Effect of Tezepelumab on Lung Function in Patients With Severe, Uncontrolled Asthma in the Phase 3 NAVIGATOR Study

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Table S1 Baseline demographics and clinical characteristics in the overall NAVIGATOR cohort

Demographic/characteristic	**Tezepelumab 210 mg Q4W (*n* = 528)**	**Placebo (*n* = 531)**
Age, years, mean (SD)	49.9 (16.3)	49.0 (15.9)
Female, *n* (%)	335 (63.4)	337 (63.5)
BMI, kg/m^2, mean (SD)	28.7 (7.1)	28.3 (6.9)
ICS dose level, *n* (%)[a]		
Medium	131 (24.8)	132 (24.9)
High	397 (75.2)	398 (75.0)
Maintenance OCS use, *n* (%)	49 (9.3)	51 (9.6)
Prebronchodilator FEV_1, L, mean (SD)	1.8 (0.7)	1.9 (0.7)
Prebronchodilator FEV_1 reversibility, %, mean (SD)	15.0 (15.6)	15.1 (15.2)
Postbronchodilator FEV_1 reversibility, *n*		
< 20%	391	388
≥ 20%	137	143
Prebronchodilator ppFEV_1, mean (SD)	62.8 (18.0)	62.7 (18.0)
Postbronchodilator FEV_1, L, mean (SD)	2.1 (0.8)	2.1 (0.8)
Morning PEF, L/min, weekly mean (SD)	261.7 (109.7)	262.5 (105.8)
Evening PEF, L/min, weekly mean (SD)	277.0 (111.3)	278.2 (106.9)

Number of exacerbations in the past 12 months, *n* (%)		
2	310 (58.7)	324 (61.0)
> 2	218 (41.3)	206 (38.8)
Serum total IgE, IU/mL, median (min, max)	194.9 (1.5, 12,823.2)	196.7 (1.5, 9740.9)
Blood eosinophil count, cells/μL, median (min, max)	250 (0, 3650)	250 (0, 8170)
FeNO, ppb, median (min, max)	31.0 (5.0, 235.0)	30.0 (5.0, 265.0)

BMI body mass index, *FeNO* fractional exhaled nitric oxide, *FEV_1* forced expiratory volume in 1 second, *$ppFEV_1$* percent predicted forced expiratory volume in 1 second, *ICS* inhaled corticosteroids, *IgE* immunoglobulin E, *max* maximum, *min* minimum, *OCS* oral corticosteroid, *PEF* peak expiratory flow, *Q4W* every 4 weeks, *SD* standard deviation

Table S2 Demographics and clinical characteristics of patients grouped by disease duration at baseline, baseline postbronchodilator FEV_1 reversibility, baseline postbronchodilator FEV_1/FVC ratio, and combined baseline postbronchodilator FEV_1 reversibility and postbronchodilator FEV_1/FVC ratio

	Subgroup									
	Disease duration		**Postbronchodilator FEV_1 reversibility**		**Postbronchodilator FEV_1/FVC ratio**		**Postbronchodilator FEV_1 reversibility and postbronchodilator FEV_1/FVC ratio**			
Demographic/characteristic	**< 20 years (*n* = 559)**	**≥ 20 years (*n* = 500)**	**Low (< 20%) (*n* = 779)**	**High (≥ 20%) (*n* = 280)**	**< 0.7 (*n* = 617)**	**≥ 0.7 (*n* = 442)**	**< 0.7 and < 20% (*n* = 433)**	**< 0.7 and ≥ 20% (*n* = 184)**	**≥ 0.7 and < 20% (*n* = 346)**	**≥ 0.7 and ≥ 20% (*n* = 96)**
Age, years, mean (SD)	46.3 (17.8)	53.0 (13.0)	49.8 (16.4)	48.5 (15.2)	53.7 (12.9)	43.5 (18.1)	55.0 (12.0)	50.7 (14.2)	43.2 (18.6)	44.3 (16.3)
Age group, *n* (%)										
Adolescent: 12 to 18 years	82 (14.7)	0 (0.0)	66 (8.5)	16 (5.7)	7 (1.1)	75 (17.0)	1 (0.2)	6 (3.3)	65 (18.8)	10 (10.4)
Adult: ≥ 18 to < 65 years	409 (73.2)	398 (79.6)	577 (74.1)	230 (82.1)	487 (78.9)	320 (72.4)	337 (77.8)	150 (81.5)	240 (69.4)	80 (83.3)
Adult: ≥ 65 years	68 (12.2)	102 (20.4)	136 (17.5)	34 (12.1)	123 (19.9)	47 (10.6)	95 (21.9)	28 (15.2)	41 (11.8)	6 (6.3)
Female, *n* (%)	334 (59.7)	338 (67.6)	483 (62.0)	189 (67.5)	371 (60.1)	301 (68.1)	252 (58.2)	119 (64.7)	231 (66.8)	70 (72.9)
BMI, kg/m^2, mean (SD)	27.5 (6.7)	29.6 (7.1)	28.6 (7.1)	28.3 (6.6)	28.3 (6.6)	28.7 (7.5)	28.4 (6.5)	28.2 (7.0)	28.8 (7.8)	28.4 (6.0)
Time since asthma diagnosis, years, median (min, max)	10.0 (1.0, 19.3)	34.0 (20.0, 69.0)	-	-	-	-	-	-	-	-
ICS dose level, *n* (%)[a]										
Medium	165 (29.5)	98 (19.6)	205 (26.3)	58 (20.7)	126 (20.4)	137 (31.0)	91 (21.0)	35 (19.0)	114 (32.9)	23 (24.0)
High	394 (70.5)	401 (80.2)	573 (73.6)	222 (79.3)	490 (79.4)	305 (69.0)	341 (78.8)	149 (81.0)	232 (67.1)	73 (76.0)

Maintenance OCS use, *n* (%)	54 (9.7)	46 (9.2)	73 (9.4)	27 (9.6)	69 (11.2)	31 (7.0)	48 (11.1)	21 (11.4)	25 (7.2)	6 (6.3)
Number of exacerbations in the past 12 months, *n* (%)										
2	321 (57.4)	313 (62.6)	470 (60.3)	164 (58.6)	350 (56.7)	284 (64.3)	246 (56.8)	104 (56.5)	224 (64.7)	60 (62.5)
> 2	237 (42.4)	187 (37.4)	308 (39.5)	116 (41.4)	267 (43.3)	157 (35.5)	187 (43.2)	80 (43.5)	121 (35.0)	36 (37.5)
Prebronchodilator FEV_1, L, mean (SD)	2.0 (0.8)	1.7 (0.6)	2.0 (0.7)	1.5 (0.6)	1.5 (0.5)	2.3 (0.7)	1.6 (0.5)	1.4 (0.5)	2.4 (0.7)	1.9 (0.5)
Prebronchodilator ppFEV_1, mean (SD)	65.5 (19.1)	59.7 (16.0)	66.4 (17.6)	52.6 (14.8)	53.9 (14.7)	75.2 (14.3)	56.7 (14.4)	47.2 (13.3)	78.6 (13.0)	62.9 (12.0)
Postbronchodilator FEV_1 reversibility, %, mean (SD)	14.6 (14.7)	15.6 (16.2)	7.9 (6.6)	35.0 (15.3)	16.4 (16.2)	13.1 (14.1)	8.3 (6.8)	35.4 (16.0)	7.3 (6.4)	34.3 (13.9)
Prebronchodilator FVC, L, mean (SD)	3.0 (1.0)	2.8 (0.9)	3.0 (0.9)	2.7 (0.9)	2.8 (0.9)	3.1 (0.9)	3.0 (0.9)	2.7 (0.9)	3.1 (0.9)	2.7 (0.8)
Prebronchodilator $FEF_{25–75}$, L/s, mean (SD)	1.3 (1.0)	0.9 (0.6)	1.3 (0.9)	0.8 (0.5)	0.7 (0.3)	1.8 (0.9)	0.7 (0.3)	0.6 (0.3)	1.9 (0.9)	1.2 (0.6)
Blood eosinophil count, cells/μL, median (min, max)	270 (0, 4640)	240 (0, 8170)	240 (0, 8170)	280 (0, 1340)	280 (0, 8170)	220 (0, 1340)	260 (0, 8170)	300 (10, 1310)	220 (0, 1240)	225 (0, 1340)
FeNO, ppb, median (min, max)	35.0 (5.0, 265.0)	26.0 (5.0, 258.0)	28.5 (5.0, 258.0)	34.0 (5.0, 265.0)	31 (5.0, 258.0)	28 (5.0, 265.0)	31 (5.0, 258.0)	33 (5.0, 193.0)	27 (5.0, 235.0)	37 (5.0, 265.0)
Serum total IgE, IU/mL, median (min, max)	209.8 (1.5, 12,823.2)	175.4 (1.5, 7406.3)	189.0 (1.5, 12,823.2)	212.7 (1.5, 9740.9)	192.7 (1.5, 12,823.2)	205 (1.5, 9740.9)	177.1 (1.5, 12,823.2)	209.3 (1.5, 5587.1)	196 (1.5, 6136.5)	254 (1.5, 9740.9)

BMI body mass index, $FEF_{25–75}$ forced expiratory flow between 25% and 75% of vital capacity, *FeNO* fractional exhaled nitric oxide, $ppFEV_1$ percent predicted forced expiratory volume in 1 second, FEV_1 forced expiratory volume in 1 second, *FVC* forced vital capacity, *ICS* inhaled corticosteroids, *IgE* immunoglobulin E, *max* maximum, *min* minimum, *OCS* oral corticosteroid, *SD* standard deviation

[a]Medium-dose ICS: fluticasone propionate 500 μg/day or equivalent; high-dose ICS: fluticasone propionate > 500 μg/day or equivalent

Table S3 Change from baseline in prebronchodilator $FEF_{25–75}$ in patients grouped by disease duration at baseline, baseline postbronchodilator FEV_1 reversibility, and baseline postbronchodilator FEV_1/FVC ratio

Subgroup	Mean at baseline (SD), L/s		LS mean change from baseline (SE), L/s		LS mean difference versus placebo (95% CI), L/s
	Tezepelumab 210 mg Q4W	Placebo	Tezepelumab 210 mg Q4W	Placebo	
Baseline disease duration, years					
< 20	1.3 (0.9)	1.3 (1.0)	0.29 (0.03)	0.13 (0.03)	0.17 (0.08, 0.25)
n	285	274	255	236	
≥ 20	0.9 (0.6)	0.9 (0.6)	0.11 (0.03)	0.03 (0.03)	0.09 (0.00, 0.18)
n	243	257	216	217	
Baseline postbronchodilator FEV_1 reversibility					
< 20%	1.3 (0.9)	1.2 (0.9)	0.17 (0.03)	0.04 (0.03)	0.13 (0.06, 0.20)
n	391	388	352	331	
≥ 20%	0.7 (0.4)	0.9 (0.6)	0.32 (0.04)	0.19 (0.04)	0.13 (0.01, 0.26)
n	137	143	119	122	
Baseline postbronchodilator FEV_1/FVC ratio					
< 0.7	0.7 (0.3)	0.7 (0.3)	0.13 (0.03)	−0.02 (0.03)	0.15 (0.07, 0.23)
n	304	313	277	263	

≥ 0.7	1.8 (0.9)	1.8 (1.0)	0.32 (0.04)	0.22 (0.04)	0.10 (0.01, 0.20)
n	224	218	194	190	
Baseline combined postbronchodilator FEV_1 reversibility and postbronchodilator FEV_1/FVC ratio					
< 20% and < 0.7	0.7 (0.4)	0.7 (0.3)	0.13 (0.04)	−0.02 (0.04)	0.15 (0.05, 0.25)
n	209	224	191	185	
≥ 20% and < 0.7	0.6 (0.3)	0.6 (0.3)	0.20 (0.05)	0.05 (0.06)	0.14 (0.00, 0.29)
n	95	89	86	78	
< 20% and ≥ 0.7	1.9 (0.9)	2.0 (1.0)	0.23 (0.04)	0.12 (0.04)	0.11 (0.00, 0.21)
n	182	164	161	146	
≥ 20% and ≥ 0.7	1.2 (0.5)	1.3 (0.6)	0.56 (0.08)	0.37 (0.07)	0.19 (−0.02, 0.40)
n	42	54	33	44	

CI confidence interval, $FEF_{25–75}$ forced expiratory flow between 25% and 75% of vital capacity, FEV_1 forced expiratory volume in 1 second, *FVC* forced vital capacity, *LS* least-squares, *Q4W* every 4 weeks, *SD* standard deviation, *SE* standard error

Table S4 Change from baseline to week 52 in postbronchodilator FEV_1 in patients grouped by disease duration

Subgroup	Mean at baseline (SD), L/s		LS mean change from baseline (SE), L/s		LS mean difference versus placebo (95% CI), L/s
	Tezepelumab 210 mg Q4W	Placebo	Tezepelumab 210 mg Q4W	Placebo	
Baseline disease duration, years					
< 20	2.2 (0.8)	2.2 (0.9)	0.19 (0.02)	0.06 (0.02)	0.13 (0.07, 0.20)
n	285	274	285	274	
≥ 20	1.9 (0.7)	2.0 (0.6)	0.10 (0.03)	0.01 (0.02)	0.09 (0.02, 0.16)
n	243	257	243	257	

CI confidence interval, *FEV_1* forced expiratory volume in 1 second, *LS* least-squares, *Q4W* every 4 weeks, *SD* standard deviation, *SE* standard error

Table S5 Lung function at baseline and at week 52 in patients grouped by disease duration

			Prebronchodilator ppFEV$_1$ at week 52, *n* (%)		
Baseline disease duration, years	**Treatment group**	**Prebronchodilator ppFEV$_1$ at baseline**	**Abnormal (< 80%)**	**Normal (≥ 80%)**	**Missing**
< 20	Tezepelumab 210 mg Q4W (*N* = 285)	Abnormal (< 80%; *n* = 214)	134 (62.6)	62 (29.0)	18 (8.4)
		Normal (≥ 80%; *n* = 71)	13 (18.3)	46 (64.8)	12 (16.9)
	Placebo (*N* = 274)	Abnormal (< 80%; *n* = 214)	157 (73.4)	24 (11.2)	33 (15.4)
		Normal (≥ 80%; *n* = 60)	17 (28.3)	38 (63.3)	5 (8.3)
≥ 20	Tezepelumab 210 mg Q4W (*N* = 243)	Abnormal (< 80%; *n* = 220)	171 (77.7)	25 (11.4)	24 (10.9)
		Normal (≥ 80%; *n* = 23)	4 (17.4)	16 (69.6)	3 (13.0)
	Placebo (*N* = 257)	Abnormal (< 80%; *n* = 227)	170 (74.9)	24 (10.6)	33 (14.5)
		Normal (≥ 80%; *n* = 30)	9 (30.0)	14 (46.7)	7 (23.3)

Baseline was defined as the last non-missing measurement recorded before randomization

ppFEV$_1$ percent predicted forced expiratory volume in 1 second, *Q4W* every 4 weeks

Table S6 Change from baseline to week 52 in prebronchodilator FEV_1 in patients grouped by number and type of additional controllers

Subgroup	Tezepelumab 210 mg Q4W		Placebo		LS mean (95% CI) difference versus placebo, L
	n	LS mean (SE), L	*n*	LS mean (SE), L	
Number of additional controllers					
1	240	0.22 (0.03)	252	0.12 (0.03)	0.10 (0.03, 0.18)
2	184	0.23 (0.03)	197	0.09 (0.03)	0.13 (0.05, 0.22)
≥ 3	103	0.26 (0.04)	82	0.04 (0.05)	0.22 (0.10, 0.34)
Additional controllers					
LABA alone	236	0.23 (0.03)	244	0.11 (0.03)	0.11 (0.04, 0.19)
LABA + LTRA	112	0.26 (0.04)	112	0.12 (0.04)	0.14 (0.03, 0.25)
LABA + LAMA	50	0.20 (0.06)	62	0.07 (0.06)	0.13 (−0.03, 0.29)
LABA + LAMA + LTRA	52	0.28 (0.06)	50	−0.01 (0.06)	0.28 (0.12, 0.45)
Other controllers	77	0.18 (0.05)	63	0.08 (0.05)	0.10 (−0.04, 0.24)
Additional controllers used by patients who were not receiving maintenance OCS at baseline					
LABA alone	225	0.22 (0.03)	234	0.11 (0.03)	0.10 (0.03, 0.18)
LABA + LTRA	107	0.26 (0.04)	102	0.14 (0.04)	0.13 (0.02, 0.24)
LABA + LAMA	47	0.21 (0.06)	48	0.10 (0.06)	0.10 (−0.06, 0.27)
LABA + LAMA + LTRA	39	0.27 (0.07)	44	−0.02 (0.06)	0.29 (0.11, 0.47)
Other controllers	60	0.14 (0.05)	52	0.09 (0.06)	0.05 (−0.10, 0.20)

CI confidence interval, *FEV_1* forced expiratory volume in 1 second, *LABA* long-acting β_2 agonist, *LAMA* long-acting muscarinic antagonist, *LS* least-squares, *LTRA* leukotriene receptor antagonist, *n* number of patients contributing to the analysis, *OCS* oral corticosteroids, *Q4W* every 4 weeks, *SE* standard error

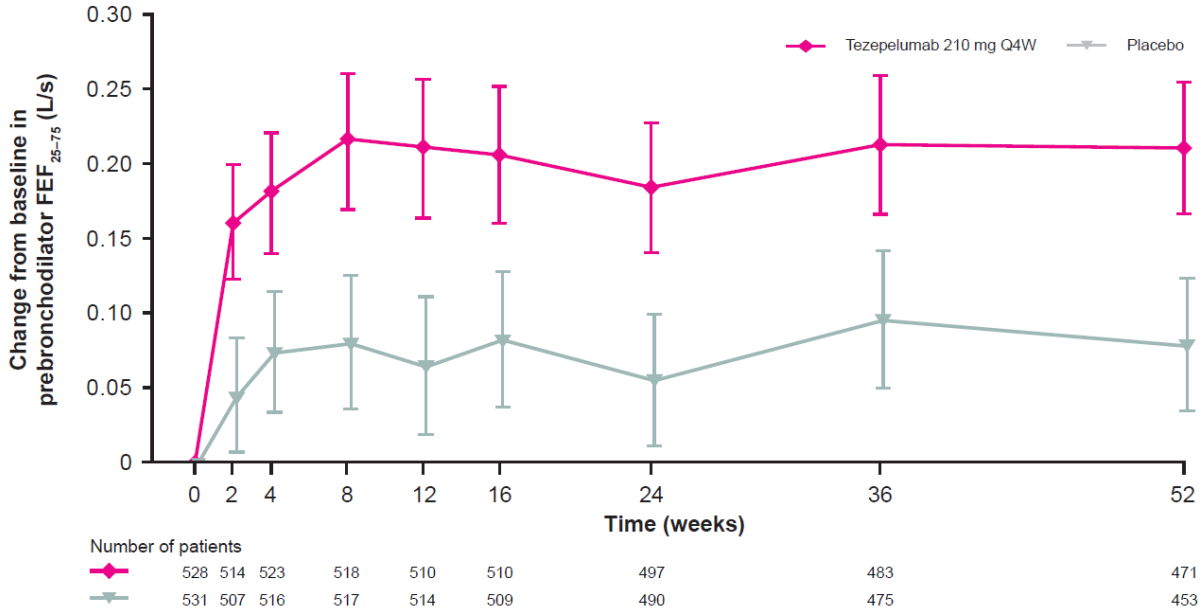

Fig. S1 Change from baseline in prebronchodilator $FEF_{25–75}$ over 52 weeks. Data are adjusted means and 95% CIs. 'Number of patients' indicates the number of patients with available data at a given time point. Patients who received at least one dose of tezepelumab or placebo with at least one change from baseline assessment were included in the model. *CI* confidence interval, *$FEF_{25–75}$* forced expiratory flow between 25% and 75% of vital capacity, *Q4W* every 4 weeks

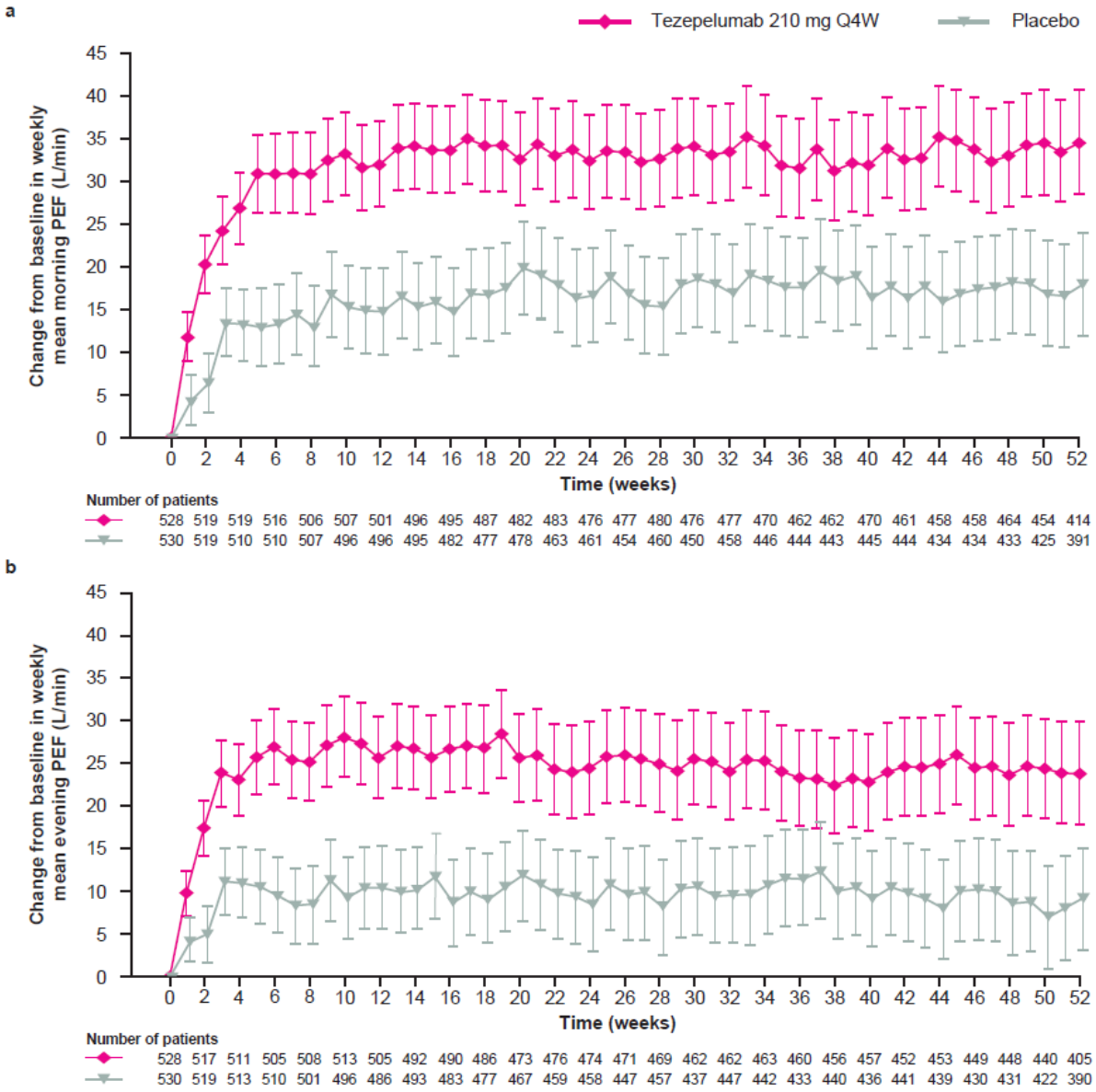

Fig. S2 Change from baseline to week 52 in (a) weekly mean morning PEF and (b) weekly mean evening PEF. 'Number of patients' indicates the number of patients with available data at a given time point. Patients who received at least one dose of tezepelumab or placebo with at least one change from baseline assessment were included in the model. Data are adjusted means and 95% CIs. *CI* confidence interval, *PEF* peak expiratory flow, *Q4W* every 4 weeks

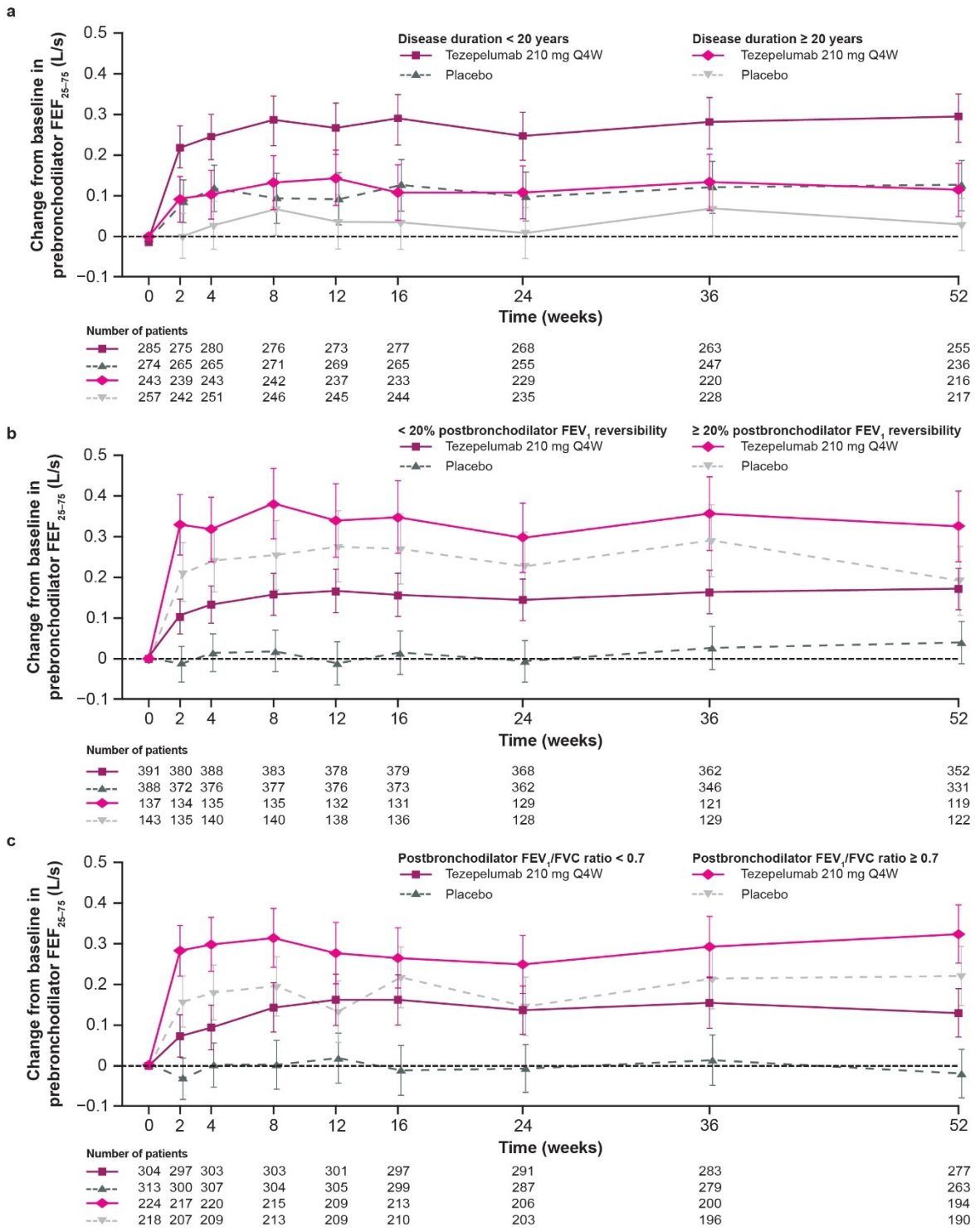

Fig. S3 Change from baseline in prebronchodilator $FEF_{25–75}$ over 52 weeks in patients grouped by (a) disease duration, (b) baseline post-bronchodilator FEV_1 reversibility, and (c) postbronchodilator FEV_1/FVC ratio. 'Number of patients' indicates the number of patients with available data at a given time point. Patients who received at least one dose of tezepelumab or placebo with at least one change from baseline assessment were included

in the model. Data are adjusted means and 95% CIs. *CI* confidence interval, $FEF_{25–75}$ forced expiratory flow between 25% and 75% of vital capacity, FEV_1 forced expiratory volume in 1 second, *FVC* forced vital capacity, *Q4W* every 4 weeks