

Tafasitamab Plus Lenalidomide and Rituximab for Relapsed or Refractory Follicular Lymphoma: Results From a Phase 3 Study (inMIND)

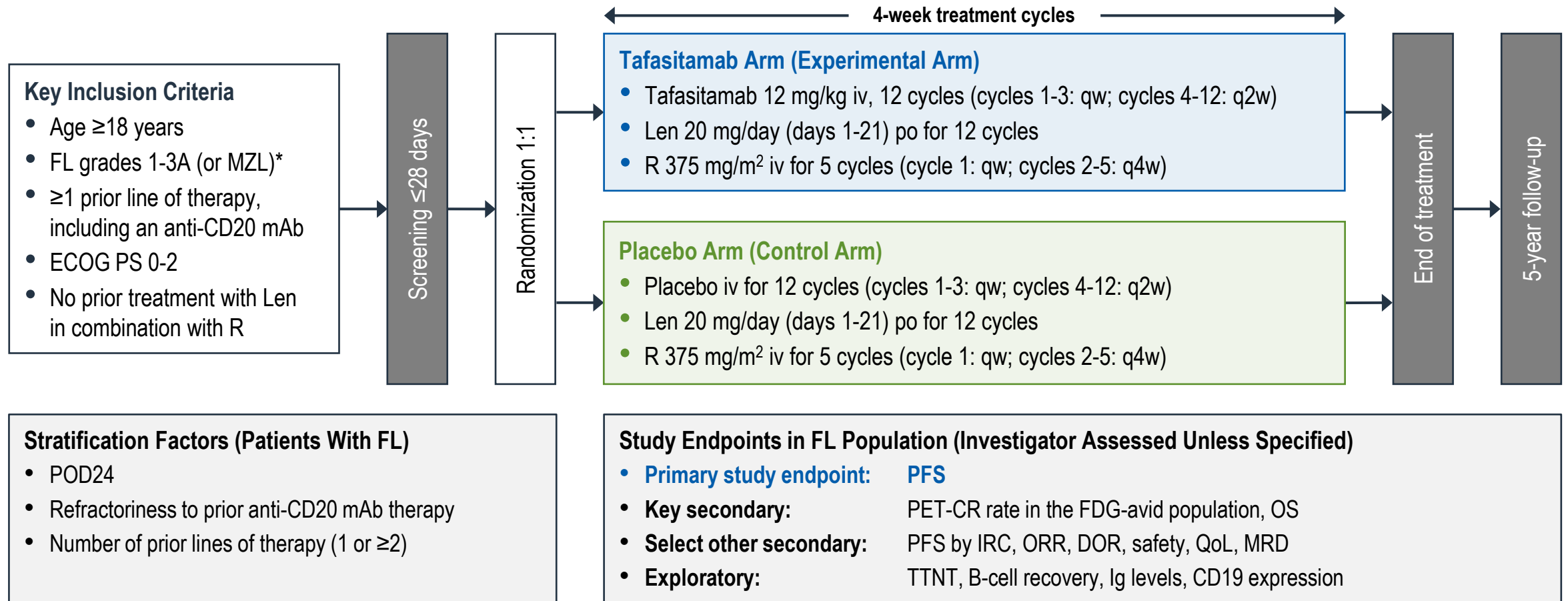
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Background

- Most patients with FL experience relapsed or refractory disease (R/R) and need multiple lines of therapy
 - Chemoimmunotherapy is often used frontline but yields shorter remissions with each treatment
 - Immunotherapy options are now preferred in the R/R setting, but improved durability is needed
- Lenalidomide (len) + rituximab (R) is approved for R/R FL based on the AUGMENT study¹
- Tafasitamab, a CD19-targeted mAb, induces direct cytotoxicity and enhances NK cell and macrophage immune-mediated mechanisms
 - Tafasitamab + len is approved for patients with transplant-ineligible R/R DLBCL based on the L-MIND study²
- **inMIND** (NCT04680052) study evaluated the efficacy and safety of adding tafasitamab to len + R in patients with R/R FL or MZL

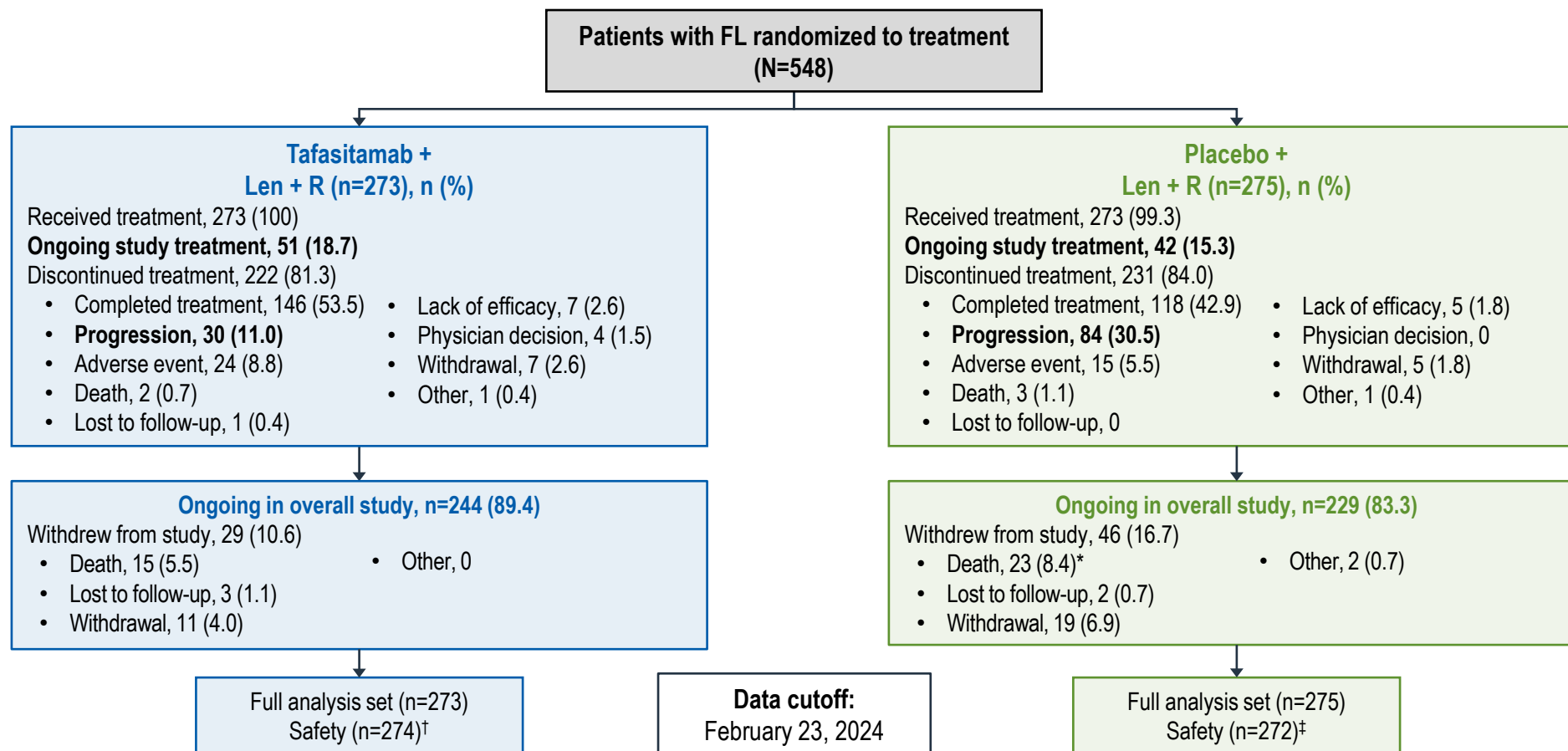
inMIND: Phase 3, Double-Blind, Placebo-Controlled, International, Multicenter Randomized Study



- Powered to assess PFS in the FL population, triggered when 174 investigator-assessed events occurred
- OS analysis planned after 5 years of follow-up

*Limited number of patients with MZL were enrolled but the study was not powered for this population; data for patients with MZL will be presented separately. DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; FL, follicular lymphoma; Ig, immunoglobulin; IRC, independent review committee; iv, intravenous; Len, lenalidomide; mAb, monoclonal antibody; MRD, minimal residual disease; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PET-CR, positron emission tomography-complete response; PFS, progression-free survival; po, orally; POD24, disease progression within 24 months of initial diagnosis; QoL, quality of life; qw, weekly; q2w, every 2 weeks; q4w, every 4 weeks; R, rituximab; TTNT, time to next treatment.

Patient Disposition



- At primary analysis, median number of cycles received was 12 with tafasitamab and 11 with placebo

*Death for 1 patient was reported but not recorded in the end-of-study form. †One patient randomized to the placebo + len + R group is included in the tafasitamab + len + R safety population because the patient erroneously received tafasitamab. ‡Three patients randomized to the placebo + len + R group are not included in the safety population because they erroneously received tafasitamab (n=1), or did not receive any study treatment due to confirmation of R hypersensitivity (n=1), or the patient withdrew from the study (n=1). FL, follicular lymphoma; Len, lenalidomide; R, rituximab.

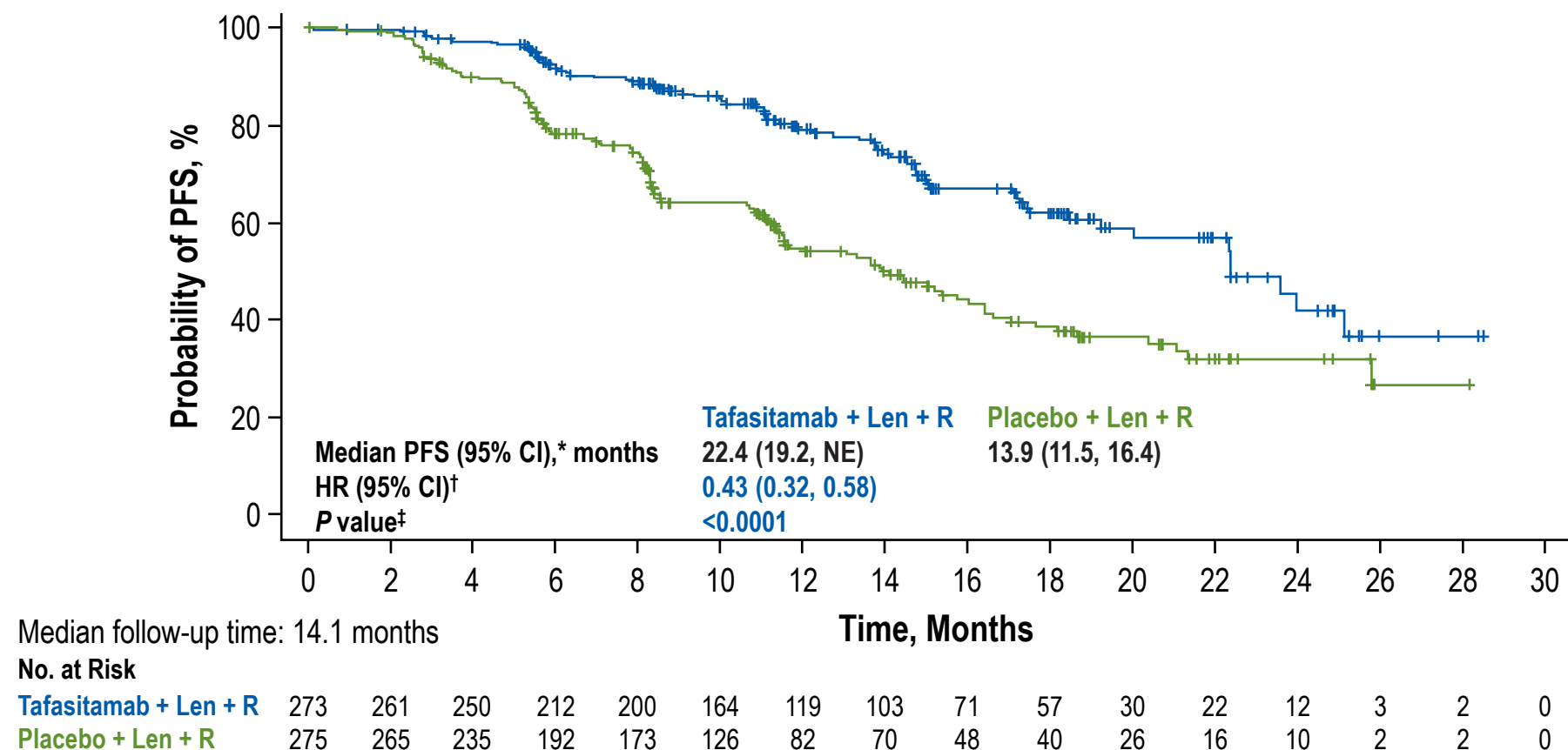
Baseline Characteristics

Variable	Tafasitamab + Len + R (n=273)	Placebo + Len + R (n=275)	Total (N=548)
Median age, years (range)	64.0 (36, 88)	64.0 (31, 85)	64.0 (31, 88)
≥75, n (%)	54 (19.8)	54 (19.6)	108 (19.7)
Male sex, n (%)	150 (54.9)	149 (54.2)	299 (54.6)
Median time since initial diagnosis of FL, years (range)	5.2 (0, 34)	5.5 (1, 33)	5.3 (0, 34)
ECOG PS at screening, n (%)			
0	181 (66.3)	192 (69.8)	373 (68.1)
1-2	92 (33.7)	83 (30.2)	175 (31.9)
Ann Arbor stage, n (%)			
I or II	52 (19.0)	50 (18.2)	102 (18.6)
III or IV	221 (81.0)	225 (81.8)	446 (81.4)
FL grade, n (%)			
1 or 2	203 (74.4)	203 (73.8)	406 (74.1)
3A	67 (24.5)	71 (25.8)	138 (25.2)
B symptoms, n (%)	63 (23.1)	67 (24.4)	130 (23.7)
FLIPI score, n (%)			
0-1	57 (20.9)	57 (20.7)	114 (20.8)
2	79 (28.9)	67 (24.4)	146 (26.6)
3-5	137 (50.2)	150 (54.5)	287 (52.4)
GELF criteria, n (%)	222 (81.3)	232 (84.4)	454 (82.8)
FL diagnosis confirmed by central pathology, n (%)	256 (93.8)	259 (90.5)	505 (92.2)

Treatment History

Variable	Tafasitamab + Len + R (n=273)	Placebo + Len + R (n=275)	Total (N=548)
Median number of prior lines of therapy (range)	1.0 (1, 7)	1.0 (1, 10)	1.0 (1, 10)
Number of prior lines of therapy, n (%)			
1	147 (53.8)	153 (55.6)	300 (54.7)
2	66 (24.2)	71 (25.8)	137 (25.0)
3	39 (14.3)	30 (10.9)	69 (12.6)
≥4	21 (7.7)	21 (7.6)	42 (7.7)
Time since last anti-lymphoma therapy, n (%)			
≤2 years	147 (53.8)	157 (57.1)	304 (55.5)
>2 years	126 (46.2)	118 (42.9)	244 (44.5)
POD24, n (%)	85 (31.1)	88 (32.0)	173 (31.6)
Relapsed/refractory status to last therapy, n (%)			
Relapsed	148 (54.2)	164 (59.6)	312 (56.9)
Refractory	112 (41.0)	97 (35.2)	209 (38.1)
Undetermined	13 (4.8)	14 (5.1)	27 (4.9)
Refractory to prior anti-CD20 therapy, n (%)	118 (43.2)	115 (41.8)	233 (42.5)

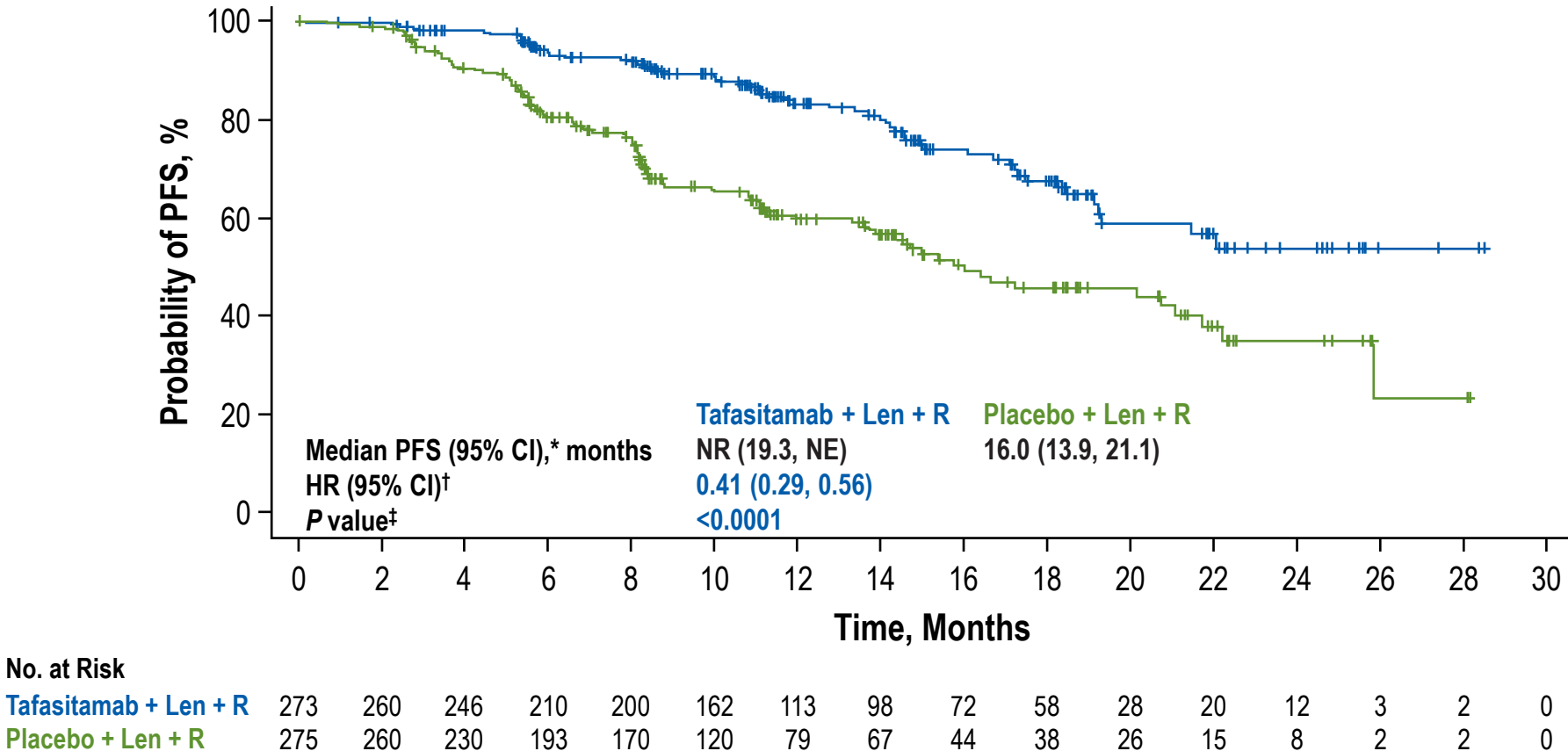
Primary Endpoint: PFS by Investigator Assessment



Significant improvement in PFS was observed with tafasitamab

ITT population. *Estimated using Kaplan-Meier method. [†]Estimated using a stratified Cox proportional hazard model. [‡]Stratified log-rank test with a 2-sided significance level of 5%. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; PFS, progression-free survival; R, rituximab.

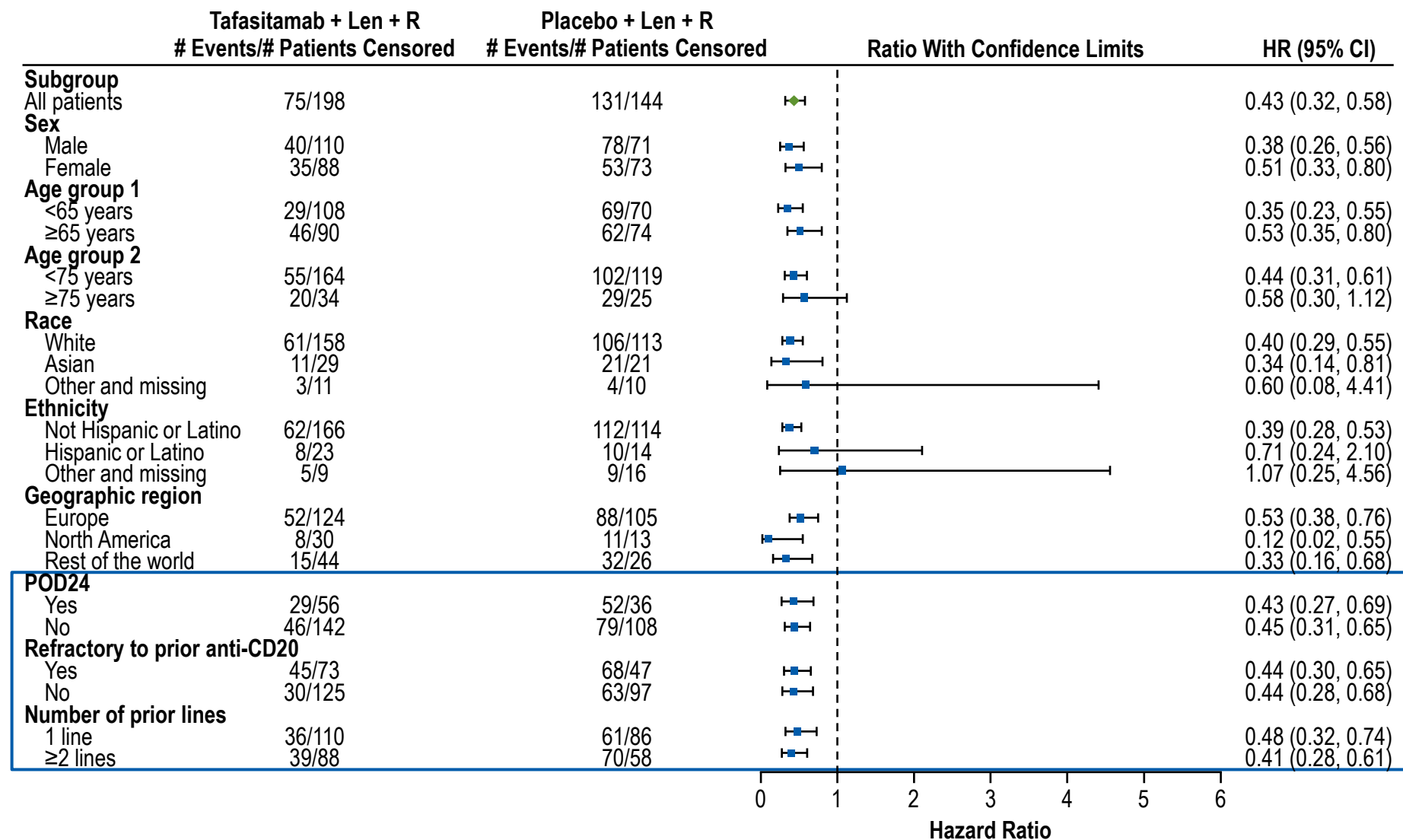
PFS by Independent Review Committee



Significant PFS benefit was confirmed by independent review committee

ITT population. *Estimated using Kaplan-Meier method. †Estimated using a stratified Cox proportional hazard model. ‡Nominal P value; stratified log-rank test with a 2-sided significance level of 5%. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; NR, not reached; PFS, progression-free survival; R, rituximab.

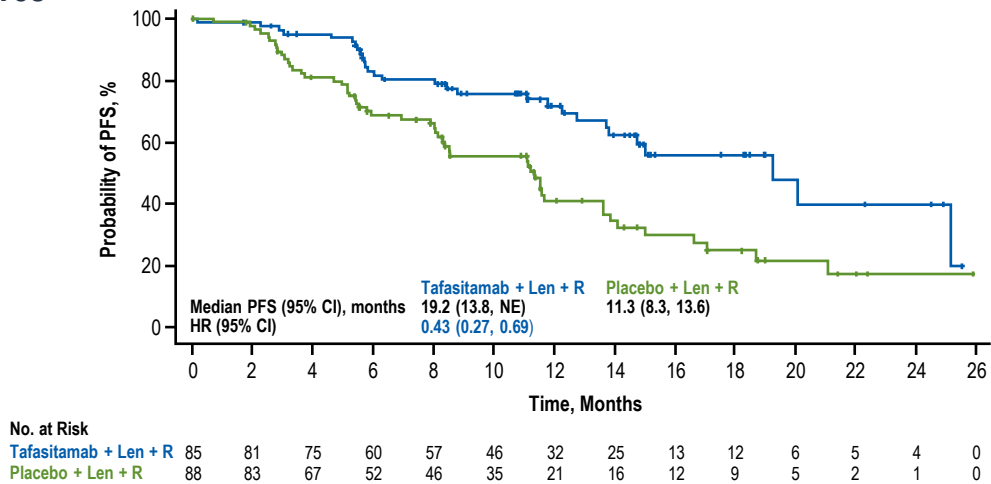
Prespecified Subgroup Analysis of PFS



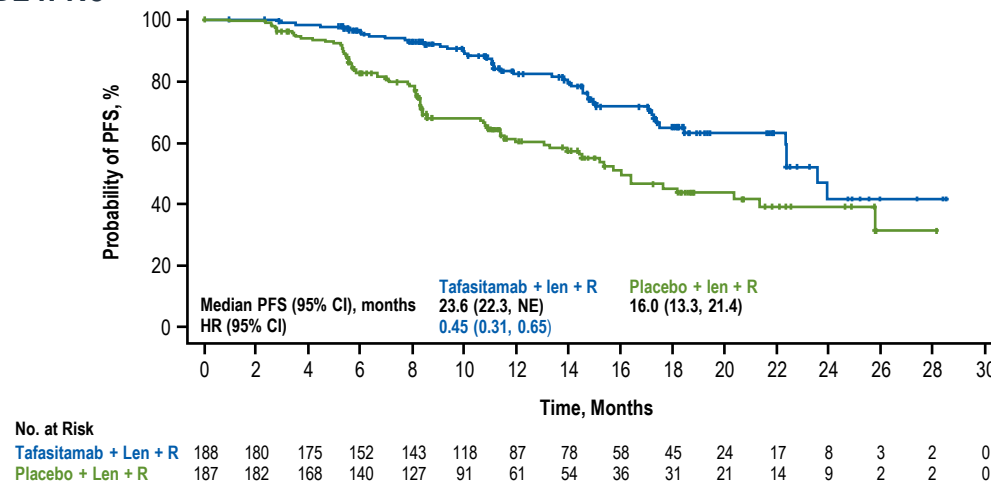
ITT population. Analysis by investigator assessment. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; PFS, progression-free survival; POD24, progression of disease within 24 months; R, rituximab.

PFS by POD24 Status and Refractoriness to Anti-CD20

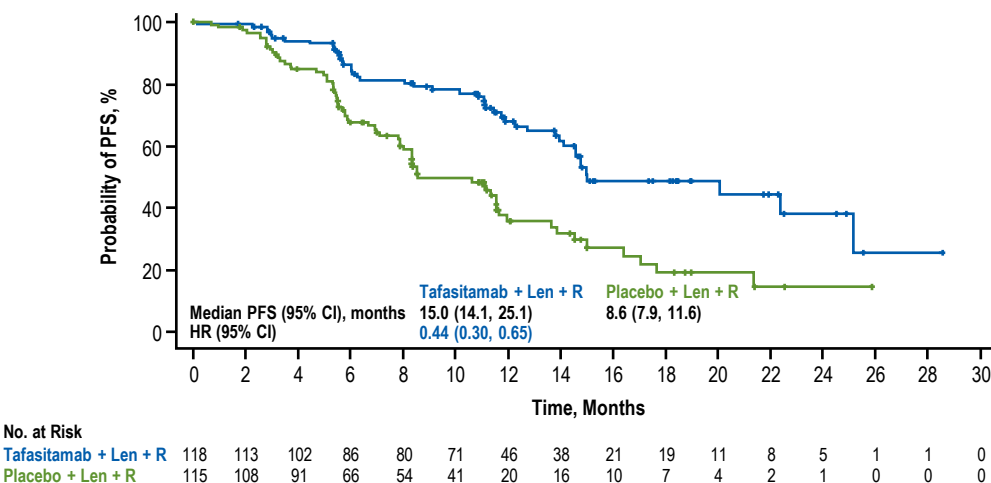
POD24: Yes



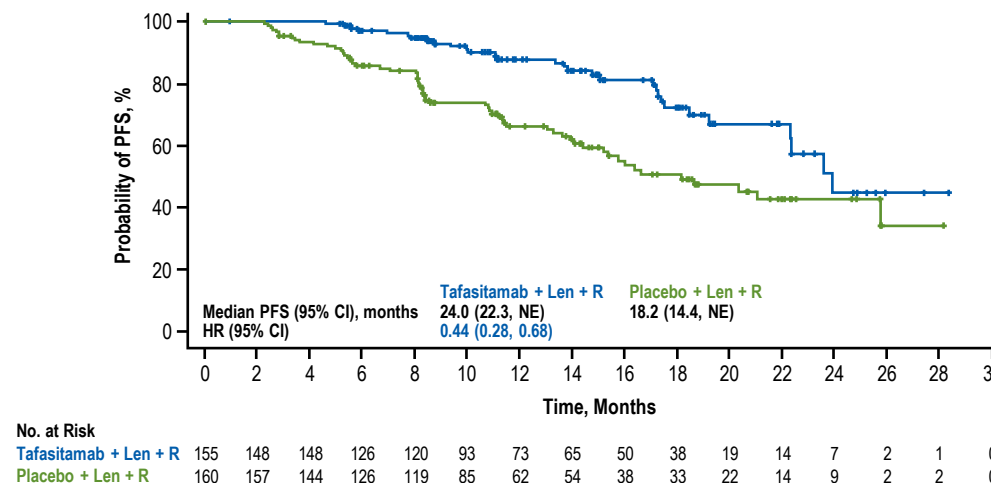
POD24: No



Anti-CD20 Refractory: Yes



Anti-CD20 Refractory: No



ITT population. Subgroup analyses are based on stratification factor. Analysis by investigator assessment. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; PFS, progression-free survival; POD24, progression of disease within 24 months of initial diagnosis; R, rituximab.

PET-CR and ORR

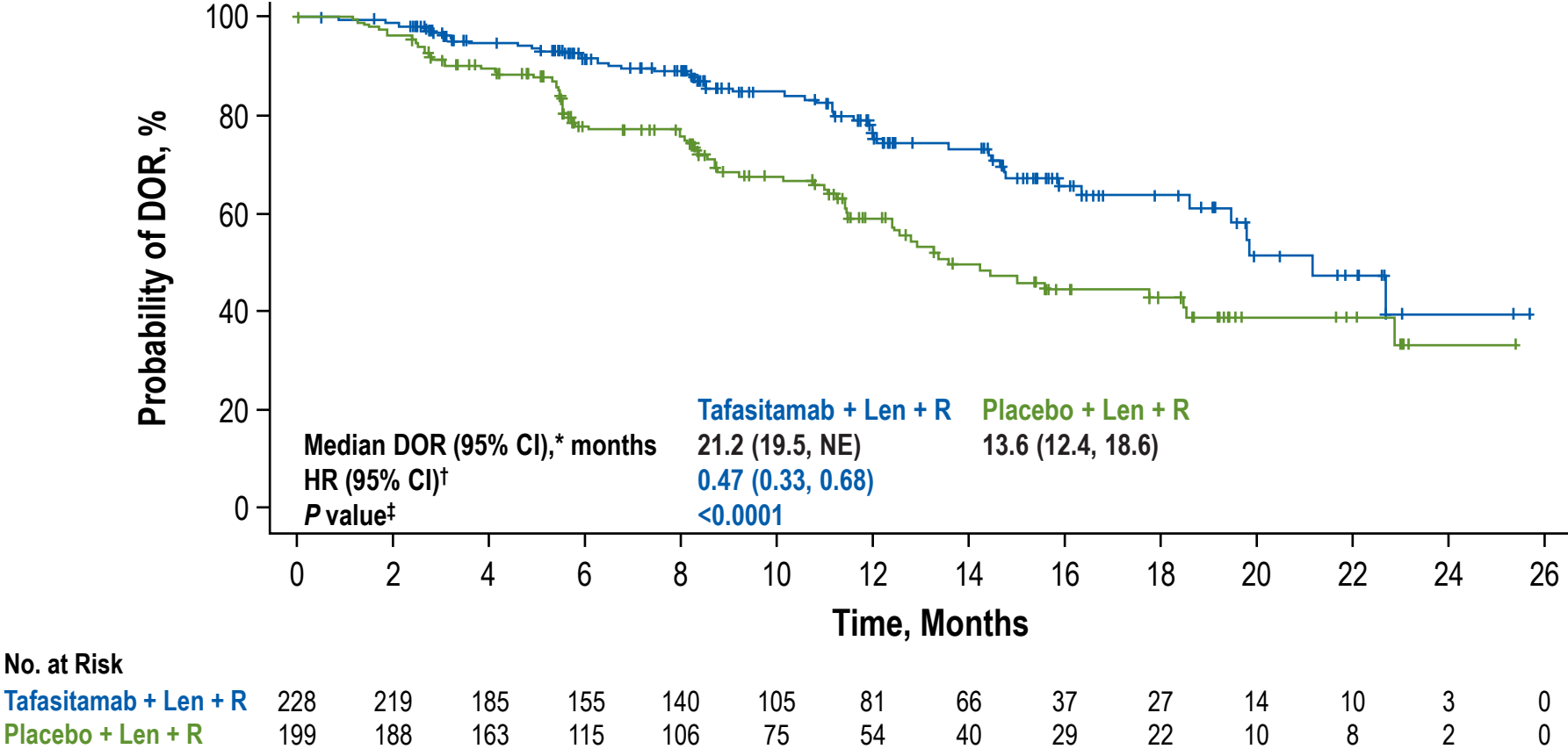
PET-CR (FDG-Avid Population)	Tafasitamab + Len + R	Placebo + Len + R
Patients with FDG-avid disease at baseline	251	254
Patients with postbaseline PET assessments, n (%) [*]	201/251 (80.1)	205/254 (80.7)
Best metabolic response based on PET, n (%) [†]		
CMR	124 (49.4)	101 (39.8)
PMR	37 (14.7)	39 (15.4)
NMR/SD	19 (7.6)	12 (4.7)
PMD	19 (7.6)	51 (20.1)
Not done	50 (19.9)	46 (19.3)
PET-CR rate, % (95% CI)	49.4 (43.1, 55.8)	39.8 (33.7, 46.1)
Odds ratio (95% CI)	1.5 (1.04, 2.13)	
Nominal <i>P</i> value	0.0286	

ORR (ITT Population)	Tafasitamab + Len + R	Placebo + Len + R
Patients, n	273	275
Best overall response, n (%) [‡]		
CR	142 (52.0)	112 (40.7)
PR	86 (31.5)	87 (31.6)
SD	28 (10.3)	46 (16.7)
PD	7 (2.6)	20 (7.3)
NE	2 (0.7)	0
Not done	8 (2.9)	10 (3.6)
ORR, % (95% CI)	83.5 (78.6, 87.7)	72.4 (66.7, 77.6)
Odds ratio (95% CI)	2.0 (1.30, 3.02)	
Nominal <i>P</i> value	0.0014	

Significant improvement in PET-CR rate and ORR was observed with tafasitamab

Analysis by investigator assessment. ^{*}Calculated based on patients with a positive PET scan at baseline, defined as having a Deauville score of 4 or 5 at baseline. [†]Two patients (0.8%) in both arms had PET after confirmed PD or new antilymphoma treatment initiation. [‡]Per Lugano 2014 classification. CI, confidence interval; CMR, complete metabolic response; CR, complete response; FDG, fluorodeoxyglucose; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; NMR, nonmetabolic response; ORR, overall response rate; PD, progressive disease; PET, positron emission tomography; PET-CR, positron emission tomography-complete response; PMD, progressive metabolic disease; PMR, partial metabolic response; PR, partial response; R, rituximab; SD, stable disease.

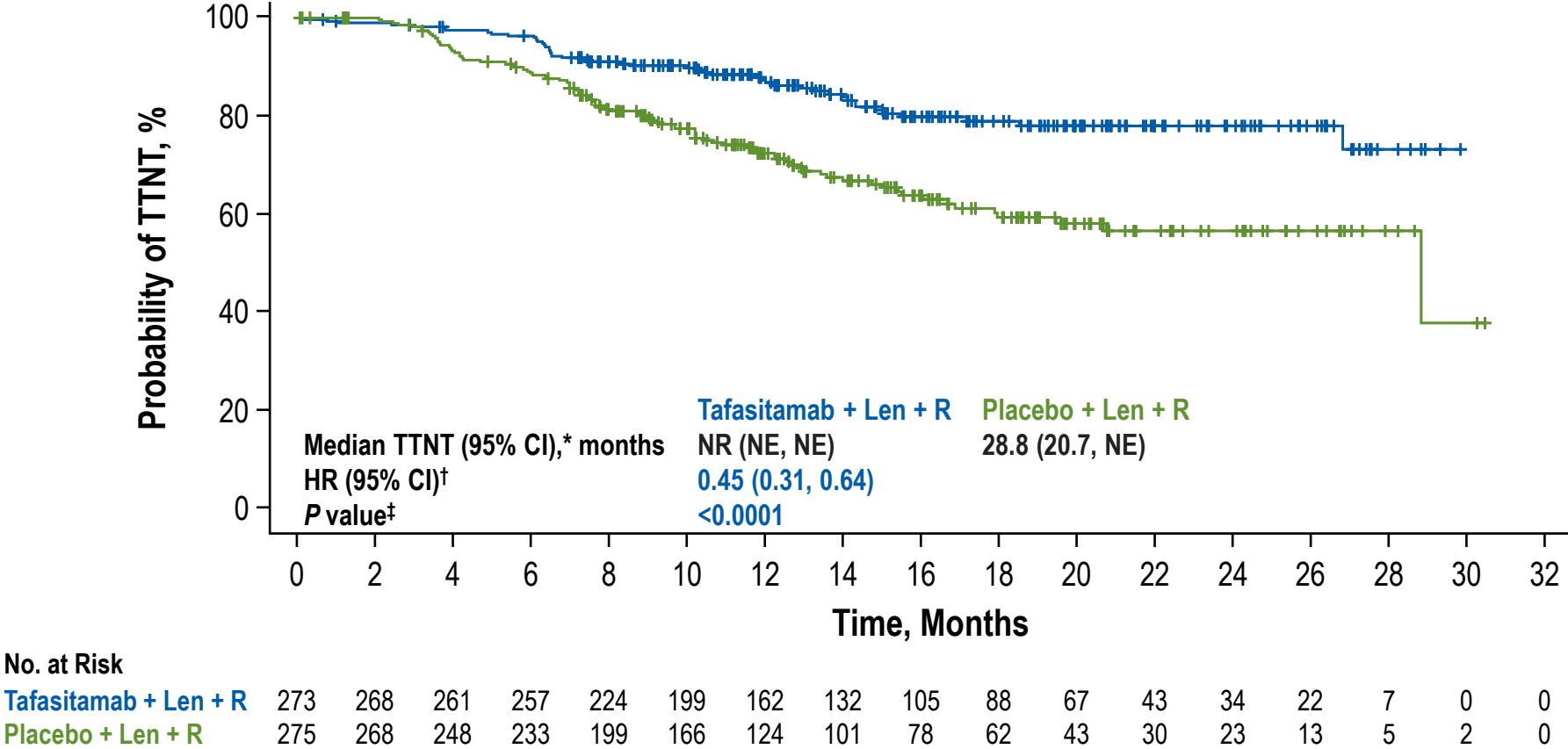
Duration of Response



Significant improvement in DOR was observed with tafasitamab

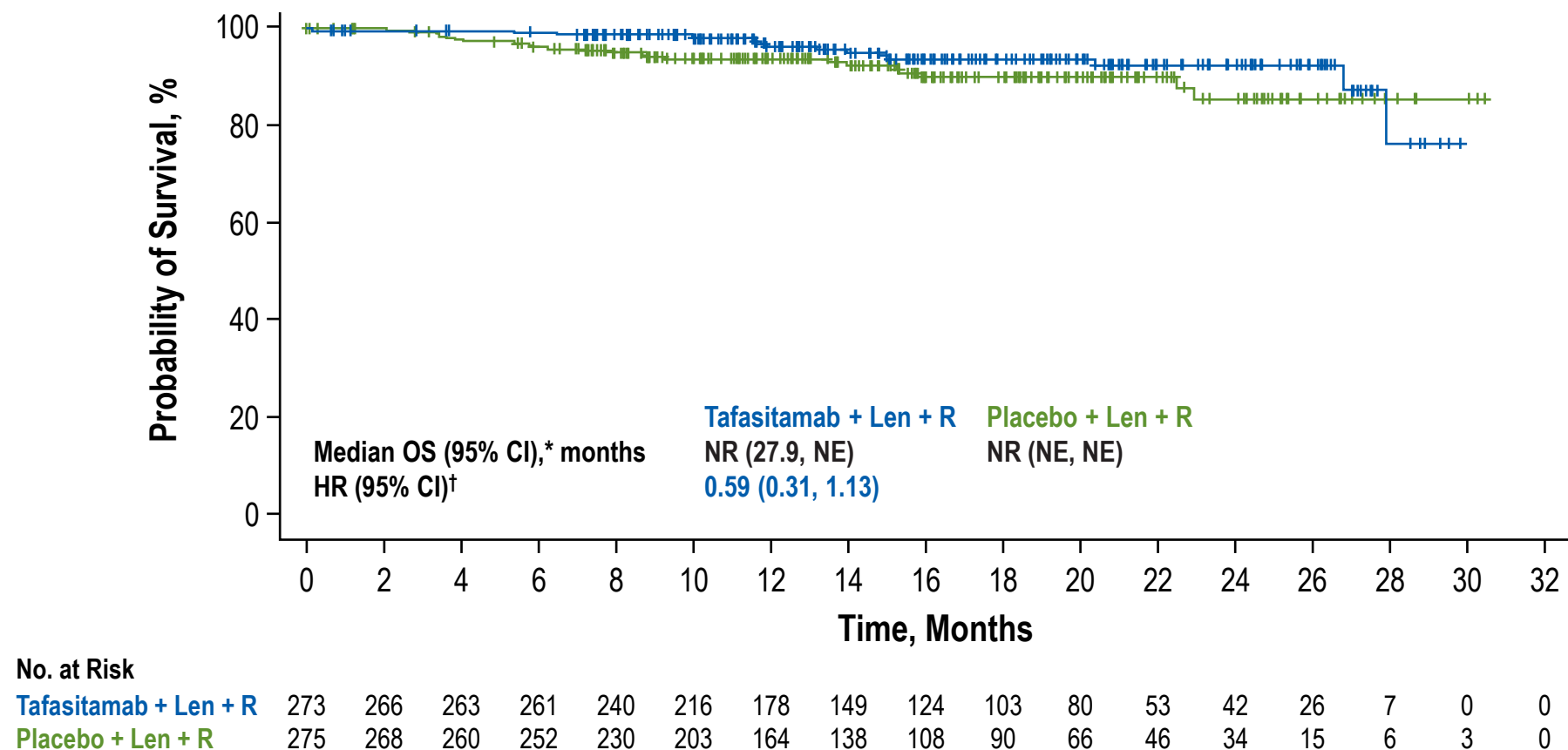
ITT population. Analysis by investigator assessment. *Estimated using Kaplan-Meier method. †Estimated using a stratified Cox proportional hazard model. ‡Nominal P value; stratified log-rank test with a 2-sided significance level of 5%. CI, confidence interval; DOR, duration of response; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; R, rituximab.

Time to Next Treatment



ITT population. Analysis by investigator assessment. *Estimated using Kaplan-Meier method. †Estimated using a stratified Cox proportional hazard model. ‡Nominal P value; stratified log-rank test with a 2-sided significance level of 5%. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; len, Lenalidomide; NE, not evaluable; NR, not reached; R, rituximab; TTNT, time to next treatment.

Overall Survival



- OS was tested only for futility at the time of the primary analysis
- After a median follow-up of 15.3 months, the futility threshold was not crossed and a positive trend was observed

ITT population. Analysis by investigator assessment. *Estimated using Kaplan-Meier method. †Estimated using a stratified Cox proportional hazard model. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; NR, not reached; OS, overall survival; R, rituximab.

Most Frequent Any-Grade TEAEs (≥15% in Any Group)

Preferred Term, n (%)	Tafasitamab + Len + R (n=274)*	Placebo + Len + R (n=272)†	Total (n=546)
Any adverse event	272 (99.3)	270 (99.3)	542 (99.3)
Neutropenia	133 (48.5)	123 (45.2)	256 (46.9)
Diarrhea	103 (37.6)	77 (28.3)	180 (33.0)
COVID-19	86 (31.4)	64 (23.5)	150 (27.5)
Constipation	80 (29.2)	67 (24.6)	147 (26.9)
Rash	60 (21.9)	58 (21.3)	118 (21.6)
Fatigue	58 (21.2)	43 (15.8)	101 (18.5)
Cough	52 (19.0)	47 (17.3)	99 (18.1)
Pyrexia	52 (19.0)	44 (16.2)	96 (17.6)
Muscle spasms	49 (17.9)	49 (18.0)	98 (17.9)
Nausea	49 (17.9)	38 (14.0)	87 (15.9)
Infusion-related reaction	43 (15.7)	41 (15.1)	84 (15.4)
Thrombocytopenia	37 (13.5)	42 (15.4)	79 (14.5)
Pruritus	44 (16.1)	28 (10.3)	72 (13.2)

Safety population. *One patient randomized to the placebo + len + R group is included in the tafasitamab + len + R safety population because the patient erroneously received tafasitamab. †Three patients randomized to the placebo + len + R group are not included in the safety population because they erroneously received tafasitamab (n=1), or did not receive any study treatment due to confirmation of R hypersensitivity (n=1), or the patient withdrew from the study (n=1). COVID-19, coronavirus disease 2019; Len, lenalidomide; R, rituximab; TEAE, treatment-emergent adverse event.

Grade 3 or 4 TEAEs and Dose Modifications

Most Common Grade 3 or 4 TEAEs (≥5% in Any Group)

Preferred Term, n (%)	Tafasitamab + Len + R (n=274)*	Placebo + Len + R (n=272)†	Total (n=546)
Neutropenia	109 (39.8)	102 (37.5)	211 (38.6)
Pneumonia	23 (8.4)	14 (5.1)	37 (6.8)
Thrombocytopenia	17 (6.2)	20 (7.4)	37 (6.8)
Neutrophil count decreased	16 (5.8)	18 (6.6)	34 (6.2)
Anemia	12 (4.4)	16 (5.9)	28 (5.1)
COVID-19	16 (5.8)	6 (2.2)	22 (4.0)
COVID-19 pneumonia	13 (4.7)	3 (1.1)	16 (2.9)

- Tafasitamab and placebo dose interruptions or discontinuations due to TEAEs were similar between treatment arms, n (%):
 - Dose delay or interruption due to TEAEs: 203 (74%) vs 190 (70%)
 - Discontinued study treatment due to TEAEs: 30 (11%) vs 18 (7%)
- Len discontinuations due to TEAEs were similar between tafasitamab and placebo arms, n (%):
 - 39 (14%) vs 31 (11%)
- Len dose reductions were similar between tafasitamab and placebo arms
 - Median relative dose intensity: 86% vs 87%

Safety population. *One patient randomized to the placebo + len + R group is included in the tafasitamab + len + R safety population because the patient erroneously received tafasitamab. †Three patients randomized to the placebo + len + R group are not included in the safety population because they erroneously received tafasitamab (n=1), or did not receive any study treatment due to confirmation of R hypersensitivity (n=1), or the patient withdrew from the study (n=1). COVID-19, coronavirus disease 2019; Len, lenalidomide; R, rituximab; TEAE, treatment-emergent adverse event.

Summary of Deaths and Fatal TEAEs

Variable, n (%)	Tafasitamab + Len + R (n=274)*	Placebo + Len + R (n=272)†	Total (n=546)
All deaths	15 (5.5)	23 (8.5)	38 (7.0)
Disease progression	5 (1.8)	17 (6.3)	22 (4.0)
Adverse event with fatal outcome	6 (2.2)	6 (2.2)	12 (2.2)
COVID-19	2 (0.7)	0	2 (0.4)
COVID-19 pneumonia	0	2 (0.7)	2 (0.4)
Sepsis	1 (0.4)	1 (0.4)	2 (0.4)
Adenocarcinoma gastric	1 (0.4)	0	1 (0.2)
Carcinoid tumor (large intestine)	1 (0.4)	0	1 (0.2)
Death‡	1 (0.4)	0	1 (0.2)
Bronchopulmonary aspergillosis	0	1 (0.4)	1 (0.2)
Cardiac failure	0	1 (0.4)	1 (0.2)
Pneumonia	0	1 (0.4)	1 (0.2)
Deaths reported after 90-day follow-up interval	4 (1.5)	0	4 (0.7)
Heart failure	1 (0.4)	0	1 (0.2)
Lung infection	1 (0.4)	0	1 (0.2)
Pneumonia	1 (0.4)	0	1 (0.2)
Respiratory failure	1 (0.4)	0	1 (0.2)

Safety population. *One patient randomized to the placebo + len + R group is included in the tafasitamab + len + R safety population because the patient erroneously received tafasitamab. †Three patients randomized to the placebo + len + R group are not included in the safety population because they erroneously received tafasitamab (n=1), or did not receive any study treatment due to confirmation of R hypersensitivity (n=1), or the patient withdrew from the study (n=1). ‡This is an unexplained death case, not related to any TEAE or other event. COVID-19, coronavirus disease 2019; Len, lenalidomide; R, rituximab; TEAE, treatment-emergent adverse event.

FL Patient Population Comparison

Variable	inMIND Tafasitamab + Len + R (n=273)	inMIND Placebo + Len + R (n=275)	AUGMENT ¹ R + Len (n=147)
Median age, years	64	64	62
Male, %	55	54	42
Ann Arbor stage IV at enrollment, %	55	59	30
FL grade 3A, %	25	26	12
FLIPI high risk (score 3-5) , %	50	55	37
ECOG PS 0, %	66	70	67
ECOG PS 1-2, %	34	30	33
B symptoms present, %	23	24	8
High tumor burden per GELF (yes), %	81	84	52
Refractory to last prior regimen, %	41	35	18
Refractory to anti-CD20, %	43	42	–

1, Leonard JP, et al. *J Clin Oncol*. 2019;37:1188-1899.
 ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; FLIPI, Follicular Lymphoma International Prognostic Index; GELF, Groupe d’Etude des Lymphomes Folliculaires; len, lenalidomide; R, rituximab.

Conclusions

- The inMIND phase 3 study met its primary endpoint of prolonging PFS in R/R FL
 - Addition of tafasitamab to lenalidomide and rituximab resulted in significant improvement in PFS, representing a 57% reduction in risk of progression, relapse, or death
 - Benefit was observed in all prespecified subgroups, including patients with POD24, refractory to prior anti-CD20 mAbs, and receiving multiple prior lines of therapy
- Although OS data are immature, a trend in favor of tafasitamab was observed
- The safety profile was manageable and consistent with expected toxicities with these agents
- This study is the first to validate the approach of combining 2 antibodies (anti-CD19 with anti-CD20) for treatment of FL
- Tafasitamab plus lenalidomide and rituximab can be administered in community as well as academic settings and represents a potential new standard of care for patients with R/R FL

Acknowledgments and Abstract Plain Language Summary

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