Clinical trial results:
A Multicentre, Single-arm, Phase 3b Efficacy and Safety Study of Tezepelumab 210 mg Administered Subcutaneously to Reduce Oral Corticosteroid Use in Adult Participants with Severe Asthma on High-dose Inhaled Corticosteroid plus Long-acting 2 Agonist and Long-term Oral Corticosteroid Therapy (WAYFINDER)

Summary

EudraCT number	2021-005457-85
Trial protocol	DE FR ES BE PL LV
Global end of trial date	09 September 2024

Results information

Result version number	v2 (current)
This version publication date	25 January 2026
First version publication date	23 October 2025
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	D5180C00037

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05274815
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	151 85, Södertälje, Sweden,
Public contact	Global Clinical Lead, AstraZeneca, +1 8772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 8772409479, 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	17 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 September 2024
Global end of trial reached?	Yes
Global end of trial date	09 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the ability of tezepelumab 210 mg subcutaneous (SC) to reduce the prescribed oral corticosteroids (OCS) dose (≤ 5 mg/day) without loss of asthma control in adult participants with OCS-dependent asthma

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with ICH/GCP, applicable regulatory requirements, and the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 May 2022
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 80
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Bulgaria: 36
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Latvia: 16
Country: Number of subjects enrolled	Mexico: 41
Country: Number of subjects enrolled	Poland: 40
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	United States: 12
Country: Number of subjects enrolled	United Kingdom: 12
Worldwide total number of subjects	298
EEA total number of subjects	153

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)	231
From 65 to 84 years	67
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 305 participants were enrolled from 68 study sites across 11 countries, including sites in Argentina, Belgium, Bulgaria, France, Germany, Latvia, Mexico, Poland, Spain, UK, and USA.

Pre-assignment

Screening details:

Of the 305 participants that initiated treatment with tezepelumab, 7 were excluded from the efficacy and safety summary due to potential data fraud. Therefore, only 298 participants were included in the summaries.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Tezepelumab

Arm description:

Tezepelumab 210 mg was administered subcutaneously (SC) every 4 weeks (Q4W) for a total of 13 doses

Induction phase (Week 0 to 4): At the screening visit, participants continued or were switched to prednisone or prednisolone. Participants started to receive tezepelumab treatment at Visit 2/Week 0 (baseline) and had to remain stable on their baseline oral corticosteroid (OCS) dose during this phase.

OCS reduction and maintenance phase (Week 4 to Week 52): Initial OCS tapering was guided by an algorithm based on baseline OCS dose until the lowest stable OCS dose (OCS discontinued or no further OCS reduction possible) was reached or until Week 48; dosages were reduced in 2.5- to 5-mg increments weekly, every 2 weeks, or Q4W.

Arm type	Experimental
Investigational medicinal product name	Tezepelumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

210 mg from a 110 mg/mL solution for injection in an accessorised pre-filled syringe (APFS) administered subcutaneously every 4 weeks (Q4W)

Number of subjects in period 1	Tezepelumab
Started	298
Completed	273
Not completed	25
Adverse event, serious fatal	2
Consent withdrawn by subject	11
Adverse event, non-fatal	1

Withdrawn - severe protocol non-compliance	1
Withdrawn - stopped visit; phone contact at Wk 52	1
Withdrawn - participant's decision to withdraw	1
Withdrawn - personal and family reasons	1
Lost to follow-up	4
Withdrawn - investigator's decision	1
Withdrawn - participant decision	1
Withdrawn - randomized to closed cohort in error	1

Baseline characteristics

Reporting groups	
Reporting group title	Tezepelumab

Reporting group description:

Tezepelumab 210 mg was administered subcutaneously (SC) every 4 weeks (Q4W) for a total of 13 doses

Induction phase (Week 0 to 4): At the screening visit, participants continued or were switched to prednisone or prednisolone. Participants started to receive tezepelumab treatment at Visit 2/Week 0 (baseline) and had to remain stable on their baseline oral corticosteroid (OCS) dose during this phase.

OCS reduction and maintenance phase (Week 4 to Week 52): Initial OCS tapering was guided by an algorithm based on baseline OCS dose until the lowest stable OCS dose (OCS discontinued or no further OCS reduction possible) was reached or until Week 48; dosages were reduced in 2.5- to 5-mg increments weekly, every 2 weeks, or Q4W.

Reporting group values	Tezepelumab	Total	
Number of subjects	298	298	
Age Categorical			
Age at Screening			
Units: Participants			
>=18 to <65 years	231	231	
>=65 years	67	67	
Age continuous			
Full Analysis Set			
Units: years			
arithmetic mean	54.4		
standard deviation	± 12.0	-	
Sex: Female, Male			
Full Analysis Set			
Units: Participants			
Female	206	206	
Male	92	92	
Ethnicity (NIH/OMB)			
Full Analysis Set			
Units: Subjects			
Hispanic or Latino	123	123	
Not Hispanic or Latino	157	157	
Missing	18	18	
Region of Enrollment			
Full Analysis Set			
Units: Subjects			
Argentina	80	80	
Belgium	13	13	
Bulgaria	36	36	
France	18	18	
Germany	22	22	
Latvia	16	16	
Mexico	41	41	
Poland	40	40	

Spain	8	8	
United States	12	12	
United Kingdom	12	12	
Race (NIH/OMB)			
Full Analysis Set			
Units: Subjects			
Black or African American	2	2	
American Indian or Alaska Native	5	5	
White	258	258	
Other	15	15	
Not reported	18	18	

End points

End points reporting groups

Reporting group title	Tezepelumab

Reporting group description:

Tezepelumab 210 mg was administered subcutaneously (SC) every 4 weeks (Q4W) for a total of 13 doses

Induction phase (Week 0 to 4): At the screening visit, participants continued or were switched to prednisone or prednisolone. Participants started to receive tezepelumab treatment at Visit 2/Week 0 (baseline) and had to remain stable on their baseline oral corticosteroid (OCS) dose during this phase.

OCS reduction and maintenance phase (Week 4 to Week 52): Initial OCS tapering was guided by an algorithm based on baseline OCS dose until the lowest stable OCS dose (OCS discontinued or no further OCS reduction possible) was reached or until Week 48; dosages were reduced in 2.5- to 5-mg increments weekly, every 2 weeks, or Q4W.

Primary: Proportion of the participants who discontinued OCS without loss of asthma control at Week 28 and Week 52

End point title	Proportion of the participants who discontinued OCS without loss of asthma control at Week 28 and Week 52[1]

End point description:

The proportion (expressed as a percentage) of participants who discontinued OCS without loss of asthma control is presented.

Loss of asthma control was defined as asthma worsening or exacerbation. Asthma worsening was defined by an increase of Asthma Control Questionnaire 6 (ACQ-6) score ≥0.5 from baseline. Asthma exacerbation was defined by worsening of asthma symptoms that led to temporary bolus/burst of systemic corticosteroids (SCS; or a temporary increase in stable OCS background dose) for at least 3 consecutive days (a single depo-injectable dose of corticosteroids being considered equivalent to a 3-day bolus/burst of SCS), and/or an emergency room (ER) or urgent care visit requiring SCS, and/or inpatient hospitalisation, both due to asthma.

End point type	Primary

End point timeframe:

Week 28 and Week 52

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were specified for the primary endpoint as the objective is descriptive.

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	32.2 (26.9 to 37.8)			
Week 52	50.3 (44.5 to 56.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of the participants who reduced daily prescribed maintenance OCS dose to ≤5 mg/day without loss of asthma control at Week 28 and Week 52

End point title	Proportion of the participants who reduced daily prescribed maintenance OCS dose to ≤5 mg/day without loss of asthma control at Week 28 and Week 52[2]

End point description:

The proportion (expressed as a percentage) of the participants who reduced daily prescribed maintenance OCS dose to ≤5 mg/day without loss of asthma control at Week 28 and Week 52 is presented.

End point type	Primary

End point timeframe:

Week 28 and Week 52

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were specified for the primary endpoint as the objective is descriptive.

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	88.9 (84.8 to 92.3)			
Week 52	89.9 (85.9 to 93.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Annual asthma exacerbation rate (AAER) over Week 28 and over Week 52

End point title	Annual asthma exacerbation rate (AAER) over Week 28 and over Week 52

End point description:

The AAER over Week 28 and over Week 52 is presented. The AAER was calculated as the total number of asthma exacerbations over the period (Week 28/52) divided by the total time at risk for the period (Week 28 or Week 52).

End point type	Secondary

End point timeframe:

Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: exacerbations/year				
number (not applicable)				
Week 28	0.66			
Week 52	0.57			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of asthma exacerbation associated with hospitalisation or ER visit over 28 weeks and over 52 weeks

End point title	Rate of asthma exacerbation associated with hospitalisation or ER visit over 28 weeks and over 52 weeks

End point description:

The AAER for exacerbations associated with hospitalisation or ER visit over 28 weeks and over 52 weeks is presented. The AAER was calculated as the total number of asthma exacerbations over the period (Week 28/52) divided by the total time at risk for the period (Week 28 or Week 52).

End point type	Secondary

End point timeframe:

Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: exacerbations/year				
number (not applicable)				
Week 28	0.13			
Week 52	0.11			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of asthma exacerbation associated with hospitalisation over 28 weeks and over 52 weeks

End point title	Rate of asthma exacerbation associated with hospitalisation over 28 weeks and over 52 weeks

End point description:

The AAER for exacerbations associated with hospitalisation over 28 weeks and over 52 weeks are presented. The AAER was calculated as the total number of asthma exacerbations over the period (Week 28/52) divided by the total time at risk for the period (Week 28 or Week 52).

End point type	Secondary

End point timeframe:

Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: exacerbations/year				
number (not applicable)				
Week 28	0.06			
Week 52	0.05			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of the participants who did not experience an exacerbation associated with hospitalisation or ER visit over 28 weeks and over 52 weeks

End point title	Proportion of the participants who did not experience an exacerbation associated with hospitalisation or ER visit over 28 weeks and over 52 weeks

End point description:

The proportion (expressed as a percentage) of participants who completed 28 or 52 weeks of treatment and did not experience an exacerbation associated with hospitalisation or ER visit over 28 weeks and over 52 weeks is presented.

End point type	Secondary

End point timeframe:

Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	95.5 (92.40 to 97.57)			
Week 52	92.7 (88.99 to 95.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of the participants who did not experience an exacerbation over 28 weeks and over 52 weeks

End point title	Proportion of the participants who did not experience an exacerbation over 28 weeks and over 52 weeks

End point description:

The proportion (expressed as a percentage) of participants who completed 28 or 52 weeks of treatment and did not experience an exacerbation over 28 weeks and over 52 weeks is presented.

End point type	Secondary

End point timeframe:

Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	76.0 (70.68 to 80.85)			
Week 52	66.9 (61.01 to 72.44)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of the participants with ≥50% reduction from baseline in daily maintenance OCS dose at Week 28 and Week 52

End point title	Proportion of the participants with ≥50% reduction from baseline in daily maintenance OCS dose at Week 28 and Week 52

End point description:

The proportion (expressed as a percentage) of participants with ≥50% reduction from baseline in daily maintenance OCS dose at Week 28 and Week 52 is presented.

The baseline OCS dose is the prescribed OCS dose prior to first dose of investigational product (IP). The final daily OCS dose was defined as the last dose reported by participants with asthma stability verified (no change in OCS dose for at least 2 consecutive weeks).

End point type	Secondary

End point timeframe:

Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	76.8 (71.6 to 81.5)			
Week 52	81.9 (77.0 to 86.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Categorised percent reduction from baseline in the daily maintenance OCS dose at Week 28 and Week 52

End point title	Categorised percent reduction from baseline in the daily maintenance OCS dose at Week 28 and Week 52

End point description:

The categorised percent reduction from baseline in the daily maintenance OCS dose (categories: ≥90% to ≤100% reduction, ≥75% to <90% reduction, ≥50% to <75% reduction, >0% to <50% reduction, no change or any increase) at Week 28 and Week 52 is presented.

The baseline OCS dose is the prescribed OCS dose prior to first dose of IP. The final daily OCS dose was defined as the last dose reported by participants with asthma stability verified (no change in OCS dose for at least 2 consecutive weeks).

End point type	Secondary

End point timeframe:

Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28: ≥90% to ≤100% reduction	35.2 (29.8 to 41.0)			
Week 28: ≥75% to <90% reduction	14.1 (10.4 to 18.6)			
Week 28: ≥50% to <75% reduction	27.5 (22.5 to 33.0)			
Week 28: >0% to <50% reduction	8.1 (5.2 to 11.7)			
Week 28: No change or any increase	15.1 (11.2 to 19.7)			
Week 52: ≥90% to ≤100% reduction	52.0 (46.2 to 57.8)			
Week 52: ≥75% to <90% reduction	9.1 (6.1 to 12.9)			
Week 52: ≥50% to <75% reduction	20.8 (16.3 to 25.9)			

Week 52: >0% to <50% reduction	4.0 (2.1 to 6.9)			
Week 52: No change or any increase	14.1 (10.4 to 18.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of the participants who did not experience an exacerbation associated with hospitalisation over 28 weeks and over 52 weeks

End point title	Proportion of the participants who did not experience an exacerbation associated with hospitalisation over 28 weeks and over 52 weeks

End point description:

The proportion (expressed as a percentage) of participants who completed 28 or 52 weeks of treatment and did not experience an exacerbation associated with hospitalisation over 28 weeks and over 52 weeks is presented.

End point type	Secondary

End point timeframe:

Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: Percentage				
number (confidence interval 95%)				
Week 28	97.9 (95.52 to 99.23)			
Week 52	96.0 (92.96 to 97.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in daily maintenance OCS dose at Week 28 and Week 52

End point title	Absolute change from baseline in daily maintenance OCS dose at Week 28 and Week 52

End point description:

The absolute change from baseline in daily maintenance OCS dose at Week 28 and Week 52 is presented.

The baseline OCS dose is the prescribed OCS dose prior to first dose of IP. The final daily OCS dose was defined as the last dose reported by participants with asthma stability verified (no change in OCS dose for at least 2 consecutive weeks).

End point type	Secondary

End point timeframe:
Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: mg				
arithmetic mean (standard deviation)				
Week 28	-6.951 (± 5.596)			
Week 52	-7.704 (± 6.294)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in daily maintenance OCS dose at Week 28 and Week 52

End point title	Percent change from baseline in daily maintenance OCS dose at Week 28 and Week 52

End point description:

The percent change from baseline in daily maintenance OCS dose at Week 28 and Week 52 is presented.

The baseline OCS dose is the prescribed OCS dose prior to first dose of IP. The final daily OCS dose was defined as the last dose reported by participants with asthma stability verified (no change in OCS dose for at least 2 consecutive weeks).

End point type	Secondary

End point timeframe:
Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: Percentage change				
arithmetic mean (standard deviation)				
Week 28	-61.919 (± 41.773)			
Week 52	-69.844 (± 43.666)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in ACQ-6 at Week 28 and Week 52

End point title	Change from baseline in ACQ-6 at Week 28 and Week 52

End point description:

The Asthma Control Questionnaire 6 (ACQ-6) is a 6-item questionnaire which includes the following questions: 1) Awakening at night by symptoms, 2) Limitations of normal daily activities, 3) Waking in the morning with symptoms, 4) Dyspnoea, 5) Wheeze, and 6) Daily rescue medication. Questions were scored from 0 (totally controlled) to 6 (severely uncontrolled) and the ACQ-6 score was computed as the unweighted mean of the responses to the 6 questions. Higher scores indicate poorer outcomes.

The change from baseline in ACQ-6 at Week 28 and Week 52 is presented.

End point type	Secondary

End point timeframe:

Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298[3]			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 28 (n=238)	-1.12 (± 1.00)			
Week 52 (n=222)	-1.20 (± 1.09)			

Notes:

[3] - The number of participants analyzed at Week 28 and Week 52 are specified in each row below.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in post-bronchodilator FEV1 at Week 28 and Week 52

End point title	Change from baseline in post-bronchodilator FEV1 at Week 28 and Week 52

End point description:

The change from baseline in post-bronchodilator FEV1 at Week 28 and Week 52 is presented. Baseline was defined as the last measurement at or prior first dose of IP.

FEV1 = forced expiratory volume in 1 second

End point type	Secondary

End point timeframe:

Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298[4]			
Units: liter (L)				
arithmetic mean (standard deviation)				
Week 28 (n=242)	0.0885 (± 0.3405)			
Week 52 (n=232)	0.0737 (± 0.3559)			

Notes:

[4] - The number of participants analyzed at Week 28 and Week 52 are specified in each row below.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in SGRQ total score at Week 28 and Week 52

End point title	Change from baseline in SGRQ total score at Week 28 and Week 52

End point description:

The St. George's Respiratory Questionnaire (SGRQ) is a 50-item instrument developed to measure the health status of participants with airway obstruction diseases. The total score indicates the impact of disease on overall health status. The total score ranges for the SGRQ are 0-100, with higher scores indicating worse health status.

The change from baseline in SGRQ total score at Week 28 and Week 52 is presented.

End point type	Secondary

End point timeframe:

Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298[5]			
Units: score				
arithmetic mean (standard deviation)				
Week 28 (n=216)	-16.2919 (± 18.1489)			
Week 52 (n=226)	-16.6593 (± 18.7749)			

Notes:

[5] - The number of participants analyzed at Week 28 and Week 52 are specified in each row below.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in standardised AQLQ(s)+12 total score at Week 28 and Week 52

End point title	Change from baseline in standardised AQLQ(s)+12 total score at Week 28 and Week 52

End point description:

The Asthma Quality of Life Questionnaire for 12 Years and Older (AQLQ[S]+12) is a questionnaire that measures the health-related quality of life experienced by asthma participants. Questions were scored from 7 (no impairment) to 1 (severe impairment). The overall score is calculated as the mean response to all questions. Higher scores indicate better outcomes.

The change from baseline in standardised AQLQ(S)+12 total score at Week 28 and Week 52 is presented.

End point type	Secondary

End point timeframe:

Week 28 and Week 52

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	298[6]			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 28 (n=220)	1.1455 (± 1.0419)			
Week 52 (n=230)	1.1932 (± 1.1551)			

Notes:

[6] - The number of participants analyzed at Week 28 and Week 52 are specified in each row below.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of first dose of IP until study completion or withdrawal date, up to 64 weeks.

Adverse event reporting additional description:

Only events that fall into the following categories were collected in this study: serious AEs, AEs leading to discontinuation of IP, and AEs of special interest. Participants with multiple occurrences in the same category were counted once per category regardless of the number of occurrences.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Tezepelumab

Reporting group description:

Tezepelumab 210 mg was administered SC Q4W for a total of 13 doses.

Induction phase (Week 0 to 4): Participants received tezepelumab treatment at Visit 2/Week 0 (baseline) and had to remain stable on their baseline OCS dose during this phase.

OCS reduction and maintenance phase (Week 4 to 52): Initial OCS tapering was guided by an algorithm based on baseline OCS dose until the lowest stable OCS dose (OCS discontinued or no further OCS reduction possible) was reached or until Week 48; dosages were reduced in 2.5- to 5-mg increments weekly, every 2 weeks, or Q4W OCS dose.

Serious adverse events	Tezepelumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 298 (9.40%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			

subjects affected / exposed	2 / 298 (0.67%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Aortic valve incompetence				
subjects affected / exposed	1 / 298 (0.34%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	2 / 298 (0.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Mitral valve incompetence				
subjects affected / exposed	1 / 298 (0.34%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	1 / 298 (0.34%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tachycardia foetal				
subjects affected / exposed	1 / 298 (0.34%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic reaction				
subjects affected / exposed	1 / 298 (0.34%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Pancreatitis acute				
subjects affected / exposed	1 / 298 (0.34%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Gastritis				

subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	13 / 298 (4.36%)		
occurrences causally related to treatment / all	0 / 15		
deaths causally related to treatment / all	0 / 1		
Endocrine disorders			
Adrenocortical insufficiency acute			
subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Costochondritis			

subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis bacterial			
subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	3 / 298 (1.01%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Covid-19			
subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 298 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Tezepelumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 298 (1.34%)		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 298 (0.34%)		
occurrences (all)	1		

Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	 1 / 298 (0.34%) 1		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 1 / 298 (0.34%) 1		
Endocrine disorders Adrenal insufficiency subjects affected / exposed occurrences (all)	 1 / 298 (0.34%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2021	Among the changes, completion of SNOT-22 was restricted to participants with a history of chronic sinusitis at baseline, as some SNOT-22 questions are relevant only to participants with chronic sinusitis. Another change was the modification of the list of adverse events of special interest (AESIs) to align the protocol with the investigator's brochure (IB) version 5.0. Another update involved replacing helminth parasitic infestation requiring hospitalisation with helminth parasitic infestation not responding to anti-helminth treatment in the list of specific criteria for discontinuation, to ensure consistency with the draft US label of tezepelumab. An additional update added AESI as a reason to record signs and symptoms of adrenal insufficiency (AI), clarifying that AI signs and symptoms had to be recorded if the participant experienced an adrenal crisis, now listed as AESI. Lastly, the description of final OCS derivation was updated to provide additional clarification of final OCS dose derivation.
10 November 2022	This amendment made several updates. An alternative method was included in case tetracosactides were not available for the adrenocorticotropic hormone (ACTH) stimulation test, as tetracosactides (required for performing ACTH stimulation test) were not registered in some countries involved in the study. Another change updated the composite strategy to hypothetical strategy for handling the intercurrent event of therapy initiation with another biologic for treatment of asthma in statistical analyses, to correct the name of the strategy. Additionally, the asthma exacerbation definition was edited to align with AstraZeneca standards related to asthma exacerbations. A further update added an interim analysis, intended for publication to inform clinical practice about interim results related to key efficacy and safety objectives. The change from baseline in Asthma Impairment and Risk Questionnaire (AIRQ) and the proportion of AIRQ responders at Week 28 were deleted from exploratory endpoints, as the study used the past 12-month recall for AIRQ, making change from baseline at Week 28 not relevant. Another was was asthma exacerbation and its treatment with additional corticosteroids were added in exclusion criterion #4 and circumstances for re-screening, as exacerbation of asthma is often linked to respiratory tract infections. One AESI (serious cardiac events) was added for consistency with the updated IB. The list of variables to be collected for serious adverse event (SAE), discontinuation of investigational product due to adverse events (DAE), and AESI was updated to collect the maximum intensity of the event. Clarification was also added to the definition of the currently or historically elevated eosinophil (EOS) population. Lastly, clarification was added that the start date of all treatment periods was the date of first investigational product (IP) dose.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported