Clinical trial results:
An open-label, multicenter, efficacy and safety study of 4-month canakinumab treatment with 5-month follow-up and long-term treatment period in patients with active recurrent or chronic TNF-receptor associated periodic syndrome (TRAPS)

Summary

EudraCT number	2010-020061-24
Trial protocol	IE GB IT
Global end of trial date	20 June 2014

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	CACZ885D2203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01242813
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to assess response induced by canakinumab in subjects with active Tumor necrosis factor (TNF) receptor associated periodic syndrome (TRAPS) after 15 days of the first dose.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed. Corticosteroids and nonsteroidal anti-inflammatory drugs NSAIDs were allowed as rescue medication during active TRAPS attacks at the discretion of the investigator. Corticosteroids were allowed either as increased corticosteroid maintenance dose or intermittent steroid treatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 October 2010
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	United Kingdom: 8
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	Italy: 10
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	2
Children (2-11 years)	4
Adolescents (12-17 years)	13

Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 6 centres in 3 countries.

Pre-assignment

Screening details:

A total of 29 subjects were screened, out of which 20 were enrolled and exposed to study medication. Nine subjects were considered as screening failures due to unacceptable laboratory value or test procedure results.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Canakinumab

Arm description:

Subjects received body-weight stratified dosage of canakinumab (2 milligram/ kilogram (mg/kg) for subjects ≤ 40 kg or 150 mg for subjects > 40 kg) through subcutaneously (s.c.) route as the starting dose at baseline and monthly for 4 months. The dose was escalated at Day 8 if dose of canakinumab was not sufficient to resolve the qualifying TRAPS flare.

Arm type	Experimental
Investigational medicinal product name	Canakinumab
Investigational medicinal product code	ACZ885
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Body weight stratified dose of canakinumab 2 mg/kg or 150 mg injected s.c. at baseline and monthly for 4 months.

Number of subjects in period 1	Canakinumab
Started	20
Completed	18
Not completed	2
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Canakinumab
Reporting group description:	
Subjects received body-weight stratified dosage of canakinumab (2 milligram/ kilogram (mg/kg) for subjects ≤ 40 kg or 150 mg for subjects > 40 kg) through subcutaneously (s.c.) route as the starting dose at baseline and monthly for 4 months. The dose was escalated at Day 8 if dose of canakinumab was not sufficient to resolve the qualifying TRAPS flare.	

Reporting group values	Canakinumab	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
Children (2--11 years)	2	2	
Adolescents (12--17 years)	4	4	
Adults (18--64 years)	13	13	
Adults (65-84 years)	1	1	
Age continuous Units: years			
arithmetic mean	34.62		
standard deviation	± 18.362	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	13	13	

End points

End points reporting groups

Reporting group title	Canakinumab

Reporting group description:

Subjects received body-weight stratified dosage of canakinumab (2 milligram/ kilogram (mg/kg) for subjects ≤ 40 kg or 150 mg for subjects > 40 kg) through subcutaneously (s.c.) route as the starting dose at baseline and monthly for 4 months. The dose was escalated at Day 8 if dose of canakinumab was not sufficient to resolve the qualifying TRAPS flare.

Primary: Percentage of subjects with complete or almost complete response at Day 15

End point title	Percentage of subjects with complete or almost complete response at Day 15[1]

End point description:

Complete response was defined as clinical remission (Physician's Global Assessment of TRAPS activity absent or minimal) and serological remission (C reactive protein (CRP) and/or Serum amyloid A protein (SAA) less than 10 milligram per litre (mg/L)). Almost complete response was defined as clinical remission and a partial serological remission (equal to or more than 70% reduction of baseline (CRP) and/or (SAA)}. The primary analysis was performed on the Full Analysis Set (FAS), defined as all subjects who received at least one dose of study treatment and had at least one post-baseline assessment for primary efficacy.

End point type	Primary

End point timeframe:

Day 15

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: Only descriptive summary statistics was planned for this outcome measure.

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of subjects				
number (confidence interval 95%)	95 (75.1 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with complete or almost complete response at Day 8

End point title	Percentage of subjects with complete or almost complete response at Day 8

End point description:

Complete response was defined as clinical remission (Physician's Global Assessment of TRAPS activity absent or minimal) and serological remission (CRP and/or SAA less than 10 mg/L). Almost complete response was defined as clinical remission and a partial serological remission (equal to or more than 70% reduction of baseline (CRP) and/or (SAA)). The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

Day 8

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of subjects				
number (confidence interval 95%)	80 (56.3 to 94.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with complete clinical remission at Day 8 and 15

End point title	Percentage of subjects with complete clinical remission at Day 8 and 15

End point description:

Complete clinical remission was defined as Physician's Global Assessment of TRAPS activity to be absent or minimal (1). TRAPS associated clinical signs and symptoms were assessed by the investigator at every visit on a 5-point scale: 0 = Absent; 1 = Minimal; 2 = Mild; 3 = Moderate; 4 = Severe. The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

Day 8 and 15

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 8	90 (68.3 to 98.8)			
Day 15	100 (83.2 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with target levels of C-reactive protein (CRP) and Serum amyloid A protein (SAA) at Day 8 and 15

End point title	Percentage of subjects with target levels of C-reactive protein (CRP) and Serum amyloid A protein (SAA) at Day 8 and 15

End point description:

The CRP and SAA were used as inflammatory markers. The target level concentration was equal to or less than 10 mg/L. The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

Day 8 and 15

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 8 Day 15	35 (15.4 to 59.2) 60 (36.1 to 80.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to physician’s assessed clinical remission

End point title	Time to physician’s assessed clinical remission

End point description:

Time period for complete remission after initial canakinumab treatment as assessed by subjects was defined as a Physician’s Global Assessment of TRAPS symptoms of scale 1 or less. The Patient’s Global Assessment was based on a 5-point scale: 0 = None/absent (no) ; 1 = Minimal; 2 = Mild; 3 = Moderate; 4 = Severe. The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

From start of treatment to Day 15

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Days				
median (confidence interval 95%)	4 (3 to 8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with complete or almost complete response at Day 15 after receiving additional dose at Day 8

End point title	Percentage of subjects with complete or almost complete response at Day 15 after receiving additional dose at Day 8

End point description:

Subjects who had not achieved a complete response at Day 8 were given an additional dose of canakinumab. Complete response was defined as clinical remission (Physician's Global Assessment of TRAPS activity absent or minimal) and serological remission (CRP and/or SAA less than 10 mg/L). Almost complete response was defined as clinical remission and a partial serological remission (equal to or more than 70% reduction of baseline (CRP) and/or (SAA)). The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

Day 15

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	4[2]			
Units: Percentage of subjects				
number (confidence interval 95%)	100 (39.8 to 100)			

Notes:

[2] - Only 4 subjects out of 20 had not achieved complete or almost complete response at Day 8.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to patient's assessed clinical remission

End point title	Time to patient's assessed clinical remission

End point description:

Time period for complete remission after initial canakinumab treatment as assessed by subjects was defined as a Patient's Global Assessment of TRAPS symptoms of scale 1 or less. The Patient's Global Assessment was based on a 5-point scale: 0 = None/absent (no) ; 1 = Minimal; 2 = Mild; 3 = Moderate; 4 = Severe. The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

Day 15

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Days				
median (confidence interval 95%)	3 (1 to 11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from baseline in C-reactive protein (CRP) and Serum amyloid A (SAA) concentration to end of study

End point title	Percentage change from baseline in C-reactive protein (CRP) and Serum amyloid A (SAA) concentration to end of study

End point description:

The CRP and SAA were used as inflammatory markers. The target level concentration was equal to or less than 10 mg/L. Negative percent change in concentration of inflammatory markers indicated improvement. The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

Baseline to end of study

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percent change				
median (full range (min-max))				
CRP	-92.19 (-99 to 43.6)			
SAA	-96.54 (-99.8 to 68.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with defined grades for skin rash, eye manifestations, extremity pain and abdominal pain

End point title	Number of subjects with defined grades for skin rash, eye manifestations, extremity pain and abdominal pain

End point description:

TRAPS signs and symptoms were assessed in 4 key categories: skin disease (skin rash), eye manifestations, extremity pain (musculoskeletal), and abdominal pain. Subjects were assessed for TRAPS associated signs and symptoms a 5-point Physician’s global assessment scale: None/absent (no); 1 = Minimal; 2 = Mild; 3 = Moderate; 4 = Severe . The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

End of study

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Number of subjects				
number (not applicable)				
Skin rash absent	19			
Skin rash minimal	1			
Skin rash mild	0			
Skin rash moderate	0			
Skin rash severe	0			
Eye manifestations absent	18			
Eye manifestations minimal	2			
Eye manifestations mild	0			
Eye manifestations moderate	0			
Eye manifestations severe	0			
Extremity pain absent	18			
Extremity pain minimal	1			
Extremity pain mild	1			
Extremity pain moderate	0			
Extremity pain severe	0			
Abdominal pain absent	19			
Abdominal pain minimal	1			
Abdominal pain mild	0			
Abdominal pain moderate	0			
Abdominal pain severe	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with defined grades in physician’s global assessment score

End point title	Percentage of subjects with defined grades in physician’s global assessment score

End point description:

Subjects were assessed based on Physician’s Global Assessment on 5-point scale for TRAPS associated signs and symptoms as: 0 = None/absent; 1 = Minimal; 2 = Mild; 3 = Moderate; 4 = Severe. The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

End of study

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	18[3]			
Units: Percent				
number (not applicable)				
None (0)	84.2			
Minimal (1)	10.5			
Mild (2)	0			
Moderate (3)	0			
Severe (4)	0			

Notes:

[3] - Total number of subjects with non-missing assessment at the specified time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with defined grades in patient's global assessment score

End point title	Percentage of subjects with defined grades in patient's global assessment score

End point description:

Subjects assessed the disease condition based on a 5-point Patient's global assessment scale for were assessed based on TRAPS associated signs and symptoms as: 0 = None/absent; 1 = Minimal; 2 = Mild; 3 = Moderate; 4 = Severe. The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

End of follow-up period

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	12[4]			
Units: Percent				
number (not applicable)				
Absent	41.7			
Minimal	33.3			
Mild	8.3			
Moderate	16.7			
Severe	0			

Notes:

[4] - Total number of subjects with non-missing assessment at the specified time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of relapsed subjects

End point title	Percentage of relapsed subjects

End point description:

Relapse was defined as a Physician's Global Assessment score of 2 (and an increase of at least 1 point compared to Day 15) and CRP and/or SAA equal to or more than 30 mg/L representing a 30% increase from Day 15. The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

At Day 15, 29, 57, 85, 113, 141, 169, 197, 225, 253, 281, 309, 337, 365, 393, 421, 449, 533, 561, 589, 617, 645, 673, 729, 785, 841, 897, 925 and 953

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20[5]			
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 15	0 (0.1 to 27.3)			
Day 29	0 (0 to 0)			
Day 57	0 (0 to 0)			
Day 85	5 (0 to 0)			
Day 113	0 (0.1 to 24.9)			
Day 141	10 (0 to 0)			
Day 169	10 (1.3 to 33.1)			
Day 197	35 (1.9 to 45.5)			
Day 225	10 (30.8 to 89.1)			
Day 253	10 (6.8 to 93.2)			
Day 281	0 (1.2 to 31.7)			
Day 309	10 (0 to 0)			
Day 337	5 (1.2 to 31.7)			
Day 365	0 (0.1 to 24.9)			
Day 393	0 (0 to 0)			
Day 421	5 (0 to 0)			
Day 449	0 (0 to 0)			
Day 477	5 (0.1 to 26)			
Day 505	0 (0 to 0)			
Day 533	0 (0 to 0)			
Day 561	0 (0 to 0)			
Day 589	0 (0 to 0)			
Day 617	0 (0 to 0)			
Day 645	5 (0 to 0)			
Day 673	15 (0.5 to 71.6)			
Day 701	0 (3.6 to 41.4)			
Day 729	5 (0.1 to 27.3)			
Day 757	0 (0 to 0)			
Day 785	0 (0 to 0)			
Day 813	0 (0 to 0)			
Day 841	10 (1.4 to 34.7)			

Day 869	0 (0 to 0)			
Day 897	10 (1.4 to 34.7)			
Day 925	0 (0 to 0)			
End of Study (Day 953)	0 (0 to 0)			

Notes:

[5] - Confidence Interval value (0.0) denotes that value was not applicable as number of subjects was 0

Statistical analyses

No statistical analyses for this end point

Secondary: Time to relapse after last dose of canakinumab

End point title	Time to relapse after last dose of canakinumab

End point description:

Relapse was defined as a Physician's Global Assessment score of 2 (and an increase of at least 1 point compared to Day 15) and CRP and/or SAA equal to or more than 30 mg/L representing a 30% increase from Day 15. The analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

Day 15 to Day 120 (4 months)

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Days				
median (confidence interval 95%)	91.5 (65 to 117)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who relapsed and took rescue medication

End point title	Percentage of subjects who relapsed and took rescue medication

End point description:

Subjects who relapsed after the last dose of canakinumab and received either corticosteroid treatment or NSAID or both corticosteroid treatment and NSAID as rescue medication. The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

Day 15 to Day 120 (4 months)

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of subjects				
number (confidence interval 95%)				
Corticosteroid	25 (8.7 to 49.1)			
NSAID	25 (8.7 to 49.1)			
Both corticosteroid and NSAID	10 (1.2 to 31.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of canakinumab

End point title	Serum concentration of canakinumab

End point description:

Canakinumab concentrations in serum were assessed for evaluating pharmacokinetics (PK) of the drug. The analysis was performed on the FAS population. The 'n' signifies those subjects evaluable for this measure at specified time points for each group, respectively.

End point type	Secondary

End point timeframe:

At Day 3, 8, 15, 29, 57, 85, 113, 141, 169, 197, 225, 253, 281, 309, 337, 365, 393, 421, 449, 533, 561, 589, 617, 645, 673, 729, 785, 841, 897, 925 and 953

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20[6]			
Units: microgram(s)/millilitre				
arithmetic mean (standard deviation)				
Day 3 (n=20)	12.737 (± 5.3158)			
Day 8 (n=19)	13.874 (± 4.5851)			
Day 15 (n=19)	13.609 (± 5.5868)			
Day 29 (n=20)	9.911 (± 4.2272)			
Day 57 (n=20)	13.605 (± 5.4975)			
Day 85 (n=20)	15.291 (± 6.4353)			
Day 113 (n=20)	15.837 (± 6.828)			
Day 141 (n=17)	8.799 (± 3.1486)			
Day 169 (n=12)	5.655 (± 2.2158)			

Day 197 (n=8)	3.906 (± 1.6446)			
Day 225 (n=2)	2.725 (± 1.2799)			
Day 253 (n=9)	10.261 (± 7.9592)			
Day 281 (n=20)	9.759 (± 4.6194)			
Day 309 (n=13)	13.088 (± 4.6648)			
Day 337 (n=11)	13.182 (± 5.464)			
Day 365 (n=9)	15.531 (± 6.7944)			
Day 393 (n=2)	20.95 (± 1.6263)			
Day 421 (n=2)	20.9 (± 2.9698)			
Day 449 (n=17)	17.319 (± 6.496)			
Day 533 (n=1)	18.4 (± 0)			
Day 561 (n=4)	15.55 (± 2.2128)			
Day 589 (n=5)	16.48 (± 3.8134)			
Day 617 (n=17)	14.124 (± 5.8931)			
Day 645 (n=1)	7.45 (± 0)			
Day 673 (n=5)	9.802 (± 4.6757)			
Day 729 (n=5)	8.912 (± 3.4413)			
Day 785 (n=18)	7.757 (± 2.2948)			
Day 841 (n=4)	8.528 (± 2.112)			
Day 897 (n=9)	8.157 (± 2.6782)			
Day 925 (n=3)	10.527 (± 7.4405)			
Day 953 (n=10)	9.56 (± 2.9375)			

Notes:

[6] - Standard deviation value (0.0) denotes that the dispersion value was not applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of total Interleukin-1β antibody (IL-1β)

End point title	Serum concentration of total Interleukin-1β antibody (IL-1β)

End point description:

Pharmacodynamics of canakinumab was assessed by total IL-1β (sum of free and bound canakinumab) concentration, determined in serum by means of competitive ELISA assay with limit of detection at 0.25 picogram/millilitre (pg/mL). The analysis was performed on the FAS population. The 'n' signifies those subjects evaluable for this measure at specified time points for each group, respectively.

End point type	Secondary

End point timeframe:

Day 1, 3, 8, 15, 29, 57, 85, 113, 141, 169, 197, 225, 253, 281, 309, 337, 365, 393, 421, 449, 533,

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20[7]			
Units: Picogram(s)/millilitre				
arithmetic mean (standard deviation)				
Day 3 (n=20)	12.616 (± 20.441)			
Day 8 (n=19)	16.811 (± 20.237)			
Day 15 (n=19)	10.662 (± 7.6915)			
Day 29 (n=20)	9.342 (± 5.1266)			
Day 57 (n=20)	10.701 (± 4.5329)			
Day 85 (n=20)	11.212 (± 4.1552)			
Day 113 (n=20)	14.401 (± 5.491)			
Day 141 (n=17)	10.779 (± 4.1092)			
Day 169 (n=12)	10.912 (± 8.2431)			
Day 197 (n=8)	30.098 (± 41.158)			
Day 225 (n=2)	3.52 (± 0.9475)			
Day 253 (n=9)	25.002 (± 28.274)			
Day 281 (n=20)	13.722 (± 7.5574)			
Day 309 (n=13)	22.478 (± 16.688)			
Day 337 (n=11)	19.904 (± 10.789)			
Day 365 (n=9)	16.338 (± 5.8318)			
Day 393 (n=2)	27.6 (± 10.182)			
Day 421 (n=2)	30.65 (± 12.94)			
Day 449 (n=17)	17.723 (± 8.8367)			
Day 533 (n=1)	25.2 (± 0)			
Day 561 (n=4)	15.008 (± 5.4952)			
Day 589 (n=5)	16.99 (± 5.2212)			
Day 617 (n=17)	14.34 (± 6.1663)			
Day 645 (n=1)	16 (± 0)			
Day 673 (n=5)	15.296 (± 11.908)			

Day 729 (n=5)	16.702 (± 12.386)			
Day 785 (n=18)	12.698 (± 6.0688)			
Day 841 (n=4)	12.478 (± 6.9548)			
Day 897 (n=9)	12.331 (± 8.032)			
Day 925 (n=3)	15.033 (± 1.7502)			
Day 953 (n=10)	11.701 (± 7.9172)			

Notes:

[7] - Standard deviation value (0.0) denotes that the dispersion value was not applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects exhibiting Anti-canakinumab antibodies at any visit

End point title	Number of subjects exhibiting Anti-canakinumab antibodies at any visit

End point description:

Immunogenicity assessment included determination of anti-canakinumab (ACZ885) antibodies in serum samples using BIAcore system. The analysis was performed on the FAS population.

End point type	Secondary

End point timeframe:

From Day 1 to end of study

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Number of subjects	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Canakinumab

Reporting group description:

Subjects received body-weight stratified dosage of canakinumab (2 mg/kg for subjects ≤ 40 kg or 150 mg for subjects > 40 kg) through s.c. route as the starting dose at baseline and monthly for 4 months. The dose was escalated at Day 8 if dose of canakinumab was not sufficient to resolve the qualifying TRAPS flare.

Serious adverse events	Canakinumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 20 (35.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Pericarditis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperkalaemia			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertriglyceridaemia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Canakinumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	6		
Phlebitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Surgical and medical procedures			
Nasal septal operation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skin neoplasm excision			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Tooth extraction			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			

Asthenia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Fatigue subjects affected / exposed occurrences (all)	7 / 20 (35.00%) 11		
Condition aggravated subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 4		
Chest pain subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 5		
Non-cardiac chest pain subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2		
Pyrexia subjects affected / exposed occurrences (all)	10 / 20 (50.00%) 25		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Reproductive system and breast disorders Breast cyst subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2		
Breast mass subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Dysmenorrhoea subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2		
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	6 / 20 (30.00%)		
occurrences (all)	10		
Dysphonia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Epistaxis			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Nasal congestion			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	11 / 20 (55.00%)		
occurrences (all)	19		
Rhinitis allergic			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Rhinorrhoea			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Sneezing			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Tonsillar hypertrophy			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Investigations			

Blood creatinine increased			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Blood iron decreased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Blood triglycerides increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Occult blood positive			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Joint dislocation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Laceration			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Muscle rupture			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Muscle strain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skeletal injury			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Sunburn			

subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Hypoaesthesia subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Presyncope subjects affected / exposed occurrences (all) Sinus headache subjects affected / exposed occurrences (all) Tremor subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 2 5 / 20 (25.00%) 5 11 / 20 (55.00%) 25 1 / 20 (5.00%) 1 3 / 20 (15.00%) 4 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Blood and lymphatic system disorders			

Lymphadenopathy			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Anaemia			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Ear pain			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Eye disorders			
Chalazion			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Conjunctivitis allergic			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Conjunctival haemorrhage			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Eye pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Dry eye			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Eye pruritus			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Eye swelling			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Eyelid oedema			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Ocular hyperaemia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Periorbital oedema			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	11 / 20 (55.00%)		
occurrences (all)	28		
Abdominal pain upper			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	5		
Constipation			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Dental caries			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	8 / 20 (40.00%)		
occurrences (all)	11		
Haemorrhoids			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Haematochezia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

Mouth ulceration subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1			
Vomiting subjects affected / exposed occurrences (all)	7 / 20 (35.00%) 7			
Toothache subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3			
Nausea subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2			
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1			
Actinic keratosis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1			
Alopecia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1			
Dermal cyst subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1			
Dry skin subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1			
Hyperhidrosis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1			
Ingrown hair subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1			
Rash				

subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	5		
Rash erythematous			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skin discolouration			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Polyuria			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Strangury			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 20 (40.00%)		
occurrences (all)	10		
Back pain			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	8		
Flank pain			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Muscle spasms			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Musculoskeletal pain			

subjects affected / exposed	6 / 20 (30.00%)		
occurrences (all)	8		
Myalgia			
subjects affected / exposed	6 / 20 (30.00%)		
occurrences (all)	8		
Neck pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Osteoporosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	4		
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	5		
Cystitis			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	4		
Ear infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Enterobiasis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Haemorrhoid infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gingivitis			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Fungal skin infection			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		

Hand-foot-and-mouth disease				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Lower respiratory tract infection				
subjects affected / exposed	3 / 20 (15.00%)			
occurrences (all)	8			
Laryngitis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences (all)	2			
Oral candidiasis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Onychomycosis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	12 / 20 (60.00%)			
occurrences (all)	23			
Oral herpes				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	3			
Pharyngitis				
subjects affected / exposed	4 / 20 (20.00%)			
occurrences (all)	5			
Pharyngitis streptococcal				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Pharyngotonsillitis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Respiratory tract infection				
subjects affected / exposed	3 / 20 (15.00%)			
occurrences (all)	6			

Rhinitis			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	16		
Sinusitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Tinea infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Tooth abscess			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Tooth infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	6 / 20 (30.00%)		
occurrences (all)	9		
Urinary tract infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Urinary tract infection viral			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Viral infection			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypertriglyceridaemia			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Hyperkalaemia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Metabolic acidosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Iron deficiency			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Vitamin D deficiency			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 November 2010	Updated the volume of blood withdrawal for biomarker component, protocol for soluble plasma protein marker sample collection and information regarding subject diaries.
10 November 2011	Site monitoring and collection of efficacy and safety data during the 24 months of continued treatment were implemented after clarification on post follow-up period. Optimized PK/PD based dosing schedule was implemented, updated the duration of the follow-up period for actual maximum duration of the withdrawal period (5 months) and clarified almost complete response and relapse endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported