

# Tafasitamab Plus Lenalidomide and R-CHOP for Patients With Previously Untreated Diffuse Large B-Cell Lymphoma: Results From the Phase 3 frontMIND Study

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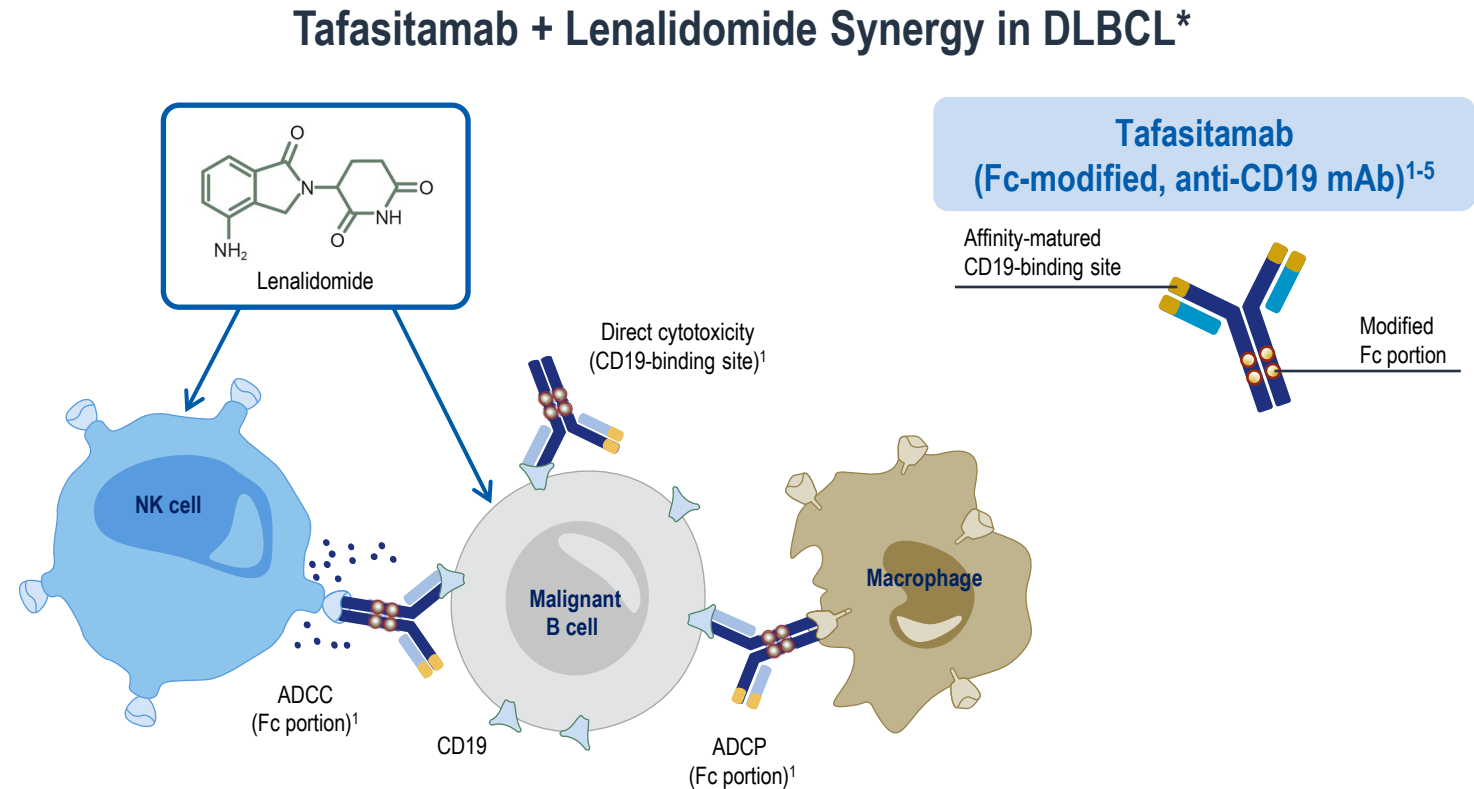
# Disclosures

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**Lenz:** Honoraria – *AbbVie, ADC, AstraZeneca, BeOne, Bristol Myers Squibb, Eli Lilly, Exscientia, Flindr, Genmab, Gilead, GSK, Hexal/Sandoz, Incyte Corporation, Miltenyi, MSD, Novartis, PentixaPharm, Pierre Fabre, Roche, Sobi*; Consultant/advisory boards – *AbbVie, ADC, AstraZeneca, BeOne, Bristol Myers Squibb, Eli Lilly, Exscientia, Flindr, Genmab, Gilead, GSK, Hexal/Sandoz, Incyte Corporation, Miltenyi, MSD, Novartis, PentixaPharm, Pierre Fabre, Roche, Sobi*; Research support – *AbbVie, AstraZeneca, Gilead, Novartis, Sobi*; Travel/accommodation/expenses – *AbbVie, AstraZeneca, BeOne, Bristol Myers Squibb, Gilead, Incyte Corporation, Novartis, Roche, Sobi*.

# 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



\*Adapted from "The use of tafasitamab in diffuse large B-cell lymphoma" by Düll J, et al. and licensed under CC BY 4.0.

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

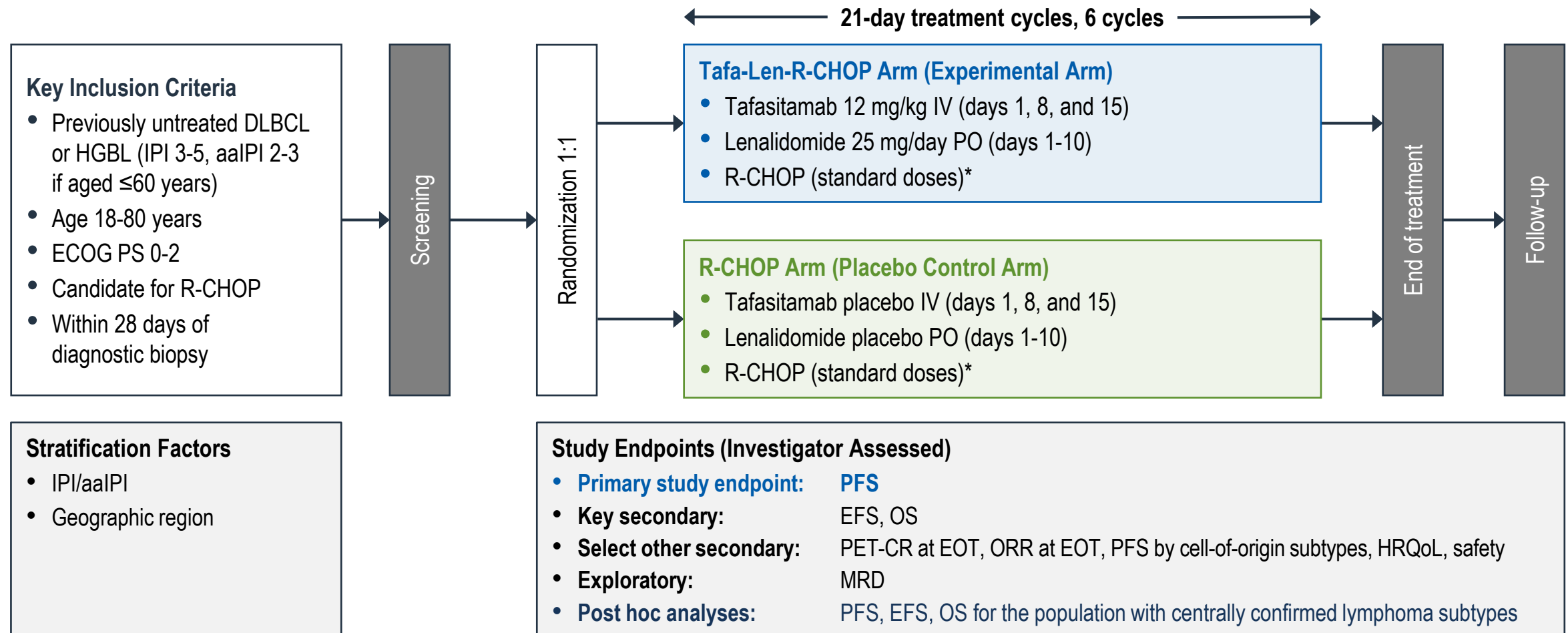
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- >40% of patients with high-risk DLBCL, are not cured with first-line R-CHOP<sup>1-3</sup>
- Tafasitamab and lenalidomide doubled the historical ORR of lenalidomide monotherapy in R/R DLBCL leading to FDA approval of the regimen for patients with R/R DLBCL<sup>4,5</sup>
- 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<sup>6</sup>
- **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.

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

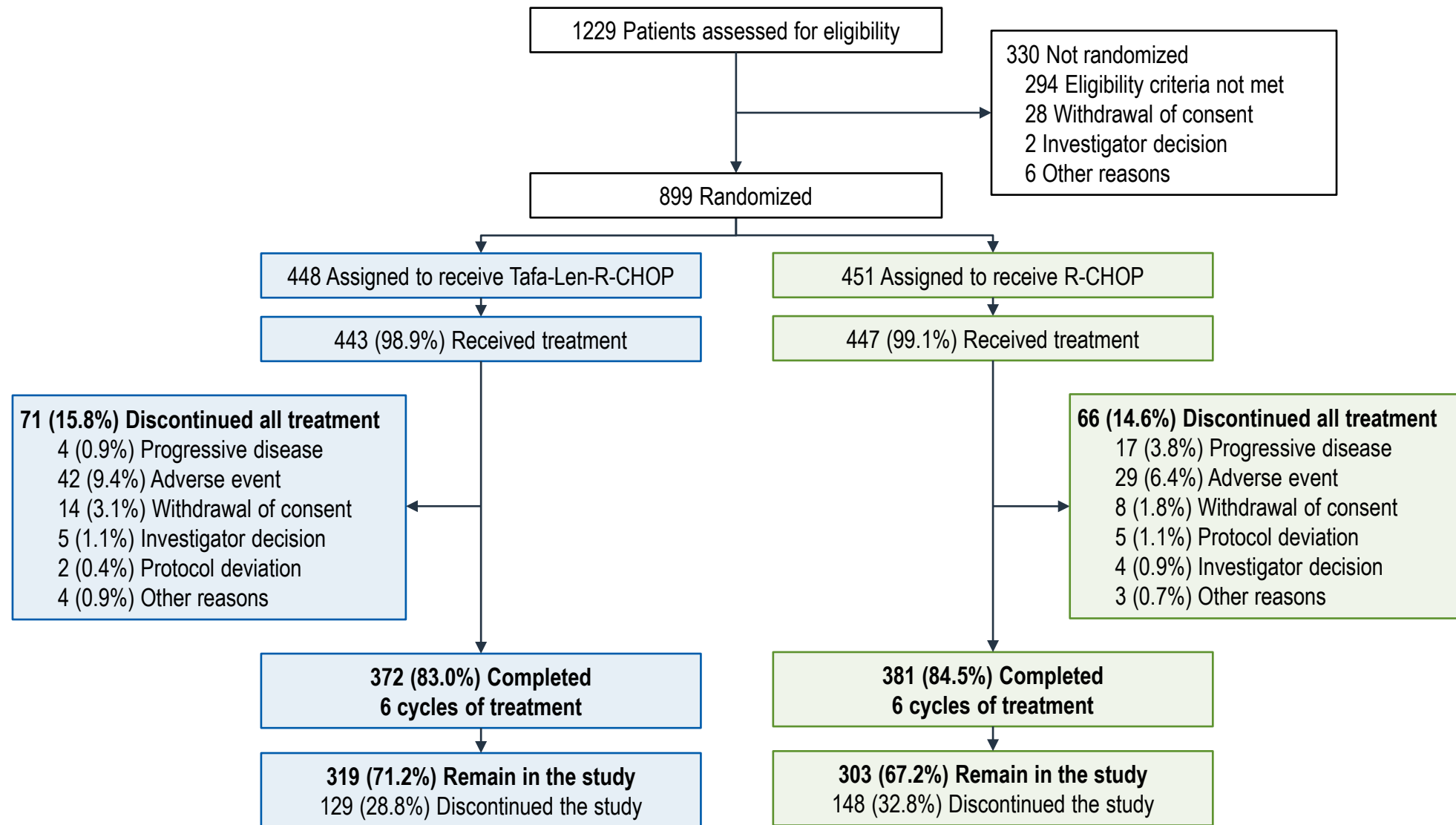


\*Rituximab administered at 375 mg/m<sup>2</sup> IV (day 1); cyclophosphamide, doxorubicin, and vincristine administered IV (day 1); prednisone/prednisolone administered PO (days 1-5).

aalPI, 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; MRD, minimal residual disease; 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

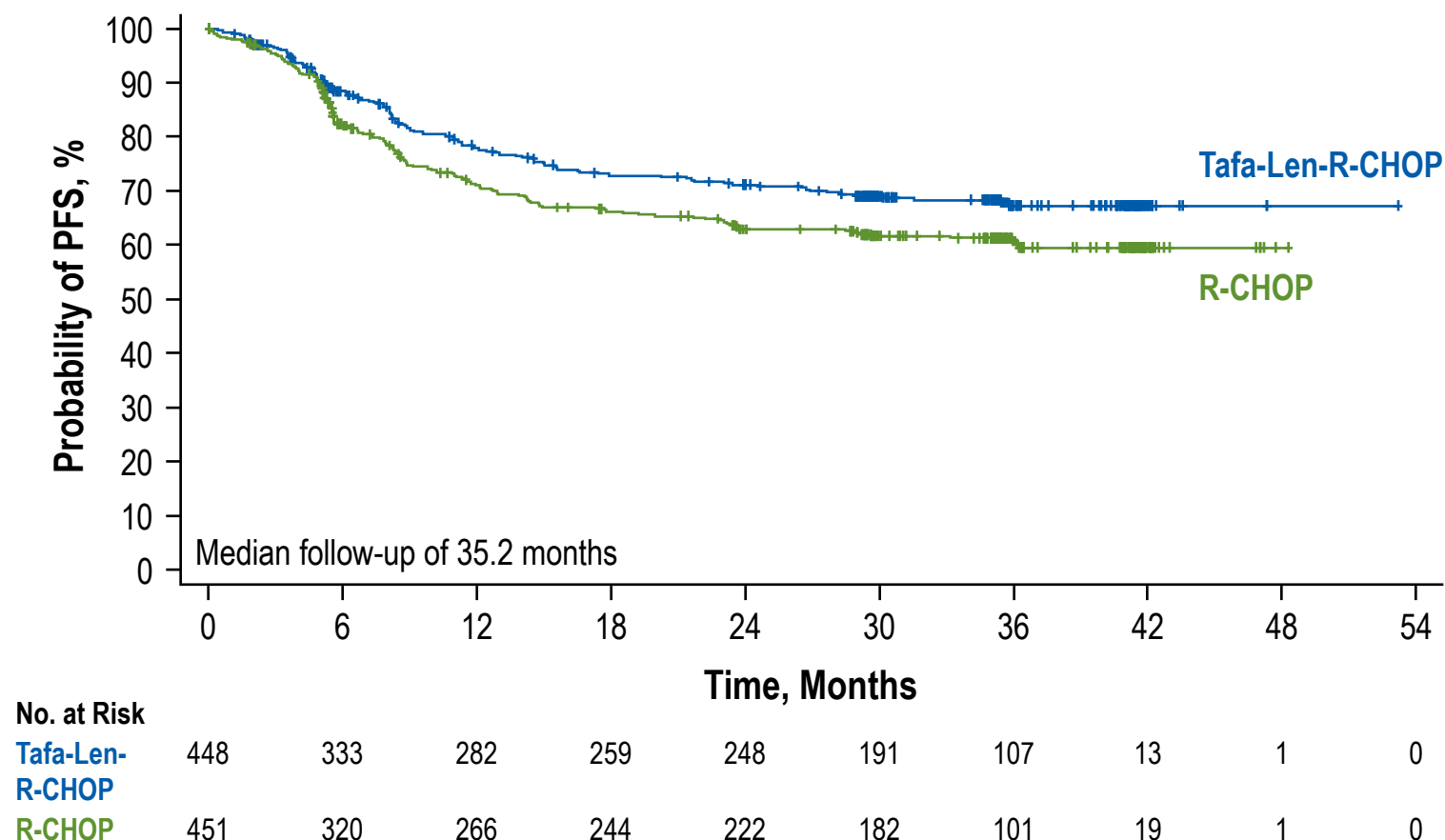
Overall ITT population

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/aalPI 2)	259 (57.8)	244 (54.1)	503 (56.0)
High risk (IPI 4-5/aalPI 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.  
aalPI, 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)



**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 ( $\Delta=8.2\%$ )
- **3-year PFS:**  
67.3% with Tafa-Len-R-CHOP vs 60.7% with R-CHOP ( $\Delta=6.6\%$ )

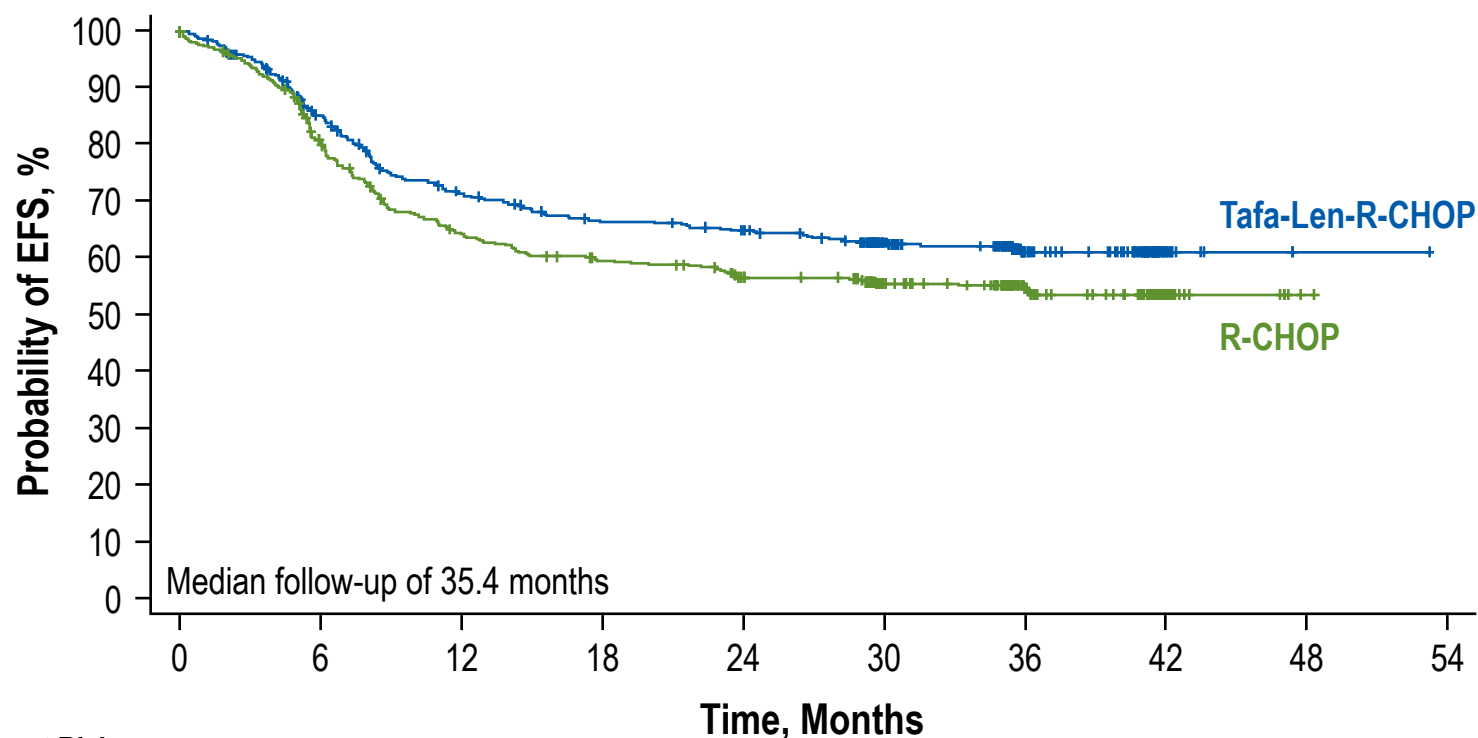
ITT population. \*Calculated using a stratified Cox proportional hazards model.

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)



**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

No. at Risk

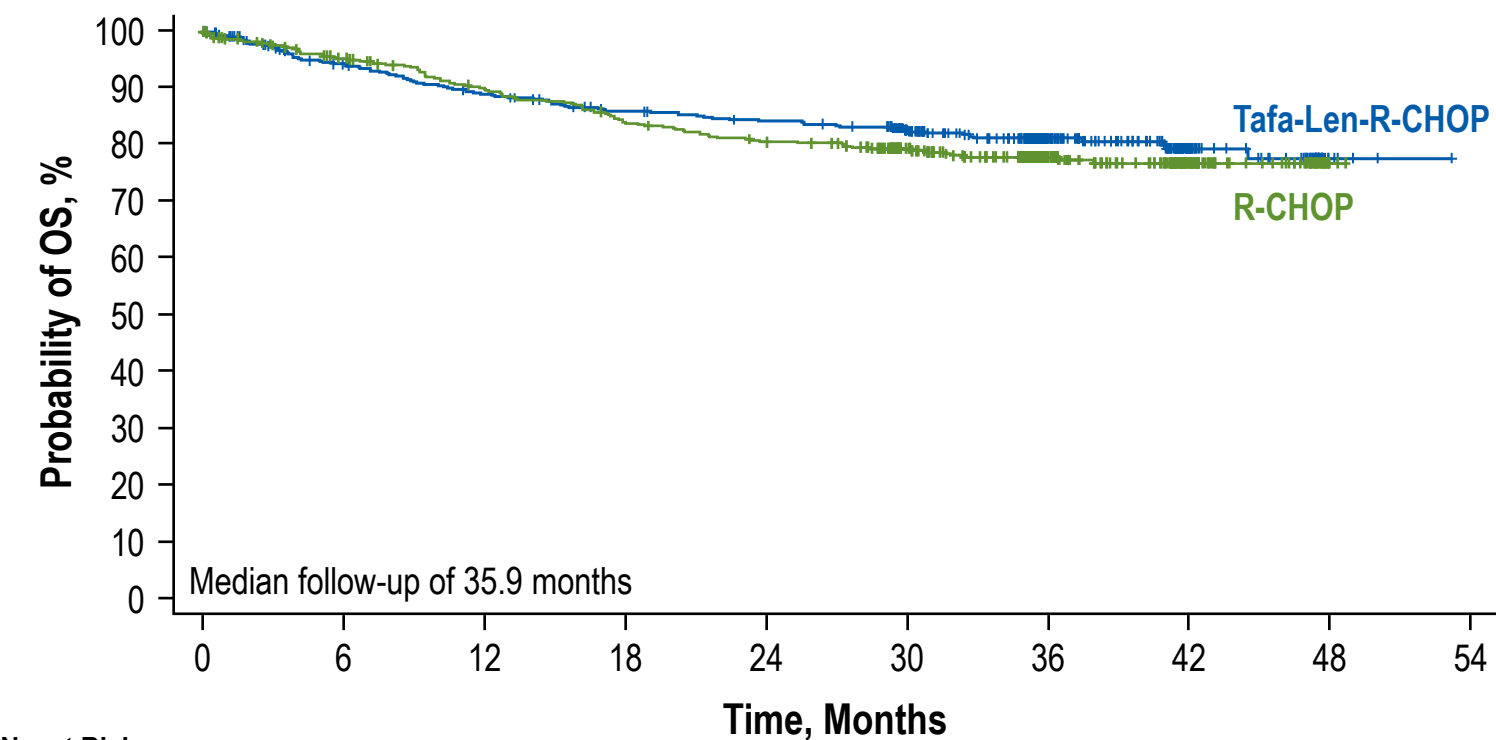
	0	6	12	18	24	30	36	42	48	54
Tafa-Len-R-CHOP	448	346	283	259	249	191	107	13	1	0
R-CHOP	451	339	267	244	222	182	101	19	1	0

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	0	6	12	18	24	30	36	42	48	54
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

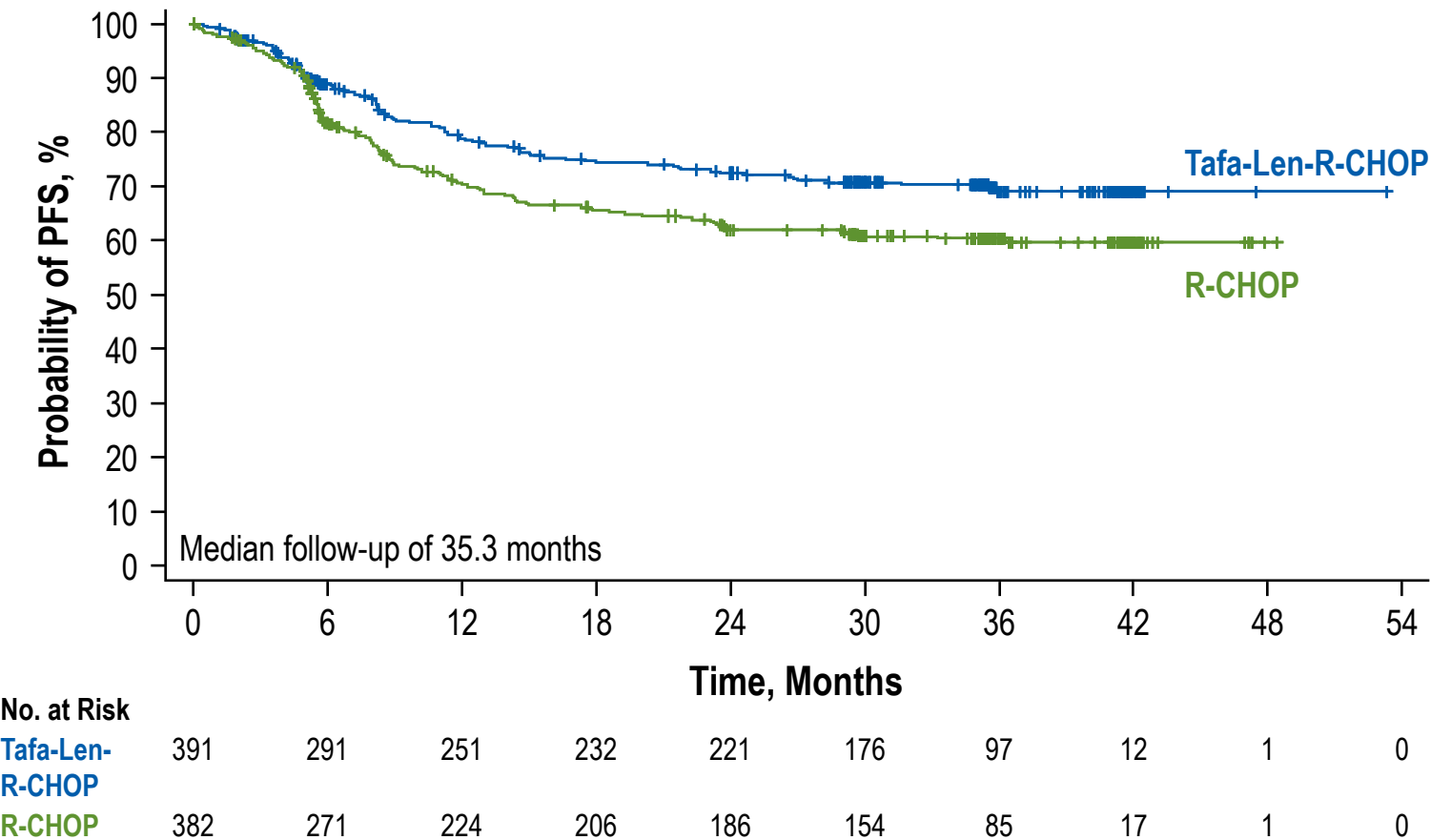
**HR 0.85\*** ( $P=0.2703$ )

**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\*** ( $P=0.0035$ )<sup>†</sup>

**95% CI: 0.52, 0.88**

*versus*

**Overall ITT population:**

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

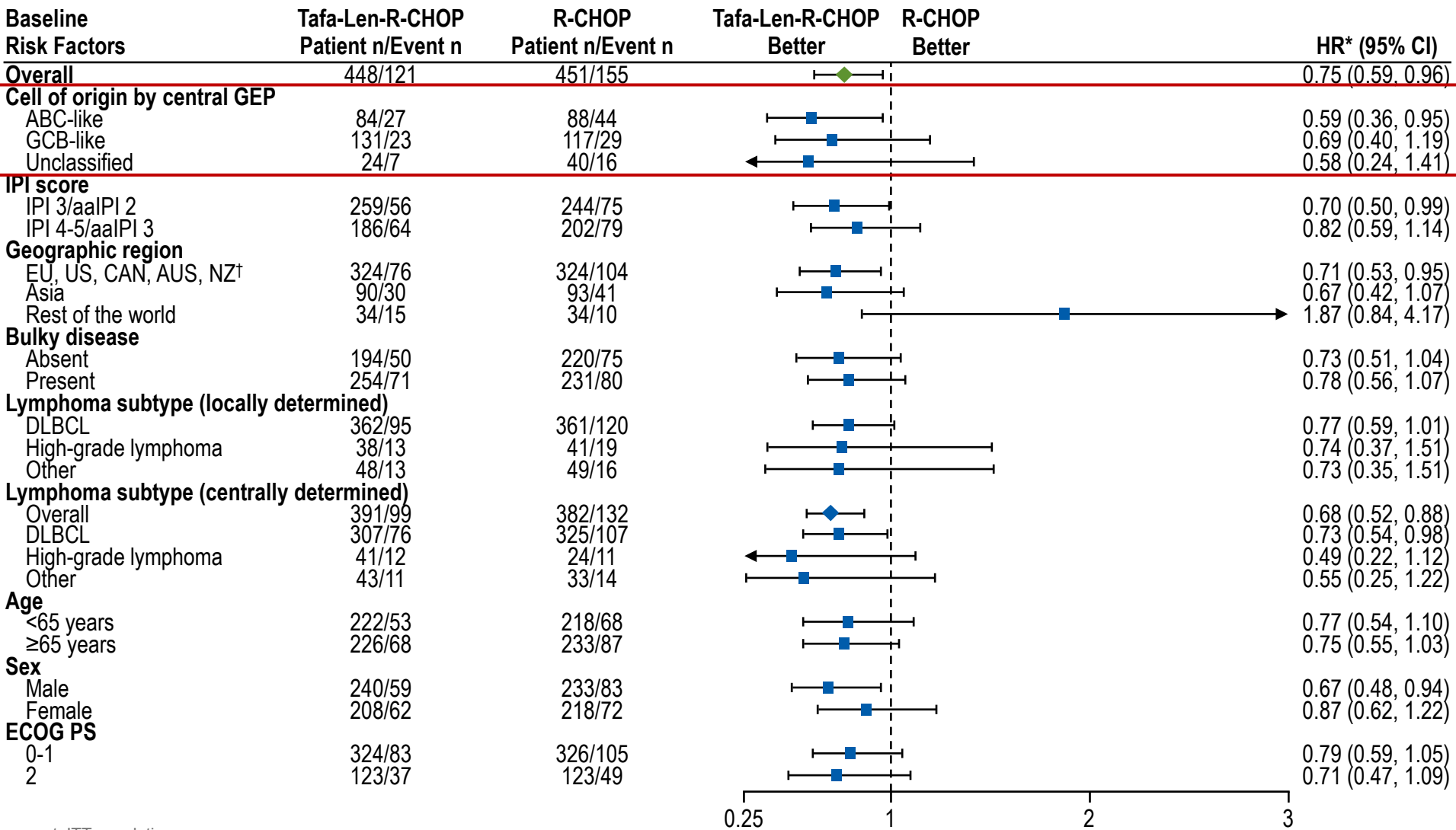
**95% CI: 0.59, 0.96**

- **2-year PFS:**  
72.7% with Tafa-Len-R-CHOP vs  
62.2% with R-CHOP
- **Differences in 2-year PFS rates:**  
 $\Delta=10.5\%$  in centrally confirmed  
 $\Delta=8.2\%$  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

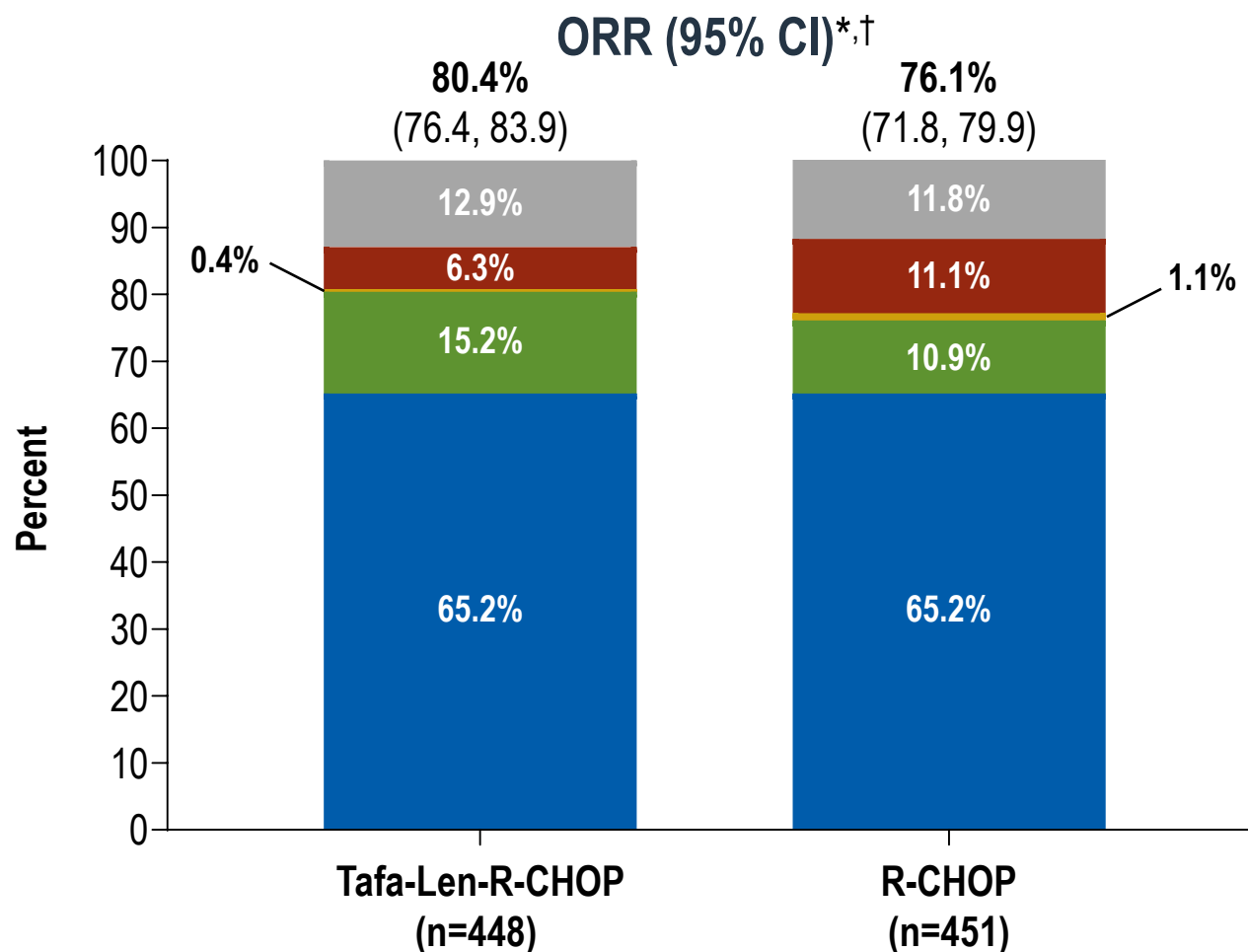
Post hoc analysis of PFS by Investigator; centrally confirmed lymphoma subtypes population. \*Calculated using a stratified Cox proportional hazards model. <sup>†</sup>Nominal  $P$  value.  
BL, Burkitt lymphoma; CI, confidence interval; FL, follicular lymphoma; HR, hazard ratio; ITT, intention-to-treat;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

# Consistent Trends Toward PFS Benefit in Prespecified Subgroups



PFS by investigator assessment; ITT population.  
\*Calculated using a stratified Cox proportional hazards model. †Europe, USA, Canada, Australia, and New Zealand.  
aalPI, 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



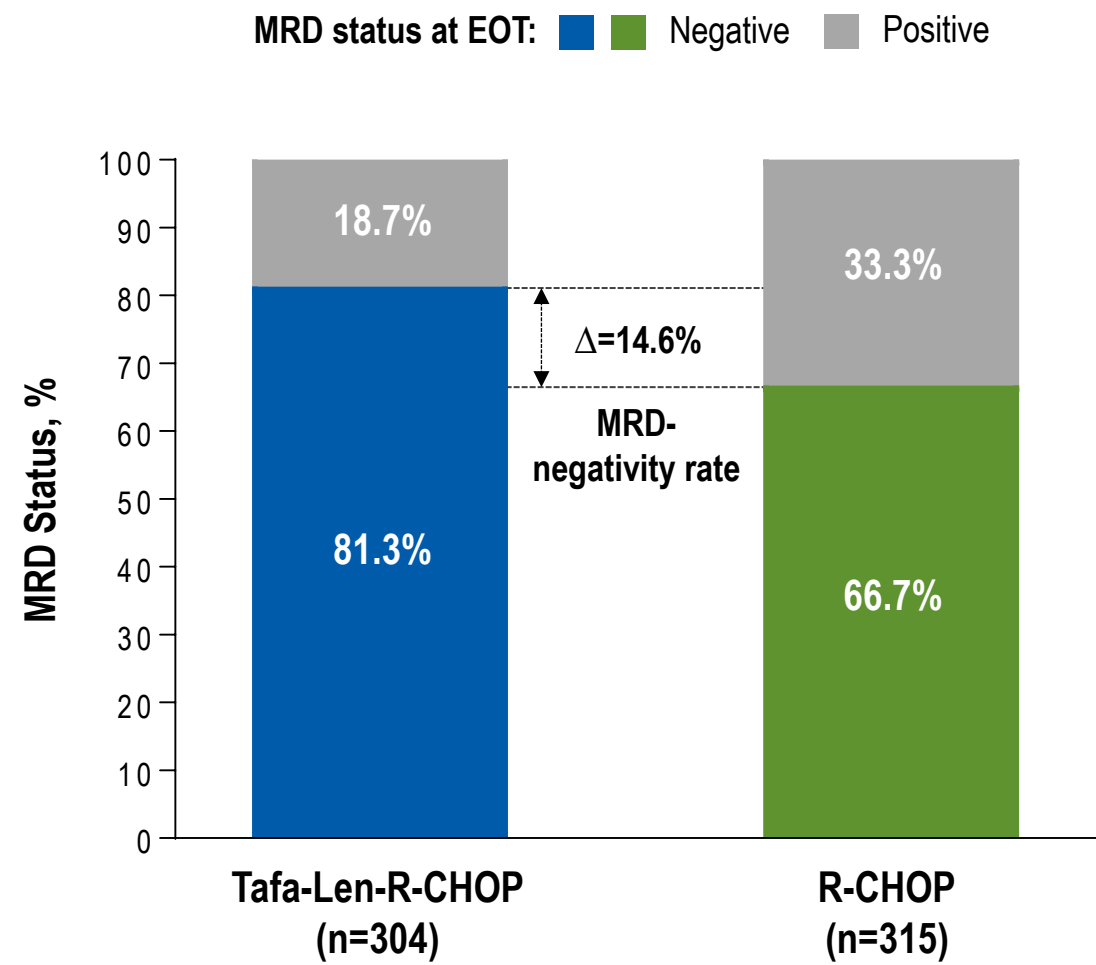
- **ORR** (OR 1.29 [95% CI: 0.94, 1.78]<sup>‡</sup>;  $P=0.1201^{\S}$ ) and **PET-negative CR rate** (OR 1.00 [95% CI: 0.76, 1.31]<sup>‡</sup>,  $P=0.9873^{\S}$ ) were **similar** between treatment arms at EOT
- **PR** rate was **numerically higher** in the Tafa-Len-R-CHOP arm

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.

<sup>‡</sup>95% CI calculated using the Wald method. <sup>§</sup>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.

# Higher MRD-Negativity Rate With Tafa-Len-R-CHOP at End of Treatment



MRD	Tafa-Len-R-CHOP	R-CHOP
MRD tested (baseline and EOT), n	336	349
MRD evaluable (baseline positive, EOT positive/negative), n*	304	315
Negative status at EOT, n (%) 95% CI	247 (81.3) (76.4, 85.5)	210 (66.7) (61.2, 71.9)

- MRD tested by a capture-based ctDNA assay

Exploratory analysis; ITT population. MRD-negativity threshold was defined for each sample as the minimum number of required genetic reads divided by the total sequencing reads (based on the 95th percentile, the lower limit of detection was  $\leq 10^{-5}$ ). \*Samples failed quality check: Tafa-Len-R-CHOP, n=7; R-CHOP, n=7. Samples with no tumor marker identified or negative at baseline: Tafa-Len-R-CHOP, n=25; R-CHOP, n=27. CI, confidence interval; ctDNA, circulating tumor DNA; EOT, end of treatment; ITT, intention-to-treat; Len, lenalidomide; MRD, minimal residual disease; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

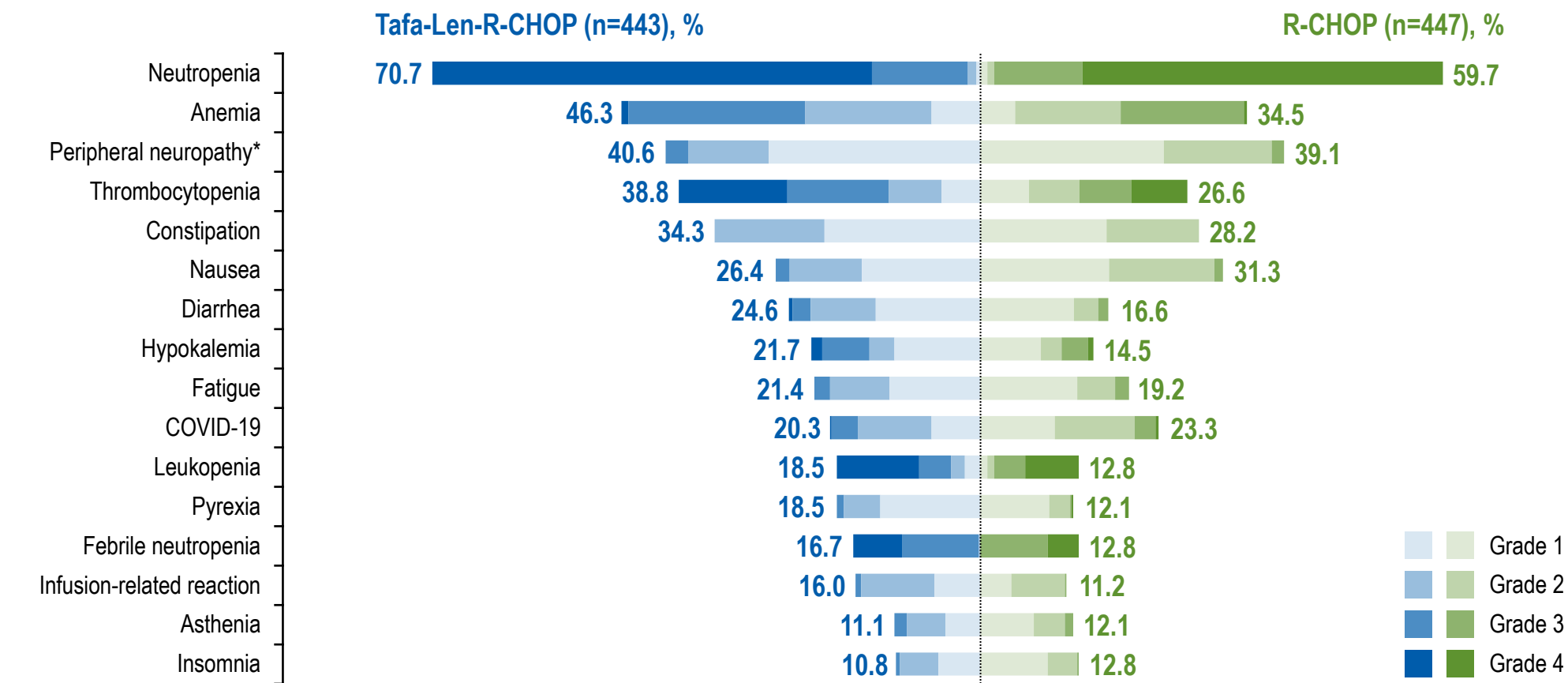
# Overall Safety Summary

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 ( $\geq 12\%$ in Any Group)



- **Most common** grade  $\geq 3$  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)
Individual R-CHOP components:		
Rituximab		
Cyclophosphamide	100	100
Doxorubicin		
Prednisone or prednisolone		
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

# Summary and Conclusions

1

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

2

Point estimates suggested trends toward **PFS advantage** in **key prespecified subgroup analyses**, and Tafa-Len-R-CHOP **improved MRD-negativity rate** at EOT

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 potential new standard first-line treatment** for patients with high-risk DLBCL or HGBL, regardless of COO molecular subtype

# Acknowledgments

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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

Georg Lenz, Marek Trněný, John M Burke, Grzegorz S Nowakowski, Christopher P Fox, Annalisa Chiappella, Johannes Duell, Young Woo Jeon, Chan Y Cheah, Jason Westin, Joseph Z Ye, Priscilla B Caguioa, David Belada, Ho-Jin Shin, Sung Yong Oh, Sandy Amorim, Matthew Ku, Heidi Mocikova, Javier López Jiménez, Gianluca Gaidano, Andreas Rosenwald, Roberto Chiarle, Philomena Colucci, Sonia Ioannidis, Lulu Cheng, Umberto Vitolo, on behalf of the frontMIND Study investigators\*



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