



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 |
|-----------------------|-------------|

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 IWSR.

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 |
|------------------|---------|

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: 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: Proportion of participants COPD exacerbation free at Week 52

| | |
|------------------------|--|
| End point title | Proportion of participants COPD exacerbation free at Week 52 |
| 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 |
| 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: Comparison of annual severe COPD exacerbation rates over 52 weeks

| | |
|-----------------|---|
| End point title | Comparison of annual severe COPD exacerbation rates over 52 weeks |
|-----------------|---|

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 |
|----------------|-----------|

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 with ≥ 1 severe COPD exacerbations over 52 weeks

| | |
|-----------------|--|
| End point title | Proportion of participants with ≥ 1 severe COPD exacerbations over 52 weeks |
|-----------------|--|

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 |
|----------------|-----------|

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: 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: 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 |
| 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 |
| 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 |
|-----------------|---|

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 |
|----------------|-----------|

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: 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 |
|-----------------|---|

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 |
|----------------|-----------|

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: 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 |
|-----------------|--|

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 |
|----------------|-----------|

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: 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 |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | Teze 420 mg Q4W |
|-----------------------|-----------------|

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).

| 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