Long-term analyses from L-MIND, a Phase II study of tafasitamab (MOR208) combined with lenalidomide (LEN) in patients with relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL)

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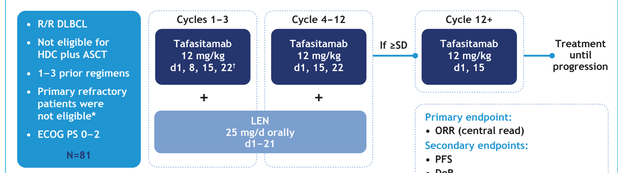
Background

- Tafasitamab (MOR208) is an Fc-modified, humanized, monoclonal antibody that targets the B-lymphocyte antigen CD19 on tumor cells[1,2]
- The CD19 molecule is broadly and homogeneously expressed across various B-cell malignancies, including diffuse large B-cell lymphoma (DLBCL)[3,4]
- The prognosis is poor for patients with relapsed or refractory (R/R) DLBCL who are ineligible for autologous stem cell transplantation (ASCT) with few alternate treatment options available.[5] Consequently, there is a vital need for novel, tolerable, and easy-to-administer treatment options for patients with R/R DLBCL, especially for those ineligible for ASCT
- In the open-label, single-arm, Phase II L-MIND study (NCT02399085) of tafasitamab combined with the immunomodulatory drug lenalidomide (LEN) in patients with R/R DLBCL ineligible for ASCT (**Figure 1**), primary analyses and 2-year efficacy results demonstrated the treatment combination was effective with a good tolerability profile[6]

Figure 1. L-MIND study design



- Sample size suitable to detect ≥15% absolute increase in ORR for tafasitamab plus LEN vs LEN monotherapy at 85% power, two-sided alpha of 5%
- Safety data from the first six patients were evaluated in a safety run-in to determine the starting dose of LEN for the remainder of the study

*Primary refractory is defined as no response to, or progression/relapse during or within 6 months of frontline therapy.
†A loading dose of tafasitamab was administered on Day 4 of Cycle 1.
ASCT, autologous stem cell transplantation; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HDC, high-dose chemotherapy; LEN, lenalidomide; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed or refractory; SD, stable disease.

- Tafasitamab combined with LEN followed by tafasitamab monotherapy is approved under accelerated approval by the United States Food and Drug Administration for adult patients with R/R DLBCL not otherwise specified, including DLBCL arising from low-grade lymphoma, and who are not eligible for ASCT[7]
- To further determine the long-term clinical efficacy and safety of tafasitamab plus LEN in patients with R/R DLBCL, here we report updated long-term data based on a follow-up of ≥35 months (data cut-off: October 30, 2020)

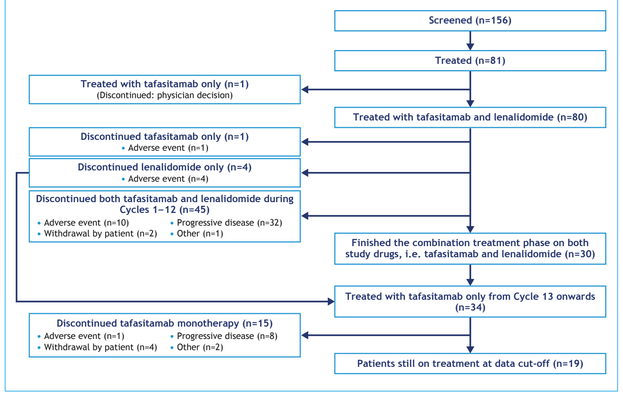
Methods

- Patients aged ≥18 years with R/R DLBCL (1–3 prior systemic therapies, including ≥1 CD20-targeting regimen), with an Eastern Cooperative Oncology Group performance status of 0–2, and who were ineligible for ASCT were enrolled[6]
- Patients received tafasitamab plus LEN, followed by tafasitamab monotherapy
  - Tafasitamab was administered over 28-day cycles (12 mg/kg intravenously), once weekly during Cycles 1–3, with a loading dose on Day 4 of Cycle 1, then every 2 weeks (Q2W) during Cycles 4–12
  - LEN (25 mg orally) was administered on Days 1–21 of Cycles 1–12
  - Following Cycle 12, progression-free patients received tafasitamab Q2W until disease progression
- The primary endpoint was objective response rate (ORR), assessed by independent review committee, based on the 2007 International Working Group response criteria[8]
- Secondary endpoints included duration of response (DoR), progression-free survival (PFS), and overall survival (OS); safety endpoints included incidence and severity of adverse events

Results

- Of 81 patients enrolled in L-MIND, 80 received ≥1 dose of both tafasitamab plus LEN, and were included in the full analysis set for efficacy, all 81 patients were included in the safety analysis (**Figure 2**)
- A total of 34 patients received tafasitamab monotherapy after discontinuing LEN, of whom 15 patients had ceased tafasitamab treatment at the data cut-off for this analysis, therefore, 19 patients were ongoing with tafasitamab monotherapy (**Figure 2**)

Figure 2. L-MIND patient disposition



- The complete baseline characteristics for patients participating in the L-MIND study have been previously published[6]
  - Patients had a median age of 72 years (range, 41–86) at enrollment, and had received a median of 2 (range, 1–4) prior lines of therapy before entering the study
- Of the 80 patients included in the full analysis set for efficacy, 40 patients had received one prior treatment, whereas the other 40 patients received ≥2 prior treatments before enrollment in L-MIND

Efficacy

- At this long-term data cut-off after at least 35 months follow-up, ORR was 57.5% (46/80; 95% confidence interval [CI]: 45.9–68.5), complete response (CR) rate was 40.0% (32/80) and partial response (PR) rate was 17.5% (14/80) (**Table 1**)

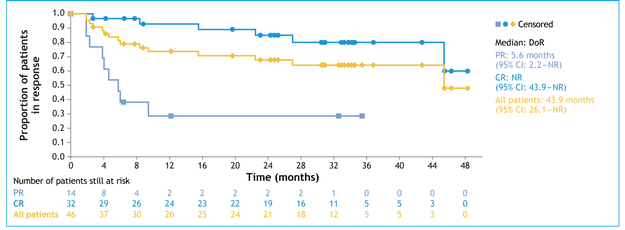
Table 1. Analysis of efficacy endpoints (IRC) by number of prior treatment lines

Tafasitamab plus LEN	1 prior treatment (N=40)	≥2 prior treatments (N=40)	Overall (N=80)
Best Objective Response, n (%)			
CR	19 (47.5)	13 (32.5)	32 (40.0)
PR	8 (20.0)	6 (15.0)	14 (17.5)
SD	7 (17.5)	6 (15.0)	13 (16.3)
PD	5 (12.5)	8 (20.0)	13 (16.3)
NE*	1 (2.5)	7 (17.5)	8 (10.0)
ORR (CR + PR), n (%) [95% CI]†	27 (67.5) [50.9–81.4]	19 (47.5) [31.5–63.9]	46 (57.5) [45.9–68.5]
Median DoR, months (95% CI)‡	43.9 (9.1–NR)	NR (15.0–NR)	43.9 (26.1–NR)
Median PFS, months (95% CI)‡	23.5 (7.4–NR)	7.6 (2.7–NR)	11.6 (6.3–45.7)
Median OS, months (95% CI)‡	45.7 (24.6–NR)	15.5 (8.6–NR)	33.5 (18.3–NR)

*No valid post-baseline response assessments. †Two-sided 95% Clopper-Pearson exact method based on a binomial distribution. ‡Kaplan-Meier estimate.
CI, confidence interval; CR, complete response; DoR, duration of response; IRC, independent review committee; LEN, lenalidomide; NE, not evaluable; NR, not reached; ORR, objective response rate; PD, disease progression; PFS, progression-free survival; PR, partial response; SD, stable disease.

- Median DoR for the full efficacy population was 43.9 months (95% CI: 26.1–not reached [NR]). For patients who reached a best response of CR, the median DoR was NR (95% CI: 43.9–NR) (**Figure 3A**)

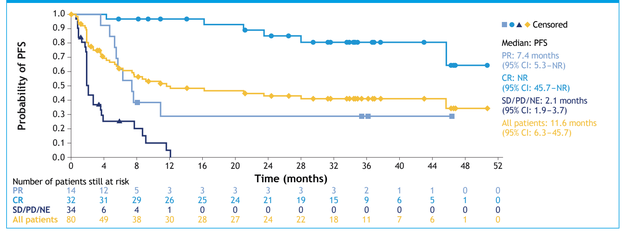
Figure 3A. Duration of response by best response



CI, confidence interval; CR, complete response; DoR, duration of response; NR, not reached; PR, partial response.

- Median PFS for the full efficacy population was 11.6 months (95% CI: 6.3–45.7), with a median follow-up of 33.9 months (**Figure 3B**)

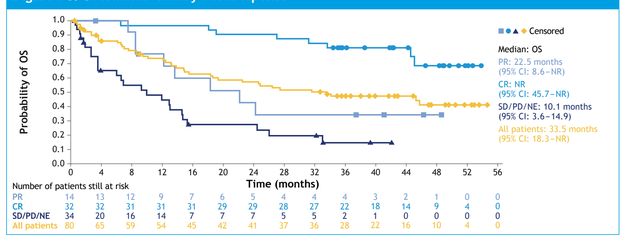
Figure 3B. Progression-free survival by best response



CI, confidence interval; CR, complete response; NE, not evaluable; NR, not reached; PD, disease progression; PFS, progression-free survival; PR, partial response; SD, stable disease.

- Median OS for the full efficacy population was 33.5 months (95% CI: 18.3–NR), with a median follow-up of 42.7 months (**Figure 3C**)

Figure 3C. Overall survival by best response



CI, confidence interval; CR, complete response; NE, not evaluable; NR, not reached; OS, overall survival; PD, disease progression; PR, partial response; SD, stable disease.

Safety

- Overall, tafasitamab plus LEN was well tolerated in long-term follow-up of the L-MIND study, no unexpected toxicities or new safety signals arose
- Similar to the primary analysis, the most common Grade 3–5 treatment-emergent adverse events (TEAEs) were neutropenia (49.4%), thrombocytopenia (17.3%), and febrile neutropenia (12.3%) with long-term follow up (**Table 2**)
- The most frequent TEAE leading to treatment interruption for tafasitamab (± LEN; combination + tafasitamab monotherapy treatment phases) and LEN (± tafasitamab; combination treatment phase) was neutropenia (28 [34.6%] patients and 24 [29.6%] patients, respectively)
- During the extended tafasitamab monotherapy phase of L-MIND, 21 (52.5%) patients had an interruption of tafasitamab treatment due to at least one TEAE; the most common reasons being neutropenia or leukopenia (9 patients each) and respiratory tract infections (6 patients)
- The burden of TEAEs, in terms of incidence, frequency, and severity, greatly decreased during the extended tafasitamab monotherapy phase compared with the combination therapy phase, which indicates a good tolerability profile for tafasitamab monotherapy until disease progression

Table 2. The most frequent hematologic TEAEs occurring in ≥10% of patients, or Grade 3–5 TEAEs in >1 patient

Event	All Grades (≥10%) n (%)	Grade 3-5 (>1 patient) n (%)
Neutropenia	41 (50.6)	40 (49.4)
Anemia	30 (37.0)	6 (7.4)
Thrombocytopenia	25 (30.9)	14 (17.3)
Leukopenia	12 (14.8)	9 (11.1)
Febrile neutropenia	10 (12.3)	10 (12.3)
Lymphopenia	6 (7.4)	3 (3.7)

TEAEs, treatment-emergent adverse events.

Conclusions

- Combination treatment with tafasitamab plus LEN followed by tafasitamab monotherapy provided durable responses in patients with R/R DLBCL not eligible for ASCT
- These data suggest that this chemotherapy-free combination treatment may have the potential to achieve prolonged remission and survival benefit in this patient population, especially at first relapse
- The long term safety data indicate the favorable benefit-risk profile of tafasitamab plus LEN, followed by tafasitamab until disease progression

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Disclosures

About Tafasitamab

Tafasitamab is a humanized Fc-modified cytolytic CD19-targeting monoclonal antibody. In 2010, MorphoSys licensed exclusive worldwide rights to develop and commercialize tafasitamab from Xencor, Inc. Tafasitamab incorporates an Xmab® engineered Fc domain, which mediates B-cell lysis through apoptosis and immune effector mechanism including antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP). In January 2020, MorphoSys and Incyte entered into a collaboration and licensing agreement to further develop and commercialize tafasitamab globally. Following approval by the U.S. Food and Drug Administration in July 2020, tafasitamab is being co-commercialized by MorphoSys and Incyte in the United States. Incyte has exclusive commercialization rights outside the United States. Xmab® is a trademark of Xencor, Inc.

JD: research funding from MorphoSys and Regeneron. **KM:** honoraria from Pharmacyclics, Celgene, Seattle Genetics, MorphoSys, Bristol-Myers Squibb, Karyopharm Therapeutics, Kite Pharma/Gilead Company, ADC Therapeutics and Genmab; research funding from Pharmacyclics, Merck and Bristol-Myers Squibb. **EGB:** consultancy fees for Janssen, Celgene, Gilead Sciences, Kyowa Kirin, EUSA Pharma and AbbVie; speaker fees from Janssen, AbbVie and Takeda; travel expenses from Janssen, AbbVie and Roche. **WJ:** research funding from Janssen-Cilag, Acerta Pharma/AstraZeneca, Merck, LOXO, TG Therapeutics and BeiGene. **AML:** consultancy fees from SERVIER; travel expenses from Bristol-Myers Squibb, Sanofi, Takeda, Roche, Celgene, Novartis, AbbVie, IQvia and Verastem; research funding from Novartis, Janssen-Cilag, AbbVie, Roche, Amgen, Sanofi, Celgene, Bristol-Myers Squibb, Takeda, Incyte, BeiGene, Oncopeptides, Verastem, Karyopharm Therapeutics, Archigen Biotech, Diobiopharm Group, MorphoSys, FibroGen and Onconova Therapeutics. **AO:** consultancy fees from Janssen; honoraria from Roche and Janssen; speaker fees from Roche; travel expenses from Roche, Gilead Sciences and Janssen. **GG:** consultancy fees from Janssen, AbbVie and AstraZeneca; speaker fees from Janssen and AbbVie; travel expenses from Janssen; honoraria from Janssen, AbbVie and AstraZeneca. **PA:** honoraria from Janssen, Celgene, AbbVie, AstraZeneca and Gilead Sciences; consultancy fees from Janssen, Celgene, AbbVie and AstraZeneca; speaker fees from Janssen, Celgene, AbbVie, AstraZeneca and Gilead Sciences. **MA:** no disclosures. **MHD:** consultancy fees from Acerta Pharma/AstraZeneca, Bayer/Vital, Celgene/Jazz, Gilead Sciences, Janssen-Cilag, Novartis, Roche and BeiGene; speaker fees from Bayer Health, Celgene, Gilead Sciences, Janssen-Cilag and Roche; travel expenses from Celgene, Janssen-Cilag and Roche; research funding from Celgene, Janssen-Cilag, Roche and AbbVie. **TM:** consultancy fees from Kite Pharma/Gilead, Celgene, Novartis, Amgen, Pfizer, Atara Biotherapeutics and Daiichi Sankyo/Lilly; speaker fees from Kite/Gilead, Roche, Novartis and Pfizer; travel expenses from Amgen, Jazz Pharmaceuticals, Janssen, Celgene and Kite/Gilead; honoraria from Takeda and Janssen; research funding from Janssen, AstraZeneca and Novartis. **MDH, JW:** employees of MorphoSys AG. **SVA:** employee of MorphoSys AG; accommodation fees from MorphoSys AG and has a patent under review. **GAS:** consultancy fees from Roche/Genentech, Gilead Sciences, Janssen, Celgene, Novartis, MorphoSys, Epizyme, Alimera Sciences, Debiopharm Group, Velosbio, Genmab, Bristol-Myers Squibb, BeiGene, Incyte and Miltenyi Biotec; honoraria from Roche/Genentech, Janssen, Celgene, Gilead Sciences, Novartis, AbbVie and MorphoSys.

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