



Clinical trial results:

A Phase 2a, Randomized, Double-blind, Placebo-controlled, Parallel-arm, Multicenter Study to Evaluate the Efficacy and Safety of CAT-354, a Recombinant Human Monoclonal Antibody Directed against Interleukin-13 (IL-13), on Asthma Control in Adults with Uncontrolled, Moderate-to-severe, Persistent Asthma

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2008-007844-33 |
| Trial protocol | DE GB BG |
| Global end of trial date | 03 August 2010 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 11 May 2016 |
| First version publication date | 11 May 2016 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | MI-CP199 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00873860 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | MedImmune, LLC |
| Sponsor organisation address | Milstein Building, Granta Park, Cambridge, United Kingdom, CB21 6GH |
| Public contact | Rene van de Merwe, Senior Director, Clinical Development, MedImmune, LLC., vandermerwer@medimmune.com |
| Scientific contact | Rene van de Merwe, Senior Director, Clinical Development, MedImmune, LLC., vandermerwer@medimmune.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 | 03 August 2010 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 03 August 2010 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effect of 3 subcutaneous (SC) treatment regimens of CAT-354 versus placebo on asthma control at Study Day 92 in adults with uncontrolled, moderate-to-severe, persistent asthma.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating participant signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 04 June 2009 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Poland: 37 |
| Country: Number of subjects enrolled | Romania: 77 |
| Country: Number of subjects enrolled | Bulgaria: 52 |
| Country: Number of subjects enrolled | Germany: 21 |
| Country: Number of subjects enrolled | United Kingdom: 7 |
| Worldwide total number of subjects | 194 |
| EEA total number of subjects | 194 |

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) | 194 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 357 participants were screened in this study, out of which 194 participants were enrolled and randomized.

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 |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Placebo matched to CAT-354 subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85.

| | |
|--|----------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo matched to CAT-354 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received Placebo matched to CAT-354 subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85.

| | |
|------------------|----------------|
| Arm title | CAT-354 150 mg |
|------------------|----------------|

Arm description:

CAT-354 150 milligram (mg) subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | CAT-354 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received CAT-354 150 mg subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85.

| | |
|------------------|----------------|
| Arm title | CAT-354 300 mg |
|------------------|----------------|

Arm description:

CAT-354 300 mg subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|------------------------|
| Investigational medicinal product name | CAT-354 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received CAT-354 300 mg subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85.

| | |
|------------------|----------------|
| Arm title | CAT-354 600 mg |
|------------------|----------------|

Arm description:

CAT-354 600 mg subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | CAT-354 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received CAT-354 600 mg subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85.

| Number of subjects in period 1 | Placebo | CAT-354 150 mg | CAT-354 300 mg |
|---------------------------------------|---------|----------------|----------------|
| Started | 48 | 47 | 51 |
| Treated | 47 | 47 | 51 |
| Completed | 44 | 47 | 48 |
| Not completed | 4 | 0 | 3 |
| Adverse event, serious fatal | 1 | - | - |
| Consent withdrawn by subject | 1 | - | 2 |
| Unspecified | 1 | - | 1 |
| Lost to follow-up | 1 | - | - |

| Number of subjects in period 1 | CAT-354 600 mg |
|---------------------------------------|----------------|
| Started | 48 |
| Treated | 48 |
| Completed | 47 |
| Not completed | 1 |
| Adverse event, serious fatal | - |
| Consent withdrawn by subject | - |
| Unspecified | - |
| Lost to follow-up | 1 |

Baseline characteristics

Reporting groups

| | |
|--|----------------|
| Reporting group title | Placebo |
| Reporting group description: Placebo matched to CAT-354 subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85. | |
| Reporting group title | CAT-354 150 mg |
| Reporting group description: CAT-354 150 milligram (mg) subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85. | |
| Reporting group title | CAT-354 300 mg |
| Reporting group description: CAT-354 300 mg subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85. | |
| Reporting group title | CAT-354 600 mg |
| Reporting group description: CAT-354 600 mg subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85. | |

| Reporting group values | Placebo | CAT-354 150 mg | CAT-354 300 mg |
|--|---------|----------------|----------------|
| Number of subjects | 48 | 47 | 51 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 48 | 47 | 51 |
| Age Continuous Units: years | | | |
| arithmetic mean | 47.2 | 43.4 | 48.7 |
| standard deviation | ± 9.8 | ± 11.1 | ± 11 |
| Gender, Male/Female Units: participants | | | |
| Female | 33 | 19 | 36 |
| Male | 15 | 28 | 15 |

| Reporting group values | CAT-354 600 mg | Total | |
|--|----------------|-------|--|
| Number of subjects | 48 | 194 | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 48 | 194 | |
| Age Continuous Units: years | | | |
| arithmetic mean | 49.8 | - | |
| standard deviation | ± 10.4 | - | |
| Gender, Male/Female Units: participants | | | |
| Female | 28 | 116 | |
| Male | 20 | 78 | |

End points

End points reporting groups

| | |
|--|----------------|
| Reporting group title | Placebo |
| Reporting group description: Placebo matched to CAT-354 subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85. | |
| Reporting group title | CAT-354 150 mg |
| Reporting group description: CAT-354 150 milligram (mg) subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85. | |
| Reporting group title | CAT-354 300 mg |
| Reporting group description: CAT-354 300 mg subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85. | |
| Reporting group title | CAT-354 600 mg |
| Reporting group description: CAT-354 600 mg subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85. | |

Primary: Change From Baseline in the Mean Asthma Control Questionnaire (ACQ) Score at Day 92

| | |
|---|---|
| End point title | Change From Baseline in the Mean Asthma Control Questionnaire (ACQ) Score at Day 92 |
| End point description: ACQ is a participant-reported questionnaire to assess the asthma control with 6 items assessing night-time waking, symptoms on waking, activity limitation, shortness of breath, wheeze, and rescue short-acting beta agonist use. Each item was rated on a 7-point Likert scale ranging from 0 (no impairment) to 6 (maximum impairment). Overall ACQ score is the mean of the 6 item scores with a score range of 0 (well controlled) to 6 (extremely poor controlled). Data collected on Day 1 prior to dosing was considered as baseline. Results were reported for overall ACQ score. Evaluable population included all participants who received at least 4 doses of investigational product or received at least 1 dose but discontinued prior to receiving 4 doses due to safety reasons. Here, 'n' signifies those participants who were evaluable for this measure at specified time points for each arm, respectively. | |
| End point type | Primary |
| End point timeframe: Day 1 (baseline), Day 92 | |

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|--------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 46 | 51 | 47 |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (n=46, 46, 50, 47) | 2.63 (± 0.51) | 2.72 (± 0.58) | 2.62 (± 0.5) | 2.72 (± 0.76) |
| Change at Day 92 (n= 46, 46, 51, 47) | -0.61 (± 0.9) | -0.73 (± 1.12) | -0.7 (± 0.93) | -0.86 (± 1.09) |

Statistical analyses

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Placebo v CAT-354 150 mg |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.573 ^[1] |
| Method | ANOVA |

Notes:

[1] - Change at Day 92: p-value was based on analysis of variance (ANOVA).

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 2 |
| Comparison groups | Placebo v CAT-354 300 mg |
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.64 ^[2] |
| Method | ANOVA |

Notes:

[2] - Change at Day 92: p-value was based on ANOVA.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 3 |
| Comparison groups | Placebo v CAT-354 600 mg |
| Number of subjects included in analysis | 93 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.224 ^[3] |
| Method | ANOVA |

Notes:

[3] - Change at Day 92: p-value was based on ANOVA.

Secondary: Time to First Observed Asthma Control

| | |
|-----------------|---------------------------------------|
| End point title | Time to First Observed Asthma Control |
|-----------------|---------------------------------------|

End point description:

Time to first asthma control defined as number of days from Study Day 1 to the post-baseline ACQ score measurement time point when greater than or equal to (\geq) 0.5 reduction from baseline in mean ACQ score was first observed. Time to first asthma control was analyzed from Day 1 through Day 92 and up to entire study duration through Day 169. The ACQ score is a participant-reported questionnaire to assess the asthma control with 6 items assessing night-time waking, symptoms on waking, activity limitation, shortness of breath, wheeze, and rescue short-acting beta agonist use. Each item was rated on 7-point Likert scale ranging from 0 (no impairment) to 6 (maximum impairment). Overall ACQ score is the mean of the 6 item scores with a score range of 0 (well controlled) to 6 (extremely poor controlled). Evaluable population included all participants who received at least 4 doses of investigational product or received at least 1 dose but discontinued treatment due to safety reasons.

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

End point timeframe:

Day 1 to Day 92 and Day 169

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 46 | 51 | 47 |
| Units: days | | | | |
| median (confidence interval 95%) | | | | |
| Day 1 to 92 | 25.5 (15 to 71) | 22 (15 to 43) | 15 (15 to 43) | 15 (15 to 36) |
| Day 1 to 169 | 25.5 (15 to 71) | 22 (15 to 43) | 15 (15 to 43) | 15 (15 to 36) |

Statistical analyses

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Placebo v CAT-354 150 mg |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4686 ^[4] |
| Method | Logrank |

Notes:

[4] - Day 1 to 92: P-value was calculated against placebo group from a stratified log-rank test with atopic asthma status and tertile of baseline mean ACQ score as the stratification factors.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 2 |
| Comparison groups | Placebo v CAT-354 300 mg |
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.317 ^[5] |
| Method | Logrank |

Notes:

[5] - Day 1 to 92: P-value was calculated against placebo group from a stratified log-rank test with atopic asthma status and tertile of baseline mean ACQ score as the stratification factors.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 3 |
| Comparison groups | Placebo v CAT-354 600 mg |
| Number of subjects included in analysis | 93 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1664 ^[6] |
| Method | Logrank |

Notes:

[6] - Day 1 to 92: P-value was calculated against placebo group from a stratified log-rank test with atopic asthma status and tertile of baseline mean ACQ score as the stratification factors.

| | |
|-----------------------------------|--------------------------|
| Statistical analysis title | Statistical analysis 4 |
| Comparison groups | Placebo v CAT-354 150 mg |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3234 ^[7] |
| Method | Logrank |

Notes:

[7] - Day 1 to 169: P-value was calculated against placebo group from a stratified log-rank test with atopic asthma status and tertile of baseline mean ACQ score as the stratification factors.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 5 |
| Comparison groups | Placebo v CAT-354 300 mg |
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3133 ^[8] |
| Method | Logrank |

Notes:

[8] - Day 1 to 169: P-value was calculated against placebo group from a stratified log-rank test with atopic asthma status and tertile of baseline mean ACQ score as the stratification factors.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 6 |
| Comparison groups | Placebo v CAT-354 600 mg |
| Number of subjects included in analysis | 93 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2108 ^[9] |
| Method | Logrank |

Notes:

[9] - Day 1 to 169: P-value was calculated against placebo group from a stratified log-rank test with atopic asthma status and tertile of baseline mean ACQ score as the stratification factors.

Secondary: Change from Baseline in Forced Expiratory Volume in 1 Second (FEV1) Recorded at Study Sites at Day 1, 15, 29, 43, 57, 71, 85, 92, 127 and 169

| | |
|-----------------|---|
| End point title | Change from Baseline in Forced Expiratory Volume in 1 Second (FEV1) Recorded at Study Sites at Day 1, 15, 29, 43, 57, 71, 85, 92, 127 and 169 |
|-----------------|---|

End point description:

FEV1 is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. Spirometry was performed with the participant in the sitting/standing (kept consistent at each visit) position at study sites by the investigator or qualified designee according to American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines. Multiple forced expiratory efforts (at least 3 but no more than 8) were performed for each office spirometry session and the 2 best efforts that met ATS/ERS acceptability and reproducibility criteria were recorded. The best efforts were based on the highest FEV1. The maximum FEV1 of the 2 best efforts was used for the analysis. Evaluable population included all participants who received at least 4 doses of investigational product or received at least 1 dose but discontinued treatment due to safety reasons. Here, "n" signifies participants evaluable for specified category for each arm, respectively.

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

End point timeframe:

Day 1 (baseline), 15, 29, 43, 57, 71, 85, 92, 127 and 169

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|--------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 46 | 51 | 47 |
| Units: liters | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (n=46,46,51,47) | 1.949 (± 0.479) | 2.178 (± 0.661) | 1.907 (± 0.586) | 1.977 (± 0.646) |
| Change at Day 15 (n=44,46,50,46) | 0.019 (± 0.42) | 0.122 (± 0.316) | 0.116 (± 0.378) | 0.134 (± 0.348) |
| Change at Day 29 (n=46,46,49,47) | 0.051 (± 0.424) | 0.138 (± 0.315) | 0.149 (± 0.303) | 0.222 (± 0.354) |
| Change at Day 43 (n=45,44,47,47) | 0.125 (± 0.399) | 0.131 (± 0.38) | 0.164 (± 0.358) | 0.147 (± 0.373) |
| Change at Day 57 (n=45,46,49,47) | 0.043 (± 0.436) | 0.127 (± 0.339) | 0.187 (± 0.349) | 0.201 (± 0.344) |
| Change at Day 71 (n=45,45,49,47) | 0.047 (± 0.397) | 0.158 (± 0.314) | 0.179 (± 0.381) | 0.19 (± 0.335) |
| Change at Day 85 (n=45,46,48,47) | 0.087 (± 0.397) | 0.135 (± 0.342) | 0.286 (± 0.393) | 0.265 (± 0.473) |
| Change at Day 92 (n=42,44,49,44) | 0.063 (± 0.476) | 0.158 (± 0.348) | 0.211 (± 0.374) | 0.262 (± 0.408) |
| Change at Day 127 (n=44,44,49,47) | 0.094 (± 0.489) | 0.144 (± 0.263) | 0.241 (± 0.381) | 0.237 (± 0.285) |
| Change at Day 169 (n=42,42,47,47) | 0.101 (± 0.442) | 0.204 (± 0.378) | 0.211 (± 0.394) | 0.236 (± 0.366) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Peak Expiratory Flow (PEF) Recorded at Home Every Week From Day 1 to 169

| | |
|-----------------|--|
| End point title | Change From Baseline in Peak Expiratory Flow (PEF) Recorded at Home Every Week From Day 1 to 169 |
|-----------------|--|

End point description:

The PEF is a participant's maximum speed of expiration, as measured with a peak flow meter. Home peak flow testing for PEF was performed every morning while sitting or standing prior to using any medication (if needed) for asthma. Mean of the data was collected over 1 week prior to dosing on Day 1 was considered as baseline. Mean PEF values for each week were used to calculate the change from baseline values starting from Day 2 to 169. Evaluable population included all participants who received at least 4 doses of investigational product or received at least 1 dose but discontinued treatment due to safety reasons. Here, 'n' signifies those participants who were evaluable for this measure at specified time points for each group, respectively.

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

End point timeframe:

Day -7 to 1 (predose), Day 2 to 169

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|--|-------------------|-------------------|-------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 46 | 51 | 47 |
| Units: liters/minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day -7 to 1 (n=46,46,51,47) | 282.63 (± 100.65) | 351.06 (± 130.41) | 291.54 (± 119.46) | 325.23 (± 123.9) |
| Change in Day 2 to 8 (n=44,46,51,47) | -5.77 (± 22.74) | 1.91 (± 23.81) | -4.53 (± 19.02) | 5.94 (± 29.93) |
| Change in Day 9 to 15 (n=45,46,51,47) | -7.46 (± 29.68) | -4.1 (± 28.15) | -2.83 (± 24.4) | 5.75 (± 42.34) |
| Change in Day 16 to 22 (n=45,46,51,47) | -8.94 (± 35.72) | -6.53 (± 32.7) | -0.37 (± 33.85) | 10.55 (± 51.26) |
| Change in Day 23 to 29 (n=44,46,51,47) | -10.53 (± 40.06) | -6.61 (± 37.95) | -0.79 (± 36.94) | 10.61 (± 52.64) |
| Change in Day 30 to 36 (n=45,46,51,47) | -5.69 (± 44.69) | -5.69 (± 41.87) | -1.98 (± 36.06) | 6.52 (± 50.15) |
| Change in Day 37 to 43 (n=44,46,50,47) | -11.08 (± 41.52) | -2 (± 49.76) | -4.07 (± 39.8) | 5.55 (± 54.28) |
| Change in Day 44 to 50 (n=44,46,50,47) | -6.37 (± 41.5) | -9.02 (± 47.51) | -5.3 (± 36.57) | -0.84 (± 50.67) |
| Change in Day 51 to 57 (n=45,46,50,47) | -7 (± 41.7) | -6.01 (± 47.36) | -4.85 (± 41.27) | -3.57 (± 52.84) |
| Change in Day 58 to 64 (n=45,46,50,46) | -9.84 (± 38.73) | -2.83 (± 47.42) | -1.42 (± 41.9) | -0.73 (± 55.98) |
| Change in Day 65 to 71 (n=45,46,50,46) | -11.81 (± 43.87) | -3.98 (± 47.2) | -0.92 (± 49.95) | -1.82 (± 49.79) |
| Change in Day 72 to 78 (n=44,45,50,47) | -3.72 (± 44.07) | -3.42 (± 53.55) | 2.54 (± 45.58) | 1.78 (± 49.45) |
| Change in Day 79 to 85 (n=45,45,50,46) | -10.83 (± 43.99) | -6.67 (± 54.49) | -0.35 (± 40.29) | 5.3 (± 60.62) |
| Change in Day 86 to 92 (n=45,46,50,47) | -3.26 (± 47.36) | -6.66 (± 51.23) | 5.04 (± 40.52) | 0.31 (± 62.86) |
| Change in Day 93 to 99 (n=45,46,50,47) | -2.52 (± 47.94) | -4.99 (± 49.91) | 5.16 (± 40.99) | 7.81 (± 58.29) |
| Change in Day 100 to 106 (n=44,46,49,47) | -9.6 (± 55.47) | -7.33 (± 52.64) | 1.93 (± 43.08) | 2 (± 62.18) |
| Change in Day 107 to 113 (n=44,45,48,47) | -7.53 (± 56.29) | -11.29 (± 57.33) | 0.53 (± 45.6) | 0.39 (± 61.52) |
| Change in Day 114 to 120 (n=42,45,47,47) | -2.19 (± 61.74) | -8.97 (± 55.61) | 4.85 (± 39.54) | -3.03 (± 59.68) |
| Change in Day 121 to 127 (n=42,46,46,46) | -3.58 (± 65.64) | -8.99 (± 64.6) | 3.61 (± 46.18) | -4.21 (± 57.88) |
| Change in Day 128 to 134 (n=42,45,45,47) | -4.39 (± 61.22) | -14.81 (± 61.39) | 4.62 (± 44.65) | -2.64 (± 56.87) |
| Change in Day 135 to 141 (n=40,45,47,47) | -0.26 (± 58.83) | -17.03 (± 58.99) | 1.11 (± 44.36) | -6.03 (± 63.13) |
| Change in Day 142 to 148 (n=40,45,47,47) | 5.16 (± 66.54) | -11.63 (± 61.02) | -2.69 (± 51.65) | -9.65 (± 65.62) |
| Change in Day 149 to 155 (n=40,45,46,47) | 0.43 (± 60.53) | -9.56 (± 60.13) | -7.65 (± 47.44) | -11.07 (± 62.16) |
| Change in Day 156 to 162 (n=40,45,46,46) | -1.38 (± 65.53) | -11.6 (± 62.14) | -10.05 (± 43.11) | -10.68 (± 66.86) |
| Change in Day 163 to 169 (n=37,41,42,40) | -0.36 (± 58.66) | -5.68 (± 60.69) | -4.71 (± 49.29) | -3.23 (± 66.84) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Puffs of Rescue Beta-2 Agonist Per Week

| | |
|--|---|
| End point title | Number of Puffs of Rescue Beta-2 Agonist Per Week |
| End point description: | |
| Number of Puffs of Rescue Beta-2 Agonist Per Week Rescue beta-2 agonist use (total number of puffs for the preceding week) was collected daily in the morning by the participants in the daily diary provided to them. Average values for each week were reported starting from Day -7 to Day 169. Evaluable population included all participants who received at least 4 doses of investigational product or received at least 1 dose but discontinued treatment due to safety reasons. Here, 'n' signifies those participants who were evaluable for this measure at specified time points for each group, respectively. | |
| End point type | Secondary |
| End point timeframe: | |
| Day -7 to 169 | |

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|--------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 46 | 51 | 47 |
| Units: puffs per week | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day -7 to 1 (n=46,46, 51,47) | 2.58 (± 1.7) | 2.84 (± 2.03) | 2.04 (± 1.51) | 2.62 (± 1.96) |
| Day 2 to 8 (n=45,46, 51,47) | 2.5 (± 1.8) | 2.4 (± 2) | 1.9 (± 1.5) | 2.3 (± 2) |
| Day 9 to 15 (n=46,46, 51,47) | 2.4 (± 1.8) | 2.5 (± 2.3) | 1.9 (± 1.5) | 2.2 (± 2) |
| Day 16 to 22 (n=46,46, 51,47) | 2.6 (± 1.9) | 2.2 (± 2) | 1.9 (± 1.7) | 2.3 (± 2.2) |
| Day 23 to 29 (n=45,46, 51,47) | 2.7 (± 2.1) | 2.2 (± 2) | 2 (± 1.9) | 2.2 (± 2.1) |
| Day 30 to 36 (n=46,46, 51,47) | 2.5 (± 2) | 2.1 (± 2.2) | 1.9 (± 2) | 2 (± 1.9) |
| Day 37 to 43 (n=45,46, 50,47) | 2.4 (± 2) | 2.1 (± 2.2) | 1.9 (± 2) | 2 (± 2) |
| Day 44 to 50 (n=45,46, 50,47) | 2.5 (± 2) | 1.9 (± 2.2) | 1.7 (± 2) | 2 (± 2) |
| Day 51 to 57 (n=45,46, 50,47) | 2.5 (± 2.1) | 2 (± 2) | 1.8 (± 1.9) | 2 (± 2.1) |
| Day 58 to 64 (n=46,46, 49,46) | 2.5 (± 2.2) | 1.9 (± 2) | 1.9 (± 2) | 1.8 (± 2) |
| Day 65 to 71 (n=46,46, 50,47) | 2.7 (± 2.3) | 2 (± 2) | 1.8 (± 2) | 2 (± 1.9) |
| Day 72 to 78 (n=45,45, 50,46) | 2.5 (± 2.2) | 2 (± 2) | 1.8 (± 2.1) | 1.9 (± 1.8) |
| Day 79 to 85 (n=46,46, 50,46) | 2.6 (± 2.3) | 2.1 (± 2.1) | 1.9 (± 2) | 1.8 (± 1.8) |
| Day 86 to 92 (n=46,46, 50,47) | 2.5 (± 2.3) | 2 (± 2.1) | 1.8 (± 2) | 1.7 (± 1.7) |
| Day 93 to 99 (n=46,46, 50,47) | 2.4 (± 2.2) | 1.7 (± 2) | 1.8 (± 2.1) | 1.6 (± 1.8) |
| Day 100 to 106 (n=45,46, 49,47) | 2.3 (± 2.1) | 1.9 (± 2.2) | 1.7 (± 2.2) | 1.8 (± 1.8) |
| Day 107 to 113 (n=45,45, 48,47) | 2.4 (± 2.1) | 1.9 (± 2.2) | 1.7 (± 1.9) | 1.7 (± 1.6) |
| Day 114 to 120 (n=43,45, 47,47) | 2.3 (± 2) | 1.9 (± 2.1) | 1.7 (± 1.9) | 1.7 (± 1.7) |
| Day 121 to 127 (n=43,46, 46,47) | 2.2 (± 1.9) | 1.9 (± 2.2) | 1.8 (± 2) | 1.6 (± 1.6) |
| Day 128 to 134 (n=44,45, 47,47) | 2.2 (± 2.1) | 1.8 (± 2) | 1.6 (± 1.9) | 1.6 (± 1.7) |
| Day 135 to 141 (n=42,45, 47,47) | 2.2 (± 2) | 1.9 (± 1.9) | 1.7 (± 2) | 1.7 (± 1.8) |
| Day 142 to 148 (n=42,45, 47,47) | 2.3 (± 2) | 1.9 (± 2.1) | 1.8 (± 2) | 1.8 (± 1.8) |
| Day 149 to 155 (n=42,45, 46,47) | 2.4 (± 2.2) | 1.9 (± 2.1) | 1.8 (± 2) | 1.8 (± 1.8) |
| Day 156 to 162 (n=42,45, 46,46) | 2.3 (± 2.1) | 1.9 (± 2.1) | 1.7 (± 2.2) | 2 (± 2) |
| Day 163 to 169 (n=39,41,42,40) | 2.7 (± 2.6) | 1.9 (± 2.1) | 1.6 (± 1.8) | 1.7 (± 1.9) |

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma Quality of Life Questionnaire (Standardized Version) (AQLQ[S]) Scores

| | |
|---|--|
| End point title | Asthma Quality of Life Questionnaire (Standardized Version) (AQLQ[S]) Scores |
| End point description: | |
| <p>AQLQ[S]: a 32-item questionnaire that measures the functional impairments experienced by adult participants including 4 domains (Symptoms, Activity Limitations, Emotional Function, and Environmental Stimuli). Participants were asked to recall their experiences during the previous 2 weeks and to score each of the 32 questions on a 7-point scale ranging from 7 (no impairment) to 1 (severe impairment). The overall score was calculated as the mean response to all questions. The 4 domain scores were the means of the responses to the questions in each of the domains. Overall AQLQ score and 4 domain scores ranged from 7 (no impairment) to 1 (severe impairment). Evaluable population included all participants who received at least 4 doses of investigational product or received at least 1 dose but discontinued treatment due to safety reasons. Here, 'n' signifies those participants who were evaluable for this measure at specified time points for each group, respectively.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Day 1, 29, 57, 92, 127 and 169 | |

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|---|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 46 | 51 | 47 |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Overall : Day 1 (n=41,41,44,39) | 4.22 (± 0.83) | 3.96 (± 0.89) | 4.12 (± 0.8) | 4.11 (± 0.94) |
| Overall: Day 29 (n=43,41,44,40) | 4.39 (± 1.04) | 4.39 (± 1.01) | 4.47 (± 0.97) | 4.6 (± 0.91) |
| Overall: Day 57 (n=44,40,43,45) | 4.57 (± 1.03) | 4.56 (± 1.15) | 4.47 (± 1.05) | 4.73 (± 0.96) |
| Overall: Day 92 (n=40,42,40,38) | 4.7 (± 1.16) | 4.88 (± 1.31) | 4.74 (± 1.15) | 4.87 (± 0.99) |
| Overall: Day 127 (n=41,42,44,42) | 4.69 (± 1.22) | 4.76 (± 1.29) | 4.64 (± 1.11) | 4.85 (± 1.13) |
| Overall: Day 169 (n=41,44,45,44) | 4.72 (± 1.29) | 4.73 (± 1.26) | 4.61 (± 1.27) | 4.76 (± 1.13) |
| Symptom: Day 1 (n=41,41,44,39) | 4.15 (± 0.88) | 3.89 (± 0.84) | 4.11 (± 0.71) | 4.08 (± 1.06) |
| Symptom: Day 29 (n=43,41,44,40) | 4.32 (± 1.08) | 4.44 (± 1.07) | 4.48 (± 0.94) | 4.56 (± 1.01) |
| Symptom: Day 57 (n=44,40,43,45) | 4.61 (± 1.02) | 4.68 (± 1.23) | 4.49 (± 1.05) | 4.73 (± 1.05) |
| Symptom: Day 92 (n=40,42,40,38) | 4.77 (± 1.17) | 4.88 (± 1.4) | 4.78 (± 1.17) | 4.92 (± 1.01) |
| Symptom: Day 127 (n=41,42,44,42) | 4.74 (± 1.33) | 4.79 (± 1.31) | 4.69 (± 1.09) | 4.95 (± 1.31) |
| Symptom: Day 169 (n=41,44,45,44) | 4.82 (± 1.3) | 4.76 (± 1.29) | 4.63 (± 1.26) | 4.77 (± 1.31) |
| Activity Limitation: Day 1 (n=41,41,44,39) | 4.38 (± 0.83) | 4.07 (± 0.88) | 4.13 (± 0.97) | 4.15 (± 0.91) |
| Activity Limitation: Day 29 (n=43,41,44,40) | 4.47 (± 1) | 4.37 (± 1.07) | 4.42 (± 1.08) | 4.59 (± 0.92) |

| | | | | |
|---|---------------|---------------|---------------|---------------|
| Activity Limitation: Day 57 (n=44,40,43,45) | 4.57 (± 1.03) | 4.42 (± 1.09) | 4.41 (± 1.14) | 4.74 (± 0.99) |
| Activity Limitation: Day 92 (n=40,42,40,38) | 4.68 (± 1.19) | 4.89 (± 1.29) | 4.73 (± 1.15) | 4.91 (± 1.04) |
| Activity Limitation: Day 127 (n=41,42,44,42) | 4.64 (± 1.2) | 4.77 (± 1.32) | 4.62 (± 1.13) | 4.66 (± 1.08) |
| Activity Limitation: Day 169 (n=41,44,45,44) | 4.68 (± 1.28) | 4.76 (± 1.26) | 4.54 (± 1.31) | 4.7 (± 1.14) |
| Emotional Function: Day 1 (n=41,41,44,39) | 4.3 (± 1.08) | 4.2 (± 1.18) | 4.45 (± 1.1) | 4.29 (± 1.24) |
| Emotional Function: Day 29 (n=43,41,44,40) | 4.64 (± 1.27) | 4.82 (± 1.17) | 4.82 (± 1.22) | 4.88 (± 1.17) |
| Emotional Function: Day 57 (n=44,40,43,45) | 4.85 (± 1.36) | 4.98 (± 1.42) | 4.87 (± 1.24) | 4.99 (± 1.13) |
| Emotional Function: Day 92 (n=40,42,40,38) | 5 (± 1.31) | 5.24 (± 1.33) | 4.99 (± 1.45) | 4.98 (± 1.02) |
| Emotional Function: Day 127 (n=41,42,44,42) | 5.08 (± 1.4) | 5.06 (± 1.48) | 4.98 (± 1.4) | 5.28 (± 1.29) |
| Emotional Function: Day 169 (n=41,44,45,44) | 5.05 (± 1.56) | 5 (± 1.5) | 5.06 (± 1.39) | 5.13 (± 1.28) |
| Environment stimuli: Day 1 (n=41,41,44,39) | 3.88 (± 1.28) | 3.55 (± 1.43) | 3.7 (± 1.11) | 3.85 (± 1.1) |
| Environment stimuli: Day 29 (n=43,41,44,40) | 4.06 (± 1.26) | 3.75 (± 1.48) | 4.13 (± 1.41) | 4.4 (± 1.2) |
| Environment stimuli: Day 57 (n=44,40,43,45) | 4.07 (± 1.34) | 4.04 (± 1.36) | 4.09 (± 1.43) | 4.37 (± 1.49) |
| Environment stimuli: Day 92 (n=40,42,40,38) | 4.16 (± 1.56) | 4.44 (± 1.63) | 4.31 (± 1.43) | 4.47 (± 1.47) |
| Environment stimuli: Day 127 (n=41,42,44,42) | 4.18 (± 1.58) | 4.3 (± 1.57) | 4.15 (± 1.56) | 4.51 (± 1.64) |
| Environment stimuli: Day 169 (n=41,44,45,44) | 4.13 (± 1.54) | 4.26 (± 1.5) | 4.18 (± 1.76) | 4.45 (± 1.51) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Asthma Quality of Life Questionnaire (Standardized Version) (AQLQ[S]) Scores at Day 29, 57, 92, 127 and 169

| | |
|-----------------|---|
| End point title | Change From Baseline in Asthma Quality of Life Questionnaire (Standardized Version) (AQLQ[S]) Scores at Day 29, 57, 92, 127 and 169 |
|-----------------|---|

End point description:

AQLQ[S]: a 32-item questionnaire that measures the functional impairments experienced by adult participants including 4 domains (Symptoms, Activity Limitations, Emotional Function, and Environmental Stimuli). Participants were asked to recall their experiences during the previous 2 weeks and to score each of 32 questions on a 7-point scale ranging from 7 (no impairment) to 1 (severe impairment). The overall score calculated as mean response to all questions. The 4 domain scores were means of the responses to questions in each of the domains. Overall AQLQ score and 4 domain scores ranged from 7 (no impairment) to 1 (severe impairment). Data collected on Day 1 prior to dosing considered as baseline. Evaluable population included all participants who received at least 4 doses of investigational product or received at least 1 dose but discontinued treatment due to safety reasons. Here, 'n' signifies participants who were evaluable at specified time points for each group, respectively.

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

End point timeframe:

Day 1, 29, 57, 92, 127 and 169

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|--|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 46 | 51 | 47 |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Overall: Day 29 (n=34,35,37,31) | 0.32 (± 0.65) | 0.38 (± 0.64) | 0.39 (± 0.88) | 0.66 (± 0.76) |
| Overall: Day 57 (n=33,33,35,34) | 0.45 (± 0.77) | 0.7 (± 0.99) | 0.38 (± 0.95) | 0.77 (± 1.04) |
| Overall: Day 92 (n=31,34,35,27) | 0.63 (± 0.88) | 0.94 (± 1.21) | 0.52 (± 1.07) | 1.05 (± 1.25) |
| Overall: Day 127 (n=32,36,34,31) | 0.71 (± 0.85) | 0.78 (± 1.21) | 0.49 (± 1.14) | 1.05 (± 1.15) |
| Overall: Day 169 (n=31,37,37,34) | 0.64 (± 1.05) | 0.78 (± 1.19) | 0.56 (± 1.09) | 0.75 (± 1.26) |
| Symptom: Day 29 (n=34,35,37,31) | 0.31 (± 0.81) | 0.49 (± 0.83) | 0.43 (± 0.83) | 0.62 (± 0.8) |
| Symptom: Day 57 (n=33,33,35,34) | 0.52 (± 0.86) | 0.87 (± 1.1) | 0.44 (± 0.85) | 0.81 (± 1.11) |
| Symptom: Day 92 (n=31,34,35,27) | 0.76 (± 1) | 1 (± 1.32) | 0.61 (± 1.11) | 1.14 (± 1.39) |
| Symptom: Day 127 (n=32,36,34,31) | 0.85 (± 1.03) | 0.87 (± 1.24) | 0.56 (± 1.14) | 1.24 (± 1.23) |
| Symptom: Day 169 (n=31,37,37,34) | 0.8 (± 1.06) | 0.86 (± 1.22) | 0.62 (± 1.17) | 0.77 (± 1.34) |
| Activity Limitation: Day 29 (n=34,35,37,31) | 0.21 (± 0.64) | 0.25 (± 0.69) | 0.32 (± 0.96) | 0.57 (± 0.9) |
| Activity Limitation: Day 57 (n=33,33,35,34) | 0.28 (± 0.79) | 0.44 (± 0.89) | 0.3 (± 1.08) | 0.71 (± 1.07) |
| Activity Limitation: Day 92 (n=31,34,35,27) | 0.42 (± 0.81) | 0.8 (± 1.12) | 0.51 (± 1.12) | 1.04 (± 1.26) |
| Activity Limitation: Day 127 (n=32,36,34,31) | 0.43 (± 0.77) | 0.65 (± 1.2) | 0.45 (± 1.14) | 0.72 (± 1.28) |
| Activity Limitation: Day 169 (n=31,37,37,34) | 0.38 (± 1.09) | 0.68 (± 1.16) | 0.44 (± 1.09) | 0.65 (± 1.37) |
| Emotional Function: Day 29 (n=34,35,37,31) | 0.5 (± 0.93) | 0.57 (± 0.76) | 0.36 (± 1.04) | 0.86 (± 0.97) |
| Emotional Function: Day 57 (n=33,33,35,34) | 0.69 (± 1.15) | 0.95 (± 1.16) | 0.42 (± 1.15) | 0.86 (± 1.21) |
| Emotional Function: Day 92 (n=31,34,35,27) | 0.87 (± 1.25) | 1.06 (± 1.25) | 0.43 (± 1.26) | 0.93 (± 1.39) |
| Emotional Function: Day 127 (n=32,36,34,31) | 1.02 (± 1.2) | 0.87 (± 1.38) | 0.41 (± 1.32) | 1.32 (± 1.42) |
| Emotional Function: Day 169 (n=31,37,37,34) | 0.88 (± 1.42) | 0.88 (± 1.36) | 0.63 (± 1.2) | 0.95 (± 1.4) |
| Environmental Stimuli: Day 29 (n=34,35,37,31) | 0.4 (± 0.85) | 0.16 (± 0.78) | 0.47 (± 1.18) | 0.76 (± 0.8) |
| Environmental Stimuli: Day 57 (n=33,33,35,34) | 0.36 (± 0.86) | 0.58 (± 1.39) | 0.38 (± 1.27) | 0.65 (± 1.4) |
| Environmental Stimuli: Day 92 (n=31,34,35,27) | 0.54 (± 0.94) | 0.97 (± 1.68) | 0.42 (± 1.17) | 0.94 (± 1.28) |
| Environmental Stimuli: Day 127 (n=32,36,34,31) | 0.64 (± 1.11) | 0.74 (± 1.68) | 0.48 (± 1.45) | 1.02 (± 1.22) |
| Environmental Stimuli: Day 169 (n=31,37,37,34) | 0.52 (± 1.17) | 0.75 (± 1.55) | 0.58 (± 1.3) | 0.74 (± 1.39) |

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression of Change (PGIC)

| | |
|------------------------|---|
| End point title | Patient Global Impression of Change (PGIC) |
| End point description: | Patient Global Impression of Change (PGIC): participant rated instrument to measure participant's change in overall status compared to baseline on a 7-point scale; range from 1 (very much worse) to 7 (very much better). Evaluable population included all participants who received at least 4 doses of investigational product or received at least 1 dose but discontinued treatment due to safety reasons. Here, 'n' signifies those participants who were evaluable for this measure at specified time points for each group, respectively. |
| End point type | Secondary |
| End point timeframe: | Day 92 and 169 |

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|--------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 46 | 51 | 47 |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 92 (n=40,42,40,38) | 5.1 (± 1.1) | 5.3 (± 1.1) | 5.3 (± 1) | 5.2 (± 1.2) |
| Day 169 (n=42,44,45,44) | 5.1 (± 1.1) | 5.3 (± 1.1) | 5 (± 1) | 5.1 (± 1.3) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Mean Asthma Control Questionnaire (ACQ) Score Less Than or Equal to 0.75 or ACQ Score Greater Than 0.75 but Less Than 1.5

| | |
|------------------------|--|
| End point title | Percentage of Participants with Mean Asthma Control Questionnaire (ACQ) Score Less Than or Equal to 0.75 or ACQ Score Greater Than 0.75 but Less Than 1.5 |
| End point description: | Percentage of participants with mean ACQ score less than or equal to (\leq) 0.75 or mean ACQ score greater than ($>$) 0.75 and less than ($<$) 1.5 were analyzed. The ACQ is a participant-reported questionnaire to assess the asthma control with 6 items assessing night-time waking, symptoms on waking, activity limitation, shortness of breath, wheeze, and rescue short-acting beta agonist use. Each item was rated on a 7-point Likert scale ranging from 0 (no impairment) to 6 (maximum impairment). Overall ACQ score is the mean of the 6 item scores with a score range of 0 (well controlled) to 6 (extremely poor controlled). Mean ACQ scores of less than or equal to (\leq) 0.75 indicated well-controlled asthma, mean ACQ scores greater than ($>$) 0.75 but less than ($<$) 1.5 indicated partly controlled asthma. Evaluable population included all participants who received at least 4 doses of investigational product or received at least 1 dose but discontinued treatment due to safety reasons. |
| End point type | Secondary |
| End point timeframe: | Day 92 and 169 |

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|-------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 46 | 51 | 47 |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| ACQ score ≤ 0.75: Day 92 | 13 | 19.6 | 11.8 | 17 |
| ACQ score > 0.75 and < 1.5: Day 92 | 15.2 | 13 | 15.7 | 19.1 |
| ACQ score ≤ 0.75: Day 169 | 13 | 19.6 | 13.7 | 19.1 |
| ACQ score > 0.75 and < 1.5: Day 169 | 21.7 | 10.9 | 17.6 | 19.1 |

Statistical analyses

| Statistical analysis title | Statistical analysis 2 |
|---|--|
| Comparison groups | Placebo v CAT-354 150 mg v CAT-354 300 mg v CAT-354 600 mg |
| Number of subjects included in analysis | 190 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.592 ^[10] |
| Method | Fisher exact |

Notes:

[10] - ACQ score ≤ 0.75, Day 169: Fisher exact test was used to compare all arms.

| Statistical analysis title | Statistical analysis 1 |
|---|--|
| Comparison groups | Placebo v CAT-354 150 mg v CAT-354 300 mg v CAT-354 600 mg |
| Number of subjects included in analysis | 190 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.934 ^[11] |
| Method | Fisher exact |

Notes:

[11] - ACQ score ≤ 0.75, Day 92: Fisher exact test was used to compare all arms.

Secondary: Serum Concentration for CAT-354

| | |
|--|---|
| End point title | Serum Concentration for CAT-354 ^[12] |
| End point description: Pharmacokinetic (PK) population included participants who received CAT-354 and had a sufficient number of serum concentration measurements for computing PK parameters. Here, 'n' signifies those participants evaluable for this measure at specified time points for each group, respectively. | |
| End point type | Secondary |
| End point timeframe: Predose on Day 15, 29, 43, 57, 71 and 85; Day 88, 92, 99, 127, and 169 | |

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No inferential statistical analysis was planned for this end-point

| End point values | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg | |
|--|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 47 | 51 | 48 | |
| Units: microgram per milliliter (mcg/mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 15 (n=46,48,48) | 14.5 (± 5.57) | 27.8 (± 10.3) | 56.4 (± 16) | |
| Day 29 (n=45,51,47) | 20.8 (± 7.2) | 40.2 (± 15) | 81.9 (± 23.5) | |
| Day 43 (n=46,50,47) | 26.9 (± 12.7) | 51 (± 16) | 98.5 (± 33.4) | |
| Day 57 (n=46,48,46) | 28.4 (± 11.3) | 58.8 (± 20.2) | 108 (± 35.8) | |
| Day 71 (n=46,49,47) | 29.3 (± 11.9) | 61 (± 21.4) | 112 (± 41.2) | |
| Day 85 (n=45,49,47) | 31.1 (± 12.5) | 62 (± 23.8) | 120 (± 44.5) | |
| Day 88 (n=46,48,45) | 43.4 (± 15.8) | 85.7 (± 32.7) | 157 (± 56.5) | |
| Day 92 (n=45,46,45) | 42 (± 16.3) | 86.8 (± 33.1) | 156 (± 46.6) | |
| Day 99 (n=46,50,46) | 31.3 (± 13) | 69.3 (± 27.2) | 125 (± 41.9) | |
| Day 127 (n=47,48,47) | 11.5 (± 6.02) | 22.9 (± 12) | 43.7 (± 20.5) | |
| Day 169 (n=47,48,46) | 2.94 (± 2.23) | 5.87 (± 3.69) | 10.1 (± 6.71) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-Drug Antibodies to CAT-354 at any Visit

| | |
|------------------------|--|
| End point title | Number of Participants With Anti-Drug Antibodies to CAT-354 at any Visit |
| End point description: | Safety population included all participants who received any dose of the investigational product. Here, 'N'(number of participants analyzed) signifies those participants who were evaluable for this measure. |
| End point type | Secondary |
| End point timeframe: | Day 1, 92 and 169 |

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 47 | 47 | 49 | 47 |
| Units: participants | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Positive Serum Antibodies to CAT-354 at any Visit

| | |
|--|---|
| End point title | Percentage of Participants With Positive Serum Antibodies to CAT-354 at any Visit |
| End point description: Safety population included all participants who received any dose of the investigational product. Here, 'N'(number of participants analyzed) signifies those participants who were evaluable for this measure. | |
| End point type | Secondary |
| End point timeframe: Day 1, 92 and 169 | |

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 47 | 47 | 49 | 47 |
| Units: percentage of participants | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

| | | | | |
|---|--|--|--|--|
| End point title | Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs) | | | |
| End point description: An adverse event (AE) was any untoward medical occurrence attributed to study drug in a participant who received study drug. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent were events between first dose of study drug and Day 169 that were absent before treatment or that worsened relative to pretreatment state. Safety population included all participants who received any dose of the investigational product. | | | | |
| End point type | Secondary | | | |
| End point timeframe: Day 1 to 169 | | | | |

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 47 | 47 | 51 | 48 |
| Units: participants | | | | |
| TEAEs | 17 | 20 | 25 | 25 |
| TESAEs | 3 | 2 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With at least 1 Moderate or Severe Exacerbation

| | |
|-----------------|--|
| End point title | Percentage of Participants With at least 1 Moderate or Severe Exacerbation |
|-----------------|--|

End point description:

Asthma exacerbation was defined as either a progressive increase of asthma symptoms (cough, wheeze, chest tightness, and/or shortness of breath) or a reduction of ≥ 20 percent (%) in PEF or FEV1 from baseline that did not resolve after the initiation of rescue medications and resulted in an administration of systemic corticosteroids by the investigator or health care provider. Asthma exacerbation severity was classified as: 1) Moderate-worsening symptoms that required systemic corticosteroids. 2) Severe-worsening symptoms that required systemic corticosteroids and hospital admission. No separate analyses were performed for moderate and severe exacerbations since only 1 participant had a severe exacerbation. Evaluable population included all participants who received at least 4 doses of investigational product or received at least 1 dose but discontinued prior to receiving 4 doses due to safety reasons.

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

End point timeframe:

Day 92 and 169

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 46 | 51 | 47 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Day 92 | 4.3 | 2.2 | 2 | 4.3 |
| Day 169 | 4.3 | 4.3 | 3.9 | 6.4 |

Statistical analyses

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Placebo v CAT-354 150 mg |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 [13] |
| Method | Fisher exact |

Notes:

[13] - Day 92: Fisher exact test was used for the analysis.

| | |
|----------------------------|--------------------------|
| Statistical analysis title | Statistical analysis 2 |
| Comparison groups | Placebo v CAT-354 300 mg |

| | |
|---|--------------------------|
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6022 ^[14] |
| Method | Fisher exact |

Notes:

[14] - Day 92: Fisher exact test was used for the analysis.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 3 |
| Comparison groups | Placebo v CAT-354 600 mg |
| Number of subjects included in analysis | 93 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 ^[15] |
| Method | Fisher exact |

Notes:

[15] - Day 92: Fisher exact test was used for the analysis.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 4 |
| Comparison groups | Placebo v CAT-354 150 mg |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 ^[16] |
| Method | Fisher exact |

Notes:

[16] - Day 169: Fisher exact test was used for the analysis.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 5 |
| Comparison groups | Placebo v CAT-354 300 mg |
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 ^[17] |
| Method | Fisher exact |

Notes:

[17] - Day 169: Fisher exact test was used for the analysis.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 6 |
| Comparison groups | Placebo v CAT-354 600 mg |
| Number of subjects included in analysis | 93 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 ^[18] |
| Method | Fisher exact |

Notes:

[18] - Day 169: Fisher exact test was used for the analysis.

Secondary: Moderate or Severe Asthma Exacerbations per Person per Annum

| | |
|-----------------|--|
| End point title | Moderate or Severe Asthma Exacerbations per Person per Annum |
|-----------------|--|

End point description:

Asthma exacerbation was defined as either a progressive increase of asthma symptoms (cough, wheeze, chest tightness, and/or shortness of breath) or a reduction of $\geq 20\%$ in PEF or FEV1 from baseline that did not resolve after the initiation of rescue medications and resulted in an administration of systemic corticosteroids by the investigator or health care provider. Asthma exacerbation rate, calculated as total asthma exacerbations per person per annum, was assessed based on asthma exacerbation data up to Day 92 and 169 (Rate = mean asthma exacerbations for all participants/X days*365 days, where X = 92 or 169). Evaluable population included all participants who received at least 4 doses of investigational product or received at least 1 dose but discontinued treatment due to safety reasons.

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

End point timeframe:

Day 1 to Day 92 and Day 169

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|--|--------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 46 | 51 | 47 |
| Units: asthma exacerbations/person/annum | | | | |
| arithmetic mean (standard error) | | | | |
| Day 1 to 92 | 0.26 (\pm 0.19) | 0.09 (\pm 0.09) | 0.08 (\pm 0.08) | 0.25 (\pm 0.19) |
| Day 1 to 169 | 0.23 (\pm 0.19) | 0.14 (\pm 0.1) | 0.08 (\pm 0.06) | 0.19 (\pm 0.11) |

Statistical analyses

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Placebo v CAT-354 150 mg |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.551 ^[19] |
| Method | Van Elteren Test |

Notes:

[19] - Day 1 to 92: P-value was calculated against placebo group from Van Elteren Test.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 2 |
| Comparison groups | Placebo v CAT-354 300 mg |
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.492 ^[20] |
| Method | Van Elteren Test |

Notes:

[20] - Day 1 to 92: P-value was calculated against placebo group from Van Elteren Test.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 3 |
| Comparison groups | Placebo v CAT-354 600 mg |
| Number of subjects included in analysis | 93 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.983 ^[21] |
| Method | Van Elteren Test |

Notes:

[21] - Day 1 to 92: P-value was calculated against placebo group from Van Elteren Test.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 4 |
| Comparison groups | Placebo v CAT-354 150 mg |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.991 ^[22] |
| Method | Van Elteren Test |

Notes:

[22] - Day 1 to 169: P-value was calculated against placebo group from Van Elteren Test.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 5 |
| Comparison groups | Placebo v CAT-354 300 mg |
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9 ^[23] |
| Method | Van Elteren Test |

Notes:

[23] - Day 1 to 169: P-value was calculated against placebo group from Van Elteren Test.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 6 |
| Comparison groups | Placebo v CAT-354 600 mg |
| Number of subjects included in analysis | 93 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.673 ^[24] |
| Method | Van Elteren Test |

Notes:

[24] - Day 1 to 169: P-value was calculated against placebo group from Van Elteren Test.

Secondary: Time to First Moderate or Severe Asthma Exacerbation

| | |
|---|--|
| End point title | Time to First Moderate or Severe Asthma Exacerbation |
| End point description: | |
| Time to first moderate or severe asthma exacerbation was defined as time to first observed progressive increase of asthma symptoms (cough, wheeze, chest tightness, and/or shortness of breath) or a reduction of $\geq 20\%$ in PEF or FEV1 from baseline that did not resolve after the initiation of rescue medications and resulted in an administration of systemic corticosteroids by the investigator or health care provider. Evaluable population included all participants who received at least 4 doses of investigational product or received at least 1 dose but discontinued treatment due to safety reasons. | |
| End point type | Secondary |

End point timeframe:

Day 1 to Day 92 and Day 169

| End point values | Placebo | CAT-354 150 mg | CAT-354 300 mg | CAT-354 600 mg |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 46 | 46 | 51 | 47 |
| Units: days | | | | |
| arithmetic mean (standard error) | | | | |
| Day 1 to 92 | 89.67 (± 1.56) | 90.43 (± 1.32) | 88.16 (± 2.12) | 89.94 (± 1.36) |
| Day 1 to 169 | 162.24 (± 3.79) | 163.5 (± 3.24) | 158.29 (± 4.41) | 161.21 (± 3.71) |

Statistical analyses

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Placebo v CAT-354 150 mg |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.546 [25] |
| Method | Logrank |

Notes:

[25] - Day 1 to 92: P-value was calculated against placebo group from a stratified log-rank test with atopic asthma status and tertile of baseline mean ACQ score as the stratification factors.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 2 |
| Comparison groups | Placebo v CAT-354 300 mg |
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.534 [26] |
| Method | Logrank |

Notes:

[26] - Day 1 to 92: P-value was calculated against placebo group from a stratified log-rank test with atopic asthma status and tertile of baseline mean ACQ score as the stratification factors.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 3 |
| Comparison groups | Placebo v CAT-354 300 mg |
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.847 [27] |
| Method | Logrank |

Notes:

[27] - Day 1 to 92: P-value was calculated against placebo group from a stratified log-rank test with atopic asthma status and tertile of baseline mean ACQ score as the stratification factors.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 4 |
| Comparison groups | Placebo v CAT-354 150 mg |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.987 ^[28] |
| Method | Logrank |

Notes:

[28] - Day 1 to 169: P-value was calculated against placebo group from a stratified log-rank test with atopic asthma status and tertile of baseline mean ACQ score as the stratification factors.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 5 |
| Comparison groups | Placebo v CAT-354 300 mg |
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.992 ^[29] |
| Method | Logrank |

Notes:

[29] - Day 1 to 169: P-value was calculated against placebo group from a stratified log-rank test with atopic asthma status and tertile of baseline mean ACQ score as the stratification factors.

| | |
|---|--------------------------|
| Statistical analysis title | Statistical analysis 6 |
| Comparison groups | Placebo v CAT-354 600 mg |
| Number of subjects included in analysis | 93 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.688 ^[30] |
| Method | Logrank |

Notes:

[30] - Day 1 to 169: P-value was calculated against placebo group from a stratified log-rank test with atopic asthma status and tertile of baseline mean ACQ score as the stratification factors.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to 169

Adverse event reporting additional description:

Safety population included all participants who received any dose of the investigational product.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 13.0 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Placebo matched to CAT-354 subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85.

| | |
|-----------------------|----------------|
| Reporting group title | CAT-354 600 mg |
|-----------------------|----------------|

Reporting group description:

CAT-354 600 mg subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85.

| | |
|-----------------------|----------------|
| Reporting group title | CAT-354 300 mg |
|-----------------------|----------------|

Reporting group description:

CAT-354 300 mg subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85.

| | |
|-----------------------|----------------|
| Reporting group title | CAT-354 150 mg |
|-----------------------|----------------|

Reporting group description:

CAT-354 150 milligram (mg) subcutaneous injection once every 2 weeks on Day 1, 15, 29, 43, 57, 71, and 85.

| Serious adverse events | Placebo | CAT-354 600 mg | CAT-354 300 mg |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| number of deaths (all causes) | 1 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |

| | | | |
|--|----------------|----------------|----------------|
| Cardio-respiratory arrest subjects affected / exposed | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Brain injury | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Post cholecystectomy syndrome | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Somatoform disorder | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Sinusitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|--|--|
| Serious adverse events | CAT-354 150 mg | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Overdose | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Brain injury | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Gastrooesophageal reflux disease | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Post cholecystectomy syndrome | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Somatoform disorder | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Placebo | CAT-354 600 mg | CAT-354 300 mg |
|--|------------------|------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 17 / 47 (36.17%) | 25 / 48 (52.08%) | 25 / 51 (49.02%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lipoma | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vascular disorders | | | |

| | | | |
|--|----------------|----------------|----------------|
| Hypertension | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 48 (4.17%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 2 | 1 |
| Labile hypertension | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | 3 / 48 (6.25%) | 2 / 51 (3.92%) |
| occurrences (all) | 2 | 4 | 2 |
| Infusion site induration | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injection site erythema | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 2 / 48 (4.17%) | 1 / 51 (1.96%) |
| occurrences (all) | 7 | 3 | 1 |
| Injection site induration | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injection site inflammation | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 2 |
| Injection site pain | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 2 / 51 (3.92%) |
| occurrences (all) | 0 | 7 | 8 |
| Injection site pruritus | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Injection site rash | | | |

| | | | |
|--|---------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Injection site reaction subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 51 (0.00%) 0 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 51 (0.00%) 0 |
| Pyrexia subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 51 (1.96%) 1 |
| Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 51 (0.00%) 0 |
| Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Menopausal disorder subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | 0 / 48 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Menstruation irregular subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 51 (1.96%) 1 |
| Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) | 3 / 47 (6.38%) 6 | 6 / 48 (12.50%) 9 | 5 / 51 (9.80%) 6 |
| Cough subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 1 / 51 (1.96%) 1 |
| Dyspnoea subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Epistaxis | | | |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 2 / 51 (3.92%) |
| occurrences (all) | 0 | 1 | 2 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 1 / 48 (2.08%) | 1 / 51 (1.96%) |
| occurrences (all) | 1 | 2 | 1 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Psychiatric disorders | | | |
| Acute psychosis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nightmare | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood bilirubin | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood chloride increased | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urea increased | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 1 / 48 (2.08%) | 1 / 51 (1.96%) |
| occurrences (all) | 3 | 1 | 1 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 2 / 48 (4.17%) | 1 / 51 (1.96%) |
| occurrences (all) | 3 | 2 | 2 |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 2 / 48 (4.17%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Reticulocyte count decreased | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urine analysis abnormal | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 1 / 48 (2.08%) | 1 / 51 (1.96%) |
| occurrences (all) | 1 | 1 | 1 |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fall | | | |

| | | | |
|--------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle rupture | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 1 | 0 | 1 |
| Headache | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | 6 / 48 (12.50%) | 1 / 51 (1.96%) |
| occurrences (all) | 3 | 7 | 1 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 2 |
| Intercostal neuralgia | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Eosinophilia | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 3 / 48 (6.25%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Leukopenia | | | |

| | | | |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Monocytopenia | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Monocytosis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Keratitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 5 / 48 (10.42%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 6 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 2 / 48 (4.17%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Nausea | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 51 (0.00%) 0 |
| Odynophagia subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 51 (1.96%) 1 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 51 (0.00%) 0 |
| Hepatobiliary disorders Biliary colic subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 1 / 51 (1.96%) 1 |
| Biliary dyskinesia subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | 1 / 48 (2.08%) 1 | 1 / 51 (1.96%) 1 |
| Hyperbilirubinaemia subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | 0 / 48 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Dermatitis contact subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 51 (0.00%) 0 |
| Renal and urinary disorders Crystalluria subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 3 / 48 (6.25%) 3 | 1 / 51 (1.96%) 1 |
| Haematuria subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 1 / 51 (1.96%) 1 |
| Leukocyturia subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 51 (0.00%) 0 |
| Nitrituria | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 51 (1.96%) 1 |
| Urinary tract inflammation subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | 0 / 48 (0.00%) 0 | 1 / 51 (1.96%) 1 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 1 / 51 (1.96%) 1 |
| Muscle spasms subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 51 (0.00%) 0 |
| Muscle tightness subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Musculoskeletal chest pain subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 1 / 48 (2.08%) 1 | 1 / 51 (1.96%) 1 |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | 0 / 48 (0.00%) 0 | 1 / 51 (1.96%) 2 |
| Infections and infestations | | | |
| Acute tonsillitis subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Bacteriuria subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 4 / 48 (8.33%) 4 | 2 / 51 (3.92%) 2 |
| Bronchitis subjects affected / exposed occurrences (all) | 3 / 47 (6.38%) 3 | 0 / 48 (0.00%) 0 | 1 / 51 (1.96%) 1 |
| Escherichia infection | | | |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| H1n1 influenza | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Influenza | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | 1 / 48 (2.08%) | 2 / 51 (3.92%) |
| occurrences (all) | 2 | 1 | 2 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 48 (4.17%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 47 (8.51%) | 4 / 48 (8.33%) | 3 / 51 (5.88%) |
| occurrences (all) | 4 | 5 | 4 |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 2 / 51 (3.92%) |
| occurrences (all) | 0 | 1 | 2 |
| Pharyngitis bacterial | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 1 | 0 | 1 |
| Rhinitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 2 / 51 (3.92%) |
| occurrences (all) | 0 | 1 | 2 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 48 (4.17%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 2 | 1 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vulvovaginitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 48 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 1 | 1 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 1 / 48 (2.08%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Type 2 diabetes mellitus subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 51 (0.00%) 0 |
|--|---------------------|---------------------|---------------------|

| | | | |
|--|--|--|--|
| Non-serious adverse events | CAT-354 150 mg | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 19 / 47 (40.43%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Lipoma subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) Labile hypertension subjects affected / exposed occurrences (all) Hypertensive crisis subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 0 / 47 (0.00%) 0 0 / 47 (0.00%) 0 | | |
| General disorders and administration site conditions Chest pain subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all) Infusion site induration subjects affected / exposed occurrences (all) Injection site erythema subjects affected / exposed occurrences (all) Injection site induration | 0 / 47 (0.00%) 0 1 / 47 (2.13%) 1 0 / 47 (0.00%) 0 0 / 47 (0.00%) 0 | | |

| | | | |
|---|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Injection site inflammation subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Injection site pain subjects affected / exposed occurrences (all) | 2 / 47 (4.26%) 3 | | |
| Injection site pruritus subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Injection site rash subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Injection site reaction subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Menopausal disorder subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Menstruation irregular | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 5 / 47 (10.64%) | | |
| occurrences (all) | 9 | | |
| Cough | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Productive cough | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 4 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| Acute psychosis | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |
| Nightmare | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Investigations | | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Blood bilirubin subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Blood chloride increased subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Blood glucose increased subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Blood urea increased subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Lymphocyte count decreased subjects affected / exposed occurrences (all) | 2 / 47 (4.26%) 2 | | |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 3 / 47 (6.38%) 3 | | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Reticulocyte count decreased | | | |

| | | | |
|--|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Urine analysis abnormal subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Fall subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Limb injury subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Muscle rupture subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 2 / 47 (4.26%) 2 | | |
| Headache subjects affected / exposed occurrences (all) | 6 / 47 (12.77%) 8 | | |
| Hypoaesthesia subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Intercostal neuralgia subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Lethargy | | | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed occurrences (all)</p> <p>Sciatica subjects affected / exposed occurrences (all)</p> <p>Somnolence subjects affected / exposed occurrences (all)</p> | <p>1 / 47 (2.13%) 1</p> <p>0 / 47 (0.00%) 0</p> <p>1 / 47 (2.13%) 5</p> | | |
| <p>Blood and lymphatic system disorders</p> <p>Eosinophilia subjects affected / exposed occurrences (all)</p> <p>Leukopenia subjects affected / exposed occurrences (all)</p> <p>Monocytopenia subjects affected / exposed occurrences (all)</p> <p>Monocytosis subjects affected / exposed occurrences (all)</p> <p>Neutropenia subjects affected / exposed occurrences (all)</p> | <p>1 / 47 (2.13%) 1</p> <p>0 / 47 (0.00%) 0</p> <p>1 / 47 (2.13%) 1</p> <p>0 / 47 (0.00%) 0</p> <p>0 / 47 (0.00%) 0</p> | | |
| <p>Ear and labyrinth disorders</p> <p>Ear pain subjects affected / exposed occurrences (all)</p> | <p>1 / 47 (2.13%) 1</p> | | |
| <p>Eye disorders</p> <p>Conjunctivitis subjects affected / exposed occurrences (all)</p> <p>Keratitis subjects affected / exposed occurrences (all)</p> | <p>0 / 47 (0.00%) 0</p> <p>0 / 47 (0.00%) 0</p> | | |
| <p>Gastrointestinal disorders</p> | | | |

| | | | |
|--|---------------------|--|--|
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Abdominal pain lower subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Gastritis subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Nausea subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Odynophagia subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Hepatobiliary disorders Biliary colic subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Biliary dyskinesia subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Hyperbilirubinaemia subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Skin and subcutaneous tissue disorders Dermatitis contact subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Pruritus | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Renal and urinary disorders | | | |
| Crystalluria | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Leukocyturia | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |
| Nitrituria | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary tract inflammation | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscle tightness | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | | |
| occurrences (all) | 2 | | |
| Pain in extremity | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Infections and infestations | | | |
| Acute tonsillitis | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |
| Bacteriuria | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | | |
| occurrences (all) | 2 | | |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | | |
| occurrences (all) | 2 | | |
| Escherichia infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |
| H1n1 influenza | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | | |
| occurrences (all) | 5 | | |
| Otitis media acute | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |

| | | | |
|-----------------------------------|----------------|--|--|
| Pharyngitis | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | | |
| occurrences (all) | 2 | | |
| Pharyngitis bacterial | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | | |
| occurrences (all) | 3 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | | |
| occurrences (all) | 3 | | |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | | |
| occurrences (all) | 1 | | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--|---------------------|--|--|
| Vulvovaginitis subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 2 | | |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 0 / 47 (0.00%) 0 | | |
| Type 2 diabetes mellitus subjects affected / exposed occurrences (all) | 1 / 47 (2.13%) 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 12 March 2009 | - Modified the description of the gene and protein expression analyses to be performed as part of the exploratory analyses. - The upper age limit for participants in the study was increased to 65 years from 55 years - The inclusion criteria was modified: 1. To place an upper limit for predicted prebronchodilator FEV1 value of less than or equal to (\leq) 80% of individual predicted value at Visits 1 and 3. 2. Provide clarification to ensure that only participants with uncontrolled asthma. 3. Clarified that participants should have an ACQ score \geq 1.5 at Visits 1 and 3. 4. Clarified for the requirement for a chest x-ray from the previous 12 months that had no findings suggestive of acute or chronic respiratory pathology other than asthma. - Exclusion criteria was amended: 1. For the modification to exclude participants with a history of ingestion of untreated water in a location known to be infected with parasites, resulting in acute or chronic diarrhea; or a diagnosis of parasitic infection within 6 months prior to screening rather than 1 month prior to randomization as previously stated. 2. To change from a history of primary immunodeficiency to a history of any known immunodeficiency disorder. 3. Addition of positive hepatitis B surface antigen, or hepatitis C virus antibody, as determined by medical history and/or participant's verbal report, A positive human immunodeficiency virus test or is taking antiretroviral medications, as determined by medical history and/or participant's verbal report. - Protocol was revised to specify that the SC injections of investigational product were to be administered into the SC tissue of the anterior thigh rather than the triceps muscle as previously written. - Gamma-glutamyl transferase was added to the serum chemistry panel. - Definition of asthma exacerbation and resolution of asthma exacerbation was modified. - Text stating that acute exacerbations were to be reported separately was been deleted from the protocol. |
| 18 November 2009 | Modified the description of the gene and protein expression analyses to be performed as part of the exploratory analyses. - The inclusion criteria was modified: 1. To remove the upper limit on the prebronchodilator FEV1 value of greater than or equal to (\geq) 40 % and \leq 80% of individual predicted value at Visits 1 and 3. 2. To increase the upper limit of body mass index (BMI) 35 to 40 kilogram per meter square (kg/m^2). 3. The use of a condom by a male sexual partner of a female subject of childbearing potential was added to the list of acceptable methods of contraception. - Additional criteria for allowing one repeat screening visit was added to the protocol. - The requirements to withhold agents prior to spirometry were clarified to be consistent with the recommendations of the American Thoracic Society/European Respiratory Society (ATS/ERS) Task Force. - The text describing visits for participants who prematurely discontinue the study was clarified. - The language describing blinding and the planned Stage 1 analysis was clarified to make it clear that group level unblinded data from the Stage 1 analysis would not be shared outside the sponsor. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported