Long-term outcomes from the phase II L-MIND study of tafasitamab (MOR208) plus lenalidomide in patients with relapsed or refractory diffuse large B-cell lymphoma

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**Supplementary Material**

**ST1. Refractoriness to last prior line (N=35, FAS)**

| Last prior treatment line | N (%) |
|---------------------------|-------|
| 1                         | 6 (17.1) |
| 2                         | 25 (71.4) |
| 3 or 4                    | 4 (11.4) |

| Last prior treatment regimen – category | N (%) |
|----------------------------------------|-------|
| Chemotherapy-based                     | 34 (97.1)† |
| Platinum-based                         | 18 (51.4)† |
| Non-platinum-based*                    | 16 (45.7)† |
| Chemotherapy-free regimens             | 1 (2.9)† |
| HD-chemo/BEAM/ASCT                    | 2 (5.7)‡ |
| Rituximab-containing                  | 28 (80)‡ |

*Composition: predominantly R-CHOP, cyclophosphamide ± doxorubicin, and R-BEN; †Percentages are also referring to the N=35 patients refractory to their last treatment line; ‡Patients are also represented among categories ‘chemotherapy-based’ and ‘chemotherapy-free regimens’.

BEAM, carmustine, etoposide, cytarabine, melphalan; BEN, bendamustine; HD-chemo, high dose chemotherapy; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone.
ST2. Selected infection- and rash-related adverse events

Changes compared with the primary analysis are indicated by an arrow

| Event                                      | All Grades, n (%) | Grade 1, n (%) | Grade 2, n (%) | Grade 3, n (%) | Grade 4, n (%) | Grade ≥3, n (%) |
|--------------------------------------------|-------------------|---------------|---------------|---------------|---------------|----------------|
| Infective pneumonia*                       |                   |               |               |               |               |                |
| All infective pneumonia                    | 8 (9.9) → 12 (14.8) | 0             | 1 (1.2) → 2 (2.5) | 6 (7.4) → 9 (11.1) | 1 (1.2) | 7 (8.6) → 10 (12.3) |
| Pneumonia                                  | 6 (7.4) → 10 (12.3) | 0             | 1 (1.2) → 2 (2.5) | 5 (6.2) → 8 (9.9) | 0         | 5 (6.2) → 8 (9.9) |
| Bronchopulmonary aspergillosis             | 1 (1.2)           | 0             | 0             | 0             | 1 (1.2) | 1 (1.2) |
| Lung infection                              | 1 (1.2) → 0‡       | 0             | 0             | 1 (1.2) → 0‡   | 0         | 1 (1.2) → 0‡   |
| Sepsis†                                     |                   |               |               |               |               |                |
| All sepsis                                  | 4 (4.9)           | 0             | 0             | 2 (2.5)       | 2 (2.5) | 4 (4.9) |
| Klebsiella sepsis                          | 1 (1.2)           | 0             | 0             | 1 (1.2)       | 0         | 1 (1.2) |
| Neutropenic sepsis                         | 1 (1.2)           | 0             | 0             | 1 (1.2)       | 0         | 1 (1.2) |
| Sepsis                                     | 1 (1.2)           | 0             | 0             | 0             | 1 (1.2) | 1 (1.2) |
| Streptococcal sepsis                       | 1 (1.2)           | 0             | 0             | 0             | 1 (1.2) | 1 (1.2) |
| Urinary tract infection‡                    |                   |               |               |               |               |                |
| All urinary tract infection                 | 14 (17.2) → 17 (21.0) | 2 (2.5) | 7 (8.6) → 9 (11.1) | 3 (3.7) | 1 (1.2) | 4 (4.9) |
| Urinary tract infection                     | 7 (8.6) → 10 (12.3) | 2 (2.5) | 3 (3.7) → 6 (7.4) | 1 (1.2) | 1 (1.2) | 2 (2.5) |
| Escherichia urinary tract infection         | 4 (4.9)           | 0             | 3 (3.7)       | 1 (1.2)       | 0         | 1 (1.2) |
| Bacterial urinary tract infection           | 2 (2.5)           | 0             | 2 (2.5)       | 0             | 0         | 0         |
| Enterococcal urinary tract infection        | 1 (1.2)           | 0             | 0             | 1 (1.2)       | 0         | 1 (1.2) |
| Rash†  | 37 (45.7) → 40 (49.4) | 18 (22.2) → 19 (23.5) | 12 (14.8) → 14 (17.3) | 7 (8.6) | 0 | 7 (8.6) |
|--------|------------------------|------------------------|------------------------|--------|---|--------|
| Pruritus | 8 (9.9) | 4 (4.9) | 3 (3.7) | 1 (1.2) | 0 | 1 (1.2) |
| Rash   | 6 (7.4) → 7 (8.6) | 2 (2.5) | 4 (4.9) → 5 (6.2) | 0 | 0 | 0 |
| Allergic dermatitis | 4 (4.9) | 0 | 1 (1.2) | 3 (3.7) | 0 | 3 (3.7) |
| Maculo-papular rash | 4 (4.9) | 3 (3.7) | 0 | 1 (1.2) | 0 | 1 (1.2) |
| Dry skin | 3 (3.7) | 2 (2.5) | 1 (1.2) | 0 | 0 | 0 |
| Erythema | 3 (3.7) | 3 (3.7) | 0 | 0 | 0 | 0 |
| Dermatitis | 1 (1.2) | 1 (1.2) | 0 | 0 | 0 | 0 |
| Eczema | 1 (1.2) → 2 (2.4) | 1 (1.2) | 0 → 1 (1.2) | 0 | 0 | 0 |
| Papule | 1 (1.2) | 1 (1.2) | 0 | 0 | 0 | 0 |
| Psoriasis | 1 (1.2) | 0 | 0 | 1 (1.2) | 0 | 1 (1.2) |
| Erythematous rash | 1 (1.2) | 0 | 0 | 1 (1.2) | 0 | 1 (1.2) |
| Pruritic rash | 1 (1.2) | 1 (1.2) | 0 | 0 | 0 | 0 |
| Rebound psoriasis | 1 (1.2) | 0 | 1 (1.2) | 0 | 0 | 0 |
| Skin lesion | 1 (1.2) → 2 (2.5) | 0 → 1 (1.2) | 1 (1.2) | 0 | 0 | 0 |
| Toxic skin eruption | 1 (1.2) | 0 | 1 (1.2) | 0 | 0 | 0 |

*Defined by Standard Medical Dictionary for Regulatory Activities query, narrow scope. Neither Pneumocystis jirovecii pneumonia nor Pneumocystis carinii pneumonia prophylaxis was administered; †Defined by customized Medical Dictionary for Regulatory Activities query; ‡At the time of data cut-off, the Preferred Term ‘lung infection’ had been discontinued. This case was re-coded and is now reported under the Preferred Term ‘pneumonia’.
Supplementary Methods

Eligibility criteria

Eligible patients were aged >18 years with histologically-confirmed R/R DLBCL (including transformed indolent lymphoma with a subsequent DLBCL relapse), had received 1–3 prior systemic regimens including ≥1 anti-CD20 therapy, had Eastern Cooperative Oncology Group performance status 0–2, and were not candidates for high-dose chemotherapy and subsequent ASCT.

Tumor assessment

Tumor assessment was based on computerized tomography scans conducted after cycles 2, 4, 6, and 9 and positron emission tomography, which was mandatory at baseline and after cycle 12. Central laboratory assessments were performed on day 1 (±2 days) of cycles 1–24. Adverse events were recorded at each visit.

Sample size determination and statistics

The sample size of 80 patients was determined using an exact binomial test with a two-sided significance level of 5% and a power of 85%, assuming a drop-out rate of 10% and that treatment with tafasitamab plus lenalidomide could increase the objective response rate by 15% vs monotherapy.

Descriptive statistics were used to summarize response rates and safety outcomes. Progression-free survival, overall survival, and duration of response were analyzed using the Kaplan–Meier method, and 95% confidence intervals for the median calculated accordingly. The median follow-up for progression-free survival and overall survival was calculated using the reverse Kaplan–Meier method. Statistical analysis was performed using SAS® Software version 9.4 or above (SAS Institute, Cary, NC).
Supplementary Results

Narratives for patients who received stem-cell transplant (SCT) after tafasitamab (n=2)

One patient who received SCT had diffuse large B-cell lymphoma (DLBCL) from marginal zone lymphoma transformation and had received autologous SCT 4 years prior to enrollment progressed after seven cycles of therapy in L-MIND, received further chemotherapy and allogenic SCT and died 4 months after allogenic SCT.

The other patient progressed after three cycles in L-MIND, received a further two lines of chemotherapy and autologous SCT but died 8 days later.

Narratives for patients who received chimeric antigen receptor T-cell therapy (CAR)-T after tafasitamab (n=2)

One patient who received CAR-T therapy had germinal center B-like DLBCL as a result of follicular lymphoma transformation and prior to L-MIND had experienced 2-year complete responses to R-EPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) and R-ICE (rituximab, ifosfamide, carboplatin, etoposide); she had also declined autologous SCT. She received six cycles of therapy in L-MIND (with a stable disease response) before progression, received further chemotherapy with R-GemOx for four cycles (with a partial response), then received CAR-T with a complete response 1 month after treatment; this patient had remained in complete response for 1 year but died approximately 2-years post CAR-T treatment due to acute myeloid leukemia.

The other patient had received autologous SCT before enrollment to L-MIND and experienced disease progression in L-MIND after eight cycles; this patient did not respond to further chemotherapy or CAR-T, and died 4 months after CAR-T therapy.
SF1. PFS in patients with (A) primary refractory DLBCL, (B) rituximab-refractory DLBCL, and (C) last-therapy refractory DLBCL

A.

B.
C.

![Graph showing progression-free survival](image)

**Median PFS**
- Yes: 7.6 months (95% CI: 2.7–NR)
- No: 16.2 months (95% CI: 7.4–NR)

| Time (months) | Yes | No |
|---------------|-----|----|
| 0             | 35  | 45 |
| 1             | 32  | 40 |
| 2             | 23  | 33 |
| 3             | 17  | 25 |
| 6             | 13  | 17 |
| 9             | 13  | 14 |
| 12            | 11  | 13 |
| 18            | 8   | 12 |
| 24            | 4   | 7  |
| 30            | 2   | 5  |
| 36            | 1   | 0  |
SF2. Swimmer plot of progression-free survival for patients with diffuse large B-cell lymphoma arising from transformation of low-grade lymphoma and double- or triple-hit lymphoma

Both patients ‘Censored: Other Reason’ had received prohibited concomitant medication.

CR, complete response; DHL, double-hit lymphoma; IPI, International Prognostic Index; IRC, independent review committee; PR, partial response; SD, stable disease; THL, triple-hit lymphoma; TL, transformed low-grade lymphoma.