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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

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References: 1. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT02399085 [Accessed April 2023]; **2.** Salles G, et al. Lancet Oncol 2020;21(7):978–88; **3.** Duell J, et al. Haematologica 2021;106(9):2417–26; **4.** Sarkozy C, Sehn LH. Ann Lymphoma 2019;3:10; **5.** Crump M, et al. Blood 2017;130(16):1800–8; **6.** Sarkozy C, Coiffier B. Clin Cancer Res 2013;19(7):1660–9; **7.** MONJUVI. Prescribing information. Boston, MA: MorphoSys. 2020 [Accessed April 2023]; **8.** European Medicines Agency. SmPC Minjuvi. 2021 [Accessed April 2023].

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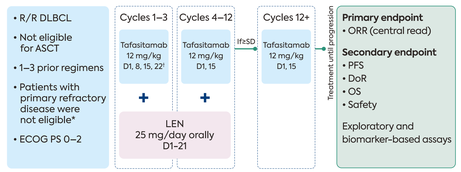
BACKGROUND

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

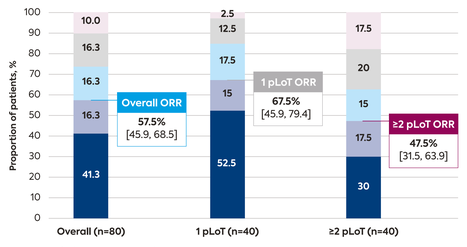
*Primary refractory is defined as no response to, or progression/relapse during or within 6 months of, front-line therapy.

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

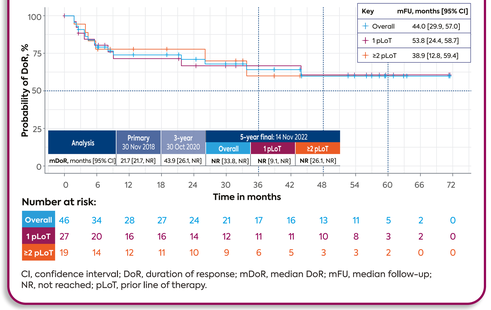
- The IRC-assessed best response at 5 years **(Figure 2)** was consistent with prior 3-year follow-up and primary analysis
  - As expected, results were better in patients with 1 vs ≥2 pLoT (complete response [CR]: 52.5%, partial response [PR]: 15% vs CR: 30%, PR: 17.5%)
- After a median follow-up of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



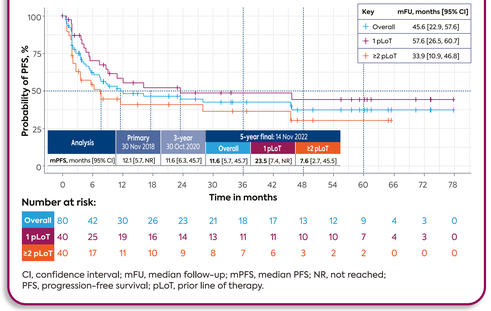
ORR, objective response rate; PD, progressive disease; pLoT, prior line of therapy; PR, partial response; SD, stable disease.

Figure 3. DoR at 5-year Follow-up



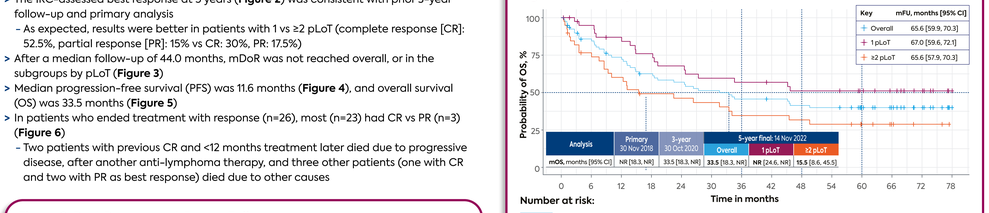
CI, confidence interval; DoR, duration of response; mDoR, median DoR; mFU, median follow-up; NR, not reached; pLoT, prior line of therapy.

Figure 4. PFS at 5-year Follow-up



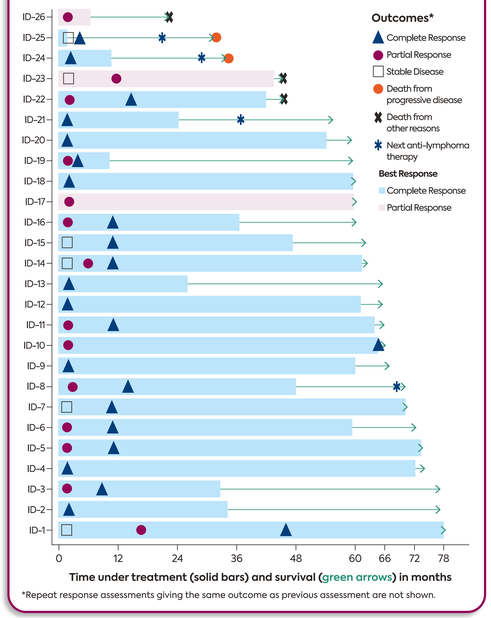
CI, confidence interval; mFU, median follow-up; mPFS, median PFS; NR, not reached; PFS, progression-free survival; pLoT, prior line of therapy.

Figure 5. OS at 5-year Follow-up



CI, confidence interval; 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)

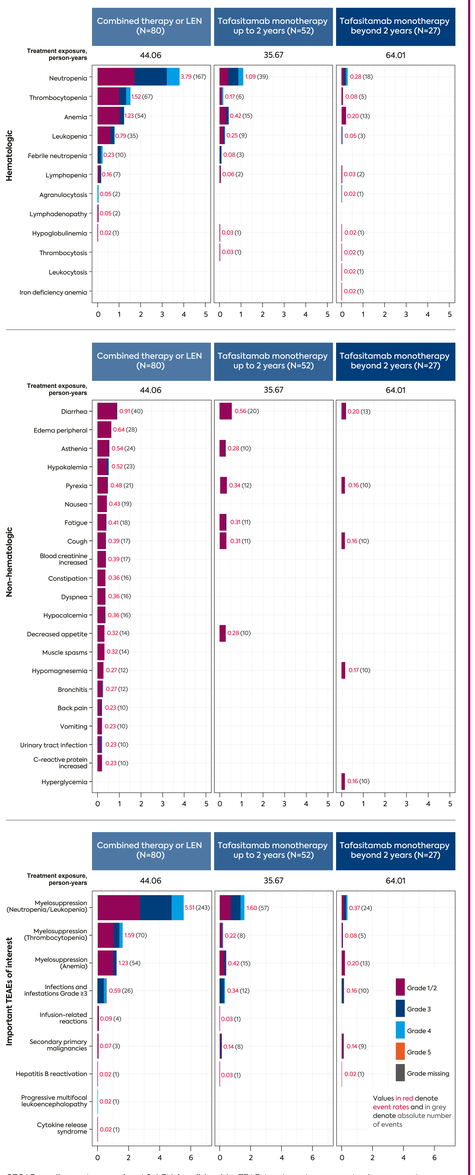


*Repeat response assessments giving the same outcome as previous assessment are not shown.

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.

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