229

Safety and efficacy of mosunetuzumab subcutaneous maintenance following mosunetuzumab plus lenalidomide induction therapy in previously untreated follicular lymphoma

Toby A. Eyre,[1*] Raul Cordoba,[2] Krish Patel,[3] Ángel Serna,[4] Roch Houot,[5] Mark Bishton,[6] Hui-Lai Zhang,[7] Liqun Zou,[8] Laura Galvez-Carvajal,[9] Wendy Osborne,[10] Emmanuel Bachy,[11] Catherine Thieblemont,[12] Andrea Knapp,[13] Jason Sit,[14] Naomi Chang,[15] Vivian Chen,[14] Elicia Penuel,[14] Michael C. Wei,[14] Enkhtsetseg Purev,[14] Franck Morschhauser[16]

***Presenting author e-mail: Toby.Eyre@ouh.nhs.uk**

[1]Oxford University Hospital, Oxford, UK; [2]Fundación Jiménez Díaz University Hospital, Madrid, Spain; [3]Swedish Cancer Institute, Seattle, WA, USA; [4]Servei d'Hematologia, Vall d'Hebron Hospital Universitari, Experimental Hematology, Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [5]CHU de Rennes, Université de Rennes, Rennes, France; [6]Nottingham University Hospitals NHS Trust and University of Nottingham, Nottingham, UK; [7]Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; [8]West China Hospital, Sichuan University, Chengdu, China; [9]Regional and Virgen de la Victoria University Hospitals, Málaga, Spain; [10]Freeman Hospital Newcastle, Newcastle University, Newcastle upon Tyne, UK; [11]Centre Hospitalier Lyon-Sud, Lyon, France; [12]Hôpital Saint-Louis, Paris, France; [13]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [14]Genentech, Inc., South San Francisco, CA, USA; [15]Hoffmann-La Roche Ltd, Mississauga, Canada; [16]CHU de Lille, Université de Lille, Lille, France.

Summary

CO41942 is a Phase Ib/II study (NCT04246086) assessing mosunetuzumab plus lenalidomide (Mosun+Len) induction and subsequent subcutaneous (SC) mosunetuzumab maintenance in patients with high tumor burden previously untreated follicular lymphoma (FL)

As of September 23, 2024, a total of 40 patients received Mosun+Len induction therapy, and 16 patients proceeded to optional mosunetuzumab maintenance

Findings highlight the promise of this chemotherapy-free regimen for the treatment of 1L FL

Further follow-up is needed to confirm these results

Mosun+Len induction with mosunetuzumab maintenance showed durable responses and manageable safety, with low rates of AEs during maintenance in patients with high tumor burden first-line (1L) FL

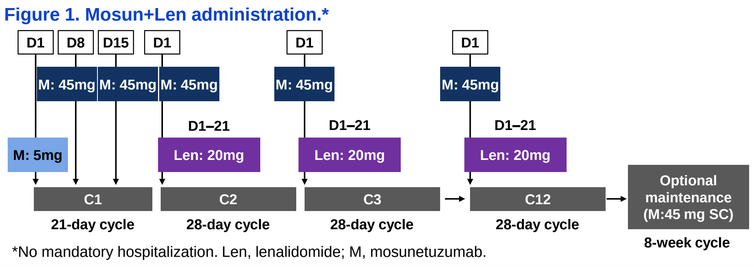
Background

- FL is the most common subtype of indolent non-Hodgkin lymphoma (NHL) and accounts for about 22% of all newly diagnosed NHL.[1]
- Therapies for FL are not yet curative and despite encouraging efficacy most patients will eventually relapse,[2,3] therefore novel therapies with increased anti-tumor activity that prolong remission in patients with 1L FL are needed. Additionally, chemotherapy-containing regimens may have substantial toxicities,[4–6] underlining the need for new therapies with improved safety.
- Mosunetuzumab, a CD20xCD3 T-cell engaging bispecific antibody, is conditionally approved as a monotherapy in the United States, European Union, and other countries for the treatment of adults with relapsed/refractory FL who have received ≥2 prior systemic therapies.[7,8]
- In the Phase Ib/II CO41942 study (NCT04246086), Mosun+Len induction therapy showed promising results in patients with 1L high tumor burden FL.[9]
- We present updated data for Mosun+Len induction and initial efficacy and safety of subsequent optional mosunetuzumab SC maintenance.

A multicenter, open-label Phase Ib/II study (NCT04246086) was conducted to assess Mosun+Len induction with mosunetuzumab SC maintenance in patients with FL

- Patients with newly diagnosed CD20+ FL Grade 1–3a who required systemic therapy per Groupe d'Etude des Lymphomes Folliculaires (GELF) criteria and had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0–2 were included.
- Patients received 12 cycles of Mosun+Len (Cycle [C]1: 21 days; C2–12: 28 days; **Figure 1**).
  - mosunetuzumab SC: C1 step-up dosing for cytokine release syndrome (CRS) mitigation (Day [D]1: 5mg; D8 and D15: 45mg) and C2–12 D1, 45mg.
  - lenalidomide [oral]: D1–21 of C2–12, 20mg.
- Responders could receive optional mosunetuzumab SC (45mg) monotherapy maintenance every 8 weeks for 9 cycles (C13–21; **Figure 1**).
- Anti-infective prophylaxis followed institutional standards.
- The primary objective of the 1L FL high tumor-burden cohort was to evaluate the efficacy of Mosun+Len induction followed by mosunetuzumab SC maintenance.
  - Response was determined through use of computed tomography (CT) or positron emission tomography (PET)-CT scans, using the Lugano 2014 criteria.

Figure 1. Mosun+Len administration.*



*No mandatory hospitalization. Len, lenalidomide; M, mosunetuzumab.

As of September 23, 2024, 40 patients received Mosun+Len induction and 16 patients opted to proceed to mosunetuzumab maintenance

- Median age was 62 years, 55% were male and 45% had a Follicular Lymphoma International Prognostic Index (FLIPI) score of 3/4 (**Table 1 and Table 2**).
  - Median time from initial diagnosis to first study treatment was 59 days (range: 15–3386).
- Median follow-up was 17.5 months (range: 6–23).

Table 1. Patient demographics.

	1L FL cohort (N=40)
Median age, years (range)	62 (28–83)
Male, n (%)	22 (55.0)
Race	
White	16 (40.0)
Asian	3 (7.5)
Black	0
Unknown*	21 (52.5)
Ethnicity	
Not Hispanic or Latino	19 (47.5)
Not stated*	20 (50.0)
Unknown	1 (2.5)
ECOG PS	
0	24 (60.0)
1	16 (40.0)

Table 2. Disease characteristics.

	1L FL cohort (N=40)
Ann Arbor Stage at study entry	
II	5 (12.5)
III–IV	35 (87.5)
FLIPI Score at study entry	
0–1	7 (17.5)
2	15 (37.5)
3	11 (27.5)
4	7 (17.5)
FL grade	
1–2	31 (77.5)
3a	7 (17.5)
1–3a	2 (5.0)
Bulky disease (>7cm)†	
Yes	19 (47.5)
No	21 (52.5)

*Country restricted inquiry. †Clinical cut-off date for bulky disease was July 20, 2023.

Mosun+Len followed by mosunetuzumab SC maintenance led to high response rates and durable responses

- The overall response rate (intention-to-treat population, N=40) was 90.0% and complete response (CR; as best response) rate was 87.5%; four patients had stable disease (SD) or progressive disease (PD).
  - Three patients with SD/PD had transformed FL (tFL) in C1.
- After a median follow-up of 18 months (range: 6–23), median duration of response (DOR), duration of CR (DOCR), progression-free survival (PFS) and overall survival (OS) were not reached.
- The 12-month event-free rates for DOR and DOCR were 94.0% (95% confidence interval [CI]: 86.0–100.0), and 94.1% (95% CI: 86.2–100.0), respectively (**Figure 2**).
- The 12-month event-free rates for PFS and OS were 86.9% (95% CI: 76.1–97.6), and 97.4% (95% CI: 92.5–100.0), respectively (**Figure 3**).
- Sustained responses were observed in patients who received maintenance (no patients had PD post-induction), and in patients who were eligible but did not receive maintenance and were observed post-induction (one patient had PD post-induction).

Figure 2. DOR (A) and DOCR (B).

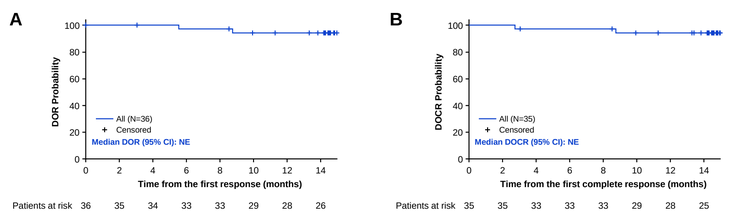
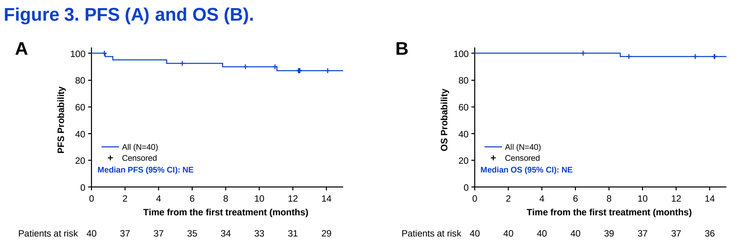


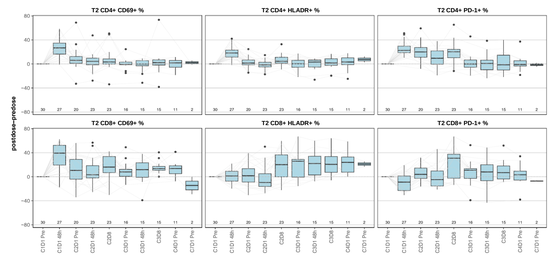
Figure 3. PFS (A) and OS (B).



Distinct activation profiles emerge with Mosun+Len induction and mosunetuzumab maintenance in peripheral CD4+ and CD8+ T cells and natural killer (NK) cells

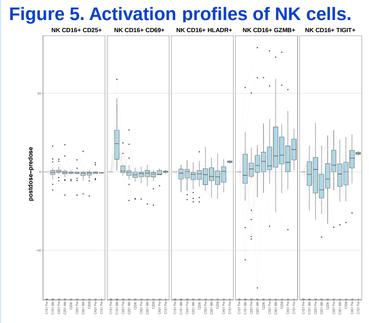
- Levels of the early activation marker CD69 increase 48 hours after initial SC dose of mosunetuzumab in both CD4+ and CD8+ T cells but return to and are maintained at near pre-dose levels with subsequent dosing (**Figure 4**).
- Levels of the activation marker human leukocyte antigen – DR isotype (HLA-DR) increase early in CD4+ T cells; in CD8+ T cells HLA-DR expression is elevated and sustained after 1 week of lenalidomide (**Figure 4**).
- PD1 levels increase on CD4+ T cells consistent with activation and levels are maintained throughout the first cycle but are reduced substantially after the first week of lenalidomide coadministration. In contrast, PD1 levels increase on CD8+ cells after a week of lenalidomide but subsequently decline with continued exposure (**Figure 4**).

Figure 4. Activation profiles of peripheral CD4+ and CD8+ T cells.



- Early activation of CD69+ expressing NK is limited to first dose of mosunetuzumab (**Figure 5**).
- Sustained expansion of granzyme B (GZMB) expressing NK cells after lenalidomide administration suggests functional NK activity (**Figure 5**).
- Despite sustained GZMB that could lead to exhaustion, higher levels of T cell immunoglobulin and ITIM domain (TIGIT) are not consistently observed (**Figure 5**).

Figure 5. Activation profiles of NK cells.



Mosun+Len induction with mosunetuzumab maintenance had a manageable safety profile, with low rates of serious AEs (SAEs) and Grade 3/4 AEs during maintenance

Safety during Mosun+Len induction

- SAEs were reported in 17 (42.5%) patients, while Grade 3/4 AEs were reported in 28 (70.0%) patients (**Table 3**).
- The most common AEs (**Table 4**) were infections (28 [70.0%] patients, pneumonia [27.5%] and coronavirus [COVID-19; 22.5%] being the most common), injection site reactions (ISRs; 27 [67.5%] patients; all Grade 1/2), neutropenia/neutrophil count decreased (25 [62.5%] patients; Grade 3/4: 20 [50.0%] patients), and CRS (21 [52.5%] patients; all Grade 1/2).
  - Grade 3/4 infections occurred in five (12.5%) patients.
  - CRS occurred mainly during C1 (three patients had CRS events in C2) and all CRS events resolved.
  - A total of 21 patients received granulocyte colony-stimulating factor prophylaxis.
- No patients experienced Grade 5 AEs, febrile neutropenia, or immune effector cell-associated neurotoxicity syndrome (ICANS).

Safety during mosunetuzumab maintenance

- Fewer SAEs (n=2, 12.5%) and Grade 3/4 AEs (n=4, 25.0%) were reported during the maintenance phase versus the induction phase (**Table 3**).
- ISRs occurred in two (12.5%) patients (all Grade 1/2) and neutropenia/neutrophil count decreased in four (25.0%) patients (Grade 3/4: three [18.8%] patients; **Table 4**).
- One patient discontinued maintenance due to an AE.
- No CRS or Grade 3/4 infections occurred.
- No patients experienced Grade 5 AEs, febrile neutropenia, or ICANS.

Table 3. Summary of AEs.*

	Induction phase (n=40)	Maintenance phase (n=16)
Patients with ≥1 AE	40 (100)	11 (68.8)
Related to mosunetuzumab	39 (97.5)	9 (56.3)
Related to lenalidomide	36 (90.0)	NA
Serious AEs	17 (42.5)	2 (12.5)
Related to mosunetuzumab	9 (22.0)	1 (6.3)
Related to lenalidomide	3 (7.5)	N/A
Grade 3/4 AEs	28 (70.0)	4 (25.0)
Grade 5 AEs	0	0
AE leading to treatment discontinuation	6 (15.0)	1 (6.3)
Withdrawal from mosunetuzumab	5 (12.5)	1 (6.3)
Withdrawal from lenalidomide	3 (7.5)	N/A
AE leading to lenalidomide dose modification	13 (32.5)	N/A
AE leading to lenalidomide dose interruption	24 (60.0)	N/A
AE leading to mosunetuzumab modification/interruption	18 (45.0)	2 (12.5)

*Reported as number of patients (%). NA, not applicable.

Table 4. Most common all grade AEs (in ≥20% of patients).

	Induction phase (n=40)	Maintenance phase (n=16)
ISR	27 (67.5)	2 (12.5)
Neutropenia/neutrophil count decreased	25 (62.5)	4 (25.0)
CRS	21 (52.5)	0
Diarrhea	13 (32.5)	1 (6.3)
Dry skin	13 (32.5)	0
Rash	13 (32.5)	0
Asthenia	12 (30.0)	0
Pneumonia	11 (27.5)	1 (6.3)
Constipation	11 (27.5)	0
Headache	10 (25.0)	0
COVID-19	9 (22.5)	0

Conclusions

- Mosun+Len induction with mosunetuzumab maintenance showed durable responses and manageable safety, with low rates of AEs during maintenance in patients with high tumor burden 1L FL.
- These results highlight the promise of this chemotherapy-free regimen, although further follow-up is needed to confirm these findings.
  - The Phase III MorningLyte trial (EUCT: 2023-505436-35-00) is studying this regimen further.

Presented at the 2025 International Conference on Malignant Lymphoma (ICML) Annual Meeting | June 17–21, 2025

References

1. Zelenetz AD, et al. J Natl Compr Canc Netw 2014;12:916–46.
2. Casulo C, et al. J Clin Oncol 2015;33:2516–22.
3. Casulo C, et al. Blood 2022;139:1684–93.
4. Rummel MJ, et al. Lancet 2013;381:1203–10.
5. Flinn IW, et al. Blood 2014;123:2944–52.
6. Morschhauser F, et al. N Engl J Med 2018;379:934–47.
7. Lunsumio® SmPC. Available at: https://www.ema.europa.eu [Accessed May 2025].
8. LUNSUMIO® USPI. 2022. Available at: https://www.accessdata.fda.gov [Accessed May 2025].
9. Morschhauser F, et al. Blood 2023;142(Suppl 1):605.

Acknowledgments

NCT04246086 was sponsored by F. Hoffmann-La Roche Ltd. Third-party medical writing assistance, under the direction of all authors, was provided by Rachel Dobb, PhD, of Ashfield Medcomms, an Inizio company, and was funded by F. Hoffmann-La Roche Ltd.

Disclosures

TAE: Honoraria (F. Hoffmann-La Roche Ltd, Gilead, KITE, Janssen, AbbVie, AstraZeneca, Loxo Oncology, BeiGene, Incyte, Autolus, Galapagos, BMS), Consulting/advisory role (F. Hoffmann-La Roche Ltd, Gilead, KITE, Janssen, AbbVie, AstraZeneca, Loxo Oncology, BeiGene, Incyte, Autolus, Galapagos, BMS), speaker's bureau (F. Hoffmann-La Roche Ltd, Gilead, KITE, Janssen, AbbVie, AstraZeneca, Loxo Oncology, BeiGene, Incyte, Autolus, Galapagos, BMS), research funding (AstraZeneca, BeiGene) and travel, accommodation, expenses (F. Hoffmann-La Roche Ltd); **RC**: Consulting/advisory role (F. Hoffmann-La Roche Ltd, AbbVie, Johnson & Johnson, Lilly, BeiGene, AstraZeneca, Gilead, BMS, Takeda, Kyowa-Kirin, Incyte, Regeneron), speaker's bureau (F. Hoffmann-La Roche Ltd, AbbVie, Johnson & Johnson, Lilly, BeiGene, AstraZeneca, Gilead, BMS, Takeda, Kyowa-Kirin, Incyte, Regeneron), expert testimony (F. Hoffmann-La Roche Ltd, AbbVie, Johnson & Johnson, Lilly, BeiGene, AstraZeneca, Gilead, BMS, Takeda, Kyowa-Kirin, Incyte, Regeneron) and travel, accommodation, expenses (F. Hoffmann-La Roche Ltd, AbbVie, Johnson & Johnson, Lilly, BeiGene, AstraZeneca, Gilead, Takeda, Kyowa-Kirin); **KP**: Honoraria (AstraZeneca, BMS, Kite Pharma), Consulting/advisory role (AbbVie, Adaptive, ADC Therapeutics, AstraZeneca, BeiGene, BMS, Caribou, Genentech, Inc., Janssen, Kite, Lilly, Merck, Nurix, Pfizer, Sana), and research funding (AbbVie, Adaptive, AstraZeneca, BMS, Caribou, Century Therapeutics, CRISPR Therapeutics, Fate Therapeutics, Genentech/Roche, Janssen/Pharmacyclics, Kite, Lilly/Loxo, Merck, Nurix, Pfizer, Sana, Xencor); **AS**: Honoraria (AstraZeneca, AbbVie, F. Hoffmann-La Roche Ltd, Incyte, Lilly, Behring, Johnson & Johnson), and travel, accommodation, expenses (AstraZeneca, AbbVie, Johnson & Johnson, F. Hoffmann-La Roche Ltd); **RH**: Honoraria (Kite/Gilead, Novartis, BMS/Celgene, Incyte, Janssen, MSD, Takeda, Amgen, AbbVie, Roche), Consulting/advisory role (Kite/Gilead, Novartis, BMS/Celgene, Tessa Therapeutics, AbbVie, F. Hoffmann-La Roche Ltd), and travel, accommodation, expenses (Novartis); **MB**: Honoraria (Roche Pharmaceuticals, Gilead, Janssen, AbbVie, Eli Lilly, Incyte, Recordati), Consulting/advisory role (Roche Pharmaceuticals, AbbVie, Incyte, AstraZeneca), and research funding (Roche Pharmaceuticals); **H-LZ**: No disclosures; **LZ**: No disclosures; **LG-C**: No disclosures; **WO**: Honoraria (F. Hoffmann-La Roche Ltd, Takeda, Kite Gilead, AstraZeneca, Kyowa Kirin, Incyte, Janssen, BMS, AbbVie), Consulting/advisory role (F. Hoffmann-La Roche Ltd, Takeda, Kite Gilead, AstraZeneca, Kyowa Kirin, Incyte, Janssen, BMS, AbbVie), speaker's bureau (F. Hoffmann-La Roche Ltd, Takeda, Kite Gilead, AstraZeneca, Kyowa Kirin, Incyte, Janssen, BMS, AbbVie), and travel, accommodation, expenses (AbbVie, F. Hoffmann-La Roche Ltd, Takeda, Kite Gilead, AstraZeneca, Kyowa Kirin, Incyte, Janssen, BMS); **EB**: Honoraria (F. Hoffmann-La Roche Ltd, Kite/Gilead, Novartis, BMS, Takeda, AbbVie, Miltenyi), Consulting/advisory role (Daiichi Sankyo, AbbVie), research funding (Amgen, BMS), and travel, accommodation, expenses (F. Hoffmann-La Roche Ltd, Kite/Gilead, Novartis, BMS, Takeda, AbbVie, Miltenyi); **CT**: Honoraria (AbbVie, F. Hoffmann-La Roche Ltd, BMS, Novartis, AstraZeneca), Consulting/advisory role (AbbVie, F. Hoffmann-La Roche Ltd, BMS, Novartis, AstraZeneca), and travel, accommodation, expenses (AbbVie, F. Hoffmann-La Roche Ltd, Incyte); **AK**: Employment (F. Hoffmann-La Roche Ltd); **JS**: Employment (Genentech, Inc.) and stock or other ownership (F. Hoffmann-La Roche Ltd); **NC**: Employment (F. Hoffmann-La Roche Ltd) and stock or other ownership (F. Hoffmann-La Roche Ltd); **VC**: Employment (F. Hoffmann-La Roche Ltd, Genentech, Inc.); **EP**: Employment (F. Hoffmann-La Roche Ltd, Genentech, Inc.) and stock or other ownership (F. Hoffmann-La Roche Ltd, Genentech, Inc.), and travel, accommodation, expenses (F. Hoffmann-La Roche Ltd, Genentech, Inc.); **MCW**: Employment (Genentech, Inc.), stock or other ownership (F. Hoffmann-La Roche Ltd), and patents, royalties, other intellectual property (Genentech, Inc.); **EP**: Employment (Genentech, Inc.), stock or other ownership (F. Hoffmann-La Roche Ltd), and travel, accommodation, expenses (Genentech, Inc.); **FM**: Honoraria (Takeda, Kite/Gilead, AstraZeneca), Consulting/advisory role (BMS, AbbVie, F. Hoffmann-La Roche Ltd, Miltenyi, Janssen, Modex therapeutics), and research funding (F. Hoffmann-La Roche Ltd, BMS, Kite/Gilead).

17th ICML International Conference on Malignant Lymphoma Lugano June 13–17 2023

Follicular Lymphoma

https://doi.org/10.1002/hon.70094_229

Poster number

229