Five-year efficacy and safety of tafasitamab in patients with relapsed or refractory DLBCL: Final results from the Phase II L-MIND study

Nagesh Kalakonda, MBBS, MRCP, FRCPath, PhD

Dept of Molecular and Clinical Cancer Medicine, University of Liverpool, Liverpool, United Kingdom

Johannes Duell,[1*] Pau Abrisqueta,[2] Marc Andre,[3] Marinela Augustin,[4] Gianluca Gaidano,[5] Eva González Barca,[6] Wojciech Jurczak,[7] Nagesh Kalakonda,[8] Anna Marina Liberati,[9] Kami J Maddocks,[10] Tobias Menne,[11] Zsolt Nagy,[12] Olivier Tournilhac,[13] Abhishek Bakuli,[14] Aasim Amin,[14] Konstantin Gurbanov,[14] Gilles Salles[15]

[1]Medizinische Klinik und Poliklinik II, Universitätsklinik Würzburg, Würzburg, Germany; [2]Department of Hematology, Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, Barcelona, Spain; [3]Department of Hematology, CHU UCL Namur, Yvoir, Belgium; [4]Department of Hematology and Oncology, Klinikum Nuernberg, Paracelsus Medical University, Nuernberg, Germany; [5]Division of Hematology, Department of Translational Medicine, University of Eastern Piedmont, Novara, Italy; [6]Institut Català d'Oncologia, Hospital Duran i Reynals, IDIBELL, Universitat de Barcelona, Barcelona, Spain; [7]Department of Clinical Oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Kraków, Poland; [8]Department of Molecular and Clinical Cancer University of Liverpool, Liverpool, United Kingdom; [9]Università degli Studi di Perugia, Azienda Ospedaliera Santa Maria di Terni, Terni, Italy; [10]Department of Internal Medicine, Arthur G James Comprehensive Cancer Center, Ohio State University Wexner Medical Center, Columbus, OH, USA; [11]Freeman Hospital, The Newcastle upon Tyne Hospitals, Newcastle upon Tyne, UK; [12]Semmelweis University, Budapest, Hungary; [13]CHU de Clermont-Ferrand, Clermont Ferrand, France; [14]MorphoSys AG, Planegg, Germany; [15]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA.

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- This presentation is a faithful reformatting of the congress oral presentation titled *Five-year efficacy and safety of tafasitamab in patients with relapsed or refractory DLBCL: Final results from the Phase II L-MIND study* presented on Sunday, April 16, 2023, at AACR 2023. Reformatting performed with permission
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Disclosure Information

Nagesh Kalakonda

I have the following relevant financial relationships to disclose:

- Employee of: University of Liverpool, Liverpool, UK and Clatterbridge Cancer Centre NHS Foundation Trust, Liverpool, UK
- Consultant for: None
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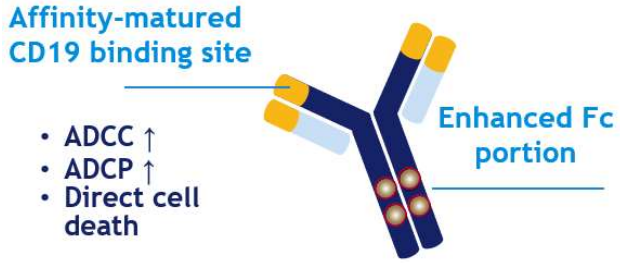
Introduction and Objective

- 1L SoC in patients with newly diagnosed DLBCL is six cycles of R-CHOP,[1] but 30–40% will have R/R disease[1,2]
- In R/R setting, many patients are ineligible for options such as HDC, ASCT, CAR-T therapy due to advanced age or comorbidities[2–4]
- Effective treatment options in 2L and beyond are much needed in patients with R/R DLBCL

Tafasitamab
Anti-CD19 monoclonal antibody immunotherapy



Tafasitamab + LEN* was effective and well tolerated in ASCT-ineligible patients with R/R DLBCL, in the **Phase II L-MIND study**[1]

	Primary 1-year analysis	3-year† analysis
ORR, %	60.0	57.5
CR, %	43.0	40.0
mDoR, months	21.7	43.9
mOS, months	NR	33.5

Objective: report final, **5-year efficacy and safety of tafasitamab + LEN** in the L-MIND study

*Tafasitamab + LEN was granted accelerated approval in the US (July 2020) and conditional marketing authorization in Europe (August 2021)[5,6]
†3-year analysis refers to ≥35 months
2L, second line; ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; ASCT, autologous stem cell transplantation; CAR-T, chimeric antigen receptor T-cell; CR, complete response; DLBCL, diffuse large B–cell lymphoma; mDoR, median duration of response; HDC, high-dose chemotherapy; LEN, lenalidomide; NR, not reached; ORR, objective response rate (ORR = CR + partial response [PR]); mOS, median overall survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; R/R, relapsed or refractory; SoC, standard of care.
1. Sarkozy C, Sehn LH. Ann Lymphoma 2019;310; 2. Crump M, et al. Blood 2017;130(16):1800–8; 3. Duell J, et al. Haematologica 2021;106(9):2417–26; 4. Sarkozy C, Coiffier B. Clin Cancer Res 2013;19(7):1660–9; 5. MONJUVI. Prescribing information. Boston, MA: MorphoSys. 2020 [Accessed March 2023]; 6. European Medicines Agency. SmPC Minjuvi. 2021 [Accessed March 2023].

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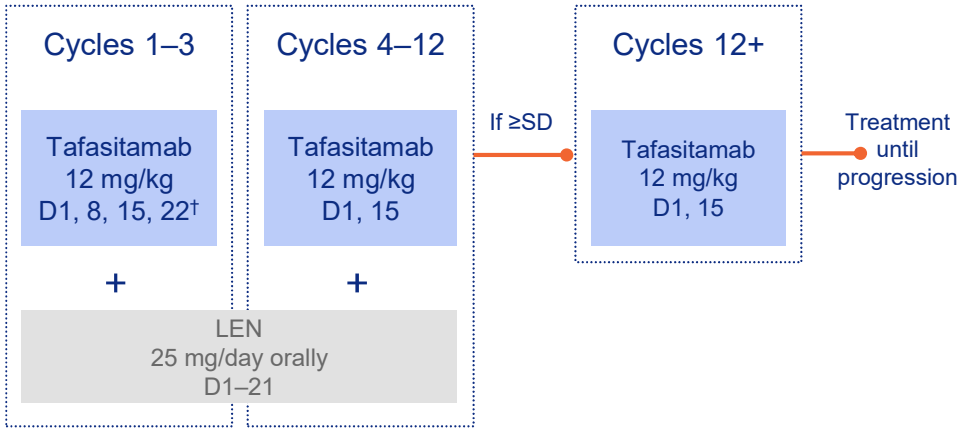
L-MIND: Study Design

Open-label, single-arm, multicenter, global, Phase II study; **N=81**

- R/R DLBCL
- Not eligible for ASCT
- 1–3 prior regimens
- Patients with primary refractory disease were not eligible*
- ECOG PS 0–2



Primary endpoint
- ORR (central read)

Secondary endpoints
- PFS
- DoR
- OS
- Safety

Exploratory and biomarker-based assays

NCT02399085[1]

*Primary refractory is defined as no response to, or progression/relapse during/within 6 months of, front-line therapy; 15 patients with refractory disease were included under an early version of the protocol.
†A loading dose of tafasitamab was administered on Day 4 of Cycle 1.
ASCT, autologous stem cell transplantation; D, days; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; LEN, lenalidomide; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed or refractory; SD, stable disease.

1. ClinicalTrials.gov NCT02399085 (accessed Apr 2023).

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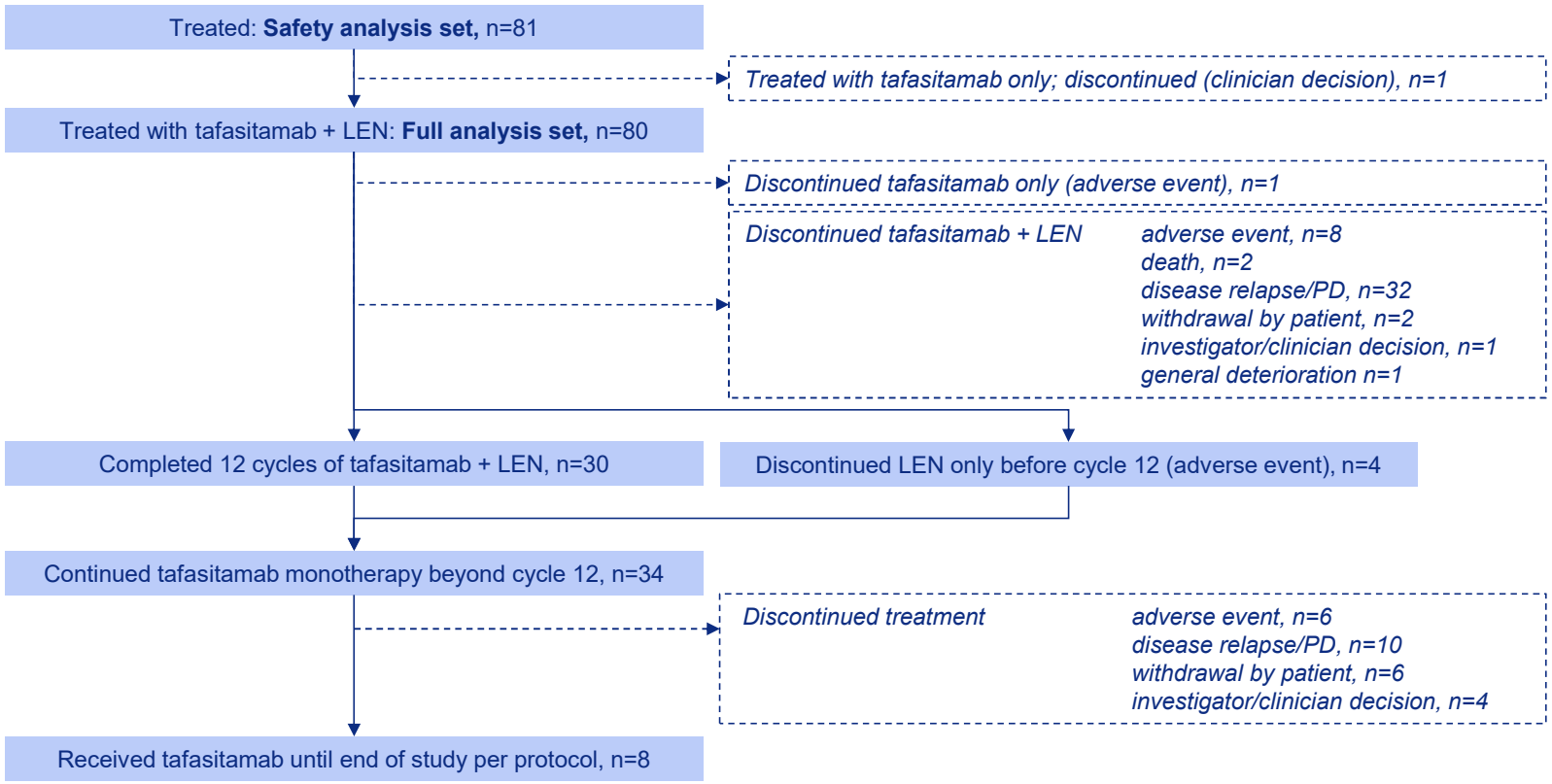
L-MIND: Patient Disposition



LEN, lenalidomide; PD, progressive disease.

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L-MIND: Baseline Characteristics

		All patients (FAS)	1 pLoT	≥2 pLoT
N		80	40	40
Median age, years (range)		72.0 (41.0–86.0)	72.0 (53.0–86.0)	70.5 (41.0–82.0)
Age >70 years, n (%)		45 (56.2)	25 (62.5)	20 (50.0)
Sex, n (%)	Female	37 (46.2)	19 (47.5)	18 (45.0)
	Male	43 (53.8)	21 (52.5)	22 (55.0)
Ann Arbor stage, n (%)	I–II	20 (25)	11 (27.5)	9 (22.5)
	III–IV	60 (75)	29 (72.5)	31 (77.5)
IPI score, n (%)	0–2	40 (50)	25 (62.5)	15 (37.5)
	3–5	40 (50)	15 (37.5)	25 (62.5)
Elevated LDH, n (%)	Yes	44 (55.0)	18 (45.0)	26 (65.0)
	No	36 (45.0)	22 (55.0)	14 (35.0)
Primary refractory*, n (%)	Yes	15 (18.8)	6 (15.0)	9 (22.5)
	No	65 (81.2)	34 (85.0)	31 (77.5)
Refractory to previous therapy line, n (%)	Yes	35 (43.8)	6 (15.0)	29 (72.5)
	No	45 (56.2)	34 (85.0)	11 (27.5)
Prior ASCT, n (%)	Yes	9 (11.2)	2 (5.0)	7 (17.5)
	No	71 (88.8)	38 (95.0)	33 (82.5)
Cell of origin (by IHC), n (%)	GCB	38 (47.5)	16 (40.0)	22 (55.0)
	Non-GCB	22 (27.5)	14 (35.0)	8 (20.0)
	Unknown / NE	20 (25.0)	10 (25.0)	10 (25.0)

*Primary refractory is defined as no response to, or progression/relapse during or within 6 months of, front-line therapy.
ASCT, autologous stem cell transplantation; FAS, full analysis set; GCB, germinal-center B-cell; IHC, immunohistochemistry; IPI, International Prognostic Index; LDH, lactate dehydrogenase; NE, not evaluable; pLoT, prior line of therapy.

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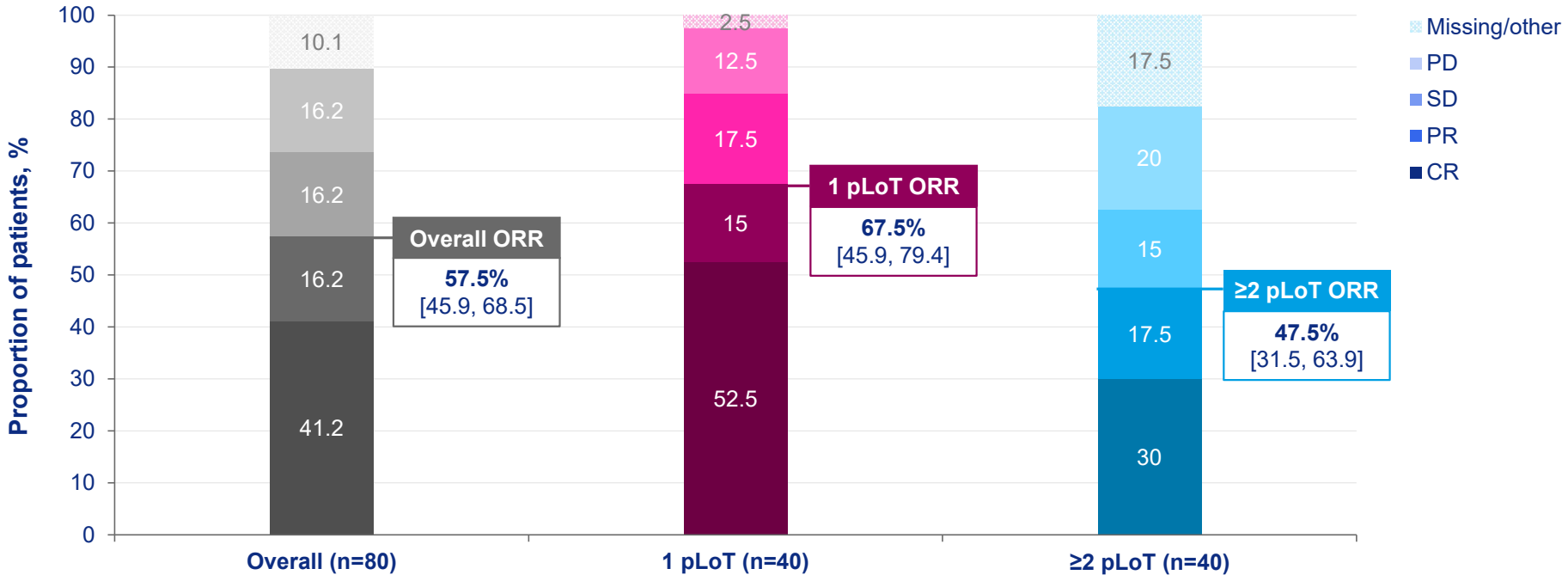
Efficacy Results: Best Response at 5-year Follow-up



CR, complete response; ORR, objective response rate; PD, progressive disease; pLoT, prior line of therapy; PR, partial response; SD, stable disease.

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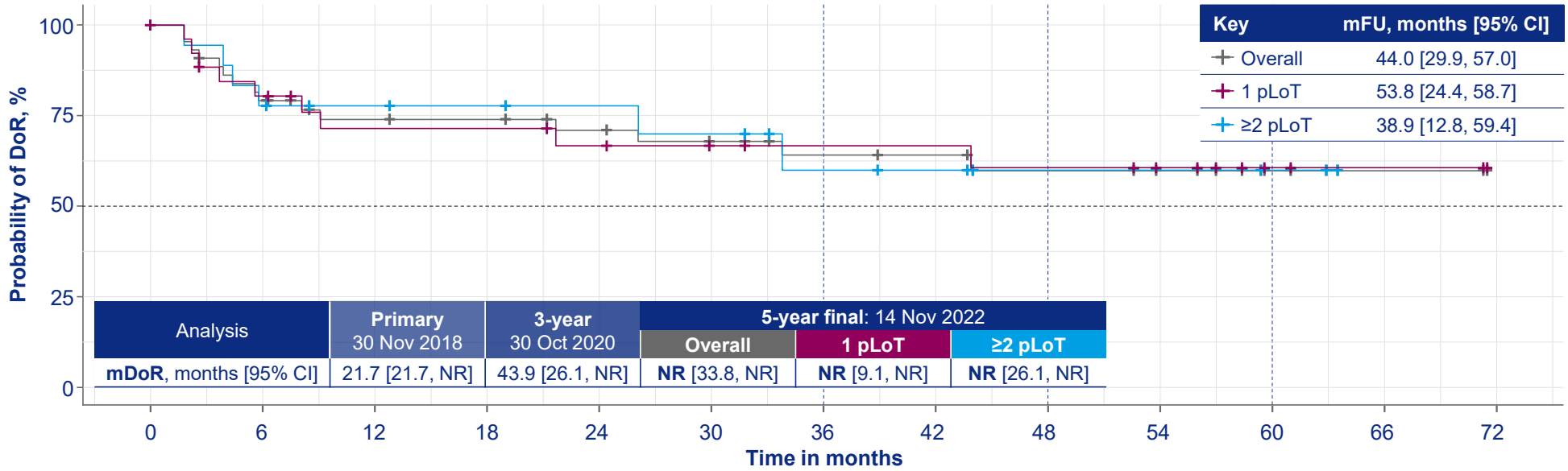
Efficacy Results: DoR at 5-year Follow-up



Number at risk:

Overall	46	34	28	27	24	21	17	16	13	11	5	2	0
1 pLoT	27	20	16	16	14	12	11	11	10	8	3	2	0
≥2 pLoT	19	14	12	11	10	9	6	5	3	3	2	0	0

DoR, duration of response; mDoR, median DoR; mFU, median follow-up; NR, not reached; pLoT, prior line of therapy.

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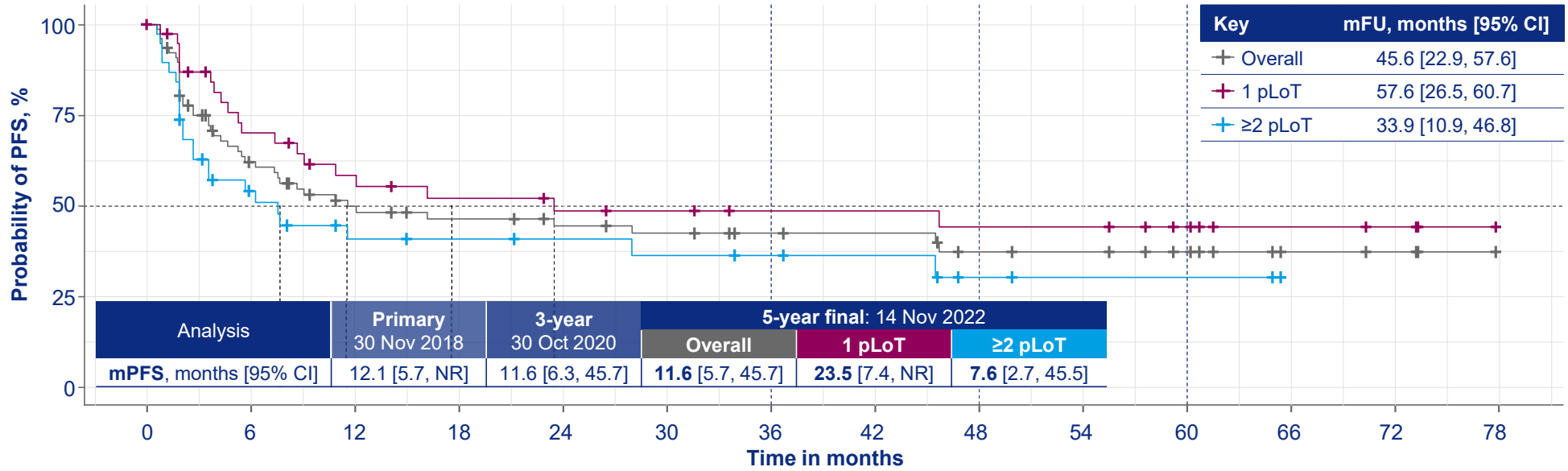
Efficacy Results: PFS at 5-year Follow-up



Number at risk:

Overall	80	42	30	26	23	21	18	17	13	12	9	4	3	0
1 pLoT	40	25	19	16	14	13	11	11	10	10	7	4	3	0
≥2 pLoT	40	17	11	10	9	8	7	6	3	2	2	0	0	0

mFU, median follow-up; mPFS, median PFS; NR, not reached; PFS, progression-free survival; pLoT, prior line of therapy.

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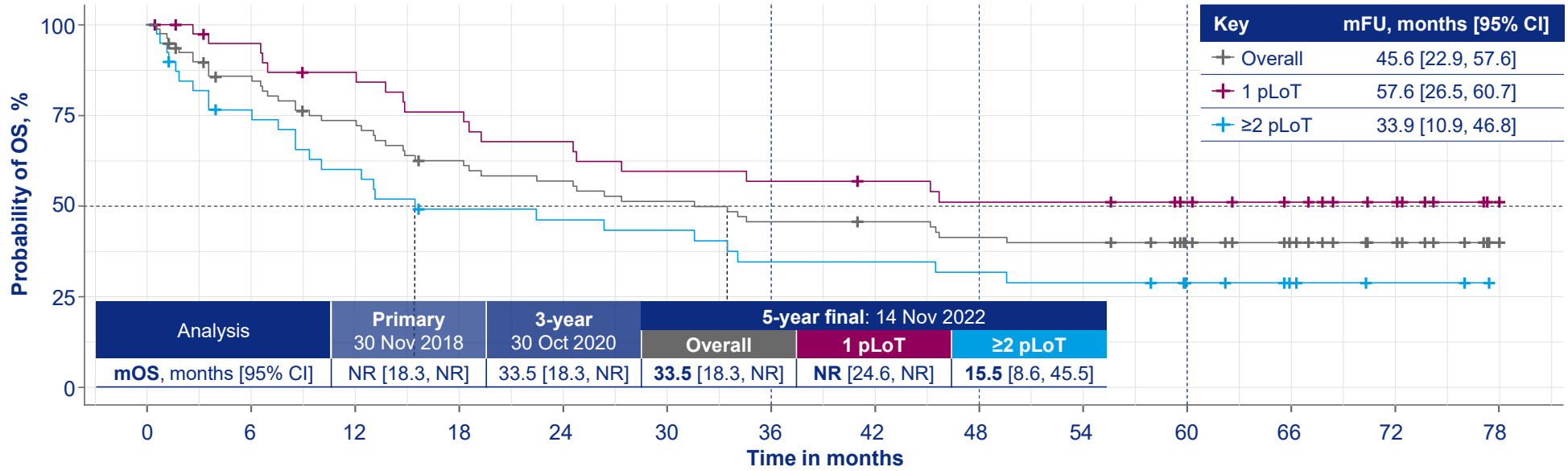
Efficacy Results: OS at 5-year Follow-up



Number at risk:

Overall	80	64	54	45	41	37	33	32	29	28	21	15	9	1
1 pLoT	40	36	32	28	25	22	21	20	18	18	14	11	7	1
≥2 pLoT	40	28	22	17	16	15	12	12	11	10	7	4	2	0

mFU, median follow-up; mOS, median OS; NR, not reached; OS, overall survival; pLoT, prior line of therapy.

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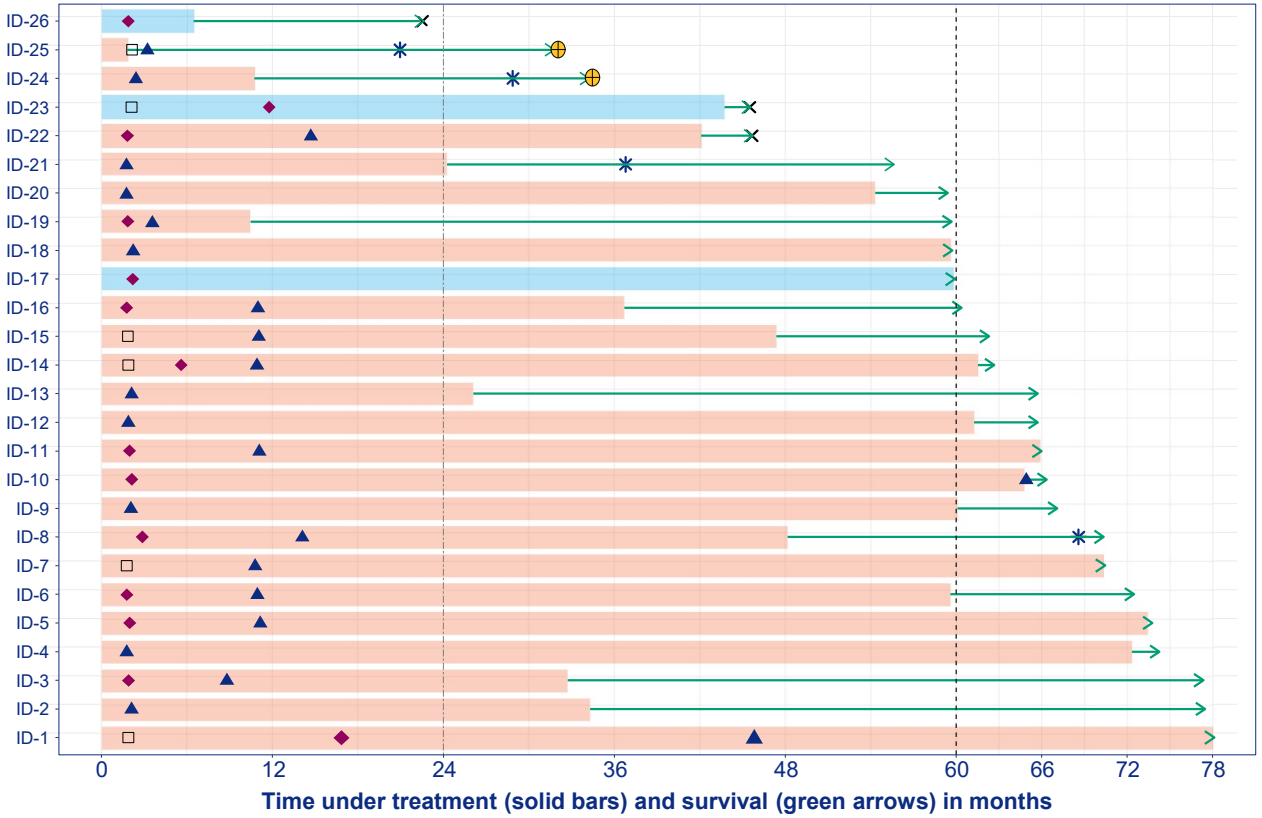
Efficacy Results: Patients who ended treatment with response (n=26)



Outcomes*
- Complete Response
- Partial Response
- Stable Disease
- Death from progressive disease
- Death from other reasons
- Next anti-lymphoma therapy

Best Response
- Complete Response
- Partial Response

*Repeat assessments giving the same outcome as previous assessment are not shown

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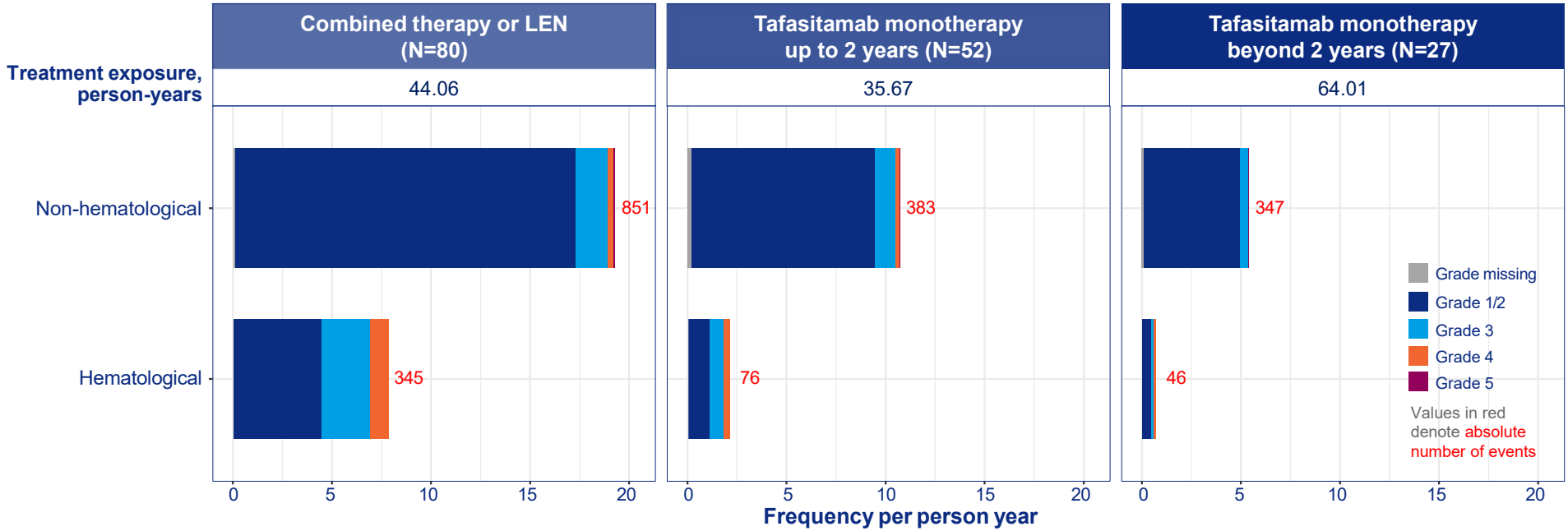
Safety Results: Exposure-Adjusted Comparison of TEAE Frequency across Treatment Periods

TEAE Summary



CTCAE grading system.
LEN, lenalidomide; TEAE, treatment-emergent adverse event.

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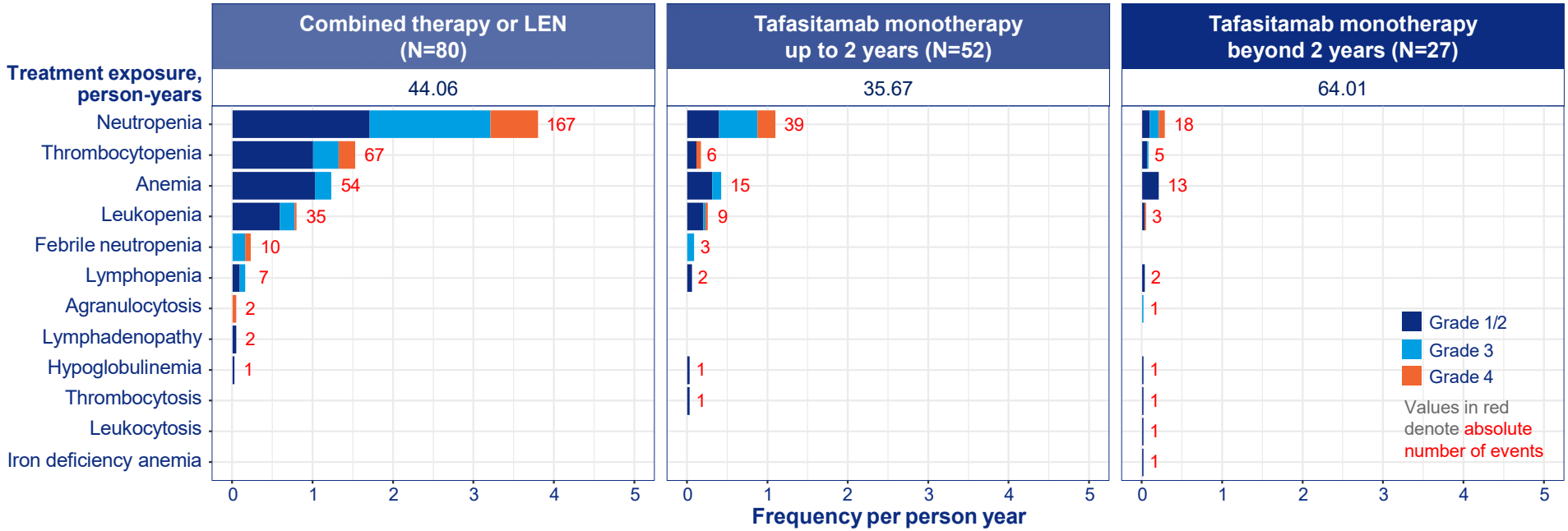
Safety Results: Exposure-Adjusted Comparison of TEAE Frequency across Treatment Periods

Hematological TEAEs



- Hematological TEAEs were less frequent during tafasitamab monotherapy compared with tafasitamab + LEN combination therapy
- The low incidence of TEAEs with tafasitamab monotherapy up to 2 years was maintained or further reduced from 2 years onwards

CTCAE grading system.
LEN, lenalidomide; TEAE, treatment-emergent adverse event.

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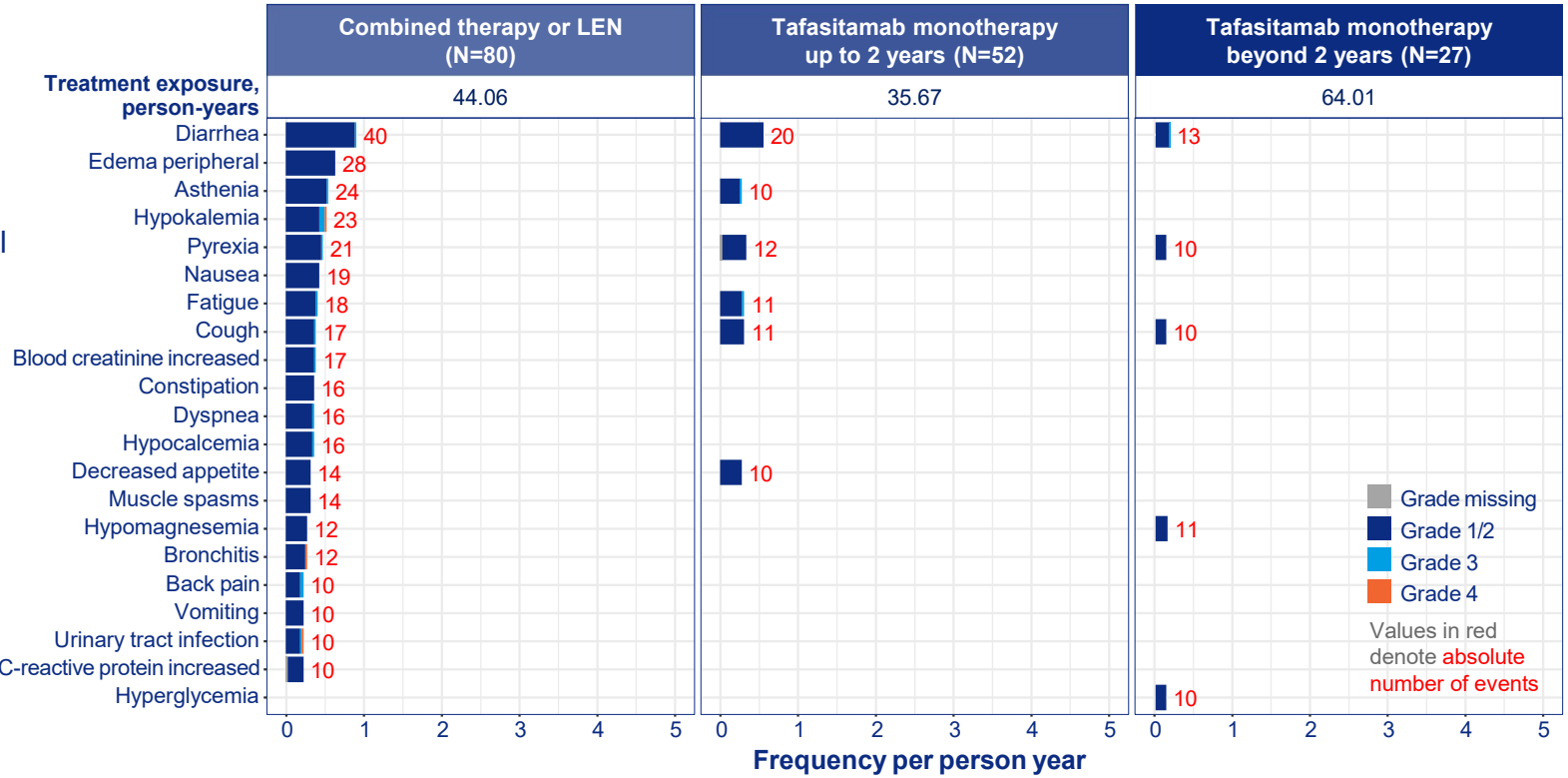
Safety Results: Exposure-Adjusted Comparison of TEAE Frequency across Treatment Periods

Non-hematological TEAEs (cut-off: ≥10 events in any treatment period)

- The most common TEAEs were diarrhea and peripheral edema during the combination therapy phase
- Most non-hematological TEAEs were Grade 1/2



CTCAE grading system.
LEN, lenalidomide; TEAE, treatment-emergent adverse event.

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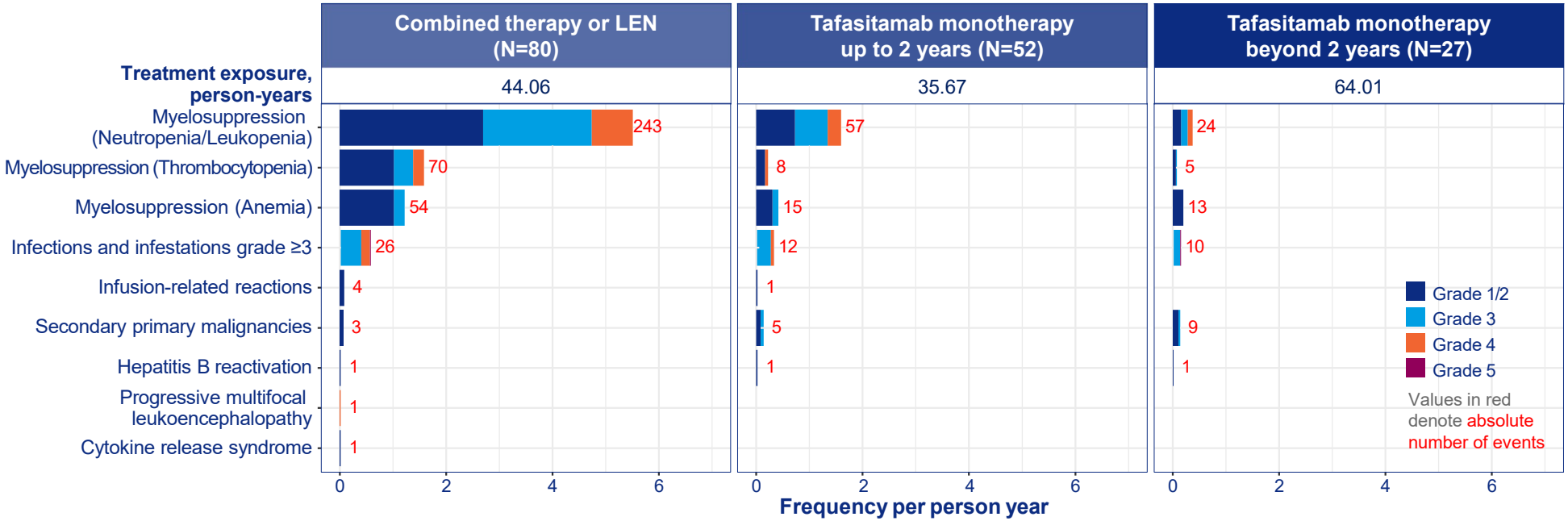
Safety Results: Exposure-Adjusted Comparison of TEAE Frequency across Treatment Periods

Important TEAEs of interest



- Most TEAEs of interest were hematological events during the tafasitamab + LEN combination period
- **Low incidence of infusion-related reactions and grade ≥3 infections and infestations**

CTCAE grading system.
LEN, lenalidomide; TEAE, treatment-emergent adverse event.

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Conclusions

- The **5-year analysis of Phase II L-MIND** study showed **durable responses** in patients with R/R DLBCL who are not eligible for ASCT
  - **Median DoR was not reached** after 44 months of median follow-up
  - As expected, patients with **1 pLoT** had better outcomes than those with **≥2 pLoT**
  - **mDoR was not reached in either subgroup** indicating durability of response irrespective of treatment line
- The frequency of **TEAEs decreased** after **patients transitioned** from combination therapy to tafasitamab monotherapy, up to 2 years (previous analysis) and further beyond 2 years
- No new safety signals were identified, confirming the tolerable safety profile seen with earlier data cuts
- These long-term data suggest that **this immunotherapy may have curative potential**, which is being explored in further studies

ASCT, autologous stem cell transplantation; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; pLoT, prior line of therapy; R/R, relapsed or refractory; TEAE, treatment-emergent adverse event.

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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 mechanisms 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 approval by the U.S. Food and Drug Administration in July 2020, tafasitamab is being co-commercialized by MorphoSys and Incyte in the United States. Conditional/accelerated approvals were granted by the European Medicines Agency and other regulatory authorities. Incyte has exclusive commercialization rights outside the United States. XmAb® is a registered trademark of Xencor, Inc.

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