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

To be presented by Brannon Flores on behalf of the authors

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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 R/R FL 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 CRS events, was consistent with previous reports and supports outpatient administration of mosunetuzumab

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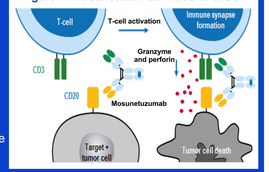
Background

- 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).

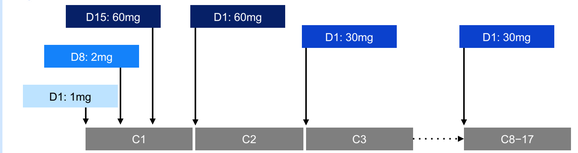
Figure 1. Mosunetuzumab mode of action



Methods

- Patients with Grade (Gr) 1–3a FL, ≥2 prior therapies (including an anti-CD20 antibody and an alkylator), and Eastern Cooperative Oncology Group (ECOG) performance status 0–1 were enrolled.
- Intravenous mosunetuzumab was administered with step-up 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



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
POD24 from start of first-line therapy	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; PI3K, phosphatidylinositol 3-kinase.

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; CI, confidence interval; DoCR, duration of complete response; DoR, duration of response; NR, not reached; OS, overall survival; PFS, progression-free survival; TTNT, time to next treatment.

Figure 2. DoR and DoCR with mosunetuzumab

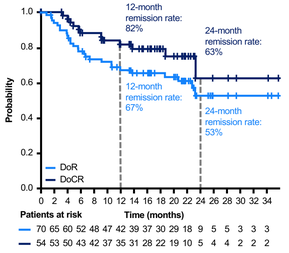
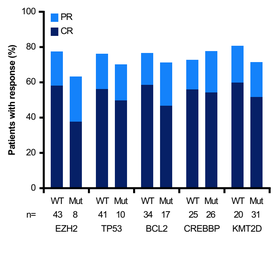


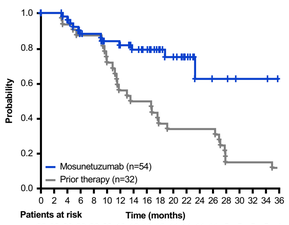
Figure 3. Response by mutation status



Mut, mutant; PR, partial response; WT, wild type.

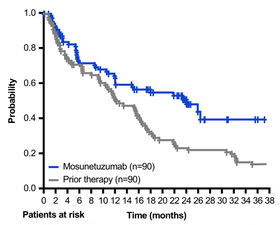
- Median DoCR and PFS were improved with mosunetuzumab compared with last prior therapy (**Figures 4** and **5**).

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)

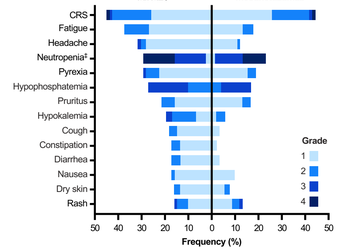
Safety

- 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'.

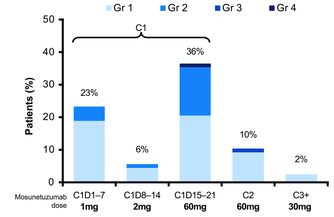
Cytokine release syndrome

- 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)	
C1D1	5.2 (1.2–24)
C1D5	27 (0.1–391)
Median CRS duration, days (range)	3 (1–29)
CRS management	
Corticosteroids	11
Tocilizumab	8
Events resolved	100

Figure 7. CRS by Cycle and Grade



ASTCT, American Society for Transplantation and Cellular Therapy.

- 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.

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.

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