frontMIND: Phase 3 Study of Tafasitamab Plus Lenalidomide and R-CHOP for Patients With Newly Diagnosed Diffuse Large B-cell Lymphoma

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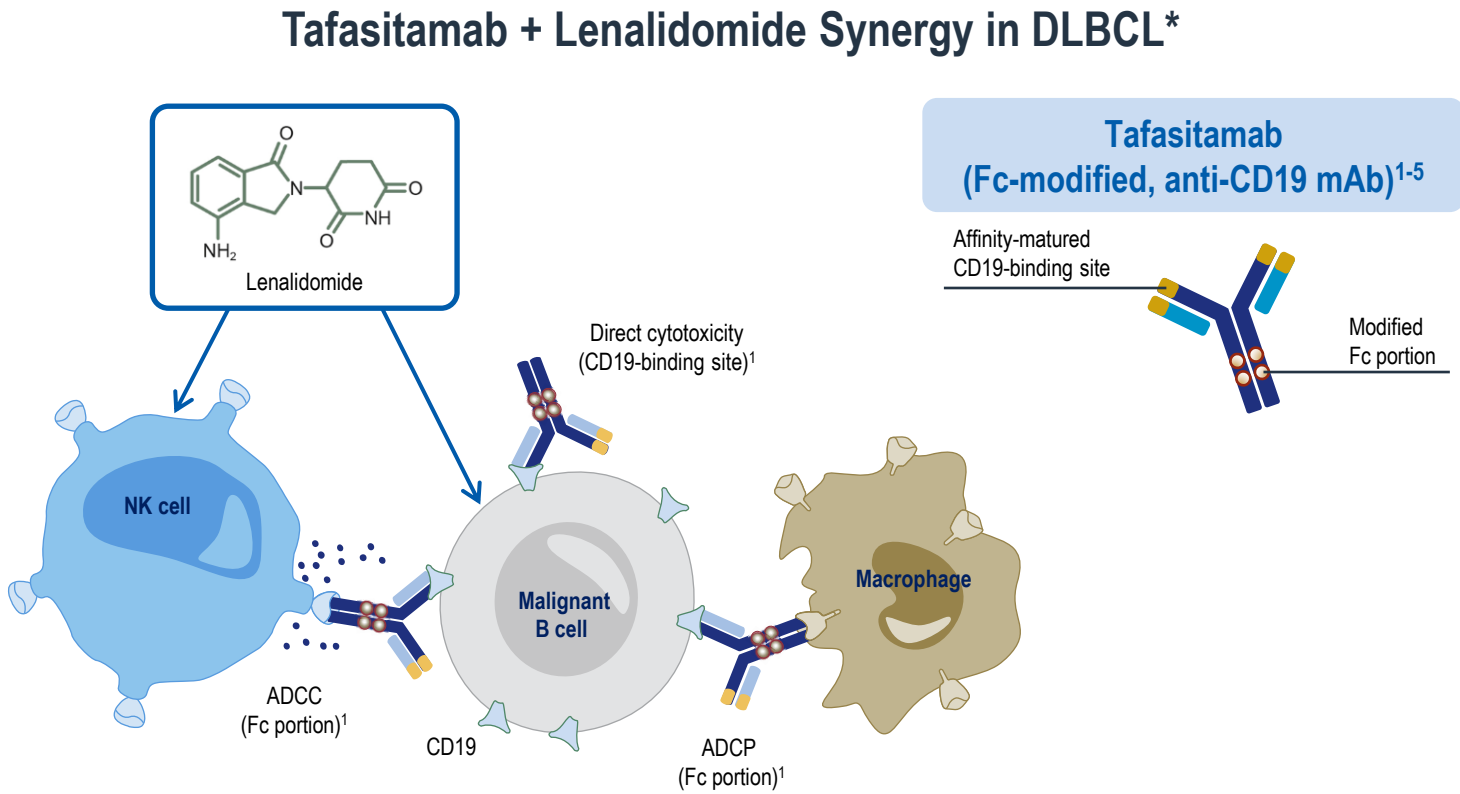
Background: Tafasitamab

- Tafasitamab, a monoclonal antibody, targets CD19 on malignant B cells
- The engineered Fc region increases affinity to immune effector cells
- Lenalidomide expands and activates effector cells and increases the ADCC, ADCP, and direct cell death caused by tafasitamab



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1. Horton HM, et al. *Cancer Res*. 2008;68:8049-8057. 2. Awan FT, et al. *Blood*. 2010;115:1204-1213. 3. Woyach JA, et al. *Blood*. 2014;124:3553-3560. 4. Jurczak W, et al. *Ann Oncol*. 2018;29:1266-1272. 5. Patra-Kneuer M, et al. *Front Immunol*. 2023;14:1220558.

ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cell-mediated phagocytosis; Fc, fragment crystallizable; mAb, monoclonal antibody; NK, natural killer.

Background: DLBCL

- >40% of patients with high-risk DLBCL, are not cured with first-line R-CHOP[1-3]
- Tafasitamab and lenalidomide doubled the historical ORR of lenalidomide monotherapy in R/R DLBCL leading to FDA approval of the regimen for patients with R/R DLBCL[4,5]
- Tafasitamab plus lenalidomide added to R-CHOP (Tafa-Len-R-CHOP) demonstrated encouraging safety and efficacy in the phase 1b First-MIND study of patients with previously untreated DLBCL[6]
- **frontMIND**, a phase 3 global study, evaluated Tafa-Len-R-CHOP vs R-CHOP in untreated patients with high intermediate- or high-risk aggressive B-cell lymphomas

1. Coiffier B, et al. *Blood*. 2010;116:2040-2045. 2. Coiffier B, et al. *N Engl J Med*. 2002;346:235-242. 3. Morschhauser F, et al. *J Clin Oncol*. 2025;43:3698-3705. 4. Salles G, et al. *Lancet Oncol*. 2020;21:978-988. 5. Li J, et al. *Front Oncol*. 2021;11:756728. 6. Belada D, et al. *Blood*. 2023;142:1348-1358.
DLBCL, diffuse large B-cell lymphoma; FDA, US Food and Drug Administration; Len, lenalidomide; ORR, overall response rate;
R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; R/R, relapsed or refractory; Tafa, tafasitamab.

Key Takeaway Points

1

Tafa-Len-R-CHOP significantly prolonged PFS compared with R-CHOP (HR 0.75) in patients with previously untreated, high-risk (IPI 3-5) DLBCL and HGBL

2

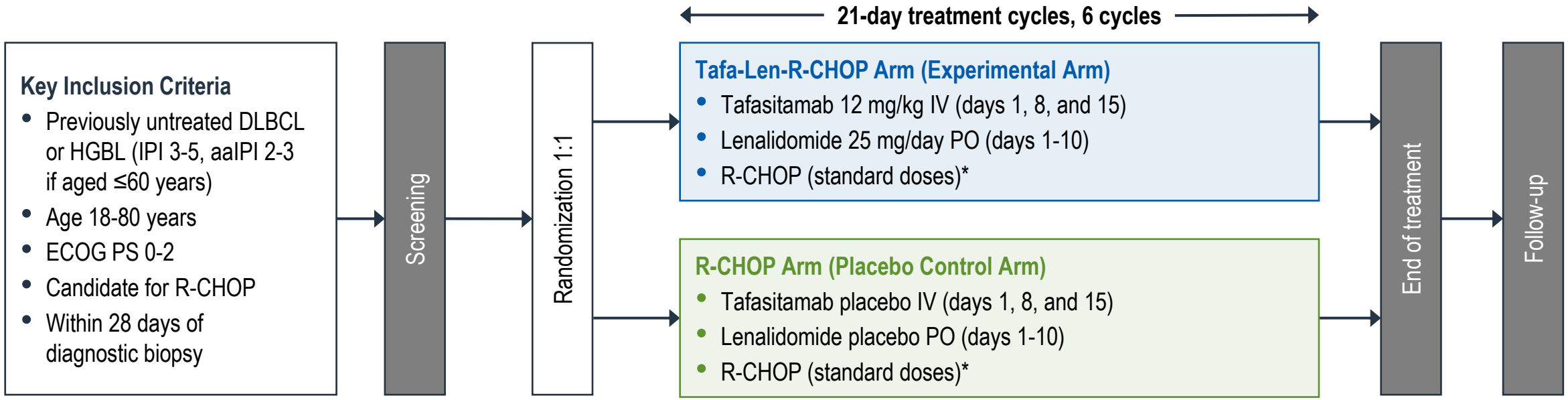
Point estimates suggested trends toward **PFS advantage** with Tafa-Len-R-CHOP in **key prespecified subgroup analyses**

3

The **incremental safety events** observed with Tafa-Len-R-CHOP were **well-managed** and **did not impact delivery of the R-CHOP** backbone

DLBCL, diffuse large B-cell lymphoma; HGBL, high-grade B-cell lymphoma; HR, hazard ratio; IPI, International Prognostic Index; Len, lenalidomide; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

frontMIND (NCT04824092): Phase 3, Global, Multicenter, Placebo-Controlled, Double-Blind, Randomized Study



Stratification Factors

- IPI/aaIPI
- Geographic region

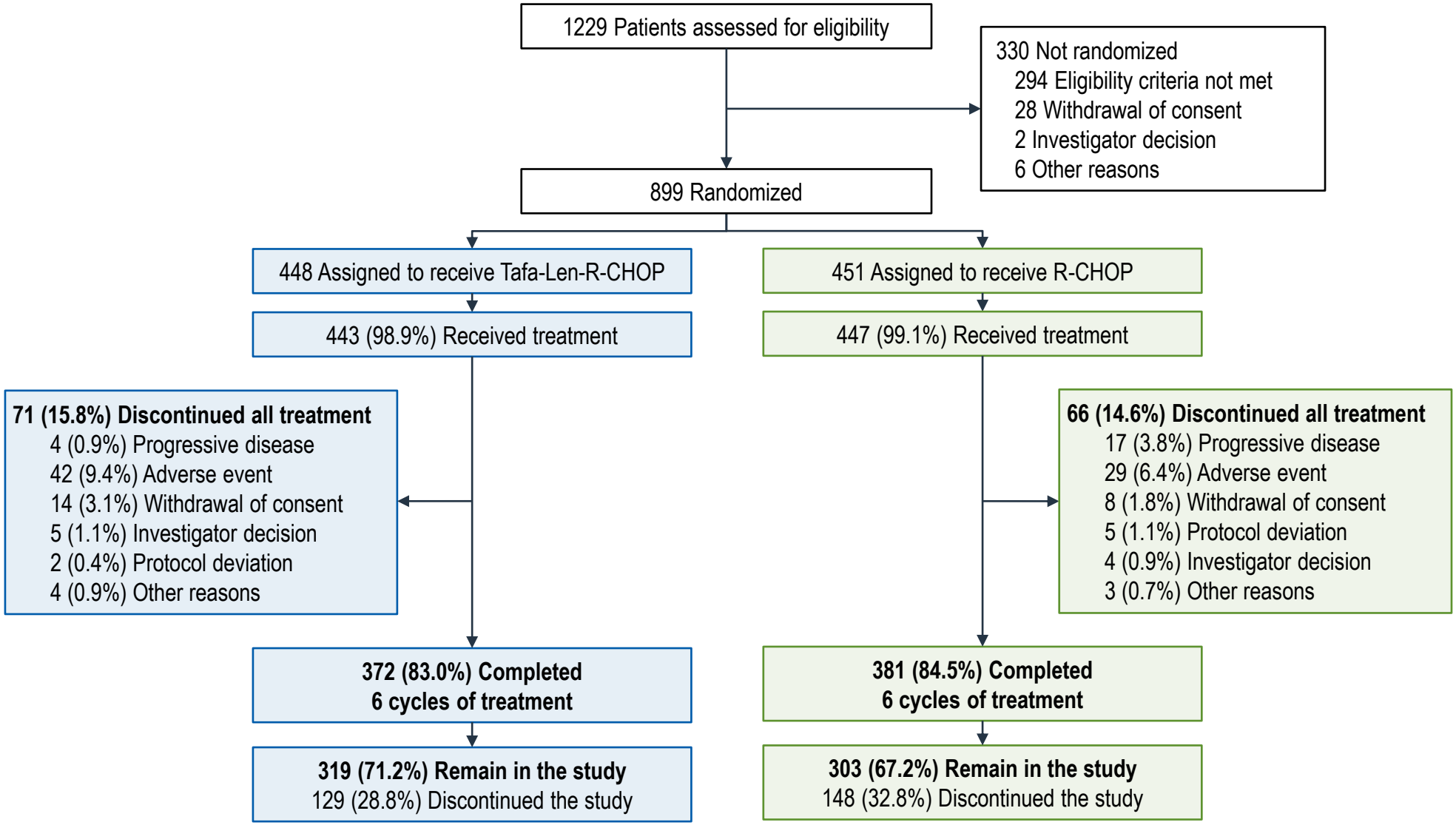
Study Endpoints (Investigator Assessed)

- **Primary study endpoint:** PFS
- **Key secondary:** EFS, OS
- **Select other secondary:** PET-CR at EOT, ORR at EOT, PFS by cell-of-origin subtypes, safety
- **Post-hoc analyses:** PFS, EFS, OS for the population with centrally confirmed lymphoma subtypes

*Rituximab administered at 375 mg/m^2 IV (day 1); cyclophosphamide, doxorubicin, and vincristine administered IV (day 1); prednisone/prednisolone administered PO (days 1-5).
aaIPI, age-adjusted IPI; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; EOT, end of treatment; HGBL, high-grade B-cell lymphoma; HRQoL, health-related quality of life; IPI, International Prognostic Index; IV, intravenously; Len, lenalidomide; ORR, objective response rate; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; PO, orally; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

Patient Disposition

Data cutoff: October 20, 2025



Data are presented for the ITT, which represents the full analysis set.

ITT, intention-to-treat; Len, lenalidomide, OS, overall survival; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

Demographics and Baseline Disease Characteristics

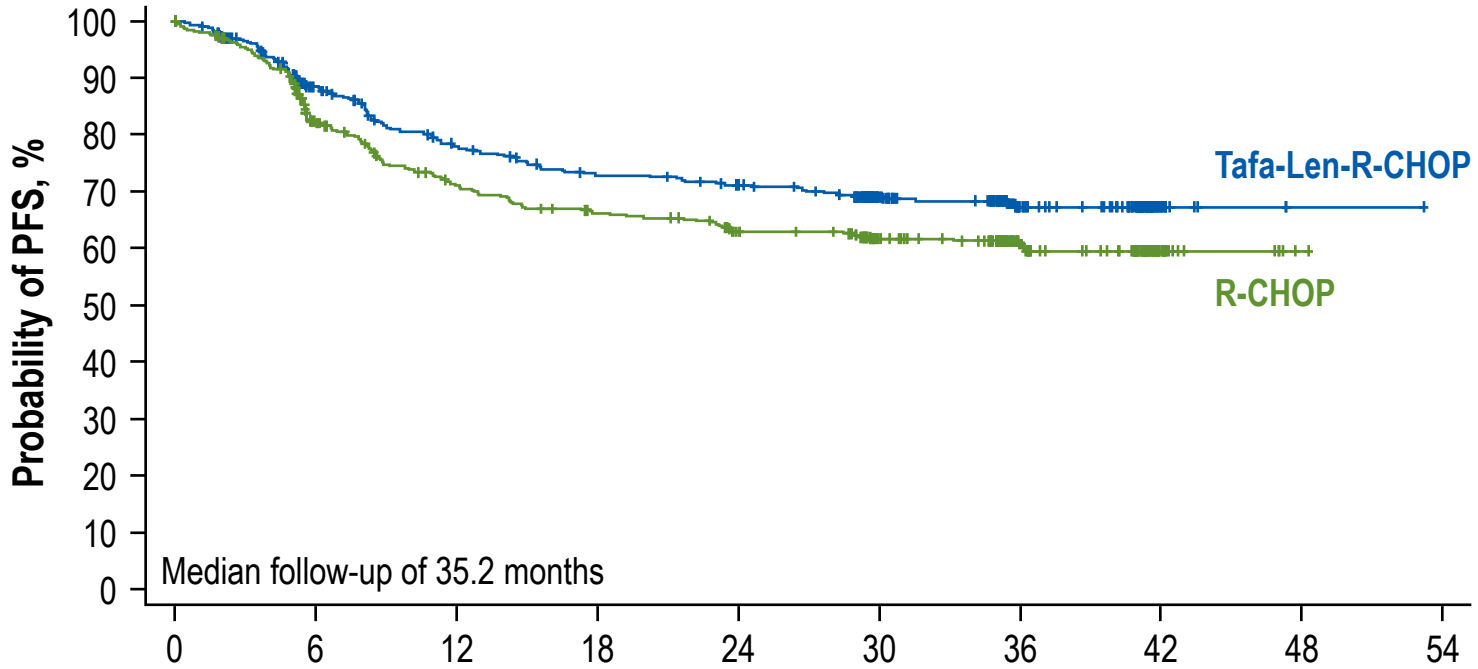
Overall ITT population

ITT Population	Tafa-Len-R-CHOP (n=448)	R-CHOP (n=451)	Total (N=899)
Median age, years (range)	65.0 (20, 80)	65.0 (18, 80)	65.0 (18, 80)
Male sex	240 (53.6)	233 (51.7)	473 (52.6)
Ann Arbor stage III or IV at enrollment	432 (96.4)	436 (96.7)	868 (96.6)
Extranodal involvement at ≥2 sites	173 (38.6)	175 (38.8)	348 (38.7)
Elevated lactate dehydrogenase level	369 (82.4)	376 (83.4)	745 (82.9)
Presence of bulky disease	254 (56.7)	231 (51.2)	485 (53.9)
ECOG PS at screening			
0-1	311 (69.4)	305 (67.6)	616 (68.5)
2	137 (30.6)	146 (32.4)	283 (31.5)
Risk group (stratification factor)			
High-intermediate risk (IPI 3/aaIPI 2)	259 (57.8)	244 (54.1)	503 (56.0)
High risk (IPI 4-5/aaIPI 3)	186 (41.5)	202 (44.8)	388 (43.2)
Median time from diagnostic biopsy to treatment initiation, days (Q1-Q3)	23.5 (17, 28)	24.0 (18, 28)	24.0 (18, 28)

Data are n (%) unless otherwise specified.
aaIPI, age-adjusted IPI; ECOG PS, Eastern Cooperative Oncology Group performance status; IPI, International Prognostic Index; ITT, intention-to-treat; Len, lenalidomide; Q, quartile; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

Tafa-Len-R-CHOP Significantly Improved PFS vs R-CHOP

PFS by investigator assessment (primary endpoint)



No. at Risk										
Tafa-Len-R-CHOP	448	333	282	259	248	191	107	13	1	0
R-CHOP	451	320	266	244	222	182	101	19	1	0

HR 0.75* (***P*=0.0194**)

95% CI: 0.59, 0.96

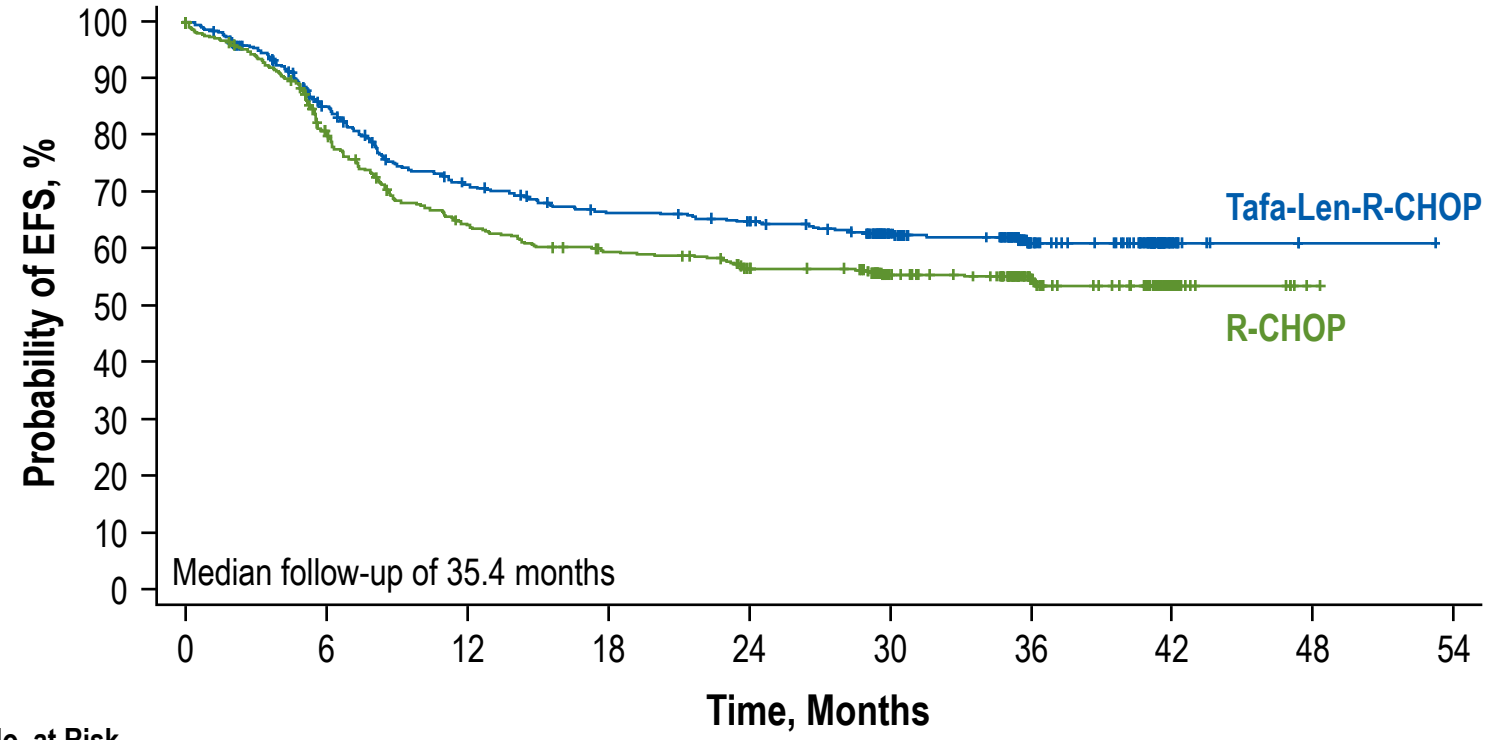
- A **25% reduction in risk of progression or death** demonstrated with Tafa-Len-R-CHOP vs R-CHOP
- **2-year PFS:** 71.1% with Tafa-Len-R-CHOP vs 62.9% with R-CHOP (**Δ=8.2%**)
- **3-year PFS:** 67.3% with Tafa-Len-R-CHOP vs 60.7% with R-CHOP (**Δ=6.6%**)

ITT population. *Calculated using a stratified Cox proportional hazards model.

CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; Len, lenalidomide; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

Tafa-Len-R-CHOP Significantly Improved EFS vs R-CHOP

EFS by investigator assessment (key secondary)



No. at Risk										
Tafa-Len-R-CHOP	448	346	283	259	249	191	107	13	1	0
R-CHOP	451	339	267	244	222	182	101	19	1	0

HR 0.79* (*P*=0.0260)

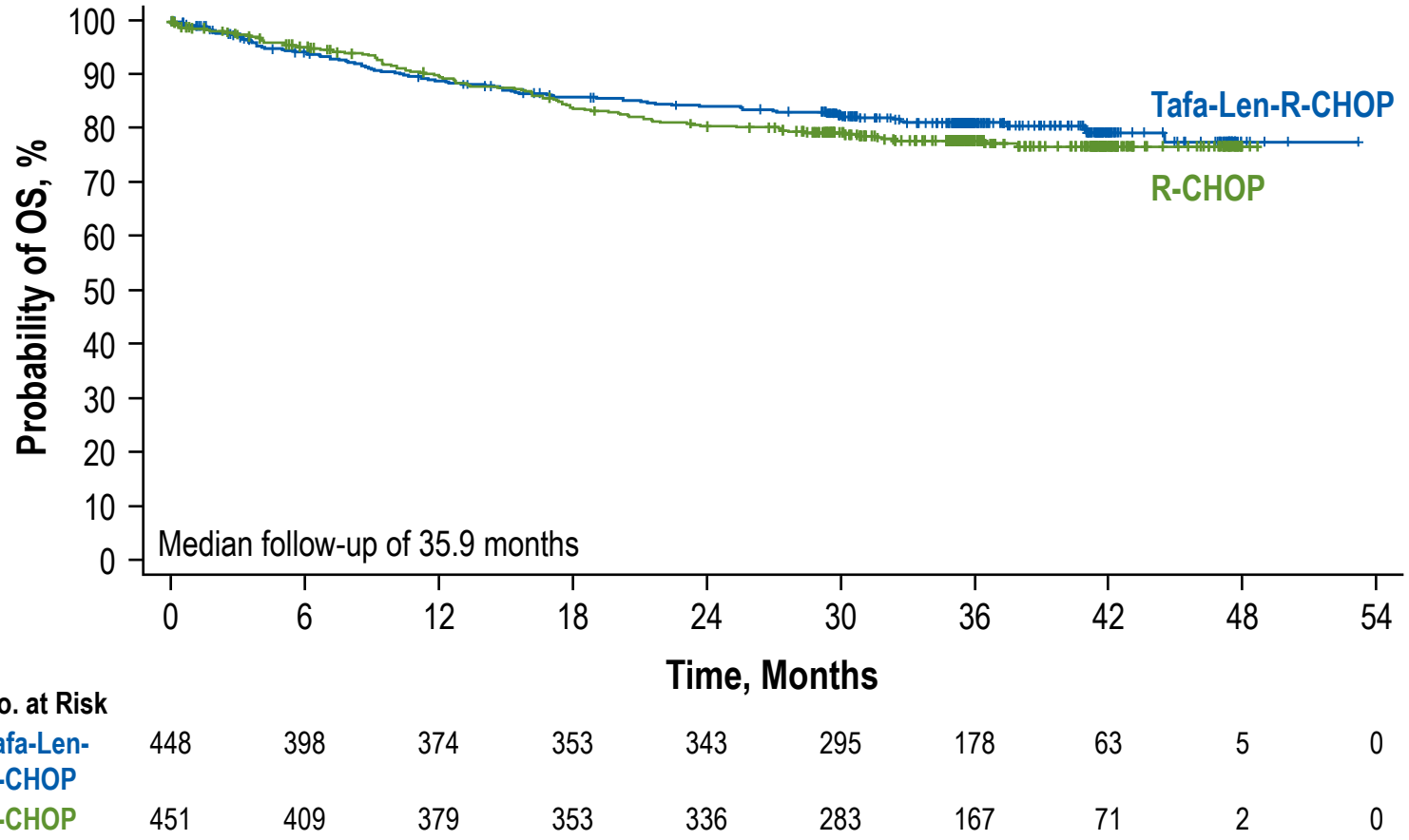
95% CI: 0.64, 0.97

- **2-year EFS:**
  65.0% with Tafa-Len-R-CHOP vs
  56.7% with R-CHOP
- **3-year EFS:**
  61.2% with Tafa-Len-R-CHOP vs
  54.8% with R-CHOP

ITT population. *Calculated using a stratified Cox proportional hazards model.
CI, confidence interval; EFS, event-free survival; HR, hazard ratio; ITT, intention-to-treat; Len, lenalidomide; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

Interim Analysis of OS Demonstrated a Positive Trend

OS (key secondary)



No. at Risk										
Tafa-Len-R-CHOP	448	398	374	353	343	295	178	63	5	0
R-CHOP	451	409	379	353	336	283	167	71	2	0

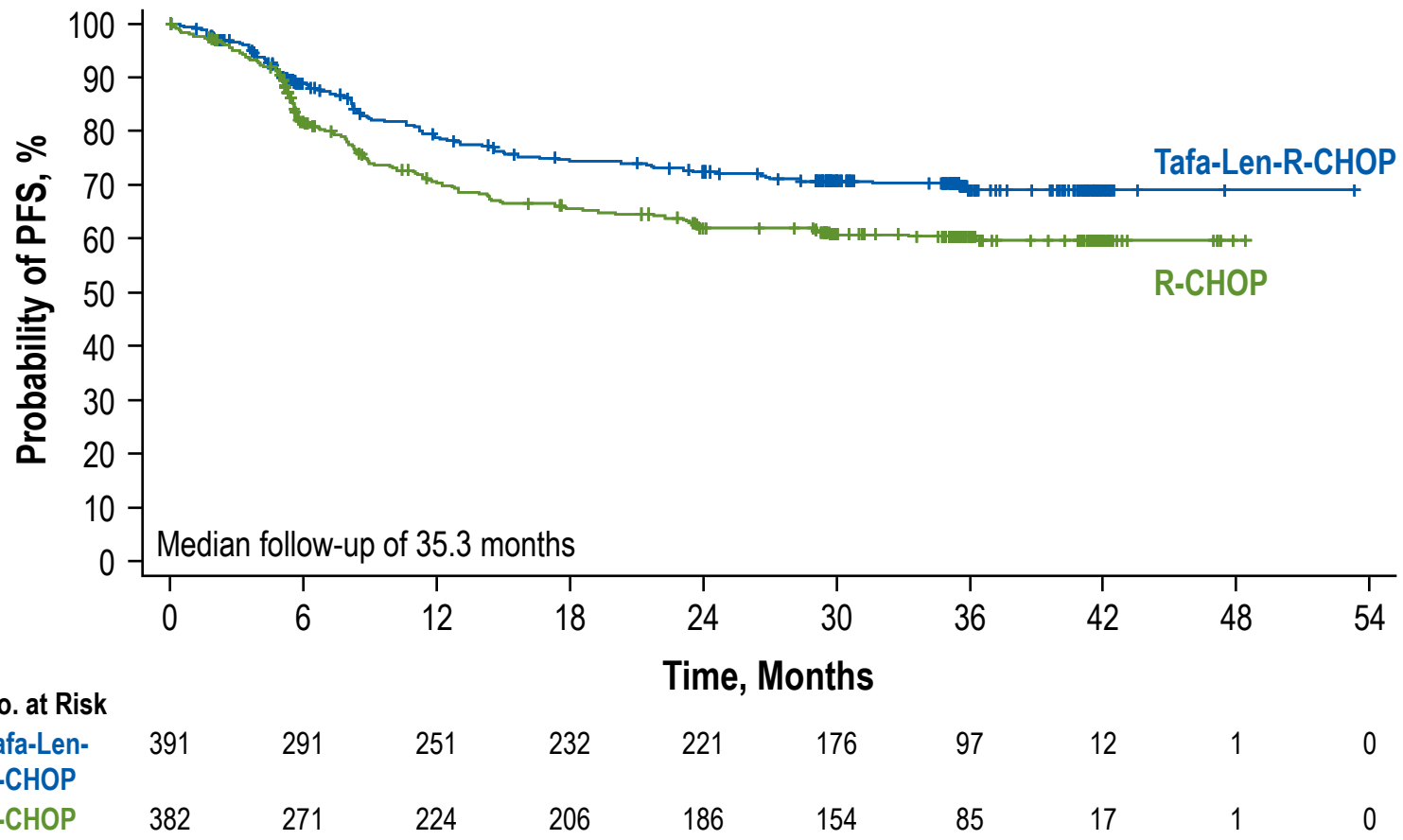
HR 0.85* (*P*=0.2703)

95% CI: 0.63, 1.14

- **2-year OS:**
  84.1% with Tafa-Len-R-CHOP vs
  80.5% with R-CHOP
- **3-year OS:**
  81.1% with Tafa-Len-R-CHOP vs
  77.8% with R-CHOP

ITT population. At the PFS primary analysis, 177 deaths had occurred. *Calculated using a stratified Cox proportional hazards model.
CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; Len, lenalidomide; OS, overall survival; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

HR for PFS Improved in Centrally Confirmed Lymphoma Subtypes (n=773)



HR 0.68* (*P*=0.0035)†
95% CI: 0.52, 0.88

versus

Overall ITT population:
HR 0.75 (*P*=0.0194)
95% CI: 0.59, 0.96

- **2-year PFS:**
  72.7% with Tafa-Len-R-CHOP vs
  62.2% with R-CHOP
- **Differences in 2-year PFS rates:**
  Δ=**10.5%** in centrally confirmed
  Δ=**8.2%** in the ITT

- On central review, 126 patients (14% of the ITT) did not have a confirmed lymphoma subtype either due to histology (eg, FL grade 1-3a, MCL, and BL) or inadequate sample

Post hoc analysis of PFS by Investigator; centrally confirmed lymphoma subtypes population. *Calculated using a stratified Cox proportional hazards model. †Nominal *P* value.
BL, Burkitt lymphoma; CI, confidence interval; FL, follicular lymphoma; HR, hazard ratio; ITT, intention-to-treat; Len, lenalidomide; MCL, mantle cell lymphoma; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

Cell-of-Origin Molecular Subtypes

Central GEP assessment

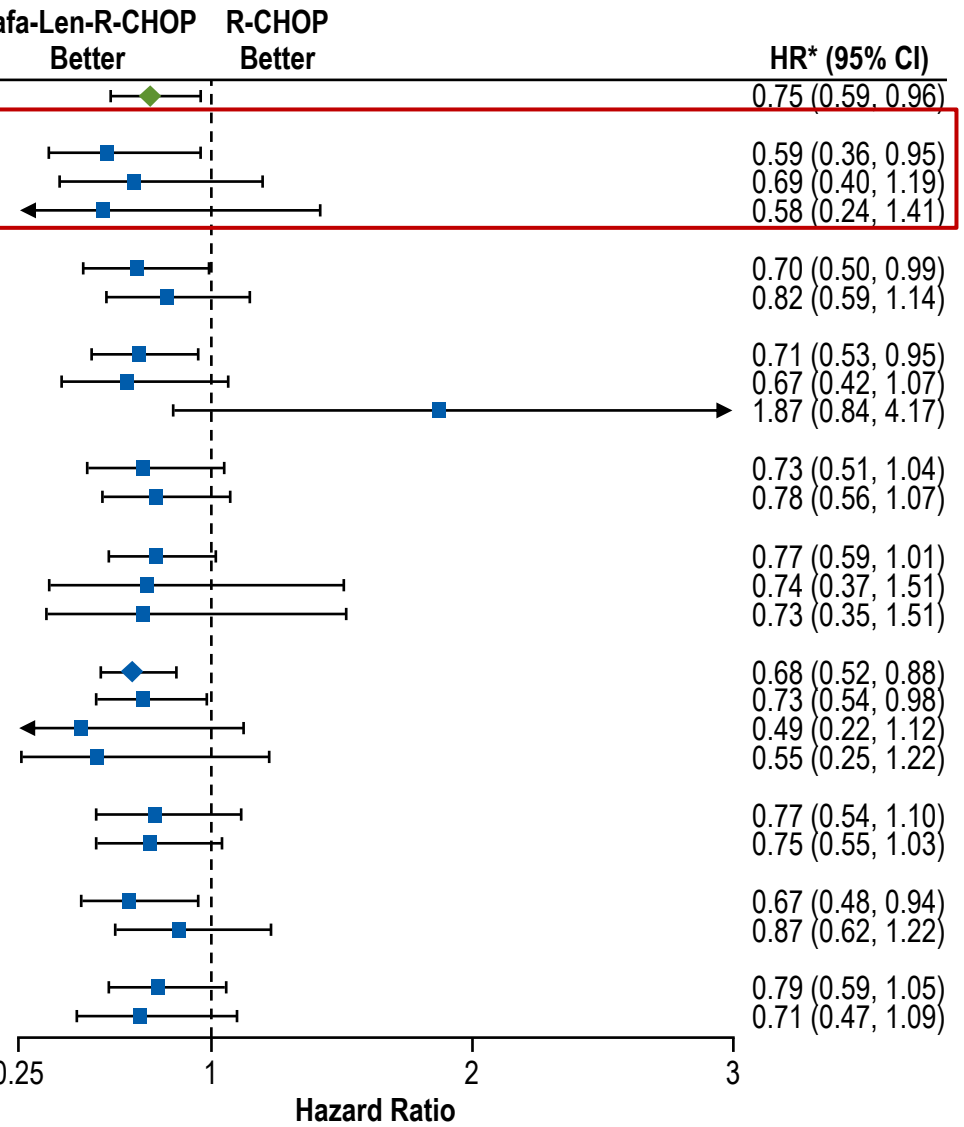
ITT Population	Tafa-Len-R-CHOP (n=448)	R-CHOP (n=451)	Total (N=899)
Cell of origin (per GEP; central assessment), n	**239**	**245**	**484**
ABC-like	84 (35.1)	88 (35.9)	172 (35.5)
GCB-like	131 (54.8)	117 (47.8)	248 (51.2)
Unclassified	24 (10.0)	40 (16.3)	64 (13.2)
Cell of origin (per GEP; central assessment) results not available, n	209	206	415

- Baseline characteristics in patients with COO subtypes determined by central GEP were very similar to the patients in the overall ITT population

Data are n (%) unless otherwise specified.
ABC, activated B cell; COO, cell of origin; GCB, germinal center B cell; GEP, gene expression profiling; ITT, intention-to-treat; Len, lenalidomide; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

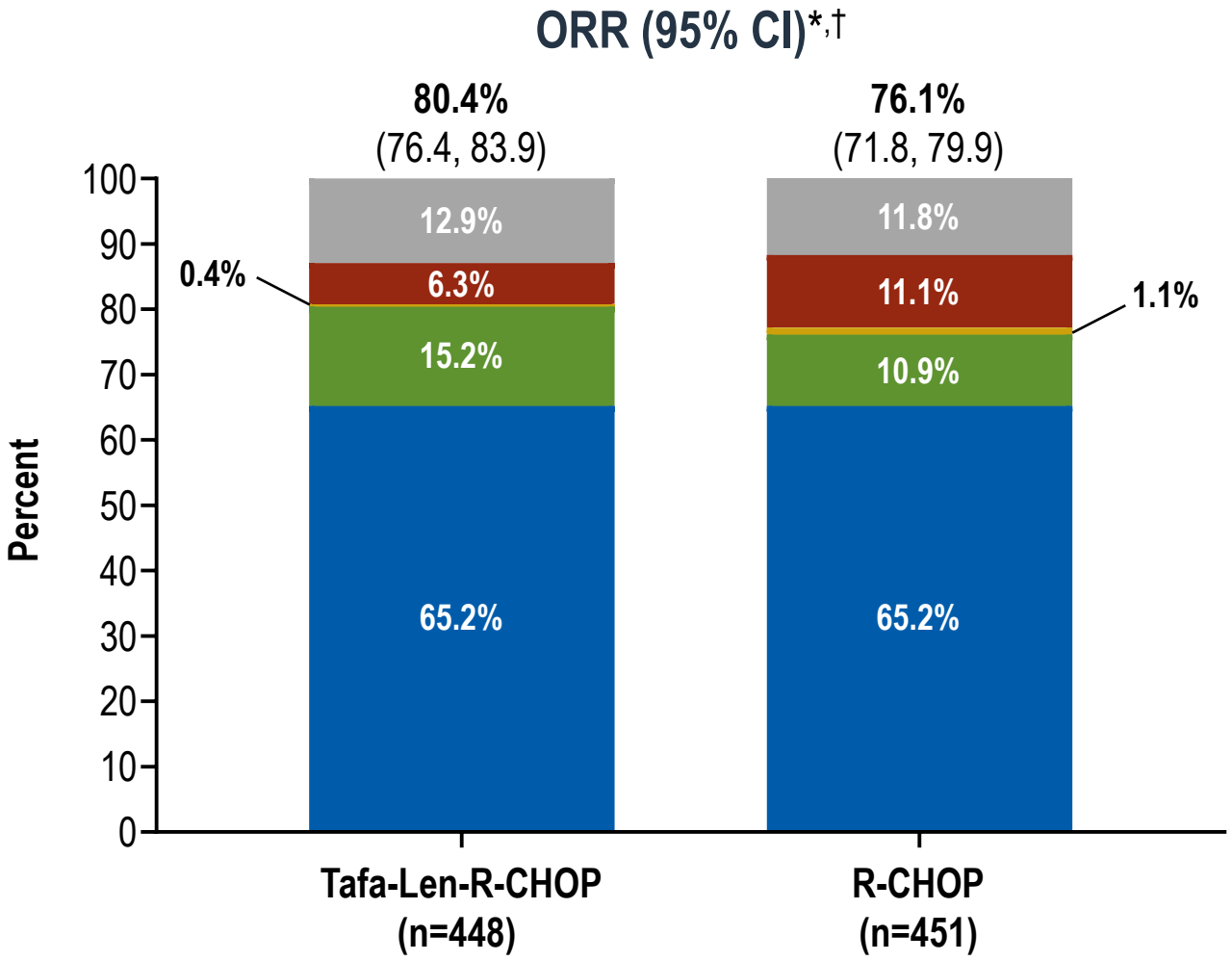
Consistent Trends Toward PFS Benefit in Prespecified Subgroups

Baseline Risk Factors	Tafa-Len-R-CHOP Patient n/Event n	R-CHOP Patient n/Event n	HR* (95% CI)
Overall	448/121	451/155	0.75 (0.59, 0.96)
Cell of origin by central GEP			
ABC-like	84/27	88/44	0.59 (0.36, 0.95)
GCB-like	131/23	117/29	0.69 (0.40, 1.19)
Unclassified	24/7	40/16	0.58 (0.24, 1.41)
IPI score			
IPI 3/aaIPI 2	259/56	244/75	0.70 (0.50, 0.99)
IPI 4-5/aaIPI 3	186/64	202/79	0.82 (0.59, 1.14)
Geographic region			
EU, US, CAN, AUS, NZ†	324/76	324/104	0.71 (0.53, 0.95)
Asia	90/30	93/41	0.67 (0.42, 1.07)
Rest of the world	34/15	34/10	1.87 (0.84, 4.17)
Bulky disease			
Absent	194/50	220/75	0.73 (0.51, 1.04)
Present	254/71	231/80	0.78 (0.56, 1.07)
Lymphoma subtype (locally determined)			
DLBCL	362/95	361/120	0.77 (0.59, 1.01)
High-grade lymphoma	38/13	41/19	0.74 (0.37, 1.51)
Other	48/13	49/16	0.73 (0.35, 1.51)
Lymphoma subtype (centrally determined)			
Overall	391/99	382/132	0.68 (0.52, 0.88)
DLBCL	307/76	325/107	0.73 (0.54, 0.98)
High-grade lymphoma	41/12	24/11	0.49 (0.22, 1.12)
Other	43/11	33/14	0.55 (0.25, 1.22)
Age			
<65 years	222/53	218/68	0.77 (0.54, 1.10)
≥65 years	226/68	233/87	0.75 (0.55, 1.03)
Sex			
Male	240/59	233/83	0.67 (0.48, 0.94)
Female	208/62	218/72	0.87 (0.62, 1.22)
ECOG PS			
0-1	324/83	326/105	0.79 (0.59, 1.05)
2	123/37	123/49	0.71 (0.47, 1.09)



PFS by investigator assessment; ITT population.
*Calculated using a stratified Cox proportional hazards model. †Europe, USA, Canada, Australia, and New Zealand.
aaIPI, age-adjusted IPI; ABC, activated B cell; CI, confidence interval; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; GCB, germinal center B cell; GEP, gene expression profiling; HR, hazard ratio; IPI, International Prognostic Index; ITT, intention-to-treat; Len, lenalidomide; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

ORR and CR Rate by Investigator Assessment



- **ORR** (OR 1.29 [95% CI: 0.94, 1.78]‡; *P*=0.1201§) **and PET-negative CR rate** (OR 1.00 [95% CI: 0.76, 1.31]‡, *P*=0.9873§) were **similar** between treatment arms at EOT
- **PR** rate was **numerically higher** in the Tafa-Len-R-CHOP arm

ITT population. *Objective response rate was defined as the proportion of patients who achieved a complete or partial response per Lugano 2014 criteria at EOT. †95% CI calculated using the Clopper-Pearson exact method. ‡95% CI calculated using the Wald method. §Nominal *P* value calculated using a stratified Cochran–Mantel–Haenszel test.
CI, confidence interval; CR, complete response; EOT, end of treatment; Len, lenalidomide; ITT, intention-to-treat; NE, not evaluable; OR, odds ratio; ORR, objective response rate; PD, progressive/relapsed disease; PET, positron emission tomography; PR, partial response; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; SD, stable disease; Tafa, tafasitamab.

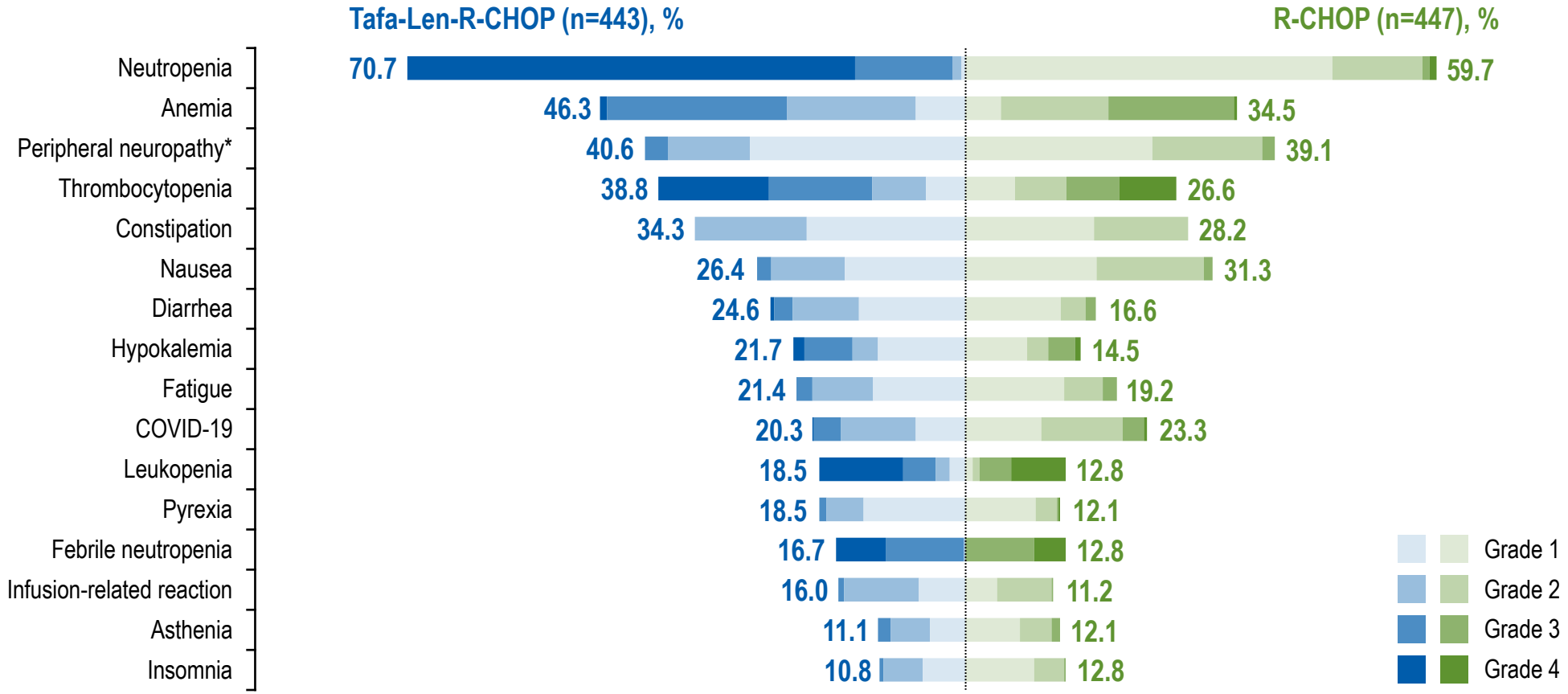
Overall Safety Summary

Variable	Tafa-Len-R-CHOP (n=443)	R-CHOP (n=447)
Patients with ≥1 TEAE, n (%)		
Any TEAE	437 (98.6)	434 (97.1)
Any treatment-related TEAE	423 (95.5)	407 (91.1)
Grade ≥3 TEAE	384 (86.7)	340 (76.1)
Serious TEAE	222 (50.1)	174 (38.9)
Fatal TEAE	26 (5.9)	17 (3.8)
TEAEs leading to discontinuation of all components of treatment, n (%)	23 (5.2)	24 (5.4)

- **Fatal TEAEs** were **predominantly balanced between groups**; exceptions included higher rates of **COVID-19 (7 [1.6%] vs 2 [0.4%])** and **sepsis (7 [1.6%] vs 3 [0.7%])** with Tafa-Len-R-CHOP
- Overall, **82 (18.5%) patients died** in the Tafa-Len-R-CHOP and **97 (21.7%)** in the R-CHOP groups

Safety population.
Len, lenalidomide; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab; TEAE, treatment-emergent adverse event.

Most Frequent TEAEs (≥12% in Any Group)



- **Most common** grade ≥3 adverse events were related to **cytopenias**
  - Rate of **serious febrile neutropenia:** 13.3% with Tafa-Len-R-CHOP and 9.8% with R-CHOP

Safety population. TEAEs are Medical Dictionary for Regulatory Activities, version 27·1, Preferred Terms. *Includes standard organ class group of preferred terms.
Len, lenalidomide; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab; TEAE, treatment-emergent adverse event.

Tafa-Len Did Not Impact Delivery of R-CHOP

Median Relative Dose Intensities, % (Across 6 Cycles)	Tafa-Len-R-CHOP (n=443)	R-CHOP (n=447)
R-CHOP component: rituximab, cyclophosphamide, doxorubicin, prednisone/prednisolone	100	100
R-CHOP component: vincristine	92.9	92.1

- **Median RDIs were high and the same** in both treatment groups across 6 treatment cycles **for each R-CHOP component**
- **Delivery of the R-CHOP backbone** was not compromised by **Tafa-Len**

Safety population.
Len, lenalidomide; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; RDI, relative dose intensity; Tafa, tafasitamab.

Summary and Conclusions

1

Tafa-Len-R-CHOP significantly prolonged PFS vs R-CHOP (HR 0.75; 2-year PFS rate, **Δ=8.2%**) in patients with previously untreated high-risk DLBCL and HGBL

2

Point estimates suggested trends toward **PFS advantage** with Tafa-Len-R-CHOP in **key prespecified subgroup analyses**

3

The **incremental safety events** observed with Tafa-Len-R-CHOP were **well-managed** and **did not impact delivery of the R-CHOP** backbone

4

The results **support the use of Tafa-Len-R-CHOP as a new standard first-line treatment option** for patients with high-risk DLBCL or HGBL, regardless of COO molecular subtype

DLBCL, diffuse large B-cell lymphoma; HGBL, high-grade B-cell lymphoma; HR, hazard ratio; IPI, International Prognostic Index; Len, lenalidomide; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

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Tafasitamab plus lenalidomide and R-CHOP versus R-CHOP for first-line treatment of patients with high-risk diffuse large B-cell lymphoma (frontMIND): a global, phase 3, randomised, double-blind, placebo-controlled trial

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