



Clinical trial results:

A Multicentre, Randomised, Double-Blind, Parallel-Group, Placebo-Controlled Phase 3 Efficacy and Safety Study of Tezepelumab in Participants with Severe Chronic Rhinosinusitis with Nasal Polyposis (WAYPOINT)

Summary

EudraCT number	2020-003062-39
Trial protocol	DE DK HU PL
Global end of trial date	11 December 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	D5242C00001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04851964
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	151 85, Sodertalje, Sweden,
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 May 2025
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	11 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy and safety of repeat dosing of tezepelumab 210 mg SC versus placebo in adult participants with severe CRSwNP.

Protection of trial subjects:

The investigator or his/her representative explained the nature of the study to the participant or his/her legally authorised representative and answered all questions regarding the study.

Participants were informed that their participation was voluntary and they were free to refuse to participate and may withdraw their consent at any time and for any reason during the study.

Participants or their legally authorised representative were required to sign a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act (HIPAA) requirements, where applicable, and the IRB/IEC or study centre.

The medical record included a statement that written informed consent was obtained before the participant was enrolled in the study and the date the written consent was obtained. The authorised person obtaining the informed consent also signed the ICF. Participants must be re-consented to the most current version of the ICF(s) during their participation in the study. A copy of the ICF(s) must be provided to the participant or the participant's legally authorised representative.

Participants who were rescreened were required to sign a new ICF.

The ICF contained a separate section that addresses and documents the collection and use of any mandatory and/or optional human biological samples. The investigator or authorized designee explained to each participant the objectives of the analysis to be done on the samples and any potential future use. Participants were told that they were free to refuse to participate in any optional samples or the future use and may withdraw their consent at any time and for any reason during the retention period.

Background therapy:

All participants used INCS for a minimum of 4 weeks prior to Randomization (Visit 3) and continued throughout the study period.

Two doses of MFNS (50µg/actuation) in each nostril twice daily (total 400µg daily) or equivalent INCS were administered unless there was a medical rationale to use the lower dose (QD) regimen. Equivalent dose referred to the highest approved country INCS dose for CRSwNP. The generic name of the INCS and the total daily dose were recorded in the eCRF.

Evidence for comparator: -

Actual start date of recruitment	22 April 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 63
Country: Number of subjects enrolled	Japan: 33

Country: Number of subjects enrolled	Canada: 49
Country: Number of subjects enrolled	Denmark: 40
Country: Number of subjects enrolled	Germany: 41
Country: Number of subjects enrolled	United Kingdom: 23
Country: Number of subjects enrolled	Hungary: 31
Country: Number of subjects enrolled	Poland: 58
Country: Number of subjects enrolled	Spain: 33
Country: Number of subjects enrolled	United States: 37
Worldwide total number of subjects	408
EEA total number of subjects	203

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	353
From 65 to 84 years	55
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 872 participants were screened between 22Apr2021 and 23Aug2023.

Pre-assignment

Screening details:

410 were randomised to either the treatment (204 participants) or placebo (206 participants) arms of the double-blind treatment period. Two participants were randomized but not dosed. Therefore, 203 participants started in the treatment arm and 205 in the placebo arm, for a total of 408 participants.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Data analyst, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Tezepelumab

Arm description:

210 mg tezepelumab injection delivered subcutaneously every 4 weeks

Arm type	Experimental
Investigational medicinal product name	210 mg Tezepelumab administered every 4 weeks subcutaneously
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

210 mg Q4W

Arm title	Placebo
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Arm description:

Matching Placebo injection delivered subcutaneously every 4 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Q4W

Number of subjects in period 1	Tezepelumab	Placebo
Started	203	205
Completed	193	174
Not completed	10	31
Adverse event, serious fatal	-	1
Other biologic treatment	-	2
Consent withdrawn by subject	8	23
Nasal polyp surgery	-	2
Severe noncompliance	-	1
Lost to follow-up	2	2

Baseline characteristics

Reporting groups

Reporting group title	Tezepelumab
Reporting group description: 210 mg tezepelumab injection delivered subcutaneously every 4 weeks	
Reporting group title	Placebo
Reporting group description: Matching Placebo injection delivered subcutaneously every 4 weeks	

Reporting group values	Tezepelumab	Placebo	Total
Number of subjects	203	205	408
Age Categorical			
Age group at screening visit			
Units:			
<=18 years	0	0	0
Between 18 and 65 years	174	179	353
>=65 years	29	26	55
Age Continuous			
Age at screening visit			
Units: years			
arithmetic mean	50.1	49.4	
standard deviation	± 13.60	± 13.69	-
Sex: Female, Male			
Gender at screening visit			
Units:			
Female	77	65	142
Male	126	140	266
Race/Ethnicity, Customized			
Units: Subjects			
Black or African American	3	3	6
White	150	149	299
Native Hawaiian or other Pacific Islander	0	0	0
American Indian or Alaska Native	0	0	0
Asian	46	51	97
Other	4	2	6
Not reported	0	0	0
Race/Ethnicity, Customized			
Ethnicity group			
Units: Subjects			
Hispanic or Latino	11	11	22
Not Hispanic or Latino	192	194	386

End points

End points reporting groups

Reporting group title	Tezepelumab
Reporting group description: 210 mg tezepelumab injection delivered subcutaneously every 4 weeks	
Reporting group title	Placebo
Reporting group description: Matching Placebo injection delivered subcutaneously every 4 weeks	

Primary: Change from baseline in total nasal polyp score at Week 52

End point title	Change from baseline in total nasal polyp score at Week 52
End point description: The total nasal polyp score (NPS) is the sum of the right and left nostril scores (maximum of 8), as evaluated by nasal endoscopy. Higher scores indicate greater symptom severity. The left and right score will be based on a central read with a scale from 0 to 4. Each nasal endoscopy is evaluated by two independent physician reviewers.	
End point type	Primary
End point timeframe: Baseline to Week 52	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)	-2.458 (-2.681 to -2.234)	-0.380 (-0.611 to -0.148)		

Statistical analyses

Statistical analysis title	Repeated measures model
Statistical analysis description: Null Hypothesis: Difference in mean change from baseline in NPS at 52 weeks (tezepelumab minus placebo) = 0	
Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	408
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	< 0.0001 ^[2]
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-2.078

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.399
upper limit	-1.757

Notes:

[1] - For participants whose NPS data collected after NP surgery were replaced with the worst possible score (WPS). Data collected after SCS for NP were replaced with the worst post-baseline observation prior to the SCS for NP (WOCF). Missing data not due to intercurrent events were imputed using MI (MAR). Analysis was repeated on 100 imputed datasets, and results were combined using Rubin's formula.

[2] - The p-value is unadjusted and it is statistically significant at 0.01 level under multiple testing strategy.

Primary: Change from baseline in bi-weekly mean nasal congestion score (NCS) at Week 52

End point title	Change from baseline in bi-weekly mean nasal congestion score (NCS) at Week 52
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End point description:

The NCS is captured by one item in the NPSD (nasal polyps symptom diary) asking participants to rate the severity of their worst NC over the past 24 hours using the following response options: 0 – None; 1 – Mild; 2 – Moderate; 3 – Severe. Baseline will be the mean of daily responses from Day -13 to Day 0. Bi-weekly (14-day) mean NCS will be calculated if at least 8 days in each 14-day period has evaluable data; otherwise the bi-weekly mean is set to missing.

End point type	Primary
End point timeframe:	
Baseline to Week 52	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)	-1.743 (-1.864 to -1.622)	-0.703 (-0.830 to -0.577)		

Statistical analyses

Statistical analysis title	Repeated measures model
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Statistical analysis description:

Null Hypothesis: Difference in mean change from baseline in bi-weekly mean NCS at 52 weeks (tezepelumab minus placebo) = 0

Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	408
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	< 0.0001 ^[4]
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-1.039

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.214
upper limit	-0.865

Notes:

[3] - For participants whose NCS data collected after NP surgery were replaced with the worst possible score (WPS). Data collected after SCS for NP were replaced with the worst post-baseline observation prior to the SCS for NP (WOCF). Missing data not due to intercurrent events were imputed using MI (MAR). Analysis was repeated on 100 imputed datasets, and results were combined using Rubin's formula.

[4] - The p-value is unadjusted and it is statistically significant at 0.01 level under multiple testing strategy.

Secondary: Change from baseline in bi-weekly mean loss of smell at Week 52

End point title	Change from baseline in bi-weekly mean loss of smell at Week 52
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End point description:

Participant reported sense of smell will be evaluated as part of the NPSD. Loss of smell is captured by the DSS item (difficulty with sense of smell) in the NPSD asking participants to rate the severity of their worst difficulty with sense of smell over the past 24 hours using the following response options: 0 – None; 1 – Mild; 2 – Moderate; 3 – Severe. Baseline will be the mean of daily responses to the from Day -13 to Day 0. Bi-weekly (14-day) mean loss of smell will be calculated if at least 8 days in each 14-day period has evaluable data; otherwise the bi-weekly mean is set to missing.

End point type	Secondary
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End point timeframe:

Baseline to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)	-1.261 (-1.382 to -1.139)	-0.255 (-0.378 to -0.133)		

Statistical analyses

Statistical analysis title	Repeated measures model
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Statistical analysis description:

Null Hypothesis: Difference in mean change from baseline in bi-weekly mean loss of smell at 52 weeks (tezepelumab minus placebo) = 0

Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	408
Analysis specification	Pre-specified
Analysis type	superiority ^[5]
P-value	< 0.0001 ^[6]
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-1.005

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.177
upper limit	-0.834

Notes:

[5] - For participants whose loss of smell data collected after NP surgery were replaced with the worst possible score (WPS). Data collected after SCS for NP were replaced with the worst post-baseline observation prior to the SCS for NP (WOCP). Missing data not due to intercurrent events were imputed using MI (MAR). Analysis was repeated on 100 imputed datasets, and results were combined using Rubin's formula.

[6] - The p-value is unadjusted, and is statistically significant at 0.01 level under multiple testing strategy.

Secondary: Change from baseline in SinoNasal Outcome Test 22 (SNOT-22) at Week 52

End point title	Change from baseline in SinoNasal Outcome Test 22 (SNOT-22) at Week 52
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End point description:

SinoNasal Outcome Test 22 scores are participant-reported and assess physical problems, functional limitations and emotional consequences of SinoNasal conditions. Patient-reported symptom severity and symptom impact over the past 2 weeks are captured via a 6-point scale (0-No Problem to 5-Problem as bad as it can be). The total score is the sum of item scores and has a range from 0 to 110 (higher scores indicate poorer outcomes).

End point type	Secondary
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End point timeframe:

Baseline to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)	-45.022 (-48.572 to -41.472)	-17.580 (-21.189 to -13.971)		

Statistical analyses

Statistical analysis title	Repeated measures model
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Statistical analysis description:

Null Hypothesis: Difference in mean change from baseline in SNOT-22 at 52 weeks (tezepelumab minus placebo) = 0

Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	408
Analysis specification	Pre-specified
Analysis type	superiority ^[7]
P-value	< 0.0001 ^[8]
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-27.441

Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.512
upper limit	-22.37

Notes:

[7] - For participants whose SNOT-22 total score collected after NP surgery were replaced with the worst possible score (WPS). Data collected after SCS for NP were replaced with the worst post-baseline observation prior to the SCS for NP (WOOF). Missing data not due to intercurrent events were imputed using MI (MAR). Analysis was repeated on 100 imputed datasets, and results were combined using Rubin's formula.

[8] - The p-value is unadjusted and it is statistically significant at 0.01 level under multiple testing strategy.

Secondary: Change from baseline in Lund Mackay score evaluated by CT at Week 52.

End point title	Change from baseline in Lund Mackay score evaluated by CT at Week 52.
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End point description:

The Lund-Mackay score scoring system is used to provide a quantitative assessment of nasal sinuses on sinus CT scans. Based on the sinus CT images, the five sinuses (maxillary, anterior ethmoid, posterior ethmoid, sphenoid and frontal) on each site are score by central radiologist as follows: (0-Normal; 1-Partial Opacification; 2-Total Opacification). The osteomeatal complex is scored for right and left sides (0 - Not occluded; 2- Occluded). The total score ranges from 0 to 24 (higher scores indicate poorer outcomes).

End point type	Secondary
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End point timeframe:

Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)	-6.270 (-6.740 to -5.799)	-0.569 (-1.046 to -0.093)		

Statistical analyses

Statistical analysis title	Repeated measures model
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Statistical analysis description:

Null Hypothesis: Difference in mean change from baseline in LMK at 52 weeks (tezepelumab minus placebo) = 0

Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	408
Analysis specification	Pre-specified
Analysis type	superiority ^[9]
P-value	< 0.0001 ^[10]
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-5.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.371
upper limit	-5.03

Notes:

[9] - For participants whose LMK score collected after NP surgery were replaced with the worst possible score (WPS). Data collected after SCS for NP were replaced with the worst post-baseline observation prior to the SCS for NP (WOOF). Missing data not due to intercurrent events were imputed using MI (MAR). Analysis was repeated on 100 imputed datasets, and results were combined using Rubin's formula.

[10] - The p-value is unadjusted and it is statistically significant at 0.01 level under multiple testing strategy.

Secondary: Time to first nasal polyp surgery decision and/or systemic corticosteroids for nasal polyposis up to Week 52

End point title	Time to first nasal polyp surgery decision and/or systemic corticosteroids for nasal polyposis up to Week 52
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End point description:

Surgery is defined as any procedure involving instruments resulting in incision and removal of tissue (e.g., polypectomy, endoscopic sinus surgery). Rescue treatment of NP is defined as requiring treatment with systemic corticosteroids (SCS) for at least 3 consecutive days (a single depo-injectable dose of corticosteroids will be considered equivalent to a 3-day course of systemic corticosteroids).

Time to first NP surgery decision or SCS for NP = (date of the first NP surgery decision or start date of first SCS for NP use – date of randomisation)+1

End point type	Secondary
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End point timeframe:

Up to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Percentage				
number (confidence interval 95%)	5.7 (1.3 to 15.0)	31.4 (25.0 to 38.0)		

Statistical analyses

Statistical analysis title	Proportional hazards regression model
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Statistical analysis description:

Null Hypothesis: Hazard ratio of time to first SCS for NP and/or surgery decision (tezepelumab/placebo) = 1

Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	408
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[11]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.08

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.16

Notes:

[11] - The p-value is unadjusted and it is statistically significant at 0.01 level under multiple testing strategy.

Secondary: Time to first nasal polyp surgery decision up to Week 52

End point title	Time to first nasal polyp surgery decision up to Week 52
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End point description:

Surgery is defined as any procedure involving instruments resulting in incision and removal of tissue (e.g., polypectomy, endoscopic sinus surgery).

Time to first NP surgery decision = (date of the first NP surgery decision - date of randomisation)+1

End point type	Secondary
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End point timeframe:

Up to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Percentage				
number (confidence interval 95%)	0.5 (0.0 to 2.5)	22.0 (16.4 to 28.2)		

Statistical analyses

Statistical analysis title	Proportional hazards regression model
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Statistical analysis description:

Null Hypothesis: Hazard ratio of time to first surgery decision (tezepelumab/placebo) = 1

Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	408
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[12]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.09

Notes:

[12] - The p-value is unadjusted and it is statistically significant at 0.01 level under multiple testing strategy.

Secondary: Time to first systemic corticosteroids for nasal polyposis up to Week 52

End point title	Time to first systemic corticosteroids for nasal polyposis up to Week 52
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End point description:

Rescue treatment of NP is defined as requiring treatment with systemic corticosteroids (SCS) for at least 3 consecutive days (a single depo-injectable dose of corticosteroids will be considered equivalent to a 3-day course of systemic corticosteroids).

Time to first SCS for NP = (start date of first SCS for NP use – date of randomisation)+1

End point type	Secondary
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End point timeframe:

Up to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Percentage				
number (confidence interval 95%)	5.2 (1.1 to 14.7)	19.3 (14.1 to 25.1)		

Statistical analyses

Statistical analysis title	Proportional hazards regression model
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Statistical analysis description:

Null Hypothesis: Hazard ratio of time to first SCS use for NP (tezepelumab/placebo) = 1

Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	408
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[13]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.25

Notes:

[13] - The p-value is unadjusted and it is statistically significant at 0.01 level under multiple testing strategy.

Secondary: Change from baseline in bi-weekly mean Nasal Polyposis Symptom Diary Total Symptom Score at Week 52

End point title	Change from baseline in bi-weekly mean Nasal Polyposis Symptom Diary Total Symptom Score at Week 52
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End point description:

The participant will complete an 11-item nasal polyposis symptom diary each morning throughout the screening, treatment and followup periods. The participant is asked to consider their experience with nasal polyposis/nasal polyps over the past 24hrs when responding to each question. Participants are

asked to report their experience with nasal polyposis symptoms (nasal blockage, nasal congestion, runny nose, postnasal drip (mucus drainage down the throat), headache, facial pain, facial pressure, difficulty with sense of smell) and symptom impacts (difficulty with sleeping due to nasal symptoms and difficulty with daily activities due to nasal symptoms). Participants report the severity of each symptom and symptom impact at its worst using a 4-point verbal rating scale (0-None to 3-Severe). A total symptom score is calculated by taking the sum of the 8 equally weighted symptom items.

End point type	Secondary
End point timeframe:	
Baseline to Week 52	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)	-10.388 (-11.174 to -9.601)	-3.429 (-4.241 to -2.617)		

Statistical analyses

Statistical analysis title	Repeated measures model
Statistical analysis description:	
Null Hypothesis: Difference in mean change from baseline in bi-weekly mean NPSD TSS at 52 weeks (tezepelumab minus placebo) = 0	
Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	408
Analysis specification	Pre-specified
Analysis type	superiority ^[14]
P-value	< 0.0001 ^[15]
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-6.959
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.085
upper limit	-5.833

Notes:

[14] - For participants whose bi-weekly mean NPSD TSS collected after NP surgery were replaced with the worst possible score (WPS). Data collected after SCS for NP were replaced with the worst post-baseline observation prior to the SCS for NP (WOCF). Missing data not due to intercurrent events were imputed using MI (MAR). Analysis was repeated on 100 imputed datasets, and results were combined using Rubin's formula.

[15] - The p-value is unadjusted and it is statistically significant at 0.01 level under multiple testing strategy.

Secondary: Change from baseline in pre-bronchodilator forced expiratory volume (L) in 1 second at Week 52.

End point title	Change from baseline in pre-bronchodilator forced expiratory volume (L) in 1 second at Week 52.
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End point description:

For participants with comorbid asthma and aspirin exacerbated respiratory disease (AERD)/nonsteroidal anti-inflammatory drug exacerbated respiratory disease (NSAID-ERD), difference in change from baseline in pre-bronchodilator forced expiratory volume in 1 second (FEV1) in the tezepelumab arm as compared to placebo at Week 52. FEV1 is defined as the volume of air exhaled from the lungs in the first second of forced expiration.

End point type	Secondary
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End point timeframe:

Baseline to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	126		
Units: Liter				
arithmetic mean (confidence interval 95%)	0.022 (-0.065 to 0.108)	0.027 (-0.055 to 0.108)		

Statistical analyses

Statistical analysis title	Repeated measures model
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Statistical analysis description:

Null Hypothesis: Difference in mean change from baseline in pre-BD FEV1 at 52 weeks (tezepelumab minus placebo) = 0

Comparison groups	Tezepelumab v Placebo
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Number of subjects included in analysis	248
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Analysis specification	Pre-specified
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Analysis type	superiority ^[16]
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P-value	= 0.9362 ^[17]
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Method	ANCOVA
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Parameter estimate	Difference in Least Squares Means
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Point estimate	-0.005
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	-0.121
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upper limit	0.111
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Notes:

[16] - Observed pre-BD FEV1 data were used in the analysis regardless of NP surgery and SCS/biologic for NP. Missing data were imputed assuming MAR. Analysis was repeated on 100 imputed datasets, and results were combined using Rubin's formula.

[17] - The p-value is unadjusted.

Other pre-specified: Change from baseline over time in Nasal Polyp Score through Week 52.

End point title	Change from baseline over time in Nasal Polyp Score through Week 52.
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End point description:

The total nasal polyp score (NPS) is the sum of the right and left nostril scores (maximum of 8), as evaluated by nasal endoscopy. Higher scores indicate greater symptom severity. The left and right score will be based on a central read with a scale from 0 to 4. Each nasal endoscopy is evaluated by two

independent physician reviewers.

End point type	Other pre-specified
End point timeframe:	
Baseline to Week 52	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)				
Week 4	-1.615 (-1.797 to -1.433)	-0.255 (-0.434 to -0.077)		
Week 12	-1.918 (-2.112 to -1.723)	-0.376 (-0.569 to -0.182)		
Week 24	-2.104 (-2.310 to -1.899)	-0.314 (-0.522 to -0.106)		
Week 36	-2.351 (-2.552 to -2.149)	-0.287 (-0.493 to -0.082)		
Week 52	-2.458 (-2.681 to -2.234)	-0.380 (-0.611 to -0.148)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Proportion of participants with ≥ 1 point reduction in the Nasal Polyp Score at Week 52

End point title	Proportion of participants with ≥ 1 point reduction in the Nasal Polyp Score at Week 52
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End point description:

The Nasal Polyp Score is the sum of the right and left nostril scores (maximum 8), as evaluated by nasal endoscopy. A participant with ≥ 1 point reduction in NPS at Week 52 in the absence of SCS for NP, biologic for NP, or NP surgery at or prior to that time point was defined as a responder, otherwise the participant was defined as a non-responder.

End point type	Other pre-specified
End point timeframe:	
Baseline to Week 52	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Participants	161	64		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Proportion of participants with ≥ 2 point reduction in the Nasal Polyp Score at Week 52

End point title	Proportion of participants with ≥ 2 point reduction in the Nasal Polyp Score at Week 52
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End point description:

The Nasal Polyp Score is the sum of the right and left nostril scores (maximum 8), as evaluated by nasal endoscopy. A participant with ≥ 2 point reduction in NPS at Week 52 in the absence of SCS for NP, biologic for NP, or NP surgery at or prior to that time point was defined as a responder, otherwise the participant was defined as a non-responder.

End point type	Other pre-specified
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End point timeframe:

Baseline to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Participants	129	39		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline over time in bi-weekly mean Nasal Congestion Score evaluated by Nasal Polyposis Symptom Diary through Week 52.

End point title	Change from baseline over time in bi-weekly mean Nasal Congestion Score evaluated by Nasal Polyposis Symptom Diary through Week 52.
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End point description:

The NCS is captured by one item in the NPSD (nasal polyps symptom diary) asking participants to rate the severity of their worst NC over the past 24 hours using the following response options: 0 – None; 1 – Mild; 2 – Moderate; 3 – Severe. Baseline will be the mean of daily responses from Day -13 to Day 0. Bi-weekly (14-day) mean NCS will be calculated if at least 8 days in each 14-day period has evaluable data; otherwise the bi-weekly mean is set to missing.

End point type	Other pre-specified
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End point timeframe:

Baseline to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)				
Week 2	-0.379 (-0.438 to -0.319)	-0.192 (-0.251 to -0.133)		
Week 4	-0.779 (-0.868 to -0.691)	-0.322 (-0.411 to -0.234)		
Week 8	-1.134 (-1.236 to -1.032)	-0.451 (-0.553 to -0.349)		
Week 12	-1.270 (-1.376 to -1.164)	-0.607 (-0.714 to -0.500)		
Week 24	-1.515 (-1.628 to -1.402)	-0.703 (-0.818 to -0.588)		
Week 36	-1.629 (-1.748 to -1.509)	-0.726 (-0.850 to -0.601)		
Week 48	-1.735 (-1.856 to -1.613)	-0.721 (-0.847 to -0.594)		
Week 52	-1.743 (-1.864 to -1.622)	-0.703 (-0.830 to -0.577)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in loss of smell evaluated by University of Pennsylvania Smell Identification Test (UPSIT) at Week 52.

End point title	Change from baseline in loss of smell evaluated by University of Pennsylvania Smell Identification Test (UPSIT) at Week 52.
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End point description:

The University of Pennsylvania Smell Identification Test is a quantitative test of olfactory function which uses microencapsulated odorants that are released by scratching standardized odour-impregnated test booklets. Scores are based on number of correctly identified odours (score range 0-40, lower scores indicate poorer outcomes).

End point type	Other pre-specified
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End point timeframe:

Baseline to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)	9.310 (8.147 to 10.474)	-0.192 (-1.378 to 0.993)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in Modified Lund Mackay score evaluated by CT at Week 52.

End point title	Change from baseline in Modified Lund Mackay score evaluated by CT at Week 52.
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End point description:

The Modified Lund-Mackay score scoring system is used to provide a semi-quantitative assessment of nasal sinuses on sinus CT scans. Based on the sinus CT images, the five sinuses (maxillary, anterior ethmoid, posterior ethmoid, sphenoid and frontal) on each site are scored by central radiologist as follows: (0-0% Opacification; 1-1-25% Opacification; 2-26-50% Opacification; 3-51-75% Opacification; 4-76-99% Opacification; 5-100% Opacification). The osteomeatal complex is scored for right and left sides (0 - Not occluded; 2- Occluded). The maximum total Modified Lund Mackay score is 50, 54 when including the Osteomeatal complex score.

End point type	Other pre-specified
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End point timeframe:

Baseline to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)	-17.520 (-18.708 to -16.332)	-1.106 (-2.291 to 0.078)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in sinus severity score by quantitative CT assessment at Week 52

End point title	Change from baseline in sinus severity score by quantitative CT assessment at Week 52
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End point description:

Quantitative assessment of sinus CT image data were used to derive an objective measure of sinus disease burden called sinus severity score. The sinus severity score is defined as: (sinus mucosal volume)/(sinus mucosal volume + sinus air volume)×100%.

End point type	Other pre-specified
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End point timeframe:

Baseline to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)	-32.754 (-35.047 to -30.461)	-1.978 (-4.267 to 0.310)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Exposure of systemic corticosteroids over 52 Weeks

End point title	Exposure of systemic corticosteroids over 52 Weeks
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End point description:

The number of courses of SCS for NP per year was analysed using a negative binomial model. The response variable was the number of courses of SCS for NP received by a participant over the planned treatment period. The model included treatment group, baseline co-morbid asthma/AERD/NSAID-ERD status, prior NP surgery status, and region as factors. The logarithm of the time at risk (in years) was used as an offset variable, to adjust different follow-up times. Time during a course was not included in the calculation of time at risk.

End point type	Other pre-specified
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End point timeframe:

Over 52 weeks

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Number of Courses	9	59		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline by domain of the Nasal Polyposis Symptom Diary through Week 52

End point title	Change from baseline by domain of the Nasal Polyposis Symptom Diary through Week 52
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End point description:

The participant will complete an 11-item nasal polyposis symptom diary each morning throughout the screening, treatment and follow-up periods. The participant is asked to consider their experience with nasal polyposis/nasal polyps over the past 24 hours when responding to each question. Participants are asked to report their experience with nasal polyposis symptoms (nasal blockage, nasal congestion, runny nose, postnasal drip (mucus drainage down the throat), headache, facial pain, facial pressure, and difficulty with sense of smell) and symptom impacts (difficulty with sleeping due to nasal symptoms and difficulty with daily activities due to nasal symptoms). Participants report the severity of each symptom and symptom impact at its worst using a 4-point verbal rating scale (0-None to 3-Severe).

End point type	Other pre-specified
End point timeframe:	
Baseline to Week 52	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)				
Nasal Blockage Week 2	-0.359 (-0.416 to -0.301)	-0.170 (-0.227 to -0.112)		
Nasal Blockage Week 4	-0.744 (-0.831 to -0.656)	-0.298 (-0.385 to -0.211)		
Nasal Blockage Week 8	-1.122 (-1.225 to -1.018)	-0.423 (-0.527 to -0.320)		
Nasal Blockage Week 12	-1.259 (-1.367 to -1.152)	-0.555 (-0.663 to -0.447)		
Nasal Blockage Week 24	-1.502 (-1.617 to -1.387)	-0.678 (-0.795 to -0.561)		
Nasal Blockage Week 36	-1.628 (-1.750 to -1.506)	-0.703 (-0.830 to -0.576)		
Nasal Blockage Week 48	-1.697 (-1.821 to -1.573)	-0.722 (-0.850 to -0.594)		
Nasal Blockage Week 52	-1.759 (-1.882 to -1.636)	-0.697 (-0.825 to -0.569)		
Nasal Congestion Week 2	-0.379 (-0.438 to -0.319)	-0.192 (-0.251 to -0.133)		
Nasal Congestion Week 4	-0.779 (-0.868 to -0.691)	-0.322 (-0.411 to -0.234)		
Nasal Congestion Week 8	-1.134 (-1.236 to -1.032)	-0.451 (-0.553 to -0.349)		
Nasal Congestion Week 12	-1.270 (-1.376 to -1.164)	-0.607 (-0.714 to -0.500)		
Nasal Congestion Week 24	-1.515 (-1.628 to -1.402)	-0.703 (-0.818 to -0.588)		
Nasal Congestion Week 36	-1.629 (-1.748 to -1.509)	-0.726 (-0.850 to -0.601)		
Nasal Congestion Week 48	-1.735 (-1.856 to -1.613)	-0.721 (-0.847 to -0.594)		
Nasal Congestion Week 52	-1.743 (-1.864 to -1.622)	-0.703 (-0.830 to -0.577)		
Runny Nose Week 2	-0.347 (-0.407 to -0.288)	-0.164 (-0.224 to -0.105)		
Runny Nose Week 4	-0.676 (-0.757 to -0.595)	-0.239 (-0.320 to -0.158)		
Runny Nose Week 8	-0.966 (-1.056 to -0.875)	-0.360 (-0.450 to -0.270)		
Runny Nose Week 12	-1.075 (-1.173 to -0.976)	-0.467 (-0.566 to -0.369)		
Runny Nose Week 24	-1.258 (-1.363 to -1.153)	-0.464 (-0.571 to -0.358)		
Runny Nose Week 36	-1.353 (-1.466 to -1.240)	-0.467 (-0.583 to -0.351)		
Runny Nose Week 48	-1.448 (-1.561 to -1.336)	-0.410 (-0.528 to -0.292)		

Runny Nose Week 52	-1.429 (-1.545 to -1.313)	-0.400 (-0.523 to -0.277)		
Postnasal Drip Week 2	-0.252 (-0.310 to -0.195)	-0.153 (-0.210 to -0.096)		
Postnasal Drip Week 4	-0.552 (-0.633 to -0.472)	-0.230 (-0.310 to -0.150)		
Postnasal Drip Week 8	-0.806 (-0.898 to -0.715)	-0.336 (-0.428 to -0.244)		
Postnasal Drip Week 12	-0.916 (-1.015 to -0.816)	-0.388 (-0.488 to -0.288)		
Postnasal Drip Week 24	-1.084 (-1.194 to -0.974)	-0.418 (-0.529 to -0.306)		
Postnasal Drip Week 36	-1.175 (-1.290 to -1.061)	-0.441 (-0.559 to -0.322)		
Postnasal Drip Week 48	-1.189 (-1.307 to -1.071)	-0.376 (-0.498 to -0.253)		
Postnasal Drip Week 52	-1.177 (-1.294 to -1.060)	-0.348 (-0.471 to -0.225)		
Headache Week 2	-0.259 (-0.318 to -0.199)	-0.185 (-0.245 to -0.126)		
Headache Week 4	-0.414 (-0.489 to -0.340)	-0.294 (-0.369 to -0.220)		
Headache Week 8	-0.673 (-0.753 to -0.594)	-0.382 (-0.461 to -0.303)		
Headache Week 12	-0.753 (-0.842 to -0.665)	-0.439 (-0.528 to -0.350)		
Headache Week 24	-0.870 (-0.970 to -0.771)	-0.470 (-0.571 to -0.369)		
Headache Week 36	-0.928 (-1.034 to -0.821)	-0.387 (-0.496 to -0.278)		
Headache Week 48	-0.962 (-1.075 to -0.849)	-0.361 (-0.476 to -0.245)		
Headache Week 52	-0.941 (-1.056 to -0.825)	-0.341 (-0.459 to -0.222)		
Facial Pain Week 2	-0.250 (-0.310 to -0.190)	-0.171 (-0.231 to -0.111)		
Facial Pain Week 4	-0.438 (-0.514 to -0.363)	-0.276 (-0.352 to -0.201)		
Facial Pain Week 8	-0.723 (-0.806 to -0.640)	-0.368 (-0.450 to -0.285)		
Facial Pain Week 12	-0.801 (-0.888 to -0.713)	-0.438 (-0.526 to -0.350)		
Facial Pain Week 24	-0.957 (-1.056 to -0.858)	-0.494 (-0.594 to -0.393)		
Facial Pain Week 36	-1.000 (-1.106 to -0.893)	-0.396 (-0.506 to -0.286)		
Facial Pain Week 48	-1.010 (-1.125 to -0.895)	-0.358 (-0.476 to -0.239)		
Facial Pain Week 52	-1.002 (-1.118 to -0.886)	-0.316 (-0.436 to -0.197)		
Facial Pressure Week 2	-0.276 (-0.338 to -0.215)	-0.170 (-0.232 to -0.109)		
Facial Pressure Week 4	-0.509 (-0.587 to -0.431)	-0.277 (-0.355 to -0.199)		
Facial Pressure Week 8	-0.778 (-0.866 to -0.689)	-0.373 (-0.461 to -0.284)		
Facial Pressure Week 12	-0.840 (-0.929 to -0.750)	-0.460 (-0.549 to -0.370)		
Facial Pressure Week 24	-0.987 (-1.087 to -0.887)	-0.501 (-0.603 to -0.400)		
Facial Pressure Week 36	-1.039 (-1.148 to -0.930)	-0.400 (-0.512 to -0.288)		

Facial Pressure Week 48	-1.093 (-1.210 to -0.975)	-0.379 (-0.499 to -0.258)		
Facial Pressure Week 52	-1.081 (-1.200 to -0.962)	-0.342 (-0.464 to -0.220)		
Difficulty with Sense of Smell Week 2	-0.126 (-0.164 to -0.088)	-0.037 (-0.074 to 0.001)		
Difficulty with Sense of Smell Week 4	-0.416 (-0.483 to -0.348)	-0.053 (-0.120 to 0.014)		
Difficulty with Sense of Smell Week 8	-0.804 (-0.897 to -0.711)	-0.107 (-0.200 to -0.015)		
Difficulty with Sense of Smell Week 12	-0.909 (-1.015 to -0.804)	-0.208 (-0.313 to -0.103)		
Difficulty with Sense of Smell Week 24	-1.078 (-1.195 to -0.961)	-0.275 (-0.392 to -0.158)		
Difficulty with Sense of Smell Week 36	-1.101 (-1.221 to -0.980)	-0.300 (-0.422 to -0.177)		
Difficulty with Sense of Smell Week 48	-1.242 (-1.364 to -1.121)	-0.289 (-0.413 to -0.166)		
Difficulty with Sense of Smell Week 52	-1.261 (-1.382 to -1.139)	-0.255 (-0.378 to -0.133)		
Difficulty with Sleeping Week 2	-0.340 (-0.399 to -0.281)	-0.188 (-0.247 to -0.129)		
Difficulty with Sleeping Week 4	-0.655 (-0.738 to -0.572)	-0.284 (-0.367 to -0.202)		
Difficulty with Sleeping Week 8	-0.994 (-1.084 to -0.904)	-0.454 (-0.544 to -0.364)		
Difficulty with Sleeping Week 12	-1.081 (-1.177 to -0.984)	-0.495 (-0.591 to -0.398)		
Difficulty with Sleeping Week 24	-1.262 (-1.365 to -1.159)	-0.516 (-0.621 to -0.411)		
Difficulty with Sleeping Week 36	-1.307 (-1.420 to -1.194)	-0.520 (-0.637 to -0.403)		
Difficulty with Sleeping Week 48	-1.307 (-1.427 to -1.188)	-0.469 (-0.595 to -0.342)		
Difficulty with Sleeping Week 52	-1.317 (-1.436 to -1.197)	-0.454 (-0.580 to -0.327)		
Difficulty with Daily Activities week 2	-0.282 (-0.340 to -0.225)	-0.183 (-0.240 to -0.126)		
Difficulty with Daily Activities week 4	-0.504 (-0.582 to -0.425)	-0.294 (-0.372 to -0.216)		
Difficulty with Daily Activities week 8	-0.836 (-0.926 to -0.747)	-0.408 (-0.497 to -0.319)		
Difficulty with Daily Activities week 12	-0.948 (-1.043 to -0.853)	-0.469 (-0.564 to -0.374)		
Difficulty with Daily Activities week 24	-1.135 (-1.242 to -1.028)	-0.520 (-0.628 to -0.412)		
Difficulty with Daily Activities week 36	-1.201 (-1.316 to -1.085)	-0.509 (-0.629 to -0.389)		
Difficulty with Daily Activities week 48	-1.213 (-1.334 to -1.091)	-0.440 (-0.568 to -0.313)		
Difficulty with Daily Activities week 52	-1.212 (-1.334 to -1.090)	-0.414 (-0.542 to -0.285)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in Nasal Peak Inspiratory Flow through

Week 52.

End point title	Change from baseline in Nasal Peak Inspiratory Flow through Week 52.
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End point description:

Nasal peak inspiratory flow evaluation represents a physiologic measure of the air flow through both nasal cavities during forced inspiration expressed in liters per minute.

End point type	Other pre-specified
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End point timeframe:

Baseline to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	205		
Units: Score				
least squares mean (confidence interval 95%)				
Week 12	21.860 (10.888 to 32.831)	-1.695 (-12.313 to 8.923)		
Week 24	29.437 (17.500 to 41.373)	6.258 (-5.563 to 18.080)		
Week 36	11.228 (0.875 to 21.581)	-4.941 (-15.570 to 5.687)		
Week 52	22.551 (11.467 to 33.635)	0.489 (-10.973 to 11.952)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in Asthma Control Questionnaire-6 at Week 52.

End point title	Change from baseline in Asthma Control Questionnaire-6 at Week 52.
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End point description:

The Asthma Control Questionnaire is an assessment of asthma symptoms (nighttime waking, symptoms on waking, activity limitation, shortness of breath, wheezing, and short acting beta-agonist use). Participants are asked to recall their level of asthma control during the previous week by responding to one bronchodilator use question and 5 symptom questions. Questions are weighted equally and scored from 0 (totally controlled) to 6 (severely uncontrolled).

End point type	Other pre-specified
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End point timeframe:

Baseline to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	126		
Units: Score				
least squares mean (confidence interval 95%)	-1.203 (-1.334 to -1.072)	-0.815 (-0.967 to -0.663)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Tezepelumab Pharmacokinetics

End point title	Tezepelumab Pharmacokinetics
End point description:	Serum concentrations of tezepelumab through Week 64. Geometric mean calculated using log transformed data.
End point type	Other pre-specified
End point timeframe:	Pre-dose samples at Baseline, Week 4, Week 12, Week 24, Week 36, Week 52, and Week 64

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	0 ^[18]		
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Week 4	12.165 (± 35.9)	()		
Week 12	21.496 (± 40.8)	()		
Week 24	23.994 (± 43.0)	()		
Week 36	25.237 (± 45.4)	()		
Week 52	24.352 (± 43.7)	()		
Week 64	2.449 (± 103.1)	()		

Notes:

[18] - Serum concentrations of Tezepelumab is not available for placebo.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Immunogenicity of tezepelumab for Non-China subjects

End point title	Immunogenicity of tezepelumab for Non-China subjects
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End point description:

Anti-drug antibodies (ADA) responses at baseline and post-baseline. ADA prevalence was defined as patients who are ADA positive at any time including baseline. Persistently positive was defined as having at least two post-baseline ADA positive measurements (with ≥ 16 weeks between first and last positive) or an ADA positive result at the last available post-baseline assessment. Transiently positive was defined as having at least one post-baseline ADA positive measurement and not fulfilling the conditions for persistently positive. Treatment boosted ADA was defined as baseline positive ADA titre that was boosted to a 4-fold or higher-level following treatment. Treatment emergent ADA (ADA incidence) was defined as the sum of treatment induced ADA and treatment boosted ADA.

End point type	Other pre-specified
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End point timeframe:

Pre-dose samples at Baseline, Week 4, Week 12, Week 24, Week 36, Week 52, and Week 64

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	171		
Units: Participants				
ADA prevalence	10	19		
ADA positive at baseline only	2	1		
Treatment-induced ADA positive	6	12		
Treatment-boosted ADA positive	0	0		
Treatment emergent ADA (ADA incidence)	6	12		
Baseline and one post-baseline ADA positive	2	4		
ADA persistently positive	4	11		
ADA transiently positive	4	7		
TE-ADA+ with max. titre > median of max. titres	1	2		
ADA positive at baseline	4	2		
Any post-baseline ADA positive	8	18		
nAb positive at baseline and/or post-baseline	2	2		
Treatment-induced nAb positive (nAb incidence)	1	2		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Immunogenicity of tezepelumab for China subjects

End point title	Immunogenicity of tezepelumab for China subjects
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End point description:

Anti-drug antibodies (ADA) responses at baseline and post-baseline. ADA prevalence was defined as patients who are ADA positive at any time including baseline. Persistently positive was defined as having at least two post-baseline ADA positive measurements (with ≥ 16 weeks between first and last positive) or an ADA positive result at the last available post-baseline assessment. Transiently positive was defined as having at least one post-baseline ADA positive measurement and not fulfilling the conditions for persistently positive. Treatment boosted ADA was defined as baseline positive ADA titre that was boosted to a 4-fold or higher-level following treatment. Treatment emergent ADA (ADA incidence) was defined as the sum of treatment induced ADA and treatment boosted ADA.

End point type	Other pre-specified
End point timeframe:	
Pre-dose samples at Baseline, Week 4, Week 12, Week 24, Week 36, Week 52, and Week 64	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	34		
Units: Participants				
ADA prevalence	3	4		
ADA positive at baseline only	1	0		
Treatment-induced ADA positive	2	3		
Treatment-boosted ADA positive	0	0		
Treatment emergent ADA (ADA incidence)	2	3		
Baseline and one post-baseline ADA positive	0	1		
ADA persistently positive	1	2		
ADA transiently positive	1	2		
TE-ADA+ with max. titre > median of max. titres	1	0		
ADA positive at baseline	1	1		
Any post-baseline ADA positive	2	4		
nAb positive at baseline and/or post-baseline	1	0		
Treatment-induced nAb positive (nAb incidence)	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until end of study up to week 76.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Matching Placebo injection delivered subcutaneously every 4 weeks

Reporting group title	Tezepelumab
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Reporting group description:

210 mg tezepelumab injection delivered subcutaneously every 4 weeks

Serious adverse events	Placebo	Tezepelumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 205 (6.83%)	11 / 203 (5.42%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 205 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 205 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			

subjects affected / exposed	0 / 205 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 205 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 205 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopericarditis			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Basal ganglia stroke			
subjects affected / exposed	0 / 205 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Anaphylactic reaction			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Epiretinal membrane			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 205 (0.98%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Graves' disease			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 205 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			

subjects affected / exposed	0 / 205 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 205 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 205 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 205 (0.49%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 205 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			

subjects affected / exposed	0 / 205 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	Tezepelumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	119 / 205 (58.05%)	119 / 203 (58.62%)	
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 205 (7.80%)	19 / 203 (9.36%)	
occurrences (all)	22	30	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	12 / 205 (5.85%)	1 / 203 (0.49%)	
occurrences (all)	15	1	
Chronic rhinosinusitis with nasal polyps			
subjects affected / exposed	56 / 205 (27.32%)	16 / 203 (7.88%)	
occurrences (all)	104	26	
Epistaxis			
subjects affected / exposed	7 / 205 (3.41%)	14 / 203 (6.90%)	
occurrences (all)	8	15	
Infections and infestations			
COVID-19			
subjects affected / exposed	44 / 205 (21.46%)	55 / 203 (27.09%)	
occurrences (all)	47	58	
Nasopharyngitis			
subjects affected / exposed	23 / 205 (11.22%)	45 / 203 (22.17%)	
occurrences (all)	42	63	
Pharyngitis			
subjects affected / exposed	1 / 205 (0.49%)	11 / 203 (5.42%)	
occurrences (all)	1	13	
Upper respiratory tract infection			

subjects affected / exposed	13 / 205 (6.34%)	23 / 203 (11.33%)	
occurrences (all)	16	26	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 January 2022	1. Added "bi-weekly mean" for NCS, loss of smell, and NPSD TSS to ensure correct evaluation of these endpoints from baseline over time. 2. Overall benefits-risk conclusion was updated to align with IB Edition 5.0 (dated 21 October 2021). 3. Exclusion Criterion for patients with a history of cancer was updated in order to align with program-level safety documentation regarding patients with a history of cancer. 4. Inclusion Criterion 15 "NCS ≥ 2 at Visit 3" removed. Inclusion 15a added to replace previous Inclusion Criterion 15. Inclusion 15a added: "At randomisation visit (Visit 3), a bi-weekly mean NCS ≥ 2 (baseline bi-weekly mean score collected from study Day -13 to study Day 0)."
17 October 2022	Update of key secondary objectives and corresponding endpoints: (1) 'Time to surgery and/or SCS for NP up to Week 52' updated to 'Time to surgery decision and/or SCS for NP up to Week 52'. (2) 'Time to NP surgery up to Week 52' updated to 'Time to NP surgery decision up to Week 52'. Adverse events of special interest updated to include 'serious cardiac events' and 'including opportunistic infections' added to AESI of serious infections. New category added to risk assessment table: "Important potential risks" including serious infections, malignancies and serious cardiac events. Previous category of "Potential risks of clinical significance" changed to "Potential risks" and text of risk of serious infections, serious hypersensitivity reactions, and COVID-19 updated.
17 January 2024	Two key secondary objectives 'resolution/near complete resolution of nasal polyps', and 'resolution/near complete resolution of nasal polyps and NPSD TSS responses' were moved to exploratory objectives. Estimand for US FDA and multiplicity testing procedure for secondary endpoints were modified to align with FDA guidance.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported