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Mosunetuzumab Retreatment is Effective and Well-Tolerated in Patients With Relapsed or Refractory B-Cell non-Hodgkin Lymphoma

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Summary

Ongoing Phase I/II study of patients with **relapsed/refractory (R/R) non-Hodgkin lymphoma (NHL)** receiving fixed-dose **mosunetuzumab (M)** treatment

Patients who **achieved a complete response (CR)** after initial M treatment **but developed progressive disease (PD)** following treatment completion were **eligible for M retreatment**

At the clinical cut-off date (August 27, 2021)

15 patients with R/R NHL received M retreatment

M retreatment had a **manageable safety profile**

No Grade 3–4 cytokine release syndrome (CRS) events were observed

During M retreatment **9/13 efficacy-evaluable patients had an objective response**; of these, **6 patients achieved a CR**

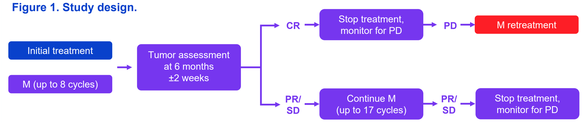
Background

- The prognosis for heavily pretreated patients with relapsed/refractory (R/R) non-Hodgkin lymphoma (NHL) is poor and there is a need for effective treatment options.[1,2]
- Mosunetuzumab (M) is a full-length, immunoglobulin G1-based, CD20xCD3 T-cell engaging bispecific monoclonal antibody that redirects T cells to eliminate malignant B cells.[3,4]
- Results from a single-arm, Phase I/II study (NCT02500407) of intravenous (IV) M in patients with R/R aggressive and indolent NHL showed durable complete response (CR) and a manageable safety profile.[4] Specifically, in patients with R/R follicular lymphoma (FL) after ≥2 prior therapies, M demonstrated a 60% CR rate and an 80% objective response (OR) rate with a median duration of response (DoR) of 22.8 months.[5]
- For patients who achieved a CR but had progressive disease (PD) after initial treatment completion, M retreatment could be provided
  - Initial M treatment had a fixed duration (8 cycles for patients who achieved CR; 17 cycles for patients with partial response [PR] or stable disease [SD] after 8 cycles).
- We report additional efficacy and safety data from this ongoing study to describe the M retreatment experience of patients with R/R NHL.

Patients with a CR after initial M treatment, who developed PD after treatment completion, were eligible for M retreatment (Figure 1)

- Patients were retreated with IV M monotherapy at a previously tested dose, and schedule, which included step-up dosing for cytokine release syndrome (CRS) mitigation.
- Response, nature and severity of adverse events (AEs), incidence of CRS events and biomarker analyses (B-cell depletion and cytokine [interferon gamma {INF_γ} and interleukin 6 {IL6}] levels) were assessed in the M retreatment population
  - Outcomes in the initial treatment phase and the retreatment phase were compared for these patients.
- All patients provided informed consent.

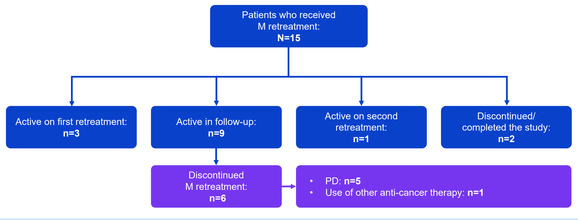
Figure 1. Study design.



At the clinical cut-off date (August 27, 2021), 15 patients received M retreatment (R/R FL n=11, R/R diffuse large B-cell lymphoma [DLBCL] n=2, R/R mantle cell lymphoma [MCL] n=1, R/R transformed follicular lymphoma [trFL] n=1)

- The patient disposition for this analysis is summarized in **Figure 2**.
- The baseline CD20 status prior to retreatment was available for 3/15 patients, all of which were CD20+; no patients received other intervening therapies between initial M treatment and M retreatment.
- The median number of M retreatment cycles received was 8.0 (range, 2–13) and the median retreatment duration was 4.9 months (range, 0.7–8.4).
- M retreatment step-up dose schedules were as follows (Cycle [C] 1, Day [D] 1/C1D8/C1D15/C2D1/C3+D1): 1/2/13.5mg (n=1), 1/2/20mg (n=1), 1/2/27mg (n=1), 1/2/40.5mg (n=1) and 1/2/60/60/30mg (n=11).
- All patients who received M retreatment were included in the safety population (n=15) and 13/15 patients were included in the efficacy population (2 patients initiated retreatment <3 months before the clinical cut-off date and therefore were not yet evaluable for efficacy).

Figure 2. Patient disposition.



The majority of the M retreatment population represented a highly refractory NHL population (Table 1)

Table 1. Baseline characteristics of the M retreatment population.

Characteristic	Total (N=15)
Median age, years (range)	61 (35–83)
Male, n (%)	11 (73.3)
Race, n (%)	
White	12 (80.0)
Asian	2 (13.3)
Unknown	1 (6.7)
NHL subtype at study entry, n (%)	
FL	11 (73.3)
DLBCL	2 (13.3)
MCL	1 (6.7)
trFL	1 (6.7)
Ann Arbor stage at study entry, n (%)	
III/IV	15 (100.0)
Bulky disease (>6cm), n (%)	5 (33.3)
ECOG PS, n (%)	
0	11 (73.3)
1	4 (26.7)
Number of prior lines of therapy (before initiation of M treatment)	
Median (range)	3.0 (1–9)
≤3, n (%)	8 (53.3)
>3, n (%)	7 (46.7)
Refractory to prior CD20 therapy, n (%)	11 (73.3)

ECOG PS, Eastern Cooperative Oncology Group performance status.

High response and CR rates were observed during M retreatment (Table 2; Figure 3)

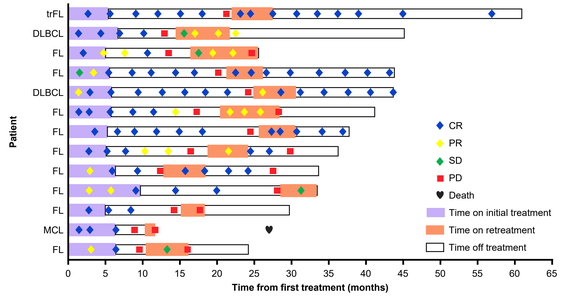
- All 13 efficacy-evaluable patients had a treatment-free period of >6 weeks.

Table 2. Best response to M retreatment.

M retreatment cohort	Best response to retreatment, n (%)	DoR range, months
All patients	**n=13**	
OR	9 (69.2)	3.2*–33.8*
CR	6 (46.2)	8.3–33.8*
PR	3 (23.1)	3.2*–6.6
PD	2 (15.4)	-
SD	2 (15.4)	-
R/R FL	**n=9**	
OR	6 (66.7)	5.4–20.7*
CR	4 (44.4)	8.3–20.7*
PR	2 (22.2)	5.4–6.6
PD	1 (11.1)	-
SD	2 (22.2)	-
R/R DLBCL	**n=2**	
OR	2 (100.0)	3.2*–17.5*
CR	1 (50.0)	17.5*
PR	1 (50.0)	3.2*
R/R trFL	**n=1**	
OR	1 (100.0)	33.8*
CR	1 (100.0)	33.8*
R/R MCL	**n=1**	
PD	1 (100.0)	-

*Value censored.

Figure 3. Time on treatment and response for patients in the M retreatment population.



The safety profile of M was consistent in the initial treatment and retreatment phases. No Grade 3–4 CRS events were observed in patients who received M retreatment (Table 3)

- During the initial treatment phase, the most common any-grade AEs were headache (n=7 [46.7%]), hypophosphatemia (n=7 [46.7%]), fatigue (n=6 [40.0%]) and CRS (n=4 [26.7%])
  - The most common Grade 3–4 AEs were hypophosphatemia (n=5 [33.3%]) and neutropenia (n=5 [33.3%]).
- During the retreatment phase, the most common any-grade AEs were hypophosphatemia (n=8 [53.3%]), hypokalemia (n=5 [33.3%]), fatigue (n=5 [33.3%]), back pain (n=5 [33.3%]) and CRS (n=5 [33.3%])
  - The most common Grade 3–4 AEs were hypophosphatemia (n=8 [53.3%]) and hypokalemia (n=3 [20.0%]).
- Grade 2 CRS events were managed using fluids and oxygen (low flow).
- All CRS events were resolved (median duration: 3 days [range, 2–16]).

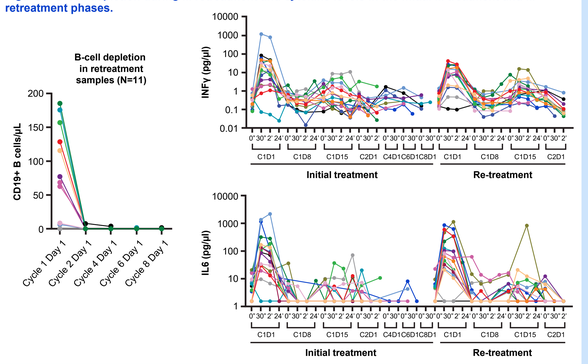
Table 3. Summary of safety (M retreatment and initial treatment phase).

AE, n (%)	Initial treatment phase (N=15)	Retreatment phase (N=15)
Any-grade AE	15 (100.0)	15 (100.0)
Any-grade AE related to M	15 (100.0)	13 (86.7)
Grade 3–4 AE	12 (80.0)	12 (80.0)
Grade 3–4 AE related to M	9 (60.0)	7 (46.7)
Serious AEs	2 (13.3)	5 (33.3)
Serious AE related to M	1 (6.7)	5 (33.3)
Grade 5 (fatal) AE	0	0
Grade 5 (fatal) AE related to M	0	0
AE leading to treatment discontinuation	0	0
M-related AE leading to treatment discontinuation	0	0
Number of patients who experienced a CRS event*		
Any-grade	4 (26.7)	5 (33.3)
Grade 1	3 (20.0)	4 (26.7)
Grade 2	1 (6.7)	1 (6.7)

*CRS events were classified as per the American Society for Transplantation and Cellular Therapy.

Rapid B-cell depletion was observed during M retreatment and the immune cytokine profile was similar to initial M treatment (Figure 4)

Figure 4. B-cell depletion during M retreatment and cytokine levels in the initial M treatment and M retreatment phases.



Conclusions

- Our results show that IV M monotherapy retreatment was efficacious in heavily pretreated patients with R/R NHL who initially achieved a CR with M treatment, but subsequently developed PD, indicating treatment activity through multiple lines of therapy.
- M retreatment had a manageable safety profile, consistent with that observed with initial treatment.
- M retreatment induced rapid B-cell depletion and an immune cytokine profile similar to initial M treatment.

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