



Clinical trial results:

A Double Blind, Randomised, Placebo Controlled Multi-Centre Field Study to Assess the Efficacy and Safety of Cat-PAD Peptide Immunotherapy in Cat Allergic Subjects

Summary

EudraCT number	2012-001733-13
Trial protocol	PL BE CZ DE HU SK LT LV EE
Global end of trial date	02 February 2016

Results information

Result version number	v1 (current)
This version publication date	03 March 2018
First version publication date	03 March 2018

Trial information

Trial identification

Sponsor protocol code	CP007
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01620762
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Circassia Limited
Sponsor organisation address	Robert Robinson Avenue, Oxford, United Kingdom, OX4 4GA
Public contact	CP007-ClinicalTrialInformation-Desk, Circassia Limited, +44 1865 598078, CP007ClinicalTrialInformationDesk@circassia.co.uk
Scientific contact	CP007-ClinicalTrialInformation-Desk, Circassia Limited, +44 1865 598078, CP007ClinicalTrialInformationDesk@circassia.co.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001054-PIP01-10
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 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 February 2016
Global end of trial reached?	Yes
Global end of trial date	02 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of the novel desensitising immunotherapy Cat-PAD in the reduction of symptoms and the use of allergy rescue medication associated with cat allergy in subjects with clinically relevant symptoms.

Protection of trial subjects:

None

Background therapy:

Subjects were permitted to use allergy rescue medications in accordance with the rescue medication plan.

Evidence for comparator:

No comparators used

Actual start date of recruitment	23 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 411
Country: Number of subjects enrolled	Slovakia: 2
Country: Number of subjects enrolled	Belgium: 28
Country: Number of subjects enrolled	Czech Republic: 103
Country: Number of subjects enrolled	Germany: 94
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Russian Federation: 91
Country: Number of subjects enrolled	Canada: 261
Country: Number of subjects enrolled	United States: 413
Worldwide total number of subjects	1408
EEA total number of subjects	643

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	90
Adults (18-64 years)	1297
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

3741 Subjects screened. 2333 Subjects were not randomised. Subjects were recruited outside of the pollen season over a total duration of 3 years. Due to poor recruitment, additional countries were added to the study after the first season.

Pre-assignment

Screening details:

Blood samples taken for measurement of specific IgE and subjects given a diary card to record symptom scores. Subjects returned for full study screening in accordance with the protocol. Once all screening tests were complete, subjects completed a daily e-diary entry for symptom scores and medication use. If successful randomisation occurred.

Period 1

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

Arms

Arm title	Randomisation
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Arm description:

All subjects randomised

Arm type	Experimental
Investigational medicinal product name	Cat-PAD
Investigational medicinal product code	Cat-PAD
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

A single course of Cat-PAD 4 x 6 nmol 4 weeks apart followed by 4 x placebo 4 weeks apart.

Investigational medicinal product name	Cat-PAD
Investigational medicinal product code	Cat-PAD
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

A single course of Cat-PAD 4 x 6 nmol 4 weeks apart followed by a second course of Cat-PAD 4 x 6 nmol 4 weeks apart

Investigational medicinal product name	placebo
Investigational medicinal product code	placebo
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

2 courses of 4 x placebo 4 weeks apart

Number of subjects in period 1	Randomisation
Started	1408
Completed	1408

Period 2

Period 2 title	Treatment and Assessment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Group 1

Arm description:

A single course of Cat-PAD 4 x 6 nmol 4 weeks apart followed by 4 x placebo 4 weeks apart.

Arm type	Experimental
Investigational medicinal product name	Cat-PAD
Investigational medicinal product code	Cat-PAD
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

A single course of Cat-PAD 4 x 6 nmol 4 weeks apart followed by 4 x placebo 4 weeks apart.

Investigational medicinal product name	placebo
Investigational medicinal product code	placebo
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

A single course of Cat-PAD 4 x 6 nmol 4 weeks apart followed by 4 x placebo 4 weeks apart.

Arm title	Treatment Group 2
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Arm description:

A single course of Cat-PAD 4 x 6 nmol 4 weeks apart followed by a second course of Cat-PAD 4 x 6 nmol 4 weeks apart.

Arm type	Experimental
Investigational medicinal product name	Cat-PAD
Investigational medicinal product code	Cat-PAD
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

A single course of Cat-PAD 4 x 6 nmol 4 weeks apart followed by a second course of Cat-PAD 4 x 6 nmol 4 weeks apart

Arm title	Treatment Group 3
Arm description: 2 courses of 4 x placebo 4 weeks apart.	
Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	placebo
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use
Dosage and administration details: 2 courses of 4 x placebo 4 weeks apart	

Number of subjects in period 2	Treatment Group 1	Treatment Group 2	Treatment Group 3
Started	468	470	470
Completed	420	412	417
Not completed	48	58	53
Use of prohibited therapies	-	1	1
Consent withdrawn by subject	23	26	27
Non specified	3	-	-
Adverse event, non-fatal	9	5	2
Protocol violation	1	1	1
Not specified	-	6	5
Lost to follow-up	11	17	10
Subject deterioration	-	1	1
Protocol deviation	1	1	6

Baseline characteristics

Reporting groups

Reporting group title	Randomisation
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Reporting group description: -

Reporting group values	Randomisation	Total	
Number of subjects	1408	1408	
Age categorical Units: Subjects			
Adolescents (12-17 years)	93	93	
Adults (18-64 years)	1312	1312	
From 65-84 years	3	3	
Gender categorical Units: Subjects			
Female	934	934	
Male	474	474	

End points

End points reporting groups

Reporting group title	Randomisation
Reporting group description: All subjects randomised	
Reporting group title	Treatment Group 1
Reporting group description: A single course of Cat-PAD 4 x 6 nmol 4 weeks apart followed by 4 x placebo 4 weeks apart.	
Reporting group title	Treatment Group 2
Reporting group description: A single course of Cat-PAD 4 x 6 nmol 4 weeks apart followed by a second course of Cat-PAD 4 x 6 nmol 4 weeks apart.	
Reporting group title	Treatment Group 3
Reporting group description: 2 courses of 4 x placebo 4 weeks apart.	

Primary: The mean Combined Score in the Cat-PAD treatment groups compared with the mean Combined Score in the placebo group

End point title	The mean Combined Score in the Cat-PAD treatment groups compared with the mean Combined Score in the placebo group
End point description:	
End point type	Primary
End point timeframe: Weeks 52-54 after randomisation	

End point values	Treatment Group 1	Treatment Group 2	Treatment Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	417	414	414	
Units: Combined Score				
least squares mean (standard error)	1.04 ($\pm$ 0.068)	1.00 ($\pm$ 0.068)	1.05 ($\pm$ 0.068)	

Statistical analyses

Statistical analysis title	Mean daily CS in PAC3 active compared to placebo
Comparison groups	Treatment Group 1 v Treatment Group 2 v Treatment Group 3

Number of subjects included in analysis	1245
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)

Secondary: Mean TRSS in Cat-PAD treatment groups compared with placebo

End point title	Mean TRSS in Cat-PAD treatment groups compared with placebo
End point description:	
End point type	Secondary
End point timeframe:	
Weeks 52-54 after randomisation	

End point values	Treatment Group 1	Treatment Group 2	Treatment Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	417	414	414	
Units: TRSS score				
least squares mean (standard error)	5.67 (± 0.358)	5.54 (± 0.356)	5.87 (± 0.357)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean daily TNSS in Cat-PAD treatment groups compared with placebo

End point title	Mean daily TNSS in Cat-PAD treatment groups compared with placebo
End point description:	
End point type	Secondary
End point timeframe:	
Weeks 52 - 54 post randomisation	

End point values	Treatment Group 1	Treatment Group 2	Treatment Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	417	414	414	
Units: TNSS				
least squares mean (standard error)	3.48 (± 0.197)	3.36 (± 0.196)	3.44 (± 0.196)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean daily TOSS in Cat-PAD compared to placebo

End point title	Mean daily TOSS in Cat-PAD compared to placebo
End point description:	
End point type	Secondary
End point timeframe:	
Weeks 52 - 54 post randomisation	

End point values	Treatment Group 1	Treatment Group 2	Treatment Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	417	414	414	
Units: TOSS				
least squares mean (standard error)	2.20 (± 0.179)	2.19 (± 0.178)	2.42 (± 0.179)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean RMS in Cat-PAD treatment groups compared with placebo

End point title	Mean RMS in Cat-PAD treatment groups compared with placebo
End point description:	
End point type	Secondary
End point timeframe:	
Weeks 52-54 post randomisation	

End point values	Treatment Group 1	Treatment Group 2	Treatment Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	417	414	414	
Units: RMS				
least squares mean (standard error)	0.34 ($\pm$ 0.038)	0.31 ($\pm$ 0.037)	0.32 ($\pm$ 0.037)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean RQLQ score in Cat-PAD treatment groups compared with placebo

End point title	Mean RQLQ score in Cat-PAD treatment groups compared with placebo
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End point description:

End point type	Secondary
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End point timeframe:

Weeks 52-54 post randomisation

End point values	Treatment Group 1	Treatment Group 2	Treatment Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	396	403	393	
Units: RQLQ score				
least squares mean (standard error)	1.26 ($\pm$ 0.080)	1.26 ($\pm$ 0.079)	1.25 ($\pm$ 0.079)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days subjects have no moderate or severe TRSS symptoms without rescue medication usage

End point title	Number of days subjects have no moderate or severe TRSS symptoms without rescue medication usage
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End point description:

End point type	Secondary
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End point timeframe:

Weeks 52-54 post randomisation

End point values	Treatment Group 1	Treatment Group 2	Treatment Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	417	414	414	
Units: Days				
least squares mean (standard error)	9.44 ($\pm$ 0.560)	10.11 ($\pm$ 0.556)	9.76 ($\pm$ 0.557)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Time from randomisation to end of study

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	Treatment Group 1
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Reporting group description:

A single course of Cat-PAD 4 x 6 nmol 4 weeks apart followed by 4 x placebo 4 weeks apart.

Reporting group title	Treatment Group 2
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Reporting group description:

A single course of Cat-PAD 4 x 6 nmol 4 weeks apart followed by a second course of Cat-PAD 4 x 6 nmol 4 weeks apart

Reporting group title	Treatment Group 3
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Reporting group description:

2 courses of 4 x placebo 4 weeks apart.

Serious adverse events	Treatment Group 1	Treatment Group 2	Treatment Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 467 (2.36%)	13 / 470 (2.77%)	9 / 470 (1.91%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 467 (0.00%)	0 / 470 (0.00%)	1 / 470 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign breast neoplasm			
subjects affected / exposed	1 / 467 (0.21%)	0 / 470 (0.00%)	0 / 470 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 467 (0.21%)	0 / 470 (0.00%)	0 / 470 (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

Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 467 (0.21%)	0 / 470 (0.00%)	1 / 470 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 467 (0.00%)	0 / 470 (0.00%)	1 / 470 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 467 (0.21%)	0 / 470 (0.00%)	0 / 470 (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
Pulmonary embolism			
subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (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
Psychiatric disorders			
Major depression			
subjects affected / exposed	1 / 467 (0.21%)	0 / 470 (0.00%)	0 / 470 (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
Suicidal ideation			

subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (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
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	0 / 467 (0.00%)	0 / 470 (0.00%)	1 / 470 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	1 / 467 (0.21%)	0 / 470 (0.00%)	0 / 470 (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
Procedural pain			
subjects affected / exposed	2 / 467 (0.43%)	0 / 470 (0.00%)	0 / 470 (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
Comminuted fracture			
subjects affected / exposed	1 / 467 (0.21%)	0 / 470 (0.00%)	0 / 470 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (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
Hand fracture			
subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (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
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Nervous system disorders			
Vascular headache			
subjects affected / exposed	1 / 467 (0.21%)	0 / 470 (0.00%)	0 / 470 (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
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 467 (0.00%)	0 / 470 (0.00%)	1 / 470 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 467 (0.21%)	0 / 470 (0.00%)	0 / 470 (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
IgA nephropathy			
subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (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
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 467 (0.00%)	0 / 470 (0.00%)	1 / 470 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 467 (0.00%)	0 / 470 (0.00%)	1 / 470 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoroacetabular impingement			
subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (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			
Acarodermatitis			

subjects affected / exposed	0 / 467 (0.00%)	0 / 470 (0.00%)	1 / 470 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 467 (0.00%)	0 / 470 (0.00%)	1 / 470 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 467 (0.21%)	1 / 470 (0.21%)	0 / 470 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 467 (0.21%)	0 / 470 (0.00%)	0 / 470 (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
Scrotal abscess			
subjects affected / exposed	1 / 467 (0.21%)	0 / 470 (0.00%)	0 / 470 (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
Infectious mononucleosis			
subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (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
Cellulitis			
subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (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
Metabolism and nutrition disorders			
Diabetic ketoacidosis			

subjects affected / exposed	0 / 467 (0.00%)	1 / 470 (0.21%)	0 / 470 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Treatment Group 1	Treatment Group 2	Treatment Group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	298 / 467 (63.81%)	299 / 470 (63.62%)	305 / 470 (64.89%)
Nervous system disorders			
Headache			
subjects affected / exposed	25 / 467 (5.35%)	39 / 470 (8.30%)	35 / 470 (7.45%)
occurrences (all)	78	86	76
General disorders and administration site conditions			
Injection site pruritus			
subjects affected / exposed	19 / 467 (4.07%)	13 / 470 (2.77%)	11 / 470 (2.34%)
occurrences (all)	51	45	41
Injection site urticaria			
subjects affected / exposed	17 / 467 (3.64%)	9 / 470 (1.91%)	7 / 470 (1.49%)
occurrences (all)	95	43	38
Pyrexia			
subjects affected / exposed	6 / 467 (1.28%)	12 / 470 (2.55%)	6 / 470 (1.28%)
occurrences (all)	6	13	7
Immune system disorders			
Allergy to animal			
subjects affected / exposed	9 / 467 (1.93%)	9 / 470 (1.91%)	11 / 470 (2.34%)
occurrences (all)	9	11	13
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	9 / 467 (1.93%)	12 / 470 (2.55%)	3 / 470 (0.64%)
occurrences (all)	10	12	3
Diarrhoea			
subjects affected / exposed	5 / 467 (1.07%)	6 / 470 (1.28%)	12 / 470 (2.55%)
occurrences (all)	6	7	15
Toothache			

subjects affected / exposed occurrences (all)	1 / 467 (0.21%) 1	11 / 470 (2.34%) 12	5 / 470 (1.06%) 5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	18 / 467 (3.85%)	18 / 470 (3.83%)	24 / 470 (5.11%)
occurrences (all)	26	27	26
Oropharyngeal pain			
subjects affected / exposed	16 / 467 (3.43%)	16 / 470 (3.40%)	16 / 470 (3.40%)
occurrences (all)	20	20	18
Asthma			
subjects affected / exposed	17 / 467 (3.64%)	14 / 470 (2.98%)	16 / 470 (3.40%)
occurrences (all)	21	15	17
Dyspnoea			
subjects affected / exposed	12 / 467 (2.57%)	7 / 470 (1.49%)	11 / 470 (2.34%)
occurrences (all)	19	13	12
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	12 / 467 (2.57%)	9 / 470 (1.91%)	15 / 470 (3.19%)
occurrences (all)	20	12	20
Arthralgia			
subjects affected / exposed	7 / 467 (1.50%)	12 / 470 (2.55%)	16 / 470 (3.40%)
occurrences (all)	8	16	16
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	85 / 467 (18.20%)	87 / 470 (18.51%)	90 / 470 (19.15%)
occurrences (all)	124	128	127
Upper respiratory tract infection			
subjects affected / exposed	37 / 467 (7.92%)	34 / 470 (7.23%)	42 / 470 (8.94%)
occurrences (all)	48	41	60
Sinusitis			
subjects affected / exposed	21 / 467 (4.50%)	24 / 470 (5.11%)	23 / 470 (4.89%)
occurrences (all)	26	29	24
Bronchitis			
subjects affected / exposed	23 / 467 (4.93%)	23 / 470 (4.89%)	19 / 470 (4.04%)
occurrences (all)	27	25	21
Pharyngitis			

subjects affected / exposed	11 / 467 (2.36%)	18 / 470 (3.83%)	14 / 470 (2.98%)
occurrences (all)	11	20	17
Influenza			
subjects affected / exposed	9 / 467 (1.93%)	5 / 470 (1.06%)	19 / 470 (4.04%)
occurrences (all)	9	5	20
Urinary tract infection			
subjects affected / exposed	9 / 467 (1.93%)	12 / 470 (2.55%)	11 / 470 (2.34%)
occurrences (all)	11	16	13
Tonsillitis			
subjects affected / exposed	9 / 467 (1.93%)	10 / 470 (2.13%)	7 / 470 (1.49%)
occurrences (all)	11	12	7
Rhinitis			
subjects affected / exposed	8 / 467 (1.71%)	4 / 470 (0.85%)	10 / 470 (2.13%)
occurrences (all)	8	5	13

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 January 2015	1. Change to the statistical analysis The study protocol has been amended to introduce a Bonferroni-Holm procedure in testing the primary hypothesis. Circassia has taken into account the scientific advice received from the Competent Authorities regarding the proposed statistical analysis and is adopting a change to the primary endpoint testing approach. This protocol amendment is designed to fulfil this requirement. 2. Increase in sample size An upper limit on the number of subjects to be randomised is being added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported