Clinical trial results:
A Multicentre, Randomized, Double-Blind, Placebo Controlled, Parallel Group, Phase 3 Study to Evaluate the Efficacy and Safety of Tezepelumab in Adults and Adolescents with Severe Uncontrolled Asthma (NAVIGATOR)

Summary

EudraCT number	2017-003078-15
Trial protocol	GB DE FR AT
Global end of trial date	12 November 2020

Results information

Result version number	v1
This version publication date	28 May 2021
First version publication date	28 May 2021

Trial information

Trial identification

Sponsor protocol code	D5180C00007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03347279
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	AstraZeneca Clinical Study Information, AstraZeneca, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001613-PIP01-14
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	12 November 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of 210 mg tezepelumab SC Q4W on asthma exacerbations in adult and adolescent subjects with severe uncontrolled asthma compared with placebo

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 or their legally authorised representative 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.

For subjects under the age of majority (adolescent subjects), the subject's legal guardian provided their informed consent in addition to the subject's informed consent.
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 or the subject's legally authorised representative.

Background therapy:

Subjects who had received a physician-prescribed asthma controller medication with medium- or high-dose ICS as per GINA guideline (GINA 2017) for at least 12 months prior to Visit 1.

Documented treatment with a total daily dose of either medium or high-dose ICS (>=500µg fluticasone propionate dry powder formulation equivalent total daily dose) for at least 3 months prior to Visit 1. The ICS could be contained within an ICS/LABA combination product.

At least one additional maintenance asthma controller medication was required according to standard practice of care. Use of additional asthma controller medications must have been documented for at least 3 months prior to Visit 1.

Evidence for comparator: -

Actual start date of recruitment	23 November 2017
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	Korea, Republic of: 126
Country: Number of subjects enrolled	Japan: 97
Country: Number of subjects enrolled	Vietnam: 20
Country: Number of subjects enrolled	Taiwan: 9
Country: Number of subjects enrolled	United States: 186
Country: Number of subjects enrolled	Canada: 36
Country: Number of subjects enrolled	Brazil: 93
Country: Number of subjects enrolled	Argentina: 81
Country: Number of subjects enrolled	Germany: 103
Country: Number of subjects enrolled	France: 41
Country: Number of subjects enrolled	Australia: 19
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	South Africa: 109
Country: Number of subjects enrolled	Israel: 47
Country: Number of subjects enrolled	Saudi Arabia: 7
Country: Number of subjects enrolled	Russian Federation: 51
Country: Number of subjects enrolled	Ukraine: 26
Worldwide total number of subjects	1059
EEA total number of subjects	152

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)	82
Adults (18-64 years)	807
From 65 to 84 years	170
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 2420 subjects were enrolled at 297 centres in 18 countries;

Pre-assignment

Screening details:

1061 subjects were randomised to receive treatment with tezepelumab 210mg Q4W or placebo. Of the 1061 randomised, 1059 (99.8%) subjects received treatment. 82 (7.7%) of the subjects randomised and treated were adolescents.

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 210mg Q4W

Arm description:

Tezepelumab administered every 4 weeks subcutaneously

Arm type	Experimental
Investigational medicinal product name	Tezepelumab 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 subcutaneously

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 210mg Q4W	Placebo
Started	528	531
Completed	513	509
Not completed	15	22
Adverse event, serious fatal	-	2
Consent withdrawn by subject	8	15
Other reasons	2	3
Lost to follow-up	5	2

Baseline characteristics

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

Reporting group values	Tezepelumab 210mg Q4W	Placebo	Total
Number of subjects	528	531	1059
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)	41	41	82
Adults (18-64 years)	391	416	807
From 65-84 years	96	74	170
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	49.9	49.0	
standard deviation	± 16.3	± 15.9	-
Gender Categorical			
Units: Subjects			
Female	335	337	672
Male	193	194	387

End points

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

Primary: Annual asthma exacerbation rate in adult and adolescent patients with uncontrolled asthma	
End point title	Annual asthma exacerbation rate in adult and adolescent patients with uncontrolled asthma
End point description:	
The annual exacerbation rate is based on unadjudicated annual exacerbation rate reported by the investigator in the eCRF. The analysis is based on the primary population (Full Analysis Set)	
End point type	Primary
End point timeframe:	
From randomisation to Study Week 52.	

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	528	531		
Units: annual rate of event over time at risk				
least squares mean (confidence interval 95%)				
Least squares means (95% confidence interval)	0.93 (0.80 to 1.07)	2.10 (1.84 to 2.39)		

Statistical analyses

Statistical analysis title	Negative binomial analysis
Comparison groups	Tezepelumab 210mg Q4W v Placebo
Number of subjects included in analysis	1059
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Negative Binomial
Parameter estimate	Rate ratio
Point estimate	0.44

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.53

Primary: Annual asthma exacerbation rate in adult and adolescent patients with uncontrolled asthma in subjects with baseline eosinophils < 300 cells/uL

End point title	Annual asthma exacerbation rate in adult and adolescent patients with uncontrolled asthma in subjects with baseline eosinophils < 300 cells/uL

End point description:

End point type	Primary

End point timeframe:

From randomisation to Study Week 52.

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	309		
Units: Annual rate of event over time at risk				
least squares mean (confidence interval 95%)				
Least squares means (95% confidence interval)	1.02 (0.84 to 1.23)	1.73 (1.46 to 2.05)		

Statistical analyses

Statistical analysis title	Negative Binomial model
Comparison groups	Tezepelumab 210mg Q4W v Placebo
Number of subjects included in analysis	618
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Negative Binomial
Parameter estimate	Rate ratio
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	0.75

Secondary: Mean change from baseline at Week 52 in pre-bronchodilator FEV1 (L) (key secondary endpoint)

End point title	Mean change from baseline at Week 52 in pre-bronchodilator FEV1 (L) (key secondary endpoint)

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	471	453		
Units: Litre				
least squares mean (standard error)				
Least square means (standard error)	0.23 (± 0.018)	0.10 (± 0.018)		

Statistical analyses

Statistical analysis title	Repeated measures model
Comparison groups	Tezepelumab 210mg Q4W v Placebo
Number of subjects included in analysis	924
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.08
upper limit	0.18

Secondary: Mean change from baseline at Week 52 in ACQ-6 (key secondary endpoint)

End point title	Mean change from baseline at Week 52 in ACQ-6 (key secondary endpoint)

End point description:

End point type	Secondary

End point timeframe:

From Randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	485	472		
Units: Scale of score				
least squares mean (standard error)				
Least squares mean (standard error)	-1.53 (± 0.045)	-1.20 (± 0.046)		

Statistical analyses

Statistical analysis title	Repeated measures model
Comparison groups	Tezepelumab 210mg Q4W v Placebo
Number of subjects included in analysis	957
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	-0.2

Secondary: Mean change from baseline at Week 52 in AQLQ(S)+12 total score (key secondary endpoint)

End point title	Mean change from baseline at Week 52 in AQLQ(S)+12 total score (key secondary endpoint)

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	480	467		
Units: Scale of score				
least squares mean (standard error)				
Least squares mean (standard error)	1.48 (± 0.049)	1.14 (± 0.049)		

Statistical analyses

Statistical analysis title	Repeated measures model
Comparison groups	Tezepelumab 210mg Q4W v Placebo
Number of subjects included in analysis	947
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.47

Secondary: Mean change from baseline at Week 52 in Asthma Symptom Diary (key secondary endpoint)

End point title	Mean change from baseline at Week 52 in Asthma Symptom Diary (key secondary endpoint)

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	355		
Units: Scale of score				
least squares mean (standard error)				
Least squares mean (standard error)	-0.70 (± 0.027)	-0.59 (± 0.027)		

Statistical analyses

Statistical analysis title	Repeated measures model
Comparison groups	Tezepelumab 210mg Q4W v Placebo
Number of subjects included in analysis	729
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	-0.04

Secondary: Annual asthma exacerbation rate resulting in emergency room visit or hospitalisation

End point title	Annual asthma exacerbation rate resulting in emergency room visit or hospitalisation

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	528	531		
Units: Annual rate of event over time at risk				
least squares mean (confidence interval 95%)				
Least squares mean (95% confidence interval)	0.06 (0.04 to 0.09)	0.28 (0.20 to 0.39)		

Statistical analyses

No statistical analyses for this end point

Secondary: Annual asthma exacerbations associated with hospitalisations

End point title	Annual asthma exacerbations associated with hospitalisations

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	528	531		
Units: Annual rate of event over time at risk				
least squares mean (confidence interval 95%)				
Least squares mean (95% Confidence interval)	0.03 (0.01 to 0.06)	0.19 (0.12 to 0.30)		

Statistical analyses

No statistical analyses for this end point

Secondary: Annual asthma exacerbation rate using adjudicated data

End point title	Annual asthma exacerbation rate using adjudicated data

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	528	531		
Units: Annual rate of event over time at risk				
least squares mean (confidence interval 95%)				
Least squares mean (95% confidence interval)	0.94 (0.81 to 1.09)	2.14 (1.88 to 2.44)		

Statistical analyses

No statistical analyses for this end point

Secondary: Annual asthma exacerbation rate associated with emergency room visit or hospitalisation using adjudicated data

End point title	Annual asthma exacerbation rate associated with emergency room visit or hospitalisation using adjudicated data

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52.

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	528	531		
Units: Annual rate of event over time at risk				
least squares mean (confidence interval 95%)				
Least squares mean (95% confidence interval)	0.08 (0.05 to 0.12)	0.31 (0.22 to 0.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with >= 1 asthma exacerbation and time to first asthma exacerbation

End point title	Proportion of subjects with >= 1 asthma exacerbation and time to first asthma exacerbation

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	528	531		
Units: Count				
Number of subjects with >=1 asthma exacerbation	231	319		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with >=1 asthma exacerbation associated with emergency room visit or hospitalisation and time to first asthma exacerbation associated with emergency room visit or hospitalisation

End point title	Proportion of subjects with >=1 asthma exacerbation associated with emergency room visit or hospitalisation and time to first asthma exacerbation associated with emergency room visit or hospitalisation

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	528	531		
Units: Count				
Number of subjects with >= 1 event	25	65		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects who had no asthma exacerbations

End point title	Proportion of subjects who had no asthma exacerbations

End point description:

The proportion of subjects with no exacerbations is defined as subjects who meet both the following criteria: (1) completed the 52 week treatment period and (2) did not report an exacerbation during this period.

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	528	531		
Units: Number of subjects				
Number of subjects with no asthma exacerbations	286	205		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with no asthma exacerbations associated with emergency room visit or hospitalisation.

End point title	Proportion of subjects with no asthma exacerbations associated with emergency room visit or hospitalisation.

End point description:

The proportion of subjects with no exacerbations associated with emergency room visit or hospitalisation. is defined as subjects who meet both the following criteria: (1) completed the 52 week treatment period and (2) did not report an exacerbation associated with emergency room visit or hospitalisation.during this period.

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	528	531		
Units: Number of subjects				
Number of subjects with no events	488	452		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline at Week 52 in clinic FeNO (ppb)

End point title	Mean change from baseline at Week 52 in clinic FeNO (ppb)

End point description:

End point type	Secondary

End point timeframe:
From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	440	426		
Units: ppb				
least squares mean (standard error)				
Least squares mean (SE)	-17.29 (± 1.156)	-3.46 (± 1.165)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline at Week 52 in Eosinophils (cells/uL)

End point title	Mean change from baseline at Week 52 in Eosinophils (cells/uL)

End point description:

End point type	Secondary

End point timeframe:
From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	458	451		
Units: cells/uL				
least squares mean (standard error)	-170.02 (± 9.222)	-40.15 (± 9.254)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline at Week 52 in IgE (IU/mL)

End point title	Mean change from baseline at Week 52 in IgE (IU/mL)

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	482	471		
Units: IU/mL				
least squares mean (standard error)	-164.38 (± 34.414)	43.61 (± 34.542)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in daily rescue medication use at Week 52

End point title	Mean change from baseline in daily rescue medication use at Week 52

End point description:

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].

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	439	428		
Units: weekly mean use				
least squares mean (standard error)	-2.53 (± 0.137)	-2.36 (± 0.137)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in night time awakenings due to asthma at Week 52

End point title	Mean change in night time awakenings due to asthma at Week 52

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	418	395		
Units: percentage of nights with awakenings				
least squares mean (standard error)	-33.51 (± 1.381)	-30.22 (± 1.387)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in home based morning PEF (L/min) at Week 52

End point title	Mean change in home based morning PEF (L/min) at Week 52

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	414	391		
Units: Weekly mean (L/min)				
least squares mean (standard error)	34.57 (± 3.051)	18.01 (± 3.074)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in home based evening PEF (L/min) at Week 52

End point title	Mean change in home based evening PEF (L/min) at Week 52

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	405	390		
Units: weekly mean (L/min)				
least squares mean (standard error)	23.87 (± 3.075)	9.01 (± 3.094)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinicians global impression of change at Week 52

End point title	Clinicians global impression of change at Week 52

End point description:

CGIC (Clinical global impression of change), is an overall evaluation of response to treatment, conducted by investigator using 7-point rating scale, ranging from 1 (very much improved), to 7 (very much worse)

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	483	477		
Units: Number of subjects				
Very much improved	96	60		
Much improved	199	132		
Minimally Improved	98	131		
No change	77	130		
Minimally worse	11	19		
Much worse	2	4		
Very much worse	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Patients global impression of change at Week 52

End point title	Patients global impression of change at Week 52

End point description:

PGIC (Patient global impression of change) is an overall evaluation of response to treatment, conducted by the patient using 7-point rating scale, ranging from 1 (very much improved), to 7 (very much worse).

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	479	466		
Units: Number of subjects				
Very much Improved	255	182		
Much improved	103	94		
Minimally improved	71	76		
No Change	39	99		
Minimally worse	6	8		
Much worse	4	6		
Very much worse	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Patients global impression of severity at Week 52

End point title	Patients global impression of severity at Week 52

End point description:

PGI-S (Patient global impression of severity) is an overall evaluation of patient's perception of overall symptom severity using a 6-point rating scale, ranging from 0 = No symptoms, 1=Very mild symptoms, 2=Mild symptoms, 3=Moderate symptoms, 4=Severe symptoms, 5=Very severe symptoms

End point type	Secondary

End point timeframe:

At Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	479	466		
Units: Number of subjects				
No symptoms	118	78		
Very mild symptoms	138	128		
Mild symptoms	110	128		
Moderate symptoms	99	111		
Severe symptoms	14	19		

Very severe symptoms	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of healthcare utilization over 52 weeks

End point title	Number of healthcare utilization over 52 weeks

End point description:

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	528	531		
Units: Number of subjects				
Hospitalisation	17	37		
Emergency room visit	23	50		
Unscheduled visit to specialist	187	231		
Home visit	9	10		
Telephone call	101	133		
Ambulance transport	4	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in work productivity loss due to asthma at Week 52

End point title	Mean change from baseline in work productivity loss due to asthma at Week 52

End point description:

WPAI+CIQ work productivity loss at Week 52

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	177		
Units: Percentage				
arithmetic mean (standard deviation)	-20.16 (± 30.31)	-16.58 (± 29.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in class productivity loss due to asthma at Week 52

End point title	Mean change from baseline in class productivity loss due to asthma at Week 52

End point description:

WPAI+CIQ productivity loss at Week 52 for subjects currently attending school.

End point type	Secondary

End point timeframe:

From randomisation to study week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	19		
Units: Percentage				
arithmetic mean (standard deviation)	-14.03 (± 33.00)	-24.72 (± 26.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Activity impairment at Week 52

End point title	Activity impairment at Week 52

End point description:

WPAI+CIQ activity impairment

End point type	Secondary

End point timeframe:

From randomisation to Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	207	196		
Units: Percentage				
arithmetic mean (standard deviation)	-20.0 (± 28.6)	-17.9 (± 27.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of tezpelumab

End point title	Pharmacokinetics of tezpelumab

End point description:

Mean serum trough PK concentrations at each visit

End point type	Secondary

End point timeframe:

Baseline, Week 4, Week 12, Week 24, Week 36, Week 52, Week 64

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	528	0[1]		
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Baseline (n=524)	0 (± 0)	()		
Week 4 (n=514)	10.1573 (± 74.51)	()		
Week 12 (n=491)	18.7396 (± 48.53)	()		
Week 24 (n=461)	20.1924 (± 51.77)	()		
Week 36 (n=464)	19.5246 (± 55.58)	()		
Week 52 (n=452)	19.8894 (± 70.04)	()		
Week 64 (n=72)	1.7675 (± 171.86)	()		

Notes:

[1] - Not applicable since it is not the experimental product.

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenecity of tezepelumab

End point title	Immunogenecity of tezepelumab

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, and from time of first dose to end of study

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	527	530		
Units: Number of subjects				
ADA positive at baseline and/or post-baseline	26	44		
Any baseline ADA positive	17	25		
Only baseline ADA positive	14	8		
Any post-baseline ADA positive	12	36		
Both baseline and >= 1 post-baseline ADA positive	3	17		
Treatment induced ADA positive	9	18		
Treatment boosted ADA positive	1	2		
Treatment emergent ADA positive	10	20		
ADA persistently positive	4	18		
ADA transiently positive	8	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline at Week 52 in EQ-5D-5L VAS

End point title	Mean change from baseline at Week 52 in EQ-5D-5L VAS

End point description:

End point type	Secondary

End point timeframe:

At Study Week 52

End point values	Tezepelumab 210mg Q4W	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	448	435		
Units: scale of score				
least squares mean (standard error)	14.64 (± 0.708)	11.86 (± 0.712)		

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	75 / 531 (14.12%)	55 / 528 (10.42%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events	2	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	2 / 531 (0.38%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of thyroid gland			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer			

subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	0 / 531 (0.00%)	2 / 528 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Cyanosis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 531 (0.00%)	2 / 528 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (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	42 / 531 (7.91%)	16 / 528 (3.03%)	
occurrences causally related to treatment / all	0 / 91	2 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilic pneumonia			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (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 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	0 / 531 (0.00%)	2 / 528 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lumbar vertebral fracture			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
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 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Aortic valve stenosis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 531 (0.00%)	2 / 528 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cubital tunnel syndrome			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Idiopathic generalised epilepsy			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelopathy			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 531 (0.19%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 531 (0.19%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uveitis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal achalasia			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis necrotising			

subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 531 (0.19%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 531 (0.19%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
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			
Bone cyst			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle necrosis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 531 (0.19%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyarthritis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast abscess			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 531 (0.38%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	2 / 531 (0.38%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 531 (0.38%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			

subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster oticus			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection bacterial			
subjects affected / exposed	2 / 531 (0.38%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 531 (0.19%)	2 / 528 (0.38%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			

subjects affected / exposed	2 / 531 (0.38%)	2 / 528 (0.38%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia streptococcal			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			

subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 531 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 531 (0.19%)	0 / 528 (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	432 / 531 (81.36%)	404 / 528 (76.52%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	22 / 531 (4.14%)	23 / 528 (4.36%)	
occurrences (all)	29	27	
Nervous system disorders			

Headache			
subjects affected / exposed	48 / 531 (9.04%)	44 / 528 (8.33%)	
occurrences (all)	73	102	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	23 / 531 (4.33%)	20 / 528 (3.79%)	
occurrences (all)	27	22	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	50 / 531 (9.42%)	38 / 528 (7.20%)	
occurrences (all)	61	43	
Rhinitis allergic			
subjects affected / exposed	17 / 531 (3.20%)	16 / 528 (3.03%)	
occurrences (all)	25	19	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	14 / 531 (2.64%)	23 / 528 (4.36%)	
occurrences (all)	15	29	
Back pain			
subjects affected / exposed	16 / 531 (3.01%)	22 / 528 (4.17%)	
occurrences (all)	17	27	
Pain in extremity			
subjects affected / exposed	8 / 531 (1.51%)	16 / 528 (3.03%)	
occurrences (all)	9	17	
Infections and infestations			
Bronchitis			
subjects affected / exposed	34 / 531 (6.40%)	27 / 528 (5.11%)	
occurrences (all)	37	41	
Bronchitis bacterial			
subjects affected / exposed	18 / 531 (3.39%)	25 / 528 (4.73%)	
occurrences (all)	21	27	
Gastroenteritis			
subjects affected / exposed	15 / 531 (2.82%)	17 / 528 (3.22%)	
occurrences (all)	17	18	
Nasopharyngitis			

subjects affected / exposed	118 / 531 (22.22%)	115 / 528 (21.78%)	
occurrences (all)	195	174	
Pharyngitis			
subjects affected / exposed	17 / 531 (3.20%)	17 / 528 (3.22%)	
occurrences (all)	19	18	
Rhinitis			
subjects affected / exposed	19 / 531 (3.58%)	15 / 528 (2.84%)	
occurrences (all)	40	19	
Sinusitis			
subjects affected / exposed	40 / 531 (7.53%)	21 / 528 (3.98%)	
occurrences (all)	57	26	
Upper respiratory tract infection			
subjects affected / exposed	92 / 531 (17.33%)	60 / 528 (11.36%)	
occurrences (all)	133	98	
Urinary tract infection			
subjects affected / exposed	23 / 531 (4.33%)	23 / 528 (4.36%)	
occurrences (all)	27	36	
Viral upper respiratory tract infection			
subjects affected / exposed	13 / 531 (2.45%)	17 / 528 (3.22%)	
occurrences (all)	21	21	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 November 2017	Inclusion of St George's Respiratory Questionnaire, clarifications on outcomes of secondary endpoints, amended inclusion/exclusion criteria, changes to concomitant medication
16 March 2018	Change in collection times of SNOT-22, added details regarding enrolment in separate extension study, clarification on adjudication committee, amended inclusion/exclusion criteria, clarification on concomitant/prohibited medication
15 April 2019	Neutralizing antibodies moved to exploratory endpoint, additional of baseline eosinophils <300/uL subgroup into the confirmatory hierarchical testing strategy, revised inclusion/exclusion criteria, clarification on dose preparation/administration, clarification on laboratories requiring treatment information for sample analyses, addition of a primary database lock, clarification on procedures for discontinuation of IP,
14 May 2020	Added appendix with guidance for changes related to the COVID-19 pandemic, clarification on subjects enrolling into long term extension study can continue with follow-up visits until an on-site visit is possible, clarification on schedule of assessments due to the COVID-19 pandemic, secondary endpoint proportion of subjects with >= 1 asthma exacerbation updated to proportion of subjects who did not experience an asthma exacerbation, clarification that pulmonology, cardiology, neurology and oncology specialists will form part of the independent adjudication committee, safety reporting period updated from post-treatment to on-study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported