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MorningSun: Open-Label Phase II Trial of the Efficacy and Safety of Subcutaneous Mosunetuzumab as Frontline Treatment in Symptomatic Patients with Marginal Zone Lymphoma (MZL)

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Summary

There is an unmet need for effective, chemotherapy-free treatments in previously untreated MZL. The MorningSun study evaluates mosunetuzumab SC in a dedicated cohort of first-line MZL patients

Clinically meaningful and durable responses were seen after ~1.5 years' median follow-up. Response rates in high-risk subgroups were comparable to the overall population

These findings support further exploration of mosunetuzumab SC in patients with previously untreated MZL

Safety and CRS profiles were manageable: mosunetuzumab SC can be administered in US community practices and outpatient settings

Background

Mosunetuzumab

- Off-the-shelf, fixed-duration treatment that can be administered in the outpatient setting[1–4]
- Intravenous (IV) mosunetuzumab is approved for the treatment of patients with relapsed or refractory (R/R) FL after ≥2 prior lines of therapy[2–4]
  - In a pivotal Phase II study, an SC formation of mosunetuzumab demonstrated PK non-inferiority to mosunetuzumab IV in this setting[5]

Ongoing Phase II MorningSun basket study (NCT05207670)

- There is an unmet need for effective, chemotherapy-free treatment options for patients with MZL in the 1L setting[6]
- The MorningSun study aims to evaluate the efficacy and safety of mosunetuzumab SC in patients with 1L FL, 1L DLBCL (elderly/unfit), 1L MZL, R/R trFL, or RT, and R/R MCL[7]
- Here we report the efficacy and safety of mosunetuzumab SC in patients with previously untreated MZL

Methods – MorningSun study design

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

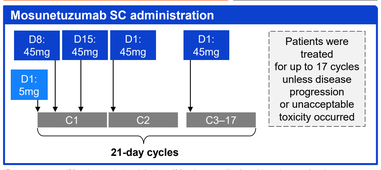
Figure 1. MorningSun study design: 1L MZL cohort

Key inclusion criteria
- Symptomatic MZL (splenic, nodal, and extranodal, including gastric/MALT)
- Previously untreated, with an indication to start systemic therapy
- ECOG performance status 0–2

CRS mitigation
- Mosunetuzumab SC step-up dosing in C1
- Corticosteroid prophylaxis* was mandatory in C1–2 and optional thereafter
- Hospitalization was not mandatory

Endpoints
- Primary: INV-assessed ORR by Lugano criteria
- Key secondary: PFS, DOR, DOCR, time to response, safety

Mosunetuzumab SC administration



*Dexamethasone (20mg) or methylprednisolone (80mg); premedication with oral acetaminophen or paracetamol and/or diphenhydramine could also be administered prior to administration of mosunetuzumab.
C, cycle; CRS, cytokine release syndrome; D, day; DOCR, duration of complete response; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; INV, investigator; MALT, mucosa-associated lymphoid tissue; MZL, marginal zone lymphoma; ORR, objective response rate; PFS, progression-free survival; SC, subcutaneous.

Results – Patient characteristics and disposition

- Overall, 36 patients were enrolled, 23 (64%) in US community sites and 13 (36%) in academic centers (**Table 1**)

Table 1. Baseline characteristics

n (%), unless stated	N=36
Median age, years (range)	69 (36–81)
Female	24 (66.7)
Race*	
White	32 (88.9)
Black or African American	1 (2.8)
Extranodal involvement	28 (77.8)
Bulky disease†	7 (19.4)
ECOG performance status	
0	20 (55.6)
1	13 (36.1)
2	3 (8.3)
B symptoms	6 (16.7)
Elevated LDH	11 (30.6)
Ann Arbor stage at study entry	
I	4 (11.1)
II	7 (19.4)
III	5 (13.9)
IV	20 (55.6)

CCOD: February 10, 2025. *Not reported, n=1; unknown, n=2. †Lesions ≥7cm.
CCOD, clinical cut-off date; LDH, lactate dehydrogenase.

- Median duration of follow-up was 18.2 months (range 1.5–30.4); 21 patients completed treatment (**Table 2**)

Table 2. Patient disposition and treatment exposure

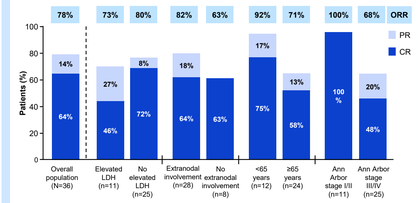
n (%), unless stated	N=36
Initial study treatment	
Ongoing	0
Completed	21 (58.3)
Discontinued[5]	15 (41.7)
AE	6 (16.7)
Physician decision	3 (8.3)
Progressive disease	3 (8.3)
Withdrawal by subject	2 (5.6)
Lost to follow-up	1 (2.8)
Median treatment duration, weeks (range)	51.0 (4–58)
Median number of cycles received, n (range)	17.0 (1–17)

CCOD: February 10, 2025. AE, adverse event.

Results – Efficacy

- CR rates across high-risk subgroups were consistent with the overall population (**Figure 2**)

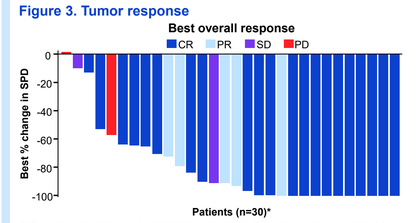
Figure 2. Best response rates



CCOD: February 10, 2025. CR, complete response; PR, partial response.

- Best overall response is shown in **Figure 3**. Time to response was 2.8 months (range 2.4–5.4); at the time of analysis, 23 patients (63.9%) were still in CMR
- Median DOR and DOCR were not reached (95% CI: NE–NE); DOR and DOCR event-free rates at 12 months were 92.3% and 100%, respectively

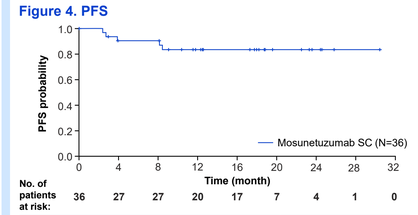
Figure 3. Tumor response



CCOD: February 10, 2025. *Analysis was conducted in all patients with a baseline and ≥1 post-baseline SPD available and Lugano response assessment before new anti-lymphoma therapy, surgery, or procedure.
CI, confidence interval; CMR, complete metabolic response; SD, stable disease; NE, not estimable; PD, progressive disease; SPD, sum of product diameters.

- Estimated PFS at 6 and 12 months was 90.5% and 83.6%, respectively (**Figure 4**). All TTE endpoints (except TTR) are immature with a low event rate and longer follow-up is needed.

Figure 4. PFS



	N=36
Median PFS, months (95% CI)	NR (NE–NE)
6-month event-free rate, % (95% CI)	90.5 (73.4–96.8)
12-month event-free rate, % (95% CI)	83.6 (64.8–92.8)

CCOD: February 10, 2025.
NR, not reached; TTE, time to event; TTR, time to response.

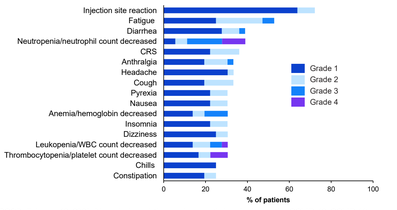
Results – Safety overview

- In total, 100% of patients experienced any-grade AEs; the most common AEs (≥25% incidence) were infections and infestations, injection site reaction, fatigue, diarrhea, and CRS (**Figure 5**)

Figure 5. AE summary

n (%)	N=36
Any grade AE	36 (100)
Grade 3/4 AEs	23 (63.9)
Most common Grade 3/4 AEs (≥10%)	
Neutropenia/neutrophil count decreased	10 (27.8)
Anemia	4 (11.1)
Grade 5 AEs	0
Select AEs of interest	
ICANS	0
Serious AEs*	14 (38.9)
AE leading to mosunetuzumab discontinuation†	6 (16.7)

Most common AEs (≥25% incidence)



CCOD: February 10, 2025. *Anemia, hemolytic anemia, necrotic lymphadenopathy, COVID-19, COVID-19 pneumonia, sepsis, norovirus, wound infection, femur fracture, platelet count decreased, colon adenocarcinoma, confusional state, pleural effusion, respiratory failure (n=1 [2.8%] each); CRS (n=3 [8.3%]); some patients may have experienced more than one AE. †Hemolytic anemia, sinusitis, femur fracture, platelet count decreased, respiratory failure, maculopapular rash (n=1 each).
COVID-19, coronavirus disease 2019; CRS, cytokine release syndrome; ICANS, immune cell-associated neurotoxicity syndrome; WBC, white blood cell.

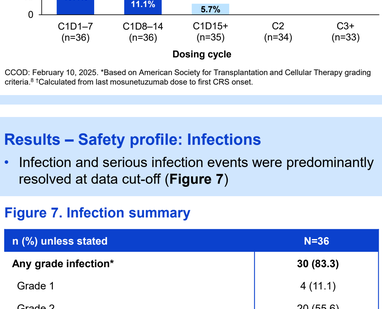
Results – Safety profile: CRS

- CRS events were predominantly Grade 1; all occurred during Cycle 1 and all resolved (**Figure 6**)

Figure 6. CRS summary

n (%) unless stated	N=36
Any grade CRS*	**13 (36.1)**
Grade 1	8 (22.2)
Grade 2	5 (13.9)
Median time to CRS onset, days (range)†	2 (1–5)
Median CRS duration, days (range)	2.5 (1–7)
Management of CRS	
Corticosteroids	5 (13.9)
Tocilizumab	5 (13.9)
Corticosteroids + tocilizumab	2 (5.6)
CRS resolution	13 (100)

Frequency of CRS events by cycle and grade



CCOD: February 10, 2025. *Based on American Society for Transplantation and Cellular Therapy grading criteria.[8] †Calculated from last mosunetuzumab dose to first CRS onset.

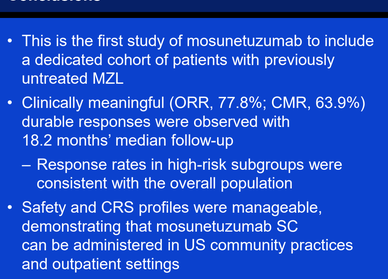
Results – Safety profile: Infections

- Infection and serious infection events were predominantly resolved at data cut-off (**Figure 7**)

Figure 7. Infection summary

n (%) unless stated	N=36
Any grade infection*	**30 (83.3)**
Grade 1	4 (11.1)
Grade 2	20 (55.6)
Grade 3	6 (16.7)
SAE of infection*	**5 (13.9)**
Grade 3	5 (13.9)
Median time from first mosunetuzumab dose to first infection, days (range)†	73.5 (3–265)
Infection events resolved, n/n (%)	57/68 (83.8)
Serious infection events resolved, n/n (%)	5/5 (100)

Most common infections (≥10% incidence)



CCOD: February 10, 2025. *System organ class (infections and infestations).
†Calculated from first mosunetuzumab dose C1D1 to first infection onset.
SAE, serious adverse event.

Conclusions

- This is the first study of mosunetuzumab to include a dedicated cohort of patients with previously untreated MZL
- Clinically meaningful (ORR, 77.8%; CMR, 63.9%) durable responses were observed with 18.2 months' median follow-up
  - Response rates in high-risk subgroups were consistent with the overall population
- Safety and CRS profiles were manageable, demonstrating that mosunetuzumab SC can be administered in US community practices and outpatient settings
  - Low grade CRS and injection site reaction AEs were observed
  - Infections were mainly low grade and manageable; no fatal infections were observed
- These data support further exploration of mosunetuzumab SC in patients with previously untreated MZL

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Disclosures

JMB has held a consultancy for AbbVie, AstraZeneca, BeiGene, Bristol Myers Squibb, CRISPR Therapeutics, Eli Lilly Genentech/Roche, Genmab, Incyte, Novartis, Regeneron and SeaGen. **AMT** has received honoraria from Curio Science and has held a consultancy for ADC Therapeutics. **JV** has held a consultancy for Curio Science, Kite/Gilead, Regeneron, TG Therapeutics and has received research funding from Aptose Biosciences, Celgene/Bristol-Myers Squibb, Enterome, Epizyme, Genentech/Roche and Regeneron. **LEB** has held a consultancy for AbbVie, AstraZeneca, BMS, CRISPR Therapeutics, Genmab, Janssen, Kite Pharma, Nurix, Roche and has received research funding from AstraZeneca. **MG** has received honoraria from MSH Pharma and has held a consultancy for Janssen and MSH Pharma. **TG** has held a consultancy for AbbVie, Adaptive Biotechnologies, AstraZeneca, Genentech, Genmab and TG Therapeutics. **She** is a member of an advisory board/steering committee for AbbVie, Bristol Myers Squibb, BeiGene, Genmab, Gilead Sciences, Eli Lilly and has participated in a speakers' bureau for AbbVie, Adaptive Biotechnologies, ADC Therapeutics, AstraZeneca, BeiGene, Genentech, Inc., Genmab, Gilead Sciences, Lilly and TG Therapeutics. **PJ** is employed by Genentech with stocks or other ownership interests in Genentech. **JMLB** is employed by Genentech with stock or other ownership interests in Roche. She has received honoraria from Genentech and has had travel, accommodation or expenses paid for by Genentech. **MW** is employed by Genentech with stock or other ownership interests in Genentech. **RF** is employed by Genentech with stocks or other ownership interests in Genentech/Roche and has had travel, accommodations or expenses paid for by Genentech/Roche. **YM** is employed by Genentech/Roche with stocks or other ownership interests in Genentech/Roche. **TL** is employed and has a leadership role at Genentech with stocks or other ownership interests in Genentech. He has had travel, accommodations or expenses paid for by Genentech **JM** has received honoraria from Curio, OncView, Physicians' Education Resource, Targeted Oncology and has held a consultancy for ADC Therapeutics, Alexion, AstraZeneca, Aurobindo, Bayer, BeiGene, Celgene/BMS, Eli Lilly, Epizyme, Fosunkite, Genentech/Roche, Genmab, Genzyme, Gilead/Kite, Janssen, Karyopharm, Kyowa, MEI, MorphoSys/Incyte, Novartis, Pfizer, Pharmacyclics/AbbVie, TG Therapeutics, Seattle Genetics and Verastem. He has received research funding from Bayer, BeiGene, Celgene, Genentech, Gilead/Kite, Janssen, Merck, Millennium, Novartis, Pharmacyclics, Portola and Seattle Genetics. **IF** has held a consultancy for AbbVie, BeiGene, Genentech, Genmab, KITE, Vincerx and has received research funding from AbbVie, AstraZeneca, BeiGene, Bristol Myers Squibb, Celgene, City of Hope National Medical Center, Epizyme, Fate Therapeutics, Genentech, Gilead Sciences, IGM Biosciences, InnoCare Pharma, Incyte, Janssen, Kite Pharma, Loxo, Marker Therapeutics, Merck, MorphoSys, Myeloid Therapeutics, Novartis, Nurix, Pfizer, Roche, Seattle Genetics, TG Therapeutics, Vincerx Pharma and 2seventy Bio.