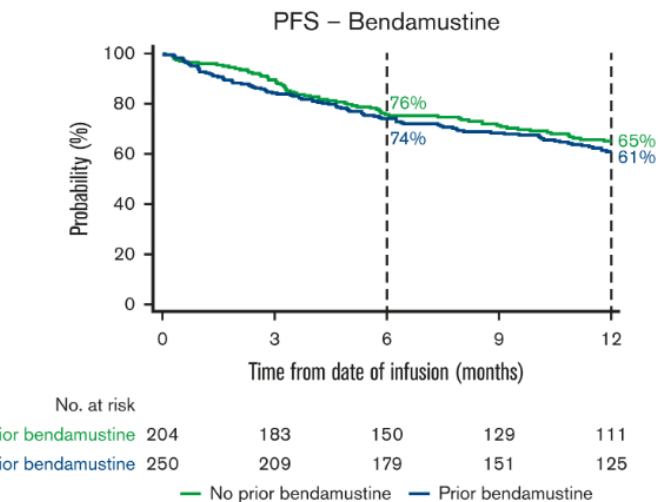
B



C



D



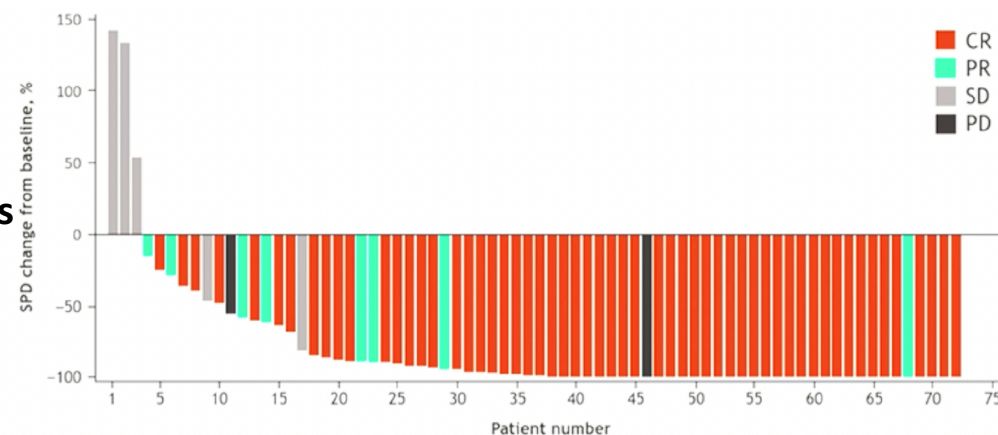
Liso-cel Efficacy in R/R MCL: Response and DOR

Best Response	Primary Analysis Set (n=74)
ORR, % (95% CI)	86.5 (76.5-93.3); $P < 0.0001$
CR, % (95% CI)	74.3 (62.8-83.8); $P < 0.0001$
PR, %	12.2
SD, %	6.8
PD, %	0
NE, %	6.8

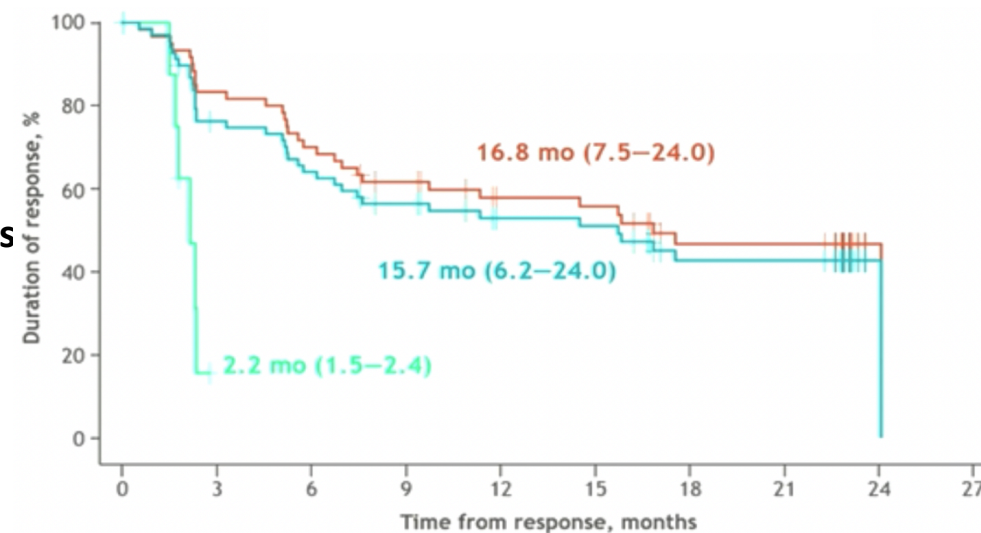
Response	Efficacy Analysis Set (n=83)
ORR, % (95% CI)	83.1 (73.3-90.5)
CR, % (95% CI)	72.3 (61.4-81.6)
Median months to first CR/PR (range)	0.95 (0.7-3.0)

DOR Per IRC		Responders (n=69)	Patients with CR (n=60)
Median, months (95% CI)		15.7 (6.2-24.0)	16.8 (7.5-24.0)
Rate, % (95% CI)	12-month	52.9 (40.1-64.2)	57.8 (44.2-69.2)
	18-month	42.7 (29.9-54.9)	46.7 (32.8-59.4)
Median follow-up, months (95% CI)		22.8 (16.7-23.0)	

Change in SPD and Response Status per IRC (Efficacy Analysis Set, n=83)



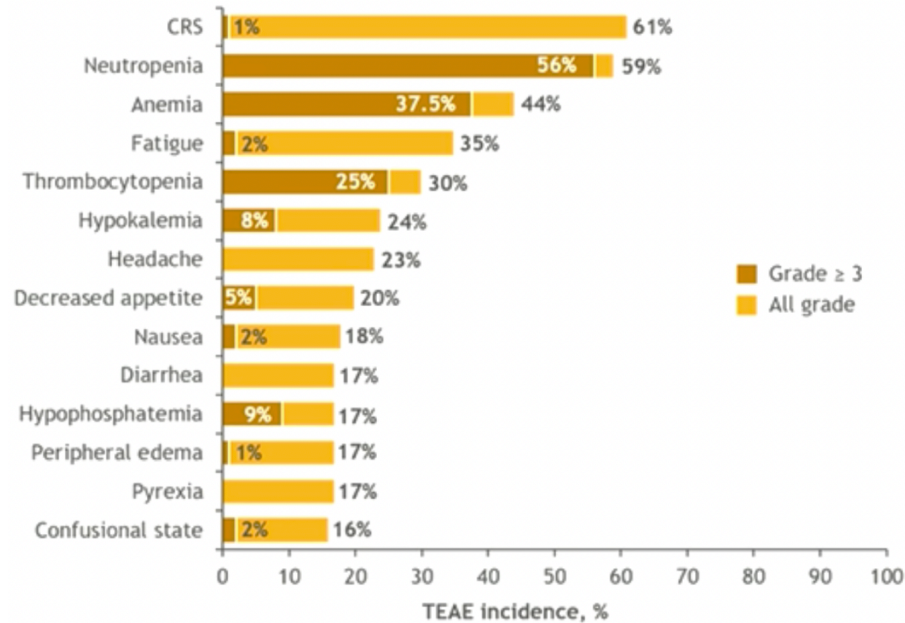
DOR per IRC (Efficacy Analysis Set, n=83)



CR	60	50	42	35	28	27	18	18	1	0
PR	9	0								
CR/PR	69	50	42	35	28	27	18	18	1	0

Primary Analysis Results From the TRANSCEND-NHL-001 Study of Liso-cel in Patients With R/R MCL: Safety

TEAEs (Liso-cel-Treated Set, n=88)

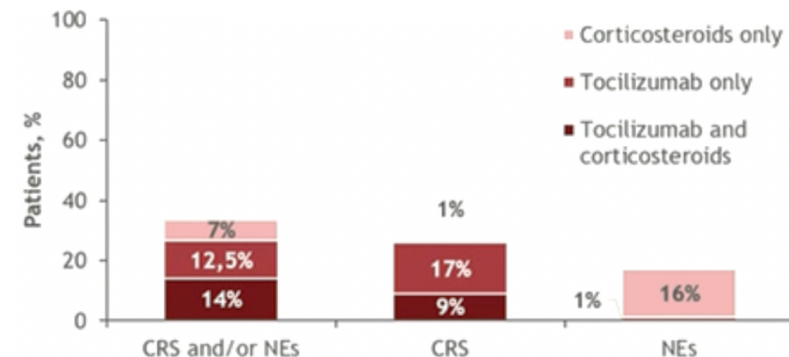


- MTD was not reached; 2 patients with a DLT among 31 DLT-evaluable patients (both at DL2)
 - Grade 5 TLS in a patient with high tumor burden
 - Grade 3 neutropenia/grade 4 thrombocytopenia
- Grade 5 TEAEs in 4 (4.5%) patients
 - 3 were considered related to liso-cel
 - 1 was considered unrelated

CRS and NEs (Liso-cel-Treated Set, n=88)	CRS	NEs
Any grade, n (%)	54 (61)	27 (31)
Grade 1/2	53 (60)	19 (22)
Grade 3	0	7 (8)
Grade 4	1 (1)	1 (1)
Grade 5	0	0
Median time to: Onset	4.0 (1-10)	8.0 (1-25)
(range), days	Resolution	4.0 (1-14)
		5.0 (1-45)

Other AEs of Special Interest, n (%)	Liso-cel-Treated Set (n=88)
Prolonged cytopenias	35 (40)
Grade ≥3 infections	13 (15)
Hypogammaglobulinemia	6 (7)

Treatment for CRS and NEs



CRS – Cytokine Release Syndrome
 DLT – Dose limiting Toxicity
 MTD – Maximum Tolerated Dose, NE – Neurological Event

Glofitamab in MCL

Glofitamab dosing schedules

Phase I dose escalation in R/R MCL

Glofitamab IV administration

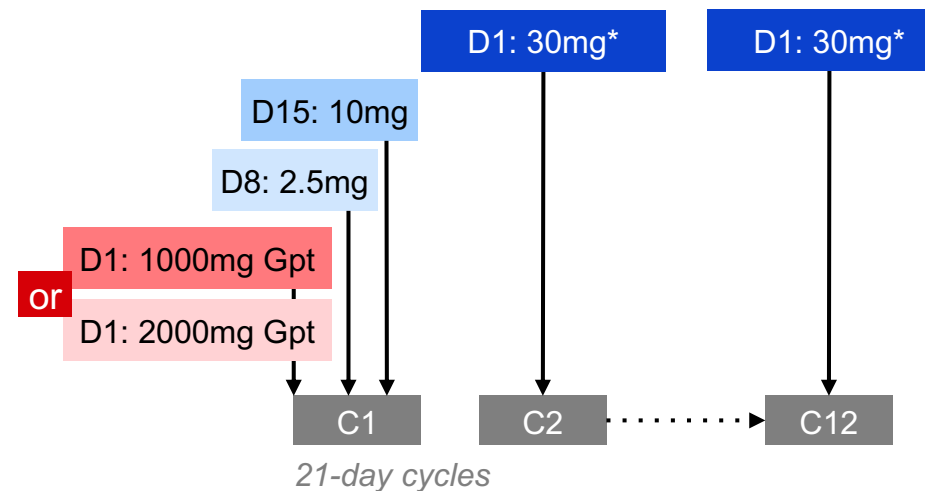
- Fixed-duration treatment: maximum 12 cycles

CRS mitigation

- Obinutuzumab pretreatment (1 x 1000mg or 1 x 2000mg)
- C1 step-up dosing
- Monitoring after first dose (2.5mg)

Population characteristics:

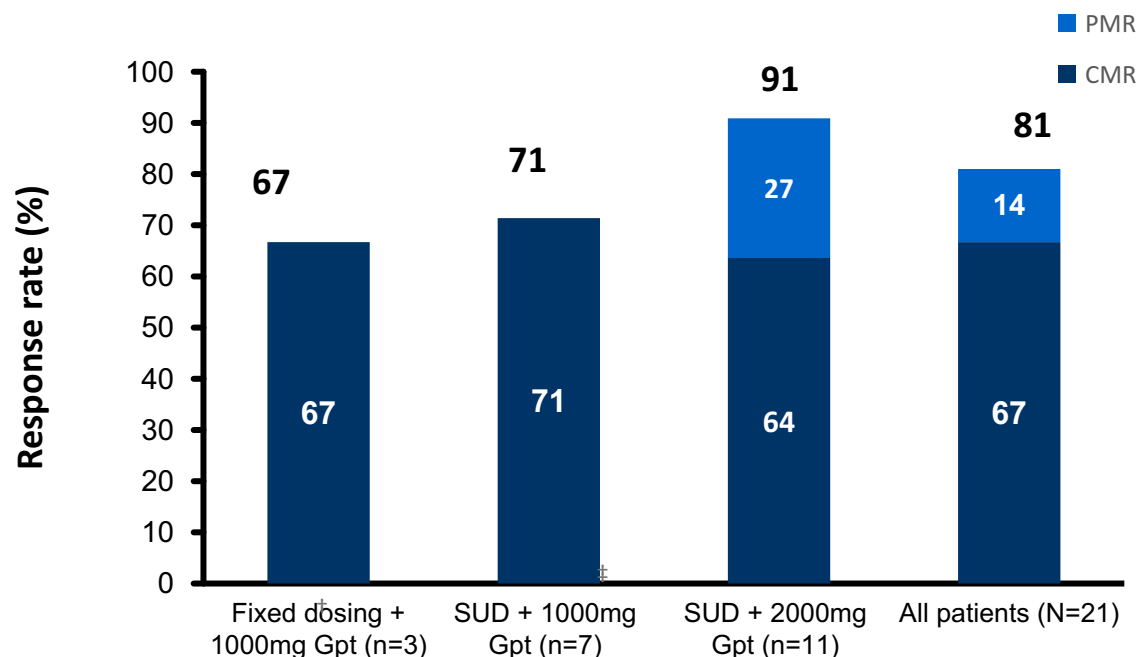
- Age ≥ 18 years
- ≥ 1 prior systemic therapy
- ECOG PS ≤ 1



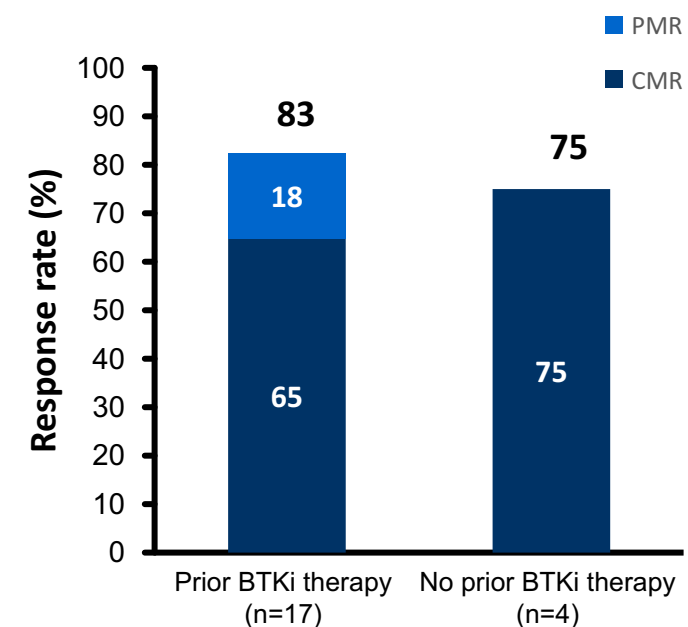
Clinical cut-off date: March 14, 2022; *In the glofitamab SUD + 1000mg Gpt cohort, two patients had 16mg glofitamab as their target dose.

Glofitamab Response rates

Response rates¹ by glofitamab regimen*



Response rates¹ by prior BTKi therapy*



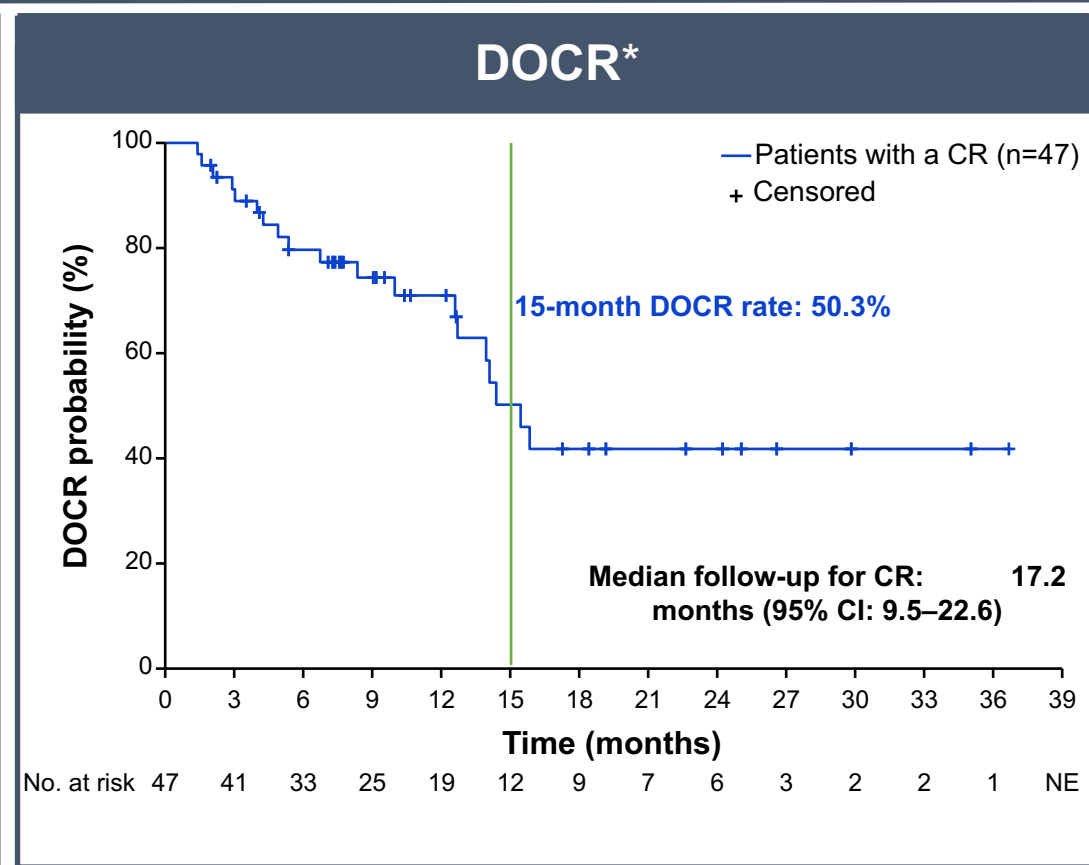
Glofitamab resulted in high response rates in patients with R/R MCL

*21/29 patients were efficacy-evaluable: the secondary efficacy-evaluable population includes all patients who had a response assessment performed (investigator-assessed), or who were still on treatment at the time of their first scheduled response assessment (Lugano 2014 criteria)¹. [†]Due to a data issue, the response (CR) from one patient is reported as missing, and two patients treated with a combination of glofitamab and obinutuzumab (G-combo); [‡]One patient treated with G-combo. CMR, complete metabolic response; PMR, partial metabolic response.

1. Cheson, BD et al. J Clin Oncol 2014

Glofitamab: Duration of response in MCL

DOCR*	Prior BTKi n=22	All patients n=47
Median DOCR, months (95% CI)	12.6 (5.4–NE)	15.4 (12.7–NE)
15-month DOCR rate, % (95% CI)	33.5 (10.6–56.4)	50.3 (32.0–68.6)
Ongoing CR, n (%)	10 (45.5)	28 (59.6)
DOR*	n=23	n=51
Median DOR, months (95% CI)	12.6 (7.4–NE)	16.2 (12.6–NE)
15-month DOR rate, % (95% CI)	38.0 (15.5–60.6)	59.7 (44.1–75.3)
Ongoing response, n (%)	10 (43.5)	28 (54.9)



With 17 months' median follow-up, fixed-duration glofitamab monotherapy achieved **durable CRs** with the **majority of CRs (59.6%) still ongoing** at data cut-off

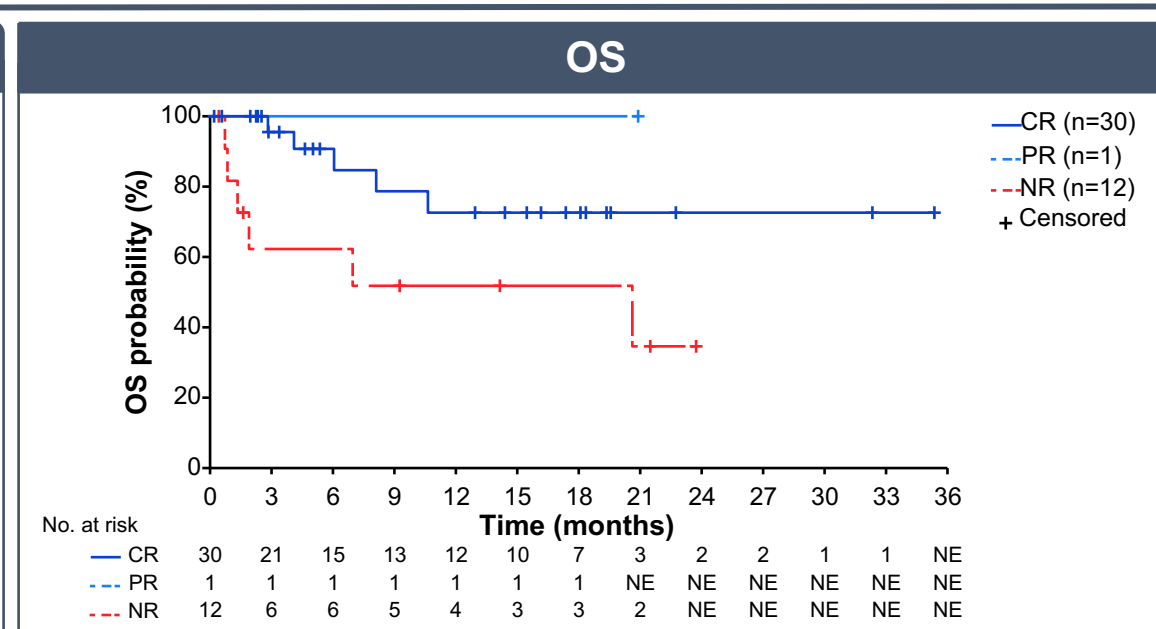
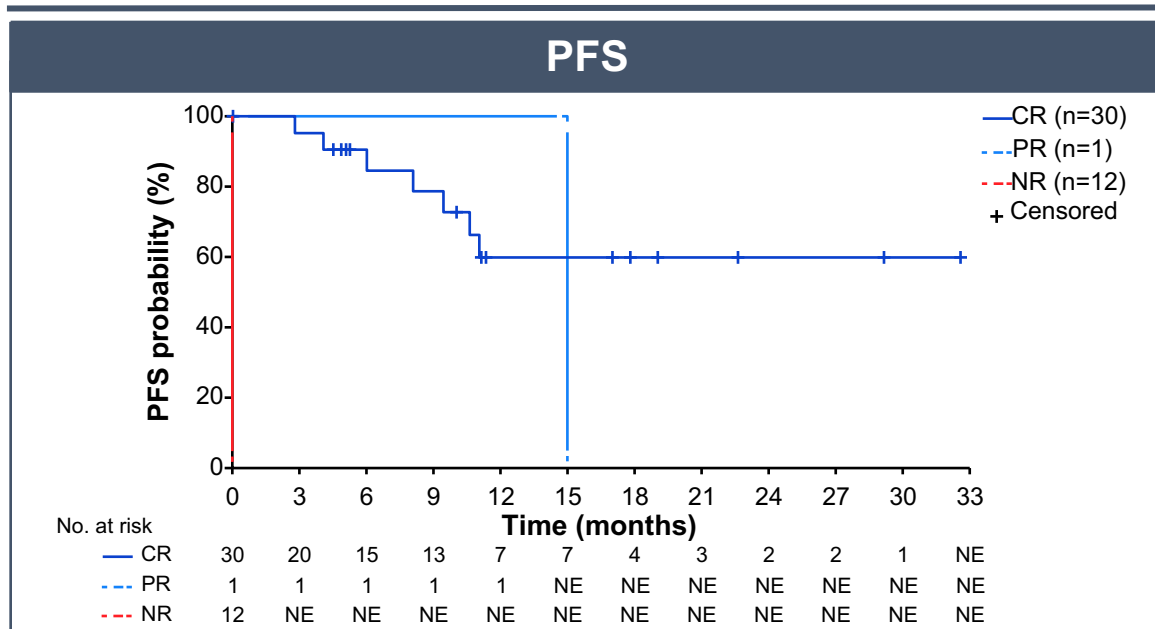
Clinical cut-off date: September 04, 2023.

*Investigator-assessed.

DOR, duration of response; DOCR, duration of complete response; NE, not estimable.

Phillips et al. EHA 2024

Glofitamab: Landmark analyses by response at EOT



Landmark PFS from EOT in patients with CR at EOT	n=30	Landmark OS from EOT in patients with CR at EOT	n=30
Median PFS, months (95% CI)	NE (10.6–NE)	Median OS, months (95% CI)	NE (NE)
15-month PFS rate, % (95% CI)	59.2 (35.5–83.0)	15-month OS rate, % (95% CI)	72.7 (51.9–93.5)

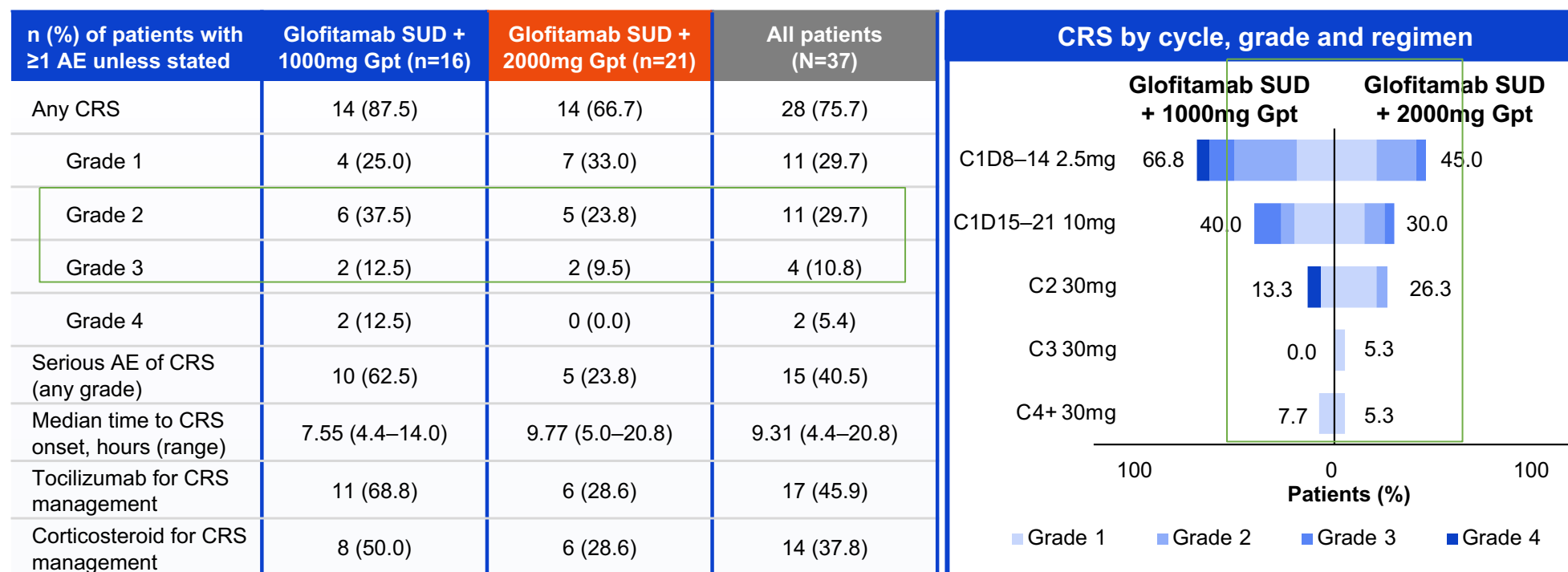
The majority of patients with a CR at EOT remained progression-free and were alive at 15 months post-EOT

Clinical cut-off date: September 04, 2023.

EOT, end of treatment; NR, no response.

Glofitmab: CRS in MCL

Cytokine release syndrome*



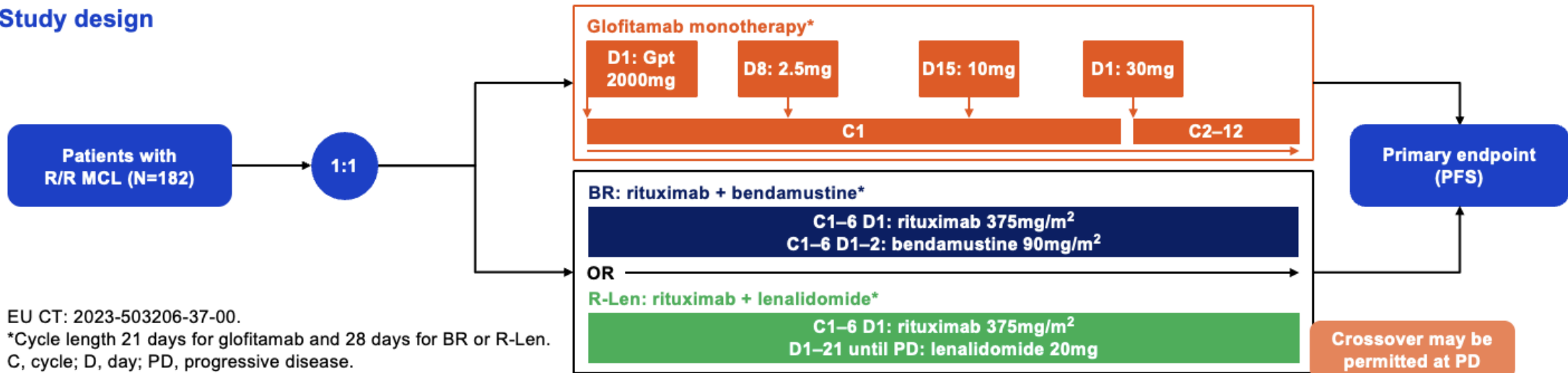
Higher Gpt (2000mg) was associated with a lower rate of CRS, with no Grade 4 events reported in this group

Lee et. Al. Biol Blood Marrow Transplant 2019, Phillips et al. ASH 2022

*By American Society for Transplantation and Cellular Therapy (ASTCT) criteria.¹

GLOBRYTE (NCT06084936) is a Phase III, open-label, multicenter, randomized, controlled trial in R/R MCL

Study design



Key eligibility criteria



Inclusion criteria

- Aged ≥18 years
- Histologically confirmed MCL with documentation of either overexpression of cyclin D1 or the presence of t(11:14)
- R/R MCL; measurable disease
- ECOG performance status 0–2
- ≥1 prior line of systemic therapy including BTKi and another option (e.g. anti-CD20 monoclonal antibody, chemotherapy, or targeted agent such as bortezomib)
- Life expectancy ≥12 weeks
- Confirmed availability of tumor biopsy tissue (pre-treatment or recent archival specimen)



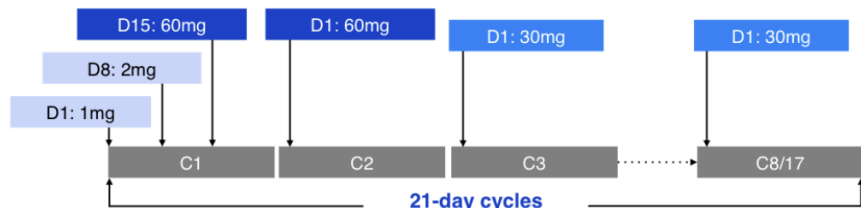
Exclusion criteria

- Leukemic, non-nodal MCL
- Prior CAR T-cell therapy or treatment with glofitamab or other CD20xCD3 bispecific antibodies
- Primary/secondary CNS lymphoma, or history of CNS lymphoma or other malignancies*
- Current or prior CNS disease (including epilepsy or CNS vasculitis; stroke or transient ischemic attack within the past 2 years)
- Significant CV disease (New York Heart Association Class III or IV cardiac disease/Objective Assessment Class C or D), MI within the last 6 months, unstable arrhythmias, or unstable angina
- Known active infection at time of enrollment

*Except for curatively-treated basal or squamous cell skin cancer, *in-situ* cervical cancer, low-grade early prostate cancer, or any other malignancy treated with curative intent and in remission for ≥2 years. CNS, central nervous system; CV, cardiovascular; ECOG, Eastern Cooperative Oncology Group; MI, myocardial infarction.

Mosunetuzumab in MCL

Figure 1. Mosunetuzumab dosing schedule.



C, cycle; D, day.

Table 1. Summary of patient demographic and baseline characteristics.

n (%) unless stated otherwise	All patients (N=25)
Median age, years (range)	70 (50–89)
Male	20 (80.0)
ECOG PS 0 / 1	9 (36.0) / 16 (64.0)
Ann Arbor stage III/IV	23 (92.0)
Ki-67 status <30% / ≥30–<50% / ≥50% / unknown	1 (4.0) / 2 (8.0) / 11 (44.0) / 11 (44.0)
MIPI score <6 / ≥6	4 (16.0) / 21 (84.0)
Bulky disease >6cm / >7cm / >10cm	10 (40.0) / 5 (20.0) / 3 (12.0)
Morphology at baseline Blastoid MCL / classic MCL not known / other	7 (28.0) / 10 (40.0) 7 (28.0) / 1 (4.0)
Bone marrow involvement	13 (52.0)
Prior autologous stem cell transplant	8 (32.0)
Median lines of prior therapy, n (range)	3 (2–6)
Number of prior lines of therapy 2 / ≥3	5 (20.0) / 20 (80.0)
Refractory to Last prior therapy / prior BTKi / prior anti-CD20 therapy	23 (92.0) / 24 (96.0) / 18 (72.0)
Failed to respond to prior BTKi	16 (64.0)

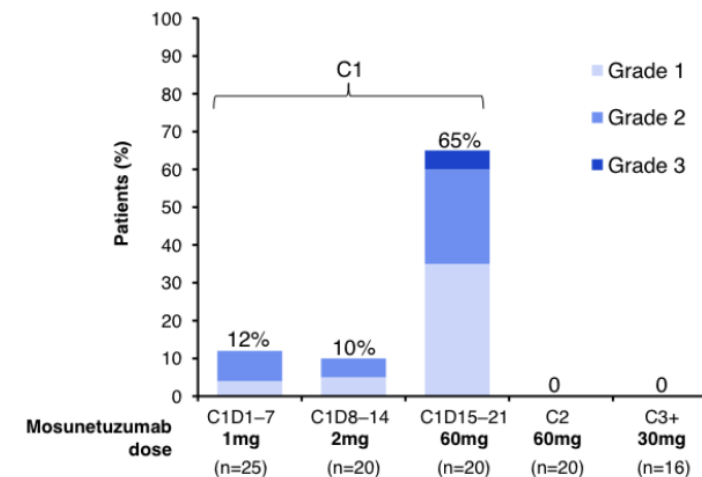
Table 5. Summary of CRS events.

n (%), unless stated otherwise	All patients (N=25)
CRS (any grade)	13 (52.0)
Grade 1	6 (24.0)
Grade 2	6 (24.0)
Grade 3	1 (4.0)
Patients with events resolved (n=13)	13 (100.0)
Median CRS duration, days (range)	3 (1–7)
Corticosteroids for CRS management*	2 (8.0)
Tocilizumab for CRS management	4 (16.0)

There were no Grade 4 or 5 CRS events. *All patients received mandatory corticosteroid premedication; patients who received corticosteroids for CRS management are defined as those who received it concurrently, not as prophylaxis, and indicated for CRS.

- Suspected immune effector cell-associated neurotoxicity syndrome events occurred in three patients (Grade 1 confusional state [n=2]; Grade 2 delirium [n=1]); two events occurred concurrently with CRS.

Figure 4. CRS events by cycle and grade.



Mosunetuzumab Efficacy in MCL

Table 2. Efficacy summary.

Months (95% CI) unless stated otherwise	All patients (N=25)
ORR, n (%) [95% CI]	11 (44.0) [24.4–65.1]
CR	6 (24.0) [9.4–45.1]
PR	5 (20.0) [6.8–40.7]
Median DoR	10.3 (2.3–19.5)
Median DoCR	18.0 (10.3–22.3)
Median PFS	3.7 (1.4–5.8)
Median OS	7.3 (3.6–25.9)

CI, confidence interval.

Table 3. Efficacy summary in high-risk subgroups.

	Patients with Ki-67 status ≥30% (n=13)	Patients with Ki-67 status ≥50% (n=11)	Patients with blastoid MCL (n=7)	Patients with MIPI ≥6 (n=21)
ORR, n (%) [95% CI]	6 (46.2) [19.2–74.9]	6 (54.5) [23.4–83.3]	2 (28.6) [3.7–71.0]	9 (42.9) [21.8–66.0]
CR, n (%)	4 (30.8)	4 (36.4)	2 (28.6)	5 (23.8)
PR, n (%)	2 (15.4)	2 (18.2)	0	4 (19.0)

Study design: Phase II dose expansion

Key inclusion criteria

- R/R MCL
- ECOG PS 0–2
- ≥2 prior therapies (including an anti-CD20 antibody, anthracycline or bendamustine therapy, and BTKi)

Objectives

- Primary: best ORR¹ by IRC
- Secondary: best ORR by INV, CR rate, DOR, DOCR, PFS, OS and safety

Mosun-Pola fixed duration administration (NCT03671018)

Mosun

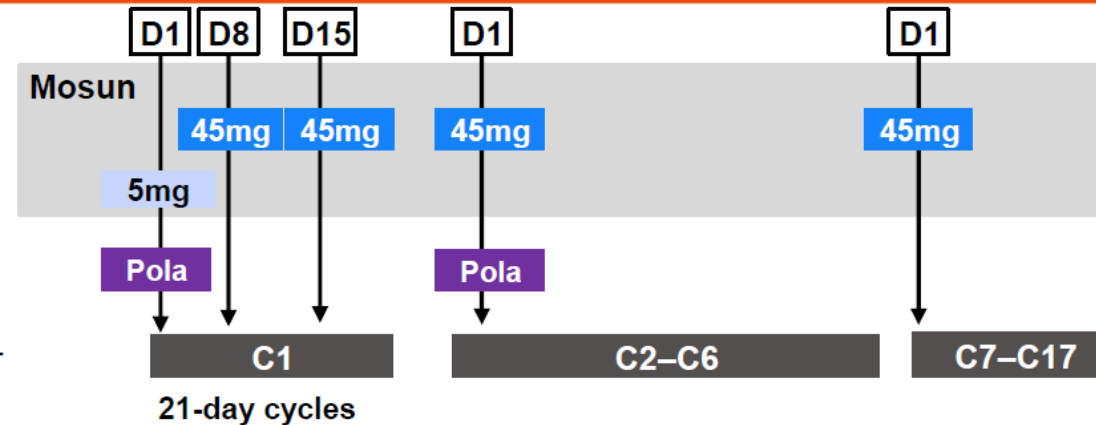
- SC administered in 21-day cycles with step-up dosing in C1; total of 17 cycles

Pola

- 1.8mg/kg IV on D1 of C1–6

No mandatory hospitalization

Corticosteroid premedication was given prior to each dose in C1*

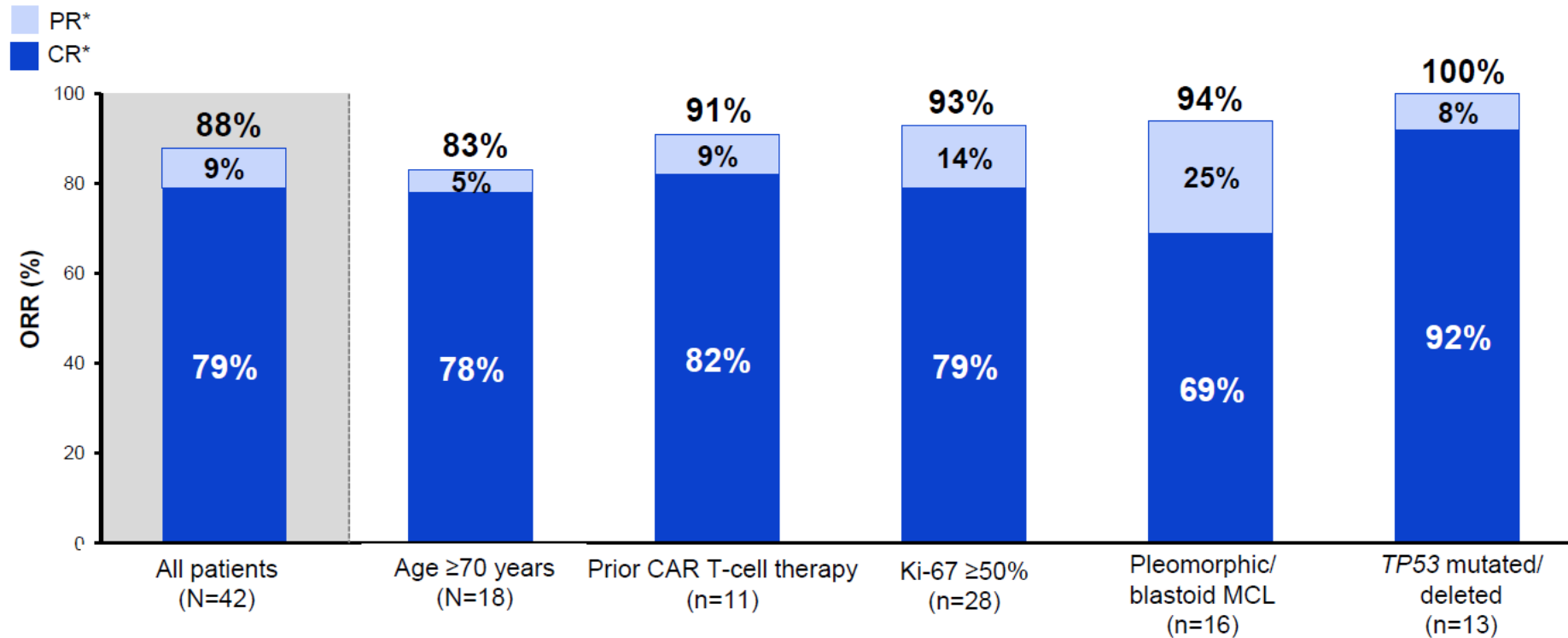


*From C2 and beyond, premedication was optional for patients who did not experience CRS in the previous cycle; corticosteroid premedication consisted of 20mg of dexamethasone or 80mg of methylprednisolone, either IV or orally. C, cycle; CR, complete response; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; CRS, cytokine release syndrome; DOCR, duration of complete response; DOR, duration of response; IRC, independent review committee; IV, intravenous; INV, investigator; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; SC, subcutaneous.

1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68.

Mosun/Pola Response

Response rates

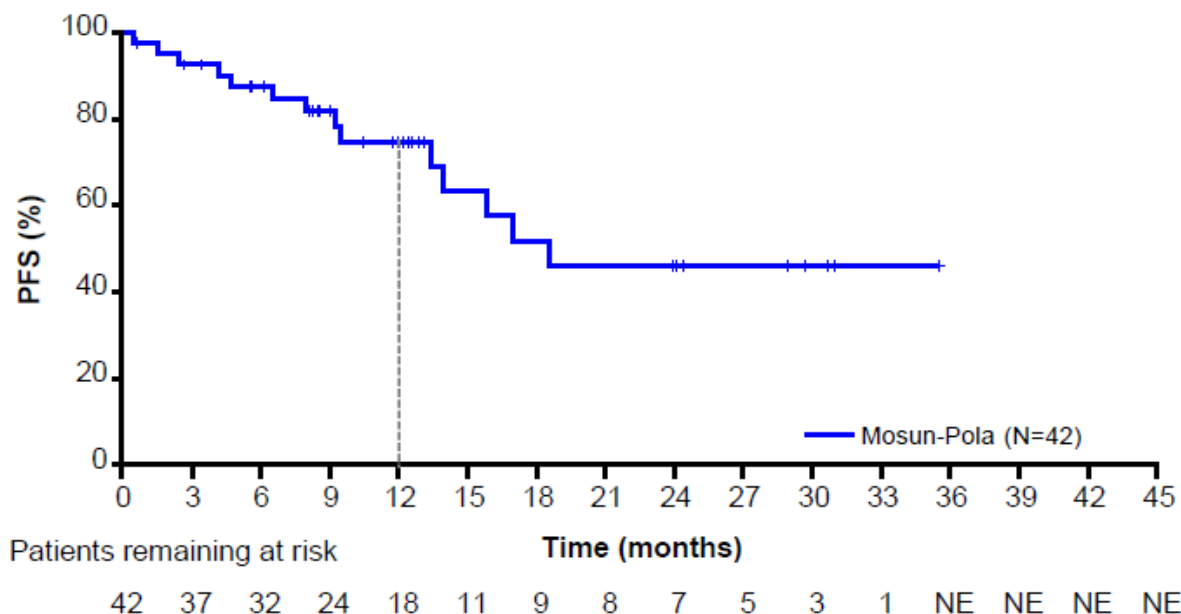


Efficacy was consistent across high-risk subgroups

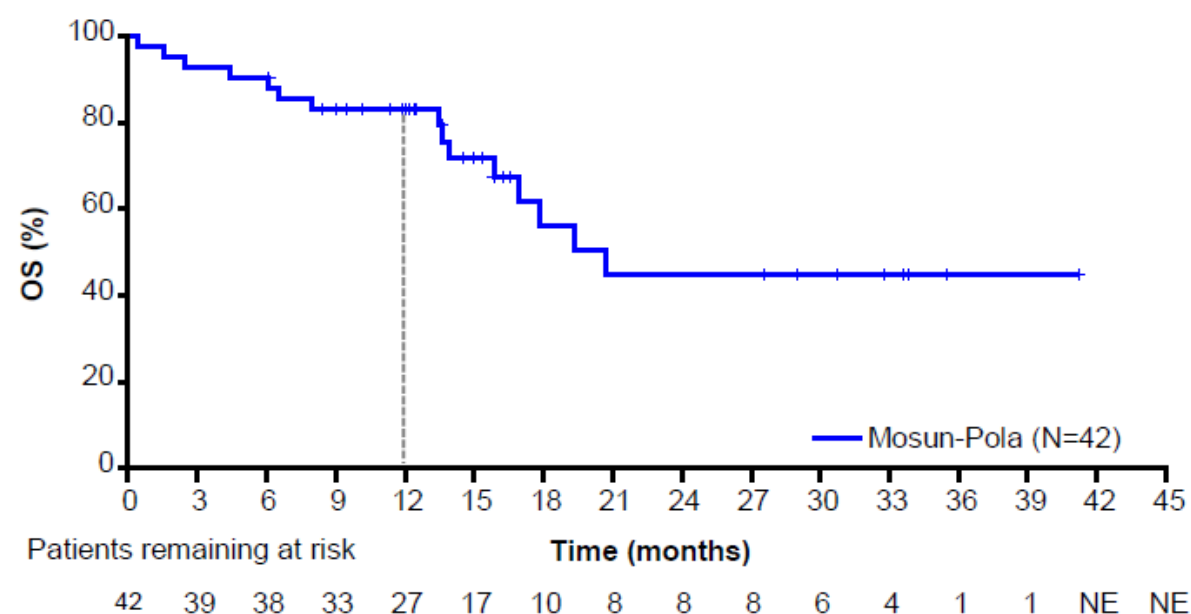
CCOD: November 8, 2024. *IRC-assessed.

PFS and OS

Progression-free survival*



Overall survival



Patient population

n=42

Median PFS, months (95% CI)

18.6 (13.9–NE)

12-month rate, % (95% CI)

74.8 (60.2–89.4)

Patient population

n=42

Median OS, months (95% CI)

20.7 (17.0–NE)

12-month rate, % (95% CI)

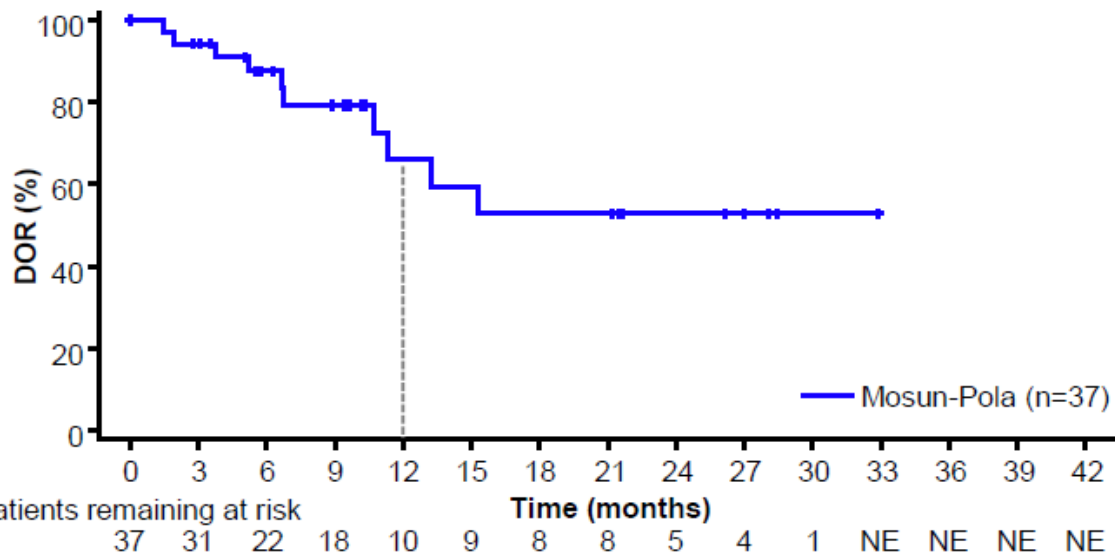
83.1 (71.7–94.5)

Mosun-Pola demonstrated promising PFS and OS

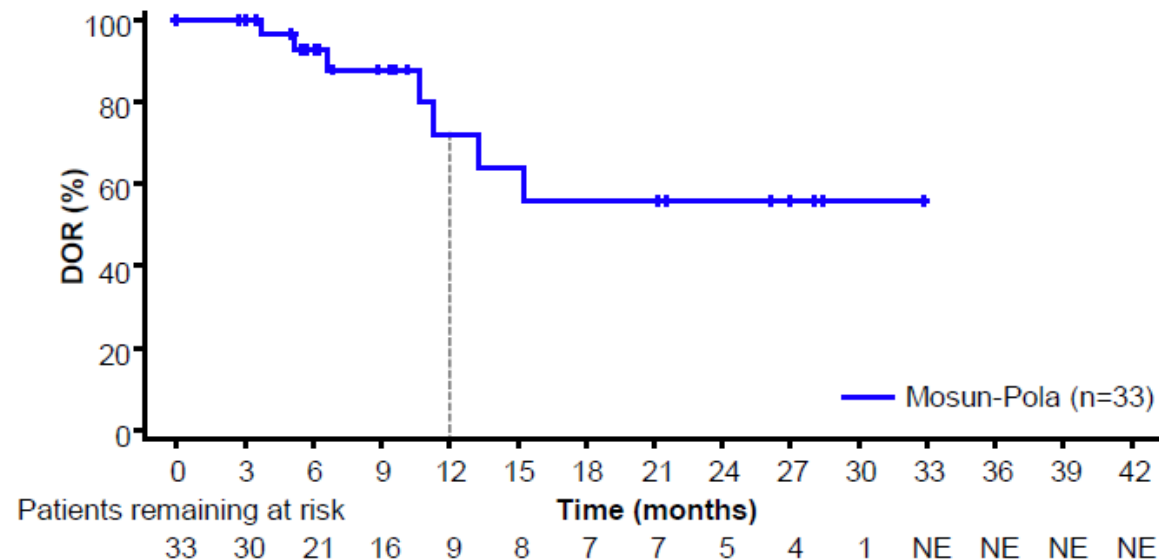
DOR and DOCR

Median follow-up: 15.9 months (95% CI: 13.6–29.0)

Duration of response*



Duration of complete response*



Patients with response

n=37

Median time to first response, months (range)	2.7 (1–7)
Median DOR, months (95% CI)	NR (11.4–NE)
12-month rate, % (95% CI)	66.0 (45.0–86.9)

Patients with complete response

n=33

Median time to first CR, months (range)	2.8 (2–18)
Median DOCR, months (95% CI)	NR (11.4–NE)
12-month rate, % (95% CI)	71.9 (49.2–94.6)

Mosun-Pola demonstrated early and durable responses

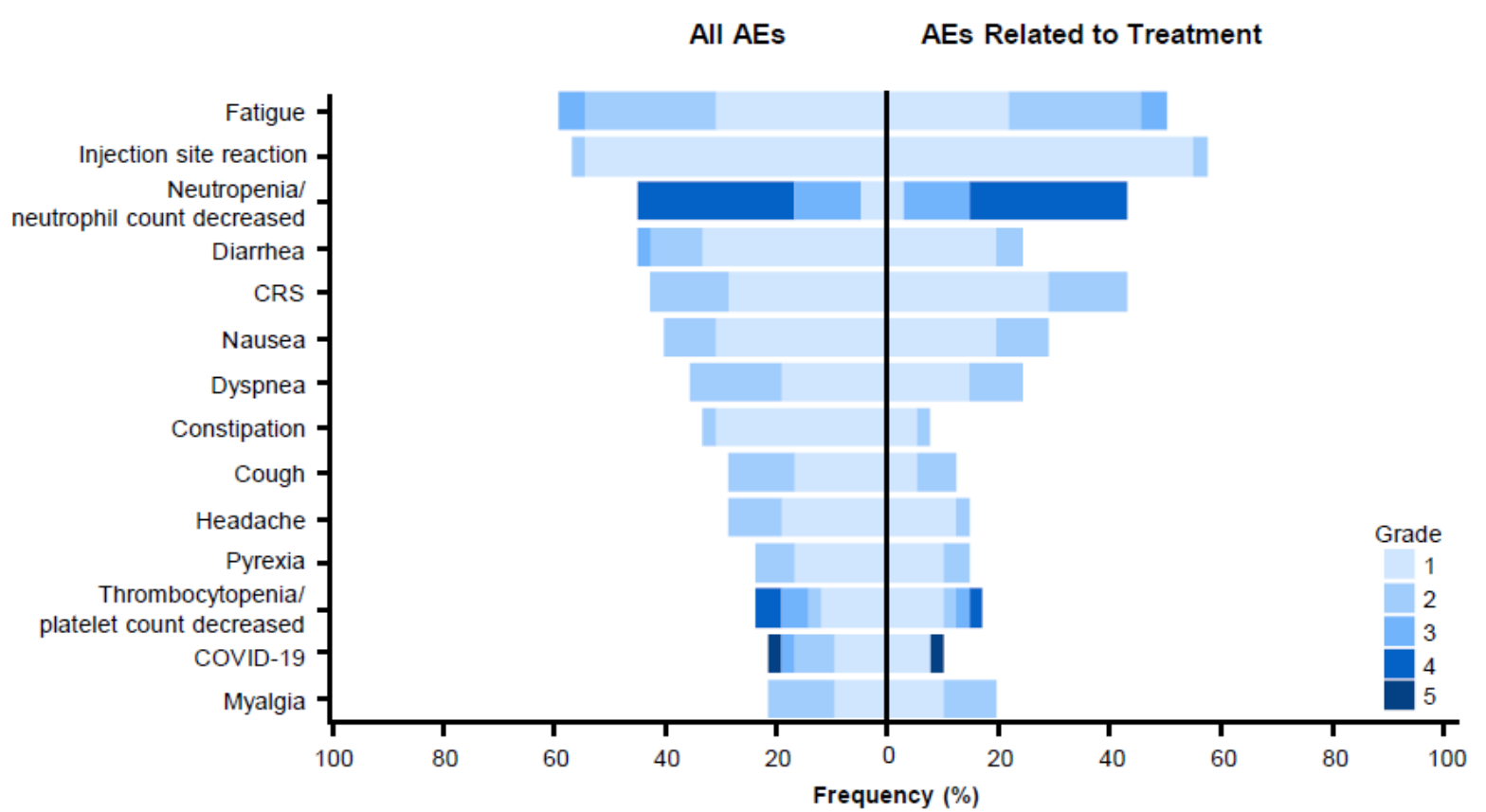
Safety summary

n (%)	N=42
AE	42 (100)
Treatment-related	39 (93)
Grade 3–4 AE	29 (69)
Treatment-related	25 (60)
Serious AE	26 (62)
Treatment-related	17 (41)
Grade 5 (fatal) AE	5 (12)*
Treatment-related	1 (2)†
AE leading to treatment discontinuation	10 (24)‡
Treatment-related	5 (12)

Median number of cycles:

- Mosun: 15 (range, 1–17)
- Pola: 6 (range, 1–6)

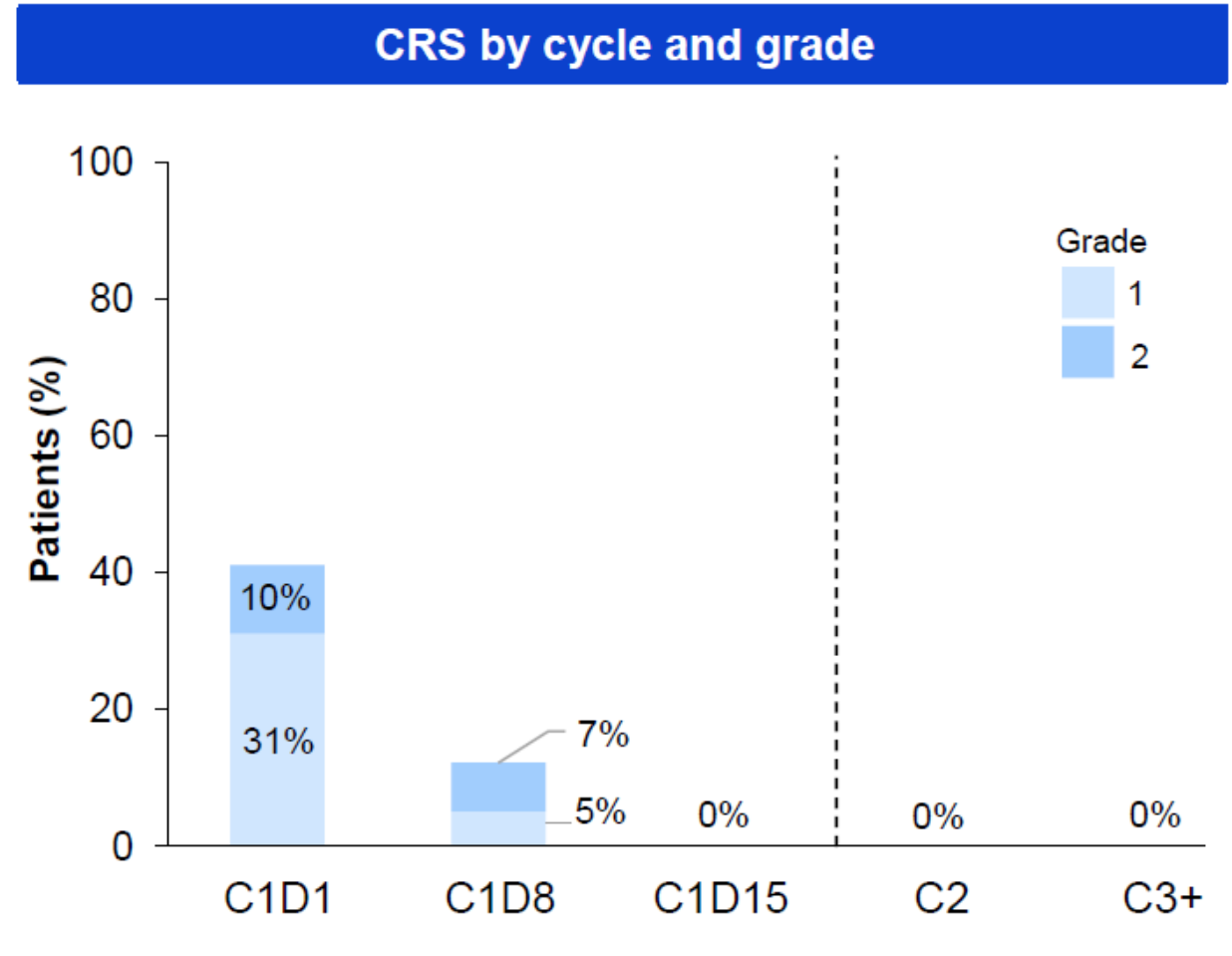
AEs occurring in ≥20% of patients by grade



CCOD: November 8, 2024. *Gr 5 events: COVID-19 pneumonia (n=3), and one each of pneumonia and West Nile virus encephalitis. †COVID-19 pneumonia (n=1). ‡Not treatment-related: COVID-19 pneumonia (n=2, Gr 5), and one each of pneumonia (Gr 3), vascular dementia (Gr 3), colorectal cancer (Gr 3, Mosun-discontinuation) and cough (Gr 2, Mosun-discontinuation); Mosun-Pola-related: one each of uveitis (Gr 3), pneumonitis (Gr 3, Pola-discontinuation), and upper respiratory tract infection (Gr 2, Mosun-discontinuation); Mosun-related: *Clostridioides difficile* colitis (n=1, Gr 3, Mosun-discontinuation); Pola-related: peripheral neuropathy (n=2, Gr 2, Pola-discontinuation). AE, adverse event; COVID-19, coronavirus disease 19; Gr, grade.

CRS summary

CRS by ASTCT criteria ¹	N=42
Any grade, n (%)	18 (43)
Grade 1	12 (29)
Grade 2	6 (14)
Grade \geq 3	0
Median time to first CRS onset relative to last dose, days (range)	2 (1–5)
Median CRS duration, days (range)	3 (1–9)
CRS management, n (%)	
Corticosteroids	6 (14)
Tocilizumab	6 (14)
Low-flow oxygen	4 (10)
Fluids	3 (7)
ICU	1 (2)



All CRS events were low grade and resolved within C1

Efficacy and Safety of BsAb and CART in MCL

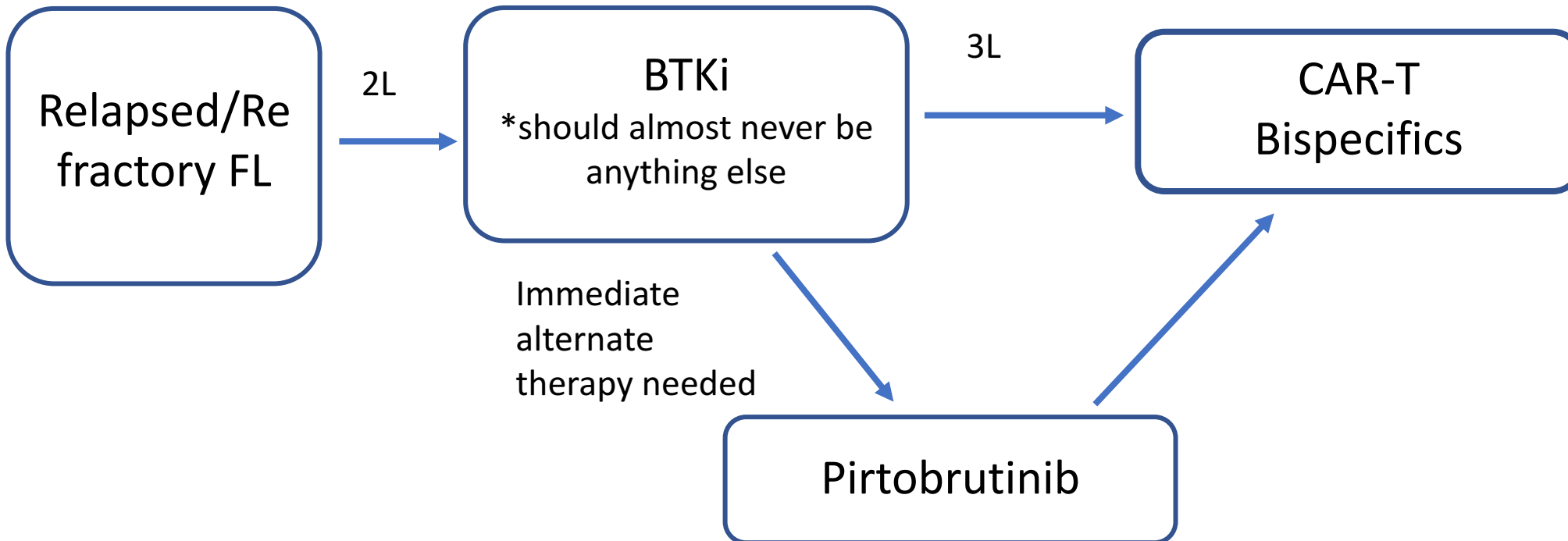
Drug	N	ORR	CR	mPFS	mOS	CRS	Grade 3+	ICANS	Grade 3+
Glofitamab	61	85%	78.3%	16.8 m	29.9 m	75.7%	16.2%	5%	0
Mosun/Pola	42	88%	79%	18.6 m	20.7 m	43%	0%	3%	0
Brexu-cel	68	91%	68%	25.8 m	46.6 m	91%	15%	63%	31%
Liso-cel	83	86.5%	74.3%	15.3 m	18.2 m	61%	1%	31%	9%

Current/Upcoming Combination Studies 2L+

- Glofitamab and pirtobrutinib
 - Australia and US
- GLOASIS
 - Glofitamab With venetoclax +/- zanubrutinib in High-risk Mantle-cell Lymphoma
 - France/Belgium
- Glofitamab + lenalidomide
 - US
- Glofitamab and Polatuzumab
 - R/R
 - US – Lycon group
- Glofitamab and Loncastuximab
 - R/R
 - US - COH

Management of R/R MCL

- Outcomes in R/R MCL remain poor especially after BTKi failure



Conclusions



- Pirtobrutinib – primarily useful as a bridge after BTKi failure

- CART in MCL
 - Brexu-cel: high response rate but high rates of CRS/ICANS
 - Liso-cel: less tox but durability?

- Bispecific Antibodies - effective but still toxicity issues
 - Glofit – CRS
 - Mosun – less efficacy/CRS
 - Mosun/Pola – excellent ORR in high-risk patient population, promising early PFS/DOR
 - Safety favorable