Clinical trial results:
A Multicentre, Randomized, Double-Blind, Placebo Controlled, Phase 3 Study
to Evaluate the Efficacy and Safety of Tezepelumab in Reducing Oral Corticosteroid Use in Adults with Oral Corticosteroid Dependent Asthma (SOURCE)

Summary

EudraCT number	2017-003079-69
Trial protocol	DE PL
Global end of trial date	25 September 2020

Results information

Result version number	v1 (current)
This version publication date	08 October 2021
First version publication date	08 October 2021

Trial information

Trial identification

Sponsor protocol code	D5180C00009

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03406078
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	151 85, Sodertalje, Sweden,
Public contact	Global Clinical Head, AstraZeneca, information.center@astrazeneca.com
Scientific contact	Global Clinical Head, AstraZeneca Clinical Study Information, AstraZeneca, information.center@astrazeneca.com, +1 302 885 1180, 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	25 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of tezepelumab compared with placebo in reducing the prescribed OCS maintenance dose in patients with asthma requiring chronic treatment with maintenance OCS in addition to high dose ICS plus LABA.

Protection of trial subjects:

The protocol, protocol amendments, informed consent form (ICF), Investigator Brochure (IB), and other relevant documents (eg, advertisements) were submitted to an Institutional Review Board/Independent Ethics Committee (IRB/IEC) by the Investigator and reviewed and approved by the IRB/IEC before the study was initiated. The Investigator or his/her representative explained the nature of the study to the subject or his/her legally authorised representative and answered all questions regarding the study. Subjects were informed that their participation was voluntary. Subjects were required to sign a statement of informed consent that met 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 must have included a statement that written informed consent was obtained before the subject was enrolled in the study and the date the written consent was obtained. The authorised person obtaining the informed consent must have also signed the ICF. Subjects must have been re-consented to the most current version of the ICF(s) during their participation in the study. A copy of the ICF(s) was provided to the subject.

Background therapy:

Subjects must have received a physician-prescribed medium- or high-dose ICS as per GINA guideline (GINA 2017) for at least 12 months prior to visit 1. Documented treatment with prescribed LABA and high dose ICS (total daily dose >500µg fluticasone propionate dry powder formulation equivalent) for at least 3 months prior to visit 1. The ICS could be contained within an ICS/LABA combination product. Additional maintenance asthma controller medications were allowed according to standard practice of care. The use of additional asthma controller medications must have been documented for at least 3 months prior to visit 1. Subjects must have received OCS for the treatment of asthma for at least 6 months prior to visit 1 and on a stable dose of between ≥ 7.5 to ≤ 30mg (prednisone or prednisolone) daily or daily equivalent for at least 1 month prior to visit 1.

Evidence for comparator: -

Actual start date of recruitment	05 March 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 30
Country: Number of subjects enrolled	Turkey: 17
Country: Number of subjects enrolled	Ukraine: 15
Country: Number of subjects enrolled	Germany: 29
Country: Number of subjects enrolled	United States: 17

Country: Number of subjects enrolled	Argentina: 21
Country: Number of subjects enrolled	Korea, Republic of: 21
Worldwide total number of subjects	150
EEA total number of subjects	59

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)	120
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 60 centres in 7 countries. A total of 243 subjects were screened between 5MAR2018 and 27SEP2019, of which 150 were randomized and treated. 93 subjects were screen failures mainly due to exclusion criteria met and/or inclusion criteria not met. Assignment was done by Interactive Voice/Web Response System(IVRS/IWRS).

Pre-assignment

Screening details:

The screening period included a Run-in (2 weeks) and an OCS optimization phase (up to 8 weeks). At the end of period, subjects were randomized in 1:1 ratio for tezepelumab or placebo. Randomization was stratified by region (Central/Eastern Europe, Western Europe and North America, Rest of the World).

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	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Tezepelumab

Arm description:

Tezepelumab 210 mg administered every 4 weeks subcutaneously

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

Dosage and administration details:

210 mg Q4W

Arm title	Placebo

Arm description:

Placebo administered every 4 weeks subcutaneously

Arm type	Placebo
Investigational medicinal product name	Placebo 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:

Q4W

Number of subjects in period 1	Tezepelumab	Placebo
Started	74	76
Completed	68	73
Not completed	6	3
Adverse event, serious fatal	1	-
Consent withdrawn by subject	5	2
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Tezepelumab
Reporting group description:	
Tezepelumab 210 mg administered every 4 weeks subcutaneously	
Reporting group title	Placebo
Reporting group description:	
Placebo administered every 4 weeks subcutaneously	

Reporting group values	Tezepelumab	Placebo	Total
Number of subjects	74	76	150
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	58	62	120
From 65-84 years	16	14	30
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	53.5	53.4	
standard deviation	± 12.1	± 11.9	-
Sex: Female, Male Units: Participants			
Male	25	31	56
Female	49	45	94

End points

End points reporting groups	
Reporting group title	Tezepelumab
Reporting group description:	
Tezepelumab 210 mg administered every 4 weeks subcutaneously	
Reporting group title	Placebo
Reporting group description:	
Placebo administered every 4 weeks subcutaneously	

Primary: Categorized percent reduction from baseline in the daily OCS dose while not losing asthma control	
End point title	Categorized percent reduction from baseline in the daily OCS dose while not losing asthma control
End point description:	
Categorized percent reduction from baseline at Week 48. Percent change from baseline is defined as {final dose-baseline dose)/baseline dose}*100, and the categories of percent change from baseline in daily OCS dose are defined as: ≥90% to ≤100% reduction, ≥75% to <90% reduction, ≥50% to <75% reduction, >0% to <50% reduction, and, no change or any increase.	
End point type	Primary
End point timeframe:	
Baseline to Week 48	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: Participants				
>=90% to <=100% reduction	40	35		
>=75% to <90% reduction	5	4		
>=50% to <75% reduction	10	14		
>0% to <50% reduction	5	9		
no change or any increase	14	14		

Statistical analyses

Statistical analysis title	Proportional odds model
Statistical analysis description:	
Response variable: categorised % reduction from baseline in final OCS dose. Covariates in the model: treatment, region and daily OCS dose at baseline.	
Comparison groups	Placebo v Tezepelumab

Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.434
Method	Proportional odds model
Parameter estimate	Cumulative Odds Ratio
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	2.35

Secondary: Annualised asthma exacerbation rate (AAER)

End point title	Annualised asthma exacerbation rate (AAER)

End point description:

The annualized exacerbation rate is based on exacerbations reported by the investigator in the eCRF over 48 weeks.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: Annual rate of event over time at risk				
least squares mean (confidence interval 95%)	1.38 (0.98 to 1.95)	2.00 (1.46 to 2.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with daily OCS dose ≤5 mg at Week 48

End point title	Proportion of subjects with daily OCS dose ≤5 mg at Week 48

End point description:

Proportion of subjects with daily OCS dose ≤5 mg at Week 48.

End point type	Secondary

End point timeframe:

Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: Participants	53	55		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with 100% reduction from baseline in daily OCS dose at Week 48

End point title	Proportion of subjects with 100% reduction from baseline in daily OCS dose at Week 48

End point description:

Proportion of subjects with 100% reduction from baseline in daily OCS dose at Week 48. Percent change from baseline is defined as {(final dose-baseline dose)/baseline dose}*100.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: Participants	40	35		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with ≥50% reduction from baseline in daily OCS dose at Week 48

End point title	Proportion of subjects with ≥50% reduction from baseline in daily OCS dose at Week 48

End point description:

Proportion of subjects with ≥50% reduction from baseline in daily OCS dose at Week 48. Percent change from baseline is defined as {(final dose-baseline dose)/baseline dose}*100.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: Participants	55	53		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in pre-bronchodilator (pre-BD) forced expiratory volume in 1 second (FEV1)

End point title	Change from baseline in pre-bronchodilator (pre-BD) forced expiratory volume in 1 second (FEV1)

End point description:

Change from baseline in pre-BD FEV1 at Week 48. FEV1 is defined as the volume of air exhaled from the lungs in the first second of a forced expiration.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	64		
Units: Litre				
least squares mean (standard error)	0.21 (± 0.046)	-0.04 (± 0.046)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Weekly mean daily Asthma Symptom Score via the daily Asthma Symptom Diary

End point title	Change from baseline in Weekly mean daily Asthma Symptom Score via the daily Asthma Symptom Diary

End point description:

Change from baseline in Asthma Symptom Diary score at Week 48. The Asthma Symptom Diary comprises of 10 items (5 items in the morning; 5 items in the evening). Asthma symptoms during night time and daytime are recorded by the patient each morning and evening in the daily diary. A daily ASD score is the mean of the 10 items. Responses for all 10 items are required to calculate the daily ASD score; otherwise, it is treated as missing. For the 7-day average asthma symptom score, scoring is done with no imputation using the mean of at least 4 of the 7 daily ASD scores as a mean weekly item score. The 7-day average ASD score ranges from 0 to 4, where 0 indicates no asthma symptoms.

End point type	Secondary
End point timeframe: Baseline to Week 48	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	68		
Units: Score on a scale				
least squares mean (standard error)	-0.36 (± 0.071)	-0.26 (± 0.068)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in weekly mean rescue medication use

End point title	Change from baseline in weekly mean rescue medication use

End point description:

Change from baseline in weekly mean rescue medication use at Week 48. Daily rescue medication use is defined as: Number of night inhaler puffs + 2 x [number of night nebulizer times] + number of daytime inhaler puffs + 2 x [number of day nebulizer times]. Each timepoint is calculated as weekly means based on daily diary data.

End point type	Secondary
End point timeframe: Baseline to Week 48	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	70		
Units: weekly mean use				
least squares mean (standard error)	-0.85 (± 0.280)	-0.37 (± 0.268)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in weekly mean home peak expiratory flow (PEF) (morning and evening)

End point title	Change from baseline in weekly mean home peak expiratory flow (PEF) (morning and evening)

End point description:

Change from baseline in weekly mean morning and evening peak expiratory flow (PEF) at Week 48. Home PEF testing will be performed by the subject in the morning upon awakening and in the evening at bedtime using an electronic, hand-held spirometer. Each timepoint is calculated as weekly means.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: L/min				
least squares mean (standard error)				
morning PEF (n teze = 59, n pbo = 70)	13.29 (± 5.653)	-9.71 (± 5.435)		
evening PEF (n teze = 59, n pbo = 69)	10.05 (± 5.980)	-11.37 (± 5.749)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in weekly mean number of night-time awakening due to asthma

End point title	Change from baseline in weekly mean number of night-time awakening due to asthma

End point description:

Change from baseline in weekly mean number of night time awakenings at Week 48. Each timepoint is calculated as weekly mean number of awakenings due to asthma based on daily diary data.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	70		
Units: Percentage of nights with awakenings				
least squares mean (standard error)	-15.71 (± 3.482)	-12.79 (± 3.317)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Asthma Control Questionnaire 6 (ACQ-6) score

End point title	Change from baseline in Asthma Control Questionnaire 6 (ACQ-6) score

End point description:

Change from baseline in ACQ-6 at Week 48. The ACQ-6 captures asthma symptoms and short-acting β2-agonist use via subject-report. Questions are weighted equally and scored from 0 (totally controlled) to 6 (severely uncontrolled). The ACQ-6 score is the mean of the responses.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	68		
Units: Score on a scale				
least squares mean (standard error)	-0.87 (± 0.125)	-0.51 (± 0.123)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Standardized Asthma Quality of Life Questionnaire for 12 years and older (AQLQ(s)+12) total score

End point title	Change from baseline in Standardized Asthma Quality of Life Questionnaire for 12 years and older (AQLQ(s)+12) total score

End point description:

Change from baseline in AQLQ(S)+12 as compared to placebo at Week 48. The AQLQ(S)+12 is a questionnaire that measures the health-related quality of life experienced by asthma subjects. The total score is defined as the average of all 32 questions in the AQLQ(S)+12 questionnaire. AQLQ(S)+12 is a 7-point scale questionnaire, ranging from 7 (no impairment) to 1 (severe impairment).

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	67		
Units: Score on a scale				
least squares mean (standard error)	0.94 (± 0.124)	0.58 (± 0.123)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in European Quality of Life – 5 Dimensions 5 Levels Questionnaire (EQ-5D-5L) score

End point title	Change from baseline in European Quality of Life – 5 Dimensions 5 Levels Questionnaire (EQ-5D-5L) score

End point description:

Change from baseline in EQ-5D-5L at Week 48. The EQ-5D-5L questionnaire assesses 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 response options (no/slight/moderate/severe/extreme problems) that reflect increasing levels of difficulty. The EQ-5D-5L scores are converted into a single index-based value (Health State Valuation), using the UK population-based weights. The Helth State Valuation is scored between 0 to 1, where higher score indicates a better health state.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	58		
Units: Score on a scale				
least squares mean (standard error)	0.07 (± 0.026)	0.00 (± 0.027)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of asthma specific resource utilizations

End point title	Number of asthma specific resource utilizations

End point description:

Number of asthma specific resource utilizations (e.g. unscheduled physician visits, unscheduled phone calls to physicians, use of other asthma medications) over 48 weeks.

End point type	Secondary

End point timeframe:

Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: Participants				
Hospitalisation	5	10		
Emergency room visit	4	7		
Unscheduled visit to specialist	29	41		
Home visit	1	2		
Telephone call	26	43		
Ambulance transport	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Work Productivity and Activity Impairment Questionnaire and Classroom Impairment Questionnaire (WPAI+CIQ) score

End point title	Change from baseline in Work Productivity and Activity Impairment Questionnaire and Classroom Impairment Questionnaire (WPAI+CIQ) score

End point description:

Change from baseline in WPAI+CIQ score at Week 48. The WPAI+CIQ consists of questions about how asthma and asthma related issues impact a subject's ability to work, attend classes, and perform regular daily activities.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76[1]		
Units: Percentage				
arithmetic mean (standard deviation)				
Work productivity loss (n teze = 22, n pbo = 21)	-6.27 (± 25.30)	-9.66 (± 36.63)		
Class productivity loss (n teze = 1, n pbo = 0)	-10.00 (± 0)	0 (± 0)		
Activity impairment (n teze = 59, n pbo = 59)	-13.2 (± 29.3)	-7.8 (± 26.4)		

Notes:

[1] - No subject in Placebo arm selected the option 'in school' on the WPAI+CIQ questionnaire at Week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in FENO

End point title	Change from baseline in FENO

End point description:

Change from baseline in fractional exhaled nitric oxide (FeNO) at week 48.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	57		
Units: ppb				
least squares mean (standard error)	-11.71 (± 2.757)	-1.40 (± 2.774)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in peripheral blood eosinophils

End point title	Change from baseline in peripheral blood eosinophils

End point description:

Change from baseline in blood eosinophil counts at week 48.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	67		
Units: cells/µL				
least squares mean (standard error)	-83.79 (± 17.078)	33.38 (± 16.605)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline from total serum IgE

End point title	Change from baseline from total serum IgE

End point description:

Change from baseline in total serum IgE at week 48.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	67		
Units: IU/mL				
least squares mean (standard error)	-80.66 (± 36.253)	37.77 (± 35.621)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Serum trough concentrations

End point title	PK: Serum trough concentrations

End point description:

Serum trough concentrations at each scheduled visit.

End point type	Secondary

End point timeframe:

Baseline, Week 4, Week 12, Week 24, Week 40, Week 48, Week 60

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	0[2]		
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Baseline	0 (± 0)	()		
Week 4	10.3298 (± 42.31)	()		
Week 12	17.9626 (± 57.85)	()		
Week 24	18.9210 (± 55.83)	()		
Week 40	16.7095 (± 181.44)	()		
Week 48	13.9224 (± 352.35)	()		
Week 60	3.5591 (± 177.36)	()		

Notes:

[2] - The placebo arm is not applicable since it is not the experimental product.

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity: Incidence of anti-drug antibodies (ADA)

End point title	Immunogenicity: Incidence of anti-drug antibodies (ADA)

End point description:

Anti-drug antibodies (ADA) responses at baseline and post baseline. Persistently positive is defined as positive at >=2 post baseline assessments (with >=16 weeks between the first and the last positive) or positive at last post baseline assessment. Transiently positive is defined as having at least one post baseline ADA positive assessment and not fulfilling the conditions of persistently positive. Treatment boosted ADA defined as baseline positive ADA that was boosted to a 4 fold or higher level following treatment. Treatment emergent ADA defined as sum of treatment induced ADA and treatment boosted ADA.

End point type	Secondary

End point timeframe:

Baseline to Week 60

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: Participants				
ADA positive at baseline and/or post-baseline	3	2		
Any baseline ADA positive	2	2		
Only baseline ADA positive	1	1		
Any post-baseline ADA positive	2	1		
Both baseline and >=1 post-baseline ADA positive	1	1		
Treatment-induced ADA positive	1	0		
Treatment-boosted ADA positive	0	0		
TE-ADA positive (ADA incidence)	1	0		
ADA persistently positive	1	1		
ADA transiently positive	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 last study visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Placebo
Reporting group description: Placebo administered subcutaneously	
Reporting group title	Teze 210 mg Q4W
Reporting group description: Tezepelumab administered every 4 weeks subcutaneously	

Serious adverse events	Placebo	Teze 210 mg Q4W	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 76 (21.05%)	12 / 74 (16.22%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive breast carcinoma			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Incisional hernia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			

subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	8 / 76 (10.53%)	4 / 74 (5.41%)	
occurrences causally related to treatment / all	0 / 11	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial secretion retention			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal polyps			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Muscle spasms			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (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			
Intervertebral discitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 76 (2.63%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Placebo	Teze 210 mg Q4W	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 76 (63.16%)	35 / 74 (47.30%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 76 (1.32%)	3 / 74 (4.05%)	
occurrences (all)	1	3	
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 76 (7.89%)	2 / 74 (2.70%)	
occurrences (all)	6	2	

Nervous system disorders			
Headache			
subjects affected / exposed	8 / 76 (10.53%)	3 / 74 (4.05%)	
occurrences (all)	9	3	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	5 / 76 (6.58%)	0 / 74 (0.00%)	
occurrences (all)	5	0	
Eye disorders			
Cataract			
subjects affected / exposed	3 / 76 (3.95%)	1 / 74 (1.35%)	
occurrences (all)	3	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	8 / 76 (10.53%)	6 / 74 (8.11%)	
occurrences (all)	15	7	
Nasal polyps			
subjects affected / exposed	4 / 76 (5.26%)	0 / 74 (0.00%)	
occurrences (all)	6	0	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 76 (1.32%)	4 / 74 (5.41%)	
occurrences (all)	2	5	
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 76 (3.95%)	4 / 74 (5.41%)	
occurrences (all)	3	4	
Bronchitis bacterial			
subjects affected / exposed	7 / 76 (9.21%)	6 / 74 (8.11%)	
occurrences (all)	10	14	
Nasopharyngitis			
subjects affected / exposed	19 / 76 (25.00%)	12 / 74 (16.22%)	
occurrences (all)	29	14	
Oral candidiasis			
subjects affected / exposed	4 / 76 (5.26%)	4 / 74 (5.41%)	
occurrences (all)	5	4	

Sinusitis subjects affected / exposed occurrences (all)	5 / 76 (6.58%) 6	1 / 74 (1.35%) 1	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	8 / 76 (10.53%) 8	9 / 74 (12.16%) 9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2018	clarifications of eligibility criteria of enrolment in the extension study and acceptable OCS dose regimen, amendment of inclusion/exclusion criteria, changes to concomitant/prohibited medication
12 March 2019	Changes to the sample size, information about two database locks and unblinding rules after primary database lock added, amendment of measures to minimise bias and study assessments, amended inclusion/exclusion criteria, clarification on concomitant/prohibited medication
14 May 2020	changes to supportive outcome of key secondary objective, added appendix with guidance for changes related to the COVID-19 pandemic, new analyses specified related to COVID-19 pandemic, threshold of partially asthma control based on ACQ-6 score updated, clarification that safety analysis will be done based on 'on-study' period instead of 'post-treatment'

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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Notes: