POSTER No. (abstract number): P1138

Five-year efficacy and safety of tafasitamab in patients with relapsed or refractory DLBCL: Final results from the Phase II L-MIND study

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OBJECTIVE

To report final, 5-year efficacy and safety of tafasitamab + lenalidomide (LEN) in the Phase II L-MIND study (NCT02399085[1])

SUMMARY

> **The 5-year analysis of L-MIND study showed durable responses in patients with relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL) who were not eligible for autologous stem cell transplant (ASCT)**
- **Median duration of response (mDoR) was not reached after 44 months of median follow-up**
- **As expected, patients with 1 prior line of therapy (pLoT) had better outcomes than those with ≥2 pLoT**
- **mDoR was not reached in either subgroup, indicating durability of response irrespective of number of prior treatment lines**

> **The frequency of treatment-emergent adverse events (TEAEs) decreased after patients transitioned from combination therapy to tafasitamab monotherapy, up to 2 years and further beyond 2 years**

> **No safety signals were identified, confirming the tolerable safety profile seen with primary and 3-year data cuts[2,3]**

> **These long-term data suggest that this immunotherapy may have curative potential, which is being explored in further studies**

Acknowledgments: Thank you to the patients, care givers, and study investigators. This study was funded by MorphoSys AG. Medical writing assistance was provided by Pavitra Joshi, MS and Emma Leah, Ph.D. of Syneos Health, UK, and funded by MorphoSys AG.

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These data were previously presented at the AACR congress 2023: Duell, J et al. Five-year efficacy and safety of tafasitamab in patients with relapsed or refractory DLBCL: Final results from the Phase II L-MIND study [abstract]. In: Proceedings of the 114th Annual Meeting of the American Association for Cancer Research; 2023 April 9-14; Orlando, FL. Philadelphia (PA): AACR; 2023. Abstract nr CT022.

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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 mechanisms 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 accelerated 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. Conditional/accelerated approvals were granted by the European Medicines Agency and other regulatory authorities. Incyte has exclusive commercialization rights outside the United States. XmAb® is a registered trademark of Xencor, Inc.

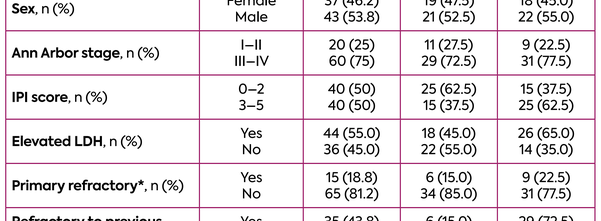
BACKGROUND

> Effective treatment options in second line and beyond are much needed in patients with R/R DLBCL; 2- and 5-year timepoints are considered important milestones of prolonged remission
> Anti-CD19 monoclonal antibody tafasitamab enhances antibody-dependent cellular cytotoxicity and phagocytosis, and received accelerated approval in the USA[7] and conditional authorization in Europe[8] in combination with LEN for patients with R/R DLBCL ineligible for ASCT based on the results of the open-label, multicenter, single-arm, Phase II L-MIND study (NCT02399085[1])
- Immunotherapy with tafasitamab + LEN was effective and well tolerated in the 1- and 3-year analyses in this population[2,3]

METHODS

> L-MIND was an open-label, single-arm, multicenter, global Phase II study (**Figure 1**)

Figure 1 Study Design



*Primary refractory is defined as no response to, or progression/relapse during/within 6 months of, front-line therapy; 15 patients with refractory disease were included under an early version of the protocol. [1]A loading dose of tafasitamab was administered on Day 4 of Cycle 1.
ASCT, autologous stem cell transplant; D, days; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; LEN, lenalidomide; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed or refractory; SD, stable disease.

RESULTS

> A total of 81 patients were enrolled and received ≥1 dose of tafasitamab (**safety analysis set**), and a total of 80 patients received tafasitamab + LEN (**full analysis set** [FAS])
- Of 80 in the FAS, 30 patients completed 12 cycles of the combination therapy, while 4 discontinued LEN before Cycle 12; these 34 patients continued tafasitamab monotherapy beyond Cycle 12, with 8 receiving it until the end of study per protocol
- The most common reason for discontinuation of the combination therapy was disease relapse/progressive disease

> Median age overall was 72.0 years (range 41–86); 50% of patients in the FAS had 1 pLoT at study entry (**Table 1**)

Table 1. Baseline characteristics

		All patients (FAS)	1 pLoT	≥2 pLoT
N		80	40	40
Median age, years (range)		72.0 (41.0–86.0)	72.0 (53.0–86.0)	70.5 (41.0–82.0)
Age >70 years, n (%)		45 (56.2)	25 (62.5)	20 (50.0)
Sex, n (%)	Female Male	37 (46.2) 43 (53.8)	19 (47.5) 21 (52.5)	18 (45.0) 22 (55.0)
Ann Arbor stage, n (%)	I–II III–IV	20 (25) 60 (75)	11 (27.5) 29 (72.5)	9 (22.5) 31 (77.5)
IPI score, n (%)	0–2 3–5	40 (50) 40 (50)	25 (62.5) 15 (37.5)	15 (37.5) 25 (62.5)
Elevated LDH, n (%)	Yes No	44 (55.0) 36 (45.0)	18 (45.0) 22 (55.0)	26 (65.0) 14 (35.0)
Primary refractory*, n (%)	Yes No	15 (18.8) 65 (81.2)	6 (15.0) 34 (85.0)	9 (22.5) 31 (77.5)
Refractory to previous therapy line, n (%)	Yes No	35 (43.8) 45 (56.2)	6 (15.0) 34 (85.0)	29 (72.5) 11 (27.5)
Prior ASCT, n (%)	Yes No	9 (11.2) 71 (88.8)	2 (5.0) 38 (95.0)	7 (17.5) 33 (82.5)
Cell of origin (by IHC), n (%)	GCB Non-GCB Unknown/NE	38 (47.5) 22 (27.5) 20 (25.0)	16 (40.0) 14 (35.0) 10 (25.0)	22 (55.0) 8 (20.0) 10 (25.0)

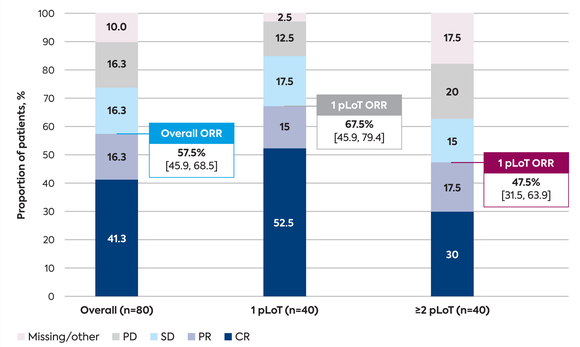
*Primary refractory is defined as no response to, or progression/relapse during or within 6 months of, front-line therapy.
ASCT, autologous stem cell transplant; FAS, full analysis set; GCB, germinal-center B-cell; IHC, immunohistochemistry; IPI, International Prognostic Index; LDH, lactate dehydrogenase; NE, not evaluable; pLoT, prior line of therapy.

EFFICACY

> The IRC-assessed best response at 5 years (**Figure 2**) was consistent with prior 3-year follow-up and primary analysis
- As expected, results were better in patients with 1 vs ≥2 pLoT (complete response [CR]: 52.5%, partial response [PR]: 15% vs CR: 30%, PR: 17.5%)

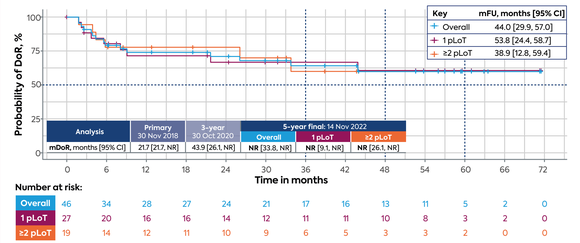
> After a median follow-up of 44.0 months, mDoR was not reached overall, or in the subgroups by pLoT (**Figure 3**)
> Median progression-free survival (PFS) was 11.6 months (**Figure 4**), and overall survival (OS) was 33.5 months (**Figure 5**)
> In patients who ended treatment with response (n=26), most (n=23) had CR vs PR (n=3) (**Figure 6**)
- Two patients with previous CR and <12 months treatment later died due to progressive disease, after another anti-lymphoma therapy, and three other patients (one with CR and two with PR as best response) died due to other causes

Figure 2: Best Response at 5-year Follow-up



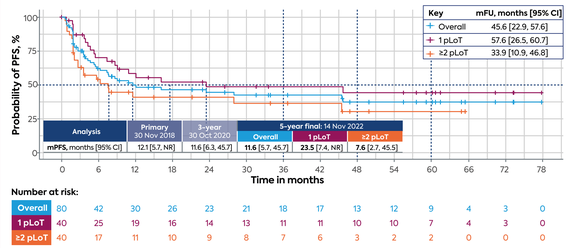
CR, complete response; ORR, objective response rate; PD, progressive disease; pLoT, prior line of therapy; PR, partial response; SD, stable disease.

Figure 3: DoR at 5-year Follow-up



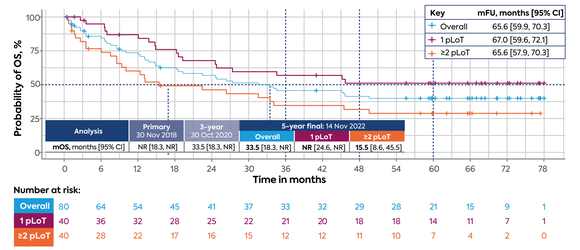
DoR, duration of response; mDoR, median DoR; mFU, median follow-up; NR, not reached; pLoT, prior line of therapy.

Figure 4: PFS at 5-year Follow-up



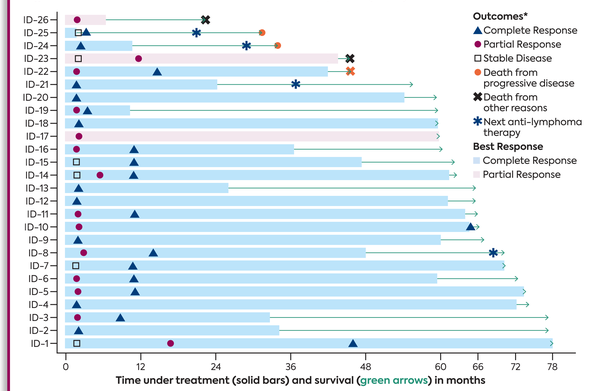
mFU, median follow-up; mPFS, median PFS; NR, not reached; PFS, progression-free survival; pLoT, prior line of therapy.

Figure 5: OS at 5-year Follow-up



mFU, median follow-up; mOS, median OS; NR, not reached; OS, overall survival; pLoT, prior line of therapy.

Figure 6: Patients who ended treatment with response (n=26)



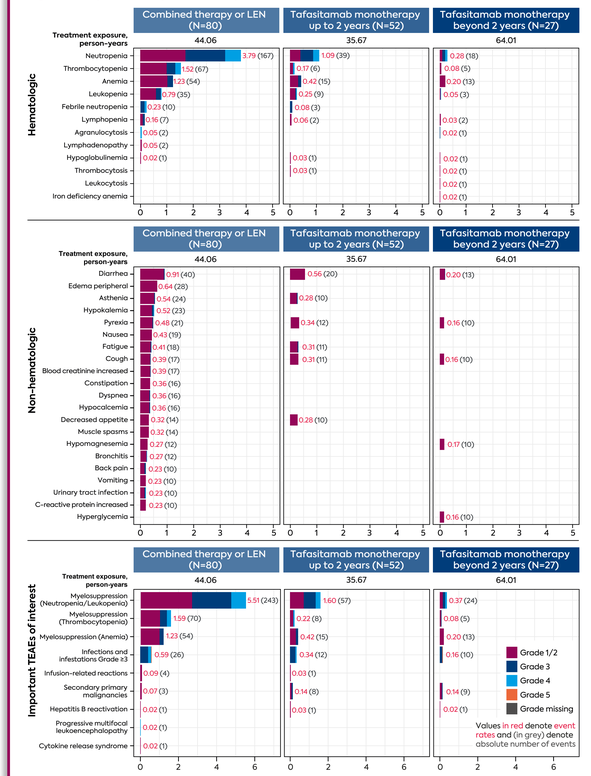
*Repeat response assessments giving the same outcome as previous assessment are not shown.

SAFETY

> TEAEs were consistent with previous reports and manageable, hematologic and non-hematologic TEAEs were less frequent during tafasitamab monotherapy compared with tafasitamab + LEN combination therapy (**Figure 7**)
- The low frequency of TEAEs during the tafasitamab monotherapy phase beyond 12 months represents a substantial improvement in the already manageable safety profile

> Most non-hematologic TEAEs were Grade 1/2, and the most common non-hematologic TEAEs were diarrhea and peripheral edema during the combination therapy phase
> Most TEAEs of interest were hematologic events during the tafasitamab + LEN combination period
- There was a low incidence of infusion-related reactions and Grade ≥3 infections and infestations
- No occurrences of progressive multiple leukoencephalopathy or cytokine release syndrome were noted after the combination phase (in which there was a single event of each AE)

Figure 7: Exposure-Adjusted Comparison of TEAE Frequency across Treatment Periods



CTCAE grading system version 4.0. LEN, lenalidomide; TEAE, treatment-emergent adverse event

Presented at European Hematology Association (EHA) 2023 Hybrid Congress; June 8–11 2023, Frankfurt, Germany.