A Phase Ib, Open-Label, Randomized Study to Assess Safety and Preliminary Efficacy of Tafasitamab (MOR208) or Tafasitamab + Lenalidomide in Addition to R-CHOP in Patients with Newly Diagnosed Diffuse Large B-cell Lymphoma (DLBCL): Preliminary Data

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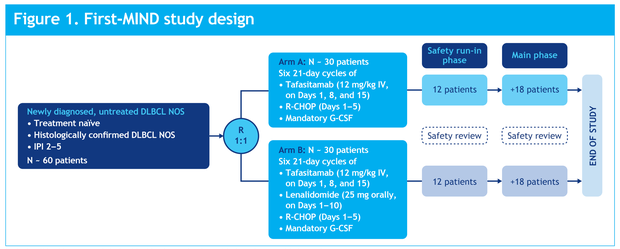
Background

- R-CHOP (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisolone) is the standard of care for newly diagnosed diffuse large B-cell lymphoma (DLBCL), with cure rates of 60–70%[1]
- However, there remains an unmet need for more effective front-line treatment options for high-risk patients[1]
- Approximately 15–20% of treatment-naïve patients with DLBCL have CD20-low-expressing tumors, which are associated with poor response to rituximab-based regimens[2,3]
- CD19 is widely expressed in B-cell malignancies and functions as a positive regulator of B-cell receptor signaling, which is important for B-cell activation and proliferation and survival[4–6]
- CD19 is expressed in ~90% of DLBCL cases,[2] and is therefore an attractive therapeutic target in addition to CD20[5,6]
- Tafasitamab (MOR208) is a humanized anti-CD19 monoclonal antibody with an engineered constant Fc region that enhances antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP), and can also cause cell death directly[6]
- Tafasitamab is approved by the FDA in combination with lenalidomide for adult patients with relapsed or refractory DLBCL not otherwise specified (NOS), including DLBCL arising from low-grade lymphoma, and for those who are not eligible for autologous stem cell transplant, under accelerated approval based on overall response rate (ORR)[7]
- First-MIND is an open-label, prospective, randomized, Phase Ib study designed to evaluate the safety and preliminary efficacy of tafasitamab or tafasitamab + lenalidomide in addition to R-CHOP in patients with newly diagnosed DLBCL (**Figure 1**)
- Enrollment is now complete and the study is ongoing. Here we report preliminary study data as of the 23 Sept 2020 data cut-off

Figure 1. First-MIND study design



In the lenalidomide arm, prophylaxis with either low-molecular weight heparins or aspirin is mandatory.
DLBCL, diffuse large B-cell lymphoma; G-CSF, granulocyte-colony stimulating factor; IPI, international prognostic index; IV, intravenous; NOS, not otherwise specified; R, randomized; R-CHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisolone.

Methods

Study details

- Recruitment of 66 patients took place across 34 sites in the US and Europe from Dec 2019 to August 2020
- The study consists of two phases (**Figure 1**):
  1. Safety run-in phase: regular safety reviews by a safety committee consisting of study investigators, including a meeting by an independent safety and data monitoring board (iDSMB) when the first 24 patients, 12 in each arm, reached Cycle 2
  2. Main phase: enrollment of remaining patients, approximately 18 in each arm, as no new safety signals were observed in either arm

Key eligibility criteria

- Patients had confirmed diagnosis of DLBCL NOS by a local pathologist, at least one measurable disease site, Eastern Cooperative Oncology Group (ECOG) performance status 0–2, international prognostic index status 2–5, and were eligible candidates for R-CHOP
- Patients were excluded from the study if they had any other histological type of lymphoma according to WHO 2016 classification of lymphoid neoplasms, known double- or triple-hit lymphoma, transformed non-Hodgkin's lymphoma (NHL) or evidence of composite lymphoma, history of radiation therapy to ≥25% of the bone marrow for other diseases, history of anthracycline therapy, known central nervous system (CNS) involvement, or active hepatitis B/C infection

Endpoints

- Primary endpoint is the incidence and severity of treatment-emergent adverse events (TEAEs)
- Key secondary endpoints: ORR and PET-negative complete response (CR) rate at the end of treatment, as assessed by Lugano 2014 classification[8]
  - Other secondary endpoints include long-term safety and efficacy, pharmacokinetics and immunogenicity

Results

- Of 83 patients screened, 17 failed to meet the inclusion criteria and 66 underwent randomization (full analysis set); 33 were allocated to each treatment arm. Enrollment is complete
  - Data cut-off for this analysis: 23 Sept 2020
- Baseline characteristics were balanced between the treatment arms (**Table 1**)
- **Table 2** shows the patient distribution per treatment cycle at the time of the data cut-off
- At data cut-off, one patient in arm A had discontinued treatment due to AEs whilst there were no discontinuations due to AEs in arm B
  - One patient discontinued the study treatment in Cycle 2 due to grade 2 myocarditis suspected to be related to R-CHOP (doxorubicin). This patient received further treatment with R-COMP with liposomal doxorubicin (Myocet) outside of the clinical trial
  - One patient discontinued the study treatment after Cycle 6 (Day 8) due to a grade 4 AE (depression suicidal), not related to study treatment

Table 1. Baseline characteristics

Characteristic		Arm A: Tafasitamab + R-CHOP (n=33)	Arm B: Tafasitamab + lenalidomide + R-CHOP (n=33)	Total (N=66)
Age at screening (years)	Median	66.0	64.0	64.5
	Min, Max	43, 86	20, 79	20, 86
Age categories at screening (years), n (%)	<60	12 (36.4)	11 (33.3)	23 (34.8)
	≥60	21 (63.6)	22 (66.7)	43 (65.2)
Sex, n (%)	Male	15 (45.5)	13 (39.4)	28 (42.4)
	Female	18 (54.5)	20 (60.6)	38 (57.6)
Pre-planned radiotherapy at screening, n (%)	Yes	4 (12.1)	4 (12.1)	8 (12.1)
	No	29 (87.9)	29 (87.9)	58 (87.9)
Pre-planned CNS prophylaxis with IV methotrexate, n (%)	Yes	6 (18.2)	8 (24.2)	14 (21.2)
	No	27 (81.8)	25 (75.8)	52 (78.8)
Pre-planned CNS prophylaxis with intrathecal chemotherapy, n (%)	Yes	7 (21.2)	3 (9.1)	10 (15.2)
	No	26 (78.8)	30 (90.9)	56 (84.8)
Ann Arbor disease stage, n (%)	Stage I	2 (6.1)	1 (3.0)	3 (4.5)
	Stage II	0	1 (3.0)	1 (1.5)
	Stage III	6 (18.2)	7 (21.2)	13 (19.7)
	Stage IV	24 (72.7)	24 (72.7)	48 (72.7)
	Missing	1 (3.0)	0	1 (1.5)
IPI risk score, n (%)	IPI 2	10 (30.3)	9 (27.3)	19 (28.8)
	IPI 3	14 (42.4)	15 (45.5)	29 (43.9)
	IPI 4	8 (24.2)	9 (27.3)	17 (25.8)
	IPI 5	0	0	0
	Missing	1 (3.0)	0	1 (1.5)
Bulky disease >10 cm, n (%)	Present	15 (45.5)	15 (45.5)	30 (45.5)
	Absent	17 (51.5)	18 (54.5)	35 (53.0)
	Missing	1 (3.0)	0	1 (1.5)
ECOG at baseline, n (%)	ECOG 0	20 (60.6)	10 (30.3)	30 (45.5)
	ECOG 1	10 (30.3)	20 (60.6)	30 (45.5)
	ECOG 2	3 (9.1)	3 (9.1)	6 (9.1)

CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; IPI, international prognostic index; IV, intravenous; R-CHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisolone.

Table 2. Treatment cycles – Ongoing study, data cut-off 23 Sept 2020

Treatment cycles, n (%)	Arm A: Tafasitamab + R-CHOP (n=33)	Arm B: Tafasitamab + lenalidomide + R-CHOP (n=33)	Total (N=66)
Total number of patients entered into:			
Cycle 1	32 (97.0)*	33 (100)	65 (98.5)
Cycle 2	29 (87.9)	30 (90.9)	59 (89.4)
Cycle 3	28 (84.8)	30 (90.9)	58 (87.9)
Cycle 4	23 (69.7)	23 (69.7)	46 (69.7)
Cycle 5	16 (48.5)	21 (63.6)	37 (56.1)
Cycle 6	13 (39.4)	14 (42.4)	27 (40.9)

*The safety analysis set does not include data for one patient in arm A because their data were not entered in the eCRF at the time of the data cut-off.
eCRF, electronic Case Report Form; R-CHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisolone.

Safety results

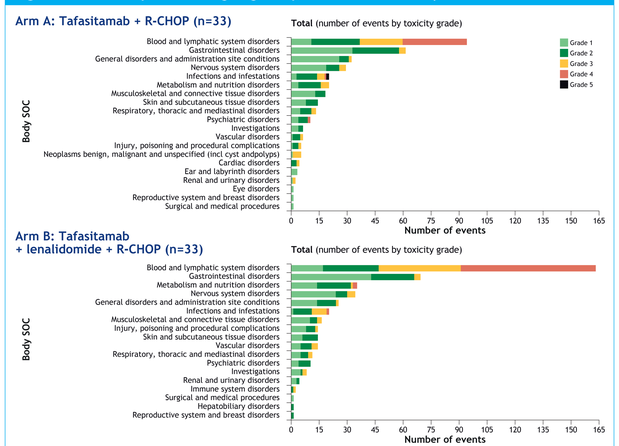
- At the data cut-off, 65 patients (98.5%) had experienced TEAEs (**Table 3**); of these, grade 3 or higher TEAEs were seen in 50 patients (75.8%; 23 patients [69.7%] in arm A and 27 [81.8%] in arm B)
- Serious TEAEs were experienced by 29 patients in total (43.9%), 13 in arm A and 16 in arm B (**Table 3**)
- The most frequent events by system organ class (SOC) were blood and lymphatic system disorders, experienced by 25 patients in each arm (75.8%)
  - More blood and lymphatic system disorder events occurred in arm B than arm A (163 vs 94), with a higher incidence of grade ≥3 events (116 vs 57 in arm B vs arm A) (**Figure 2**)
  - This was driven by a higher rate of neutropenia and thrombocytopenia with lenalidomide than without
  - Ten patients [30.3%] vs three patients [9.1%] had thrombocytopenia), of whom eight patients (24.2%) with lenalidomide experienced grade ≥3 events compared with two patients without (6.1%) (**Table 4, Figure 3**)
- In arm A, three patients (9.1%) had febrile neutropenia compared with four patients (12.1%) in arm B (**Table 4**)
- Six (18.2%) and seven (21.2%) patients experienced a grade 3 or higher infection event in arms A and B, respectively
  - One patient died due to a urinary tract infection in arm A, considered unrelated to the study treatment
- Infusion-related reactions (IRRs) with any study treatment occurred in four patients (12.1%) in each arm, which for one patient (3.0%) in arm B was grade ≥3 (**Table 4**)
- No new safety signals were identified with either tafasitamab + R-CHOP or tafasitamab + lenalidomide + R-CHOP in patients with newly diagnosed DLBCL compared with previous Phase III studies with tafasitamab, R-CHOP, or R2-CHOP[9–11]

Table 3. Summary of TEAEs – Ongoing study, data cut-off 23 Sept 2020

Overall summary by toxicity grade, n (%) [E]	Arm A: Tafasitamab + R-CHOP (n=33)	Arm B: Tafasitamab + lenalidomide + R-CHOP (n=33)	Total (N=66)
Patients with TEAEs and the total number of events	32* (97.0) [345]	33 (100) [443]	65 (98.5) [788]
Grade 1	26 (78.8) [140]	27 (81.8) [161]	53 (80.3) [301]
Grade 2	27 (81.8) [120]	28 (84.8) [135]	55 (83.3) [255]
Grade 3	21 (63.6) [48]	22 (66.7) [72]	43 (65.2) [120]
Grade 4	13 (39.4) [36]	19 (57.6) [75]	32 (48.5) [111]
Grade 5	1 (3.0) [1]	0	1 (1.5) [1]
Grade 3 or higher	23 (69.7) [85]	27 (81.8) [147]	50 (75.8) [232]
Overall summary of serious TEAEs, n (%) [E]	**Arm A: Tafasitamab + R-CHOP (n=33)**	**Arm B: Tafasitamab + lenalidomide + R-CHOP (n=33)**	**Total (N=66)**
Patients with serious TEAEs and the total number of events	13 (39.4) [28]	16 (48.5) [27]	29 (43.9) [55]

*The safety analysis set does not include data for one patient in arm A because their data were not entered in the eCRF at the time of the data cut-off.
E, events; R-CHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisolone; TEAEs, treatment-emergent adverse events.

Figure 2. TEAEs by SOC – Ongoing study, data cut-off 23 Sept 2020



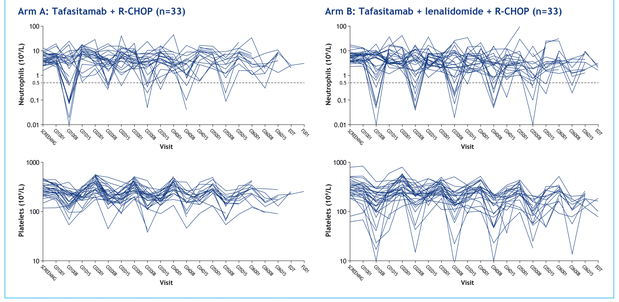
R-CHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisolone; SOC, system organ class; TEAE, treatment-emergent adverse events.

Table 4. Adverse events of interest – Ongoing study, data cut-off 23 Sept 2020

Adverse event, n (%) [E]		Arm A: Tafasitamab + R-CHOP (n=33)	Arm B: Tafasitamab + lenalidomide + R-CHOP (n=33)	Total (N=66)
Neutropenia	Any grade	15 (45.5) [39]	19 (57.6) [64]	34 (51.5) [103]
	Grade 3 or higher	14 (42.4) [32]	19 (57.6) [52]	33 (50.0) [84]
Anemia	Any grade	14 (42.4) [27]	10 (30.3) [22]	24 (36.4) [49]
	Grade 3 or higher	5 (15.2) [7]	6 (18.2) [10]	11 (16.7) [17]
Thrombocytopenia	Any grade	3 (9.1) [7]	10 (30.3) [29]	13 (19.7) [36]
	Grade 3 or higher	2 (6.1) [3]	8 (24.2) [18]	10 (15.2) [21]
Pulmonary embolism	Any grade	1 (3.0) [1]	1 (3.0) [1]	2 (3.0) [2]
	Grade 3 or higher	1 (3.0) [1]	1 (3.0) [1]	2 (3.0) [2]
Deep vein thrombosis	Any grade	1 (3.0) [1]	1 (3.0) [1]	2 (3.0) [2]
	Grade 2	1 (3.0) [1]	1 (3.0) [1]	2 (3.0) [2]
Febrile neutropenia	Any grade	3 (9.1) [3]	4 (12.1) [5]	7 (10.6) [8]
	Grade 3 or higher	3 (9.1) [3]	4 (12.1) [5]	7 (10.6) [8]
Diarrhea	Any grade	7 (21.2) [8]	9 (27.3) [17]	16 (24.2) [25]
	Grade 3 or higher	1 (3.0) [1]	0	1 (1.5) [1]
Tumor lysis syndrome (TLS)	Any grade	1 (3.0) [1]	0	1 (1.5) [1]
	Grade 3 or higher	1 (3.0) [1]	0	1 (1.5) [1]
Infections	Any grade	13 (39.4) [20]	16 (48.5) [20]	29 (43.9) [40]
	Grade 3 or higher	6 (18.2) [6]	7 (21.2) [9]	13 (19.7) [15]
	Pneumonia (any grade)	0	2 (6.1) [2]	2 (3.0) [2]
Infusion-related reaction (with any treatment)	Any grade	4 (12.1) [4]	4 (12.1) [6]	8 (12.1) [10]
	Grade 3 or higher	0	1 (3.0) [1]	1 (1.5) [1]

E, events; R-CHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisolone.

Figure 3. Absolute neutrophil and platelet counts by cycle – Ongoing study, data cut-off 23 Sept 2020



R-CHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisolone.

Conclusions

- Preliminary data from this ongoing study suggest R-CHOP can be combined with tafasitamab or tafasitamab + lenalidomide in patients with newly diagnosed treatment-naïve DLBCL
- Grade 3 or higher neutropenia and thrombocytopenia events were more frequent in arm B than arm A; events were manageable and the average relative dose intensity of R-CHOP was maintained (**Figures 2** and **3**, **Table 4**)
- The incidence of febrile neutropenia was comparable between both arms
- The incidence of other TEAEs was generally comparable between the two treatment arms – the safety profiles were as would be expected for R-CHOP alone[9] or in combination with lenalidomide (R2-CHOP),[10,11] with no new safety signals observed
- These early data from our ongoing study are encouraging and warrant further investigation

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Disclosures

About Monjuvi® (tafasitamab-cxix)

Monjuvi 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 License Agreement to further develop and commercialize Monjuvi globally. Monjuvi will be co-commercialized by Incyte and MorphoSys in the United States. Incyte has exclusive commercialization rights outside the United States. XmAb® is a trademark of Xencor, Inc.

DB – consultancy: Gilead, Janssen, Roche, Takeda; research funding: Celgene; membership of an entity: Gilead, Janssen, Roche, Takeda. **GN** – consultancy – Celgene, MorphoSys, Ryvu, Kite, Kymera, Curis, Seattle Genetics; research funding: Celgene, MorphoSys, NanoString; membership of an entity: Ryvu. **JB** – no disclosures. **MA** – employment: CHU UCL Namur; consultancy: Takeda, Bristol-Myers Squibb, Karyopharm, Gilead, Novartis, Seattle Genetics, Abbvie; research funding: Novartis, Roche, Amgen, Johnson & Johnson, Celgene; travel grants: Roche, Bristol-Myers Squibb, Amgen, Celgene, Gilead. **KK** – no disclosures. **DS** – consultancy: Amgen, MorphoSys. **MT** – employment: First Faculty of Medicine, Charles University General Hospital, Prague; consultancy: Takeda, Bristol-Myers Squibb, Incyte, AbbVie, Amgen, Roche, Gilead, Janssen, Celgene, MorphoSys; honoraria: Janssen, Gilead, Takeda, Bristol-Myers Squibb, Amgen, AbbVie, Roche, MorphoSys, Incyte. **EP** – consultancy: Celgene, Roche, Janssen, Amgen, Abbvie, Takeda; speakers bureau: Celgene, Roche, Janssen, Abbvie. **PP** – no disclosures. **PK** – employment: MorphoSys. **BB** – employment: MorphoSys. **EL** – employment: MorphoSys. **AL** – employment: MorphoSys. **NS** – employment: MorphoSys. **GF** – employment: MorphoSys. **WB** – employment: MorphoSys. **JMB** – consultancy: Gilead, Bristol-Myers Squibb, Roche, AbbVie, Bayer, Astra Zeneca, Verastem, MorphoSys, Adaptive, Epizyme, Kura, Celgene, Adaptive Biotechnologies; speakers bureau: Seattle Genetics.

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Footnotes and references

*The safety analysis set does not include data for one patient in arm A because their data were not entered in the eCRF at the time of the data cut-off.

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