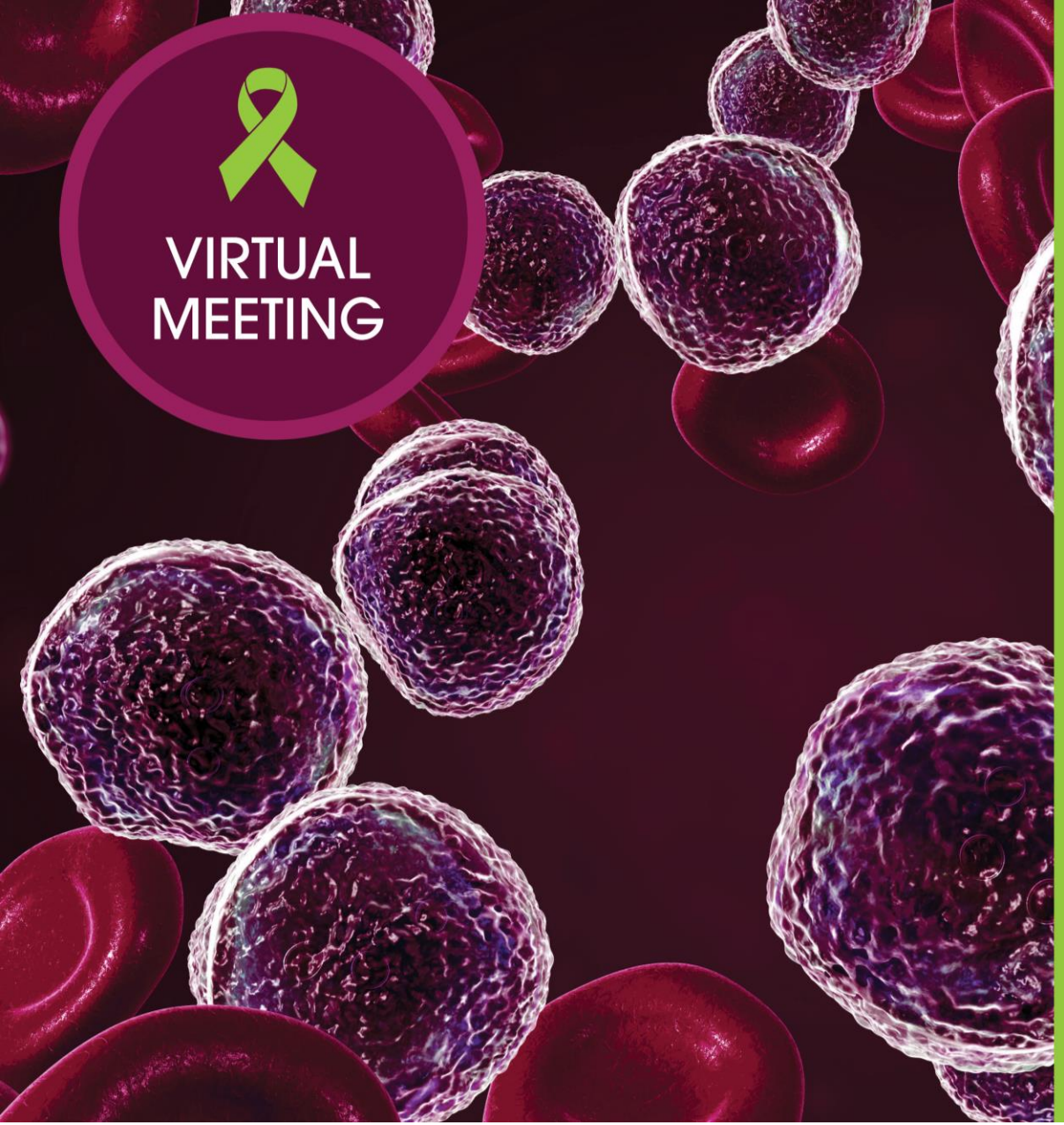


BEYOND THE CONGRESS

Key Conversations from the 2021 Hematology Annual Meeting™

FRIDAY, FEBRUARY 4, 2022

This activity is jointly provided by PIM Postgraduate Institute for Medicine and Bio Ascend™

ASH 2021 Updates: FL and MCL

Brad Kahl, MD

Disclosures

- Research Funding
  - Genentech, ADC Therapeutics, Abbvie, AstraZeneca, BeiGene

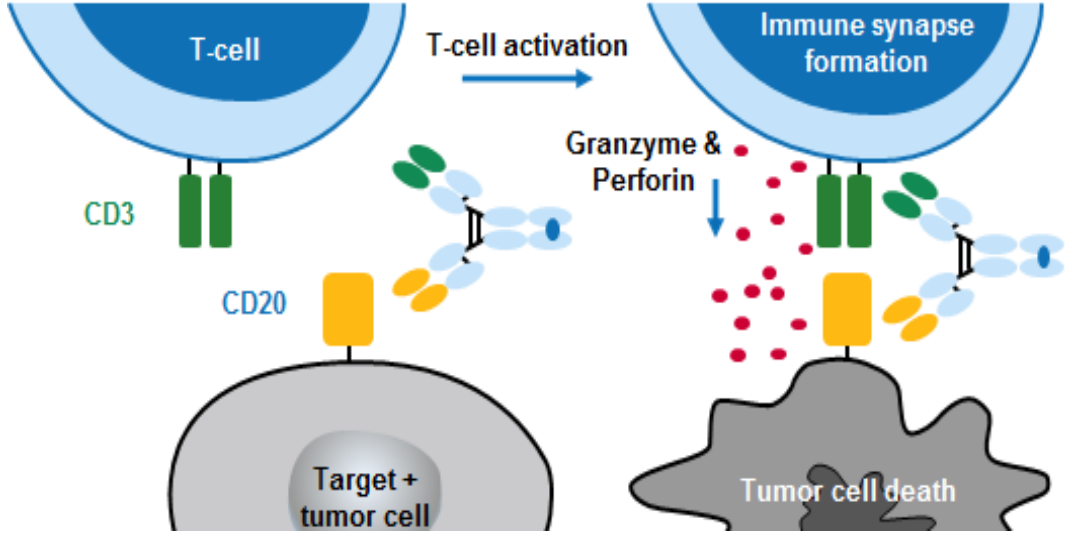
- Consulting
  - Genentech, ADC Therapeutics, Abbvie, AstraZeneca, BeiGene, Pharmacyclics, Celgene/BMS, TG Therapeutics, Hutchmed, MEI, MTEM, Kite, Epizyme, Takeda, Genmab, Incyte, Lilly

Newsworthy FL/MCL abstracts ASH 2021

- Follicular Lymphoma
  - How good are bi-specific monoclonal antibodies?
    - Abstract #127, Budde et al
  - How is CAR-T therapy looking with longer term follow up?
    - Abstract #93, Neelapu et al
    - Abstract #131, Thieblemont et al
- MCL
  - Do bi-specifics work in MCL?
    - Abstract # 130, Phillips et al

Background

- Mosunetuzumab
  - Full-length, fully humanized IgG1 bispecific antibody[1]
  - Redirects T cells to engage and eliminate B cells; T-cell activation, cytokine elevation and increase in TILs observed
  - No ex-vivo T cell manipulation required ('off-the-shelf' and no delay in treatment)



Registry number: NCT02500407

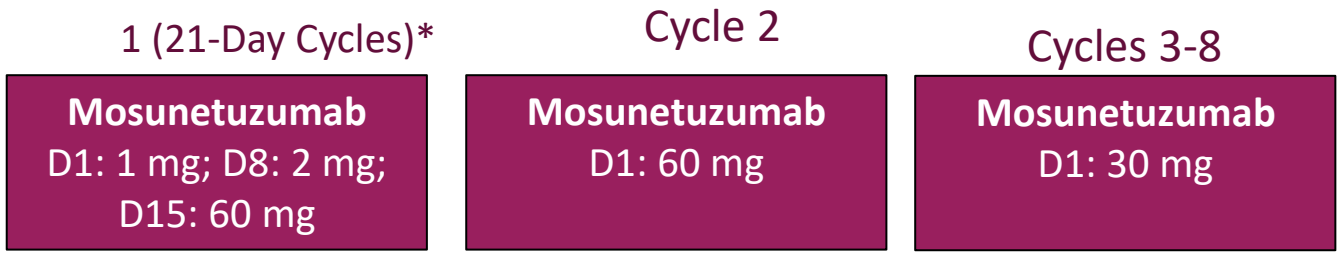
CRS, cytokine release syndrome; NHL, non-Hodgkin lymphoma; pts, patients; R/R, relapsed or refractory; TILs, tumor-infiltrating lymphocytes

1. Sun et al. Sci Transl Med 2015
2. Budde et al. ASH 2018; 3 Bartlett et al. ASCO 2019

Pivotal Phase II of Mosunetuzumab in R/R FL

- Single-arm, pivotal phase II expansion study[1]

Patients aged ≥18 yr with R/R FL grades 1-3a; CD20+; ECOG PS ≤1; ≥2 prior systemic therapies including ≥1 anti-CD20 antibody and ≥1 alkylating agent (N = 90)



*Cycle 1 step-up dosing for CRS mitigation

Discontinue if CR by cycle 8; if PR or SD, continue treatment for 17 cycles, unless PD or unacceptable toxicity occurs

- **Primary endpoint:** CR (best response) rate by IRF, assessed vs 14% historical control CR rate[2]
- **Secondary endpoints:** ORR, DoR, PFS, safety and tolerability

No mandatory hospitalization for treatment administration.

1. Budde. ASH 2021. Abstr 127. 2. Dreyling. JCO. 2017;35:3898.

Pivotal Phase II of Mosunetuzumab in R/R FL: Baseline Characteristics

Characteristic	All Patients (N = 90)
Median age, yr (range)	60 (29-90)
Male, n (%)	55 (61.1)
ECOG PS, n (%)	
▪ 0	53 (58.9)
▪ 1	37 (41.1)
Ann Arbor stage, n (%)	
▪ I-II	21 (23.3)
▪ III-IV	69 (76.7)
Median prior lines, n (range)	3 (2-10)

- Median follow-up, mo (range): 18.3 (2.0-27.5)
- 21 (23.3%) of patients received <8 cycles, 53 (58.9%) received 8 cycles, 5 (5.6%) received >8 and <17 cycles, and 11 (12.2%) received 17 cycles

Prior Therapy	All Patients (N = 90)
Prior systemic therapy, n (%)	
▪ Anti-CD20 therapy	90 (100)
▪ Alkylator therapy	90 (100)
▪ PI3K inhibitor	17 (18.9)
▪ IMiD	13 (14.4)
▪ CAR T-cell therapy	3 (3.3)
Prior ASCT, n (%)	19 (21.1)
Refractory to, n (%)	
▪ Last prior therapy	62 (68.9)
▪ Any prior anti-CD20 therapy	71 (78.9)
▪ Any prior anti-CD20 therapy and alkylator (double refractory)	48 (53.3)
Progressed within 24 mo of initial therapy, n (%)	47 (52.2)

Budde. ASH 2021. Abstr 127.

Pivotal Phase II of Mosunetuzumab in R/R FL: Response

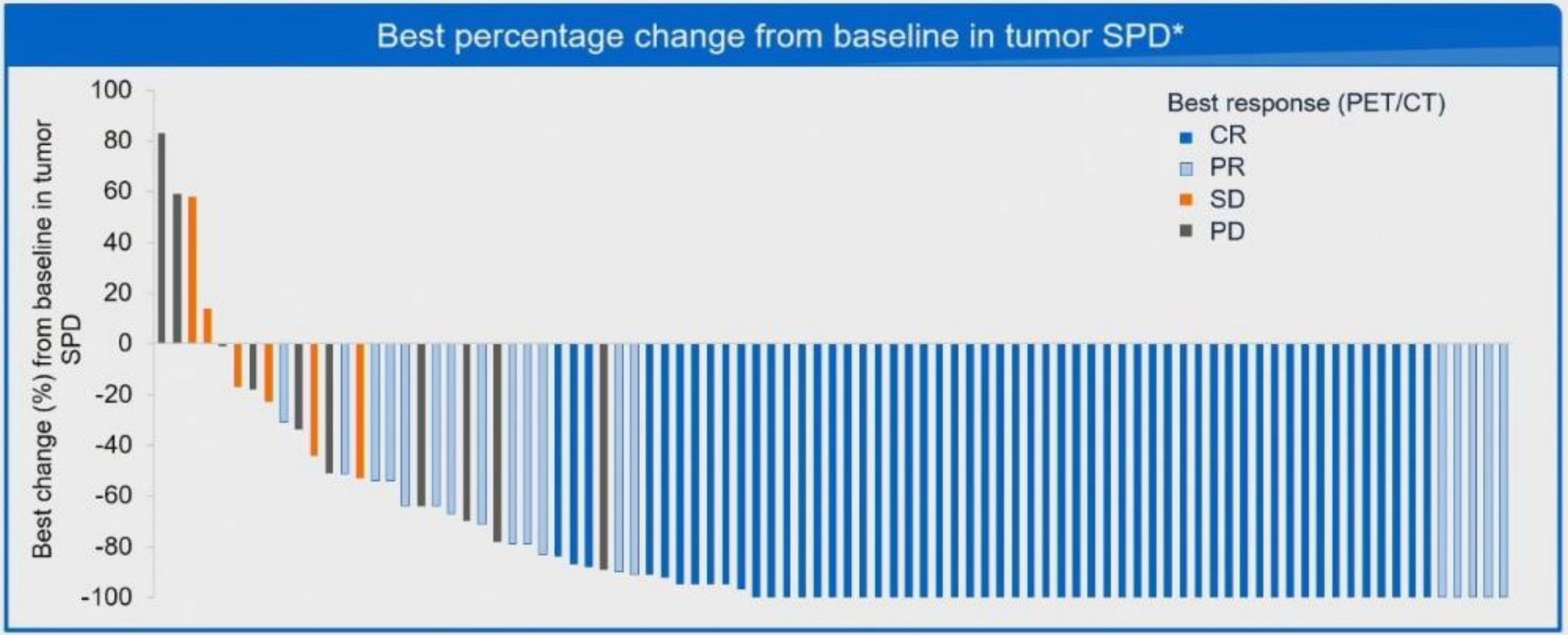
Outcome, % (95% CI)[1]	By IRF (N = 90)	By INV (N = 90)
ORR	80 (70-88)	78 (68-86)
▪ CR	60 (49-70)	60 (49-70)

- Concordance between IRF and INV[1]
  - For ORR: 96%
  - For CR: 93%
- CR rate by IRF is significantly higher than 14% historical control CR rate (*P* <.0001)[2]

Response by Double Refractory Disease Status, % (95% CI)[1]	Yes (n = 48)	No (n = 42)
ORR	71 (56-83)	90 (77-97)
▪ CR	50 (35-65)	71 (55-84)
Response by POD ≥24 Mo of Initial Tx, % (95% CI)[1]	**Yes (n = 47)**	**No (n = 43)**
ORR	85 (72-94)	74 (59-86)
▪ CR	57 (42-72)	63 (47-77)

1. Budde. ASH 2021. Abstr 127. 2. Dreyling. JCO. 2017;35:3898.

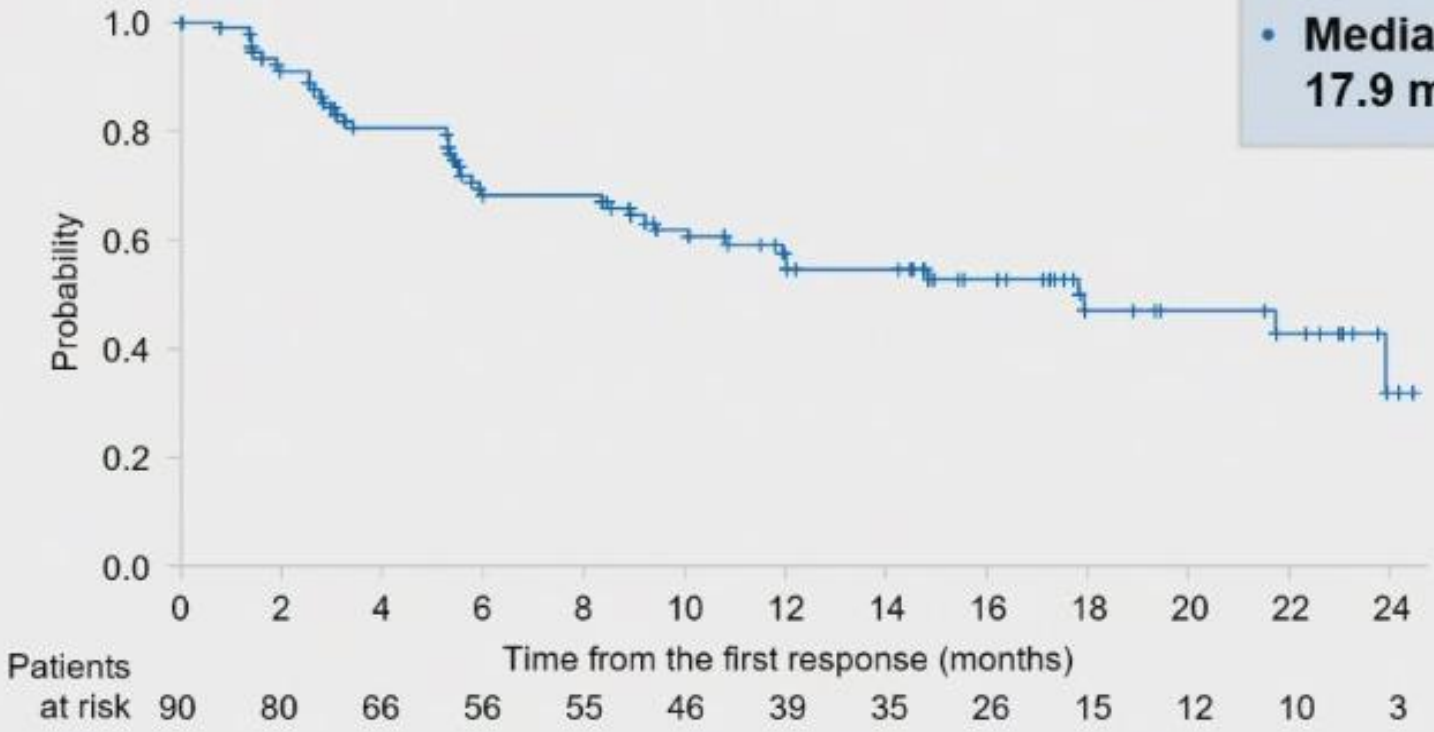
Anti-tumor efficacy



*in all patients with a baseline and ≥1 post-baseline SPD available; PD, progressive disease; SPD, sum of product diameters

Progression-free survival

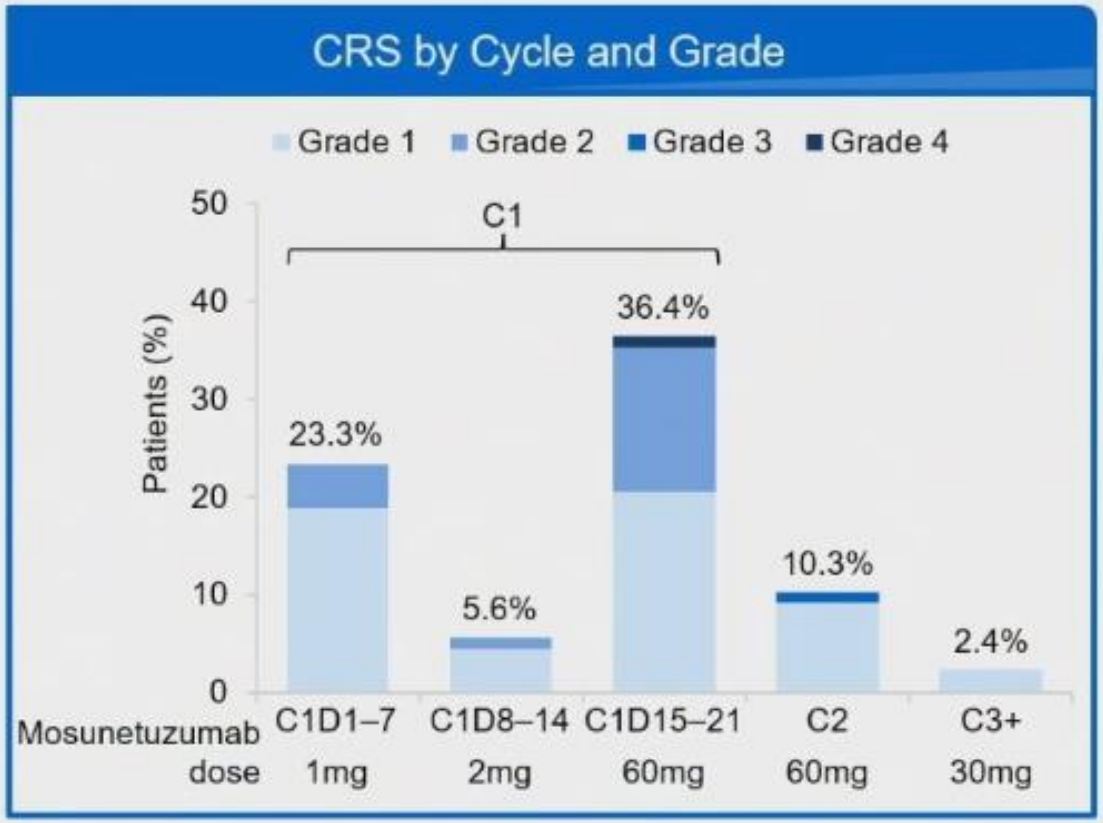
Progression-free survival (N=90)



- **Median PFS: 17.9 months (95% CI: 10.1, NE)**

Cytokine release syndrome

N (%)	N=90
CRS (any Grade)*	40 (44.4%)
Grade 1	23 (25.6%)
Grade 2	15 (16.7%)
Grade 3	1 (1.1%)
Grade 4	1 (1.1%)†
Median time to CRS onset, hours (range)	
C1D1	5.2 (1.2–23.7)
C1D15	26.6 (0.1–390.9)
Median CRS duration, days (range)	3 (1–29)
Corticosteroids for CRS management	10 (11.1%)
Tocilizumab for CRS management	7 (7.8%)



- **CRS was predominately low Grade and in Cycle 1. All events resolved.**

*assessed using ASTCT criteria[1]; †patient with leukemic phase FL

1. Lee et al. Biol Blood Marrow Transplant 20192019;25:625–38

Conclusions

- Pivotal Phase II study of mosunetuzumab, a CD20xCD3 T-cell-engaging bispecific antibody, met primary efficacy endpoint (CR rate: 60%, $p<0.0001$; ORR: 80%)
- Deep and durable responses achieved in heavily pre-treated/high-risk R/R FL with fixed-duration treatment
- Favorable tolerability profile, with most CRS confined to Cycle 1 and low Grade; treatment administration without mandatory hospitalization
- First T-cell-engaging bispecific antibody to demonstrate clinically meaningful outcomes for patients with R/R FL in pivotal Phase II setting
  - potentially promising off-the-shelf, outpatient therapy

Long-Term Follow-Up Analysis of ZUMA-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

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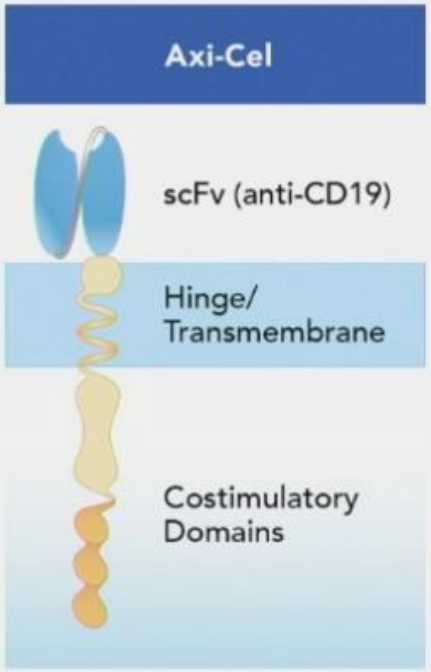
**Equal contributors*

Background

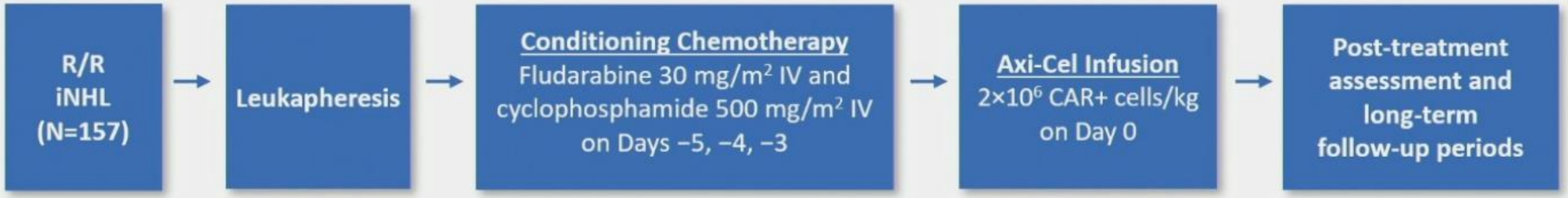
- Axi-cel is an autologous anti-CD19 CAR T-cell therapy approved for the treatment of adults with R/R LBCL and R/R FL, both after ≥2 lines of systemic therapy[1,2]
- ZUMA-5 is a multicenter, single-arm Phase 2 study of axi-cel in patients with R/R iNHL, including FL and MZL
  - In the primary analysis (N=104), the ORR was 92% (76% CR rate) after a 17.5-month median follow-up[3]
  - Median peak CAR T-cell levels were numerically greater in patients with FL who were in ongoing response at data cutoff than in those who relapsed[3]
- Here, we report updated clinical and pharmacologic outcomes from ZUMA-5 with ≥2 years of follow-up



1. YESCARTA® (axicabtagene ciloleucel) Prescribing information. Kite Pharma, Inc; 2021. 2. YESCARTA® (axicabtagene ciloleucel) [Summary of Product Characteristics]. Amsterdam, The Netherlands: Kite Pharma EU B.V.; 2021. 3. Jacobson CA, et al. ASH 2020. Abstract #700.

Axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CR, complete response; FL, follicular lymphoma; iNHL, indolent non-Hodgkin lymphoma; LBCL, large B-cell lymphoma; MZL, marginal zone lymphoma; ORR, overall response rate; R/R, relapsed/refractory; scFv, single-chain variable fragment.

ZUMA-5 Study Design



Key ZUMA-5 Eligibility Criteria

- R/R FL (Grades 1–3a) or MZL (nodal or extranodal)[a]
- ≥2 Prior lines of therapy that must have included an anti-CD20 mAb combined with an alkylating agent[b]

Primary Endpoint

- ORR (IRRC assessed per the Lugano classification[1])

Key Secondary Endpoints

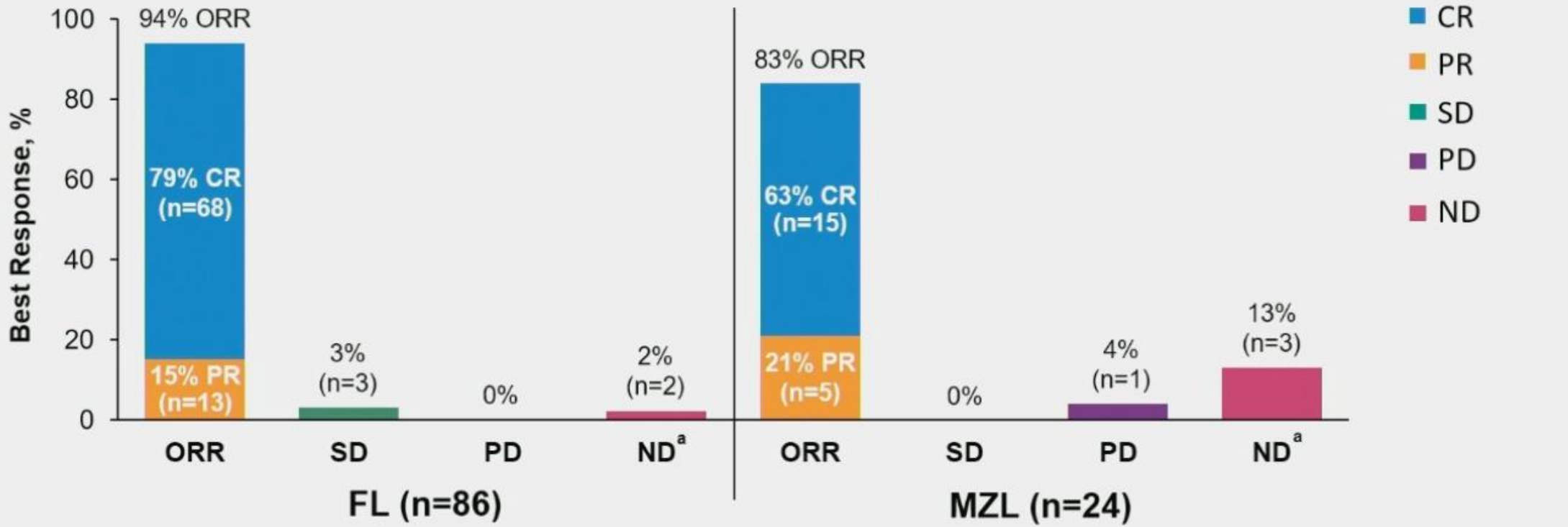
- CR rate (IRRC assessed)
- Investigator-assessed ORR[a]
- DOR, PFS, OS
- AEs
- CAR T-cell and cytokine levels

[a] Patients with stable disease (without relapse) >1 year from completion of last therapy were not eligible. [b] Single-agent anti-CD20 antibody did not count as line of therapy for eligibility.

1. Cheson BD, et al. *J Clin Oncol*. 2014;32:3059-3068.

AE, adverse event; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CR, complete response; DOR, duration of response; FL, follicular lymphoma; iNHL, indolent non-Hodgkin lymphoma; IRRC, Independent Radiology Review Committee; IV, intravenous; mAb, monoclonal antibody; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed/refractory.

ORR by Central Review

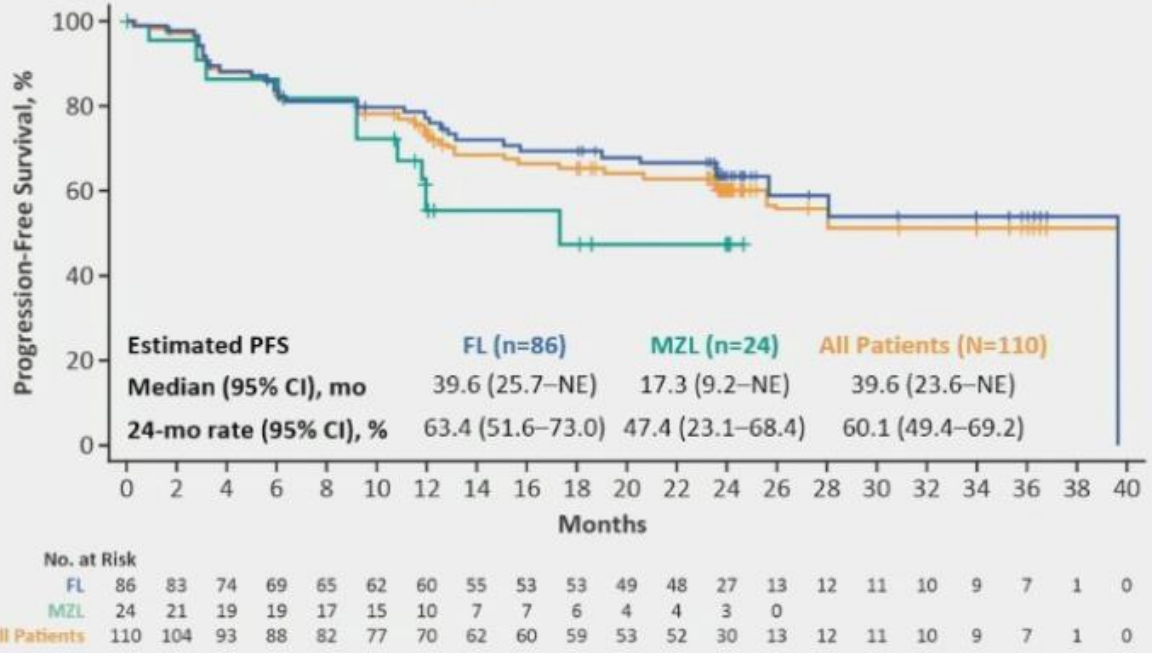


- Among efficacy-eligible patients with iNHL (n=110), the ORR was 92% (95% CI, 85–96), with a 75% CR rate
- Among all treated patients with iNHL (n=149), the ORR was 92% (95% CI, 86–96), with a 77% CR rate

Assessed in efficacy-eligible patients (n=110) by an IRRC according to the Lugano Classification (Cheson BD, et al. *J Clin Oncol.* 2014;32:3059-3068).
[a] Among the 5 patients reported as ND, 4 (1 FL; 3 MZL) had no disease at baseline and post-baseline per IRRC but were considered with disease by the investigator; 1 patient with FL died before the first disease assessment.
CR, complete response; FL, follicular lymphoma; iNHL, indolent non-Hodgkin lymphoma; IRRC, Independent Radiology Review Committee; MZL, marginal zone lymphoma; ND, not done/undefined; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.

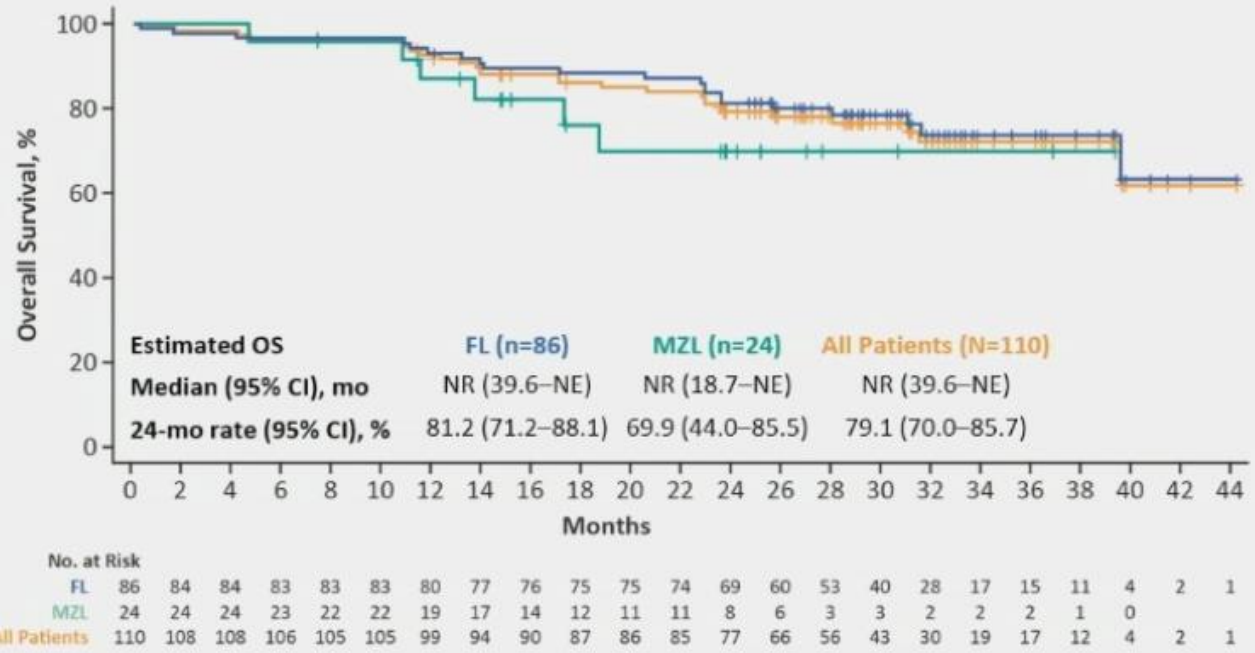
PFS and OS

Progression-Free Survival



No. at Risk																					
FL	86	83	74	69	65	62	60	55	53	53	49	48	27	13	12	11	10	9	7	1	0
MZL	24	21	19	19	17	15	10	7	7	6	4	4	3	0							
All Patients	110	104	93	88	82	77	70	62	60	59	53	52	30	13	12	11	10	9	7	1	0

Overall Survival



No. at Risk																									
FL	86	84	84	83	83	83	80	77	76	75	75	74	69	60	53	40	28	17	15	11	4	2	1
MZL	24	24	24	23	22	22	19	17	14	12	11	11	8	6	3	3	2	2	2	1	0		
All Patients	110	108	108	106	105	105	99	94	90	87	86	85	77	66	56	43	30	19	17	12	4	2	1

- Median OS was not yet reached in efficacy-eligible patients with FL or MZL
- Among patients with FL, 3 deaths occurred after Month 24[a]; no disease progression events occurred after Month 24

[a] Of the 3 deaths, 2 were from COVID-19 and 1 was from sepsis.

FL, follicular lymphoma; MZL, marginal zone lymphoma; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival.

Efficacy Outcomes in Patients With FL by POD24 Status

Parameter (95% CI)	Follicular Lymphoma (n=78)[a]	
	With POD24 (n=49)	Without POD24 (n=29)
Median DOR, months	38.6 (14.5–NE)	NR (24.7–NE)
24-month rate, %	61.1 (44.3–74.3)	72.4 (50.2–85.9)
Median PFS, months	39.6 (13.1–NE)	NR (25.7–NE)
24-month rate, %	57.3 (41.2–70.4)	73.0 (51.1–86.2)
Median OS, months	NR (39.6–NE)	NR (NE–NE)
24-month rate, %	77.6 (63.1–86.9)	85.9 (66.7–94.5)

- Patients with FL who had POD24 benefitted from axi-cel, with estimated medians and 24-month rates of DOR and PFS consistent with all efficacy-eligible patients
  - Medians of DOR and PFS among patients without POD24 were not yet reached at data cutoff

[a] Axi-cel–treated patients with FL and available efficacy data on progression after an anti-CD20 mAb + alkylating agent were included in the POD24 analysis.
Axi-cel, axicabtagene ciloleucel; DOR, duration of response; FL, follicular lymphoma; mAb, monoclonal antibody; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival; POD24, progression of disease <24 months from initiating the first anti-CD20–containing chemoimmunotherapy.

Safety Results

- Consistent with prior reports, the most common Grade ≥3 AEs were neutropenia (33%), decreased neutrophil count (28%), and anemia (25%)

- Grade ≥3 CRS and NEs occurred in 7% of patients (6% FL; 8% MZL) and 19% of patients (15% FL; 36% MZL), respectively
  - Most CRS cases (120 of 121) and NEs (82 of 87) of any grade resolved by data cutoff[a]
  - Nearly half of NEs (49%) resolved ≤2 weeks after onset; most NEs (76%) resolved ≤8 weeks after onset

- Grade ≥3 cytopenias present ≥30 days post-infusion were reported in 34% of patients (33% FL; 36% MZL), most commonly neutropenia in 29% of patients (27% FL; 36% MZL)

CRS was graded according to Lee DW, et al. *Blood*. 2014;124:188-195. NEs were identified using the modified blinatumomab registrational study (Topp MS, et al. *Lancet Oncol*. 2015; 16;57-66). The severity of all AEs, including NEs and symptoms of CRS, was graded with the use of the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03.

[a] One patient with FL died of multisystem organ failure in the context of CRS (Day 7) prior to the resolution of CRS. Ongoing NEs in FL included Grade 1 attention disturbance, Grade 1 memory impairment, and Grade 1 paresthesia. Ongoing NEs in patients with MZL included Grade 2 facial paresthesia, and Grade 1 memory impairment.

AE, adverse event; CRS, cytokine release syndrome; FL, follicular lymphoma; MZL, marginal zone lymphoma; NE, neurologic event.

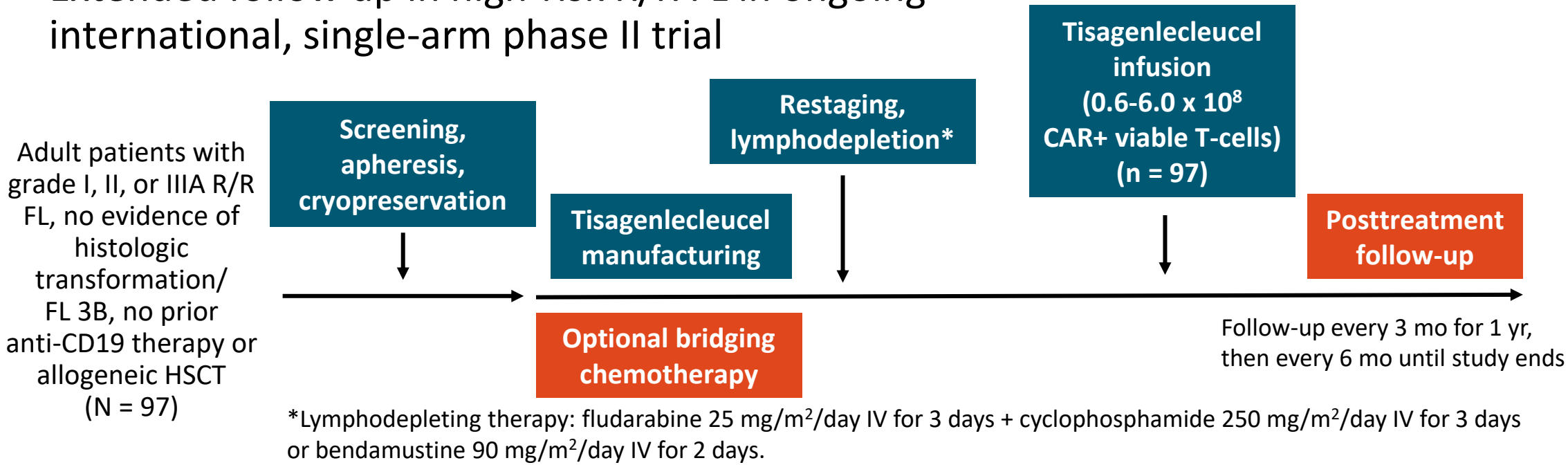
ELARA: Tisagenlecleucel for R/R FL

- Tisagenlecleucel: anti-CD19 CAR T-cell therapy approved for younger patients with R/R ALL and for adults with R/R DLBCL after ≥2 therapies[2]
- Phase II ELARA study evaluating tisagenlecleucel in adults with R/R FL[3]
  - Primary analysis reported ORR 86%, CR 66% at median follow-up of 11 mo
- Current analysis reports extended follow-up at median 17-mo follow-up and efficacy in patients with high-risk disease (descriptive analysis)[4]

1. Casulo. Blood. 2019;133:1540. 2. Tisagenlecleucel PI.
3. Schuster. ASCO 2021. Abstr 7508. 4. Thieblemont. ASH 2021. Abstr 131.

ELARA: Study Design

- Extended follow up in high-risk R/R FL in ongoing international, single-arm phase II trial



*Lymphodepleting therapy: fludarabine 25 mg/m^2/day IV for 3 days + cyclophosphamide 250 mg/m^2/day IV for 3 days or bendamustine 90 mg/m^2/day IV for 2 days.

- **Primary endpoint:** CRR by IRC
- **Secondary endpoints:** ORR, DoR, PFS, OS, safety, cellular kinetics

Thieblemont. ASH 2021. Abstr 131.

ELARA Extended Follow-up: Efficacy

Response at Median Follow-up of 17 Mo, % (95% CI)	Evaluable Patients (n = 94)
ORR	86.2 (77.5-92.4)
CRR	69.1 (58.8-78.3)
12-mo PFS	
▪ All patients	67.0 (56.0-75.8)
▪ In patients achieving CR	85.5 (74-92)
9-mo DoR	
▪ All patients	76.0 (64.6-84.2)
▪ In patients achieving CR	86.5 (75-93)

- At median follow-up of 21 mo, median PFS was 29.5 mo (95% CI: 17.9-NE)

Thieblemont. ASH 2021. Abstr 131.

ELARA Subgroup Analysis: PFS in POD24 and High TMTV Subgroups

Disease Characteristic	Descriptive Analysis		Multivariate Analysis
	High-Risk 12-Mo PFS, %	Low-Risk 12-Mo PFS, %	HR (95% CI)
POD24	60.8	77.9	2.3 (1.0-5.3)
TMTV	54.5	68.5	2.5 (1.3-5.6)

Thieblemont. ASH 2021. Abstr 131.

ELARA Extended Follow-up: CRS Events

CRS Events Occurring Within 8 Wk of Infusion	All Patients (N = 97)
Patients with CRS (Lee scale), %	48.5
Maximum CRS grade, %	
▪ 1	27.8
▪ 2	20.6
▪ 3/4	0
Median onset CRS, days	4.0
▪ Min/max	1/14
Median duration CRS, days	4.0
▪ Min/max	1/24

CRS Events Occurring Within 8 Wk of Infusion, n (%)	Patients With CRS (n = 47)
Concurrent infections	7 (14.9)
Admitted to ICU	4 (8.5)
Median duration ICU stay, days	4
Tocilizumab	16 (34.0)
Corticosteroids	3 (6.4)
Hypotension requiring IV fluids and/or vasopressors	19 (40.4)
One vasopressor administered	3 (6.4)
High-dose vasopressors	0
Hypoxia	9 (19.1)
Low-flow oxygen supplementation	9 (19.1)

Thieblemont. ASH 2021. Abstr 131.

CART in FL Conclusions

- Very high response rates
  - Axi-cel:94% ORR, 79% CRR
  - Tisa-cel: 86% ORR, 69% CRR
- Durability: So far, pretty good
  - Axi-cel: 2 yr PFS: 63%
  - Tisa-cel: 1 yr PFS: 67%
- Activity promising in high risk subgroups like POD24
- Toxicity
  - Appears to be more CRS and neurotox with axi-cel
  - Long term cytopenias remain a concern with any CART product
- May turn out to be a good option for selected FL patients

Glofitamab Step-Up Dosing Induces High Response Rates in Pts With R/R MCL, Most of Whom Had Failed Prior BTKi Therapy

Tycel Phillips,[1] Michael Dickinson,[2] Franck Morschhauser,[3] Emmanuel Bachy,[4] Michael Crump,[5] Marek Trněný,[6] Nancy Bartlett,[7] Jan Zaucha,[8] Kathryn Humphrey,[9] David Perez-Callejo,[10] Linda Lundberg,[10] James Relf,[9] Audrey Filezac de L'Etang,[10] David Carlile,[9] Emma Clark,[9] Carmelo Carlo-Stella[11]

[1]University of Michigan Medical School, Ann Arbor, MI, USA; [2]Peter MacCallum Cancer Centre, Royal Melbourne Hospital and The University of Melbourne, Melbourne, Australia; [3]CHU Lille, Service des Maladies du Sang, Lille, France; [4]Hospices Civils de Lyon and Université Claude Bernard, Pierre-Bénite, France; [5]Princess Margaret Hospital, Toronto, ON, Canada; [6]1st Faculty of Medicine, Charles University, General Hospital, Prague, Czech Republic; [7]Washington University, Siteman Cancer Center St. Louis, MO, USA; [8]Medical University of Gdańsk, Gdańsk, Poland; [9]Roche Products Ltd, Welwyn Garden City, United Kingdom; [10]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [11]Humanitas University and Humanitas Research Hospital, Milan, Italy.

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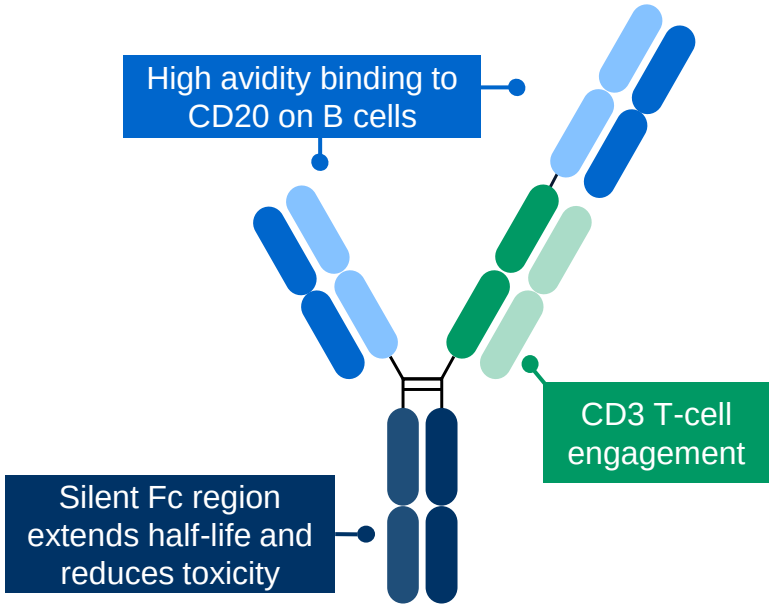
Background

- **Mantle cell lymphoma**
  - Aggressive subtype of NHL
  - Patients with PD after BTKi therapy have a poor prognosis[1]
- **Glofitamab**
  - Engages and redirects T cells to eliminate malignant B cells[2]
  - Off-the-shelf availability and fixed duration of treatment[2,3]
- **Phase I experience (NCT03075696)**[3]
  - Promising efficacy and manageable safety as monotherapy and in combination with obinutuzumab in patients with heavily pre-treated R/R B-NHL[4,5]
  - Effective CRS mitigation with obinutuzumab pre-treatment (Gpt) and/or C1 SUD[4,5]

Glofitamab: *CD20×CD3 bispecific antibody with 2:1 configuration for increased potency vs 1:1 configuration*[2]

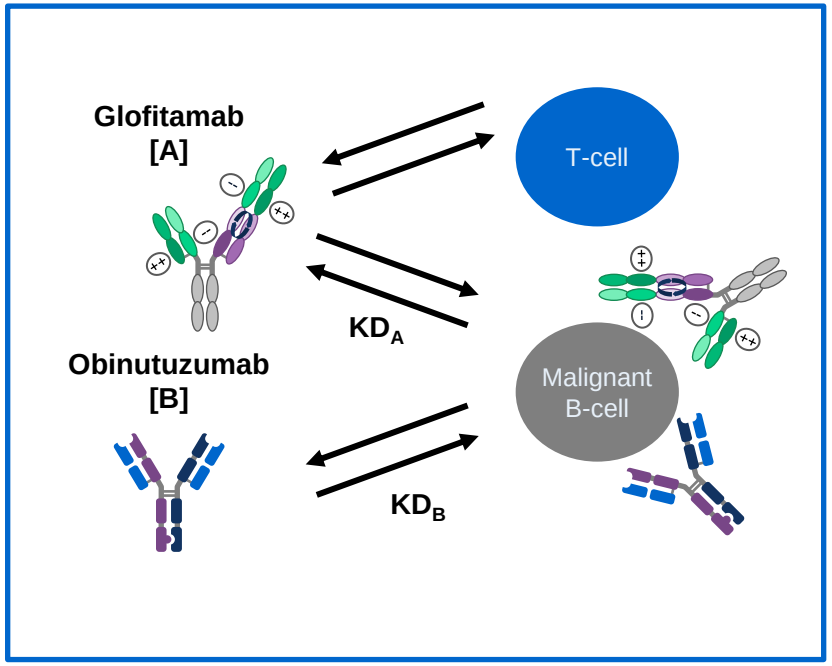


Aim: Report data – 1000mg or 2000mg obinutuzumab pretreatment prior to glofitamab monotherapy in R/R MCL

B-NHL, B-cell non-Hodgkin lymphoma; BTKi, Bruton's tyrosine kinase inhibitor; C, cycle; CRS, cytokine release syndrome; Gpt, pretreatment with obinutuzumab; MCL, mantle cell lymphoma; NHL, non-Hodgkin lymphoma; PD, progressive disease; R/R relapsed/refractory; SUD, step-up dosing.

1. Martin, P et al. Blood 2016; 2. Bacac, M et al. Clin Cancer Res 2018; 3. NCT03075696. Available at: https://clinicaltrials.gov; 4. Hutchings, M et al. JCO 2021; 5. Morschhauser, F et al. ASH 2019

Glofitamab dosing in R/R MCL



CD20 – receptor occupancy (RO; tumor cell)

- Glofitamab and obinutuzumab compete for binding to the same epitope on CD20 receptors
- Gpt reduces glofitamab RO, which aims to mitigate CRS incidence and severity, by competitive binding

Patients with MCL have:

- Higher clearance of obinutuzumab (2-fold) compared with other NHL histologies[1]
- Lower obinutuzumab concentration which leads directly to higher glofitamab RO[2]

CRS

- Direct relationship between glofitamab RO and CRS at the first dose in NHL
- A higher Gpt dose prior to glofitamab SUD may further reduce risk of CRS in MCL

Response

- Direct relationship between glofitamab RO and CR rate at Cycle 3 in aNHL

aNHL, aggressive non-Hodgkin lymphoma; CR, complete response.

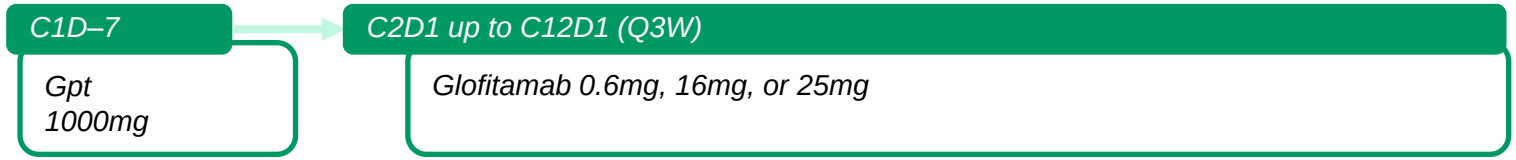
1. Gibiansky, E et al. CPT Pharmacometrics Syst Pharmacol 2014;
2. Djebli, N et al. Blood 2020

Glofitamab regimens investigated in R/R MCL

Dose escalation (Phase I)

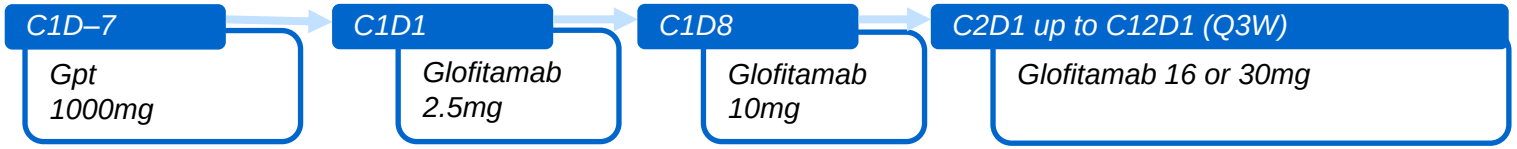
Glofitamab fixed dosing

Gpt 1000mg
Glofitamab
0.6, 16 or 25mg*:
n=3

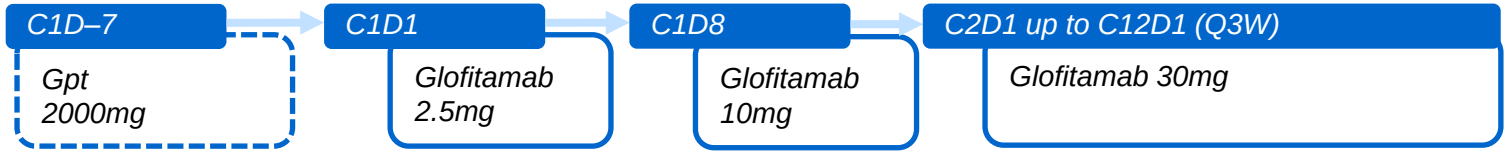


Glofitamab SUD

Gpt 1000mg
Glofitamab
2.5/10/16mg or
2.5/10/30mg†: n=7



Gpt 2000mg
Glofitamab
2.5/10/30mg: n=19



Population characteristics:

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

Clinical cut-off date: May 18, 2021. *Two patients received Gpt 1000mg, glofitamab 0.6mg (n=1) or 16mg (n=1) plus obinutuzumab 1000mg on D1 of Cycles 2–12. †One patient received extended SUD (0.5/2.5/10/30mg) and one patient received Gpt 1000mg, glofitamab SUD 2.5/10/30mg, plus obinutuzumab 1000mg on D1 of Cycles 2–12
D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; Q3W, every three weeks.

Baseline characteristics

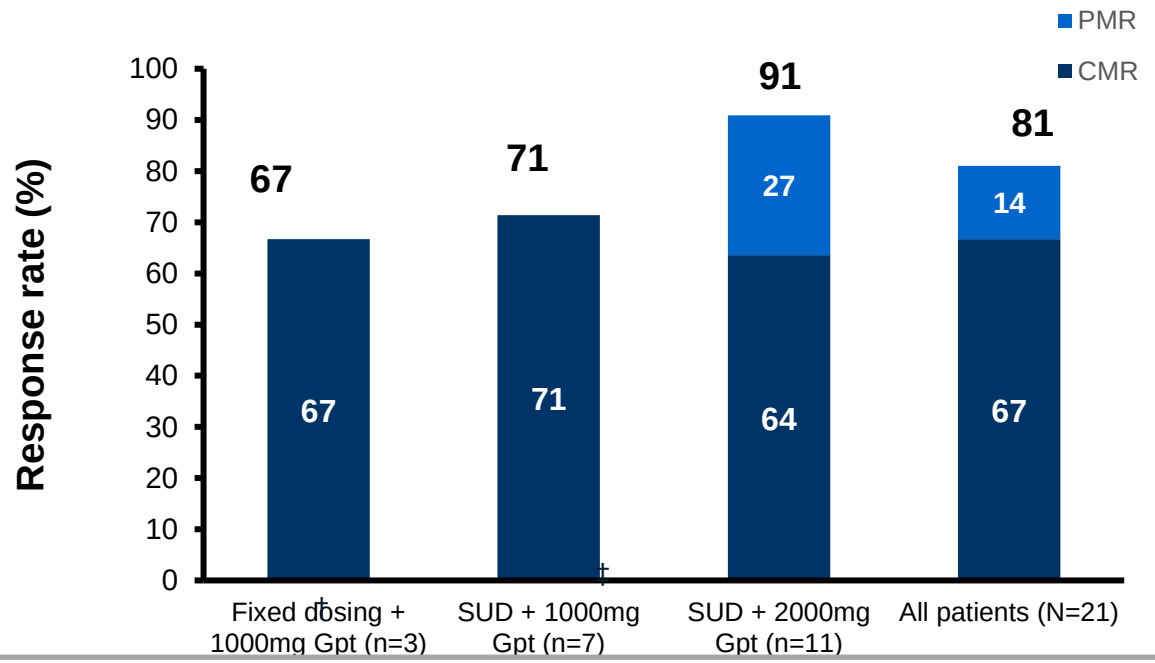
n (%) of patients unless stated		Glofitamab fixed dosing + 1000mg Gpt (n=3)	Glofitamab SUD + 1000mg Gpt (n=7)	Glofitamab SUD + 2000mg Gpt (n=19)	All patients (N=29*)
Median age, years (range)		81.0 (66–84)	69.0 (64–75)	66.0 (41–84)	69.0 (41–84)
Male		2 (66.7)	6 (85.7)	12 (63.2)	20 (69.0)
Ann Arbor stage III–IV at study entry		2 (66.7)	6 (85.7)	16 (84.2)	24 (82.8)
MCL IPI score ≥6 at study entry		3 (100)	3 (42.9)	12 (63.2)	18 (62.1)
Prior therapy	Median time since last therapy, months (range)	1.1 (1.0–8.5)	3.4 (1.2–53.2)	1.6 (0.1–107.5)	1.7 (0.1–107.5)
	Prior lines of therapy, median (range)	3 (2–5)	4 (3–5)	3 (1–6)	3 (1–6)
	BTKi	3 (100)	6 (85.7)	11 (57.9)	20 (69.0)
	Lenalidomide	0	1 (14.3)	3 (15.8)	4 (13.8)
	Chemotherapy	3 (100)	7 (100)	18 (94.7)	28 (96.6)
	Alkylator	0	6 (85.7)	7 (36.8)	13 (44.8)
	Anti-CD20 monoclonal antibody	3 (100)	6 (85.7)	14 (73.7)	23 (79.3)
Refractory status	Refractory to any prior therapy	3 (100)	7 (100)	16 (84.2)	26 (89.7)
	Refractory to prior anti-CD20 therapy	2 (66.7)	3 (42.9)	10 (52.6)	15 (51.7)
	Refractory to first-line therapy	2 (66.7)	2 (28.6)	11 (57.9)	15 (51.7)
	Refractory to last prior therapy	2 (66.7)	5 (71.4)	13 (68.4)	20 (69.0)

Most patients had received prior BTKi therapy

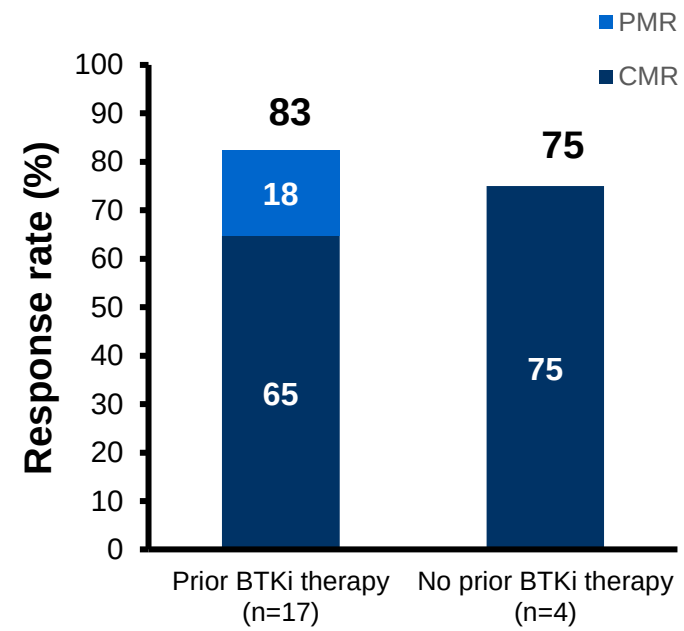
*Three patients were treated with glofitamab in combination with obinutuzumab (G-combo). IPI, International Prognostic Index.

Response rates

Response rates[1] by glofitamab regimen*



Response rates[1] by prior BTKi therapy*



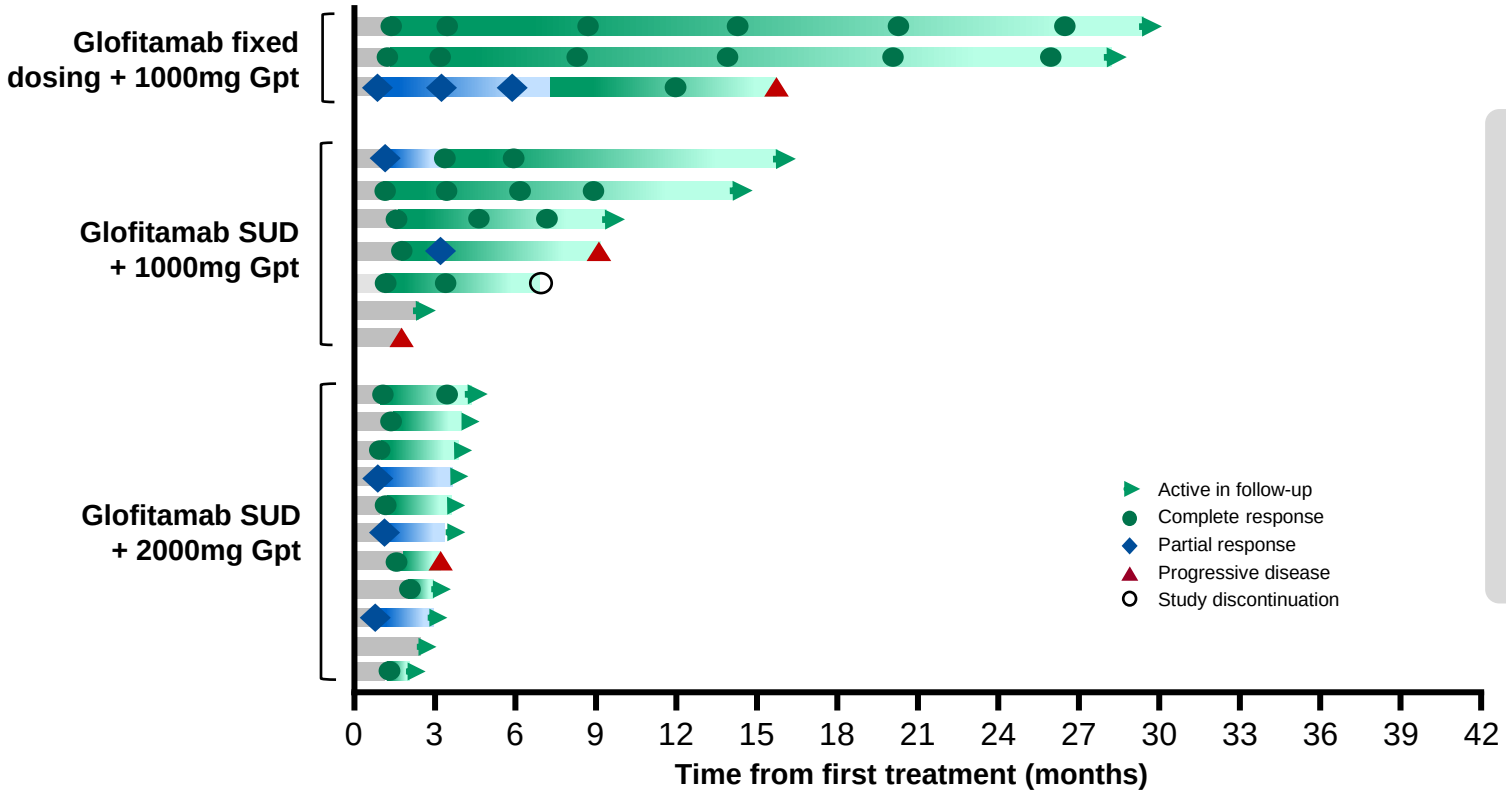
Glofitamab resulted in high response rates in patients with R/R MCL

*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

Time on treatment and response

Duration of response in efficacy-evaluable patients*



- Median follow-up (months):
  - *Glofitamab fixed dosing + 1000mg Gpt:* ***25.9 months***
  - *Glofitamab SUD + 1000mg Gpt:* ***7.3 months***
  - *Glofitamab SUD + 2000mg Gpt:* ***1.3 months***
  - *All patients:* ***1.4 months***
- Median DOCR follow-up: 2.4 months (range, 0.0–25.0)
- Median DOR follow-up: 2.2 months (range, 0.0–25.0)
- At data cut-off, 85.7% (12/14) of patients with a CR remained in remission
- Median DOR and median DOCR not reached

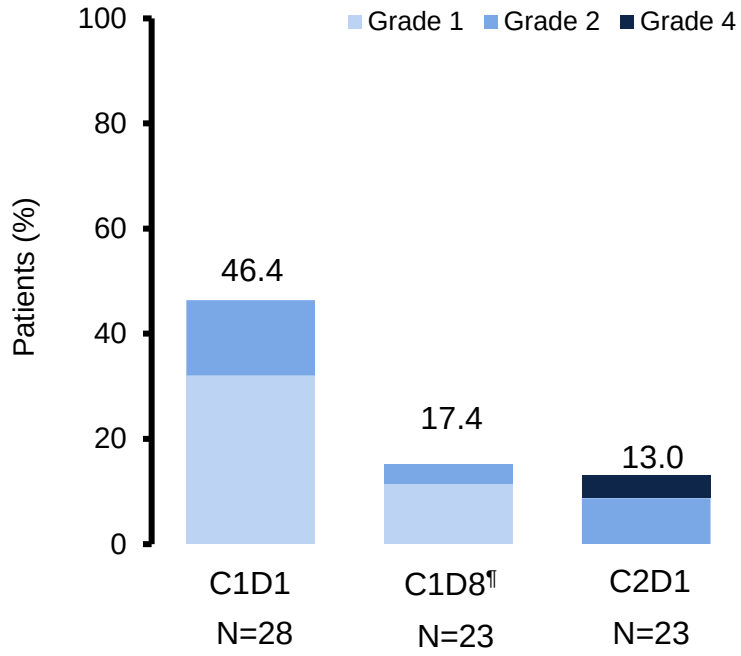
Most patients had ongoing responses at the time of the data cut-off

*Secondary efficacy-evaluable population. DOCR, duration of complete response; DOR, duration of response; Gpt, obinutuzumab pretreatment; SUD, step-up dosing.

Cytokine release syndrome*

n (%) of patients with ≥1 AE unless stated	Glofitamab fixed dosing + 1000mg Gpt (n=3)	Glofitamab SUD + 1000mg Gpt (n=7)	Glofitamab SUD + 2000mg Gpt (n=19)	All patients (N=29)
Any CRS	3 (100)	5 (71.4)	9 (47.4)	17 (58.6)
Grade 1	3 (100)	2 (28.6)	5 (26.3)	10 (34.5)
Grade 2	0	2 (28.6)	4 (21.1)	6 (20.7)
Grade 3	0	0	0	0
Grade 4†	0	1 (14.3)	0	1 (3.4)
Serious AE of CRS (any grade)	2 (66.7)	5 (71.4)	4 (21.1)	11 (37.9)
Median time to first CRS event, hrs (range)	5.5 (3.0–32.7)	9.6 (6.6–21.7)	12.1 (7.7–19.8)	9.9 (3.0–32.7)
Tocilizumab use in patients with CRS	0	4 (57.1)	3 (15.8)	7 (24.1)
CRS events resolved	3 (100)	4 (80)	6 (66)‡	13 (76.5)§
Median time to CRS resolution, hrs (range)	23.0 (10.9–171.4)	38.8 (20.6–49.0)	51.4 (3.8–142.0)	38.8 (3.8–171.4)

CRS by cycle and grade (all patients)



Most CRS events occurred during C1, were Grade 1 or 2 and resolved

*By American Society for Transplantation and Cellular Therapy (ASTCT) criteria[1]; †Grade 4 CRS in the SUD + 1000mg Gpt cohort (patient died due to cardiopulmonary insufficiency as a result of rapid PD; at time of death CRS was persisting). ‡3/3 remaining CRS events resolved post data cut off; §3/4 remaining CRS events resolved post data cut-off; ¶Patients in the fixed-dosing cohort (n=3) did not receive glofitamab on C1D8.

1. Lee, DW et al. Biol Blood Marrow Transplant 2019

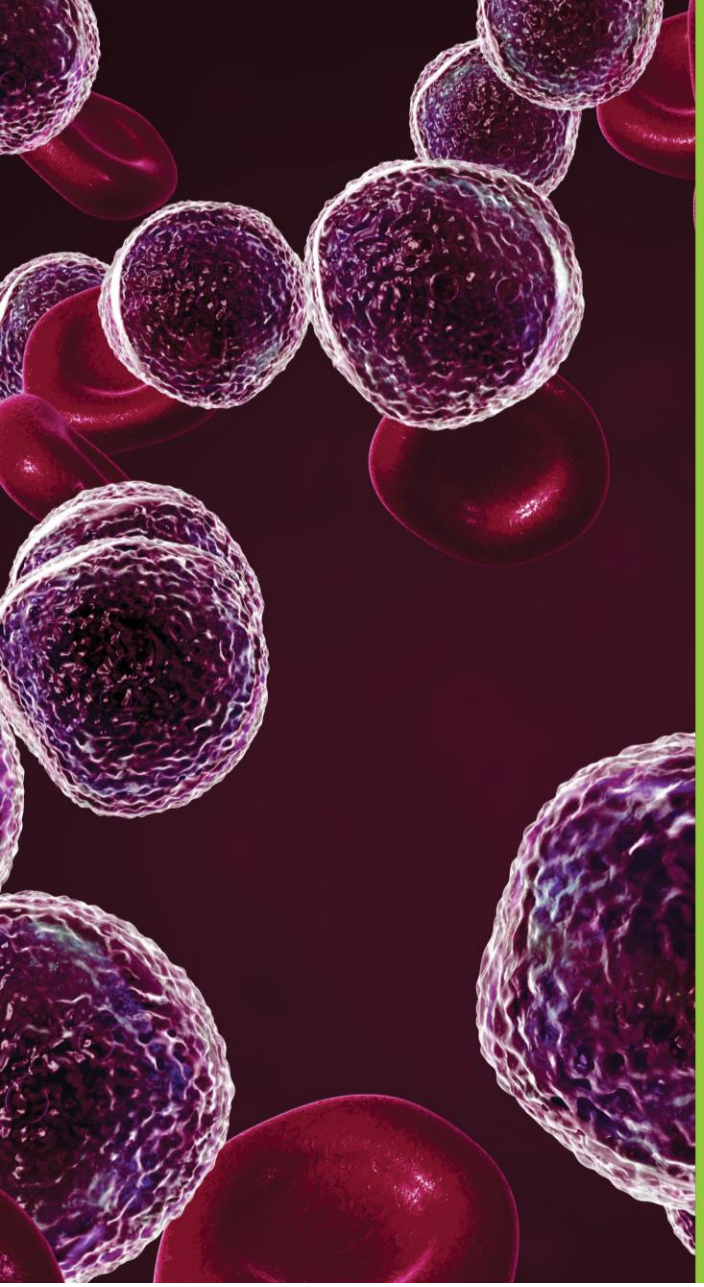
Conclusions

- Glofitamab, a 2:1 CD20xCD3 T-cell engaging bispecific antibody with a fixed-duration treatment and off-the-shelf availability,[1,2] demonstrated promising efficacy and favourable safety in R/R MCL
- Glofitamab SUD induced high response rates in patients with R/R MCL, most of whom had failed prior BTKi therapy
- CRS was manageable and mostly low grade; ICANS AEs were infrequent, low grade and resolved within 1 day
- Glofitamab continues to be evaluated in the post-BTKi R/R MCL setting: these results support a future confirmatory trial

1. Bacac, M et al. Clin Cancer Res 2018; 2. NCT03075696. Available at: https://clinicaltrials.gov

Conclusions

- Immunotherapy showing increasing promise in FL
  - Bi-specific monoclonal antibodies (mosunetuzumab)
  - CART
- And in MCL
  - Glofitamab



Breaker Slide

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