



## Clinical trial results:

### A Multicentre, Randomized, Double-Blind, Placebo Controlled, Phase 3 Study

### to Evaluate the Efficacy and Safety of Tezepelumab in Reducing Oral Corticosteroid Use in Adults with Oral Corticosteroid Dependent Asthma (SOURCE)

#### Summary

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

#### Results information

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

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | D5180C00009 |
|-----------------------|-------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | AstraZeneca AB   |
| Sponsor organisation address | 151 85, Sodertalje, Sweden,  |
| Public contact               | Global Clinical Head, AstraZeneca,<br>information.center@astrazeneca.com   |
| Scientific contact           | Global Clinical Head, AstraZeneca Clinical Study Information,<br>AstraZeneca, information.center@astrazeneca.com, +1 302<br>885 1180, information.center@astrazeneca.com |

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 25 September 2020 |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 25 September 2020 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

The protocol, protocol amendments, informed consent form (ICF), Investigator Brochure (IB), and other relevant documents (eg, advertisements) were submitted to an Institutional Review Board/Independent Ethics Committee (IRB/IEC) by the Investigator and reviewed and approved by the IRB/IEC before the study was initiated. The Investigator or his/her representative explained the nature of the study to the subject or his/her legally authorised representative and answered all questions regarding the study. Subjects were informed that their participation was voluntary. Subjects were required to sign a statement of informed consent that met the requirements of 21 CFR 31.23, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act (HIPAA) requirements, where applicable, and the IRB/IEC or study centre. The medical record must have included a statement that written informed consent was obtained before the subject was enrolled in the study and the date the written consent was obtained. The authorised person obtaining the informed consent must have also signed the ICF. Subjects must have been re-consented to the most current version of the ICF(s) during their participation in the study. A copy of the ICF(s) was provided to the subject.

Background therapy:

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

Evidence for comparator: -

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

Notes:

## Population of trial subjects

### Subjects enrolled per country

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

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

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 120 |
| From 65 to 84 years                       | 30  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

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

### Pre-assignment

Screening details:

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

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | Overall Study (overall period)                                |
| Is this the baseline period? | Yes   |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

### Arms

|                              |             |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes         |
| <b>Arm title</b>             | Tezepelumab |

Arm description:

Tezepelumab 210 mg administered every 4 weeks subcutaneously

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

Dosage and administration details:

210 mg Q4W

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

Placebo administered every 4 weeks subcutaneously

|  |   |
|--|---|
| Arm type                               | Placebo   |
| Investigational medicinal product name | Placebo administered every 4 weeks subcutaneously |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Solution for injection                            |
| Routes of administration               | Subcutaneous use                                  |

Dosage and administration details:

Q4W

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

## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Tezepelumab |
|-----------------------|-------------|

Reporting group description:

Tezepelumab 210 mg administered every 4 weeks subcutaneously

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo administered every 4 weeks subcutaneously

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

## End points

### End points reporting groups

|  |             |
|--|-------------|
| Reporting group title  | Tezepelumab |
| Reporting group description:<br>Tezepelumab 210 mg administered every 4 weeks subcutaneously |             |
| Reporting group title  | Placebo     |
| Reporting group description:<br>Placebo administered every 4 weeks subcutaneously            |             |

### Primary: Categorized percent reduction from baseline in the daily OCS dose while not losing asthma control

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

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

### Statistical analyses

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

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

### Secondary: Annualised asthma exacerbation rate (AAER)

|  |  |
|--|--|
| End point title  | Annualised asthma exacerbation rate (AAER) |
| End point description:   |  |
| The annualized exacerbation rate is based on exacerbations reported by the investigator in the eCRF over 48 weeks. |  |
| End point type   | Secondary                                  |
| End point timeframe:   |  |
| Baseline to Week 48  |  |

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

### Statistical analyses

No statistical analyses for this end point

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

|  |   |
|--|---|
| End point title  | Proportion of subjects with 100% reduction from baseline in daily OCS dose at Week 48 |
| End point description:   |   |
| Proportion of subjects with 100% reduction from baseline in daily OCS dose at Week 48. Percent change from baseline is defined as $\{(\text{final dose}-\text{baseline dose})/\text{baseline dose}\} \times 100$ . |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Baseline to Week 48  |   |



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

## Statistical analyses

No statistical analyses for this end point

### Secondary: Proportion of subjects with daily OCS dose $\leq 5$ mg at Week 48

|  |   |
|--|---|
| End point title  | Proportion of subjects with daily OCS dose ≤5 mg at Week 48 |
| End point description:<br>Proportion of subjects with daily OCS dose ≤5 mg at Week 48. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Week 48  |   |

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

## Statistical analyses

No statistical analyses for this end point

### Secondary: Proportion of subjects with $\geq 50\%$ reduction from baseline in daily OCS dose at Week 48

|   |   |
|---|---|
| End point title   | Proportion of subjects with ≥50% reduction from baseline in daily OCS dose at Week 48 |
| End point description:<br>Proportion of subjects with ≥50% reduction from baseline in daily OCS dose at Week 48. Percent change from baseline is defined as {(final dose-baseline dose)/baseline dose}*100. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Baseline to Week 48   |   |

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

## Statistical analyses

No statistical analyses for this end point

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

|                        |   |
|------------------------|---|
| End point title        | Change from baseline in pre-bronchodilator (pre-BD) forced expiratory volume in 1 second (FEV1)   |
| End point description: | Change from baseline in pre-BD FEV1 at Week 48. FEV1 is defined as the volume of air exhaled from the lungs in the first second of a forced expiration. |
| End point type         | Secondary   |
| End point timeframe:   | Baseline to Week 48   |

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

## Statistical analyses

No statistical analyses for this end point

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

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

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

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in weekly mean rescue medication use

|   |   |
|---|---|
| End point title   | Change from baseline in weekly mean rescue medication use |
| End point description:<br>Change from baseline in weekly mean rescue medication use at Week 48. Daily rescue medication use is defined as: Number of night inhaler puffs + 2 x [number of night nebulizer times] + number of daytime inhaler puffs + 2 x [number of day nebulizer times]. Each timepoint is calculated as weekly means based on daily diary data. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Baseline to Week 48   |   |

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

## Statistical analyses

No statistical analyses for this end point

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

|   |   |
|---|---|
| End point title   | Change from baseline in weekly mean home peak expiratory flow (PEF) (morning and evening) |
| End point description:<br>Change from baseline in weekly mean morning and evening peak expiratory flow (PEF) at Week 48. Home PEF testing will be performed by the subject in the morning upon awakening and in the evening at bedtime using an electronic, hand-held spirometer. Each timepoint is calculated as weekly means. |   |
| End point type  | Secondary   |

End point timeframe:

Baseline to Week 48

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 48

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Change from baseline in ACQ-6 at Week 48. The ACQ-6 captures asthma symptoms and short-acting  $\beta_2$ -agonist use via subject-report. Questions are weighted equally and scored from 0 (totally controlled) to 6 (severely uncontrolled). The ACQ-6 score is the mean of the responses.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 48

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

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 48

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

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 48

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

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of asthma specific resource utilizations**

|                 |   |
|-----------------|---|
| End point title | Number of asthma specific resource utilizations |
|-----------------|---|

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 48

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

## Statistical analyses

No statistical analyses for this end point

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

|  |   |
|--|---|
| End point title  | Change from baseline in Work Productivity and Activity Impairment Questionnaire and Classroom Impairment Questionnaire (WPAI+CIQ) score |
| End point description:<br>Change from baseline in WPAI+CIQ score at Week 48. The WPAI+CIQ consists of questions about how asthma and asthma related issues impact a subject's ability to work, attend classes, and perform regular daily activities. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Baseline to Week 48  |   |

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

Notes:

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

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in FENO

|  |                              |
|--|------------------------------|
| End point title  | Change from baseline in FENO |
| End point description:<br>Change from baseline in fractional exhaled nitric oxide (FeNO) at week 48. |                              |
| End point type   | Secondary                    |
| End point timeframe:<br>Baseline to Week 48  |                              |

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

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in peripheral blood eosinophils

|                        |   |
|------------------------|---|
| End point title        | Change from baseline in peripheral blood eosinophils        |
| End point description: | Change from baseline in blood eosinophil counts at week 48. |
| End point type         | Secondary   |
| End point timeframe:   |   |
| Baseline to Week 48    |   |

| End point values                    | Tezepelumab            | Placebo               |  |  |
|-------------------------------------|------------------------|-----------------------|--|--|
| Subject group type                  | Reporting group        | Reporting group       |  |  |
| Number of subjects analysed         | 63                     | 67                    |  |  |
| Units: cells/ $\mu$ L               |                        |                       |  |  |
| least squares mean (standard error) | -83.79 ( $\pm$ 17.078) | 33.38 ( $\pm$ 16.605) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline from total serum IgE

|                        |   |
|------------------------|---|
| End point title        | Change from baseline from total serum IgE           |
| End point description: | Change from baseline in total serum IgE at week 48. |
| End point type         | Secondary   |
| End point timeframe:   |   |
| Baseline to Week 48    |   |



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

## Statistical analyses

No statistical analyses for this end point

## Secondary: PK: Serum trough concentrations

|                        |   |
|------------------------|---|
| End point title        | PK: Serum trough concentrations                               |
| End point description: | Serum trough concentrations at each scheduled visit.          |
| End point type         | Secondary   |
| End point timeframe:   | Baseline, Week 4, Week 12, Week 24, Week 40, Week 48, Week 60 |

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

Notes:

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

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 60

| End point values                                      | Tezepelumab     | Placebo         |  |  |
|---|-----------------|-----------------|--|--|
| Subject group type                                    | Reporting group | Reporting group |  |  |
| Number of subjects analysed                           | 74              | 76              |  |  |
| Units: Participants                                   |                 |                 |  |  |
| ADA positive at baseline and/or post-baseline         | 3               | 2               |  |  |
| Any baseline ADA positive                             | 2               | 2               |  |  |
| Only baseline ADA positive                            | 1               | 1               |  |  |
| Any post-baseline ADA positive                        | 2               | 1               |  |  |
| Both baseline and $\geq 1$ post-baseline ADA positive | 1               | 1               |  |  |
| Treatment-induced ADA positive                        | 1               | 0               |  |  |
| Treatment-boosted ADA positive                        | 0               | 0               |  |  |
| TE-ADA positive (ADA incidence)                       | 1               | 0               |  |  |
| ADA persistently positive                             | 1               | 1               |  |  |
| ADA transiently positive                              | 1               | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until last study visit

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo administered subcutaneously

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | Teze 210 mg Q4W |
|-----------------------|-----------------|

Reporting group description:

Tezepelumab administered every 4 weeks subcutaneously

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

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

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

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

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

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

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

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



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

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

Notes: