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

Gilles Salles[1], Johannes Duell[2], Eva González-Barca[3], Wojciech Jurczak[4], Anna Marina Liberati[5], Sven de Vos[6], Zsolt Nagy[7], Aleš Obr[8], Gianluca Gaidano[9], Pau Abrisqueta[10], Nagesh Kalakonda[11], Marc André[12], Martin Dreyling[13], Tobias Menne[14], Olivier Tournilhac[15], Marinela Augustin[16], Maren Dirnberger-Hertweck[17], Johannes Weirather[17], Sumeet Ambarkhane[17], Kami J Maddocks[18]

[1]Hématologie, Hospices Civils de Lyon and Université de Lyon, Lyon, France; [2]Medizinische Klinik und Poliklinik II, Universitätsklinik Würzburg, Würzburg, Germany; [3]Department of Hematology, Institut Català d'Oncologia (ICO), Hospital Duran i Reynals, IDIBELL, Barcelona, Spain; [4]Maria Sklodowska Curie National Institute of Oncology, Kraków, Poland; [5]Università degli Studi di Perugia, Azienda Ospedaliera Santa Maria di Terni, Terni, Italy; [6]Department of Medicine, Ronald Reagan UCLA Medical Center, Santa Monica, CA; [7]1st Department of Internal Medicine, Semmelweis University, Budapest, Hungary; [8]Department of Hemato-Oncology, Palacký University and University Hospital, Olomouc, Czech Republic; [9]Division of Hematology, Department of Translational Medicine, University of Piemonte Orientale Amedeo Avogadro, Novara, Italy; [10]Department of Hematology, Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, Barcelona, Spain; [11]Molecular and Clinical Cancer Medicine, University of Liverpool and The Clatterbridge Cancer Centre, Liverpool, United Kingdom; [12]Department of Haematology, Université Catholique de Louvain, CHU UCL Namur, Yvoir, Belgium; [13]Department of Medicine III, University Hospital Großhadern, Ludwig Maximilians University, Munich, Germany; [14]Department of Haematology, Freeman Hospital, Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom; [15]Service d'Hématologie Clinique et de Thérapie Cellulaire, CHU Estaing, Clermont-Ferrand, France; [16]Klinik für Innere Medizin 5, Universitätsklinik der Paracelsus Medizinischen Privatuniversität, Nürnberg, Germany; [17]MorphoSys AG, Planegg, Germany; [18]Department of Internal Medicine, Arthur G James Comprehensive Cancer Center, Ohio State University Wexner Medical Center, Columbus, OH.

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Introduction

- Tafasitamab (MOR208) is an Fc-enhanced, humanized, monoclonal antibody that targets CD19 on tumor cells[1,2]
  - CD19 is broadly and homogeneously expressed across different B-cell malignancies, including diffuse large B-cell lymphoma (DLBCL)[3,4]
- Patients with relapsed or refractory (R/R) DLBCL have a poor prognosis, with few available treatment options[5]
- Tafasitamab in combination with the immunomodulatory drug lenalidomide (LEN) has shown encouraging activity with durable responses in autologous stem cell transplant (ASCT)-ineligible patients with R/R DLBCL in the open-label, single-arm, Phase II L-MIND study (NCT02399085)[6]
- In the L-MIND primary analysis (data cut-off: November 30, 2018), the primary endpoint of best objective response rate as assessed by an independent review committee (IRC) was 60.0% (95% confidence interval [CI]: 48.4–70.8)[6]
  - Of responders, median duration of response (DOR) was 21.7 months (95% CI: 21.7–not reached [NR]) and median follow-up was 17.3 months[6]

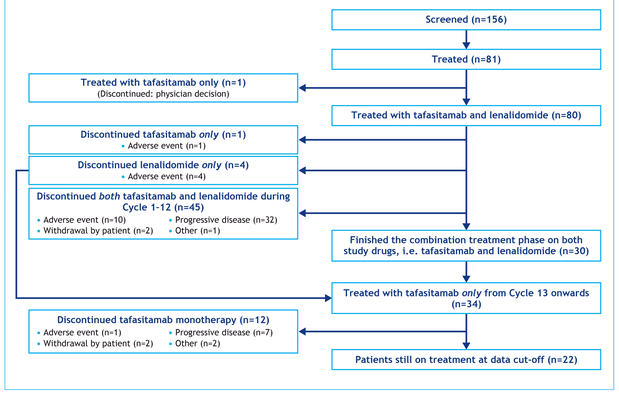
Objective

- Here, we report the long-term clinical efficacy and safety of tafasitamab + LEN in the L-MIND study after ≥2 years of follow-up from the last patient enrolled (data cut-off: November 30, 2019)

Methods

- In L-MIND, 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 and LEN, followed by tafasitamab monotherapy
  - Tafasitamab was administered in 28-day cycles (12 mg/kg intravenously), once weekly during Cycles 1–3 with a loading dose on Cycle 1 Day 4, then every 2 weeks during Cycles 4–12
  - LEN (25 mg orally) was administered on Days 1–21 of Cycles 1–12
  - After Cycle 12, progression-free patients received tafasitamab every 2 weeks until disease progression
- The primary endpoint was ORR, as assessed by an IRC
- Secondary endpoints included DOR, progression-free survival (PFS), overall survival (OS) and safety analyses

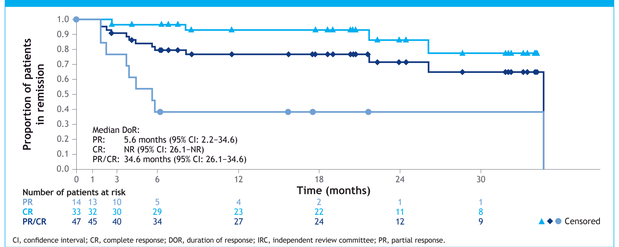
Figure 1. CONSORT diagram: L-MIND (data cut-off: November 30, 2019)



Results: Efficacy

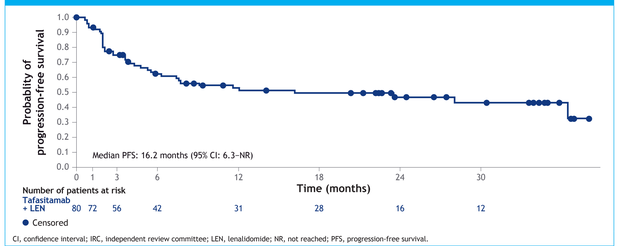
- In L-MIND, 80/81 enrolled patients received tafasitamab + LEN and were included in the full analysis set for efficacy; all 81 enrolled patients were included in the analysis set for safety
- After ≥2 years of follow-up, 22 patients were still receiving tafasitamab monotherapy and 59 had discontinued treatment (**Figure 1**)
  - Of those that discontinued, 38 patients had died, 14 were in survival follow-up and seven were lost to follow-up
- IRC-assessed ORR was 58.8% (n=47/80) and was consistent with the primary analysis
  - 41.3% (33/80) patients demonstrated a complete response (CR) and 17.5% (14/80) partial response (PR)
  - 15.0% (12/80) had stable disease, 16.3% (13/80) progressive disease, and 10.0% (8/80) were not evaluable
- Of responders, IRC-assessed median DOR was 34.6 months (95% CI: 26.1–34.6; **Figure 2a**)
  - Median DOR in patients with CR and PR was NR (95% CI: 26.1–NR) and 5.6 months (95% CI: 2.2–34.6), respectively

Figure 2a. IRC-assessed DOR after ≥24 months of follow-up



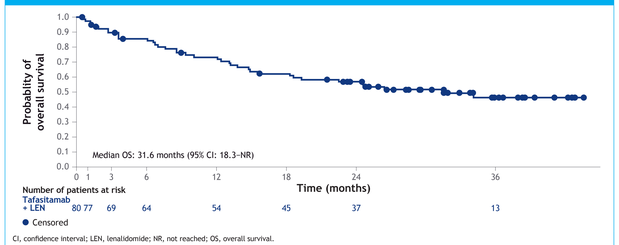
CI, confidence interval; CR, complete response; DOR, duration of response; IRC, independent review committee; PR, partial response.

Figure 2b. IRC-assessed PFS after ≥24 months of follow-up



CI, confidence interval; IRC, independent review committee; LEN, lenalidomide; NR, not reached; PFS, progression-free survival.

Figure 2c. OS of patients after ≥24 months of follow-up



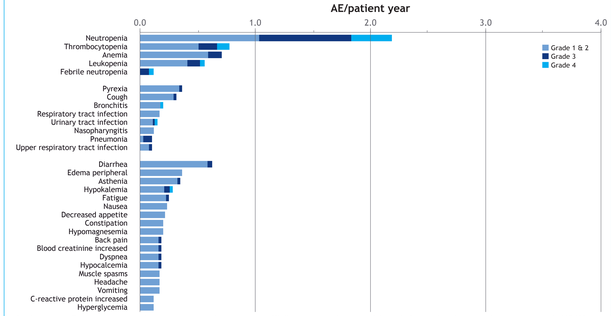
CI, confidence interval; LEN, lenalidomide; NR, not reached; OS, overall survival.

- IRC-assessed median PFS was 16.2 months (95% CI: 6.3–NR) with a median follow-up of 22.6 months (95% CI: 22.2–27.4; **Figure 2b**)
- Median OS was 31.6 months (95% CI: 18.3–NR) with a median follow-up of 31.8 months (95% CI: 27.2–35.9; **Figure 2c**)

Results: Safety

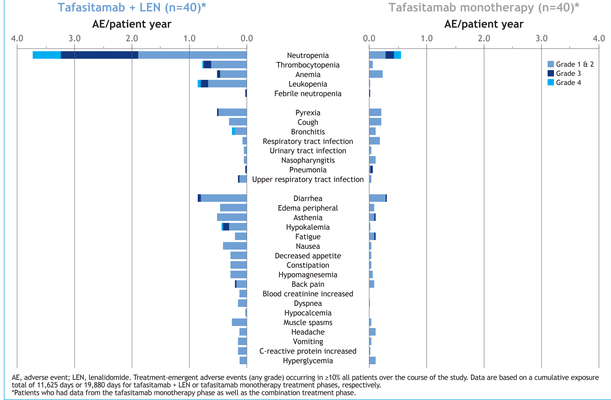
- Overall, tafasitamab plus LEN was well tolerated after long-term follow-up of the L-MIND study
  - The most frequently reported grade ≥3 hematological treatment-emergent adverse events (TEAEs) were neutropenia (49.4% incidence), thrombocytopenia (17.3%) and febrile neutropenia (12.3%)
  - The most frequently reported grade ≥3 non-hematological TEAEs were pneumonia (8.6%) and hypokalemia (6.2%)
  - The most common serious adverse events (in ≥2 patients) were pneumonia (8.6%), febrile neutropenia (6.2%), pulmonary embolism (3.7%), as well as bronchitis, lower respiratory tract infection, atrial fibrillation and congestive cardiac failure (2.5% each)

Figure 3. Number of adverse events per patient year (n=81)



AE, adverse event. Treatment-emergent adverse events (any grade) occurring in ≥10% all patients over the course of the study. Data are based on a cumulative exposure total of 35,252 days.

Figure 4. Adverse events per patient year by L-MIND treatment phase



AE, adverse event; LEN, lenalidomide. Treatment-emergent adverse events (any grade) occurring in ≥10% 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.
*Patients who had data from the tafasitamab monotherapy phase as well as the combination treatment phase.

- To better understand the burden of TEAEs on patients, the frequency and duration of TEAEs were calculated per patient year (PY) of exposure to the study medication (**Figure 3**)
  - For the most frequently reported grade ≥3 hematological TEAEs, neutropenia was reported at a rate of 1.14/PY, thrombocytopenia at 0.26/PY and febrile neutropenia at 0.11/PY (**Figure 3**)
  - For the most frequently reported grade ≥3 non-hematological TEAEs, pneumonia was reported at a rate of 0.07/PY and hypokalemia at 0.06/PY (**Figure 3**)
- An assessment of TEAE burden in each treatment phase of the study showed the rate of TEAEs per PY were reduced, in severity and incidence, during the tafasitamab monotherapy phase compared with the prior combination therapy phase (**Figure 4**)

Conclusions

- After a minimum of two years' follow-up, outcomes from the L-MIND study are consistent with the primary analysis[6]
- Data confirm the long durability of the response and a meaningful OS benefit of tafasitamab plus LEN followed by tafasitamab monotherapy in ASCT-ineligible patients with R/R DLBCL
- Tafasitamab in combination with LEN followed by tafasitamab monotherapy was well tolerated with no unexpected toxicities following ≥2 years of follow-up
- The TEAEs observed reflect the established safety profile of LEN[7]
- These long-term data are clinically relevant and show the benefit of this immunotherapy combination for patients with R/R DLBCL

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Disclosures

About tafasitamab (MOR208)

Tafasitamab (MOR208) is an investigational, humanized, Fc-engineered monoclonal antibody directed against CD19. In 2010, MorphoSys licensed exclusive worldwide rights to develop and commercialize tafasitamab from Xencor, Inc. Tafasitamab incorporates an XmAb® engineered Fc domain, which is intended to lead to a significant potentiation of antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP), thus aiming to improve a key mechanism of tumor cell killing. XmAb® is a trademark of Xencor, Inc.

GS: honoraria from MorphoSys, BMS, Acerta, Abbvie, Janssen, Merck, Novartis, Gilead/Kite, Epizyme, Pfizer, Servier, Celgene, Roche and Takeda; consultancy fees from Autolus and Genmab; their institution received patient fees from MorphoSys; and has a patent issued. JD, AML, ZN and MA's institutions have received patient fees from MorphoSys. **AO:** nothing to disclose. **EGB:** consultancy fees from Janssen, Gilead, Sandoz, Celtrion, Keona and Celgene; honoraria from Abbvie, Janssen, Takeda and Roche; institution received patient fees from MorphoSys. **JW:** financing of scientific research from MorphoSys, Roche, Sandoz and Celtrion; institution received patient fees from MorphoSys. **SdV:** consultancy fees from Verastem and Bayer; member on the board of directors or advisory committee at Portola Pharmaceuticals. **GG:** consultancy fees from Janssen, Abbvie, Astra-Zeneca and Sunesys; institution received patient fees from MorphoSys. **PA:** consultancy fees from Janssen, Roche, Celgene; honoraria from Janssen, Roche, Gilead and Abbvie. **NK:** research funding from Celgene. **MD:** consultancy fees from MorphoSys and Celgene; honoraria from Celgene; institution received patient fees from MorphoSys; institutional support of IITs from Celgene. **TM:** honoraria from and is a member on the board of directors or advisory committee at Kite/Gilead, Amgen, Novartis, Celgene, Daiichi Sankyo, Takeda, Janssen, Roche, Astra Zeneca, Jazz, Pfizer, Bayer and Kyowa Kirin; research funding from Kite/Gilead, Amgen, Novartis, Celgene, Takeda, Janssen, Roche, Astra Zeneca, Jazz, Pfizer, Bayer and Kyowa Kirin; travel grants from Kite/Gilead, Amgen, Celgene, Jazz, Pfizer, Bayer and Kyowa Kirin. **OT:** personal fees from Roche, Gilead, Abbvie, Celgene, Janssen, Sandoz and Iquone; travel grants from Roche, Gilead, Abbvie, Celgene and Janssen; institution received patient fees from MorphoSys. **MDH, JW and SA:** employees of MorphoSys AG. **KM:** advisory/consulting fees from Seattle Genetics, Pharmacyclics, Celgene and MorphoSys.

Correspondence

Email: gilles.salles@chu-lyon.fr

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