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Fixed-Duration Subcutaneous Mosunetuzumab in Patients with Previously Untreated High-Tumor Burden Follicular Lymphoma (FL): Interim Results from the Phase II MorningSun Study

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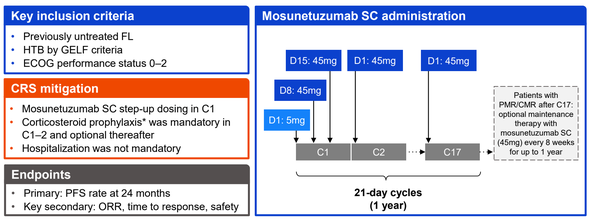
Background

- Mosunetuzumab, a CD20xCD3 bispecific antibody, is an off-the-shelf, fixed-duration treatment that can be administered in the outpatient setting[1–4]
  - Intravenous mosunetuzumab is approved for the treatment of patients with relapsed/refractory (R/R) FL after ≥2 prior lines of therapy[2–4]
  - Subcutaneous (SC) mosunetuzumab achieved high response rates with a manageable safety profile in patients with R/R FL after ≥2 prior lines of therapy in a pivotal Phase II study[5]
- The ongoing Phase II MorningSun basket study (NCT05207670) is evaluating the efficacy, safety, and pharmacodynamic profile of mosunetuzumab SC in patients with B-cell non-Hodgkin lymphoma, including FL[6,7]
  - Patients were enrolled across 55 sites within the US, including 45 community sites
  - Mosunetuzumab SC induced durable responses with a manageable safety profile in patients with previously untreated, low-tumor burden FL[7]
- Here we report interim efficacy and safety data for mosunetuzumab SC in patients with high-tumor burden (HTB) FL

MorningSun Phase II study design: HTB FL cohort

- MorningSun is an ongoing open-label Phase II trial (**Figure 1**)

Figure 1. Study overview: HTB FL cohort.



Patients were enrolled in the HTB FL cohort between March 3, 2022, and June 21, 2024.
*Dexamethasone (20mg) or methylprednisolone (80mg); premedication with oral acetaminophen or paracetamol and/or diphenhydramine could also be administered prior to mosunetuzumab administration.
C, cycle; CMR, complete metabolic response; CRS, cytokine release syndrome; D, day; ECOG, Eastern Cooperative Oncology Group; GELF, Groupe d'Études des Lymphomes Folliculaires; ORR, objective response rate; PFS, progression-free survival; PMR, partial metabolic response.

As of May 29, 2024, 103 patients were enrolled from US community (n=82) and academic (n=21) centers

- Most patients had Ann Arbor stage III/IV (91.2%) and FLIPI score ≥2 (78.4%) (**Table 1**)
- As of the clinical cut-off date, 55 patients had completed initial treatment (17 cycles), 31 had discontinued, and 16 were receiving ongoing initial treatment; 42 patients received maintenance treatment (ongoing in 38 patients)
- Median duration of follow-up was 13.9 months (range: 0.7–25.1) and the median number of cycles received was 17.0 (range: 1–23)

Table 1. Baseline characteristics.

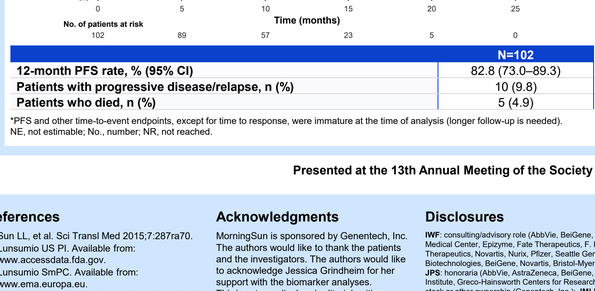
n (%), unless stated	N=102*
Median age, years (range)	64.5 (24–86)
Female	53 (52.0)
Race	
White	81 (79.4)
Asian	5 (4.9)
American Indian or Alaska Native	3 (2.9)
Black or African American	2 (2.0)
Not reported	8 (7.8)
Unknown	3 (2.9)
B symptoms	23 (22.5)
Elevated LDH	
Yes	25 (24.5)
No	77 (75.5)
ECOG performance status	
0	71 (69.6)
1	30 (29.4)
2	1 (1.0)
FL grade	
Grade 1–2	79 (77.5)
Grade 3A	20 (19.6)
Ungraded	2 (2.0)
Missing	1 (1.0)
Ann Arbor stage	
II	9 (8.8)
III	38 (37.3)
IV	55 (53.9)
Extranodal involvement	39 (38.2)
Bulky disease	
Yes	40 (39.2)
No	54 (52.9)
Unknown	8 (7.8)
FLIPI score	
0–1	22 (21.6)
2	34 (33.3)
3–5	46 (45.1)

*One patient was reassigned to a different cohort due to a protocol deviation.
FLIPI, Follicular Lymphoma International Prognostic Index; LDH, lactate dehydrogenase.

A 12-month PFS rate of 82.8% was observed with a low event rate

- Median PFS was not reached (**Figure 2**), and the 12-month PFS rate was 82.8% (95% confidence interval [CI]: 73.0–89.3)

Figure 2. Efficacy: PFS.



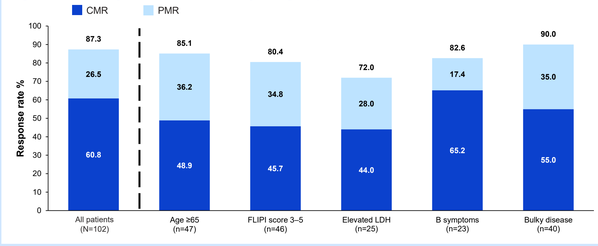
	N=102
12-month PFS rate, % (95% CI)	82.8 (73.0–89.3)
Patients with progressive disease/relapse, n (%)	10 (9.8)
Patients who died, n (%)	5 (4.9)

*PFS and other time-to-event endpoints, except for time to response, were immature at the time of analysis (longer follow-up is needed).
NE, not estimable; No., number; NR, not reached.

Consistent response rates were seen among high-risk subgroups

- ORR and CMR rates were 87.3% and 60.8%, respectively (**Figure 3**)
- Among patients with a response (n=89), the median time to response was 2.7 months (range: 1.2–5.8)

Figure 3. Efficacy: Response rates by subgroup.



All injection-site reaction and CRS adverse events (AEs), and most infections, were low grade

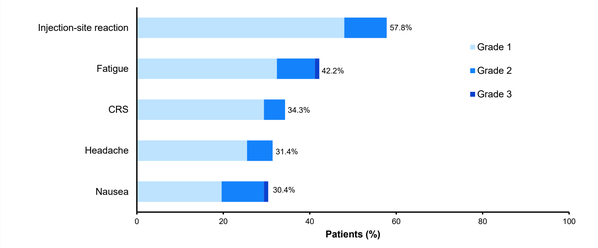
- Grade ≥3 and serious AEs occurred in 44.1% and 29.4% of patients, respectively (**Table 2**)
- The most common AEs (≥30%) were injection-site reaction (57.8%), fatigue (42.2%), CRS (34.3%), headache (31.4%), and nausea (30.4%) (**Figure 4**)
- CRS events were all Grade 1/2 and serious CRS occurred in 10.8% of patients; all events resolved (managed with steroids [7.8%], tocilizumab [5.9%], or both [2.9%])

Table 2. Safety overview.

n (%)	N=102
Any grade AE	**102 (100)**
Grade 3/4 AE	**41 (40.2)**
Most common Grade 3/4 AE (≥10%)	
Neutropenia/neutrophil count decreased	14 (13.7)
Grade 5 AEs	**4 (3.9)**
COVID-19 pneumonia	2 (2.0)
Cardiogenic shock	1 (1.0)
Death (unexplained)	1 (1.0)
Serious AE	**30 (29.4)**
Most common serious AEs (≥10%)	
Infections and infestations*	13 (12.7)
CRS	11 (10.8)
Select AEs of interest	
Infections and infestations	75 (73.5)†
Grade 3	13 (12.7)
Grade 4	2 (2.0)
Grade 5	2 (2.0)‡
ICANS (Grade 4)	1 (1.0)
AE leading to mosunetuzumab discontinuation	8 (7.8)§

*System organ class. †Most common infections (≥10%): COVID-19/COVID-19 pneumonia (26.5%), sinusitis (13.7%), urinary tract infection (12.7%), and pneumonia (11.8%). ‡COVID-19 pneumonia (n=2). §Cardiogenic shock, COVID-19 pneumonia, upper respiratory tract infection, neutrophil count decreased, amnesia, ICANS, nasal congestion, pneumonitis (n=1 each).
ICANS, immune effector cell-associated neurotoxicity syndrome.

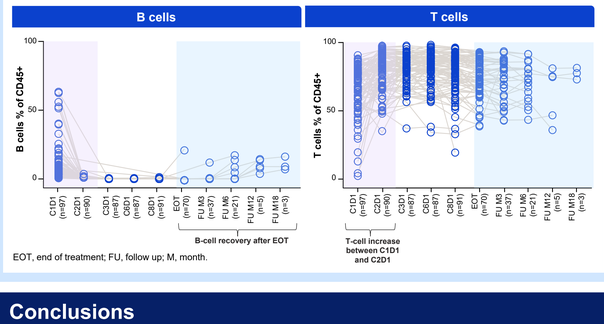
Figure 4. Most common AEs (≥30% incidence).



B cells were depleted (but recovered following treatment), and T-cell levels increased

- B-cell depletion was observed during treatment and subsequent recovery was observed following completion of fixed-duration mosunetuzumab SC treatment (**Figure 5**)
- T-cell levels increased from C1D1 to C2D1 (**Figure 5**); natural killer cell levels were unchanged

Figure 5. Biomarker results: cell subset profiling.



EOT, end of treatment; FU, follow up; M, month.

Conclusions

- Fixed-duration mosunetuzumab SC monotherapy demonstrated a 12-month PFS rate of 82.8%, ORR of 87.3%, and CMR rate of 60.8% in previously untreated HTB FL
- The safety profile was manageable and supports outpatient administration, including in US community practice settings; the CRS rate was consistent with that observed in R/R FL[1]
- Following initial B-cell depletion, B-cell recovery was observed after the completion of fixed-duration mosunetuzumab SC treatment
- These data support further exploration of mosunetuzumab-based therapy in patients with previously untreated HTB FL

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Disclosures

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