Figure 1A

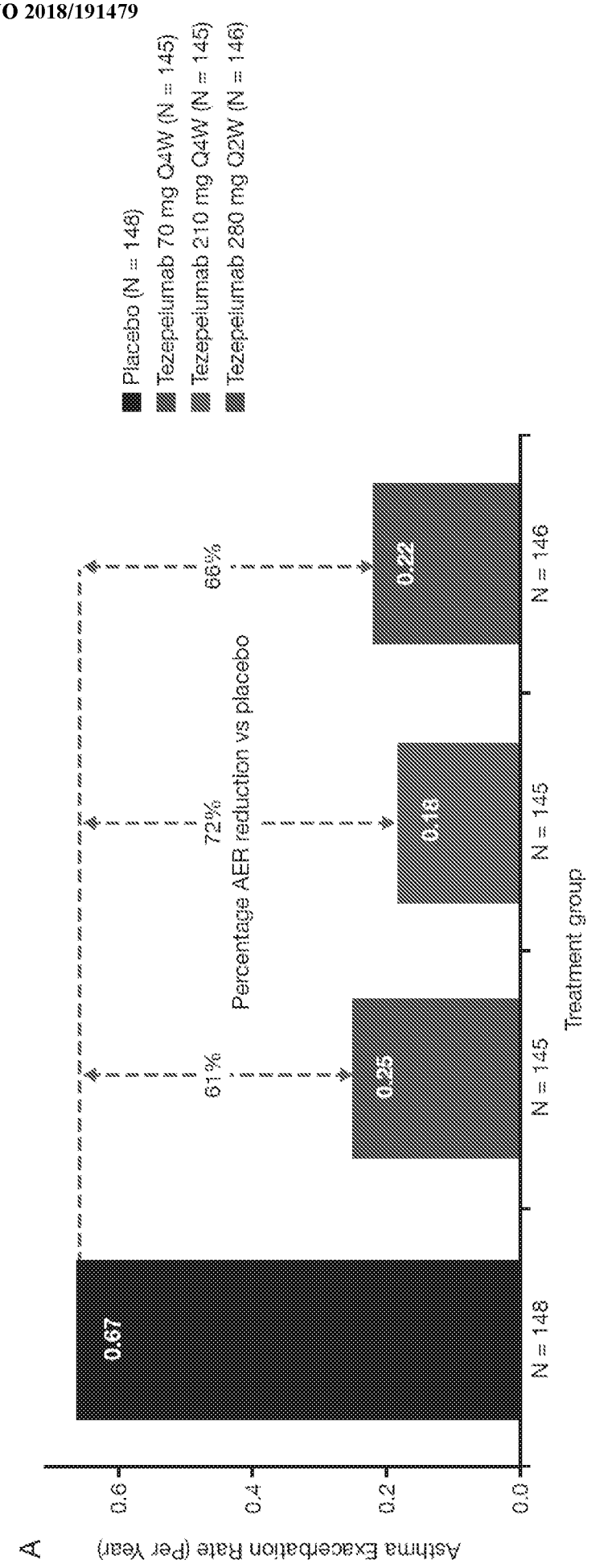

A
Asthma Exacerbation Rate (Per Year)
0.0
0.2
0.4
0.6
0.67
0.25
0.18
0.22
N = 148
N = 145
N = 145
N = 146
Treatment group
61%
72%
66%
Percentage AER reduction vs placebo
Placebo (N = 148)
Tezepelumab 70 mg Q4W (N = 145)
Tezepelumab 210 mg Q4W (N = 145)
Tezepelumab 280 mg Q2W (N = 146)

Figure 1B

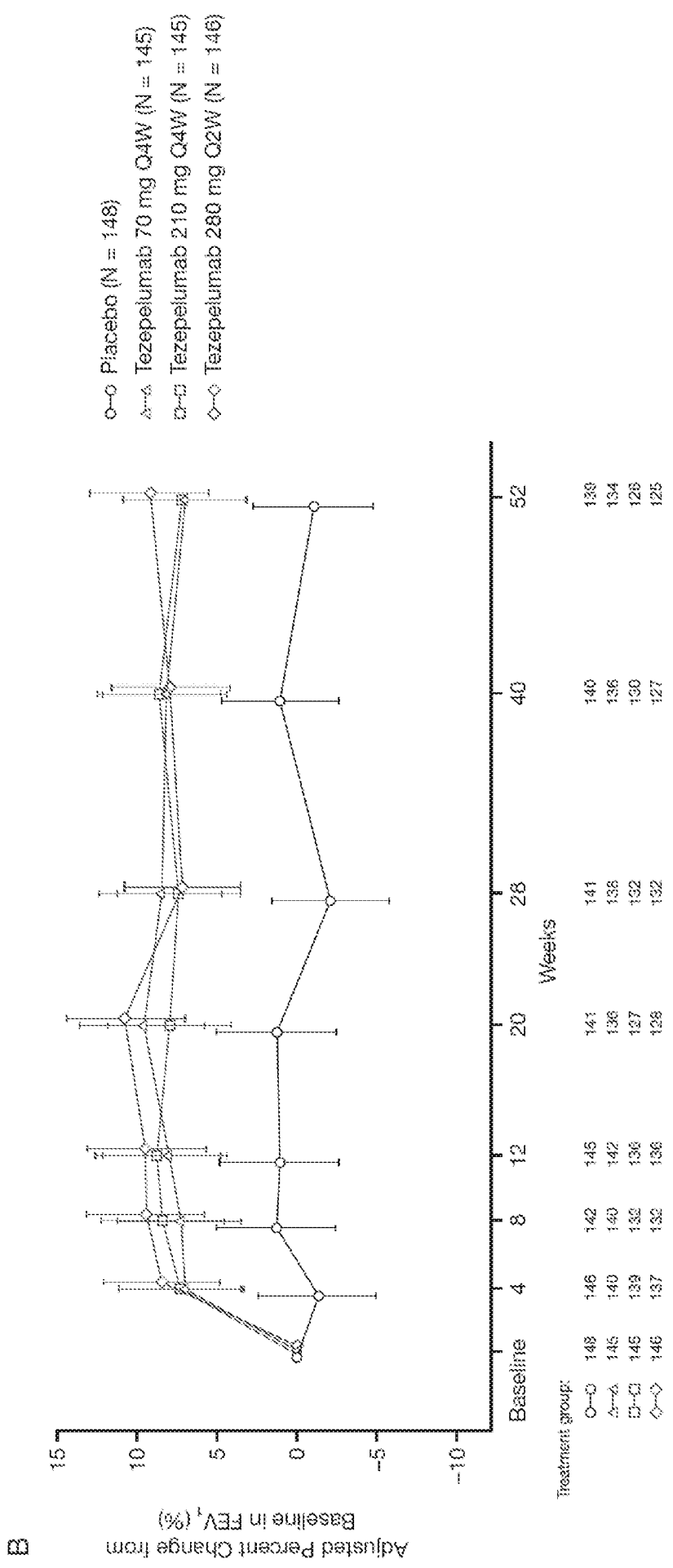

B
Adjusted Percent Change from Baseline in FEV1 (%)
15
10
5
0
−5
−10
Baseline
4
8
12
20
28
40
52
Weeks
Placebo (N = 148)
Tezepelumab 70 mg Q4W (N = 145)
Tezepelumab 210 mg Q4W (N = 145)
Tezepelumab 280 mg Q2W (N = 146)
Treatment group:
148 146 142 145 141 141 140 139
145 140 140 142 136 136 136 134
145 139 132 136 127 132 130 128
146 137 132 136 128 132 127 125

Figure 1C

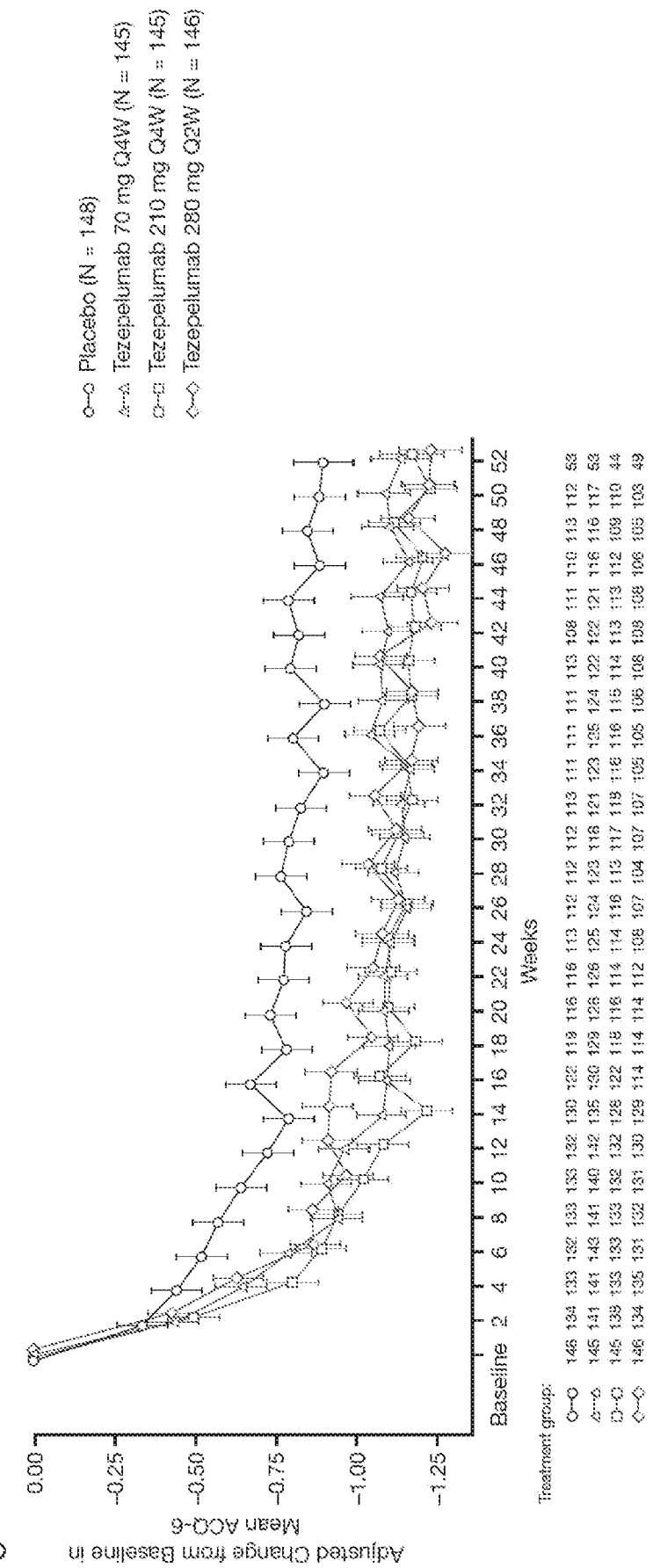

Placebo (N = 148)
Tezepelumab 70 mg Q4W (N = 145)
Tezepelumab 210 mg Q4W (N = 145)
Tezepelumab 280 mg Q2W (N = 146)
Adjusted Change from Baseline in Mean ACQ-6
0.00
−0.25
−0.50
−0.75
−1.00
−1.25
Baseline 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44 46 48 50 52
Weeks
Treatment group:
146 134 133 132 133 133 132 130 122 119 116 116 113 112 112 113 111 111 111 113 108 111 110 113 112 53
145 141 141 143 141 140 142 135 130 129 126 126 125 124 123 116 121 123 125 124 122 122 121 116 116 117 53
145 139 133 133 133 132 132 126 122 118 116 114 114 116 115 117 118 116 116 115 114 113 113 112 109 110 44
146 134 135 131 132 131 130 129 114 114 114 112 108 107 104 107 107 105 105 106 108 108 108 106 105 103 49

Figure 1D

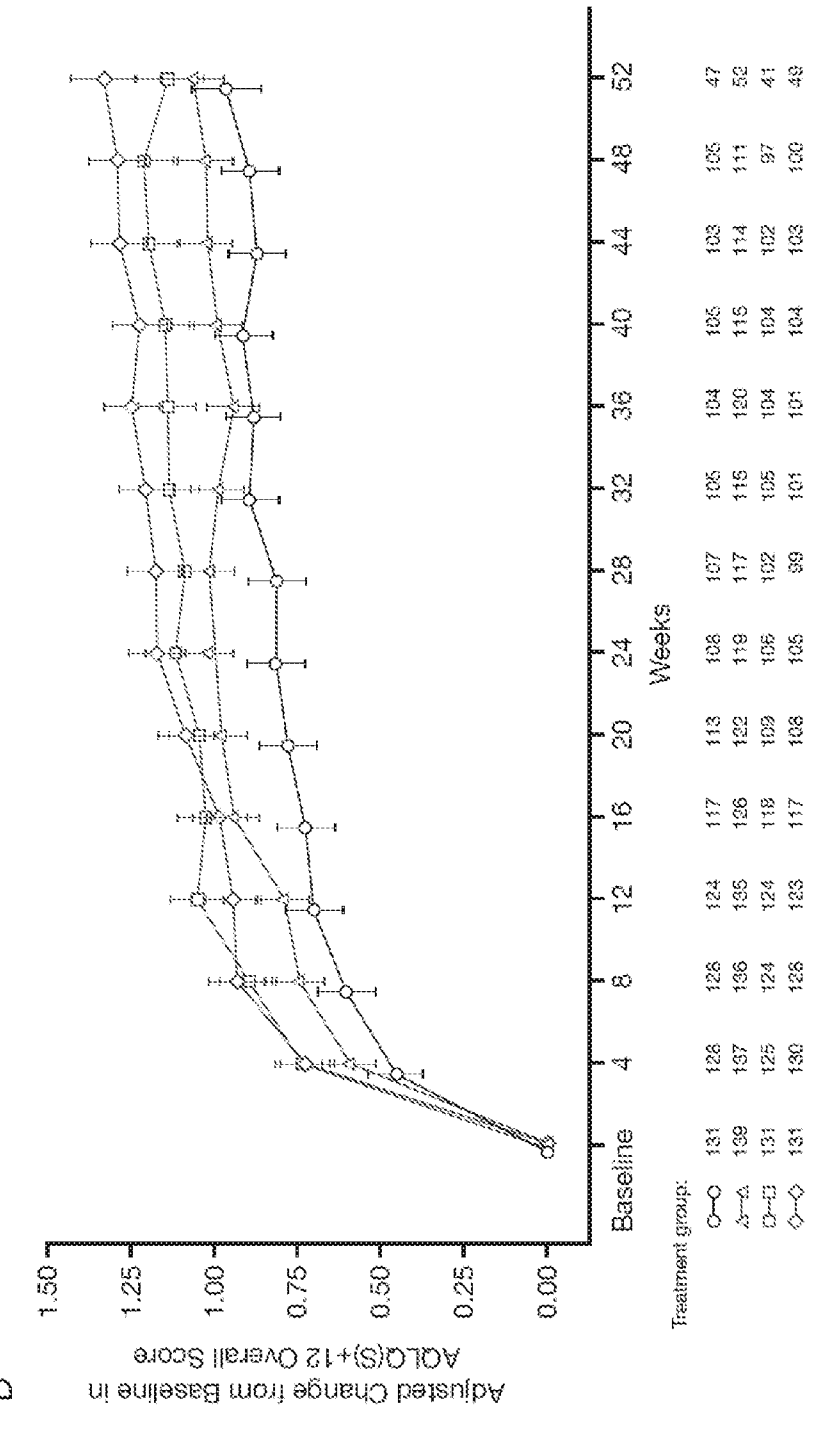

D
Adjusted Change from Baseline in
AQLQ(S)+12 Overall Score
1.50
1.25
1.00
0.75
0.50
0.25
0.00
Baseline
4
8
12
16
20
24
28
32
36
40
44
48
52
Weeks
Placebo (N = 148)
Tezepelumab 70 mg Q4W (N = 145)
Tezepelumab 210 mg Q4W (N = 145)
Tezepelumab 280 mg Q2W (N = 146)
Treatment group:
131 126 126 124 117 113 108 107 105 104 105 103 105 47
139 137 136 135 126 122 119 117 115 120 115 114 111 52
131 125 124 124 118 109 106 102 105 104 104 102 97 41
131 130 126 123 117 108 105 99 101 101 104 103 100 49

Figure 2A

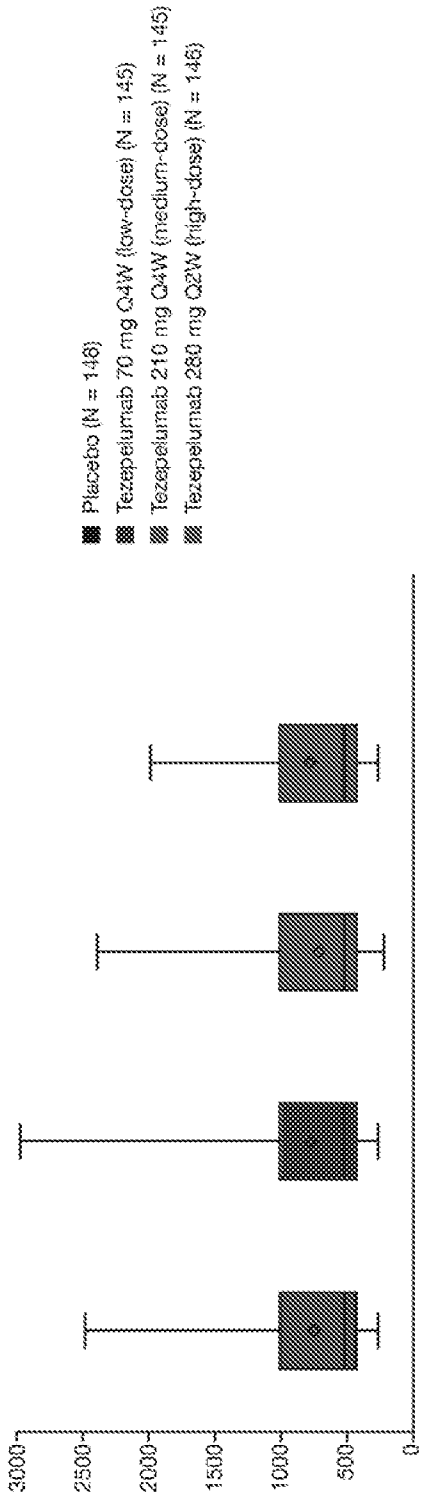


Figure 2B

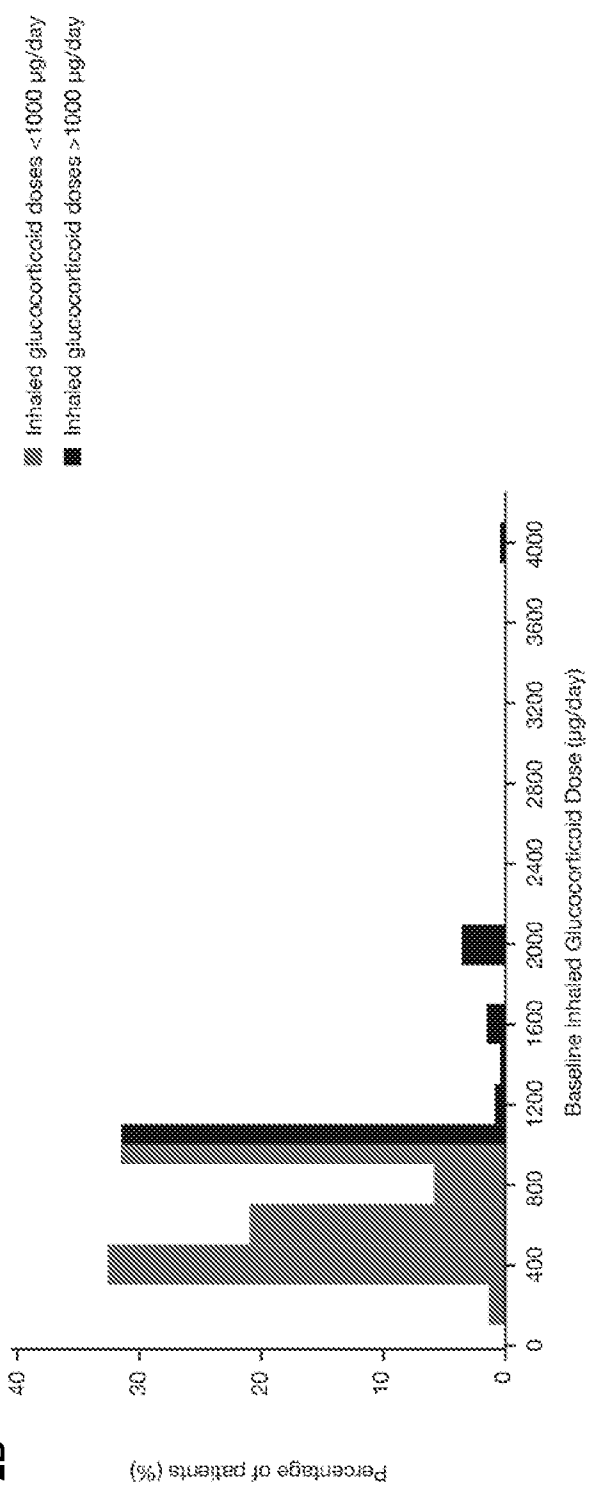


Figure 3 Kaplan-Meier Curve for Time to First Asthma Exacerbation through Week 52 in the Intention-to-Treat Population.

*P-values are nominal and without multiplicity adjustment. CI, confidence intervals; NA, not applicable; Q2W, every 2 weeks; Q4W, every 4 weeks.

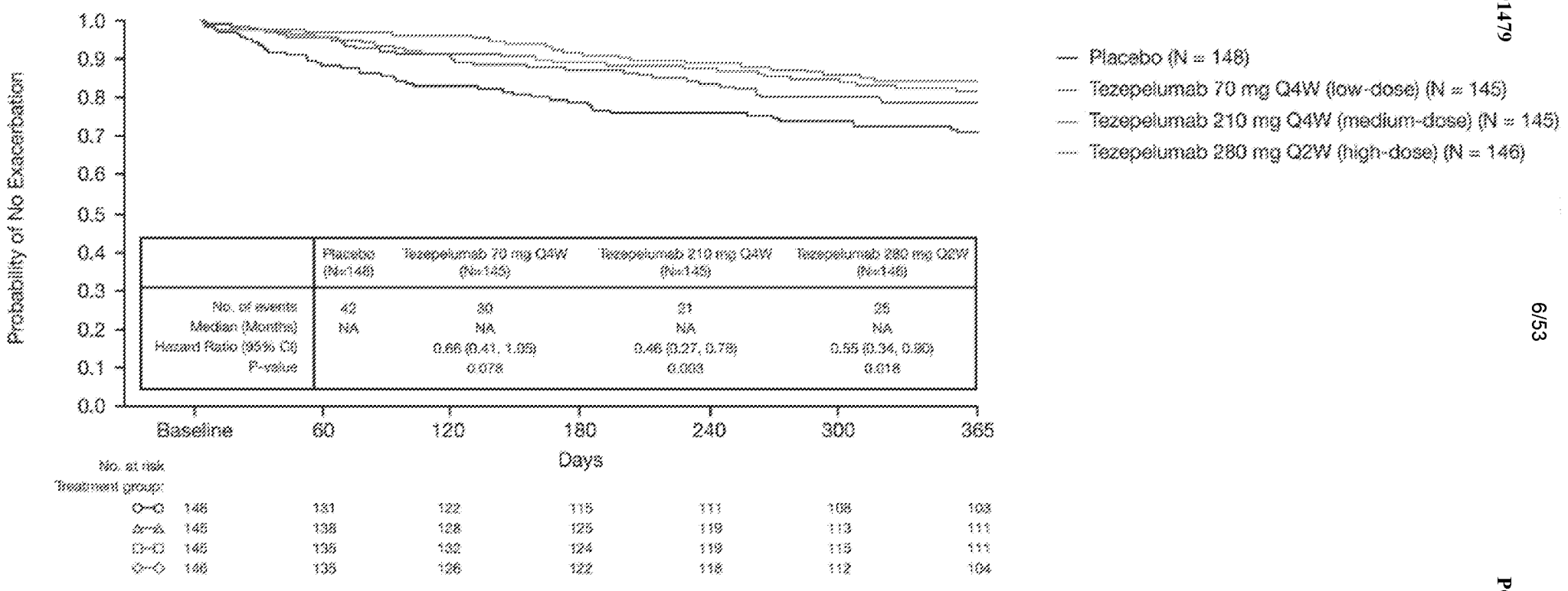


Figure 4A Change from Baseline in Peripheral Blood Eosinophils (cell/µl) over Time in the Intention-to-Treat Population

Error bars are representative of standard errors. IgE, immunoglobulin E; Th2, Q2W, every 2 weeks; Q4W, every 4 weeks

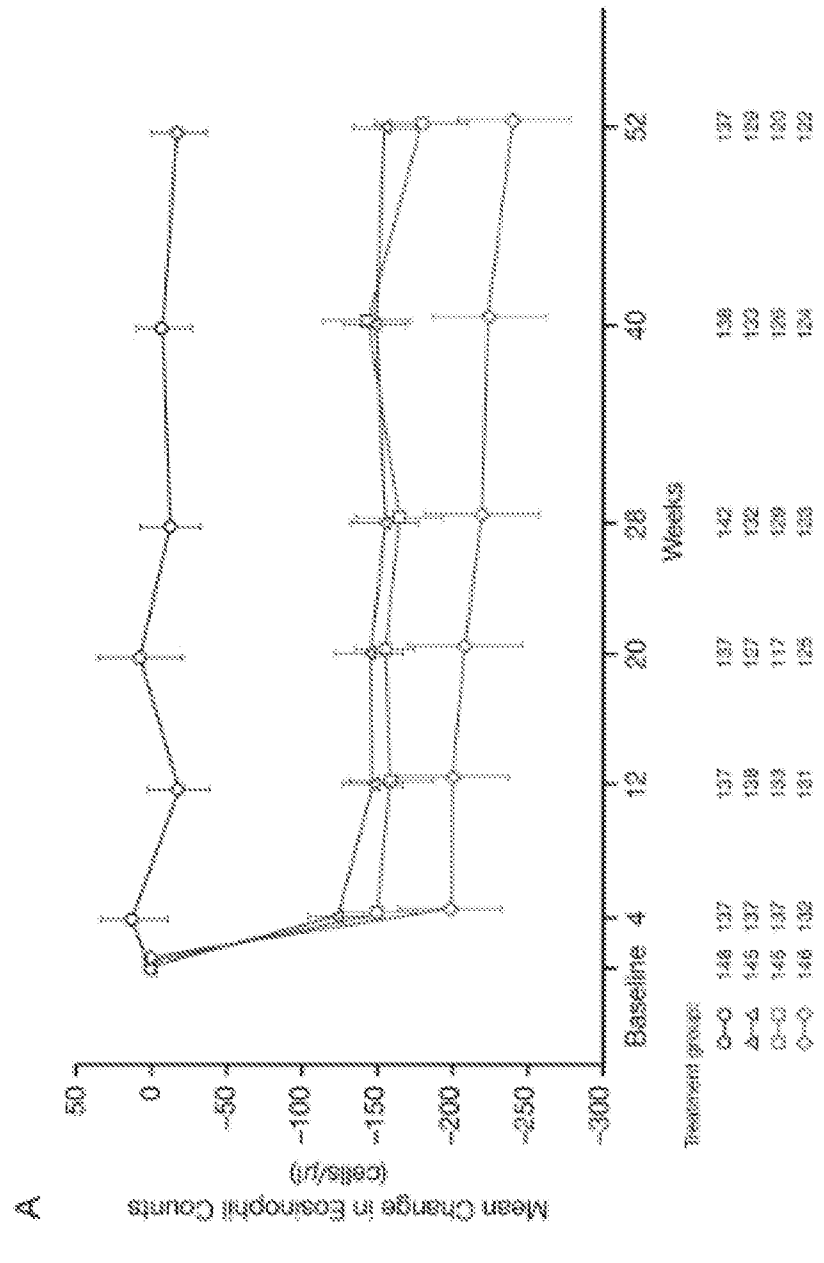


Figure 4B Change from Baseline in Total IgE (IU/ml) over Time in the Intention-to-Treat Population

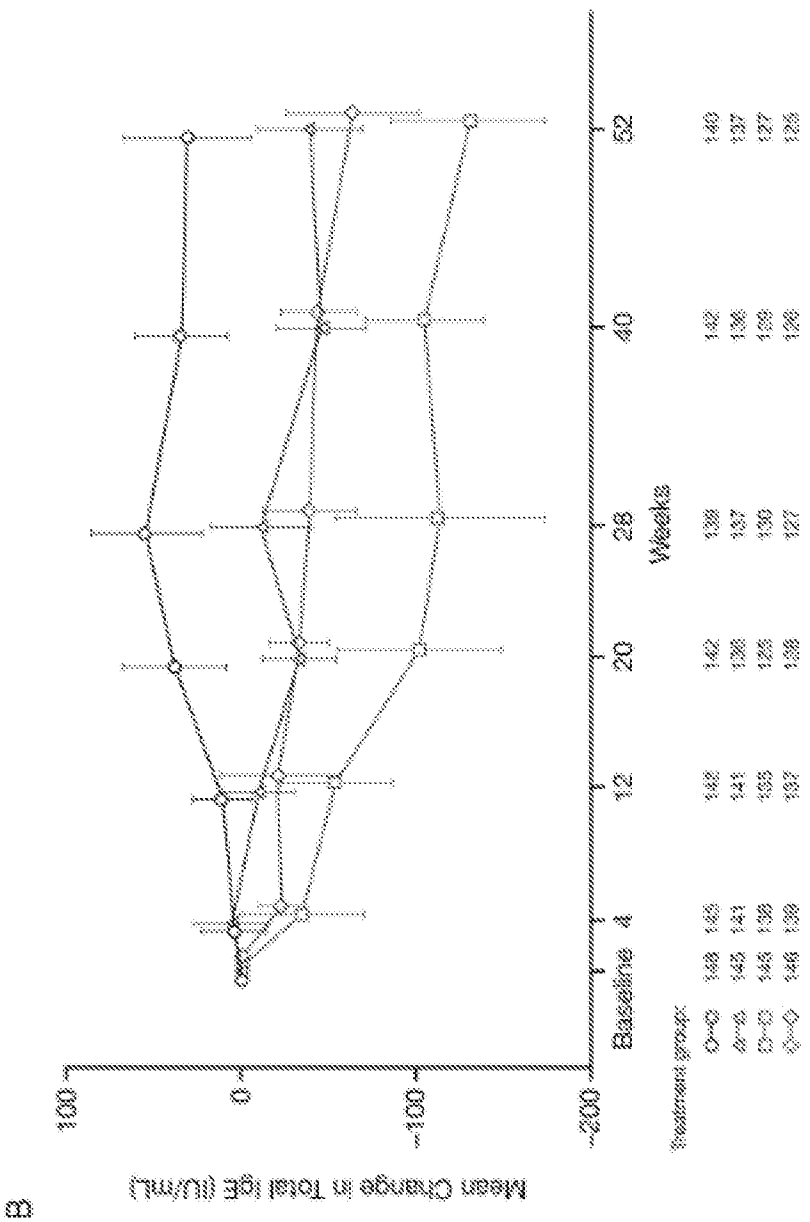
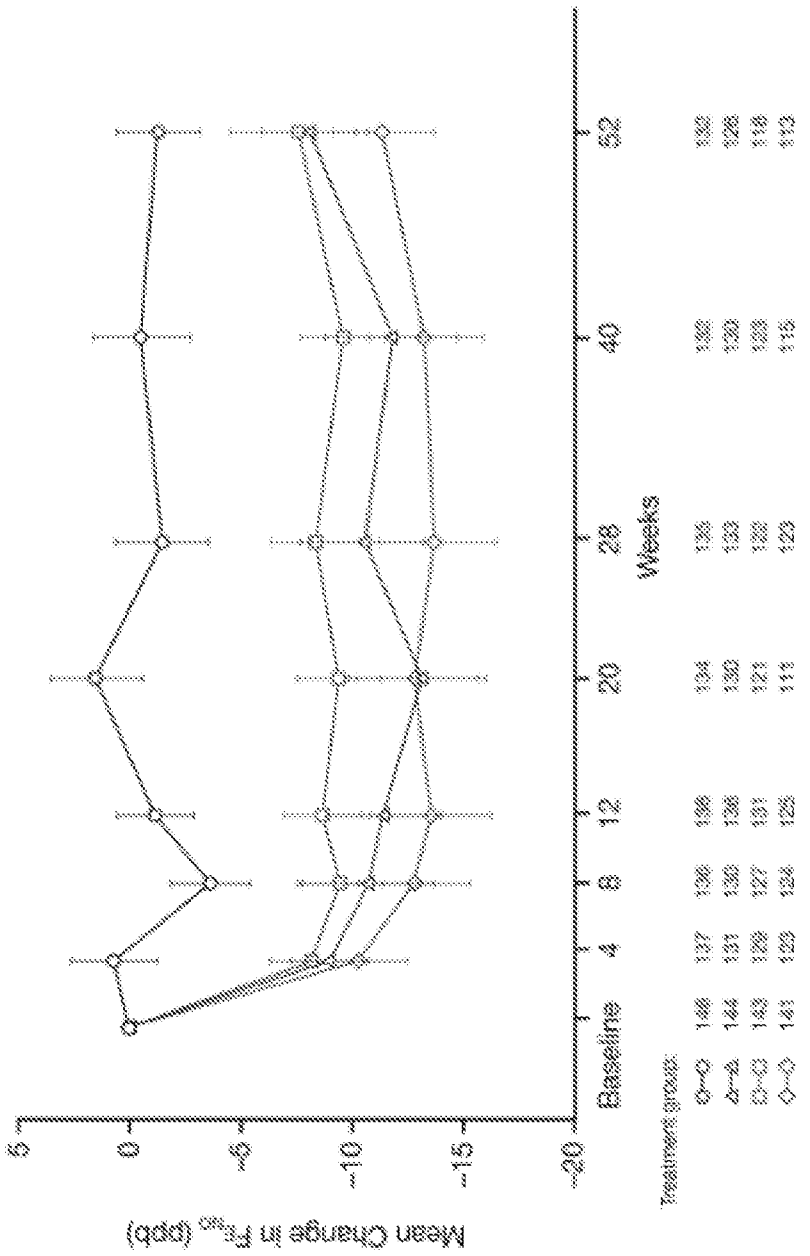


Figure 5. Change from Baseline in the Fraction of Exhaled Nitric Oxide (FENO)

CI bars indicate standard errors. FENO values included in the analysis represent averages of up to 3 measurements with a minimum of 10% reproducibility.[1] If there were not at least 2 values with 10% reproducibility, the first measurement was utilized. CI, confidence interval.



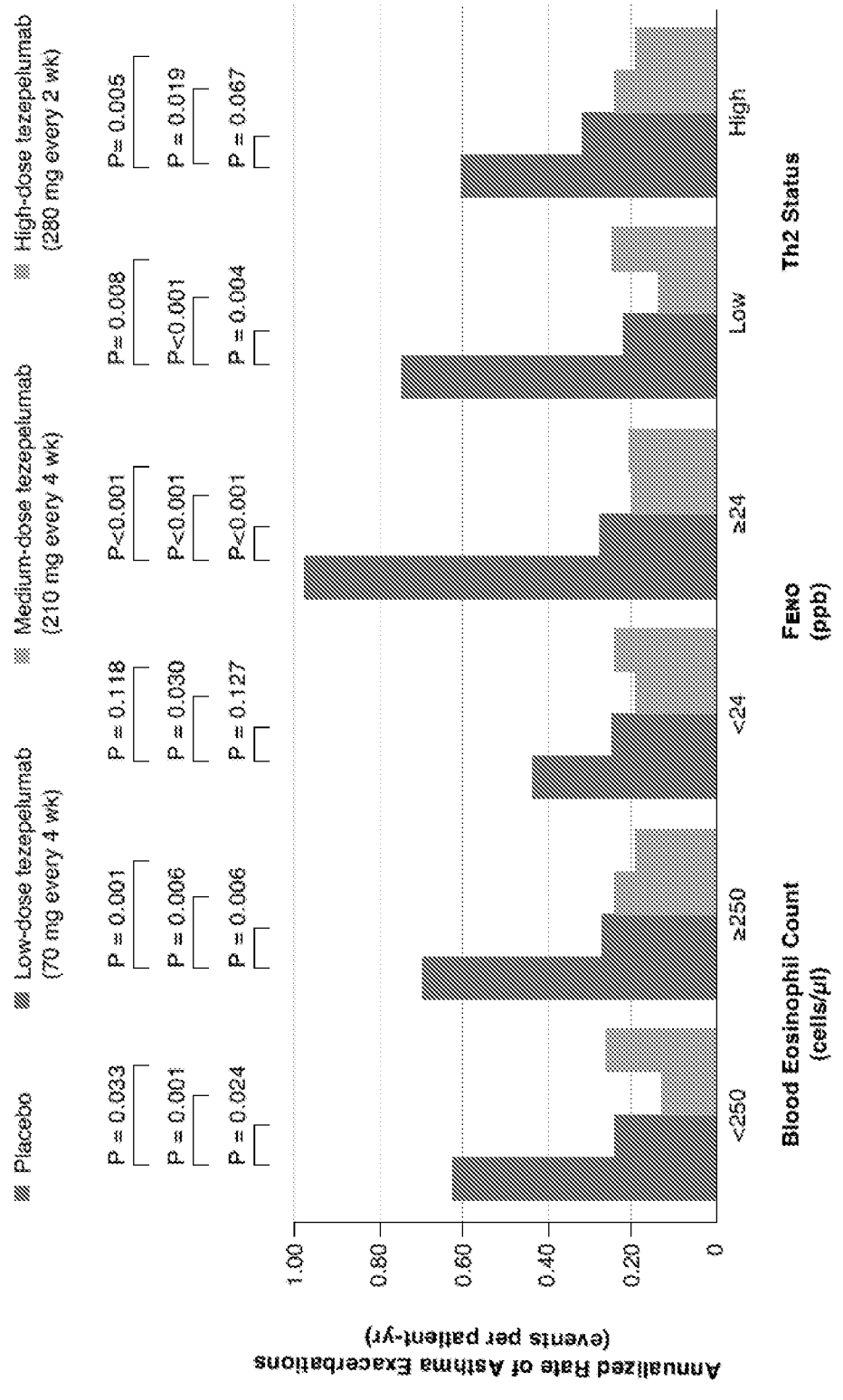


Figure 6A. Subpopulation analysis

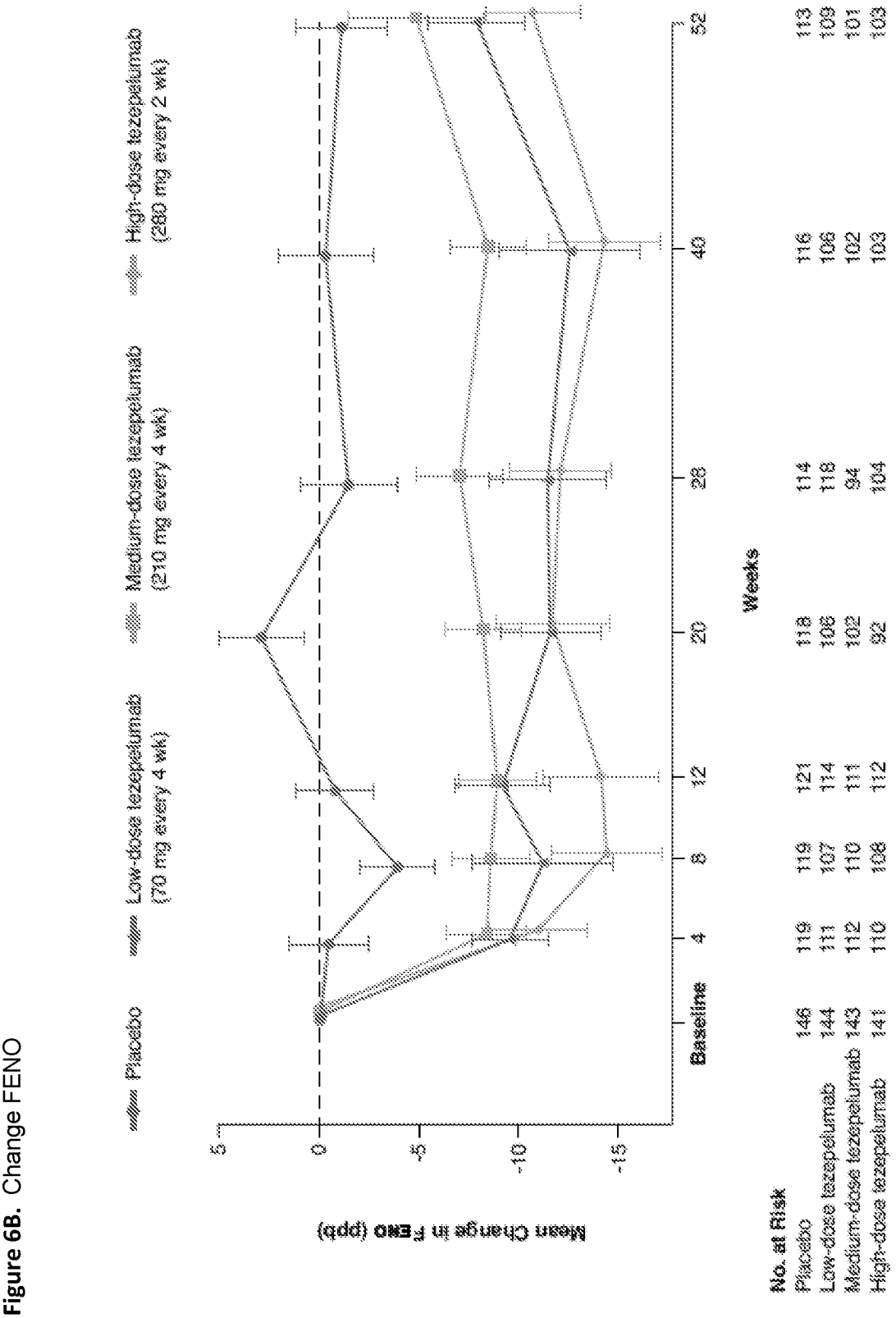


Figure 6B. Change FENO

Figure 7

Table 1A. Inclusion and Exclusion Criteria.

Inclusion criteria
Age 18–75 years, inclusive at the time of visit 1 (week –5).
Written informed consent and any locally required authorization (e.g., Health Insurance Portability and Accountability Act [HIPAA] in the USA, European Union [EU] Data Privacy Directive in the EU) obtained from the patient/legal representative prior to performing any protocol-related procedures, including screening evaluations.
Body mass index between 18–40 kg/m^2, inclusive, and weight ≥40 kg at visit 1 (week –5).
Documented physician-diagnosed asthma for at least 12 months prior to visit 1 (week –5) and post-BD reversibility of FEV_1 ≥12% and ≥200 ml during screening. Documented history of post-BD FEV_1 reversibility in the past 12 months will be accepted in place of reversibility during screening.
For patients 65 years or older at visit 1 (week –5), a chest radiograph taken during the screening period or a chest radiograph or chest computed tomography scan within 12 months prior to visit 1 (week –5) that, according to the investigator, is normal for an asthmatic patient and excludes significant alternative respiratory disease, is required.
Patients must have received a physician-prescribed asthma controller regimen with medium-dose plus LABA or high-dose inhaled glucocorticoid plus LABA for at least 6 months prior to visit 1 (week –5), and the dose of inhaled glucocorticoid must be stable for at least 15 days prior to visit 1 (week –5) and throughout the screening/run-in period. • To be classified as being on high-dose inhaled glucocorticoid, the patients will be on a total daily dose of >500 µg fluticasone dry powder inhaler, or a total daily dose of >440 µg fluticasone MDI or equivalent. • To be classified as being on medium-dose inhaled glucocorticoid, the patients will be on a total daily dose (sum of all inhaled glucocorticoid) of 250 to 500 µg fluticasone dry powder inhaler or a total daily dose of 220 to 440 µg fluticasone MDI or equivalent. • Equivalent inhaled glucocorticoid doses will be based upon the GINA guidelines (GINA, 2012).
If on asthma controller medications in addition to inhaled glucocorticoid plus LABA, the dose of the other asthma controller medications (leukotriene receptor inhibitors, theophylline, secondary inhaled glucocorticoid, LAMA, cromones, or maintenance oral prednisone or equivalent, up to a maximum of 10 mg daily or 20 mg every other day for the maintenance treatment of asthma) must be stable for at least 15 days prior to visit 1 (week –5).
Patients must have a morning pre-BD FEV_1 value of ≥40% and ≤80%, predicted at two screening visits. The first time must be at either visit 1 (week –5) or visit 2 (week –4), and the second time must be at visit 3 (week –1).
Patients must have an ACQ-6 score of ≥1.5 twice during screening. The first time must be at visit 1 (week –5). The second time may be at either week –2 (taken from home

Figure 7 cont'd

recording on the ePRO device) or at visit 3 (week –1).

At visit 4 (week 0, day 1), patients must have at least one of the following over the previous seven days from the ePRO device:

- Two days with a daytime or night-time symptoms score ≥1 (ASMA); or
- ≥1 awakening due to asthma leading to rescue medication use; or
- Rescue/reliever SABAuse >2 days.

Patients must have a documented history of at least 2 asthma exacerbation events OR at least 1 severe asthma exacerbation resulting in hospitalization (admission to the hospital for at least 24 hours) within the 12 months prior to visit 1 (week –5). To qualify as an asthma exacerbation event, administration of a burst of systemic glucocorticoids for at least 3 consecutive days must have been required for the treatment of the asthma exacerbation, or the asthma exacerbation resulted in an emergency department visit which led to systemic glucocorticoids for at least 3 consecutive days or hospitalization. For patients receiving maintenance oral glucocorticoids, a temporary doubling of the stable existing maintenance dose for at least three days qualifies.

If on allergen-specific immunotherapy patients must be on a maintenance dose and schedule for at least two months prior to visit 1 (week –5).

Patients must meet the all of following criteria at visit 4 (week 0, day 1) prior to randomization:

- Patients must demonstrate acceptable inhaler, peak flow meter, and spirometry techniques during screening/run-in period (from visit 2 to visit 4).
- Patients must demonstrate ≥70% compliance with usual asthma controller inhaled glucocorticoid/LABA during the screening/run-in period (from visit 2 to visit 4) based on ASMA.
- Patients must demonstrate ≥80% compliance with required use of the ePRO device; 80% compliance is defined as completing the ASMA for any eight mornings and any eight evenings in the previous ten days of the screening/run-in period.

Females of childbearing potential who are sexually active with a nonsterilized male partner must use a highly effective method of contraception from the time informed consent is obtained and must agree to continue using such precautions through week 64 of the study; cessation of contraception after this point should be discussed with a responsible physician. Periodic abstinence, the rhythm method, and the withdrawal method are not acceptable methods of contraception.

- Females of childbearing potential are defined as those who are not surgically sterile (i.e., bilateral tubal ligation, bilateral oophorectomy, or complete hysterectomy) or postmenopausal (defined as 12 months with no menses without an alternative medical cause).
- A highly effective method of contraception is defined as one that results in a low failure rate (i.e., less than 1% per year) when used consistently and correctly. Acceptable methods of contraception include: Male condom plus spermicide, copper T intrauterine device, levonorgesterel-releasing intrauterine device, implants, hormone shot or injection, combined pill, mini pill, and patch.

Exclusion criteria

Diagnosis of vocal cord dysfunction, reactive airways dysfunction syndrome, hyperventilation and panic attacks, or other mimics of asthma.

An established diagnosis of occupational asthma.

Current smokers or patients with a smoking history of ≥10 pack years (number of pack years = number of cigarettes per day/20 × number of years smoked). Former smokers with

Figure 7 cont'd

<10 pack years must have stopped for at least 6 months to be eligible.
Previous medical history or evidence of an uncontrolled intercurrent illness that in the opinion of the investigator and/or medical monitor may compromise the safety of the patient in the study or interfere with evaluation of the investigational product or reduce the patient's ability to participate in the study. Patients with well-controlled comorbid disease (e.g., hypertension, hyperlipidemia, gastroesophageal reflux disease) on a stable treatment regimen for 15 days prior to visit 1 (week -5) are eligible.
Any concomitant respiratory disease that, in the opinion of the investigator and/or medical monitor, will interfere with the evaluation of the investigational product or interpretation of patient safety or study results (e.g., chronic obstructive pulmonary disease, cystic fibrosis, pulmonary fibrosis, bronchiectasis, allergic bronchopulmonary aspergillosis, Churg–Strauss syndrome).
Any clinically relevant abnormal findings in hematology, clinical chemistry, or urinalysis (laboratory results from visit 1 [week –5] and visit 3 [week –1]), physical examination, vital signs during the screening/run-in period which, in the opinion of the investigator, may put the patient at risk because of his/her participation in the study, or may influence the results of the study, or the patient's ability to participate in the study.
Evidence of active liver disease, including jaundice or aspartate transaminase, alanine transaminase, or alkaline phosphatase greater than twice the upper limit of normal (laboratory results from visit 1 [week –5] and visit 3 [week –1]).
History of cancer: • Patients who have had basal cell carcinoma or in situ carcinoma of the cervix are eligible to participate in the study provided that curative therapy was completed at least 12 months prior to visit 1 (week –5) • Patients who have had other malignancies are eligible provided that curative therapy was completed at least five years prior to visit 1 (week -5).
Acute upper or lower respiratory infections leading to antibiotics or antiviral medications within 15 days prior to visit 1 (week -5), during the screening/run-in period, or at visit 4 (week 0, day 1).
Evidence of a clinically significant infection, or receiving treatment with antibiotics or antiviral medications at visit 4 (week 0, day 1).
A helminth parasitic infection diagnosed within 24 weeks of visit 1 (week -5) that has not been treated, or has not responded to standard of care therapy.
Known history of active TB or a positive QFT-G test for TB during screening. Patients with a positive or indeterminate QFT-G result may be enrolled if they have ALL of the following: • No symptoms of TB: productive, prolonged cough (>3 weeks); coughing up blood; fever; night sweats; unexplained appetite loss; unintentional weight loss • No known exposure to a case of active TB after most recent prophylaxis (prophylaxis required only if positive) • No evidence of active TB on chest radiograph within three months prior to the first dose of investigational product. Patients with an indeterminate QFT-G result will have repeat QFT-G testing during the study (weeks 12, 28, 40, and 52).
Positive hepatitis B surface antigen, or hepatitis C virus antibody serology at screening, or a positive medical history for hepatitis B or C. Patients with a history of hepatitis B vaccination without history of hepatitis B are allowed to enrol.

Figure 7 cont'd

A positive human immunodeficiency virus test at screening or patient taking antiretroviral medications, as determined by medical history and/or patient's verbal report.
History of sensitivity to any component of the investigational product formulation or a history of drug or other allergy that, in the opinion of the investigator or medical monitor contraindicates their participation.
History of anaphylaxis to any biologic therapy.
History of documented immune complex disease (type 3 hypersensitivity reactions) to monoclonal antibody administration.
History of any known primary immunodeficiency disorder excluding asymptomatic selective immunoglobulin A or immunoglobulin G subclass deficiency.
Systemic glucocorticoid burst including taper within 15 days prior to visit 1 (week –5) or during the screening/run-in period.
Use of 5-lipoxygenase inhibitors (e.g., zileuton) within 15 days prior to visit 1 (week –5).
Use of immunosuppressive medication (e.g., methotrexate, troleandomycin, oral gold, cyclosporine, azathioprine, intramuscular long-acting depot glucocorticoid, or any experimental anti-inflammatory therapy) within three months prior to visit 1 (week –5). Chronic oral prednisone or equivalent up to a maximum of 10 mg daily or 20 mg every other day for the maintenance treatment of asthma is permitted.
Receipt of any of the following within 30 days prior to visit 1 (week –5) • Immunoglobulin or blood products.
Receipt of any investigational non-biologic agent within 30 days or 5 half-lives prior visit 1 (week –5), whichever is longer.
Receipt of any marketed (including omalizumab) or investigational biologic agent within 4 months or 5 half-lives prior to visit 1 (week -5), whichever is longer.
Pregnant, breastfeeding or lactating females.
History of chronic alcohol or drug abuse within 12 months prior to visit 1 (week –5).
Planned surgical procedures requiring general anesthesia or in-patient status for >1 day during the conduct of the study.
Unwillingness or inability to follow the procedures outlined in the protocol to week 64.
Concurrent enrollment in another clinical study involving an investigational treatment.
Receipt of any oral or ophthalmic β-adrenergic antagonists (e.g., propranolol) within 15 days prior to visit 1 (week –5).
Receipt of the Th2 cytokine inhibitor suplatast within 15 days prior to visit 1 (week –5).
Receipt of any live or attenuated vaccines within 15 days prior to visit 1 (week –5).

Figure 8

Figure 8 (Table 1B). Baseline Demographics and Clinical Characteristics in the Intention-To-Treat Population.

Demographics		**Placebo (N = 148)**	**Low-dose tezepelumab (70 mg Q4W) (N = 145)**	**Medium-dose tezepelumab (210 mg Q4W) (N = 145)**	**High-dose tezepelumab (280 mg Q2W) (N = 146)**	**Tezepelumab Total (N =436)**
Age (years)	Mean (SD)	52.2 (11.5)	50.6 (12.4)	52.6 (12.5)	50.1 (12.2)	51.1 (12.4)
Male sex	no. (%)	48 (32.4)	50 (34.5)	54 (37.2)	53 (36.3)	157 (36.0)
Race	no. (%)					
Asian		6 (4.1)	3 (2.1)	5 (3.4)	5 (3.4)	13 (3.0)
Black		6 (4.1)	4 (2.8)	3 (2.1)	8 (5.5)	15 (3.4)
White		133 (89.9)	138 (95.2)	136 (93.8)	129 (88.4)	403 (92.4)
Other		2 (1.4)	0	0	2 (1.4)	2 (0.5)
BMI (kg/m^2)	Mean (SD)	28.5 (5.5)	28.3 (5.1)	28.4 (4.9)	27.7 (5.0)	28.1 (5.0)
Former smoker	Yes/no, n	16/132	25/120	35/110	28/118	88/348
Clinical characteristics		**Placebo (N = 148)**	**Low-dose tezepelumab (N = 145)**	**Medium-dose tezepelumab (N = 145)**	**High-dose tezepelumab (N = 146)**	**Tezepelumab Total**

Figure 8 cont'd

						(N = 436)
Pre-BD FEV1 (L)	Mean (SD)	1.83 (0.58)	1.91 (0.66)	1.83 (0.58)	1.87 (0.60)	1.87 (0.61)
FEV1 % predicted/ reversibility	Mean (SD)	60.4 (13.6)/ 21.5 (18.9)	60.7 (13.5)/ 23.7 (18.9)	59.2 (12.4)/ 20.6 (18.6)	59.3 (11.8)/ 23.1 (23.0)	59.7 (12.6)/ 22.5 (20.3)
Mean ACQ-6*	Mean (SD)	2.66 (0.67)	2.76 (0.80)	2.71 (0.81)	2.63 (0.75)	2.70 (0.78)
Overall AQLQ(S)+12†	Mean (SD)	4.06 (0.86)	4.14 (0.94)	4.19 (0.90)	4.09 (0.90)	4.14 (0.91)
Asthma symptom score‡	Mean (SD)	1.72 (0.58)	1.70 (0.63)	1.76 (0.57)	1.68 (0.61)	1.72 (0.60)
Inhaled glucocorticoid dose level	Medium (%)/High (%)	73 (49.3)/75 (50.7)	71 (49.0)/74 (51.0)	70 (48.3)/75 (51.7)	72 (49.3)/74 (50.7)	213 (48.9)/223 (51.1)
FEIA IgE	Positive (%)/Negative (%)	83 (61.5)/52 (38.5)	71 (53.0)/63 (47.0)	80 (60.2)/53 (39.8)	74 (55.2)/60 (44.8)	225 (56.1)/176 (43.9)
Eosinophil count (cells/µl)	Mean (SD)	366 (323)	345 (284)	359 (347)	378 (423)	361 (356)
	Median (min, max)	270.0 (0, 1870)	270.0 (10, 1600)	275.0 (0, 3180)	255.0 (0, 3990)	270.0 (0, 3990)
	≥250, no. (%)	86 (58.1)	85 (58.6)	83 (57.2)	85 (58.2)	253 (58.0)
	<250, no. (%)	62 (41.9)	60 (41.4)	62 (42.8)	61 (41.8)	183 (42.0)
Total serum IgE	Mean (SD)	447 (1232)	314 (870)	464 (1366)	344 (579)	374 (992)

Figure 8 cont'd

(IU/ml)	Median (min, max)	135.0 (4, 11860)	109.3 (2, 7423)	135.4 (2, 11430)	138.1 (2, 3814)	126.8 (2, 11430)
Th2 status^	Low, no. (%)	71 (48.3)	81 (56.3)	76 (53.1)	78 (53.8)	235 (54.4)
	High, no. (%)	76 (51.7)	63 (43.8)	67 (46.9)	67 (46.2)	197 (45.6)
FENO (ppb)	(n) Mean (SD)	(146) 36.3 (38.9)	(144) 34.5 (46.9)	(143) 30.4 (29.4)	(141) 32.6 (33.9)	(428) 32.5 (37.5)
	Median (min, max)	21.5 (3.5, 276.3)	22.0 (2.5, 349.0)	20.5 (4.0, 152.5)	19.7 (2.0, 217.5)	21.0 (2.0, 349.0)
	<24 ppb, no. (%)	80 (54.8)	77 (53.5)	83 (58.0)	79 (56.0)	239 (55.8)
	≥24 ppb, no. (%)	66 (45.2)	67 (46.5)	60 (42.0)	62 (44.0)	189 (44.2)
Number of asthma exacerbations in the past 12 months	1 or 2(%)/ ≥3(%)	120 (81.1)/28 (18.9)	116 (80.0)/29 (20.0)	113 (77.9)/32 (22.1)	126 (86.3)/20 (13.7)	355 (81.4)/81 (18.6)

*Mean ACQ-6 score: ≤0.75 = well-controlled; >0.75 and <1.5 = partly controlled; ≥1.5 = uncontrolled.

†Mean AQLQ(S) score: 7 = no impairment; 1 = severe impairment.

‡Asthma symptom score ranges from zero (no symptom) to 4 (worst possible symptom) and includes daytime severity, daytime frequency, and night time severity.

^Th2-high: IgE > 100 IU/ml and blood eosinophil count ≥140 cells/µl.

+A clinically meaningful cutoff of 24 ppb was used for the FE_{NO} sub-population analysis.[2,3]

ACQ, Asthma Control Questionnaire; AQLQ(S)+12, asthma quality of life questionnaire; BD, bronchodilator; BMI, body mass index; FE_{NO}, fractional exhaled nitric oxide; FEIA, fluorescent immunoassay; FEV_1, forced expiratory volume in 1 second; IgE, immunoglobulin E; Th2, T helper 2; Q4W, every 4 weeks; Q2W, every 2 weeks; SD, standard deviation.

Figure 9

Figure 9 (Table 2) - Annualized Asthma Exacerbation Rate Reduction, and Change from Baseline in FEV_1, ACQ and AQLQ in the Eosinophil Sub-Populations <250 cells/µl and ≥250 cells/µl.

	Placebo (N = 148)	Low-dose tezepelumab (70 mg Q4W) (N = 145)	Medium-dose tezepelumab (210 mg Q4W) (N = 145)	High-dose tezepelumab (280 mg Q2W) (N = 146)
≥250 Eosinophils per µl				
n	86	85	83	85
Annualized AER (95% CI)	0.70 (0.54, 0.91)	0.27 (0.17, 0.41)	0.24 (0.14, 0.38)	0.19 (0.11, 0.31)
Reduction vs placebo (95% CI)	-	62% (24%, 81%)	65% (26%, 84%)	73% (41%, 88%)
P-value*	-	0.006	0.006	0.001
n	84	82	72	72
LS mean percentage change from baseline at week 52 in Pre-BD FEV_1 (L)	0.67	10.88	10.27	14.57
Difference vs placebo (95% CI) P-value*	-	10.21 (2.74, 17.69) 0.008	9.60 (1.91, 17.29) 0.015	13.91 (6.28, 21.53) <0.001
LS mean change from baseline at week 52 in Pre-BD FEV_1 (L)	–0.03	0.12	0.10	0.17
Difference vs placebo (95% CI) P-value*	-	0.15 (0.03, 0.27) 0.017	0.13 (0.01, 0.26) 0.041	0.20 (0.07, 0.32) 0.002
n	68	70	60	56
LS mean ACQ-6 change from baseline at week 50†	–0.86	–1.07	–1.29	–1.15
Difference vs placebo (95% CI) P-value*	-	–0.22 (–0.51, 0.08) 0.152	–0.43 (–0.74, –0.13) 0.005	–0.29 (–0.59, 0.01) 0.062

Figure 9 cont'd

n	62	69	54	55
LS mean AQLQ(S)+12 change from baseline at week 48†	0.87	1.04	1.23	1.18
Difference vs placebo (95% CI) P-value*	-	0.17 (–0.16, 0.49) 0.312	0.36 (0.02, 0.70) 0.036	0.31 (–0.03, 0.64) 0.071
<250 Eosinophils per µl				
n	62	60	62	61
Annualized AER (95% CI)	0.63 (0.45, 0.87)	0.24 (0.13, 0.41)	0.13 (0.06, 0.26)	0.26 (0.14, 0.43)
Reduction vs placebo (95% CI)	-	59% (11%, 81%)	79% (46%, 91%)	56% (7%, 80%)
P-value*	-	0.024	0.001	0.033
n	57	55	56	53
LS mean percentage change from baseline at week 52 in Pre-BD FEV_1 (L)	–3.20	1.04	2.94	2.09
Difference vs placebo (95% CI) P-value*	-	4.25 (–4.71, 13.21) 0.351	6.14 (–2.69, 14.97) 0.172	5.30 (–3.64, 14.24) 0.244
LS mean change from baseline at week 52 in Pre-BD FEV_1 (L)	–0.08	–0.02	0.01	0.02
Difference vs placebo (95% CI) P-value*	-	0.06 (–0.09, 0.20) 0.464	0.08 (–0.06, 0.23) 0.268	0.09 (–0.06, 0.24) 0.231
n	44	47	50	47
LS mean ACQ-6 change from baseline at week 50†	–0.91	–1.09	–1.16	–1.29
Difference vs placebo (95% CI) P-value*	-	–0.18 (–0.52, 0.15) 0.284	–0.25 (–0.58, 0.09) 0.147	–0.38 (–0.72,–0.04) 0.028
n	43	42	43	45
LS mean AQLQ(S)+12 change from baseline at week 48†	0.92	1.00	1.18	1.43

Figure 9 cont'd

Difference vs placebo (95% CI) P-value*	-	0.07 (–0.26, 0.41) 0.667	0.26 (–0.08, 0.60) 0.131	0.51 (0.17, 0.85) 0.003

*P-values are nominal and without multiplicity adjustment.

†A substantially lower proportion of patients completed the eDiary at week 52 than at weeks 48 and 50 due to a programming flaw within the eDiary which prevented patients from completing all of the questionnaires at week 52.

FEV_1: increase in value indicates improvement. MCID: 100 ml to 200 ml.

ACQ-6: range: 0–6. Decrease in value indicates improvement. MCID: 0.5.

AQLQ: range: 1–7. Increase in value indicates improvement. MCID: 0.5.

AER, asthma exacerbation rate; ACQ, Asthma Control Questionnaire; AQLQ(S)+12, asthma quality of life questionnaire; BD, bronchodilator; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; LS mean, least squares mean; Q4W, every 4 weeks; Q2W, every 2 weeks.

Figure 10

Figure 10 (Table 3) - Change from Baseline in ACQ-6 (week 50) and AQLQ(S)+12 (week 48) in the Intention-to-Treat Population

	Placebo (N = 148)	Low-dose tezepelumab (70 mg Q4W) (N = 145)	Medium-dose tezepelumab (210 mg Q4W) (N = 145)	High-dose tezepelumab (280 mg Q2W) (N = 146)
n	112	117	110	103
LS mean ACQ-6 change from baseline at week 50	–0.88	–1.08	–1.23	–1.21
Difference vs placebo (95% CI)	-	–0.20 (–0.42, 0.02)	–0.34 (–0.57, –0.12)	–0.33 (–0.56, –0.10)
P-value*	-	0.077	0.003	0.004
n	105	111	97	100
LS mean AQLQ(S)+12 change from baseline at week 48	0.89	1.02	1.21	1.29
Difference vs placebo (95% CI)	-	0.13 (–0.10, 0.37)	0.32 (0.08, 0.56)	0.40 (0.16, 0.64)
P-value*	-	0.268	0.009	0.001

Figure 11

Figure 11 (Table 4) *- Annualized Asthma Exacerbation Rate Reduction and Change from Baseline in FEV_1 (week 52), ACQ-6 (week 50), and AQLQ(S)+12 (week 48) in Patient Sub-populations: Th2 status, Serum Periostin.*

		Placebo (N = 148)		Low-dose tezepelumab (70 mg Q4W) (N = 145)		Medium-dose tezepelumab (210 mg Q4W) (N = 145)		High-dose tezepelumab (280 mg Q2W) (N = 146)	
Th2 status (High = IgE >100 IU/ml and eosinophil count ≥140 cells/µl; Low = IgE ≤100 IU/ml or eosinophil count <140 cells/µl)									
		High	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**
Annualized AER									
	n	76	71	63	81	67	76	67	78
	AER (95% CI)	0.61 (0.45, 0.81)	0.75 (0.56, 0.98)	0.32 (0.20, 0.50)	0.22 (0.13, 0.35)	0.24 (0.13, 0.40)	0.14 (0.07, 0.26)	0.19 (0.10, 0.34)	0.25 (0.15, 0.39)
	AER reduction vs placebo (95% CI)	-	-	51% (–5%, 78%)	65% (29%, 83%)	63% (15%, 83%)	82% (58%, 92%)	71% (31%, 87%)	63% (22%, 82%)
	P-value*	-	-	0.067	0.004	0.019	<0.001	0.005	0.008
Pre-BD FEV_1 (L)	n	74	66	60	76	59	67	58	66

Figure 11 cont'd

percent change from baseline (week 52)	LS mean	1.85	–2.04	8.79	7.52	9.55	6.61	16.25	6.44
	Difference vs placebo	-	-	6.93	9.56	7.70	8.66	14.40	8.48
	(95% CI)			(–1.96, 15.83)	(2.05, 17.07)	(–1.11, 16.50)	(0.97, 16.34)	(5.54, 23.25)	(0.80, 16.17)
	P-value*	-	-	0.126	0.013	0.087	0.027	0.002	0.031
Pre-BD FEV_1 (L) change from baseline (week 52)	LS mean	–0.05	–0.03	0.04	0.12	0.04	0.09	0.18	0.08
	Difference vs placebo	-	-	0.09	0.15	0.09	0.13	0.23	0.11
	(95% CI)			(–0.06, 0.23)	(0.03, 0.27)	(–0.05, 0.24)	(0.00, 0.25)	(0.09, 0.38)	(–0.01, 0.24)
	P-value*	-	-	0.231	0.018	0.207	0.053	0.002	0.076
ACQ-6 (week 50)†	n	64	47	54	62	52	56	46	56
	LS mean	–1.00	–0.69	–1.06	–1.08	–1.29	–1.13	–1.20	–1.18
	Difference vs placebo	-	-	–0.06	–0.38	–0.30	–0.43	–0.20	–0.49
	(95% CI)			(–0.37, 0.26)	(–0.70, –0.06)	(–0.61, 0.02)	(–0.76, –0.11)	(–0.52, 0.12)	(–0.81, –0.16)
	P-value*	-	-	0.725	0.019	0.065	0.009	0.224	0.003
AQLQ(S)+12 (week	n	60	44	52	58	45	51	45	54

Figure 11 cont'd

48)[†]	LS mean	1.08	0.61	1.17	0.89	1.18	1.19	1.19	1.33
	Difference vs placebo (95% CI)	-	-	0.08 (–0.26, 0.42)	0.28 (–0.06, 0.61)	0.09 (–0.25, 0.44)	0.58 (0.23, 0.92)	0.10 (–0.24, 0.45)	0.72 (0.38, 1.07)
	P-value[*]	-	-	0.632	0.104	0.595	0.001	0.556	<0.001
Serum periostin (High = > Median, Low = < Median)									
		High	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**
Annualized AER	n	72	76	65	79	79	65	74	69
	AER (95% CI)	0.75 (0.56, 0.98)	0.60 (0.43, 0.80)	0.28 (0.16, 0.44)	0.25 (0.15, 0.39)	0.18 (0.09, 0.30)	0.22 (0.11, 0.37)	0.20 (0.11, 0.33)	0.25 (0.14, 0.41)
	AER reduction vs placebo (95% CI)	-	-	68% (29%, 85%)	55% (9%, 78%)	78% (53%, 90%)	60% (2%, 84%)	73% (43%, 88%)	56% (3%, 80%)
	P-value[*]	-	-	0.005	0.027	<0.001	0.045	<0.001	0.041
Pre-BD FEV_1 (L) percent change from baseline (week 52)	n	70	71	63	73	71	56	67	55
	LS mean	–0.46	1.40	11.69	6.82	14.03	2.48	14.34	6.33
	Difference vs placebo	-	-	12.15	5.42	14.49	1.09	14.80	4.93

Figure 11 cont'd

	(95% CI)			(2.84, 21.46)	(–1.10, 11.93)	(5.58, 23.40)	(–5.83, 8.00)	(5.78, 23.82)	(–1.91, 11.77)
	P-value*	-	-	0.011	0.103	0.002	0.758	0.001	0.157
Pre-BD FEV_1 (L) change from baseline (week 52)	LS mean	–0.01	–0.03	0.15	0.06	0.17	–0.01	0.19	0.08
	Difference vs placebo	-	-	0.16	0.09	0.18	0.02	0.20	0.10
	(95% CI)			(0.02, 0.30)	(–0.03, 0.22)	(0.05, 0.32)	(–0.11, 0.15)	(0.06, 0.34)	(–0.02, 0.23)
	P-value*	-	-	0.029	0.128	0.008	0.755	0.005	0.108
ACQ-6 (week 50)†	n	60	52	56	60	58	51	55	46
	LS mean	–0.89	–0.87	–1.01	–1.13	–1.46	–0.94	–1.18	–1.26
	Difference vs placebo	-	-	–0.12	–0.25	–0.57	–0.06	–0.29	–0.39
	(95% CI)			(–0.44,0.21)	(–0.56, 0.05)	(–0.89, –0.26)	(–0.38, 0.26)	(–0.61, 0.03)	(–0.71, –0.06)
	P-value*	-	-	0.475	0.101	<0.001	0.694	0.076	0.019
AQLQ(S)+12 (week 48)†	n	59	46	53	57	47	49	55	43
	LS mean	0.89	0.90	1.01	1.01	1.40	0.99	1.29	1.28
	Difference vs placebo	-	-	0.13	0.10	0.52	0.09	0.40	0.38

Figure 11 cont'd

	(95% CI)			(–0.22, 0.48)	(–0.22, 0.43)	(0.17, 0.86)	(–0.25, 0.42)	(0.06, 0.74)	(0.04, 0.72)
	P-value*	-	-	0.470	0.524	0.004	0.621	0.020	0.028

Figure 12

Figure 12 (Table 5) *Annualized Asthma Exacerbation Rate Reduction and Change from Baseline in FEV_1 (week 52), ACQ-6 (week 50), and AQLQ(S)+12 (week 48) in Patient Sub-populations: FE_{NO}, Allergic status, Current post-BD reversibility*

		Placebo (N = 148)		Low-dose tezepelumab (70 mg Q4W) (N = 145)		Medium-dose tezepelumab (210 mg Q4W) (N = 145)		High-dose tezepelumab (280 mg Q2W) (N = 146)	
FE_{NO} <24 ppb and ≥24 ppb		**≥24 ppb**	**<24 ppb**	**≥24 ppb**	**<24 ppb**	**≥24 ppb**	**<24 ppb**	**≥24 ppb**	**<24 ppb**
Annualized AER	n	66	80	67	77	60	83	62	79
	AER	0.98	0.44	0.28	0.25	0.20	0.19	0.21	0.24
	(95% CI)	(0.75, 1.25)	(0.31, 0.61)	(0.17, 0.44)	(0.15, 0.39)	(0.10, 0.35)	(0.11, 0.32)	(0.11, 0.36)	(0.14, 0.38)
	AER reduction vs placebo (95% CI)	-	-	72% (43%, 86%)	43% (–18%, 73%)	77% (50%, 90%)	62% (9%, 84%)	78% (53%, 90%)	46% (–17%, 75%)
	P-value*	-	-	<0.001	0.127	<0.001	0.030	<0.001	0.118
Pre-BD FEV_1 (L) percent	n	61	78	61	75	52	74	52	69

Figure 12 cont'd

change from baseline (week 52)	LS mean	–1.55	1.93	8.51	7.99	12.09	6.47	11.18	10.51
	Difference vs placebo (95% CI)	-	-	10.06 (0.72, 19.40)	6.06 (–1.08, 13.21)	13.64 (3.95, 23.33)	4.55 (–2.55, 11.64)	12.73 (3.09, 22.37)	8.59 (1.37, 15.80)
	P-value*	-	-	0.035	0.096	0.006	0.208	0.010	0.020
Pre-BD FEV_1 (L) change from baseline (week 52)	LS mean	–0.05	0.05	0.10	0.13	0.15	0.09	0.14	0.17
	Difference vs placebo (95% CI)	-	-	0.15 (0.00, 0.31)	0.08 (–0.03, 0.20)	0.21 (0.05, 0.37)	0.04 (–0.07, 0.16)	0.20 (0.04, 0.36)	0.12 (0.00, 0.23)
	P-value*	-	-	0.050	0.164	0.011	0.449	0.015	0.046
ACQ-6 (week 50)†	n	50	62	52	64	48	60	40	60
	LS mean	–0.83	–0.89	–1.18	–1.03	–1.50	–0.99	–1.27	–1.15
	Difference vs placebo (95% CI)	-	-	–0.35 (–0.69, –0.01)	–0.14 (–0.43, 0.15)	–0.67 (–1.02, –0.32)	–0.10 (–0.39, 0.19)	–0.44 (–0.79, –0.08)	–0.26 (–0.55, 0.04)
	P-value*	-	-	0.046	0.348	<0.001	0.507	0.016	0.086
AQLQ(S)+12 (week	n	49	56	49	62	44	51	39	58

Figure 12 cont'd

48)[+]	LS mean	0.83	0.96	1.06	0.99	1.48	0.97	1.21	1.33
	Difference vs placebo (95% CI)	-	-	0.24 (–0.13, 0.60)	0.04 (–0.27, 0.35)	0.65 (0.27, 1.03)	0.02 (–0.30, 0.33)	0.39 (0.01, 0.77)	0.38 (0.07, 0.69)
	P-value[*]	-	-	0.204	0.805	<0.001	0.911	0.047	0.017
Allergic status (allergic/non-allergic)									
		Allergic	**Non-allergic**	**Allergic**	**Non-allergic**	**Allergic**	**Non-allergic**	**Allergic**	**Non-allergic**
Annualized AER	n	83	52	71	63	80	53	74	60
	AER (95% CI)	0.73 (0.55, 0.94)	0.62 (0.43, 0.88)	0.24 (0.14, 0.38)	0.21 (0.11, 0.37)	0.13 (0.06, 0.25)	0.24 (0.13, 0.42)	0.22 (0.12, 0.36)	0.21 (0.11, 0.37)
	AER reduction vs placebo (95% CI)	-	-	66% (25%, 85%)	67% (29%, 84%)	82% (56%, 93%)	57% (3%, 81%)	66% (26%, 85%)	64% (17%, 84%)
	P-value[*]	-	-	0.008	0.004	<0.001	0.043	0.007	0.017
Pre-BD FEV_1 (L) Percent change from baseline	n	78	50	68	59	73	44	60	54
	LS mean	–0.52	–3.38	11.61	3.00	8.35	8.15	6.52	8.55

Figure 12 cont'd

(week 52)	Difference vs placebo (95% CI)	-	-	12.13 (4.07, 20.18)	6.38 (–2.49, 15.25)	8.87 (0.99, 16.75)	11.54 (2.20, 20.87)	7.04 (–1.04, 15.11)	11.93 (2.86, 21.00)
	P-value*	-	-	0.003	0.157	0.028	0.016	0.087	0.010
Pre-BD FEV_1 (L) change from baseline (week 52)	LS mean	–0.04	–0.04	0.14	0.06	0.08	0.13	0.07	0.17
	Difference vs placebo (95% CI)	-	-	0.18 (0.05, 0.31)	0.09 (–0.06, 0.25)	0.12 (–0.01, 0.25)	0.17 (0.01, 0.33)	0.11 (–0.03, 0.24)	0.20 (0.05, 0.36)
	P-value*	-	-	0.008	0.230	0.071	0.040	0.110	0.011
ACQ-6 (week 50)†	n	66	39	60	50	62	40	50	45
	LS Mean	–0.99	–0.76	–1.18	–0.96	–1.24	–1.18	–1.31	–1.25
	Difference vs placebo (95% CI)	-	-	–0.19 (–0.49, 0.12)	–0.21 (–0.56, 0.15)	–0.25 (–0.54, 0.05)	–0.42 (–0.80, –0.05)	–0.32 (–0.63, –0.01)	–0.49 (–0.85, –0.12)
	P-value*	-	-	0.227	0.253	0.106	0.027	0.041	0.009
AQLQ(S)+12 (week 48)†	n	63	35	57	47	57	34	49	43
	LS mean	1.05	0.53	1.15	0.88	1.18	1.20	1.20	1.44

Figure 12 cont'd

	Difference vs placebo	-	-	0.09	0.35	0.13	0.66	0.15	0.91
	(95% CI)			(–0.22, 0.41)	(–0.04, 0.73)	(–0.19, 0.44)	(0.25, 1.08)	(–0.17, 0.47)	(0.51, 1.30)
	P-value*	-	-	0.555	0.078	0.427	0.002	0.367	<0.001
Current post-BD reversibility (Yes [≥12% and ≥200 ml] or No [<12% and <200 ml])									
		Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
Annualized AER	n	135	13	129	16	121	24	134	12
	AER	0.56	1.85	0.25	0.38	0.16	0.37	0.20	0.44
	(95% CI)	(0.44,0.70)	(1.18,2.75)	(0.17, 0.35)	(0.14, 0.83)	(0.09, 0.25)	(0.16, 0.73)	(0.13, 0.29)	(0.14, 1.03)
	AER reduction vs placebo (95% CI)	-	-	57% (24%, 75%)	83% (57%, 93%)	72% (46%, 85%)	79% (45%, 92%)	65% (37%, 80%)	74% (13%, 92%)
	P-value*	-	-	0.003	<0.001	<0.001	0.001	<0.001	0.029
Pre-BD FEV_1 (L) percent change from baseline (week 52)	n	129	12	123	14	108	20	114	11
	LS mean	–1.08	–4.44	7.60	4.35	6.98	11.70	8.97	13.15
	Difference vs placebo	-	-	8.68	8.79	8.06	16.14	10.05	17.59

Figure 12 cont'd

	(95% CI)			(2.48, 14.88)	(–2.75, 20.32)	(1.69, 14.43)	(4.75, 27.53)	(3.79, 16.30)	(4.97, 30.22)
	P-value*	-	-	0.006	0.133	0.013	0.006	0.002	0.007
Pre-BD FEV_1 (L) change from baseline (week 52)	LS mean	–0.07	–0.10	0.06	0.02	0.03	0.16	0.08	0.21
	Difference vs placebo	-	-	0.13	0.12	0.11	0.26	0.15	0.31
	(95% CI)			(0.03, 0.23)	(–0.08, 0.33)	(0.00, 0.21)	(0.06, 0.46)	(0.05, 0.25)	(0.08, 0.53)
	P-value*	-	-	0.013	0.226	0.045	0.013	0.005	0.008
ACQ-6 (week 50)†	n	104	8	103	14	91	19	92	11
	LS mean	–0.87	–1.11	–1.08	–1.10	–1.13	–1.73	–1.21	–1.33
	Difference vs placebo	-	-	–0.21	0.01	–0.26	–0.62	–0.34	–0.22
	(95% CI)			(–0.44, 0.03)	(–0.66, 0.68)	(–0.50, –0.02)	(–1.26, 0.02)	(–0.57, –0.10)	(–0.93, 0.50)
	P-value*	-	-	0.085	0.980	0.034	0.057	0.006	0.555
AQLQ(S)+12 (week 48)†	n	98	7	98	13	79	18	89	11
	LS mean	0.89	0.98	1.00	1.22	1.19	1.38	1.28	1.39
	Difference vs placebo	-	-	0.11	0.24	0.30	0.40	0.39	0.41

Figure 12 cont'd

	(95% CI)			(–0.14, 0.35)	(–0.50, 0.98)	(0.04, 0.56)	(–0.29, 1.10)	(0.14, 0.64)	(–0.36, 1.18)
	P-value*	-	-	0.405	0.520	0.026	0.256	0.003	0.296

Figure 13

Figure 13 (Table 6) *Change from Baseline in Post-BD FEV_1 and Pre- and Post-BD Forced Vital Capacity at Week 52 in the Intention-To-Treat population*

		Placebo (N = 148)	Low-dose tezepelumab (70 mg Q4W) (N = 145)	Medium-dose tezepelumab (210 mg Q4W) (N = 145)	High-dose tezepelumab (280 mg Q2W) (N = 146)
Post-BD FEV_1 (L)					
Change from baseline	n	140	137	128	124
	Mean	–0.05	0.11	0.08	0.11
	SD	0.35	0.39	0.45	0.42
	Median	–0.02	0.04	0.04	0.04
	(Min, max)	(–1.31, 0.94)	(–0.76, 2.31)	(–1.04, 2.68)	(–1.10, 1.37)
Percentage change from baseline	n	140	137	128	124
	Mean	–1.35	6.14	6.69	7.43

Figure 13 cont'd

	SD	16.33	20.19	27.35	22.52
	Median	–1.07	1.46	1.32	2.11
	(Min, max)	(–45.92, 51.16)	(–26.77, 126.23)	(–30.54, 188.73)	(–37.50, 118.35)
Pre-BD FVC (L)					
Change from baseline	n	141	137	128	125
	Mean	0.08	0.24	0.19	0.20
	SD	0.47	0.55	0.60	0.48
	Median	0.03	0.12	0.09	0.08
	(Min, max)	(–1.25, 2.03)	(–0.85, 2.39)	(–2.22, 2.58)	(–0.91, 2.14)
Percentage change from baseline	n	141	137	128	125
	Mean	3.81	10.14	8.95	8.34
	SD	18.02	23.25	25.45	19.88

Figure 13 cont'd

	Median	1.22	4.35	3.65	3.36
	(Min, max)	(–32.76, 84.62)	(–30.83, 134.52)	(–49.12, 133.73)	(–22.81, 110.88)
Post-BD FVC (L)					
Change from baseline	n	140	137	128	124
	Mean	–0.07	0.08	0.09	0.07
	SD	0.36	0.43	0.50	0.43
	Median	–0.05	0.05	0.03	0.01
	(Min, max)	(–1.69, 1.03)	(–0.76, 2.23)	(–1.32, 2.28)	(–0.94, 1.81)
Percentage change from baseline	n	140	137	128	124
	Mean	–1.57	3.43	4.26	2.93
	SD	11.73	17.45	19.14	14.49
	Median	–1.30	1.29	0.90	0.13
	(Min, max)	(–50.60, 47.69)	(–22.44, 117.99)	(–29.91, 125.97)	(–26.22, 85.38)

Figure 14

Figure 14 (Table 7) *Annualized Rate of Severe Asthma Exacerbations, Time to First Asthma Exacerbation/Severe Asthma Exacerbation, and Proportion of Patients With One or More Asthma Exacerbation at Week 52 in the Intention-To-Treat population*

		Placebo (N = 148)	Low-dose tezepelumab (70 mg Q4W) (N = 145)	Medium-dose tezepelumab (210 mg Q4W) (N = 145)	High-dose tezepelumab (280 mg Q2W) (N = 146)
Annualized rate of severe asthma exacerbations					
	Severe asthma exacerbation rate	0.13	0.04	0.02	0.03
	(95% CI)	(0.08, 0.20)	(0.01, 0.08)	(0.00, 0.06)	(0.01, 0.07)
	Reduction vs placebo	-	72%	85%	74%
	(95% CI)		(–6%, 93%)	(27%, 97%)	(–10%, 94%)
	P-value*	-	0.060	0.019	0.067
Time to asthma exacerbations					
	Event	43	30	21	25
	Censored	105	115	124	121

Figure 14 cont'd

	Hazard ratio	-	0.66	0.46	0.55
	95% CI	-	0.41, 1.05	0.27, 0.78	0.34, 0.90
	P-value*	-	0.078	0.003	0.018
Time to severe exacerbations					
	Event	9	5	3	4
	Censored	139	140	142	142
	Hazard ratio	-	0.55	0.34	0.45
	95% CI	-	0.18, 1.64	0.09, 1.24	0.14, 1.47
	P-value*	-	0.284	0.085	0.168
Patients with asthma exacerbations/severe asthma exacerbations					
Patients with ≥1 asthma exacerbation, n (%)	Yes	43 (29.1)	30 (20.7)	21 (14.5)	25 (17.1)
	No	105 (70.9)	115 (79.3)	124 (85.5)	121 (82.9)
	P-value*	-	0.098	0.003	0.015

Figure 14 cont'd

Patients with ≥1 severe asthma exacerbation, n (%)	Yes	9 (6.1)	5 (3.4)	3 (2.1)	4 (2.7)
	No	139 (93.9)	140 (96.6)	142 (97.9)	142 (97.3)
	P-value*	-	0.291	0.083	0.163

Figure 15

Figure 15 (Table 8) *Post-hoc Analysis of Annualized Asthma Exacerbation Rate Reduction Stratified by Blood Eosinophil Count <400 cells/µL vs ≥400 cells/µL Through Week 52*

		Placebo (N = 148)		Low-dose tezepelumab (70 mg Q4W) (N = 145)		Medium-dose tezepelumab (210 mg Q4W) (N = 145)		High-dose tezepelumab (280 mg Q2W) (N = 146)	
Eosinophils per µl		**<400**	**≥400**	**<400**	**≥400**	**<400**	**≥400**	**<400**	**≥400**
Annualized AER	n	98	50	100	45	100	45	96	50
	AER	0.59	0.84	0.24	0.32	0.19	0.19	0.27	0.13
	(95% CI)	(0.44, 0.76)	(0.61, 1.14)	(0.15, 0.35)	(0.17, 0.53)	(0.11, 0.30)	(0.08, 0.37)	(0.17, 0.40)	(0.05, 0.27)
	AER reduction vs placebo (95% CI)	-	-	60% (24%, 79%)	58% (0%, 82%)	68% (34%, 84%)	75% (31%, 91%)	53% (11%, 75%)	84% (53%, 95%)
	P-value*	-	-	0.005	0.050	0.002	0.007	0.021	<0.001

*P-values are nominal and without multiplicity adjustment.

AER, asthma exacerbation rate; CI, confidence interval; Q4W, every 4 weeks; Q2W, every 2 weeks

Figure 16

Figure 16 (Table 9) *Annualized Asthma Exacerbation Rate Reduction Stratified by Patients on a Medium- or High-Dose of Inhaled Glucocorticoid and by Patients on Maintenance Oral Glucocorticoids Through Week 52*

		Placebo (N = 148)		Low-dose tezepelumab (70 mg Q4W) (N = 145)		Medium-dose tezepelumab (210 mg Q4W) (N = 145)		High-dose tezepelumab (280 mg Q2W) (N = 146)	
Inhaled glucocorticoid dose		**Medium inhaled glucocorticoid**	**High inhaled glucocorticoid**	**Medium inhaled glucocorticoid**	**High inhaled glucocorticoid**	**Medium inhaled glucocorticoid**	**High inhaled glucocorticoid**	**Medium inhaled glucocorticoid**	**High inhaled glucocorticoid**
Annualized AER	n	73	75	71	74	70	75	72	74
	AER	0.38	0.96	0.19	0.33	0.15	0.23	0.20	0.24
	(95% CI)	(0.26, 0.55)	(0.75, 1.22)	(0.10, 0.32)	(0.21, 0.49)	(0.07, 0.28)	(0.13, 0.37)	(0.10, 0.34)	(0.14, 0.39)
	AER reduction vs placebo (95% CI)	-	-	51% (–8%, 78%)	66% (33%, 83%)	60% (5%, 83%)	76% (49%, 89%)	49% (–13%, 77%)	75% (47%, 88%)
	P-value*	-	-	0.076	0.002	0.038	<0.001	0.096	<0.001
Maintenance oral glucocorticoid use		**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**

Figure 16 cont'd

Annualized AER	n	14	134	15	130	9	136	13	133
	AER	2.08	0.54	0.61	0.22	0.51	0.17	0.24	0.22
	(95% CI)	(1.37, 3.03)	(0.42, 0.68)	(0.28, 1.16)	(0.15, 0.32)	(0.14, 1.32)	(0.11, 0.26)	(0.05, 0.70)	(0.14, 0.32)
	AER reduction vs placebo (95% CI)	-	-	72% (31%, 89%)	59% (25%, 77%)	75% (11%, 93%)	68% (40%, 83%)	88% (49%, 97%)	59% (27%, 77%)
	P-value*	-	-	0.006	0.003	0.033	<0.001	0.004	0.003

Figure 17

Figure 17 (Table 10) Annualized Asthma Exacerbation Rate Reduction Stratified by Number of Prior Asthma Exacerbations and by Smoking History Through Week 52*

		Placebo (N = 148)		**Low-dose tezepelumab (70 mg Q4W) (N = 145)**		**Medium-dose tezepelumab (210 mg Q4W) (N = 145)**		**High-dose tezepelumab (280 mg Q2W) (N = 146)**	
Number of prior asthma exacerbations in the previous 12 months		**1 or 2**	**≥3**	**1 or 2**	**≥3**	**1 or 2**	**≥3**	**1 or 2**	**≥3**
Annualized AER	n	120	28	116	29	113	32	126	20
	AER	0.34	2.13	0.18	0.60	0.10	0.52	0.18	0.48

Figure 17 cont'd

	(95% CI)	(0.24, 0.46)	(1.62, 2.75)	(0.11, 0.27)	(0.35, 0.95)	(0.05, 0.18)	(0.29, 0.85)	(0.11, 0.27)	(0.22, 0.91)
	AER reduction vs placebo (95% CI)	-	-	49% (−1%, 74%)	70% (45%, 84%)	70% (34%, 87%)	75% (51%, 87%)	50% (3, 75%)	74% (43%, 88%)
	P-value[†]	-	-	0.052	<0.001	0.003	<0.001	0.040	<0.001
Smoking history		**Former smoker**	**Non-smoker**	**Former smoker**	**Non-smoker**	**Former smoker**	**Non-smoker**	**Former smoker**	**Non-smoker**
Annualized AER	n	16	132	25	120	35	110	28	118
	AER	0.72	0.67	0.53	0.20	0.18	0.19	0.25	0.21
	(95% CI)	(0.36, 1.29)	(0.53, 0.82)	(0.28, 0.90)	(0.13, 0.30)	(0.07, 0.40)	(0.12, 0.30)	(0.09, 0.53)	(0.14, 0.32)
	AER reduction vs placebo (95% CI)	-	-	28% (−72%, 70%)	69% (42%, 83%)	72% (19%, 90%)	70% (41%, 85%)	61% (−13%, 87%)	67% (39%, 83%)
	P-value[†]	-	-	0.455	<0.001	0.018	<0.001	0.083	<0.001

Figure 18

Figure 18 (Table 11) Change from Baseline in MedImmune ASMA Score at week 52

	Placebo (N = 148)		Low-dose tezepelumab (70 mg Q4W) (N = 145)		Medium-dose tezepelumab (210 mg Q4W) (N = 145)		High-dose tezepelumab (280 mg Q2W) (N = 146)	
Overall intention-to-treat population								
n	128		125		113		112	
LS mean	–0.53		–0.60		–0.67		–0.74	
Difference vs placebo	-		–0.07		–0.13		–0.21	
95% CI	-		(–0.21, 0.07)		(–0.28, 0.01)		(–0.35, –0.06)	
P-value*	-		0.329		0.067		0.005	
Eosinophils (per µl)								
	≥250	**<250**	**≥250**	**<250**	**≥250**	**<250**	**≥250**	**<250**
n	78	50	77	48	65	48	63	49
LS mean	–0.56	–0.51	–0.61	–0.60	–0.74	–0.58	–0.75	–0.73

Figure 18 cont'd

Difference vs placebo	-		–0.06	–0.09	–0.18	–0.08	–0.20	–0.22
(95% CI)			(–0.25, 0.13)	(–0.30, 0.13)	(–0.38, 0.01)	(–0.29, 0.14)	(–0.39, 0.00)	(–0.44, 0.00)
P-value*	-		0.539	0.431	0.068	0.493	0.047	0.045
Th2 Status (High = IgE >100 IU/ml and eosinophil count ≥140 cells/ul; Low = IgE ≤100 IU/ml or eosinophil count <140 cells/ul)								
	High	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**
n	66	61	55	69	53	58	53	58
LS mean	–0.55	–0.50	–0.67	– 0.55	–0.59	–0.72	–0.76	–0.73
Difference vs placebo (95% CI)	-	-	–0.12 (–0.32, 0.08)	–0.05 (–0.26, 0.16)	–0.05 (–0.25, 0.15)	–0.23 (–0.44, –0.02)	–0.21 (–0.41, –0.02)	–0.23 (–0.44, –0.02)
P-value*	-	-	0.229	0.639	0.631	0.036	0.035	0.032
FE_{NO} <24 ppb and ≥24 ppb								
	≥24 ppb	**<24 ppb**	**≥24 ppb**	**<24 ppb**	**≥24 ppb**	**<24 ppb**	**≥24 ppb**	**<24 ppb**
n	57	70	55	69	44	67	42	66
LS mean	–0.49	–0.53	–0.68	–0.54	–0.76	–0.59	–0.74	–0.71

Figure 18 cont'd

Difference vs placebo	-	-	–0.19	–0.01	–0.27	–0.06	–0.25	–0.18
(95% CI)			(–0.40, 0.02)	(–0.21, 0.18)	(–0.50, –0.05)	(–0.26, 0.13)	(–0.47, –0.03)	(–0.37, 0.02)
P-value*	-	-	0.082	–0.915	0.016	0.511	0.027	0.074
Serum periostin (High = > Median, Low = < Median)								
	High	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**
n	66	62	59	65	62	50	58	51
LS mean	–0.51	–0.55	–0.57	–0.60	–0.82	–0.47	–0.74	–0.74
Difference vs placebo	-	-	–0.05	–0.06	–0.31	0.08	–0.23	–0.19
(95% CI)			(–0.26, 0.16)	(–0.25, 0.14)	(–0.51, –0.10)	(–0.13, 0.28)	(–0.43, –0.02)	(–0.39, 0.01)
P-value*	-	-	0.619	0.569	0.003	0.464	0.030	0.058
Allergic status (allergic/non-allergic)								
	Allergic	**Non-allergic**	**Allergic**	**Non-allergic**	**Allergic**	**Non-allergic**	**Allergic**	**Non-allergic**
n	69	48	59	57	63	39	51	49

Figure 18 cont'd

LS mean	–0.53	–0.51	–0.59	–0.59	–0.63	–0.68	–0.67	–0.86
Difference vs placebo (95% CI)	-	-	–0.07 (–0.26, 0.13)	–0.09 (–0.31, 0.14)	–0.10 (–0.29, 0.09)	–0.17 (–0.41, 0.07)	–0.15 (–0.34, 0.05)	–0.36 (–0.59, –0.13)
P-value*	-	-	0.500	0.453	0.300	0.162	0.144	0.002
Current post-BD reversibility (Yes [≥12% and ≥200 ml] or no [<12% and <200 ml])								
	Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
n	117	11	112	13	94	19	101	11
LS mean	–0.55	–0.35	–0.59	–0.63	–0.63	–0.87	–0.73	–0.84
Difference vs placebo (95% CI	-	-	–0.04 (–0.19, 0.11)	–0.28 (–0.69, 0.13)	–0.07 (–0.23, 0.08)	–0.52 (–0.91, –0.14)	–0.18 (–0.33, –0.03)	–0.49 (–0.93, –0.05)
P-value*	-	-	0.580	0.183	0.348	0.008	0.022	0.030

Figure 19

Figure 19 (Table 12). All Treatment-Emergent Serious Adverse Events in the As-Treated Population

Patients* with at least one serious adverse event	Placebo (N = 148)	Low-dose tezepelumab (70 mg Q4W) (N = 145)	Medium-dose tezepelumab (210 mg Q4W) (N = 145)	High-dose tezepelumab (280 mg Q2W) (N = 146)	Tezepelumab Total (N = 436)
Cardiac disorders	2 (1.4%)	2 (1.4%)	1 (0.7%)	0	3 (0.7%)
Atrial fibrillation	1 (0.7%)	0	0	0	0
Atrial flutter	0	1 (0.7%)	0	0	1 (0.2%)
Cardiac failure	1 (0.7%)	0	1 (0.7%)	0	1 (0.2%)
Myocardial infarction	0	1 (0.7%)	0	0	1 (0.2%)
Gastrointestinal disorders	1 (0.7%)	1 (0.7%)	0	3 (2.1%)	4 (0.9%)
Abdominal pain	0	1 (0.7%)	0	0	1 (0.2%)
Abdominal pain lower	1 (0.7%)	0	0	0	0
Hiatus hernia	0	0	0	1 (0.7%)	1 (0.2%)
Large intestinal polyp	0	0	0	1 (0.7%)	1 (0.2%)
Pancreatitis acute	0	0	0	1 (0.7%)	1 (0.2%)
General disorders and administration site	1 (0.7%)	0	1 (0.7%)	0	1 (0.2%)

Figure 19 cont'd

conditions					
Non-cardiac chest pain	1 (0.7%)	0	1 (0.7%)	0	1 (0.2%)
Hepatobiliary disorders	0	0	0	1 (0.7%)	1 (0.2%)
Cholelithiasis	0	0	0	1 (0.7%)	1 (0.2%)
Immune system disorders	0	0	0	1 (0.7%)	1 (0.2%)
Anaphylactic shock	0	0	0	1 (0.7%)	1 (0.2%)
Infections and infestations	4 (2.7%)	6 (4.1%)	1 (0.7%)	4 (2.7%)	11 (2.5%)
Bronchitis	0	1 (0.7%)	0	0	1 (0.2%)
Cellulitis	1 (0.7%)	0	0	0	0
Chronic sinusitis	1 (0.7%)	1 (0.7%)	0	0	1 (0.2%)
Erysipelas	0	0	0	1 (0.7%)	1 (0.2%)
Genitourinary tract infection	0	0	0	1 (0.7%)	1 (0.2%)
Influenza	0	1 (0.7%)	0	0	1 (0.2%)
Pneumonia	1 (0.7%)	3 (2.1%)	0	2 (1.4%)	5 (1.1%)
Pyelonephritis chronic	0	1 (0.7%)	0	0	1 (0.2%)
Sinusitis	1 (0.7%)	0	0	0	0
Staphylococcal infection	0	0	1 (0.7%)	0	1 (0.2%)

Figure 19 cont'd

Tooth abscess	1 (0.7%)	0	0	0	0
Urinary tract infection	0	1 (0.7%)	0	0	1 (0.2%)
Viral infection	0	0	1 (0.7%)	0	1 (0.2%)
Injury, poisoning and procedural complications	0	2 (1.4%)	2 (1.4%)	2 (1.4%)	6 (1.4%)
Cartilage injury	0	0	1 (0.7%)	0	1 (0.2%)
Concussion	0	0	0	1 (0.7%)	1 (0.2%)
Foreign body aspiration	0	0	1 (0.7%)	0	1 (0.2%)
Ligament sprain	0	0	1 (0.7%)	0	1 (0.2%)
Lower limb fracture	0	1 (0.7%)	0	0	1 (0.2%)
Lumbar vertebral fracture	0	0	0	1 (0.7%)	1 (0.2%)
Post procedural complication	0	1 (0.7%)	0	0	1 (0.2%)
Upper limb fracture	0	1 (0.7%)	0	0	1 (0.2%)
Musculoskeletal and connective tissue disorders	1 (0.7%)	0	3 (2.1%)	1 (0.7%)	4 (0.9%)
Intervertebral disc protrusion	0	0	1 (0.7%)	0	1 (0.2%)
Osteoarthritis	1 (0.7%)	0	1 (0.7%)	0	1 (0.2%)
Osteochondrosis	0	0	0	1 (0.7%)	1 (0.2%)
Rhabdomyolysis	0	0	1 (0.7%)	0	1 (0.2%)

Figure 19 cont'd

Neoplasms benign, malignant and unspecified (including cysts and polyps)	1 (0.7%)	0	3 (2.1%)	2 (1.4%)	5 (1.1%)
Adenocarcinoma of colon	0	0	0	1 (0.7%)	1 (0.2%)
Basal cell carcinoma	0	0	1 (0.7%)	0	1 (0.2%)
Lipoma	0	0	0	1 (0.7%)	1 (0.2%)
Pancreatic carcinoma metastatic	0	0	1 (0.7%)	0	1 (0.2%)
Prostate cancer	1 (0.7%)	0	1 (0.7%)	0	1 (0.2%)
Nervous system disorders	0	2 (1.4%)	2 (1.4%)	0	4 (0.9%)
Cerebrovascular accident ("stroke")	0	1 (0.7%)	0	0	1 (0.2%)
Cervicobrachial syndrome	0	0	1 (0.7%)	0	1 (0.2%)
Guillain-Barré syndrome	0	0	1 (0.7%)	0	1 (0.2%)
Sciatica	0	1 (0.7%)	0	0	1 (0.2%)
Pregnancy, puerperium and perinatal conditions	0	0	1 (0.7%)	1 (0.7%)	2 (0.5%)
Abortion threatened	0	0	1 (0.7%)	1 (0.7%)	2 (0.5%)
Hyperemesis gravidarum	0	0	1 (0.7%)	0	1 (0.2%)
Renal and urinary disorders	0	1 (0.7%)	0	0	1 (0.2%)
Calculus urinary	0	1 (0.7%)	0	0	1 (0.2%)

Figure 19 cont'd

Reproductive system and breast disorders	0	1 (0.7%)	0	2 (1.4%)	3 (0.7%)
Cervical leukoplakia	0	0	0	1 (0.7%)	1 (0.2%)
Ovarian cyst	0	0	0	1 (0.7%)	1 (0.2%)
Testicular pain	0	1 (0.7%)	0	0	1 (0.2%)
Respiratory, thoracic and mediastinal disorders	10 (6.8%)	6 (4.1%)	4 (2.8%)	6 (4.1%)	16 (3.7%)
Asthma	10 (6.8%)	5 (3.4%)	4 (2.8%)	6 (4.1%)	15 (3.4%)
Pulmonary embolism	0	1 (0.7%)	0	0	1 (0.2%)
Skin and subcutaneous tissue disorders	1 (0.7%)	1 (0.7%)	0	0	1 (0.2%)
Dermatitis atopic	1 (0.7%)	0	0	0	0
Dermatitis contact	0	1 (0.7%)	0	0	1 (0.2%)
Vascular disorders	0	1 (0.7%)	1 (0.7%)	1 (0.7%)	3 (0.7%)
Deep vein thrombosis	0	1 (0.7%)	1 (0.7%)	0	2 (0.5%)
Hypertensive crisis	0	0	0	1 (0.7%)	1 (0.2%)