



Clinical trial results:

A Randomised, Double-blind, Placebo-controlled, Parallel Group, Multicentre, Phase 2a Study to Explore the Efficacy and Safety of Tezepelumab in Subjects with Moderate to Very Severe Chronic Obstructive Pulmonary Disease (COPD) (COURSE)

Summary

EudraCT number	2019-001363-67
Trial protocol	DK NL FR DE ES GB
Global end of trial date	31 January 2024

Results information

Result version number	v1 (current)
This version publication date	01 February 2025
First version publication date	01 February 2025

Trial information

Trial identification

Sponsor protocol code	D5241C00001
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	151 85, Sodertalje, Sweden,
Public contact	Global Clinical Lead, AstraZeneca, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, 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	31 January 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	31 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of tezepelumab as compared with placebo on COPD exacerbations in subjects with moderate to very severe COPD

Protection of trial subjects:

The protocol, protocol amendments, ICF, Investigator Brochure, and other relevant documents (e.g., advertisements) were submitted to an IRB/IEC by the Investigator and reviewed and approved by the IRB/IEC before the study is 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. 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:

All subjects were treated with maintenance locally approved triple inhaled therapy (ICS/LABA/LAMA) for COPD for at least 12 months prior to enrolment (Visit 1) with a stable dose of ICS for the 3 months prior to Visit 1.

Evidence for comparator: -

Actual start date of recruitment	30 July 2019
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: 33
Country: Number of subjects enrolled	Israel: 53
Country: Number of subjects enrolled	Germany: 29
Country: Number of subjects enrolled	Denmark: 28
Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Netherlands: 18
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	United States: 70
Country: Number of subjects enrolled	Canada: 46
Worldwide total number of subjects	333
EEA total number of subjects	105

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)	113
From 65 to 84 years	220
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 80 centres in 10 countries. A total of 579 participants were enrolled of which 337 were randomised. Of the 337 randomised, 333 participants received treatment. 4 participants randomised in error and did not receive treatment. 187 participants not randomised were due to screen failures.

Pre-assignment

Screening details:

The study consisted of a screening period for approximately 6 weeks. At the end of the screening period, participants were randomised in 1:1 ratio for tezepelumab or placebo. Randomisation was stratified by region (North America, Europe, Asia), and number of prior exacerbations (2, ≥ 3) recorded at randomisation in IWRS.

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:

420 mg Tezepelumab injection delivered subcutaneously every 4 weeks up to maximum of 52 weeks (last dose given at week 48).

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

Dosage and administration details:

420 mg Q4W

Arm title	Placebo
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Arm description:

Matching Placebo injection delivered subcutaneously every 4 weeks up to maximum of 52 weeks (last dose given at week 48).

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

Dosage and administration details:

Q4W

Number of subjects in period 1	Tezepelumab	Placebo
Started	165	168
Completed Treatment	138 ^[1]	138 ^[2]
Completed	146	150
Not completed	19	18
Adverse event, serious fatal	2	4
Site Closure	6	-
Consent withdrawn by subject	8	11
Adverse event, non-fatal	2	2
Lost to follow-up	1	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Number of subjects are correct as reported.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Number of subjects are correct as reported.

Baseline characteristics

Reporting groups

Reporting group title	Tezepelumab
Reporting group description: 420 mg Tezepelumab injection delivered subcutaneously every 4 weeks up to maximum of 52 weeks (last dose given at week 48).	
Reporting group title	Placebo
Reporting group description: Matching Placebo injection delivered subcutaneously every 4 weeks up to maximum of 52 weeks (last dose given at week 48).	

Reporting group values	Tezepelumab	Placebo	Total
Number of subjects	165	168	333
Age Categorical			
Age groups in years			
Units: Participants			
Age Group : ≥ 40 - < 65	52	61	113
Age Group : ≥ 65 - ≤ 80	113	107	220
Age Continuous			
Units: Years			
arithmetic mean	67.4	67.1	
standard deviation	± 6.75	± 7.24	-
Sex: Female, Male			
Units: Participants			
Female	77	68	145
Male	88	100	188
Race/Ethnicity, Customized			
Other also includes Native Hawaiian or Other Pacific Islander and American Indian or Alaska Native categories			
Units: Subjects			
White	147	146	293
Black or African American	2	2	4
Asian	16	18	34
Other	0	2	2
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	7	3	10
Not Hispanic or Latino	158	165	323
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Tezepelumab
Reporting group description: 420 mg Tezepelumab injection delivered subcutaneously every 4 weeks up to maximum of 52 weeks (last dose given at week 48).	
Reporting group title	Placebo
Reporting group description: Matching Placebo injection delivered subcutaneously every 4 weeks up to maximum of 52 weeks (last dose given at week 48).	

Primary: Rate of moderate or severe COPD exacerbations in participants with moderate to very severe COPD.

End point title	Rate of moderate or severe COPD exacerbations in participants with moderate to very severe COPD.
End point description: A COPD exacerbation was defined as a change in the participant's usual COPD symptoms that is beyond normal day-to-day variation, is acute in onset, lasts 2 or more days, and may warrant a change in regular medication and leads to any of the following: Use of systemic corticosteroids for at least 3 days, use of antibiotics for at least 3 days, an inpatient hospitalisation due to COPD, or results in death. Analysis was done using a negative binomial model with the response variable as the number of COPD exacerbations experienced during the follow-up for exacerbations. The model included covariates of treatment group, region, and number of exacerbations reported at randomisation as recorded in IWRS (2, >=3). The logarithm of the time at risk (in years) for exacerbation in the study is used as an offset variable.	
End point type	Primary
End point timeframe: From randomisation up to Week 52	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: exacerbations per year				
least squares mean (confidence interval 90%)	1.75 (1.45 to 2.11)	2.11 (1.77 to 2.53)		

Statistical analyses

Statistical analysis title	Negative binomial analysis
Comparison groups	Tezepelumab v Placebo

Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1042 ^[1]
Method	Negative Binomial
Parameter estimate	Rate Ratio
Point estimate	0.83
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.64
upper limit	1.06

Notes:

[1] - 1-sided p-value

Secondary: Comparison of annual severe COPD exacerbation rates over 52 weeks

End point title	Comparison of annual severe COPD exacerbation rates over 52 weeks
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End point description:

An exacerbation was considered severe if it results in at least 1 of the following: Hospitalisation due to the COPD exacerbation (defined as a participant being admitted for ≥ 24 hours to an observation area, the emergency department, or other equivalent healthcare facility), or death related to COPD or COPD exacerbation.

End point type	Secondary
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End point timeframe:

From randomisation up to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: exacerbations per year				
least squares mean (confidence interval 90%)	0.13 (0.07 to 0.24)	0.25 (0.15 to 0.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants COPD exacerbation free at Week 52

End point title	Proportion of participants COPD exacerbation free at Week 52
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End point description:

An exacerbation event was defined as described in primary analysis. A participant was exacerbation free if they did not experience any moderate or severe exacerbations from randomisation to Week 52 (EOT).

End point type	Secondary
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End point timeframe:

From randomisation up to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: participants	71	63		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first moderate/severe COPD exacerbation

End point title	Time to first moderate/severe COPD exacerbation
End point description: Time to first moderate/severe COPD exacerbation post-randomisation, presented as number of subjects with at least one moderate/severe COPD exacerbation.	
End point type	Secondary
End point timeframe: From randomisation up to Week 52	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: Participants	94	105		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first severe COPD exacerbation

End point title	Time to first severe COPD exacerbation
End point description: Time to first severe COPD exacerbation post-randomisation, presented as number of subjects with at least one severe COPD exacerbation.	
End point type	Secondary
End point timeframe: From randomisation up to Week 52	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: Participants	16	22		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants with ≥ 1 severe COPD exacerbations over 52 weeks

End point title	Proportion of participants with ≥ 1 severe COPD exacerbations over 52 weeks
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End point description:

An exacerbation was considered severe if it results in at least 1 of the following: Hospitalisation due to the COPD exacerbation (defined as a participant being admitted for ≥ 24 hours to an observation area, the emergency department, or other equivalent healthcare facility), or death related to COPD or COPD exacerbation.

End point type	Secondary
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End point timeframe:

From randomisation up to Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: participants	16	22		

Statistical analyses

No statistical analyses for this end point

Secondary: Least square (LS) mean difference in change from baseline in pre-bronchodilator forced expiratory volume in 1 (FEV1) at Week 52

End point title	Least square (LS) mean difference in change from baseline in pre-bronchodilator forced expiratory volume in 1 (FEV1) at Week 52
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End point description:

Pre-Bronchodilator FEV1 (L) was determined by spirometry at the clinic visit. FEV1 is defined as the volume of air exhaled from the lungs in the first second of a forced expiration. Change from baseline was obtained as an absolute difference between Week 52 measure and the baseline value. Baseline was defined as the last assessment recorded prior to the first dose of study treatment.

End point type	Secondary
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End point timeframe:

Baseline and Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	166		
Units: Liters				
least squares mean (standard error)	0.026 ($\pm$ 0.015)	-0.029 ($\pm$ 0.015)		

Statistical analyses

No statistical analyses for this end point

Secondary: Lease square (LS) mean difference in change from baseline in St. George's Respiratory Questionnaire (SGRQ) total score at Week 52

End point title	Lease square (LS) mean difference in change from baseline in St. George's Respiratory Questionnaire (SGRQ) total score at Week 52
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End point description:

The SGRQ is a 50-item PRO instrument to measure the health status of participants with airway obstruction diseases. The total score indicates the impact of disease on overall health status. This total score is expressed as a percentage of overall impairment, in which 100 represents the worst possible health status and 0 indicates the best possible health status. Baseline is the measurement recorded at Week 0 (Visit 3).

End point type	Secondary
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End point timeframe:

Baseline and Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: units on a scale				
least squares mean (standard error)	-4.796 ($\pm$ 1.176)	-1.863 ($\pm$ 1.189)		

Statistical analyses

No statistical analyses for this end point

Secondary: Least square (LS) mean difference in change from baseline in COPD assessment tool (CAT) total score at Week 52

End point title	Least square (LS) mean difference in change from baseline in COPD assessment tool (CAT) total score at Week 52
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End point description:

The CAT is an 8-item PRO developed to measure the impact of COPD on health status. A CAT total score is the sum of item responses. Scores range from 0-40 with higher scores indicative of greater COPD impact on health status. Baseline was defined as the value at the randomisation visit (Visit 3). If the Visit 3 measurement was missing, the screening value was used as baseline instead.

End point type	Secondary
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End point timeframe:

Baseline and Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	162		
Units: units on a scale				
least squares mean (standard error)	-3.037 ($\pm$ 0.524)	-1.182 ($\pm$ 0.524)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants achieving a minimum clinically important difference of 4 units or more in St. George's Respiratory Questionnaire (SGRQ) total score at Week 52

End point title	Proportion of participants achieving a minimum clinically important difference of 4 units or more in St. George's Respiratory Questionnaire (SGRQ) total score at Week 52
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End point description:

The SGRQ is a 50-item PRO instrument to measure the health status of participants with airway obstruction diseases. The total score indicates the impact of disease on overall health status. This total score is expressed as a percentage of overall impairment, in which 100 represents the worst possible health status and 0 indicates the best possible health status. A responder was defined as an individual who had "improvement" at Week 52 (≥ 4 point decrease in SGRQ total score).

End point type	Secondary
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End point timeframe:

Baseline and Week 52

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	163		
Units: participants	65	59		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of Tezepelumab

End point title	Serum concentration of Tezepelumab
End point description: Blood samples were collected to determine the serum concentration of Tezepelumab. With the exception of Week 0 and Week 64, only pre-dose data from samples collected between 21 and 35 days after previous dose of investigational product were included. Week 0 arithmetic mean values are below the lower limit of quantification (LLOQ). The LLOQ is 0.010 micrograms per milliliter.	
End point type	Secondary
End point timeframe: Pre-dose at weeks 0, 4, 12, 24, 36 and also at weeks 52 and 64 where no dosing was scheduled	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	0 ^[2]		
Units: microgram per milliliter (mg/mL)				
arithmetic mean (standard deviation)				
Week 0	0 (± 0)	()		
Week 4	25.881 (± 11.8828)	()		
Week 12	44.316 (± 19.0716)	()		
Week 24	49.093 (± 21.2414)	()		
Week 36	48.667 (± 22.2241)	()		
Week 52	52.659 (± 26.1703)	()		
Follow-up Week 64	6.602 (± 6.1832)	()		

Notes:

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

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Anti-Drug Antibody (ADA) response to Tezepelumab

End point title	Number of participants with Anti-Drug Antibody (ADA) response to Tezepelumab
End point description: Blood samples were measured for the presence of ADAs for tezepelumab using validated assays. Treatment-induced ADA positive was defined as ADA negative at baseline and post-baseline ADA positive. Treatment-boosted ADA positive was defined as baseline positive ADA titre that was boosted to a 4 fold or higher level following IP administration. TE-ADA positive was defined as the sum of treatment-induced ADA positive and treatment-boosted ADA positive. ADA incidence is the proportion of TE-ADA positive subjects in a population. ADA persistently positive was defined as ADA positive at ≥ 2 post-baseline assessments or ADA positive at last post-baseline assessment. ADA transiently positive was defined as having at least one post-baseline ADA positive assessment and not fulfilling the conditions of ADA persistently positive. Treatment-induced nAb positive was defined as nAb negative or ADA negative at baseline and nAb positive at any post-baseline visit.	

End point type	Secondary
End point timeframe:	
Pre-dose at weeks 0, 4, 12, 24, 36 and also at weeks 52 and 64 where no dosing was scheduled	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: Participants				
ADA positive at baseline and/or post-baseline	10	19		
Any baseline ADA positive	5	8		
Only baseline ADA positive	2	1		
Any post-baseline ADA positive	8	18		
Baseline and at least 1 post-baseline ADA positive	3	7		
Treatment-induced ADA positive	5	11		
Treatment-boosted ADA positive	0	0		
TE-ADA positive (ADA incidence)	5	11		
ADA persistently positive	5	15		
ADA transiently positive	3	3		
nAb positive at baseline and/or post-baseline	0	0		
Treatment-induced nAb positive (nAb incidence)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until end of study at Week 64.

Adverse event reporting additional description:

All AE data is based off the Safety Analysis Set, which includes all subjects who received at least one dose of study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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Reporting groups

Reporting group title	Teze 420 mg Q4W
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Reporting group description:

420 mg Tezepelumab injection delivered subcutaneously every 4 weeks up to maximum of 52 weeks (last dose given at week 48).

Reporting group title	Placebo
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Reporting group description:

Matching Placebo injection delivered subcutaneously every 4 weeks up to maximum of 52 weeks (last dose given at week 48).

Serious adverse events	Teze 420 mg Q4W	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	56 / 165 (33.94%)	58 / 168 (34.52%)	
number of deaths (all causes)	3	6	
number of deaths resulting from adverse events	3	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Non-small cell lung cancer			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma pancreas			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal melanoma			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma stage I			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma stage II			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung carcinoma cell type unspecified stage I			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal squamous cell carcinoma stage IV			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal adenocarcinoma stage IV			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Small cell lung cancer metastatic subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma of lung subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coeliac artery occlusion subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery dissection subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			

subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Vascular stent stenosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 165 (0.61%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	2 / 165 (1.21%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary artery thrombosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax spontaneous			

subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	20 / 165 (12.12%)	26 / 168 (15.48%)	
occurrences causally related to treatment / all	0 / 27	0 / 39	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			
subjects affected / exposed	2 / 165 (1.21%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gun shot wound			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Limb traumatic amputation			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pelvic fracture			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural dizziness			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pneumothorax			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
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 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Left ventricular failure			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			

subjects affected / exposed	2 / 165 (1.21%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angina pectoris			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 165 (0.61%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorder			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
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	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular extrasystoles			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	2 / 165 (1.21%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			

subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	2 / 165 (1.21%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood loss anaemia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Alcoholic pancreatitis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			

subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ileus			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (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	2 / 165 (1.21%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis alcoholic			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 165 (0.61%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery occlusion			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			

subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	1 / 165 (0.61%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Herpes zoster			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diverticulitis			
subjects affected / exposed	2 / 165 (1.21%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 165 (0.61%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 165 (1.21%)	3 / 168 (1.79%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (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			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (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	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	7 / 165 (4.24%)	5 / 168 (2.98%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	3 / 165 (1.82%)	3 / 168 (1.79%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pseudomonal			
subjects affected / exposed	1 / 165 (0.61%)	0 / 168 (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 / 165 (0.61%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas bronchitis			

subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 165 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Teze 420 mg Q4W	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 165 (47.27%)	56 / 168 (33.33%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	11 / 165 (6.67%)	10 / 168 (5.95%)	
occurrences (all)	12	12	
Contusion			
subjects affected / exposed	10 / 165 (6.06%)	0 / 168 (0.00%)	
occurrences (all)	11	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	12 / 165 (7.27%)	5 / 168 (2.98%)	
occurrences (all)	13	5	
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all)	9 / 165 (5.45%) 11	1 / 168 (0.60%) 1	
Headache subjects affected / exposed occurrences (all)	3 / 165 (1.82%) 4	10 / 168 (5.95%) 24	
General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all)	11 / 165 (6.67%) 11	8 / 168 (4.76%) 8	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	9 / 165 (5.45%) 10	4 / 168 (2.38%) 4	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	25 / 165 (15.15%) 26	16 / 168 (9.52%) 17	
Nasopharyngitis subjects affected / exposed occurrences (all)	17 / 165 (10.30%) 18	9 / 168 (5.36%) 9	
Urinary tract infection subjects affected / exposed occurrences (all)	5 / 165 (3.03%) 6	10 / 168 (5.95%) 12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 March 2022	Added "Tezepelumab has been well tolerated with an acceptable safety profile and no safety signals in subjects with severe, uncontrolled asthma identified in the completed studies to date." to Benefit/Risk Assessment. Added to Medical Devices: regarding sponsor manufactured medical device use in this study and all medical device deficiencies should be documented and reported by investigator through the study. Added definitions of medical device deficiency and requirements to fulfil regulatory reporting obligations worldwide and investigator's responsibility for detection and documentation of events meeting the definition of device deficiency occurring during the study. Added Appendix J - Medical device AEs, ADEs, SAEs, SADEs, US ADEs and Medical Device Deficiencies: Definitions and Procedures for Recording, Evaluating and Follow-up.
18 October 2022	Added serious cardiac events as an event requiring adjudication. Added that the IAC will assess whether there is a causal relationship between IP use and MACE events, serious cardiac events, and deaths. "Important potential risks" added including serious infections, malignancies, and serious cardiac events; "Potential risks" added including serious hypersensitivity reactions, and helminth infections; "Study procedures" added including COVID 19. Added new AESI: 'Serious cardiac events'. Removed "Injection Site reactions". Replaced "Anaphylactic reactions" and "Immune complex disease (Type III hypersensitivity reactions)" with "Serious hypersensitivity reactions". Replaced "Severe infections" and Opportunistic infections" with "Serious infections", and added a footnote clarifying when to complete the eCRF Severe infection pages.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported