SUPPLEMENTARY MATERIAL

Effectiveness and Safety of Tezepelumab in a Diverse Population of US Patients with Severe Asthma: Initial Results of the PASSAGE Study

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Inclusion Criteria

Participants are eligible to be included in the study only if all of the following criteria apply:

1. Male or female participant must be 12 years of age or older, at the time of signing the informed consent form or assent.
2. Documented physician-diagnosed asthma for at least 12 months prior to visit 1 and confirmed by the Investigator not to be due to alternative diagnoses.
3. Documented treatment with medium- to high-dose inhaled corticosteroids (ICS) as per GINA guidelines [1] for at least 12 months prior to visit 1.
4. Use of additional asthma maintenance controller medication(s) in addition to ICS (e.g., long-acting bronchodilator inhaler [LABA], leukotriene receptor inhibitors, theophylline, long-acting muscarinic agent and cromones) for at least 12 months prior to visit 1. The additional maintenance controller medication may be contained in a combination product (e.g., ICS/LABA).
5. Documented history of at least two asthma exacerbations during the 12 months prior to visit 1. Asthma exacerbations are defined as follows.
    - A temporary bolus/burst of systemic corticosteroids (or a temporary increase in stable oral corticosteroid background dose) for at least 3 consecutive days to treat symptoms of asthma worsening; a single depo-injectable dose of corticosteroids will be considered equivalent to a 3-day bolus/burst of systemic corticosteroids.
    - An emergency department (ED) or urgent care (UC) visit (defined as evaluation and treatment for < 24 hours in an ED/UC center) due to asthma that required systemic corticosteroids (as per the above).
    - An inpatient hospitalization (defined as admission to an inpatient facility and/or evaluation and treatment in a healthcare facility for ≥ 24 hours) due to asthma.
6. Physician decision that participant is eligible for treatment with tezepelumab according to the approved US prescribing information [2].

7. Currently receiving care from specialist physicians (e.g., pulmonologists and/or allergists) at the Investigator's or sub-Investigator's site.
8. Provision of signed and dated written informed consent prior to any mandatory study-specific procedures, sampling and analyses for participants who are at, or over, the age of majority (as per local law). For participants who are less than the age of majority, in addition to their providing informed assent, the participants' legally authorized representative must also provide their informed consent.

Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply.

1. Any contraindication to tezepelumab as per the US prescribing information [2] or in the opinion of the Investigator.
2. Comorbid diagnosis of severe or very severe COPD per GOLD guidelines [3].
3. Use of biologics that are approved for the treatment of asthma within 4 months or 5 half-lives (whichever is longer) prior to visit 1.
4. Participation in an interventional clinical trial for asthma within 12 months prior to visit 1.
5. Judgment by the Investigator that the participant is unlikely to comply with study procedures, restrictions and requirements.

Supplementary Figures

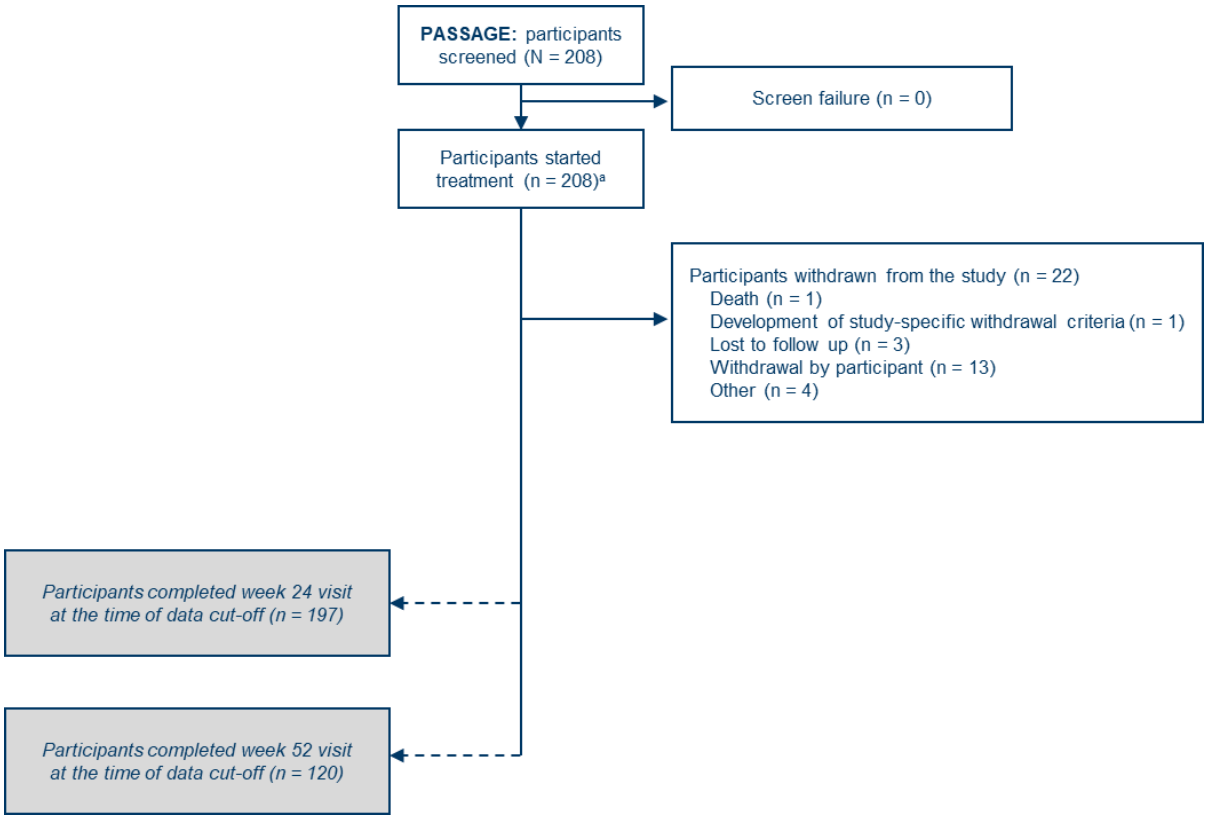

Fig. S1 Participant disposition

[a]This protocol pre-specified interim analysis included all participants who received at least one dose of tezepelumab and reached week 24 or who had withdrawn at any time from the study at the time of the data cut-off date (June 7, 2024).

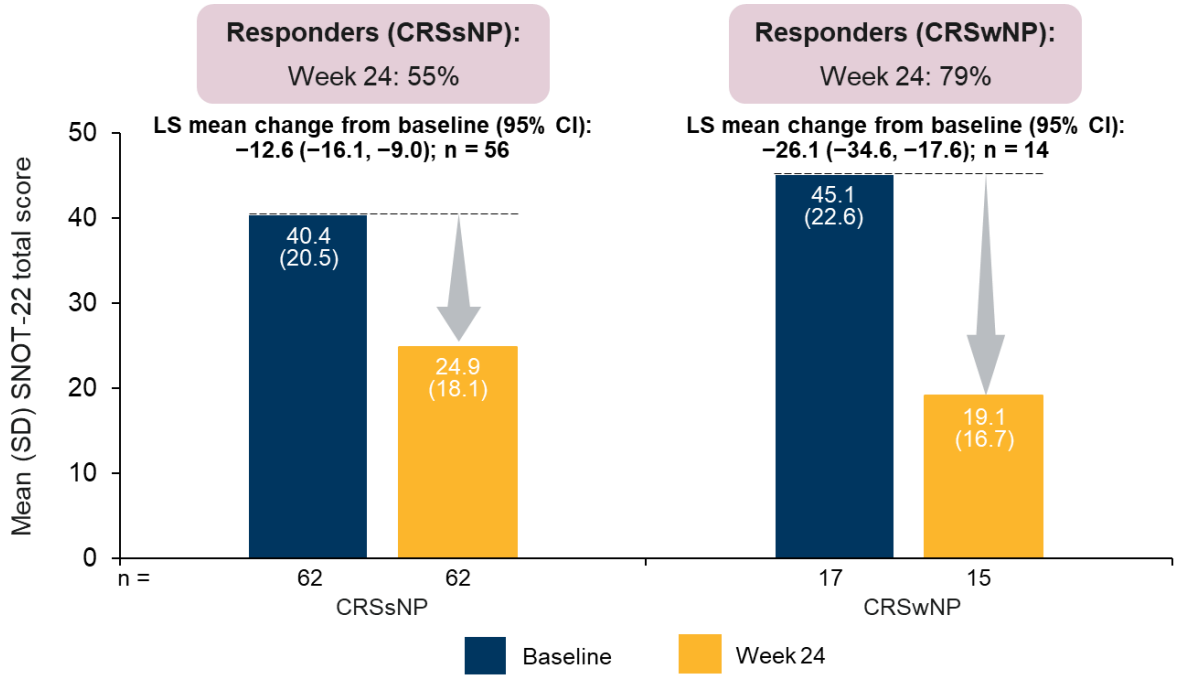

Fig. S2 Change from baseline to week 24 in SNOT-22 total score in participants without and with an ongoing diagnosis of nasal polyposis (CRSsNP and CRSwNP). Responder definition was based on the MCID threshold for SNOT-22 total score, which was an absolute change from baseline of ≥ 8.9. Responder rates are based on the n used for LS mean comparisons, which excludes participants with missing data. Baseline is the last nonmissing assessment on or before the first dose of tezepelumab at week 0. *CI* confidence interval, *CRSsNP* chronic rhinosinusitis without nasal polyps, *CRSwNP* chronic rhinosinusitis with nasal polyps, *LS* least-squares, *MCID* minimal clinically important difference, *SD* standard deviation, *SNOT* Sino-Nasal Outcome Test

Supplementary Tables

Table S1 Pre-BD FEV_1 at baseline and week 24 across phenotypes and underrepresented groups

Mean (SD), L	Overall		Baseline percent predicted pre-BD FEV_1 ≤ 80%	
	Baseline	**Week 24**	**Baseline**	**Week 24**
Asthma phenotype				
Nonallergic and BEC < 300 cells/μL	2.2 (0.7)	2.3 (0.7)	1.8 (0.5)	1.9 (0.7)
Allergic and BEC < 300 cells/μL	2.3 (0.8)	2.3 (0.7)	1.9 (0.6)	2.1 (0.6)
Nonallergic and BEC ≥ 300 cells/μL	2.0 (0.6)	2.1 (0.6)	1.8 (0.4)	2.0 (0.5)
Allergic BEC ≥ 300 cells/μL	2.2 (0.9)	2.5 (1.1)	1.9 (0.6)	2.2 (0.9)
Underrepresented groups				
Black/African American	1.8 (0.6)	1.9 (0.6)	1.7 (0.4)	1.9 (0.6)
Adolescents	3.1 (0.9)	3.3 (1.1)	2.3 (0.1)	2.7 (0.4)
Mild to moderate COPD	1.6 (0.5)	1.8 (0.6)	1.5 (0.5)	1.7 (0.6)
Smokers (≥ 10 pack-years)	1.9 (0.6)	2.0 (0.6)	1.6 (0.4)	1.8 (0.5)

Baseline is the last nonmissing assessment on or before the first dose of tezepelumab at week 0

BD bronchodilator, *BEC* blood eosinophil count, *COPD* chronic obstructive pulmonary disease, *FEV_1* forced expiratory volume in 1 second, *SD* standard deviation

Table S2 ACQ-6, AIRQ and SGRQ total scores at baseline and week 24 across asthma phenotypes

Asthma phenotype (n)	ACQ-6 score		AIRQ score		SGRQ total score	
	LS mean change from baseline to week 24 (95% CI)	Responders, %	LS mean change from baseline to week 24 (95% CI)	Responders, %	LS mean change from baseline to week 24 (95% CI)	Responders, %
Nonallergic and BEC < 300 cells/µL (49)	−1.0 (−1.3, −0.7)	63	−2.6 (−3.3, −1.9)	67	−22.8 (−28.1, −17.6)	88
Allergic and BEC < 300 cells/µL (58)	−1.1 (−1.3, −0.9)	79	−3.1 (−3.7, −2.5)	67	−24.1 (−28.8, −19.3)	86
Nonallergic and BEC ≥ 300 cells/µL (32)	−1.4 (−1.7, −1.1)	78	−3.5 (−4.2, −2.8)	69	−22.3 (−29.0, −15.6)	78
Allergic and BEC ≥ 300 cells/µL (45)	−1.1 (−1.4, −0.8)	67	−2.6 (−3.3, −1.9)	56	−21.0 (−26.5, −15.5)	80

Responder definitions were based on the MCID thresholds for the outcomes, which were an absolute change from baseline (decrease) of ≥ 0.5 for ACQ-6 score, ≥ 2 for AIRQ score and ≥ 4 for SGRQ total score. Responder rates are based on the n used for LS mean comparisons, which excludes participants with missing data. Baseline is the last nonmissing assessment on or before the first dose of tezepelumab at week 0.

ACQ-6 Asthma Control Questionnaire-6, *AIRQ* Asthma Impairment and Risk Questionnaire, *BEC* blood eosinophil count, *CI* confidence interval, *LS* least-squares, *MCID* minimal clinically important difference, *SGRQ* St George's Respiratory Questionnaire.

Table S3 Change from baseline to week 52 in BECs, total IgE and specific IgE levels to perennial aeroallergens

Biomarker	Mean (SD) change from baseline to week 52
BEC (cells/µL), n = 97	−142 (300)
Total IgE (IU/mL), n = 91	−81.65 (274.89)
Alternaria alternata antigen (U/mL), n = 16	−1.13 (4.79)
American cockroach antigen (U/mL), n = 2	−0.19 (0.43)
Aspergillus fumigatus IgE antibody (U/mL), n = 21	−2.97 (3.67)
Cat dander antigen IgE antibody (U/mL), n = 29	−7.44 (13.97)
Cladosporium herbarum IgE antibody (U/mL), n = 6	−1.23 (1.97)
Dermatophagoides farinae antigen IgE antibody (U/mL), n = 17	−2.15 (7.31)
D. pteronyssinus antigen IgE antibody (U/mL), n = 16	−0.85 (4.55)
Dog dander antigen IgE antibody (U/mL), n = 25	−5.87 (8.18)
German cockroach antigen IgE antibody (U/mL), n = 5	−1.38 (2.65)
IgE, *Aspergillus niger* allergen (U/mL), ND	ND
IgE, mouse urine protein allergen (U/mL), n = 5	−3.48 (5.88)
Penicillium notatum IgE antibody (U/mL), n = 6	−0.62 (1.04)

Perennial aeroallergens listed in the table represent the list of allergens used in the FEIA test (≥ 0.35 kUA/L) for serum-specific IgE to determine allergy status at baseline

Patients who reached visit 15 (week 52) or dropped out before visit 15, at the time of the data cut-off, June 7, 2024, are included in this analysis. Baseline is the last nonmissing assessment on or before the first dose of tezepelumab at week 0

BEC blood eosinophil count, *FEIA* fluorescence enzyme immunoassay, *IgE* immunoglobulin E, *ND* not detected, *SD* standard deviation

List of ethics committees and/or IRBs

IRB number	IRB name	City	State/country	IRB type
IRB00000971	Advarra (Central IRB)[a]	Columbia (USA); Aurora (Canada)	MD, USA; ON, Canada	OHRP/FDA
IRB00000428	New York Medical College IRB #1	Valhalla	NY, USA	OHRP/FDA
IRB00002528	New York Medical College IRB #2	Valhalla	NY, USA	OHRP/FDA
IRB00000244	University of Michigan IRBMED A-1 #1	Ann Arbor	MI, USA	OHRP/FDA
IRB00000245	University of Michigan IRB #2 – Health Sciences and Behavioral Sciences Maize	Ann Arbor	MI, USA	OHRP only
IRB00000246	University of Michigan IRB #3 – Health Sciences and Behavioral Sciences Blue	Ann Arbor	MI, USA	OHRP only

IRB00001995	University of Michigan IRBMED B-2 #6	Ann Arbor	MI, USA	OHRP/FDA
IRB00001996	University of Michigan IRBMED A-2 #7	Ann Arbor	MI, USA	OHRP/FDA
IRB00001999	University of Michigan IRBMED B-1 #8	Ann Arbor	MI, USA	OHRP/FDA
IRB00005467	University of Michigan IRB #1 – IRBMED C-1 #9	Ann Arbor	MI, USA	OHRP/FDA
IRB00012211	University of Michigan IRB #11 – IRBMED C-2 #11	Ann Arbor	MI, USA	OHRP/FDA
IRB00002040	Eisenhower Medical Center IRB #1	Rancho Mirage	CA, USA	OHRP/FDA

[a]The Advarra central IRB covers all study sites (see list below), except Children's and Women's Physicians of Westchester, LLP (covered by New York Medical College, Valhalla, NY), University of Michigan, Michigan Medicine (covered by University of Michigan, Ann Arbor, MI), Pulmonary Clinic and Eisenhower Health Center (covered by Rancho Mirage, CA).

Sites covered by the Advarra Central IRB included:

Clinical Research Associates of Central PA, LLC;

JPS Health Network;

Respiratory Medicine Research Institute of MI, PLC;

Allergy & Asthma Family Care of Queens, P.C.;

Temple University Health System – Temple Lung Center;

UNC at Chapel Hill – Adult Asthma Program;

Advanced Asthma Allergy & S.C.;

Allergy, Asthma & Immunology Assoc., Pc;

Methodist Physicians Clinic Westroads Office Park – Pulmonology;

Toledo Institute of Clinical Research Inc.;

American Institute of Research;

Allergy & Asthma Center of Minnesota – Allergology;

Yale University School of Medicine;

Washington University;

STAAMP Research;

The Vancouver Clinic;

University of Virginia;

Asthma and Allergy Assoc PC and Research Center;

Allianz Research Institute;

Allergy, Asthma and Clinical Research Center;

Allergy & Asthma Associates, PSC;

Metroplex Pulmonary and Sleep Center; ADAC Research, PA;

Northwestern Medical Group – Allergy & Immunology;

Tulane School of Medicine;

URMC Strong Memorial Hospital;

ARK Clinical Research, LLC;

Tennessee Comprehensive Lung & Sleep Center;

Accellacare.

FDA US Food and Drug Administration, *IRB* institutional review board, *OHRP* Office for Human Research Protections

Supplementary References

1. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. Available at: https://ginasthma.org/. Accessed December 12, 2024.
2. TEZSPIRE™ (tezepelumab) prescribing information 2021. AstraZeneca. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761224s001lbl.pdf. Accessed December 12, 2024.
3. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2024 report. Available at: https://goldcopd.org/2024-gold-report/. Accessed December 12, 2024.