MCL-1493

Fixed-duration outpatient subcutaneous mosunetuzumab + polatuzumab vedotin shows robust efficacy in a Phase II study of relapsed/refractory post-BTKi mantle cell lymphoma

Michael L. Wang,[1]* Manali Kamdar,[2] Sarit Assouline,[3] Nilanjan Ghosh,[4] Seema Naik,[5] Shazia K. Nakhoda,[6] Julio Chavez,[7] Thomas A. Ollila,[8] Daniel Hodson,[9] Dipenkumar Modi,[10] Mariana Bastos-Oreiro,[11] Wahib Ead,[12] Iris To,[12] Song Pham,[13] Jue Wang,[12] Hao Wu,[12] Sneha Makadia,[12] Connie Lee Batlevi,[12] Michael C. Wei,[12] L. Elizabeth Budde[14]

***e-mail: miwang@mdanderson.org**

[1]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Hematologic Malignancies and Stem Cell Transplantation, University of Colorado Cancer Center, Denver, CO, USA; [3]Jewish General Hospital, McGill University, Montreal, Quebec, Canada; [4]Levine Cancer Institute/Atrium Health, Charlotte, NC, USA; [5]Penn State University College of Medicine, Hershey, PA, USA; [6]Fox Chase Cancer Center, Philadelphia, PA, USA; [7]Moffitt Cancer Center, Tampa, FL, USA; [8]Cancer Institute, Rhode Island Hospital, Providence, RI, USA; [9]Cambridge University Hospitals NHS Foundation Trust - Addenbrookes Hospital, Cambridge, UK; [10]Karmanos Cancer Institute, Detroit, MI, USA; [11]Hospital General Universitario Gregorio Marañón, Madrid, Spain; [12]Genentech, Inc., South San Francisco, CA, USA; [13]Hoffmann-La Roche Ltd, Mississauga, Ontario, Canada; [14]City of Hope National Medical Center, Duarte, CA, USA

Summary

Fixed-duration subcutaneous mosunetuzumab plus polatuzumab vedotin (Mosun-Pola) demonstrates promising efficacy in patients with relapsed/refractory (R/R) mantle cell lymphoma (MCL) who had previously received a Bruton tyrosine kinase inhibitor (BTKi)

High overall response rate (ORR) and complete response (CR) were observed, and were consistent across high-risk subgroups; responses to Mosun-Pola were durable

Mosun-Pola is an effective off-the-shelf regimen for patients with post-BTKi R/R MCL

Mosun-Pola is a well-tolerated outpatient regimen and B-cell recovery occurs after completion of fixed-duration treatment

Previously presented at the 18th International Conference on Malignant Lymphoma (ICML) | June 17–21, 2025

Background

- Patients with R/R MCL who progress after BTKi therapy have suboptimal outcomes.[1]
- There is a high unmet need for safe and effective off-the-shelf treatments for patients with R/R MCL.[1,2]
- Mosun-Pola has demonstrated promising efficacy and manageable safety in patients with B-cell lymphoma.[3,4]
- We report updated data from the Phase II expansion cohort (NCT03671018) in patients with R/R MCL who had received prior BTKi therapy.

Open-label, multicenter, Phase Ib dose-escalation and Phase II single-arm dose-expansion study

- Data reported herein are from the Phase II dose-expansion part of the study.
- Mosun was administered subcutaneously (SC) in 21-day cycles with step-up dosing in Cycle (C)1 for a total of 17 cycles (**Figure 1**).
- Pola 1.8mg/kg was administered intravenously (IV) on Day (D)1 of C1–6 (**Figure 1**).

Figure 1. Study overview.

Key inclusion criteria

- R/R MCL
- ECOG PS 0–2
- ≥2 prior therapies (including an anti-CD20 antibody, anthracycline or bendamustine therapy, and BTKi)

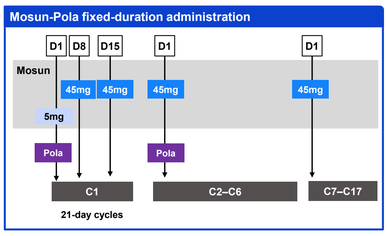
CRS mitigation

- Mosunetuzumab SC step-up dosing in C1
- Corticosteroid premedication was given prior to each dose in C1*
- Hospitalization was not mandatory

Endpoints

- Primary: best ORR by IRC[5]
- Secondary: best ORR by INV, CR rate, DOR, DOCR, PFS, OS and safety

Mosun-Pola fixed-duration administration



*From C2 and beyond, premedication was optional for patients who did not experience CRS in the previous cycle; corticosteroid premedication consisted of 20mg of dexamethasone or 80mg of methylprednisolone, either IV or orally.
ECOG PS, Eastern Cooperative Oncology Group performance status; CRS, cytokine release syndrome; DOCR, duration of complete response; DOR, duration of response; IRC, independent review committee; INV, investigator; OS, overall survival; PFS, progression-free survival.

At data cut-off (November 8, 2024), 42 patients had received Mosun-Pola

- Median age was 68 (range: 44–82) years, 91% had Ann Arbor stage III/IV, and 48% had a simplified MCL International Prognostic Index (sMIPI) score of ≥6 (**Table 1**).
- Overall, 71% of patients had ≥3 high-risk features, including *TP53* mutation, Ki-67 ≥50% and blastoid/pleomorphic morphology.

Table 1. Baseline characteristics.

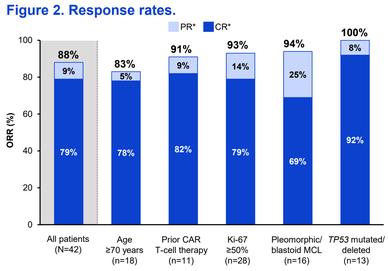
n (%), unless stated	N=42
Median age, years (range)	68 (44–82)
Male	31 (74)
ECOG PS score	
0–1	38 (90)
2	4 (10)
Ann Arbor stage III–IV	38 (91)
Number of prior lines of therapy	
Median, n (range)	3 (2–9)
2	13 (31)
3	14 (33)
≥4	15 (36)
Prior therapy	
BTKi	42 (100)
CAR T cell	11 (26)
ASCT	13 (31)
Refractory to last prior therapy	39 (93)
TP53 aberration*	
Mutation or deletion	13/33† (39)
Wild type	20/33† (61)
Blastoid/pleomorphic	16 (38)
Bone marrow involvement	18 (43)
Ki-67	
≥30%	32 (76)
≥50%	28 (67)
sMIPI score ≥6	20 (48)
Bulky disease (>7.5cm)	7 (17)
Extranodal involvement	34 (81)
Elevated LDH‡	15 (36)

*Reported by clinicians; †Of patients with known TP53 status, with an unknown mutation status in n=9/42 (21%) of patients; ‡Defined as >1x ULN.
ASCT, autologous stem cell transplant; CAR, chimeric antigen receptor; LDH, lactate dehydrogenase; ULN, upper limit of normal.

Fixed-duration Mosun-Pola demonstrated early and durable responses

- ORR and CR rate were 88% (95% confidence interval [CI]: 74–96) and 79% (95% CI: 63–90), respectively (**Figure 2**)
  - Efficacy was consistent across high-risk subgroups.

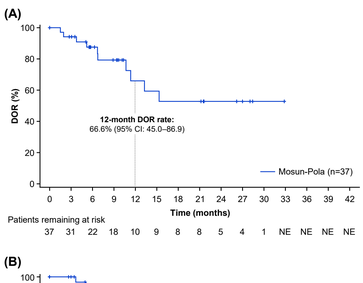
Figure 2. Response rates.

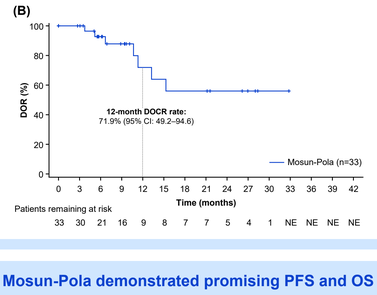


*IRC-assessed.
PR, partial response

- Median time to first response was 2.7 months (range: 1–7) and median time to CR was 2.8 months (range: 2–18).
- Median DOR and DOCR were both not reached (95% CI: 11.4–not evaluable [NE]; median follow-up: 15.9 months [95% CI: 13.6–29.0]; **Figure 3**).

Figure 3. (A) DOR and (B) DOCR.

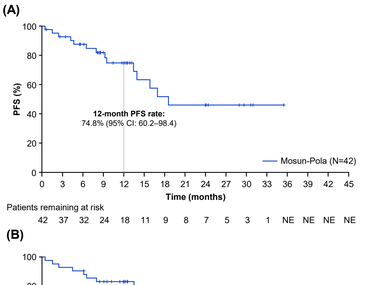


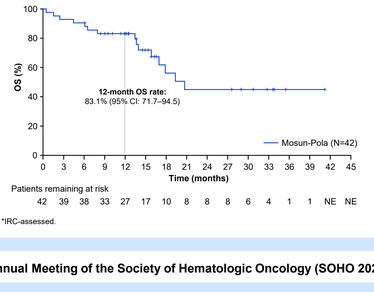


Mosun-Pola demonstrated promising PFS and OS

- Median PFS was 18.6 months (95% CI: 13.9–NE; **Figure 4A**).
- Median OS was 20.7 months (95% CI: 17.0–NE; **Figure 4B**).

Figure 4. (A) PFS and (B) OS.





*IRC-assessed.

Mosun-Pola showed a manageable safety profile

- The median number of cycles was 15 (range: 1–17) for Mosun and 6 (range: 1–6) for Pola.
- A total of five Grade 5 adverse events (AEs) occurred.
- One patient had Grade 2 immune effector-cell associated neurotoxicity syndrome (ICANS; **Table 2**).
- The most common treatment-related AEs were injection site reaction (57%), fatigue (50%), CRS (43%), and neutrophil count decreased (33%).

Table 2. Safety summary.

n (%)	N=42
AE	42 (100)
Treatment-related	39 (93)
Grade 3–4 AE	29 (69)
Treatment-related	25 (60)
Serious AE	26 (62)
Treatment-related	17 (41)
Grade 5 (fatal) AE	5 (12)*
Treatment-related	1 (2)†
AE leading to treatment discontinuation	10 (24)‡
Treatment-related	5 (12)
AE of special interest	
Injection site reaction	
Grade 1	22 (52)
Grade 2	2 (5)
Peripheral neuropathy	
Grade 1	12 (29)
Grade 2	5 (12)
ICANS§	
Grade 2	1 (2)
Infections	30 (71)
Grade 3–4	6 (14)
Grade 5	5 (12)
Tumor flare	
Grade 1	2 (5)
Grade 2	3 (7)
Neutropenia/neutrophil count decreased	
Any grade	19 (45)
Grade 3–4	17 (41)
Febrile neutropenia	
Grade 3	2 (5)

*COVID-19 pneumonia (n=3), and one each of pneumonia and West Nile virus encephalitis. †COVID-19 pneumonia (n=1). ‡Not treatment-related: COVID-19 pneumonia (n=2, Grade 5), and one each of pneumonia (Grade 3), vascular dementia (Grade 3), colorectal cancer (Grade 3, Mosun-discontinuation) and cough (Grade 2, Mosun-discontinuation); Mosun-Pola-related: one each of uveitis (Grade 3), pneumonitis (Grade 3, Pola-discontinuation), and upper respiratory tract infection (Grade 2, Mosun-discontinuation); Mosun-related: *Clostridioides difficile* colitis (n=1, Grade 3, Mosun-discontinuation); Pola-related: peripheral neuropathy (n=2, Grade 2, Pola-discontinuation). §Preferred term. Grade 2 ICANS event (confusion) occurred 3 days after C2D1, with no concurrent CRS. The event resolved with dexamethasone. COVID-19, coronavirus disease 19.

All CRS events were low grade and resolved within C1

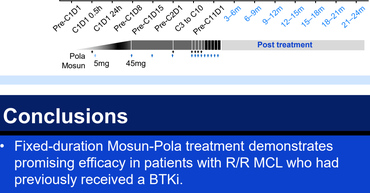
- CRS occurred in 18 patients, and all events were low grade (Grade 1–2; **Table 3**).
- All CRS events occurred and resolved within C1 (**Figure 6**).

Table 3. CRS summary.

CRS by ASTCT criteria[6]	N=42
Any grade, n (%)	18 (43)
Grade 1	12 (29)
Grade 2	6 (14)
Grade ≥3	0
Median time to first CRS onset relative to last dose, days (range)	2 (1–5)
Median CRS duration, days (range)	3 (1–9)
CRS management, n (%)	
Corticosteroids	6 (14)
Tocilizumab	6 (14)
Low-flow oxygen	4 (10)
Fluids	3 (7)
ICU	1 (2)

ASTCT, American Society for Transplantation and Cellular Therapy; ICU, intensive care unit.

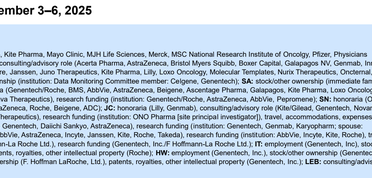
Figure 6. CRS by cycle and grade.



B-cell depletion was rapid

- B-cell depletion occurred rapidly, and recovery was observed following Mosun-Pola treatment (**Figure 7**).

Figure 7. B-cell depletion and recovery



Conclusions

- Fixed-duration Mosun-Pola treatment demonstrates promising efficacy in patients with R/R MCL who had previously received a BTKi.
- Mosun-Pola is a well-tolerated outpatient regimen.
- B-cell recovery occurred following fixed-duration treatment.
- Mosun-Pola is an effective off-the-shelf regimen for patients with post-BTKi R/R MCL.

Presented at the 13th Annual Meeting of the Society of Hematologic Oncology (SOHO 2025) | September 3–6, 2025

References

1. Martin P, et al. *Blood* 2016;127:1559–63
2. Jain P & Wang M. *Blood* 2025;145:683–95
3. Budde LE, et al. *Nat Med* 2024;30:229–39
4. Wang ML, et al. *Blood* 2023;142:734
5. Cheson BD, et al. *J Clin Oncol* 2014;32:3059–68
6. Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25:625–38.

Acknowledgments

This study was sponsored by F. Hoffmann-La Roche Ltd. The authors thank the patients and their families, the study investigators, and the study coordinators and nurses. Third-party medical writing assistance, under the direction of all authors, was provided by Deirdre Kelly, PhD, of Ashfield MedComms, an Inizio company, and was funded by F. Hoffmann-La Roche Ltd.

Disclosures

MLW: honoraria (AstraZeneca, BeiGene, Binaytara Foundation, Bristol Myers Squibb, CAHON, Editorial Medica AWWE SA, East Virtinia Medical School, Instituto Scientifico Romagnolo, Janssen, Kite Pharma, Mayo Clinic, MJH Life Sciences, Merck, MSC National Research Institute of Oncolgy, Pfizer, Physicians Education Resources (PER), Plexus Communications, PromCon S.R.E., Research to Practice, Studio ER Congressi, South African Clinical Hematology Society, Medscape/WebMD, V.Ihemonc), consulting/advisory role (Acerta Pharma, AstraZeneca, Bristol Myers Squibb, Boxer Capital, Galapagos NV, Genmab, InnoCare, Janssen, Kite Pharma, Lilly, Merck, PER, Pfizer, Oncternal), research funding (Abbvie, Acerta Pharma, AstraZeneca, Bantam Pharma, BeiGene, Biolnvent, Celgene, Genmab, Genentech, Innocare, Janssen, Juno Therapeutics, Kite Pharma, Lilly, Loxo Oncology, Molecular Templates, Nurix Therapeutics, Oncternal, Pharmacyclics, Velosbio, Vincerx); **MK:** consulting/advisory role (institution: AbbVie, AstraZeneca, Bristol-Myers Squibb, Beigene, Genentech), research funding (institution: Novartis), other relationship (institution: Data Monitoring Committee member: Celgene, Genentech); **SA:** stock/other ownership (immediate family member; Kura), honoraria (Novartis, Beigene, Roche, Abbvie), consulting/advisory role (Novartis, Beigene, Roche, Abbvie), speaker's bureau (Novartis), research funding (Novartis); **NG:** honoraria (Genentech/Roche, BMS, AbbVie, AstraZeneca, Beigene, Ascentage Pharma, Galapagos, Kite Pharma, Loxo Oncology, Ipsen, Janssen, Lava Therapeutics), consulting/advisory role (Genentech/Roche, BMS, AbbVie, AstraZeneca, Beigene, Ascentage Pharma, Galapagos, Kite Pharma, Loxo Oncology, Ipsen, Janssen, Lava Therapeutics), research funding (institution: Genentech/Roche, AstraZeneca, AbbVie, Peprotech); **SN:** honoraria (OncLive), consulting/advisory role (Janssen Biotech); **SKN:** honoraria (BTG/SERB, Astra Zeneca, Beigene), consulting/advisory role (BTG/SERB, Astra Zeneca, Beigene), research funding (institution: AstraZeneca, Roche, Beigene, ADC); **JC:** honoraria (Lilly, Genmab), consulting/advisory role (Kite/Gilead, Genentech, Novartis, Allogene, Cripsr, Autolus, BMS, AstraZeneca), research funding (Merck, Kite, Genmab), travel, accommodations, expenses (Lilly); **TAO:** honoraria (ONO Pharma), consulting/advisory role (ADC Therapeutics), research funding (institution: ONO Pharma [site principal investigator]), travel, accommodations, expenses (Genentech); **DH:** honoraria (AstraZeneca), consulting/advisory role (AstraZeneca), research funding (AstraZeneca, GSK); **DM:** consulting/advisory role (self: ADC therapeutics, Genmab; spouse: Genentech, Daiichi Sankyo, AstraZeneca), research funding (institution: Genentech, Genmab, Karyopharm; spouse: AstraZeneca); **MB-O:** honoraria (AbbVie, AstraZeneca, Incyte, Janssen, Kite, Roche), consulting/advisory role (AbbVie, AstraZeneca, Incyte, Janssen, Kite, Novartis, Roche), speaker's bureau (AbbVie, AstraZeneca, Incyte, Janssen, Kite, Roche, Takeda), research funding (institution: AbbVie, Incyte, Kite, Roche), travel, accommodations, expenses (Hospital General Universitario Gregorio Marañón); **WE:** employment (Genentech, Inc./F. Hoffmann-La Roche Ltd.), stock/other ownership (Genentech, Inc./F. Hoffmann-La Roche Ltd.), research funding (Genentech, Inc./F. Hoffmann-La Roche Ltd.); **IT:** employment (Genentech, Inc), stock/other ownership (Genentech, Inc), patents, royalties, other intellectual property (Genentech, Inc.); **SP:** employment (Roche Canada); **JW:** employment (Genentech), stock/other ownership (Roche), patents, royalties, other intellectual property (Roche); **HW:** employment (Genentech, Inc.), stock/other ownership (Genentech, Inc.); **SM:** employment (Genentech), stock/other ownership (Genentech); **CLB:** employment (Roche/Genentech), stock/other ownership (Roche); **MCW:** employment (Genentech, Inc.), stock/other ownership (F. Hoffman LaRoche, Ltd.), patents, royalties, other intellectual property (Genentech, Inc.); **LEB:** consulting/advisory role (Kite Pharma, BMS, AstraZeneca, Roche, Crispr Therapeutics, AbbVie, Jessen, Nurix, Genmab), research funding (AstraZeneca).