RE-MIND study: comparison of tafasitamab + lenalidomide (L-MIND) vs lenalidomide monotherapy (real-world data) in transplant-ineligible patients with relapsed/refractory diffuse large B-cell lymphoma

Pier Luigi Zinzani,[1] Thomas Rodgers,[2] Dario Marino,[3] Maurizio Frezzato,[4] Anna Maria Barbui,[5] Claudia Castellino,[6] Erika Meli,[7] Annarita Conconi,[8] Nicola Cascavilla,[9] Federica Cavallo,[10] Nathan H. Fowler,[11] Bruce Feinberg,[12] Sascha Tillmanns,[13] Stephan Parche,[13] Günter Fingerle-Rowson,[13] Mark Winderlich,[13] Sumeet Ambarkhane,[13] Gilles Salles,[14] Grzegorz Nowakowski[15]

[1]Institute of Hematology L e A Seràgnoli, University of Bologna, Bologna, Italy; [2]University of Rochester Medical Center, Rochester, NY, United States;
[3]Medical Oncology 1, Department of Oncology, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy; [4]Azienda ULSS 8 Berica, Vicenza, Italy;
[5]ASST Papa Giovanni XXIII, Bergamo, Italy; [6]Hematology Division, Santa Croce and Carle Hospital, Cuneo, Italy;
[7]ASST Grande Ospedale Metropolitano Niguarda, Dipartimento di Ematologia e Oncologia, S.C. Ematologia, Milan, Italy;
[8]SSD Ematologia, Ospedale degli Infermi di Biella, Ponderano, Italy; [9]Istituto di Ematologia, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy;
[10]Divisione Ematologia dell'Università di Torino, A.O.U. Citta della Salute e della Scienza di Torino, Turin, Italy;
[11]Department of Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, United States;
[12]Cardinal Health Inc., Dublin, OH, United States; [13]MorphoSys AG, Planegg, Germany;
[14]Hématologie, Hospices Civils de Lyon and Université de Lyon, Lyon, France; [15]Division of Hematology, Mayo Clinic, Rochester, MN, United States.

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. Tafasitamab is being developed by MorphoSys and Incyte under a collaboration and license agreement dated January 12, 2020, to further develop and commercialize MorphoSys' proprietary anti-CD19 antibody tafasitamab (MOR208) globally.

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RE-MIND: background

- **Patients with non-transplant-eligible R/R DLBCL have a poor prognosis, with few available treatment options[1]**
- **Tafasitamab is an Fc-enhanced humanized monoclonal anti-CD19 antibody that mediates increased ADCC, ADCP, and direct tumor cytotoxicity[2,3]**
- **Lenalidomide (LEN), an immunomodulatory drug, is active in patients with R/R DLBCL, albeit with modest activity[4–7]**
- **L-MIND (NCT02399085) is an ongoing, open-label, single-arm, Phase II study of tafasitamab + LEN in patients with R/R DLBCL who are ineligible for ASCT[8]**
  - In the primary analysis of L-MIND, the IRC-assessed ORR was 60% with a CR rate of 42.5% and a median DoR of 21.7 months[8]
- **RE-MIND, a global real-world data study of LEN monotherapy, established a matched comparative cohort for the L-MIND study to isolate the contribution of tafasitamab to the tafasitamab + LEN combination[9]**

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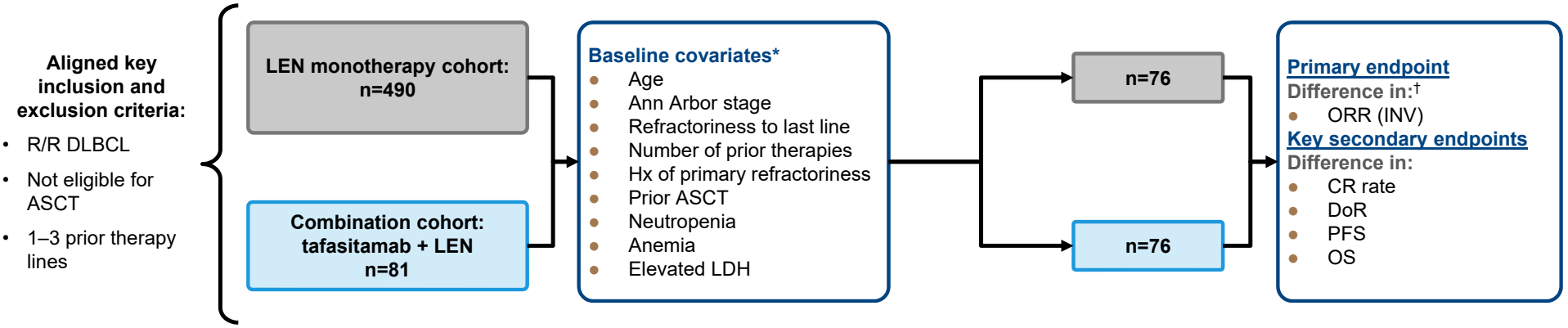
6. Wiernik PH, et al. J Clin Oncol 2008;26(30):4952–7
7. Broccoli A, et al. Oncologist 2019;24(9):1246–52
8. Salles G, et al. ICML 2019 (Abstract 124)
9. Nowakowski G, et al. ASCO 2020 (Abstract 8020)

ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; ASCT, autologous stem cell transplantation; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; IRC, independent review committee; LEN, lenalidomide; ORR, overall response rate; R/R, relapsed/refractory.

RE-MIND: trial design

NCT04150328

- **Inclusion/exclusion criteria were aligned with those of the L-MIND trial[1]**
- **Health record data of 490 patients were retrospectively collected via eCRF**
- **A control cohort for L-MIND comprised 76 patients with a LEN starting dose of 25 mg/day and matching for nine baseline characteristics via 1:1 ePS**
- **Multiple predefined sensitivity analyses, including alternative cohort balancing methodology and applying multiple imputation for missing values, demonstrated the robustness of the comparison**

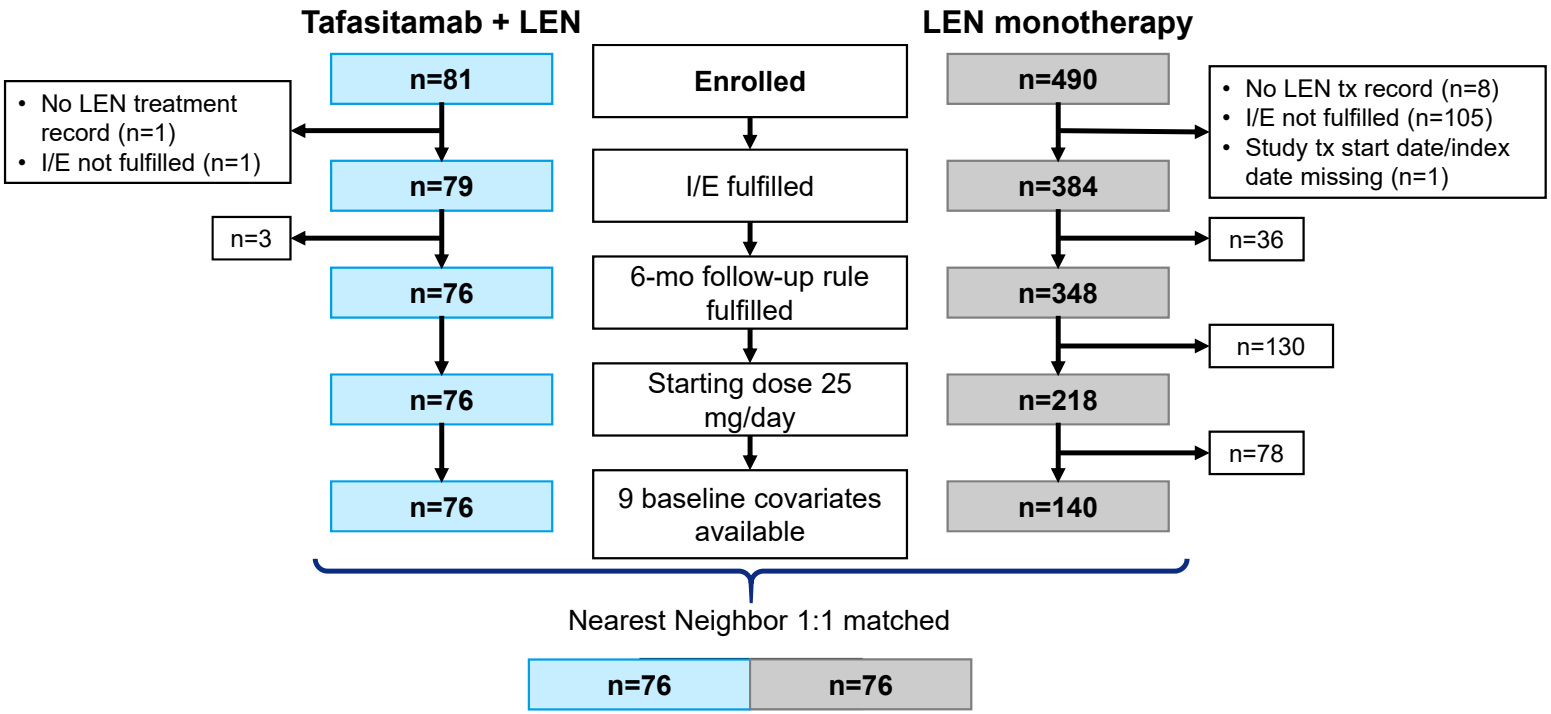


*Age (<70 vs ≥70 years); Ann Arbor stage (I/II vs III/IV); refractoriness to last therapy line (yes vs no); number of prior lines of therapy (1 vs 2 or 3); history of primary refractoriness (yes vs no); prior ASCT (yes vs no); elevated LDH (LDH >ULN vs LDH ≤ULN); neutropenia (ANC <1.5 x 10^9/L vs ANC ≥1.5 x 10^9/L); anemia (Hb <10 g/dL vs Hb ≥10 g/dL). †With an assumed difference of 23% in ORR, the achieved power is 80% and minimal detectable statistical difference is 17% under Fisher's exact test for unpaired data.

ANC, absolute neutrophil count; eCRF, electronic case report form; ePS, estimated propensity score; Hb, hemoglobin; Hx, history; INV, investigator-assessed; LDH, lactate dehydrogenase; OS, overall survival; PFS, progression-free survival; ULN, upper limit of normal.

1. Salles G, et al. ICML 2019 (Abstract 124)

RE-MIND: patient disposition



I/E, inclusion or exclusion criteria; tx, treatment.

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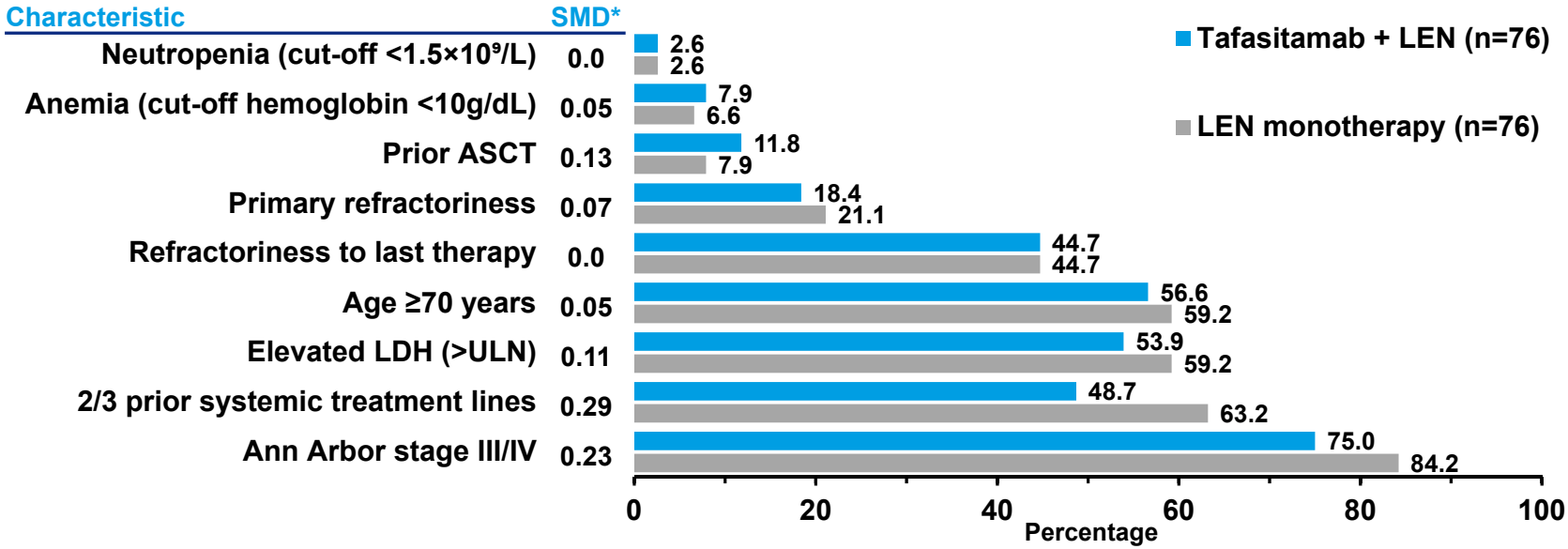
RE-MIND: baseline characteristics used for cohort balancing



Baseline characteristics were well balanced across the lenalidomide monotherapy and combination cohorts after the matching procedure

*SMD is defined as the ratio of the difference of proportions of a baseline characteristic to the standard deviation of the pooled difference. This standardization allows for comparison of the relative balance achieved across different baseline characteristics occurring in a low or high proportion.

SMD, standardized mean difference.

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RE-MIND: comparison of cohort characteristics

	Tafasitamab + LEN n=76	LEN monotherapy n=76
Median lenalidomide dose intensity,* mg/d (range)	17.6 (6.9–25.0)	19.0 (7.3–25.0)
Median follow-up for OS,† months	21.5	20.9
Median time to first post-baseline response assessment, months	1.9	3.1
Median frequency of response assessments, months	2.1	3.2
Imaging modality (CT or PET/CT), %	96	82

Cohort characteristics were comparable

*Cumulative dose divided by exposure time; †Reverse Kaplan–Meier analysis.

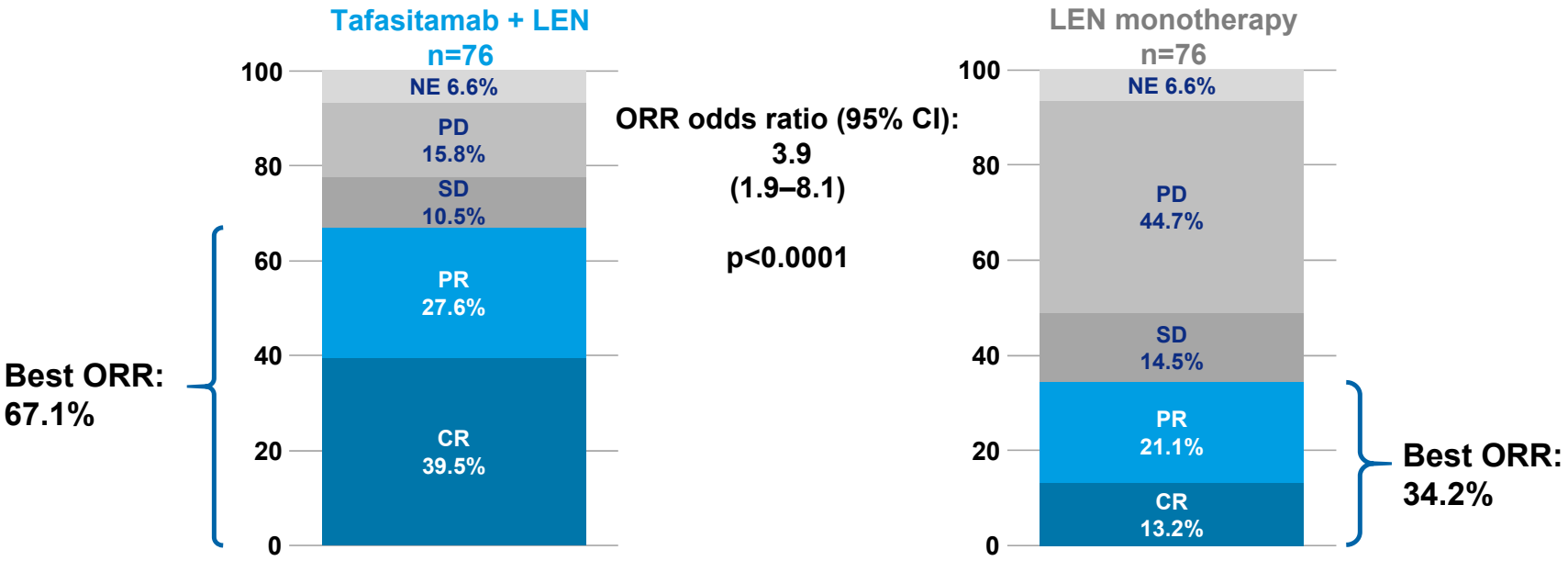
CT, computerized tomography; PET, positron emission tomography.

Nowakowski G, et al. ASCO 2020 (Abstract 8020)

EHA, June 11–14, 2020. Abstract: S238

RE-MIND: best overall response rate (primary endpoint)

Investigator-assessed



The primary endpoint was met:
a significantly better ORR in the combination cohort versus the lenalidomide monotherapy cohort was shown

CI, confidence interval; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

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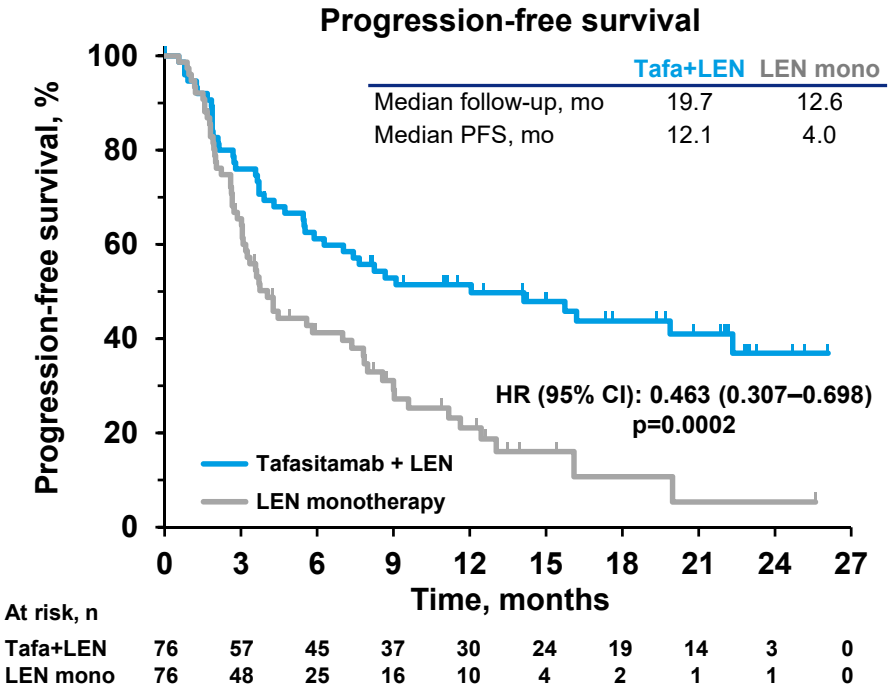
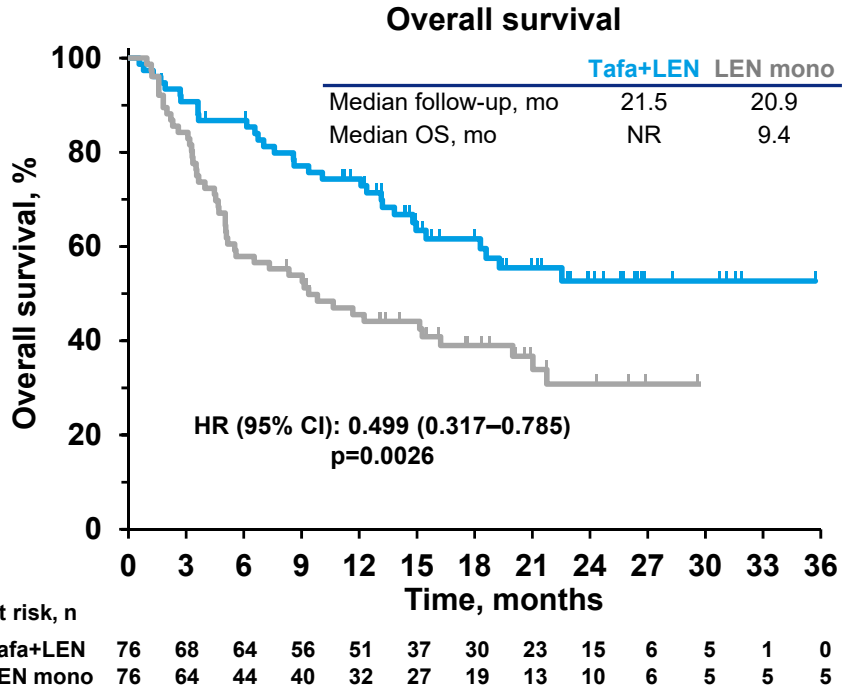
RE-MIND: PFS and OS (secondary endpoints)





Significantly improved clinical efficacy (PFS and OS) was demonstrated for tafasitamab + lenalidomide compared with lenalidomide monotherapy

HR, hazard ratio.

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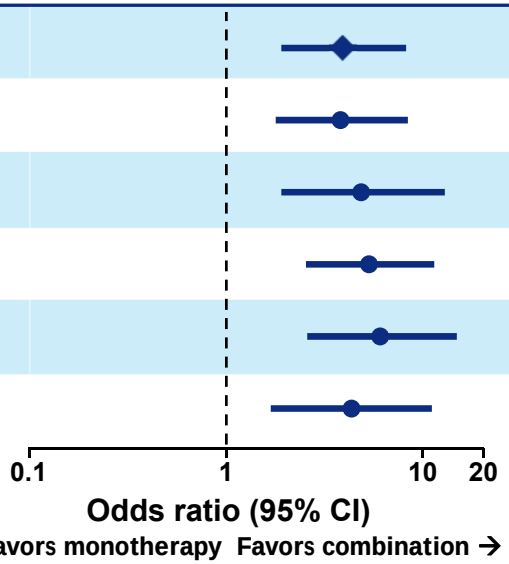
RE-MIND: sensitivity analyses for ORR

Population	LEN mono, n (overlap, %)	Tafa+LEN, n	Odds ratio (95% CI)
Primary analysis	**76 (100)**	**76**	**3.9 (1.9–8.1)**
Higher degree of balance (SMD ≤0.18)	68 (89.5)	68	3.8 (1.8–8.3)
Higher degree of balance (SMD <0.1)	48 (52.6)	48	4.8 (1.9–12.9)
Missing data imputed	76 (63.2)	76	5.3 (2.5–11.4)
Balanced for 10 covariates (+ECOG)	59 (61.8)	59	6.0 (2.6–14.7)
Alternative balancing (weighting)*	140 (NA)	76	4.3 (1.7–11.0)



Sensitivity analyses, including achieving a higher degree of balance, utilizing alternative cohort balancing approaches and applying a multiple imputation technique, confirmed the primary analysis results

*Balancing weight approaches use weights based on the ePS to create a sample in which the distribution of measured baseline covariates is independent of treatment assignment, and estimate the average treatment effect in this population.

ECOG, Eastern Cooperative Oncology Group.

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RE-MIND: summary

- **RE-MIND is a prospectively designed, high-quality real-world data study[1]**
- **Outcomes observed for LEN monotherapy in RE-MIND compare well with published data from clinical trials[2–5]**
- **A robust estimation of the additional treatment effect attributable to tafasitamab in the combination with LEN in transplant-ineligible R/R DLBCL was determined**
- **Tafasitamab + LEN provides significant and clinically meaningful improvements in ORR, CR rate, DoR, and OS compared with LEN monotherapy**
- **Effect sizes in all time-to-event endpoints and all sensitivity analyses support the primary endpoint results**
- **The study provides an important example of the utilization of real-world data to accelerate drug development**

RE-MIND demonstrates the significant contribution of tafasitamab to the efficacy observed in the combination with LEN, which represents a potential therapy option in R/R DLBCL

1. Nowakowski G, et al. ASCO 2020 (Abstract 8020)
2. Witzig TE, et al. Ann Oncol 2011;22(7):1622–7
3. Czuczman MS, et al. Clin Cancer Res 2017;23(15):4127–37
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5. Broccoli A, et al. Oncologist 2019;24(9):1246–52