

inMIND: A Phase 3 Study of Tafasitamab + Lenalidomide Add-on to Rituximab vs Placebo + Lenalidomide Add-on to Rituximab for Relapsed/Refractory (R/R) Follicular Lymphoma (FL) or Marginal Zone Lymphoma (MZL)

Laurie H. Sehn,¹ Christian W. Scholz,² Stefano Luminari,³ Antonio Salar,⁴ Björn E. Wahlin,⁵ Ajay K. Gopal,⁶ Christophe Bonnet,⁷ Marek Trněný,⁸ Shankara Paneesha,⁹ Oliver Manzke,¹⁰ Francis Seguy,¹⁰ Di Li,¹¹ Kai Hübel¹²

¹BC Cancer Centre for Lymphoid Cancer and The University of British Columbia, Vancouver, BC, Canada; ²Department of Hematology and Oncology, Vivantes Klinikum Am Urban, Berlin, Germany; ³Hematology Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy; ⁴Department of Hematology, Hospital del Mar-IMIM, Barcelona, Spain; ⁵Department of Medicine, Unit of Hematology, Karolinska Institute, Stockholm, Sweden; ⁶Division of Medical Oncology, University of Washington Medicine, Seattle, WA, USA; ⁷Clinical Hematology, Centre Hospitalier Universitaire, University of Liège, Liège, Belgium; ⁸First Department of Medicine, First Faculty of Medicine, Charles University, General Hospital, Prague, Czech Republic; ⁹University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; ¹⁰Incyte Biosciences International Sàrl, Morges, Switzerland; ¹¹Incyte Corporation, Wilmington, DE, USA; ¹²Department of Internal Medicine I Oncology and Hematology, University Hospital Cologne, Cologne, Germany

Introduction

- Follicular lymphoma (FL) and marginal zone lymphoma (MZL) are indolent subtypes of non-Hodgkin lymphoma (NHL)¹ that account for 22% and 8% of NHL cases in the Western world, respectively²
 - Most patients respond to first-line treatment but relapse is common, and there is no single standard treatment for patients with relapsed/refractory (R/R) disease^{3,4}
 - Recently approved therapies include R² (rituximab plus lenalidomide [LEN]),⁵ phosphoinositide 3-kinase inhibitors (copanlisib, duvelisib, idelalisib, umbralisib),^{6–9} and EZH2 (enhancer of zeste homolog 2) inhibitor (tazemetostat)¹⁰
 - Additional treatment options with improved clinical outcomes and safety are needed for these patients
- CD19 is broadly expressed in FL and MZL, and regulates B-cell proliferation via B-cell receptor signaling^{11,12}
- Tafasitamab is a humanized anti-CD19 monoclonal antibody (mAb) that is Fc-engineered for increased affinity to Fcγ receptors on immune effector cells
 - Tafasitamab triggers malignant B-cell death by binding to CD19 and inducing direct cytotoxicity as well as by enhancing immune-mediated mechanisms, ie, natural killer cell-mediated antibody-dependent cell-mediated cytotoxicity and macrophage-mediated antibody-dependent cellular phagocytosis
- Tafasitamab demonstrated preclinical activity in NHL cell lines in combination with anti-CD20 mAb rituximab and the immunomodulator LEN¹³
- In the United States, tafasitamab received accelerated approval by the US Food and Drug Administration in combination with LEN for adult patients with R/R diffuse large B-cell lymphoma not otherwise specified, including diffuse large B-cell lymphoma arising from low-grade lymphoma, who are not eligible for autologous stem cell transplant based on data from L-MIND, an ongoing phase 2 single-arm study (NCT02399085)^{14,15}
 - In the primary analysis of L-MIND (November 2018 data cutoff), tafasitamab plus LEN was associated with an objective response rate (ORR) of 60% (95% confidence interval [CI], 48–71)¹⁴
 - In a subsequent analysis (November 2019 data cutoff), after a median follow-up of 31.8 months, the median duration of response (DOR) was 34.6 months (95% CI, 26.1–not reached [NR]) and median overall survival was 31.6 months (95% CI, 18.3–NR)¹⁶
 - In the most recent analysis (October 2020 data cutoff), after a median follow-up of ≥35 months, the median DOR was 43.9 months (95% CI, 26.1–NR)¹⁷
- In a phase 2a study in patients with R/R NHL (NCT01685008), tafasitamab monotherapy was associated with an investigator-assessed ORR of 29% (n/N = 10/34) in patients with FL and 33% (n/N = 3/9) in patients with MZL¹⁸
- These clinical findings, along with preclinical observations, suggest a potential for clinical benefit of tafasitamab plus LEN and rituximab for patients with R/R FL or MZL

Objective

- inMIND is designed to investigate whether tafasitamab plus LEN as an add-on to rituximab provides improved clinical benefit compared with LEN alone as an add-on to rituximab in R/R FL or R/R MZL

Study Design

- inMIND (NCT04680052; EudraCT2020-004407-13) is a global, phase 3, double-blind, placebo-controlled, randomized study in patients with R/R FL of grade 1 to 3a, or R/R MZL
- Approximately 528 R/R FL and 60–90 R/R MZL patients eligible for enrollment will be randomized 1:1 with stratification to receive either:
 - Tafasitamab (12 mg/kg intravenous [IV] on days 1, 8, 15, and 22 of a 28-day cycle [cycles 1–3], then days 1 and 15 [cycles 4–12]) plus LEN (20 mg orally once daily [PO QD; 10 mg PO QD if creatinine clearance ≥30 to <60 mL/min], days 1–21/cycle for 12 cycles), and rituximab (375 mg/m² IV on days 1, 8, 15, and 22 of cycle 1, then day 1 of cycles 2–5)
- OR**
 - Placebo (0.9% saline solution IV) plus LEN and rituximab
- Stratified randomization will be performed separately for patients with R/R FL and R/R MZL

Figure 1. inMIND Study Design

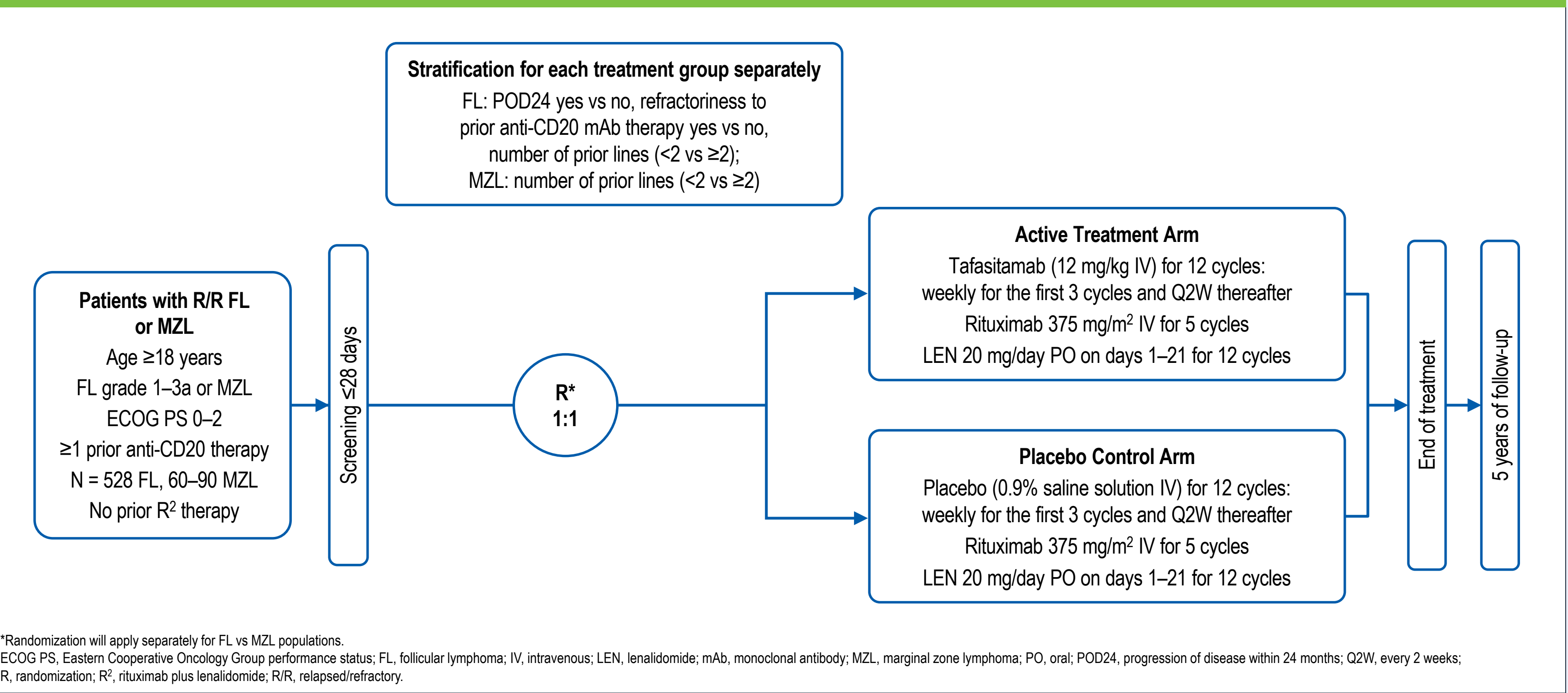


Table 1. Key Patient Eligibility Criteria

Inclusion Criteria
- Age ≥18 years - Histologically confirmed FL (grade 1, 2, or 3a) or MZL (nodal, splenic, or extranodal) - Patients with gastric MZL and evidence of <i>Helicobacter pylori</i> must have documented nonresponse to antibiotic therapy ≥1 prior systemic anti-CD20 therapy (anti-CD20 refractory disease is eligible) - Documented relapsed, refractory, or PD after systemic treatment - Need of treatment for relapsed, refractory, or PD as assessed by the investigator per GELF criteria, with ≥1 measurable lesion - ECOG performance status ≤2 - Adequate hematologic, liver, and renal function
Exclusion Criteria
- NHL histology other than FL or MZL including transformed lymphoma - Prior rituximab plus LEN treatment - History of nonhematologic malignancy - Congestive heart failure (LVEF <50%) - Active systemic infection - Severe immunocompromised state - Known CNS lymphoma

CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; FL, follicular lymphoma; GELF, Groupe d'Etude des Lymphomes Foliculaires; LEN, lenalidomide; LVEF, left ventricular ejection fraction; MZL, marginal zone lymphoma; NHL, non-Hodgkin lymphoma; PD, progressive disease.

Table 2. Key Study Assessments

Assessments	Screening	Treatment Period											EOT (90 Days After Last Dose)	Follow-up Period
	Day -28 to Day -1	Cycle 1 (± 1 Day)				Cycles 2 and 3 (± 1 Day)				Cycle ≥4 (± 2 Days)				
Safety														
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X		
Survival follow-up													X	
Efficacy														
Bone marrow core biopsy	X											X*		
Bone marrow aspirate (for MRD)	X											X		
PET	X											X†		
CT with contrast or MRI	X										X‡,§	X‡,§	X‡	
Quality-of-life questionnaires														
EORTC QLQ-C30, EQ-5D-5L, FACT-Lym		X				X					X	X	X	

*If positive at baseline and at time of radiological CR. †Within 4 (± 2) weeks to confirm a PD per CT/MRI if earlier than EOT. ‡The assessments are performed every 12 (± 2) weeks in year 1, every 16 (± 2) weeks in years 2 and 3, and every 24 (± 3) weeks in years 4 to 6; PET and CT can be combined. §Patients with negative PET at baseline will have a CT scan or MRI only at EOT. ¶Every 6 months after EOT until PD, and 6 months after PD. CR, complete response; CT, computed tomography; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-30; EOT, end of treatment; EQ-5D-5L, EuroQol 5-Dimensional 5-Level Scale; FACT-Lym, Functional Assessment of Cancer Therapy – Lymphoma; MRD, minimum residual disease; MRI, magnetic resonance imaging; PD, progressive disease; PET, positron emission tomography.

Table 3. Key Study Endpoints

Primary endpoint	PFS by investigator assessment in the FL population
Key secondary endpoints	- PFS by investigator assessment in the overall population (FL + MZL) - PET-CR rate at EOT* by investigator in the FL population - OS in the FL population
Other secondary endpoints	- PET-CR rate at EOT* by investigator in the overall population - MRD-negativity rate (at thresholds of 10^{–4} and 10^{–5}) at EOT in the FL and overall population - ORR and DOR by investigator in the FL and overall population - OS in the overall population - HRQoL in the FL and overall population - Safety (incidence and severity of TEAEs) in the FL and overall population

All clinical efficacy endpoints will be assessed based on the Lugano 2014 criteria.¹⁹

*90 days after last dose.
DOR, duration of response; EOT, end of treatment; FL, follicular lymphoma; HRQoL, health-related quality of life; MRD, minimal residual disease; MZL, marginal zone lymphoma; ORR, objective response rate; OS, overall survival; PET-CR, positron emission tomography-complete response; PFS, progression-free survival; TEAE, treatment-emergent adverse event.

Summary

- inMIND (NCT04680052, EudraCT2020-004407-13) is currently enrolling patients, with a planned enrollment of 528 patients with R/R FL and 60–90 patients with R/R MZL**
- Approximately 275 centers in North America, Europe, and Asia Pacific are anticipated to participate in this study**

Disclosures

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 mechanism 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 US Food and Drug Administration in July 2020, tafasitamab is being co-commercialized by MorphoSys and Incyte in the United States. Incyte has exclusive commercialization rights outside the United States. XmAb® is a trademark of Xencor, Inc.

Sehn: Advisory board – AbbVie, Acerta, Apobiologix, AstraZeneca, Celgene, Debiopharm, Genentech, Genmab, Gilead Sciences, Incyte Corporation, Janssen, Karyopharm Therapeutics, Kite Pharma, Lundbeck, Merck, MorphoSys, Novartis, Sandoz, Takeda, TG Therapeutics, Verastem Oncology; Advisory board/research grants – Teva; Advisory board/speakers' bureau – Roche, Seattle Genetics. **Scholz:** Advisory board – Roche. **Luminari:** Advisory board – Bristol Myers Squibb, Genmab, Janssen, Regeneron, Roche. **Salar:** Advisory board – Roche. **Wahlin:** Research grant – Gilead Sciences. **Gopal:** Honoraria – Incyte Corporation, MorphoSys. **Bonnet:** Advisory board – Roche. **Trněný:** Honoraria – AbbVie, Amgen, Bristol Myers Squibb, Gilead Sciences, Incyte Corporation, Janssen, MorphoSys, Roche, Takeda; Consultant/Advisory board – AbbVie, Amgen, Bristol Myers Squibb, Celgene, Gilead Sciences, Incyte Corporation, Janssen, MorphoSys, Roche, Takeda; Travel/Accommodations/Expenses – AbbVie, Bristol Myers Squibb, Gilead Sciences, Janssen, Roche, Takeda. **Paneesha:** Honoraria – Celgene, Roche. **Manzke, Seguy, Li:** Employment and stock ownership – Incyte Corporation. **Hübel:** Advisory board/speakers' bureau – Celgene, EUSA, Gilead Sciences, Incyte Corporation, Roche, Servier.

Acknowledgments

The authors wish to thank the patients, investigators, and site personnel who participate in this study. This study is sponsored by Incyte Corporation (Wilmington, DE). Medical writing assistance was provided by Matthew Bidgood of Envision Pharma Group (Philadelphia, PA), and funded by Incyte Corporation.

References

- Armitage JO, et al. *Lancet*. 2017;390:298–310.
- Thandra KC, et al. *Med Sci (Basel)*. 2021;9:5.
- Lumish M, et al. *J Hematol Oncol*. 2021;14:5.
- Nastoupil LJ. *Curr Hematol Malig Rep*. 2021;16:45–51.
- REVLIMID (lenalidomide) capsules [prescribing information]. Summit, NJ: Celgene Corporation; 2019.
- ALIQOPA (copanlisib) for injection [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; 2020.
- COPIKTRA (duvelisib) capsules [prescribing information]. Needham, MA: Verastem, Inc.; 2019.
- ZYDELIG (idelalisib) tablets [prescribing information]. Foster City, CA: Gilead Sciences, Inc.; 2020.
- UKONIQ (umbralisib) tablets [prescribing information]. Edison, NJ: TG Therapeutics, Inc.; 2021.
- TAZVERIK (tazemetostat) tablets [prescribing information]. Cambridge, MA: Epizyme, Inc.; 2020.
- Cheson BD, et al. *Blood Cancer J*. 2021;11:68.
- Kost CB, et al. *Cytometry B Clin Cytom*. 2008;74:282–286.
- Data on file. MorphoSys AG (Planegg, Germany).
- Salles G, et al. *Lancet Oncol*. 2020;21:978–988.
- MONJUVI (tafasitamab-cxix) for injection [prescribing information]. Boston, MA: MorphoSys US Inc.; 2020.
- Jurczak W, et al. *Ann Oncol*. 2018;29:1266–1272.
- Duell J, et al. *Haematologica*. 2021 Jul 1. doi: 10.3324/haematol.2020.275958. Online ahead of print.
- Maddocks KJ, et al. *Blood*. 2020;136(Suppl. 1):19–21.
- Cheson BD, et al. *J Clin Oncol*. 2014;32:3059–3068.



Scan code to download a copy of the poster.