Clinical trial results:
An Open Label Study to Assess the Safety, Tolerability and Efficacy of Canakinumab (ACZ885) in Patients Aged 4 Years or Older Diagnosed With Cryopyrin-associated Periodic Syndromes (CAPS) in Canada

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Summary

EudraCT number	2015-003491-69
Trial protocol	Outside EU/EEA
Global end of trial date	17 May 2012

Results information

Result version number	v1 (current)
This version publication date	06 July 2018
First version publication date	06 July 2018

Trial information

Trial identification

Sponsor protocol code	CACZ885DCA01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01105507
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 May 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 May 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate safety and tolerability of canakinumab in Canadian patients with CAPS defined as:
• Familial Cold Autoinflammatory Syndrome (FCAS)/ Familial Cold Urticaria (FCU);
• Muckle-Wells Syndrome (MWS);
• Neonatal-Onset Multisystem Inflammatory Disease (NOMID)/ Chronic Infantile Neurological, Cutaneous, Articular Syndrome (CINCA).
To assess the maintenance of response over time under routine medical care in patients with the following CAPS related diseases: FCAS/FCU, MWS, NOMID/CINCA.

Protection of trial subjects:

In order to avoid relapse, rescue medication with canakinumab was allowed during the course of the study with the stipulation that once a patient received this medication, telephone contact with the patient was necessary to determine if there was a response to treatment. In addition, investigators advised Novartis of the occurrence of such events so that investigational drug stocks could be replenished.
Some patients may have required rescue medication for a brief period of time. In this case, patients returned to their previous dosing regimen if the reason for rescue medication had subsided, based on the Investigator's judgment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 August 2010
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	Canada: 4
Worldwide total number of subjects	4
EEA total number of subjects	0

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)	2
Adolescents (12-17 years)	0
Adults (18-64 years)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Informed consent was obtained for patient’s > 18 years of age in writing before any assessment was performed. For patients < 18 years of age, the parent or legal guardian provided informed consent and an Assent Form was available for the children when appropriate. Consent was obtained at the Screening/Baseline visit.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	ACZ885

Arm description:

Canakinumab was administered subcutaneously. Individuals whose body weight was > 40 kg received 1 mL of solution for injection at a concentration of 150 mg/mL. For patients with a body weight ≥ 15 kg and ≤ 40 kg, a dose of 2 mg/kg subcutaneous was administered.

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

Dosage and administration details:

Canakinumab for injection in 6 mL glass vials each containing nominally 150 mg study drug as a lyophilized cake. Reconstitution was achieved by addition of 1.0 mL water for injection and canakinumab was administered subcutaneously.

Number of subjects in period 1	ACZ885
Started	4
Completed	3
Not completed	1
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	4	4	
Age categorical Units: Subjects			
Children (2-11 years)	2	2	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	2	2	
Age continuous Units: years			
arithmetic mean	27.4		
standard deviation	± 22.7	-	
Gender categorical Units: Subjects			
Female	4	4	

End points

End points reporting groups

Reporting group title	ACZ885
Reporting group description:	
Canakinumab was administered subcutaneously. Individuals whose body weight was > 40 kg received 1 mL of solution for injection at a concentration of 150 mg/mL. For patients with a body weight ≥ 15 kg and ≤ 40 kg, a dose of 2 mg/kg subcutaneous was administered.	
Subject analysis set title	Subject A
Subject analysis set type	Full analysis
Subject analysis set description:	
Health related quality of life evaluation per subject.	
Subject analysis set title	Subject B
Subject analysis set type	Full analysis
Subject analysis set description:	
Health related quality of life evaluation per subject.	
Subject analysis set title	Subject C
Subject analysis set type	Full analysis
Subject analysis set description:	
Health related quality of life evaluation per subject.	
Subject analysis set title	Subject D
Subject analysis set type	Full analysis
Subject analysis set description:	
Health related quality of life evaluation per subject.	

Primary: The percentage of patients with complete response to treatment at Day 8

End point title	The percentage of patients with complete response to treatment at Day 8[1]
End point description:	
Complete response is defined as Investigator's clinical assessment of disease activity ≤ minimal (using a 5-point scale ranging from absent to severe); assessment of skin disease ≤ minimal (using a 5-point scale ranging from absent to severe) and normal serum values of CRP and/or SAA (< 10 mg/L) .	
End point type	Primary
End point timeframe:	
Day 8	

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: Statistical analyses have not been reported for this primary end point.

End point values	ACZ885			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: percent				
number (not applicable)	100			

Statistical analyses

No statistical analyses for this end point

Primary: The percentage of complete responders who relapsed after showing a complete response at Day 8

End point title	The percentage of complete responders who relapsed after showing a complete response at Day 8[2]

End point description:

For complete responders, relapse was defined as the following criteria (assessed on the same day): CRP and/or SAA value > 30 mg/L AND Investigator's clinical assessment of disease activity > minimal or the investigator's clinical assessment of disease activity ≥ minimal AND assessment of skin disease > minimal.

End point type	Primary

End point timeframe:

Day 169 (Month 6 visit)

Notes:

[2] - 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: Statistical analyses have not been reported for this primary end point.

End point values	ACZ885			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: percent				
number (not applicable)	25			

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of health-related quality of life and productivity assessed using the medical outcome short form (36) health survey (SF-36®)

End point title	Evaluation of health-related quality of life and productivity assessed using the medical outcome short form (36) health survey (SF-36®)

End point description:

Each patient completed the SF-36 scale (Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH) Vitality (VT), Social Functioning(SF), Role Emotional (RE) and Mental Health (MH)) and Physical Component (PCS) and Mental Component (MCS) summary scores was computed and plotted using the norm-based scoring.
The SF-36 consists of eight scaled scores, which are the weighted sums of the questions in their section. Each scale is directly transformed into a 0-100 scale on the assumption that each question carries equal weight. The lower the score the more disability. The higher the score the less disability.

End point type	Secondary

End point timeframe:

Every 6 months until the end of study (Baseline, Month 6, 12 and 18)

End point values	Subject A	Subject B	Subject C	Subject D
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1[3]	1[4]	1	1
Units: scores on a scale				
number (not applicable)				
Baseline - Mental	999.99	52.2	59.4	55.2
Baseline - Physical	999.99	40.9	39.9	52.7
Month 6 - Mental	54.2	54.9	58.1	54.4
Month 6 - Physical	47.9	50.4	28.1	58.7
Month 12 - Mental	10.1	999.99	59	60
Month 12 - Physical	57	999.99	33.9	55.1
Month 18 - Mental	999.99	53.5	48.6	59.5
Month 18 - Physical	999.99	43.1	21.8	55.8

Notes:

[3] - 999.99 = no data reported

[4] - 999.99 = no data reported

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of health-related quality of life and productivity assessed using the Health Assessment Questionnaire (HAQ©)

End point title	Evaluation of health-related quality of life and productivity assessed using the Health Assessment Questionnaire (HAQ©)

End point description:

Twenty specific activities are assessed on a 4-point Likert scale where 0 = without difficulty, 1 = with some difficulty, 2 = with much difficulty, and 3 = unable to do. The 20 activities are grouped into 8 functional categories with each category given a single score equal to the maximum value of their component activities (0, 1, 2, or 3).

End point type	Secondary

End point timeframe:

Every 6 months until the end of study (Baseline, Month 6, 12 and 18)

End point values	Subject A	Subject B	Subject C	Subject D
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1[5]	1	1	1
Units: scores on a scale				
number (not applicable)				
Baseline - Alternative Disability Index	0.6	0.4	0.1	0
Baseline - Standard Disability Index	1	0.8	0.1	0
Month 6 - Alternative Disability Index	0.1	0	0	0
Month 6 - Standard Disability Index	0.1	0	0	0
Month 12 - Alternative Disability Index	0.1	0	0	0
Month 12 - Standard Disability Index	0.1	0	0	0
Month 18 - Alternative Disability Index	999.99	0.3	0.3	0
Month 18 - Standard Disability Index	999.99	0.5	0.4	0

Notes:
[5] - 999.99 = no data reported

Statistical analyses

No statistical analyses for this end point

Secondary: Subject's treatment adherence with canakinumab for the duration of the study

End point title	Subject's treatment adherence with canakinumab for the duration of the study

End point description:

End point type	Secondary

End point timeframe:
Baseline through week 72

End point values	ACZ885			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Dose interruption				
number (not applicable)				
incidence of dose interruption	3			

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	15.0

Reporting groups

Reporting group title	Canakinumab

Reporting group description:

Canakinumab

Serious adverse events	Canakinumab		
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		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
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: 5 %

Non-serious adverse events	Canakinumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Surgical and medical procedures			
Hospitalisation			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	4		
Aphthous stomatitis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Diarrhoea			

subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2 1 / 4 (25.00%) 6 1 / 4 (25.00%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Dysphonia subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Sinus congestion subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1 2 / 4 (50.00%) 2 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all) Purpura subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Infections and infestations			
Ear infection			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Gastroenteritis norovirus			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Gastroenteritis viral			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Lower respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Urinary tract infection			

subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 February 2011	The main purpose of this amendment was to clarify information related to rescue medication, concomitant therapy and efficacy and safety assessment sections of the clinical study protocol. The rescue medication section was updated to provide more clarity regarding alternative dosing for patients experiencing insufficient symptomatic relief. A correction was required regarding the washout time frame for Anakinra; the protocol was amended to be more in line with washout time frames currently prescribed in other Novartis protocols evaluating similar indications. The efficacy assessment section was modified in order to reflect study operational changes. The self-injection and health utilization patient questionnaires were removed from the study protocol as patients were not required to self inject and information initially planned to be collected using the health utilization questionnaire was already being collected via the other patient reported outcomes. No safety assessments were added to the protocol; however more detailed wording was provided in the safety section to clarify the procedures. The sample size was reduced in line with more realistic estimates; since there was no formal statistical hypothesis the reduction of sample size does not alter the trial objectives or planned analysis. Timelines, typographical errors and minor inconsistencies were corrected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Notes: