Long-term outcomes from the phase II L-MIND study of tafasitamab (MOR208) plus lenalidomide in patients with relapsed or refractory diffuse large B-cell lymphoma

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 doi:10.3324/haematol.2020.275958

Received: November 13, 2020.

Accepted: May 11, 2021.

Pre-published: July 1, 2021.

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Supplementary Material

ST1. Refractoriness to last prior line (N=35, FAS)

Prior treatment regimens	
Last prior treatment line	N (%)
1	6 (17.1)
2	25 (71.4)
3 or 4	4 (11.4)
Last prior treatment regimen – category	
Chemotherapy-based	34 (97.1)†
Platinum-based	18 (51.4)†
Non-platinum-based*	16 (45.7)†
Chemotherapy-free regimens	1 (2.9)†
HD-chemo/BEAM/ASCT	2 (5.7)†‡
Rituximab-containing	28 (80)†‡
Patients with 3 or 4 lines refractory to all their prior lines	0

*Composition: predominantly R-CHOP, cyclophosphamide ± doxorubicin, and R-BEN; †Percentages are also referring to the N=35 patients refractory to their last treatment line; ‡Patients are also represented among categories ‘chemotherapy-based’ and ‘chemotherapy-free regimens’.

BEAM, carmustine, etoposide, cytarabine, melphalan; BEN, bendamustine; HD-chemo, high dose chemotherapy; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone.

ST2. Selected infection- and rash-related adverse events

Changes compared with the primary analysis are indicated by an arrow

Event	All Grades, n (%)	Grade 1, n (%)	Grade 2, n (%)	Grade 3, n (%)	Grade 4, n (%)	Grade ≥3, n (%)
Infective pneumonia*						
All infective pneumonia	8 (9.9) → 12 (14.8)	0	1 (1.2) → 2 (2.5)	6 (7.4) → 9 (11.1)	1 (1.2)	7 (8.6) → 10 (12.3)
Pneumonia	6 (7.4) → 10 (12.3)	0	1 (1.2) → 2 (2.5)	5 (6.2) → 8 (9.9)	0	5 (6.2) → 8 (9.9)
Bronchopulmonary aspergillosis	1 (1.2)	0	0	0	1 (1.2)	1 (1.2)
Lung infection	1 (1.2) → 0‡	0	0	1 (1.2) → 0‡	0	1 (1.2) → 0‡
Sepsis†						
All sepsis	4 (4.9)	0	0	2 (2.5)	2 (2.5)	4 (4.9)
Klebsiella sepsis	1 (1.2)	0	0	1 (1.2)	0	1 (1.2)
Neutropenic sepsis	1 (1.2)	0	0	1 (1.2)	0	1 (1.2)
Sepsis	1 (1.2)	0	0	0	1 (1.2)	1 (1.2)
Streptococcal sepsis	1 (1.2)	0	0	0	1 (1.2)	1 (1.2)
Urinary tract infection†						
All urinary tract infection	14 (17.2) → 17 (21.0)	2 (2.5)	7 (8.6) → 9 (11.1)	3 (3.7)	1 (1.2)	4 (4.9)
Urinary tract infection	7 (8.6) → 10 (12.3)	2 (2.5)	3 (3.7) → 6 (7.4)	1 (1.2)	1 (1.2)	2 (2.5)
Escherichia urinary tract infection	4 (4.9)	0	3 (3.7)	1 (1.2)	0	1 (1.2)
Bacterial urinary tract infection	2 (2.5)	0	2 (2.5)	0	0	0
Enterococcal urinary tract infection	1 (1.2)	0	0	1 (1.2)	0	1 (1.2)

Rash†						
All rash	37 (45.7) → 40 (49.4)	18 (22.2) → 19 (23.5)	12 (14.8) → 14 (17.3)	7 (8.6)	0	7 (8.6)
Pruritus	8 (9.9)	4 (4.9)	3 (3.7)	1 (1.2)	0	1 (1.2)
Rash	6 (7.4) → 7 (8.6)	2 (2.5)	4 (4.9) → 5 (6.2)	0	0	0
Allergic dermatitis	4 (4.9)	0	1 (1.2)	3 (3.7)	0	3 (3.7)
Maculo-papular rash	4 (4.9)	3 (3.7)	0	1 (1.2)	0	1 (1.2)
Dry skin	3 (3.7)	2 (2.5)	1 (1.2)	0	0	0
Erythema	3 (3.7)	3 (3.7)	0	0	0	0
Dermatitis	1 (1.2)	1 (1.2)	0	0	0	0
Eczema	1 (1.2) → 2 (2.4)	1 (1.2)	0→ 1 (1.2)	0	0	0
Papule	1 (1.2)	1 (1.2)	0	0	0	0
Psoriasis	1 (1.2)	0	0	1 (1.2)	0	1 (1.2)
Erythematous rash	1 (1.2)	0	0	1 (1.2)	0	1 (1.2)
Pruritic rash	1 (1.2)	1 (1.2)	0	0	0	0
Rebound psoriasis	1 (1.2)	0	1 (1.2)	0	0	0
Skin lesion	1 (1.2) → 2 (2.5)	0 → 1 (1.2)	1 (1.2)	0	0	0
Toxic skin eruption	1 (1.2)	0	1 (1.2)	0	0	0

*Defined by Standard Medical Dictionary for Regulatory Activities query, narrow scope. Neither Pneumocystis jirovecii pneumonia nor Pneumocystis carinii pneumonia prophylaxis was administered; †Defined by customized Medical Dictionary for Regulatory Activities query; ‡At the time of data cut-off, the Preferred Term ‘lung infection’ had been discontinued. This case was re-coded and is now reported under the Preferred Term ‘pneumonia’.

Supplementary Methods

Eligibility criteria

Eligible patients were aged >18 years with histologically-confirmed R/R DLBCL (including transformed indolent lymphoma with a subsequent DLBCL relapse), had received 1–3 prior systemic regimens including ≥1 anti-CD20 therapy, had Eastern Cooperative Oncology Group performance status 0–2, and were not candidates for high-dose chemotherapy and subsequent ASCT.

Tumor assessment

Tumor assessment was based on computerized tomography scans conducted after cycles 2, 4, 6, and 9 and positron emission tomography, which was mandatory at baseline and after cycle 12. Central laboratory assessments were performed on day 1 (±2 days) of cycles 1–24. Adverse events were recorded at each visit.

Sample size determination and statistics

The sample size of 80 patients was determined using an exact binomial test with a two-sided significance level of 5% and a power of 85%, assuming a drop-out rate of 10% and that treatment with tafasitamab plus lenalidomide could increase the objective response rate by 15% vs monotherapy.

Descriptive statistics were used to summarize response rates and safety outcomes. Progression-free survival, overall survival, and duration of response were analyzed using the Kaplan–Meier method, and 95% confidence intervals for the median calculated accordingly. The median follow-up for progression-free survival and overall survival was calculated using the reverse Kaplan–Meier method. Statistical analysis was performed using SAS® Software version 9.4 or above (SAS Institute, Cary, NC).

Supplementary Results

Narratives for patients who received stem-cell transplant (SCT) after tafasitamab (n=2)

One patient who received SCT had diffuse large B-cell lymphoma (DLBCL) from marginal zone lymphoma transformation and had received autologous SCT 4 years prior to enrollment progressed after seven cycles of therapy in L-MIND, received further chemotherapy and allogenic SCT and died 4 months after allogenic SCT.

The other patient progressed after three cycles in L-MIND, received a further two lines of chemotherapy and autologous SCT but died 8 days later.

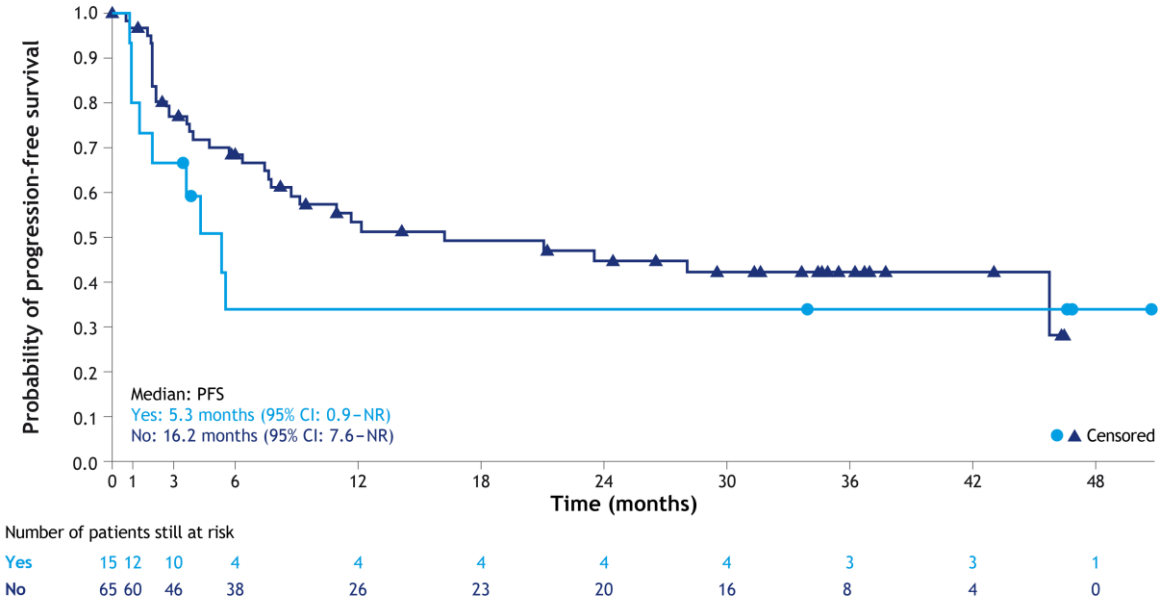
Narratives for patients who received chimeric antigen receptor T-cell therapy (CAR)-T after tafasitamab (n=2)

One patient who received CAR-T therapy had germinal center B-like DLBCL as a result of follicular lymphoma transformation and prior to L-MIND had experienced 2-year complete responses to R-EPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) and R-ICE (rituximab, ifosfamide, carboplatin, etoposide); she had also declined autologous SCT. She received six cycles of therapy in L-MIND (with a stable disease response) before progression, received further chemotherapy with R-GemOx for four cycles (with a partial response), then received CAR-T with a complete response 1 month after treatment; this patient had remained in complete response for 1 year but died approximately 2-years post CAR-T treatment due to acute myeloid leukemia.

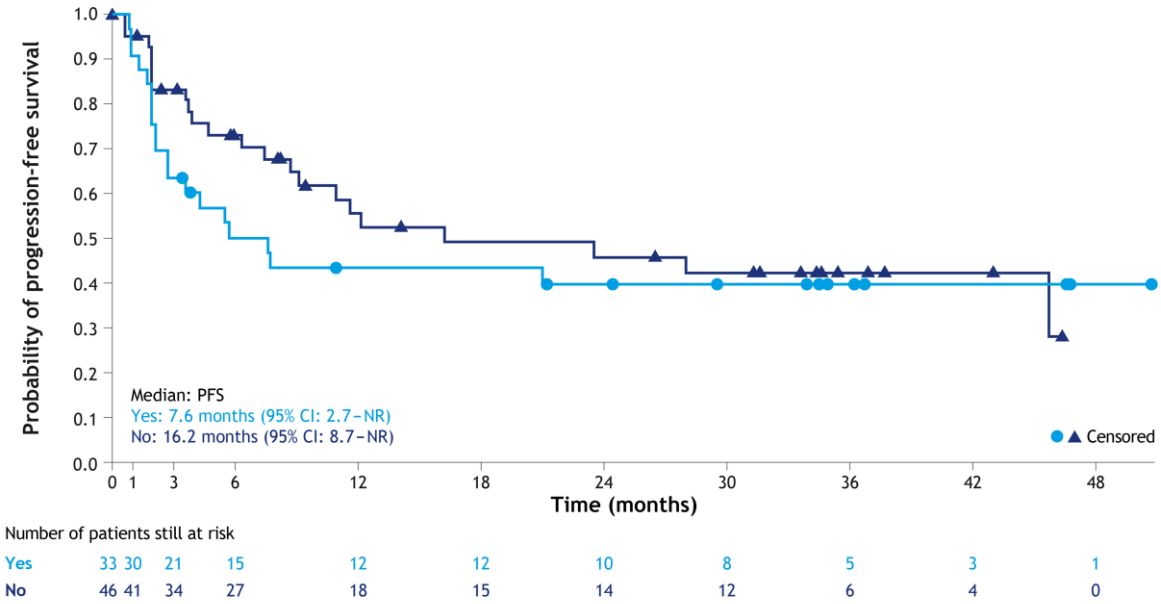
The other patient had received autologous SCT before enrollment to L-MIND and experienced disease progression in L-MIND after eight cycles; this patient did not respond to further chemotherapy or CAR-T, and died 4 months after CAR-T therapy.

SF1. PFS in patients with (A) primary refractory DLBCL, (B) rituximab-refractory DLBCL, and (C) last-therapy refractory DLBCL

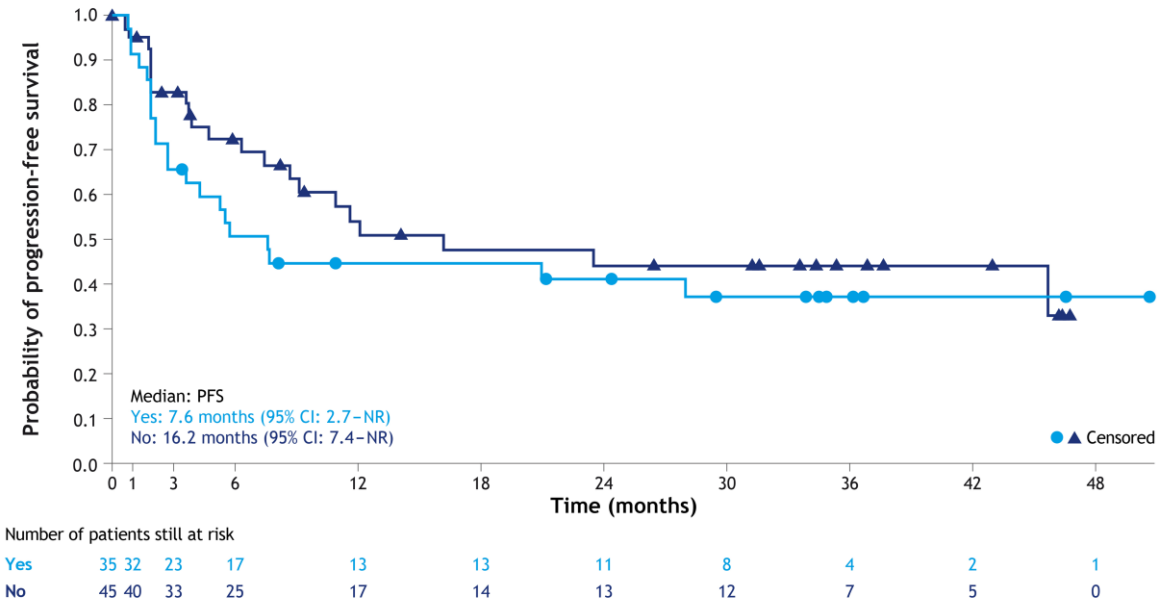
A.



B.



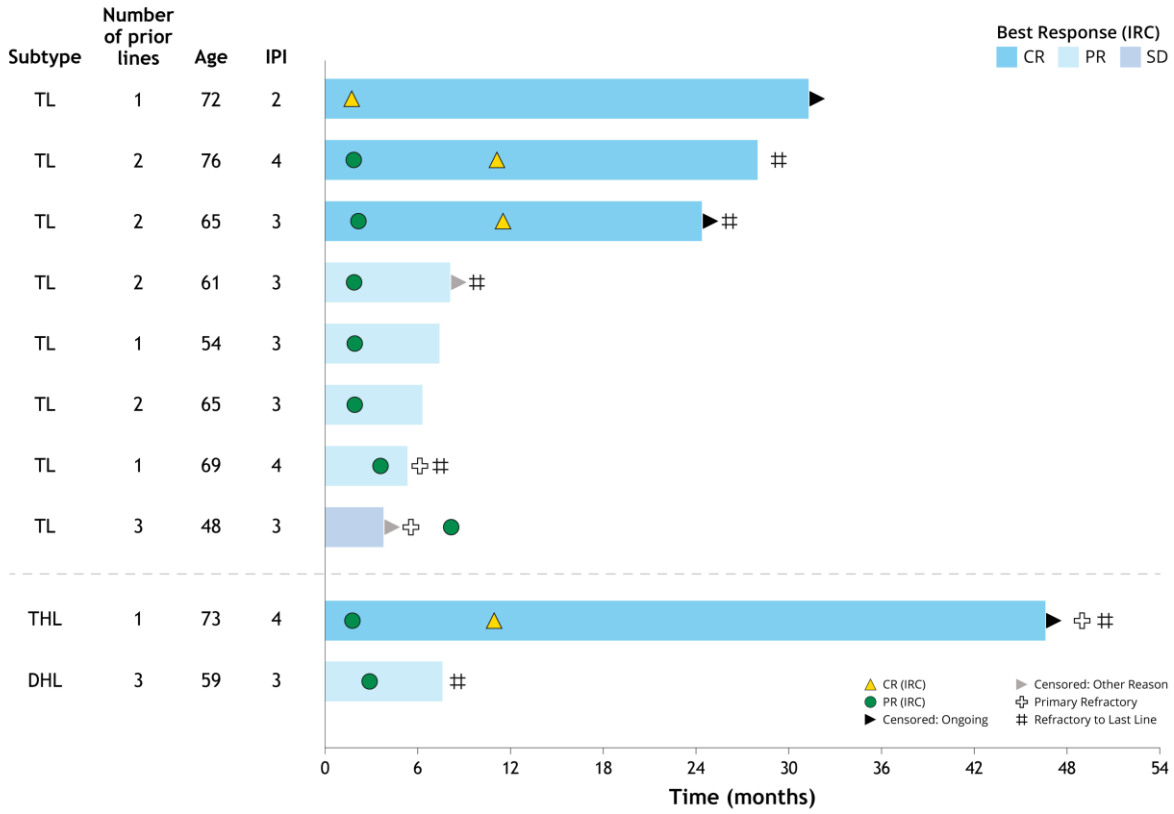
C.



Number of patients still at risk

Yes	35	32	23	17	13	13	11	8	4	2	1
No	45	40	33	25	17	14	13	12	7	5	0

SF2. Swimmer plot of progression-free survival for patients with diffuse large B-cell lymphoma arising from transformation of low-grade lymphoma and double- or triple-hit lymphoma



Both patients 'Censored: Other Reason' had received prohibited concomitant medication.

CR, complete response; DHL, double-hit lymphoma; IPI, International Prognostic Index; IRC, independent review committee; PR, partial response; SD, stable disease; THL, triple-hit lymphoma; TL, transformed low-grade lymphoma.