IBCL-458

Mosunetuzumab Monotherapy Demonstrates Durable Efficacy With a Manageable Safety Profile in Patients With Relapsed/Refractory Follicular Lymphoma Who Received ≥2 Prior Therapies: Updated Results From a Pivotal Phase II Study

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Summary

Updated efficacy and safety data (median 28.3 months of follow-up) are presented from a pivotal, single-arm, Phase II study in patients with relapsed/refractory follicular lymphoma and ≥2 prior therapies

Durable responses continued to be observed with mosunetuzumab

Comparable clinical response was observed regardless of CRS occurrence

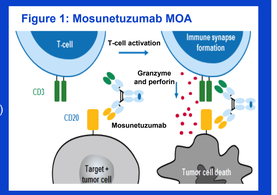
The safety profile, with predominantly low-grade cytokine release syndrome (CRS) events, was consistent with previous reports and supports outpatient administration of mosunetuzumab

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Background

- Mosunetuzumab is a CD20xCD3 T-cell-engaging bispecific antibody that redirects T cells to engage and eliminate malignant B cells.[1,2]
- Mosunetuzumab is approved in the EU and USA for the treatment of relapsed/refractory (R/R) follicular lymphoma (FL) after ≥2 prior systemic therapies.[3,4]
  - Objective response rate (ORR) 80%, complete response (CR) rate 60%, majority maintaining response after 18 months.[5]
  - Consistent benefit in patients with double-refractory disease and progression of disease within 24 months (POD24).[5]
  - Off-the-shelf, fixed-duration treatment that can be administered in the outpatient setting.[5]
- A pivotal, single-arm, multicenter, Phase II study (NCT02500407) in patients with R/R FL and ≥2 prior therapies met its primary endpoint, with a 60% CR rate versus 14% for a historical control ($p<0.0001$).[5,6]
- Here we present updated efficacy and safety data with a median 28.3 months of follow-up (10 months after the previous report; cut-off date: July 8, 2022).

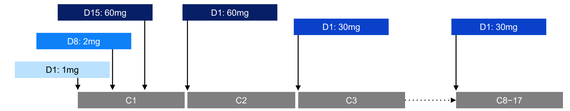
Figure 1: Mosunetuzumab MOA



Methods

- Patients with Grade (Gr) 1–3a FL, ≥2 prior therapies (including an anti-CD20 antibody and an alkylator), and ECOG Performance Status 0–1 were enrolled.
- Intravenous mosunetuzumab was administered with step dosing in Cycle (C) 1 (**Figure 1**). Treatment was of fixed duration: 8 cycles (21-day cycles) if CR by C8; 17 cycles if partial response or stable disease by C8.
- Re-treatment with mosunetuzumab was permitted at relapse for patients who achieved CR. There was no mandatory hospitalization.
- Whole exome sequencing was performed in 51 available baseline biopsy samples to assess activity of mosunetuzumab in patients with known prognostic variants.

Figure 1. Mosunetuzumab treatment schedule



C, Cycle; D, Day

Baseline characteristics

- Ninety patients were enrolled. Median age was 60 years (range: 29–90), and 77% had stage III/IV disease (**Table 1**). Median number of prior lines of therapy was 3.
- Median time on study was 28.3 months (range: 2–38) and 62% of patients completed therapy. The majority of patients (59%) received 8 cycles of therapy.

Table 1. Baseline characteristics

% unless stated	N=90
Median age, years (range)	60 (29–90)
Male	61
ECOG Performance Status	
0	59
1	41
Ann Arbor stage	
I/II	23
III/IV	77
Median time since last prior therapy, months (range)	6.7 (0–89)
Median lines of prior therapy, n (range)	3 (2–10)
Last therapy prior to mosunetuzumab	
Chemoimmunotherapy	63
PI3K inhibitor-containing regimen	8
Anti-CD20 antibody plus lenalidomide	2
CAR T-cell therapy	2
Other*	24
Refractory to last prior therapy	69
Refractory to any prior anti-CD20 therapy	79
Progression of disease within 24 months from start of first-line therapy (POD24)	52
Double refractory to prior anti-CD20 and alkylator therapy	53
Prior autologous stem cell transplant	21

*other common therapies included anti-CD20 antibody monotherapy, chemotherapy, and radioimmunotherapy; CAR, chimeric antigen receptor

Efficacy

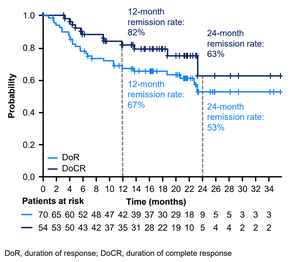
- Objective response and CR rates (**Table 2**) were consistent with published results.[5] Median time to first response was 1.4 months (range: 1–11) and median time to first CR was 3.0 months (1–19).
- Responses were durable, with the majority of patients in remission after 2 years (**Table 2** and **Figure 2**).
- Response rates were substantially improved with mosunetuzumab versus last prior therapy (**Table 2**).
- Clinically meaningful response rates were observed in patients with common mutations, including those associated with poor prognosis (**Figure 3**). Single nucleotide variants were found at a similar frequency to reported prevalence rates.[7]

Table 2. Response to mosunetuzumab versus last prior therapy

Efficacy endpoint*	Mosunetuzumab (N=90)	Last prior therapy (N=90)
Response rates, % (95% CI)		
ORR	78 (68–86)	56 (45–66)
CR	60 (49–70)	36 (26–46)
Median DoR, months (range)	NR (21–NR)†	12 (10–17)‡
24-month DoR, % (95% CI)	53 (38–68)†	29 (16–41)‡
Median DoCR, months (range)	NR (23–NR)§	15 (11–26)¶
24-month DoCR, % (95% CI)	63 (38–88)§	34 (18–51)¶
Median PFS, months (range)	24 (12–NR)	12 (10–16)
24-month PFS, % (95% CI)	48 (36–60)	23 (14–32)
Median TTNT, months (range)	NR (18–NR)	17 (14–20)
24-month TTNT, % (95% CI)	56 (45–67)	33 (24–43)
Median OS, months (range)	NR (NR–NR)	–
24-month OS, % (95% CI)	87 (80–94)	–

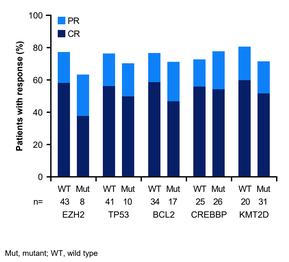
*by investigator assessment; †n=70; ‡n=50; §n=54; ¶n=32; CR, complete response; DoCR, duration of complete response; DoR, duration of response; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; TTNT, time to next treatment

Figure 2. DoR and DoCR with mosunetuzumab



DoR, duration of response; DoCR, duration of complete response

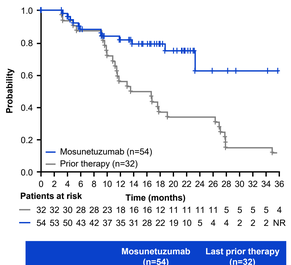
Figure 3. Response by mutation status



Mut, mutant; WT, wild type

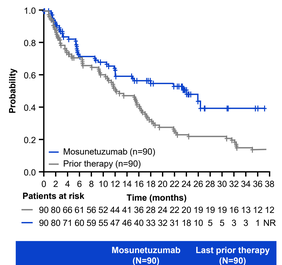
- Median duration of CR (DoCR) and progression-free survival were improved with mosunetuzumab compared with last prior therapy (**Figures 4** and **5**).

Figure 4. DoCR with mosunetuzumab versus last prior therapy



	Mosunetuzumab (n=54)	Last prior therapy (n=32)
Median DoCR, months (95% CI)	NR (23–NR)	15 (11–26)

Figure 5. PFS with mosunetuzumab versus last prior therapy



	Mosunetuzumab (N=90)	Last prior therapy (N=90)
Median PFS, months (95% CI)	24 (12–NR)	12 (10–16)

DoCR, duration of complete response; NR, not reached; PFS, progression-free survival

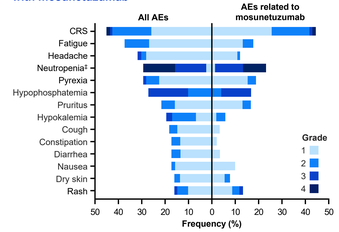
Safety

- No new serious adverse events (AEs), Gr ≥3 AEs, or treatment-related AEs were reported with 10 additional months of follow-up (**Table 3** and **Figure 6**).

Table 3. AE summary

%	N=90
Any Gr AEs	100
Mosunetuzumab related	92
Gr 3–4 AEs	70
Mosunetuzumab related	51
Serious AEs	47
Mosunetuzumab related	33
Gr 5 (fatal) AEs	2*
Mosunetuzumab related	0
AEs leading to treatment discontinuation	4†
Mosunetuzumab related	2

Figure 6. AEs (≥15%) by Grade and relationship with mosunetuzumab



*malignant neoplasm progression (n=1) and unexplained death (n=1); †mosunetuzumab related: CRS (n=2); mosunetuzumab unrelated: Epstein-Barr viremia and Hodgkin's disease (n=1 each); ‡grouped term including preferred term 'neutropenia' and 'neutrophil count decreased'; AE, adverse event; CRS, cytokine release syndrome; Gr, Grade

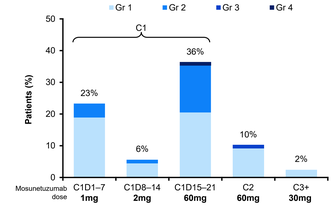
Cytokine release syndrome

- CRS was predominantly low grade and occurred during C1 (**Table 4** and **Figure 7**). All CRS events resolved. No new events were reported with 10 months of additional follow-up.

Table 4. CRS by ASTCT criteria[8]

% unless stated	N=90
CRS	
Any Gr	44
Gr 1	26
Gr 2	17
Gr 3	1
Gr 4	1
Median time to CRS onset, hours (range)	5.2 (1.2–24)
C1D1	27 (0.1–391)
C1D5	
Median CRS duration, days (range)	3 (1–29)
CRS management	
Corticosteroids	11
Tocilizumab	8
Events resolved	100

Figure 7. CRS by Cycle and Grade



C, Cycle; CRS, cytokine release syndrome; D, Day; Gr, Grade

- No correlation was observed between the occurrence of CRS and tumor response (**Table 5**).

Table 5. Tumor response and CRS occurrence

Efficacy endpoints by investigator assessment	CRS (n=40)	No CRS (n=50)
ORR, %	78	78
CR, %	65	56
Median DoR, months (95% CI)	23 (11–NR)*	NR (19–NR)†
18-month DoR, % (95% CI)	65 (48–83)*	66 (51–81)†
Median DoCR, months (95% CI)	23 (12–NR)‡	NR (NR–NR)§
18-month DoCR, % (95% CI)	66 (47–86)‡	91 (80–100)§

*n=31; †n=39; ‡n=26; §n=28; CR, complete response; CRS, cytokine release syndrome; DoR, duration of response; DoCR, duration of complete response; NR, not reached; ORR, objective response rate

Conclusions

- This pivotal Phase II study of mosunetuzumab continues to demonstrate:
  - Clinically meaningful outcomes in heavily pre-treated patients with R/R FL after >2 years of follow-up: CR rate, 60%; 24-month DoCR, 63%.
  - A manageable safety profile, with no new CRS events and no late-onset or chronic toxicities.
- Mosunetuzumab substantially improved tumor response and PFS versus last prior therapy.
- Mosunetuzumab is an efficacious treatment for patients with R/R FL and ≥2 prior therapies that is available off-the-shelf and can be given as an outpatient therapy with a fixed duration of treatment.

Presented at the 11th Annual Meeting of the Society of Hematologic Oncology (SOHO 2023) | September 6–9, 2023

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Acknowledgements

These data have been previously been presented at the American Society of Hematology Annual Meeting 2022 and the Hematology/Oncology Pharmacy Association Annual Conference 2023. This study is sponsored by Genentech, Inc. Third-party medical writing assistance, under the direction of all authors, was provided by Emily Lynch, PhD and Martha Warren, MSci, of Ashfield MedComms, an Inizio company, and was funded by F. Hoffmann-La Roche Ltd.

Disclosures

NLB has received research funding (ADC Therapeutics, Autolus, BMS, Celgene, Forty Seven, Janssen, Kite, Pharma, Merck, Millennium, Pharmacyclics, Roche/Genentech, Seattle Genetics); current employment (Washington University School of Medicine), Membership on an entity's Board of Directors or advisory committees (ADC Therapeutics, Roche/Genentech, Seattle Genetics); **LHS** has received consultancy (Abbvie, Acerta, Amgen, Apobiologix, Astra Zeneca, BMS/Celgene, Gilead, Incyte, Janssen, Kite, Karyopharm, Lundbeck, Merck, Morphosys, Roche/Genentech, Sandoz, Seattle Genetics, Servier, Teva, Takeda, TG Therapeutics, Verastem), honoraria (Abbvie, Acerta, Amgen, Apobiologix, Astra Zeneca, BMS/Celgene, Gilead, Incyte, Janssen, Kite, Karyopharm, Lundbeck, Merck, Morphosys, Roche/Genentech, Sandoz, Seattle Genetics, Servier, Teva, Takeda, TG Therapeutics, Verastem), research funding (Abbvie, Acerta, Amgen, Apobiologix, Astra Zeneca, BMS/Celgene, Gilead, Incyte, Janssen, Kite, Karyopharm, Lundbeck, Merck, Morphosys, Roche/Genentech, Sandoz, Seattle Genetics, Servier, Teva, Takeda, TG Therapeutics, Verastem); **MM** has received honoraria (ADC Therapeutics, Bayer, Daiichi Sankyo, Epizyme, IMV Therapeutics, Janssen, MEI Pharma, Pharmacyclics, Genentech, Roche, Seattle Genetics), research funding (Astra Zeneca, Bayer, Genentech, IGM Biosciences, Janssen, Pharmacyclics, Roche, Seattle Genetics), stock ownership (Merck), consultancy (ADC Therapeutics, Astra Zeneca, Bayer, Daiichi Sankyo, Epizyme, F. Hoffmann-La Roche Ltd, Genentech Inc., IMV Therapeutics, Juno Therapeutics, Karyopharm, Merck, MEI Pharma, Rocket Medical, Seattle Genetics, TG Therapeutics, Teva, Bayer), current employment (Memorial Sloan Kettering Cancer Center); **SJS**, **JM** and **CRB** have no conflicts to declare; **SA** has received consultancy (Genentech/Roche, Astra Zeneca, Novartis, BMS, Jazz, Gilead, Amgen, Beigene, Abbvie, Paladin), research funding (Novartis), honoraria (Genentech/Roche, Astra Zeneca, Novartis, BMS, Jazz, Gilead, Amgen, Beigene, Abbvie, Paladin); **PG** has received honoraria (Roche), advisory committee (Roche), current employment (Royal Adelaide Hospital); **JK** has received consultancy (Abbvie, Antengene, BMS, Gilead, Karyopharm, Medison Ventures, Merck, Roche, Seattle Genetic), research funding (Roche, Astra Zeneca, Merck), honoraria (Abbvie, Amgen, Astra Zeneca, BMS, Gilead, Incyte, Janssen, Karyopharm, Merck, Novartis, Pfizer, Roche, Seattle Genetics), other (DSMB Karyopharm); **MC** has received consultancy (Beigene, BMS, Kite, Incyte, Janssen, Karyopharm, Kyowa, Novartis, Roche, Sanofi, Takeda), current employment (La Paz University Hospital), speaker's bureau (Amgen, Kite, Janssen, Kyowa, Novartis, Roche, Sandoz, Takeda); **SD** has received consultancy (Kite, Gilead, Roche), current employment (Clinical Haematologist, University Hospital Heidelberg); **KF** has received current employment (St Vincent's Hospital, Sydney, Australia); **MK** has received consultancy (Antengene, Genor BioPharma, Roche), current employment (Clinical Haematologist, St Vincent's Hospital, Melbourne); **LN** has received research funding (BMS, Caribou Biosciences, Epizyme, Genentech, Gilead/Kite, Genmab, Janssen, IGM Biosciences, Novartis, Takeda), honoraria (ADC Therapeutics, BMS, Caribou Biosciences, Epizyme, Genentech/Roche, Gilead/Kite, Genmab, Janssen, MEI, Morphosys, Novartis, Takeda), other (DSMC - Genentech/Roche, MEI, Takeda); **MCW** has received stock ownership (Roche), current employment (Roche), patents and royalties (Roche); **SY** has received stock ownership (F. Hoffmann-La Roche), current employment (Genentech, Inc.), patents and royalties (Genentech, Inc.); **IT** has received stock ownership (Genentech, Inc.) current employment (Genentech, Inc.); **HH** has received current employment (F. Hoffmann-La Roche); **EP** has received stock ownership (Genentech, Inc.) current employment (Genentech, Inc.); **LEB** has received research funding (Merck, Amgen, MustangBio, AstraZeneca), consulting or advisory role (Roche/Genentech, Kite/Gilead, Novartis, BeiGene), Patents, royalties, other intellectual property (CCR4 CAR T cells for treatment of patients with CCR4 positive cancer, CD33CAR for treatment of patients with CD33+ acute myeloid leukemia), Travel, accommodation, expenses (Roche/Genentech, Kite/Gilead).