



Clinical trial results:

A Double-Blind, Placebo-Controlled Parallel-Group Study to Assess the Efficacy, Safety and Tolerability of CAT-354

Summary

EudraCT number	2007-002090-31
Trial protocol	GB DE NL
Global end of trial date	10 October 2008

Results information

Result version number	v2 (current)
This version publication date	16 February 2017
First version publication date	19 June 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CAT-354-0603
-----------------------	--------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00640016
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 der Merwe, MedImmune, LLC, +44 3013980000, vandermerwer@medimmune.com
Scientific contact	Rene van der Merwe, MedImmune, LLC, +44 3013980000, 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	10 October 2008
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	10 October 2008
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to investigate the effects of CAT-354 on airway hyperresponsiveness (AHR) in uncontrolled (refractory) 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 March 2008
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	Germany: 2
Country: Number of subjects enrolled	United Kingdom: 12
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	14
From 65 to 84 years	0

85 years and over	0
-------------------	---

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Ninety (90) participants were screened for this study, and a total of 14 participants were randomized. Thirteen (13) of the 14 randomized participants were included in the safety population.

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	Investigator, Monitor, Carer, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo matched to CAT-354 intravenous infusion over 60 minutes on Day 0, 28 and 56.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo matched to CAT-354 intravenous infusion over 60 minutes on Day 0, 28 and 56.

Arm title	CAT-354 1 mg/kg
------------------	-----------------

Arm description:

CAT-354 1 milligram/kilogram (mg/kg) of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.

Arm type	Experimental
Investigational medicinal product name	CAT-354
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

CAT-354 1 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.

Arm title	CAT-354 5 mg/kg
------------------	-----------------

Arm description:

CAT-354 5 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.

Arm type	Experimental
Investigational medicinal product name	CAT-354
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

CAT-354 5 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.

Arm title	CAT-354 10 mg/kg
Arm description: CAT-354 10 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.	
Arm type	Experimental
Investigational medicinal product name	CAT-354
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

CAT-354 10 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.

Number of subjects in period 1	Placebo	CAT-354 1 mg/kg	CAT-354 5 mg/kg
Started	3	3	4
Treated	3	2	4
Completed	1	1	1
Not completed	2	2	3
Consent withdrawn by subject	-	1	-
Study termination	2	1	3
Adverse event, non-fatal	-	-	-

Number of subjects in period 1	CAT-354 10 mg/kg
Started	4
Treated	4
Completed	1
Not completed	3
Consent withdrawn by subject	-
Study termination	2
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Placebo matched to CAT-354 intravenous infusion over 60 minutes on Day 0, 28 and 56.	
Reporting group title	CAT-354 1 mg/kg
Reporting group description: CAT-354 1 milligram/kilogram (mg/kg) of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.	
Reporting group title	CAT-354 5 mg/kg
Reporting group description: CAT-354 5 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.	
Reporting group title	CAT-354 10 mg/kg
Reporting group description: CAT-354 10 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.	

Reporting group values	Placebo	CAT-354 1 mg/kg	CAT-354 5 mg/kg
Number of subjects	3	3	4
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	3	4
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	34	34	37.75
standard deviation	± 11.136	± 14.933	± 9.878
Gender, Male/Female Units: participants			
Female	3	3	2
Male	0	0	2

Reporting group values	CAT-354 10 mg/kg	Total	
Number of subjects	4	14	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	

Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	14	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years arithmetic mean standard deviation	40.75 ± 15.086	-	
Gender, Male/Female Units: participants			
Female	3	11	
Male	1	3	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo matched to CAT-354 intravenous infusion over 60 minutes on Day 0, 28 and 56.	
Reporting group title	CAT-354 1 mg/kg
Reporting group description: CAT-354 1 milligram/kilogram (mg/kg) of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.	
Reporting group title	CAT-354 5 mg/kg
Reporting group description: CAT-354 5 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.	
Reporting group title	CAT-354 10 mg/kg
Reporting group description: CAT-354 10 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.	
Subject analysis set title	Therapeutic-dose (CAT-354 5mg/kg and CAT-354 10mg/kg)
Subject analysis set type	Per protocol
Subject analysis set description: Subjects (N=8) included who received CAT-354 5 mg/kg or 10 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.	
Subject analysis set title	Sub-therapeutic Dose (placebo or CAT-354 1mg/kg)
Subject analysis set type	Per protocol
Subject analysis set description: Subjects (N=5) included who received Placebo or CAT-354 1 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.	

Primary: Change From Baseline in Doubling Concentration of Methacholine at Day 28

End point title	Change From Baseline in Doubling Concentration of Methacholine at Day 28 ^[1]
End point description: Change in doubling concentrations of methacholine was calculated as Log2 PC20 (Visit x) - Log2 PC20 (Baseline), where x was the post-baseline assessment (Day 28) and PC20 was provocative concentration of methacholine causing 20 percent fall in forced expiratory volume in 1 second (FEV1). FEV1 was the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. Change in doubling concentration was summarized as per planned analysis.	
End point type	Primary
End point timeframe: Baseline and Day 28	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Therapeutic-dose (CAT-354 5mg/kg and CAT-354 10mg/kg)	Sub-therapeutic Dose (placebo or CAT-354 1mg/kg)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	5		
Units: log2 milligram/deciliter (mg/dL)				
arithmetic mean (standard deviation)				

Baseline (n=8, 5)	-0.604 (± 2.408)	-1.545 (± 0.8952)		
Change at Day 28 (n=5, 4)	-0.207 (± 1.045)	0.125 (± 2.3433)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Doubling concentration of Methacholine at Day 56, 84 or Early Termination

End point title	Change From Baseline in Doubling concentration of Methacholine at Day 56, 84 or Early Termination
-----------------	---

End point description:

Change in doubling concentrations of methacholine was calculated as Log2 PC20 (Visit x) - Log2 PC20 (Baseline), where x was the post-baseline assessment (Day 28) and PC20 was provocative concentration of methacholine causing 20 percent fall in forced expiratory volume in 1 second (FEV1). FEV1 was the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. Change in doubling concentration was summarized as per planned analysis. Safety population included all participants who received at least 1 dose of study medication. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure, and '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:

Baseline, Day 56, 84 or early termination (any time before Day 84)

End point values	Therapeutic-dose (CAT-354 5mg/kg and CAT-354 10mg/kg)	Sub-therapeutic Dose (placebo or CAT-354 1mg/kg)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3	2		
Units: log2 mg/dL				
arithmetic mean (standard deviation)				
Change at Day 56 (n=2, 2)	0.062 (± 1.1309)	-1.423 (± 0.4059)		
Change at Day 84 (n=2, 2)	-0.038 (± 0.141)	-1.846 (± 0.0431)		
Change at Early termination (n=3, 2)	-0.514 (± 0.8636)	0.417 (± 0.984)		

Statistical analyses

No statistical analyses for this end point

Secondary: Forced expiratory volume in 1 second (FEV1)

End point title	Forced expiratory volume in 1 second (FEV1)
-----------------	---

End point description:

The FEV1 was maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. FEV1 was summarized as per planned analysis.

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

End point timeframe:

Predose, 30 minutes and 6 hours post-end of infusion on Day 0, 28 and 56; Day 4, 14, 35, 63, 84 or early termination (any time before Day 84)

End point values	Therapeutic-dose (CAT-354 5mg/kg and CAT-354 10mg/kg)	Sub-therapeutic Dose (placebo or CAT-354 1mg/kg)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	5		
Units: liters				
arithmetic mean (standard deviation)				
Day 0: Predose (n=8, 5)	2.718 (± 0.5458)	2.64 (± 0.3994)		
Day 0: 30 minutes postdose (n=8, 5)	2.684 (± 0.5695)	2.624 (± 0.4126)		
Day 0: 6 hours postdose (n=8, 5)	2.606 (± 0.5731)	2.55 (± 0.4304)		
Day 4 (n=8, 5)	2.814 (± 0.6048)	2.606 (± 0.2919)		
Day 14 (n=6, 5)	2.323 (± 0.5703)	2.52 (± 0.0812)		
Day 28: Predose (n=5, 4)	2.598 (± 0.4676)	2.85 (± 0.2082)		
Day 28: 30 minutes postdose (n=4, 4)	2.535 (± 0.5639)	2.918 (± 0.2822)		
Day 28: 6 hours postdose (n=4, 4)	2.4 (± 0.5254)	2.665 (± 0.2748)		
Day 35 (n= 4, 4)	2.26 (± 0.5464)	2.778 (± 0.4228)		
Day 56: Predose (n=2, 2)	2.555 (± 0.6718)	2.7 (± 0.3677)		
Day 56: 30 minutes postdose (n=2, 2)	2.705 (± 0.799)	2.83 (± 0.1697)		
Day 56: 6 hours postdose (n=2, 2)	2.51 (± 0.7071)	2.69 (± 0.2404)		
Day 63 (n= 2, 2)	2.505 (± 0.6859)	2.58 (± 0.0283)		
Day 84: (n=2, 2)	2.68 (± 0.7778)	2.54 (± 0.4101)		
Early Termination (n=4, 3)	3.018 (± 0.5803)	2.867 (± 0.44)		

Statistical analyses

No statistical analyses for this end point

Secondary: Forced Vital Capacity (FVC)

End point title	Forced Vital Capacity (FVC)
End point description: The FVC was volume of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. FVC was summarized as per planned analysis.	
End point type	Secondary
End point timeframe: Predose, 30 minutes and 6 hours post-end of infusion on Day 0, 28 and 56; Day 4, 14, 35, 63, 84 or early termination (any time before Day 84)	

End point values	Therapeutic-dose (CAT-354 5mg/kg and CAT-354 10mg/kg)	Sub-therapeutic Dose (placebo or CAT-354 1mg/kg)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	5		
Units: liters				
arithmetic mean (standard deviation)				
Day 0: Predose (n= 8, 5)	3.828 (± 0.8215)	3.666 (± 0.6068)		
Day 0: 30 minutes postdose (n= 8, 5)	3.823 (± 0.65)	3.722 (± 0.6752)		
Day 0: 6 hours postdose (n= 8, 5)	3.808 (± 0.7718)	3.722 (± 0.7297)		
Day 4 (n= 8, 5)	3.988 (± 0.6058)	3.824 (± 0.7415)		
Day 14 (n=6, 5)	3.462 (± 0.5926)	3.71 (± 0.522)		
Day 28: Predose (n=5, 4)	3.908 (± 0.767)	3.883 (± 0.6412)		
Day 28: 30 minutes postdose (n=4, 4)	3.878 (± 0.7876)	3.98 (± 0.7951)		
Day 28: 6 hours postdose (n=4, 4)	3.81 (± 0.7409)	3.79 (± 0.483)		
Day 35 (n=4, 4)	3.613 (± 0.6874)	3.92 (± 0.7777)		
Day 56: Predose (n=2, 2)	3.7 (± 0.5233)	3.41 (± 0.3818)		
Day 56: 30 minutes postdose (n=2, 2)	3.775 (± 0.5303)	3.54 (± 0.4667)		
Day 56: 6 hours postdose (n=2, 2)	3.715 (± 0.6435)	3.545 (± 0.3748)		
Day 63 (n=2, 2)	3.705 (± 0.5162)	3.575 (± 0.502)		
Day 84: (n=2, 2)	3.71 (± 0.6505)	3.415 (± 0.3323)		
Early Termination (n=4, 3)	3.908 (± 0.807)	4.193 (± 0.8364)		

Statistical analyses

No statistical analyses for this end point

Secondary: Forced Expiratory Volume in 1 second (FEV1) as Percentage of Forced Vital Capacity (FVC)

End point title	Forced Expiratory Volume in 1 second (FEV1) as Percentage of Forced Vital Capacity (FVC)
-----------------	--

End point description:

Percentage of FEV1 was calculated as $(FEV1/FVC) \times 100$. It signified the percentage of the total amount of air exhaled from the lungs during the first second of forced exhalation. FEV1 was the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. FVC was the volume of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. Result was summarized as per planned analysis.

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

End point timeframe:

Predose, 30 minutes and 6 hours post-end of infusion on Day 0, 28 and 56; Day 4, 14, 35, Day 63, 84 or early termination (any time before Day 84)

End point values	Therapeutic-dose (CAT-354 5mg/kg and CAT-354 10mg/kg)	Sub-therapeutic Dose (placebo or CAT-354 1mg/kg)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	5		
Units: percentage of FVC				
arithmetic mean (standard deviation)				
Day 0: Predose (n=8, 5)	71.875 (\pm 10.3156)	72.6 (\pm 11.4149)		
Day 0: 30 minutes postdose (n=8, 5)	70.25 (\pm 9.1613)	71.6 (\pm 13.1833)		
Day 0: 6 hours postdose (n=8, 5)	69.125 (\pm 12.5178)	69.6 (\pm 12.1984)		
Day 4 (n=8, 5)	71 (\pm 13.1909)	69.4 (\pm 8.7063)		
Day 14 (n=6, 5)	66.667 (\pm 7.5011)	68.8 (\pm 8.167)		
Day 28: Predose (n=5, 4)	67.4 (\pm 13.1263)	74.5 (\pm 11.2694)		
Day 28: 30 minutes postdose (n=4, 4)	66.5 (\pm 13.9881)	74.5 (\pm 9.6782)		
Day 28: 6 hours postdose (n=4, 4)	63.75 (\pm 12.339)	71.25 (\pm 13.8173)		
Day 35 (n=4, 4)	62.5 (\pm 7.5498)	71.75 (\pm 7.8049)		
Day 56: Predose (n=2, 2)	68 (\pm 8.4853)	80 (\pm 19.799)		
Day 56: 30 minutes postdose (n=2, 2)	71 (\pm 11.3137)	81 (\pm 15.5563)		
Day 56: 6 hours postdose (n=2, 2)	67 (\pm 7.0711)	76.5 (\pm 14.8492)		
Day 63 (n=2, 2)	66.5 (\pm 9.1924)	72.5 (\pm 9.1924)		
Day 84 (n=2, 2)	71.5 (\pm 9.1924)	75.5 (\pm 19.0919)		
Early Termination (n=4, 3)	77.75 (\pm 9.8107)	69 (\pm 5.5678)		

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma Control Questionnaire (ACQ) Total Score

End point title	Asthma Control Questionnaire (ACQ) Total Score
-----------------	--

End point description:

The ACQ is questionnaire that comprises of 7-questions evaluating participant's asthma control. Six self-administered questions assess asthma control over the past week covering nocturnal waking, morning symptoms, activity limitations, shortness of breath, wheezing, and short-acting bronchodilator use; using 7-point ordinal rating scale from 0 (good control) to 6 (poor control). Seventh question is completed by a health professional on forced expiratory volume in 1 second (FEV1) percentage (%) predicted; scale: 0 (greater than [$>$] 95% predicted) to 6 (less than [$<$] 50% predicted). Final score is the average score of the 7 questions, with a score range of 0 (well controlled) to 6 (extremely poor controlled). Result was summarized as per planned analysis.

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

End point timeframe:

Baseline, Day 28, 56, 84 or early termination (any time before Day 84)

End point values	Therapeutic-dose (CAT-354 5mg/kg and CAT-354 10mg/kg)	Sub-therapeutic Dose (placebo or CAT-354 1mg/kg)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	5		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=8, 5)	2.44 (\pm 0.737)	1.77 (\pm 0.861)		
Day 28 (n=5, 4)	2 (\pm 0.416)	1.46 (\pm 0.914)		
Day 56 (n=2, 2)	1.43 (\pm 0.808)	1.5 (\pm 1.111)		
Day 84 (n=2, 2)	1.57 (\pm 1.01)	2.36 (\pm 0.101)		
Early Termination (n=5, 3)	1.72 (\pm 1.304)	0.57 (\pm 0.378)		

Statistical analyses

No statistical analyses for this end point

Secondary: Post-bronchodilator Forced Expiratory Volume in 1 Second (FEV1)

End point title	Post-bronchodilator Forced Expiratory Volume in 1 Second (FEV1)
-----------------	---

End point description:

The FEV1 was maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration.

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

End point timeframe:

Day 0 to 84

End point values	Therapeutic-dose (CAT-354 5mg/kg and CAT-354 10mg/kg)	Sub-therapeutic Dose (placebo or CAT-354 1mg/kg)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 ^[2]	0 ^[3]		
Units: liters				
arithmetic mean (standard deviation)	()	()		

Notes:

[2] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[3] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Diary Data

End point title	Number of Participants With Diary Data
End point description:	
Participants recorded asthma symptoms, use of reliever inhalers (beta-agonist use for symptom relief and as prophylaxis), and morning and evening peak expiratory flow (PEF) measurements in a diary.	
End point type	Secondary
End point timeframe:	
Day 0, 4, 14, 28, 35, 56, 63 to Day and 84	

End point values	Placebo	CAT-354 1 mg/kg	CAT-354 5 mg/kg	CAT-354 10 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[4]	0 ^[5]	0 ^[6]	0 ^[7]
Units: participants				

Notes:

[4] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[5] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[6] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[7] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Exacerbations

End point title	Number of Participants With Exacerbations
End point description:	
Exacerbation was defined as: Mild (determined from diary data) - 2 consecutive days satisfying the same or 1 of the following criteria: any night with awakening(s) due to asthma or morning PEF 20 % or more below baseline where baseline = average of the 10 days before randomization or as-needed medication use of 2 inhalations or more in 24 hours above baseline where baseline = average of the 10	

days before randomization. Severe (determined by taking an exacerbation update and history): deterioration of asthma resulting in emergency treatment or hospitalization or need for oral steroids for 3 days or more (as judged by the Investigator).

End point type	Secondary
End point timeframe:	
Day 0 to Day 84	

End point values	Placebo	CAT-354 1 mg/kg	CAT-354 5 mg/kg	CAT-354 10 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[8]	0 ^[9]	0 ^[10]	0 ^[11]
Units: participants				

Notes:

[8] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[9] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[10] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[11] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Morning Peak Flow and Peak Flow Variability

End point title	Morning Peak Flow and Peak Flow Variability
End point description:	
Peak flow is a participant's maximum speed of expiration.	
End point type	Secondary
End point timeframe:	
Day 0 to Day 84	

End point values	Placebo	CAT-354 1 mg/kg	CAT-354 5 mg/kg	CAT-354 10 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[12]	0 ^[13]	0 ^[14]	0 ^[15]
Units: liters/minute				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[12] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[13] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[14] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[15] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Adult Asthma Quality of Life (QoL) Questionnaire Final Score

End point title	Adult Asthma Quality of Life (QoL) Questionnaire Final Score
-----------------	--

End point description:

The AQLQ: a 32-item questionnaire evaluating quality of life of participants with asthma including 4 domains (symptoms, activity limitations, emotional function, and environmental stimuli). Participants are 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 is calculated as the mean response to all questions. The 4 domain scores are 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).

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

End point timeframe:

Day 0, 28, 84 or early termination (any time before Day 84)

End point values	Placebo	CAT-354 1 mg/kg	CAT-354 5 mg/kg	CAT-354 10 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[16]	0 ^[17]	0 ^[18]	0 ^[19]
Units: units on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[16] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[17] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[18] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

[19] - Study was prematurely terminated, hence data was not collected and analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) for CAT-354

End point title	Maximum Observed Serum Concentration (Cmax) for CAT-
-----------------	--

End point description:

In the below table, '99999' indicates that data was not estimable due to only 1 participant was evaluable in the reporting group. Pharmacokinetic (PK) population included all participants who received at least 1 dose of study medication and had sufficient post-dose blood samples to estimate Cmax. Here 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure.

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

End point timeframe:

Predose, 10 minutes and 6 hours post-end of infusion on Day 0, 28 and 56

Notes:

[20] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	CAT-354 1 mg/kg	CAT-354 5 mg/kg	CAT-354 10 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	1	1	
Units: microgram/milliliter (mcg/mL)				
arithmetic mean (standard deviation)				
After first dose (Day 0)	27.7 (± 99999)	219 (± 99999)	163 (± 99999)	
After second dose (Day 28)	34.5 (± 99999)	255 (± 99999)	235 (± 99999)	

After third dose (Day 56)	33.4 (± 99999)	338 (± 99999)	251 (± 99999)	
---------------------------	----------------	---------------	---------------	--

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Serum Concentration (Cmin) for CAT-354

End point title	Minimum Observed Serum Concentration (Cmin) for CAT-
-----------------	--

End point description:

In the below table, '99999' indicates that data was not estimable due to only 1 participant was evaluable in the reporting group. PK population included all participants who received at least 1 dose of study medication and had sufficient post-dose blood samples to estimate Cmax. Here 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure.

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

End point timeframe:

Predose, 10 minutes and 6 hours post-end of infusion on Day 0, 28 and 56

Notes:

[21] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	CAT-354 1 mg/kg	CAT-354 5 mg/kg	CAT-354 10 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	1	1	
Units: mcg/mL				
arithmetic mean (standard deviation)				
After first dose (Day 0)	4.84 (± 99999)	51.8 (± 99999)	52.8 (± 99999)	
After second dose (Day 28)	7.91 (± 99999)	54.1 (± 99999)	64.4 (± 99999)	
After third dose (Day 56)	9.7 (± 99999)	85.5 (± 99999)	68.4 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Serum Concentration Time Curve From Time Zero to Last Measurable Concentration (AUC [0 - t]) for CAT-354

End point title	Area Under the Serum Concentration Time Curve From Time Zero to Last Measurable Concentration (AUC [0 - t]) for CAT-354 ^[22]
-----------------	---

End point description:

In the below table, '99999' indicates that data was not estimable due to only 1 participant was evaluable in the reporting group. PK population included all participants who received at least 1 dose of study medication and had sufficient post-dose blood samples to estimate Cmax. Here 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure.

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

End point timeframe:

Predose, 10 minutes and 6 hours post-end of infusion on Day 0, 28 and 56

Notes:

[22] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	CAT-354 1 mg/kg	CAT-354 5 mg/kg	CAT-354 10 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	1	1	
Units: microgram*day/milliliter (mcg*day/mL)				
arithmetic mean (standard deviation)				
After first dose (Day 0)	335 (± 99999)	2820 (± 99999)	2090 (± 99999)	
After second dose (Day 28)	408 (± 99999)	4720 (± 99999)	3080 (± 99999)	
After third dose (Day 56)	499 (± 99999)	3690 (± 99999)	3420 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Accumulation Ratio for CAT-354 (RA)

End point title	Accumulation Ratio for CAT-354 (RA) ^[23]
-----------------	---

End point description:

Accumulation ratio (RA) is calculated for C_{max}, C_{min} and AUC as RA for C_{max} = C_{max} (56 - 84)/C_{max} (0 - 28); Similarly, RA for C_{min} = C_{min} (56 - 84)/C_{min} (0 - 28) and RA for AUC = AUC (56 - 84)/AUC (0 - 28) where C_{max} (0 - 28) and C_{max} (56 - 84) are the maximum observed serum concentration after first dose (Day 0 to Day 28) and after third dose (Day 56 to Day 84), respectively; C_{min} (0 - 28) and C_{min} (56 - 84) are the minimum observed serum concentration after first and third dose, respectively; AUC (0 - 28) and AUC (56 - 84) are the area under the serum concentration time curve over a dosage interval determined after first and third dose, respectively. In the below table, '99999' indicates that data was not estimable due to only 1 participant was evaluable in the reporting group. Here 'N' (number of participants analyzed) signifies, evaluable participants for this measure, and 'n' signifies, evaluable participants at specified time points for each group, respectively.

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

End point timeframe:

Predose, 10 minutes and 6 hours post-end of infusion on Day 0, 28 and 56

Notes:

[23] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	CAT-354 1 mg/kg	CAT-354 5 mg/kg	CAT-354 10 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1 ^[24]	1 ^[25]	1 ^[26]	
Units: ratio				
arithmetic mean (standard deviation)				
RA for C _{min}	1.2 (± 99999)	1.54 (± 99999)	1.73 (± 99999)	

RA for Cmax	2 (± 99999)	1.65 (± 99999)	1.3 (± 99999)	
RA for AUC	1.49 (± 99999)	1.31 (± 99999)	1.64 (± 99999)	

Notes:

[24] - PK population

[25] - PK population

[26] - PK population

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Participants Reporting Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)
-----------------	---

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. 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 up to Day 84 that were absent before treatment or that worsened relative to pre-treatment state. Safety population included all participants who received at least 1 dose of study medication. Here, number of participants analysed, "N" signifies evaluable participants for the respective reporting group.

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

End point timeframe:

Day 0 to 84

End point values	Placebo	CAT-354 1 mg/kg	CAT-354 5 mg/kg	CAT-354 10 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	4	4
Units: participants				
TEAEs	2	2	4	3
TESAEs	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 0 to 84

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

Dictionary used

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

Dictionary version	9.0
--------------------	-----

Reporting groups

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

Reporting group description:

Placebo matched to CAT-354 intravenous infusion over 60 minutes on Day 0, 28 and 56

Reporting group title	CAT-354 1mg/kg
-----------------------	----------------

Reporting group description:

CAT-354 1 milligram/kilogram (mg/kg) of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.

Reporting group title	CAT-354 5mg/kg
-----------------------	----------------

Reporting group description:

CAT-354 5 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.

Reporting group title	CAT-354 10mg/kg
-----------------------	-----------------

Reporting group description:

CAT-354 10 mg/kg of body weight intravenous infusion over 60 minutes on Day 0, 28 and 56.

Serious adverse events	Placebo	CAT-354 1mg/kg	CAT-354 5mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 2 (0.00%)	0 / 4 (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 10mg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	1 / 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 1mg/kg	CAT-354 5mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	2 / 2 (100.00%)	4 / 4 (100.00%)
Investigations			
Forced expiratory volume decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Constipation			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 2 (0.00%) 0	1 / 4 (25.00%) 1
Diarrhoea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 2 (0.00%) 0	1 / 4 (25.00%) 1
Nausea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 2 (0.00%) 0	1 / 4 (25.00%) 1
Vomiting subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 2 (0.00%) 0	1 / 4 (25.00%) 2
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	0 / 2 (0.00%) 0	1 / 4 (25.00%) 1
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 2 (50.00%) 1	0 / 4 (0.00%) 0
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 2 (0.00%) 0	1 / 4 (25.00%) 1
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 2 (0.00%) 0	1 / 4 (25.00%) 1
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 2 (50.00%) 1	0 / 4 (0.00%) 0
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	2 / 2 (100.00%) 2	1 / 4 (25.00%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0

Non-serious adverse events	CAT-354 10mg/kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)		
Investigations			
Forced expiratory volume decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Inflammation			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	3		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nausea			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 4 (0.00%)</p> <p>0</p> <p>1 / 4 (25.00%)</p> <p>1</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Asthma</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea exertional</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p>		
<p>Skin and subcutaneous tissue disorders</p> <p>Pruritus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 4 (0.00%)</p> <p>0</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Muscle spasms</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Musculoskeletal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p>		
<p>Infections and infestations</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urinary tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 4 (25.00%)</p> <p>1</p> <p>0 / 4 (0.00%)</p> <p>0</p>		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 June 2007	- Determination of the atopic status of participants was to be required. Participants were considered atopic if they had documented hypersensitivity to a seasonal or perennial allergen as determined by skin test (prick or intradermal) or Radioallergosorbent Test (RAST) or equivalent test within 12 months prior to enrolment. - Coffee, tea, other caffeinated drinks, chocolate drinks, and chocolate foodstuffs were not to be consumed on challenge days before the test was completed. In addition, vigorous exercise was to be avoided on the day of the challenge before completion of the challenge test. - The means of determining the severity of exacerbations were clarified: mild-determined from diary data at each clinic visit and severe determined by taking an exacerbation update and history at each clinic visit.
17 August 2007	- Two additional exclusion criterion added: Significant, uncontrolled disease including serious psychological disorders, chronic renal failure, uncontrolled hypertension - systolic blood pressure greater than (>) 200 millimeter of mercury (mmHg), or diastolic blood pressure > 100 mmHg, heart disease, psoriasis requiring treatment and participants who have had a heart attack or stroke within the 3 months preceding Visit 1, or who have a known aneurysm. Known hypersensitivity to CAT-354 or its components, to the challenge agents used in the study or to related drugs. - Detail on study drug formulation was added. - Concomitant medications/treatments were adjusted to state that parenteral corticosteroids from one month prior to Visit 1 were not permissible, and corticosteroids (oral or injected) were allowed.
13 August 2008	- To remove all US specific reference as it was decided not to proceed with the study in the US due to feasibility and Key Opinion Leader feedback. - To document the changes resulting from reduced recruitment on the study design, interim analyses, and anticipated study objectives. - Changes were made to reduce the risk of hypersensitivity or infusion-related reactions and to remove investigations that were relatively invasive, and may have contributed to a number of adverse events. Specifically, planned changes in this regard were to: a. increase the infusion time of investigational medical product (IMP) from 30 to 60 minutes; b. to remove the mannitol challenge at all-time points; c. to remove the induced sputum collection at all-time points; d. to collect extra blood samples pre- and post-infusion of IMP in order to assess participant safety; e. to perform additional vital signs pre- and post-infusion of IMP in order to assess participant safety; f. to add that chlorphenamine and paracetamol could be administered 1.5 hours before infusion at Visits 5 and 7 for participants who experienced minor infusion reactions (without hemodynamic or respiratory compromise) after the infusion at Visit 2.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
10 October 2008	Study was prematurely terminated by the sponsor due to slow recruitment rate, delay due to temporary halt and potential for expiry date of study drug.	-

Notes:

Limitations and caveats

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

Study was prematurely terminated by the sponsor due to slow recruitment rate, delay due to temporary halt and potential for expiry date of study drug. It was not considered possible to draw meaningful conclusions from the small dataset.

Notes: