Long-Term Subgroup Analyses from L-MIND, a Phase II Study of Tafasitamab (MOR208) Combined with Lenalidomide in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma

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Disclosures

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L-MIND: Background

- Tafasitamab (MOR208) is an Fc-modified, humanized, monoclonal antibody that targets CD19 on tumor cells[1,2]
  - CD19 is broadly and homogeneously expressed across different B-cell malignancies, including DLBCL[3,4]
- Patients with R/R DLBCL who are ineligible for ASCT have a poor prognosis, with few available treatment options[5]
- L-MIND (NCT02399085) is an ongoing, open-label, single-arm, Phase II study of tafasitamab + the immunomodulatory drug LEN in patients with R/R DLBCL who are ineligible for ASCT
- Tafasitamab + LEN has shown clinical activity with durable responses in the L-MIND study primary analysis (data cut-off: Nov 30, 2018)[6]
  - Tafasitamab is approved by the FDA in combination with LEN for adult patients with relapsed or refractory DLBCL NOS, including DLBCL arising from low-grade lymphoma, and who are not eligible for ASCT[7]
- L-MIND results from prespecified patient subgroup analyses were presented previously (primary analysis: data cut-off: Nov 30, 2018).[8] Here, we report long-term clinical efficacy and safety from the L-MIND study after a median follow-up of 31.8 months for OS (data cut-off: Nov 30, 2019)

1. Awan FT, et al. Blood 2010;115:1204–13;
2. Horton HM, et al. Cancer Res 2008;68:8049–57;
3. Olejniczak SH, et al. Immunol Invest 2006;35:93–114;
4. Poe JC, et al. J Immunol 2012;189:2318–25;
5. Friedberg JW. Hematology Am Soc Hematol Educ Program 2011;2011:498–505;
6. Salles G, et al. Lancet Oncol 2020;21:978–88;
7. Monjuvi (tafasitamab) US PI. Aug 2020;
8. Duell J, et al. Blood 2019;134(Suppl.1):1582.

ASCT, autologous stem cell transplantation; DLBCL, diffuse large B-cell lymphoma; LEN, lenalidomide; NOS, not otherwise specified; OS, overall survival; R/R, relapsed/refractory.

L-MIND: Study design

- R/R DLBCL
- Not eligible for HDC + ASCT
- 1–3 prior regimens
- Primary refractory patients were not eligible*
- ECOG PS 0-2

N=81

Cycles 1–3

Tafasitamab 12 mg/kg q4w; d1, 8, 15, 22†

+

LEN 25 mg/d orally d1–21

Cycles 4–12

Tafasitamab 12 mg/kg q4w; d1, 15

+

LEN 25 mg/d orally d1–21

If ≥ SD

Cycle 12+

Tafasitamab 12 mg/kg d1, 15

Treatment until progression

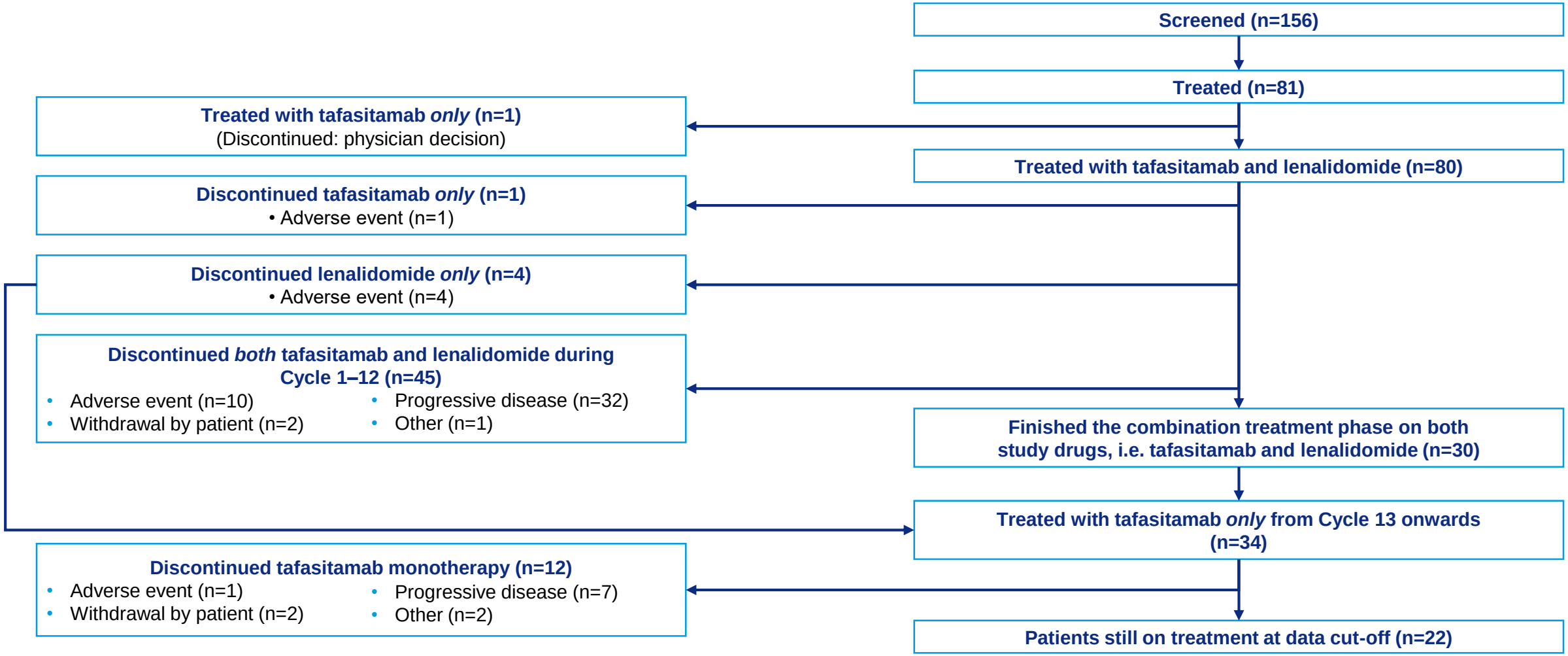
Primary endpoint:
- ORR (central read)

Secondary endpoints:
- PFS
- DOR
- OS
- Safety of the tafasitamab + LEN combination
- Exploratory and biomarker-based assays

- Sample size suitable to detect ≥15% absolute increase in ORR for tafasitamab/LEN combination 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

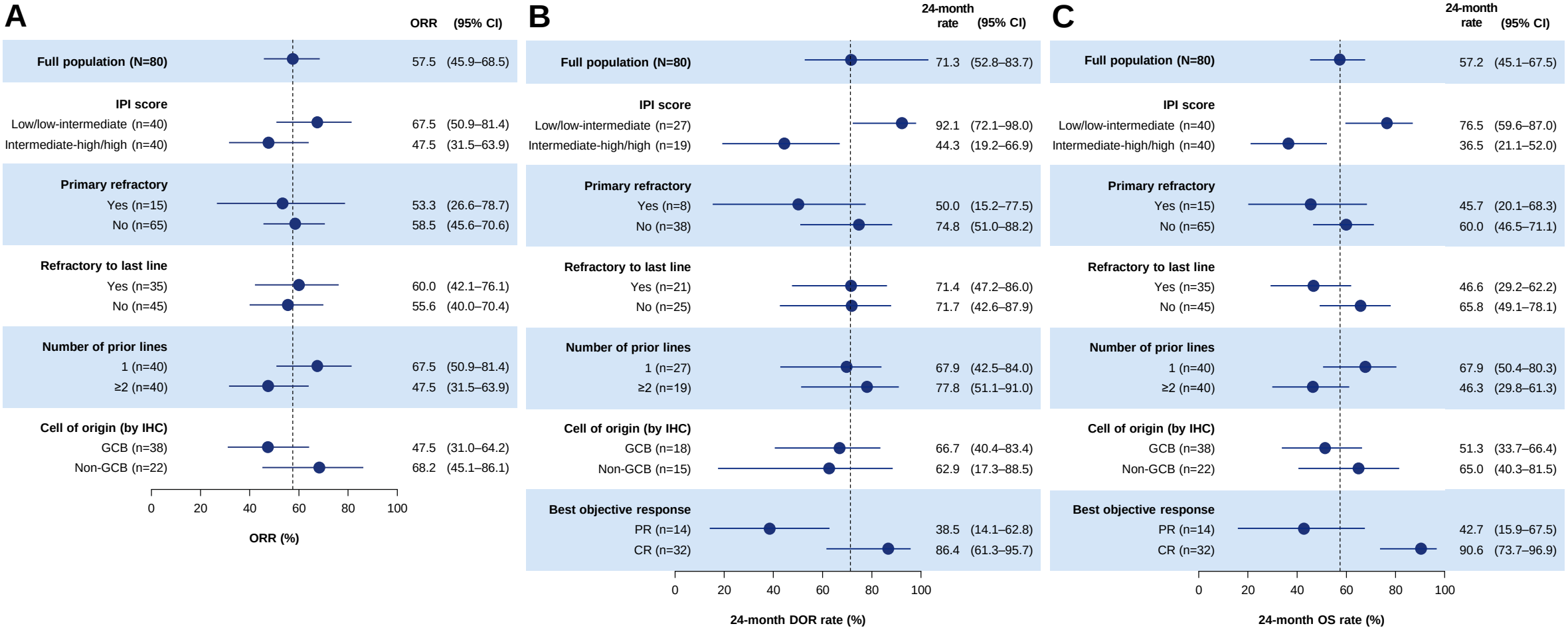
*Primary refractory defined as no response to, or progression/relapse during or within 6 months of frontline therapy; †A loading dose of tafasitamab was administered on Day 4 of Cycle 1.
DOR, duration of response; ECOG PS; Eastern Cooperative Oncology Group performance status; HDC, high-dose chemotherapy; ORR, objective response rate; PFS, progression-free survival; q4w, every 4 weeks; SD, stable disease.

L-MIND (Nov 30, 2019 data cut-off) CONSORT diagram



Subgroup analysis

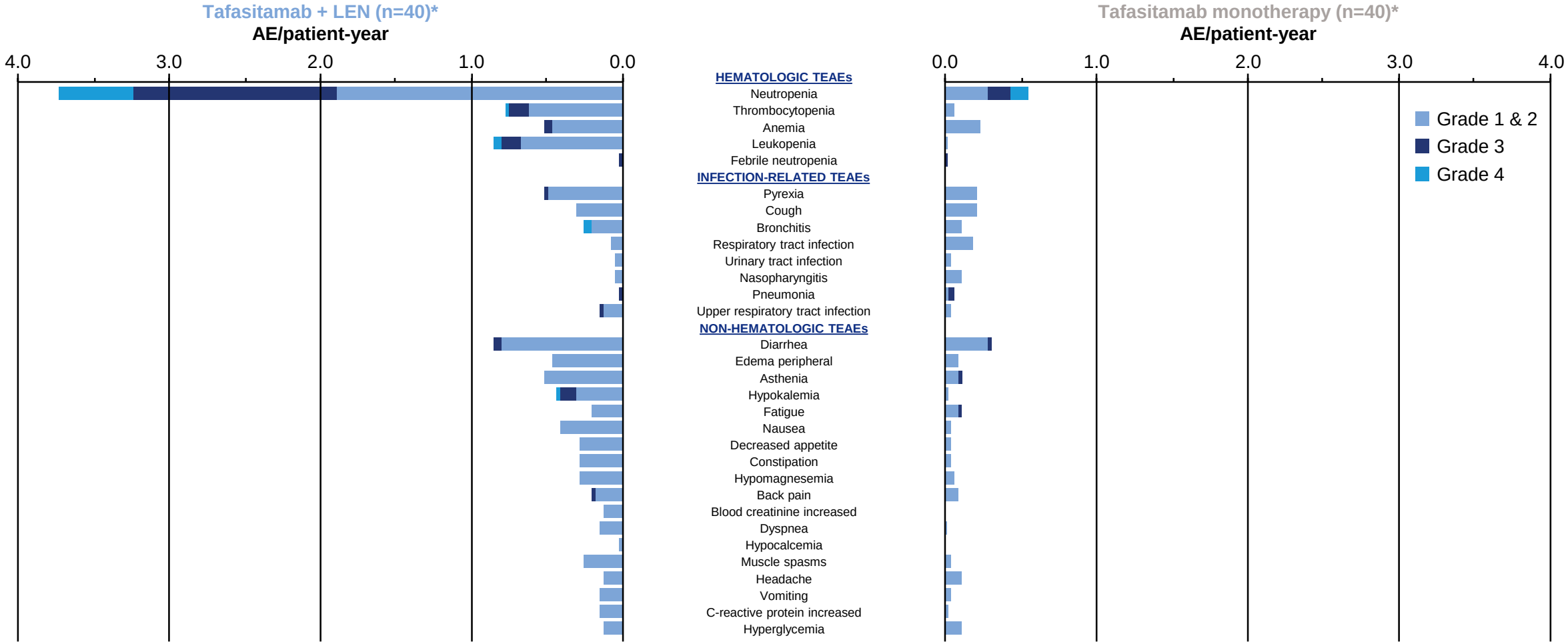
Objective response rate (A), duration of response (B) and overall survival (C)



CI, confidence interval; CR, complete response; GCB, germinal center B-cell like; IHC, immunohistochemistry; IPI, International Prognostic Index; PR, partial response.

Safety analysis

Adverse events per patient-year by L-MIND treatment phase



*Patients who had data from the tafasitamab monotherapy phase as well as the combination treatment phase – patients had completed the combination therapy phase and had received subsequent tafasitamab monotherapy. TEAEs (any grade) occurring in ≥10% of all patients over the course of the study. Data are based on a cumulative exposure total of 11,625 days or 19,880 days for tafasitamab + LEN or tafasitamab monotherapy treatment phases, respectively.

AE, adverse event; TEAE, treatment-emergent adverse events.

Conclusions

- Long-term L-MIND subgroup data show that the encouraging activity observed at primary analysis remains durable after ≥2 years of follow-up
- Patients with CR continue to experience long DOR and high OS
- The long-term safety data showed that tafasitamab plus LEN for 12 cycles, followed by tafasitamab until progression, was well-tolerated and did not result in any unexpected safety signal
- Although the influence of poor prognosis risk factors is still evident, the clinical activity of tafasitamab in combination with LEN followed by tafasitamab monotherapy continues to show promise in difficult-to-treat ASCT-ineligible patients with R/R DLBCL