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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Disclosures

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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.

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First-MIND: Background and introduction

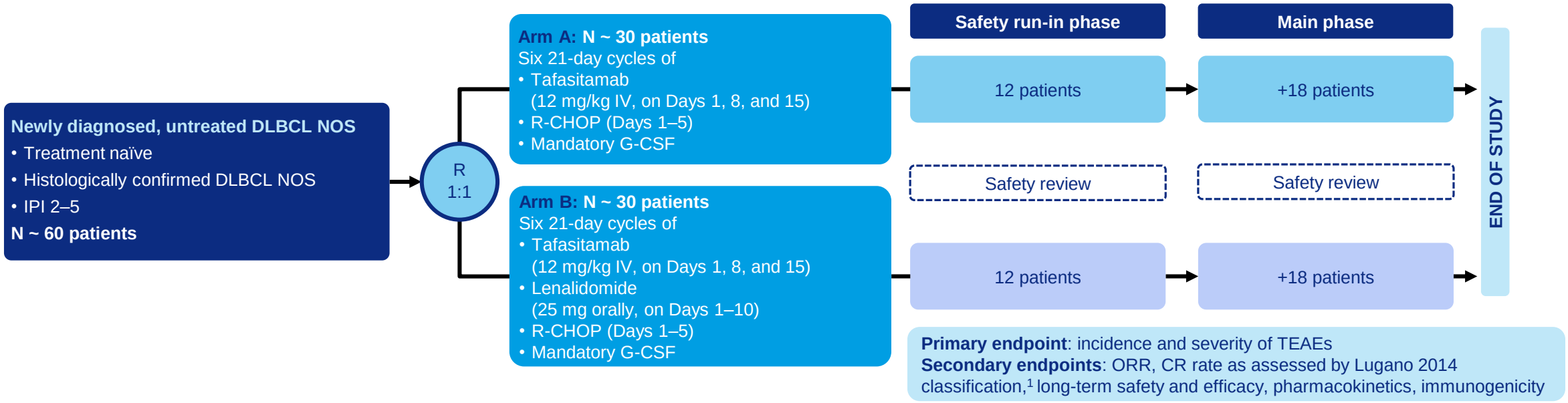
- R-CHOP is the standard of care for newly diagnosed DLBCL, with cure rates of 60–70%[1]
- However, there remains an unmet need for more effective front-line treatment options for high-risk patients[1]
- Approximately 14–17% of treatment-naïve patients with DLBCL have CD20-low-expressing tumors, which are associated with poor response to rituximab-based regimens[2,3]
- CD19 is expressed in ~90% DLBCL cases,[2] and is therefore an attractive therapeutic target in addition to CD20[4,5]
- Tafasitamab (MOR208) is a humanized anti-CD19 monoclonal antibody that enhances ADCC and ADCP, and can also cause cell death directly[5]
- Tafasitamab is approved by the FDA in combination with lenalidomide for adult patients with relapsed or refractory DLBCL NOS, including DLBCL arising from low-grade lymphoma, and who are not eligible for ASCT[6]
- Here we present safety data from the ongoing study with a cut-off date 23 Sept 2020

ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis;
ASCT, autologous stem cell transplantation; DLBCL, diffuse large B-cell lymphoma;
NOS, not otherwise specified;
R-CHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisolone.

1. Sehn LH, Gascoyne RD. Blood 2015;125:22–32;
2. Johnson NA, et al. Blood 2009;113:3773–80;
3. Prevodnik VK, et al. Diagnostic Pathol 2011;6:33;
4. Woyach JA, et al. Blood 2014;124:3553–60;
5. Jurczak W, et al. Ann Oncol 2018;29:1266–72;
6. Monjuvi (tafasitamab) US PI. Aug 2020.

First-MIND: Study design

- 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



In the lenalidomide arm, prophylaxis with either low-molecular weight heparins or aspirin is mandatory.

CR, complete response; G-CSF, granulocyte-colony stimulating factor;
IPI, international prognostic index; IV, intravenous; ORR, overall response rate; R, randomized;
TEAEs, treatment-emergent adverse events.

1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68.

First-MIND: Baseline characteristics

From Dec 2019 to August 2020, 83 patients were screened and 66 underwent randomization; 33 were allocated to each treatment arm

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 CT, 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.

First-MIND: Treatment cycles received at data cut-off

- All patients entered into the first treatment cycle* and 82% (54/66) of patients are still on treatment
  - At the data cut-off, 3 patients had discontinued treatment early, 1 patient had discontinued treatment, 1 patient died and 7 patients had completed the entire treatment including the end of treatment PET-CT
- At data cut-off, two patients in arm A had discontinued treatment due to AEs, while 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

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.

First-MIND: Summary of TEAEs

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]

- Overall, 98.5% of patients experienced TEAEs; of these, 75.8% were grade 3 or higher
- Serious TEAEs were experienced by 29 patients in total (43.9%), 13 patients in arm A and 16 in arm B (39.4% vs 48.5%)
- No new safety signals were identified with either tafasitamab + R-CHOP or tafasitamab + lenalidomide + R-CHOP compared with previous Phase III studies with R-CHOP or R2-CHOP[1–3]

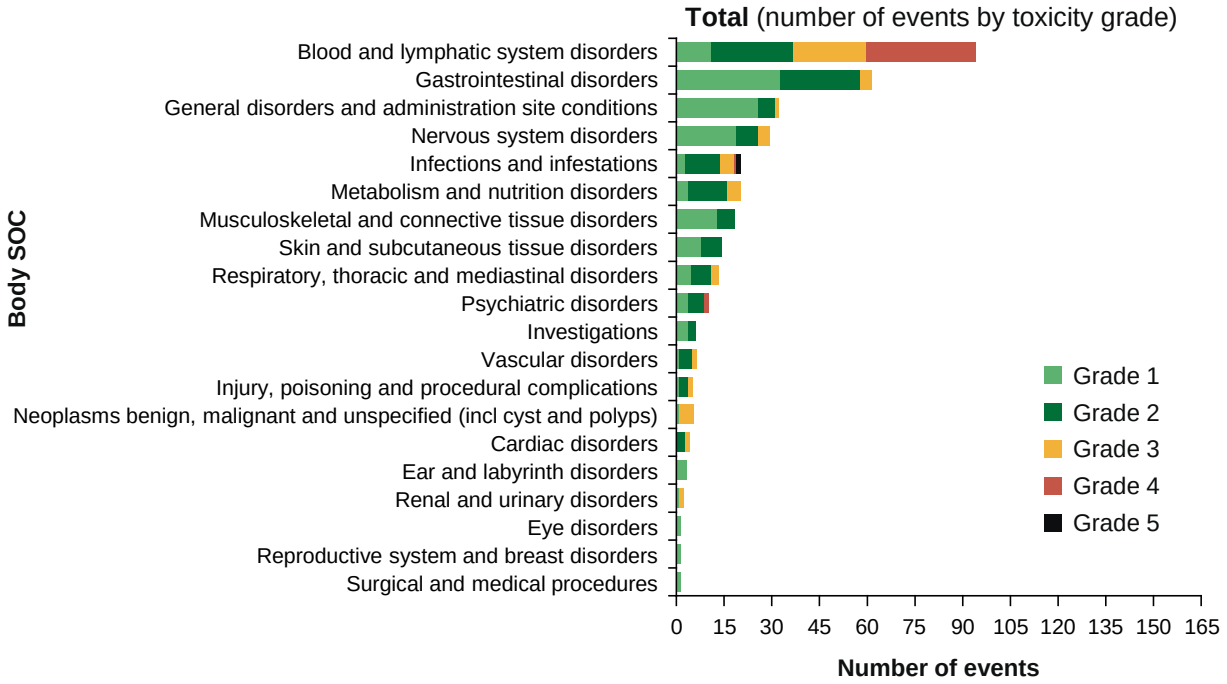
*The safety analysis set does not include data for one patient in arm A because their data were not entered in the eCRF at the time of the data cut-off.
E, events.

1. Sehn LH, et al. Blood 2019;134(Supplement_1):4088;
2. Vitolo U, et al. Hematol Oncol 2019;37:36–7;
3. Nowakowski GS, et al. Presented at ICML 2019. Article no. 006.

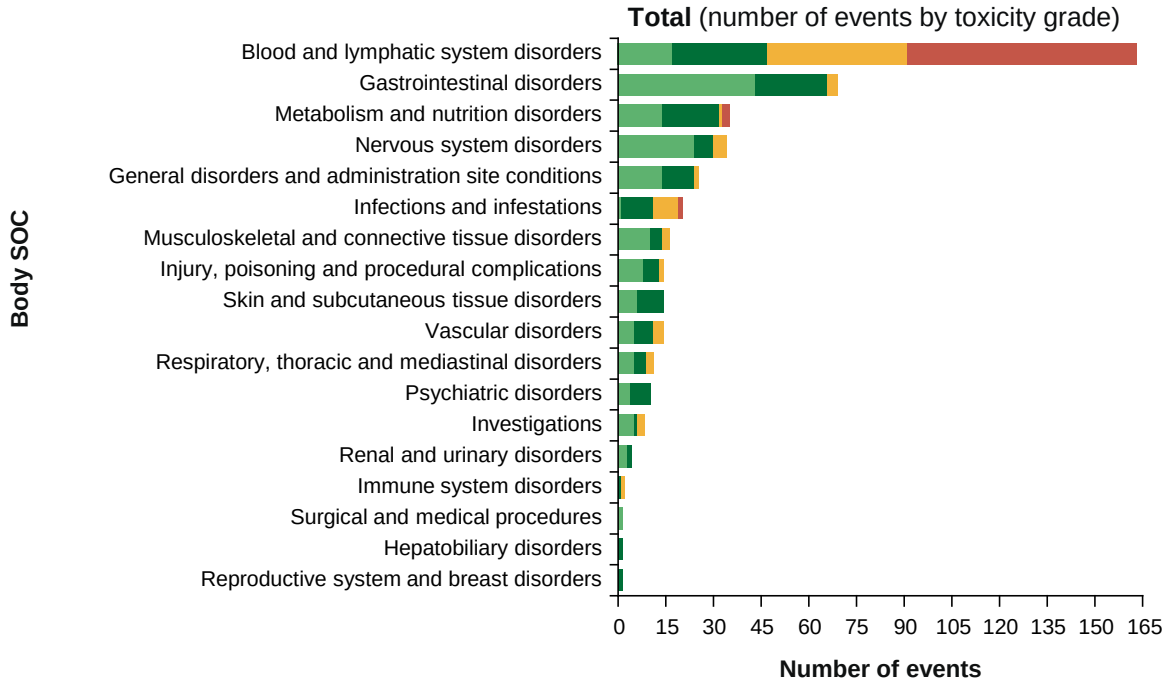
First-MIND: TEAEs by SOC

- The most frequent events by 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)

Arm A: Tafasitamab + R-CHOP (n=33)



Arm B: Tafasitamab + lenalidomide + R-CHOP (n=33)

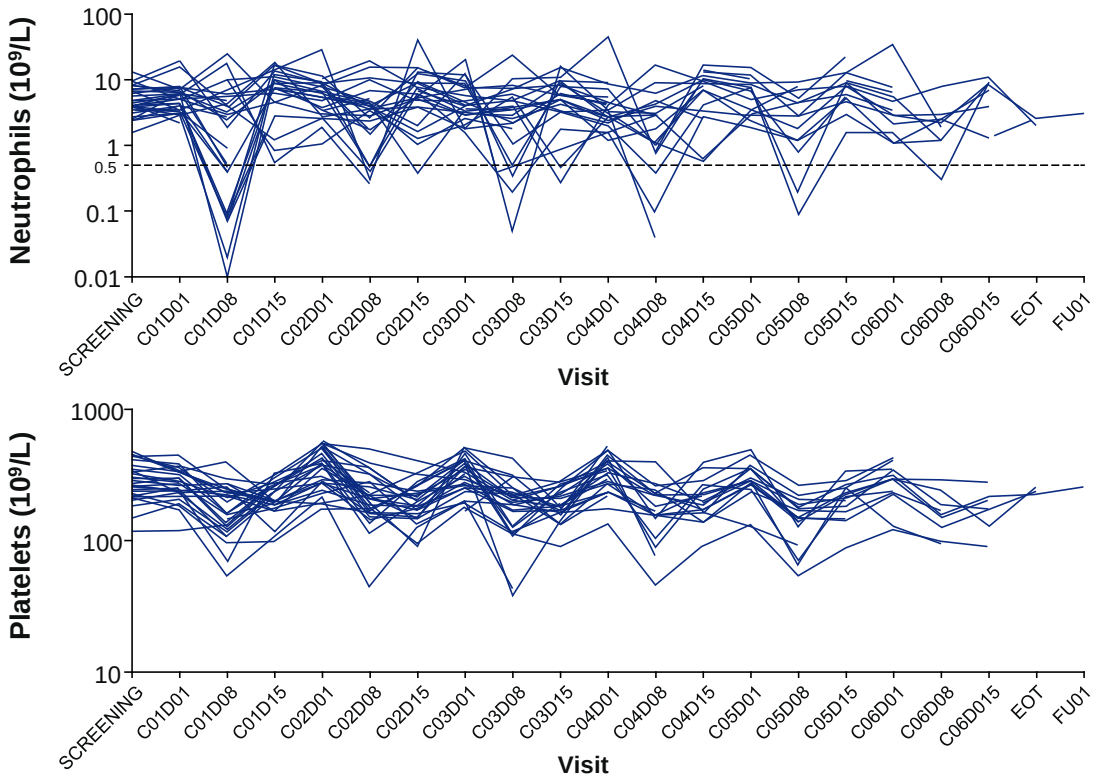


SOC, system organ class.

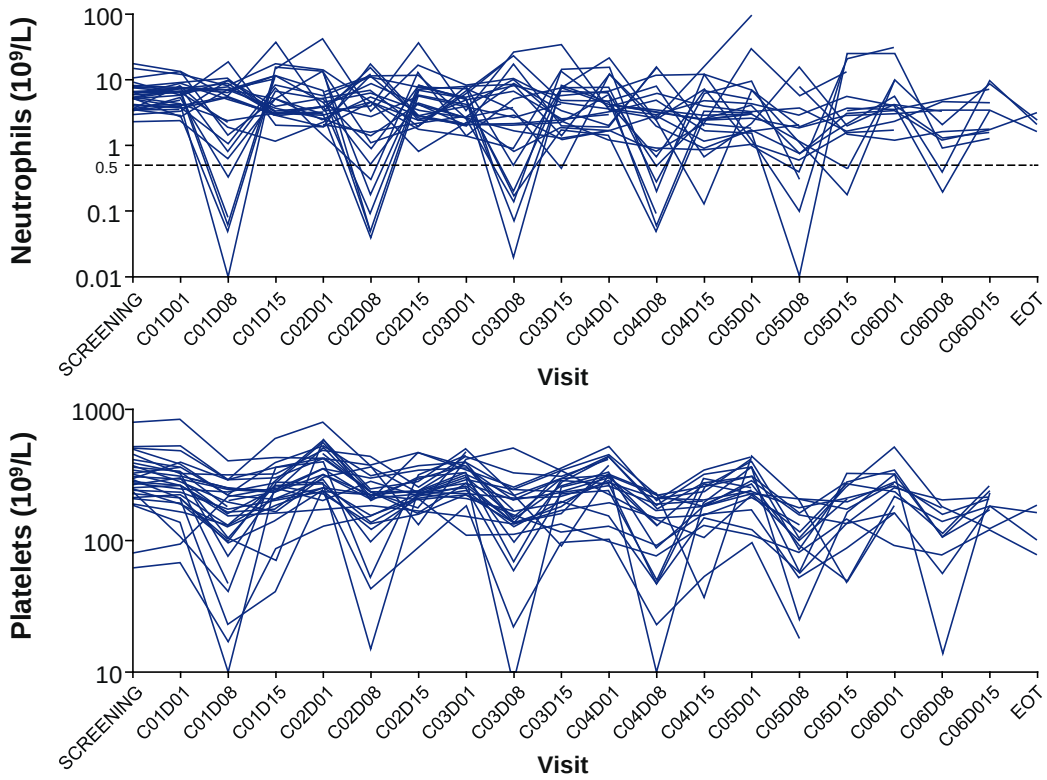
First-MIND: Absolute neutrophil and platelet counts by cycle

- The higher rate of blood and lymphatic system disorder events in arm B was driven by a higher incidence of neutropenia and thrombocytopenia with lenalidomide than without
- Ten patients [30.3%] vs three patients [9.1%] had thrombocytopenia. Of these patients, eight (24.2%) experienced grade ≥3 events with lenalidomide compared with two patients without (6.1%)

Arm A: Tafasitamab + R-CHOP (n=33)



Arm B: Tafasitamab + lenalidomide + R-CHOP (n=33)



First-MIND: Adverse events of interest

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

- In arm A, three patients (9.1%) had febrile neutropenia compared with four patients (12.1%) in arm B
- Grade 3 or higher infection events were experienced by six (18.2%) and seven (21.2%) patients in arm A and B, respectively
  - One patient died due to a urinary tract infection in arm A, considered unrelated to the study treatment

First-MIND: 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
- The incidence of TEAEs was generally comparable between the two treatment arms, with no new safety signals observed to those expected with R-CHOP alone[1] or in combination with lenalidomide (R2-CHOP)[2,3]
- 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
- The incidence of febrile neutropenia was comparable between both arms
- Interim response assessments after 3 cycles were available in 45 patients (68.2%). In total, in both arms combined 41/45 (91.1%) had an objective response as per Lugano 2014[4]
- These early data from our ongoing study are encouraging and warrant further investigation

1. Sehn LH, et al. Blood 2019;134(Supplement_1):4088;
2. Vitolo U, et al. Hematol Oncol 2019;37:36–7;
3. Nowakowski GS, et al. Presented at ICML 2019. Article no. 006;
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