Clinical trial results:
An Open-label, Exploratory Study to Establish the Safety and Efficacy of 3 Months Treatment With Canakinumab in Patients With Colchicine Resistant Familial Mediterranean Fever

Summary

EudraCT number	2015-003527-57
Trial protocol	Outside EU/EEA
Global end of trial date	25 October 2011

Results information

Result version number	v1 (current)
This version publication date	29 September 2016
First version publication date	29 September 2016

Trial information

Trial identification

Sponsor protocol code	CACZ885DTR01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01088880
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharmaceuticals AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharmaceuticals 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	25 October 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 October 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

to measure the effect of canakinumab on the frequency of FMF
attacks defined as percentage of subjects with at least 50% reduction in the attack frequency during 3 month treatment period.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 December 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	Turkey: 9
Worldwide total number of subjects	9
EEA total number of subjects	0

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)	1
Adults (18-64 years)	8
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients who signed an informed consent and meet all inclusion and exclusion criteria in the screening period entered into a 30-day Run-in observation period.

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	Canakinumab

Arm description:

150 mg sc canakinumab every 4 weeks

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:

Subjects weighing less than 40 kg were administered canakinumab 2 mg/kg/month s.c., those weighting ≥ 40 kg were administered canakinumab 150 mg/month s.c in every 4 weeks during “Treatment Period”. The dose was doubled to 4 mg/kg/month for subjects weighing less than 40 kg and 300 mg/month for those weighing ≥ 40 kg at the second dosing if an attack occurs during the previous month. Canakinumab was supplied as a 180 mg white lyophilized powder for solution for subcutaneous injection.

Number of subjects in period 1	Canakinumab
Started	9
Completed	9

Baseline characteristics

Reporting groups	
Reporting group title	Canakinumab
Reporting group description:	
150 mg sc canakinumab every 4 weeks	

Reporting group values	Canakinumab	Total	
Number of subjects	9	9	
Age categorical Units: Subjects			
Adolescents (12-17 years)	1	1	
Adults (18-64 years)	8	8	
Age continuous Units: years			
arithmetic mean	22.33		
standard deviation	± 6.34	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	2	2	

End points

End points reporting groups

Reporting group title	Canakinumab
Reporting group description:	
150 mg sc canakinumab every 4 weeks	

Primary: Percentage of participants with at least 50% reduction in the attack frequency during 3 month treatment period

End point title	Percentage of participants with at least 50% reduction in the attack frequency during 3 month treatment period[1]
End point description:	
End point type	Primary
End point timeframe:	
Baseline to 3 months (adjusted for 84 days)	
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 provided for this primary end point.	

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent				
number (confidence interval 95%)				
Not observed	0 (0 to 33.6)			
Observed	100 (66.4 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of attacks during treatment period

End point title	Number of attacks during treatment period
End point description:	
End point type	Secondary
End point timeframe:	
Baseline through 3 months	

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent				
number (confidence interval 95%)				
No attack	88.9 (51.8 to 99.7)			
1 attack	11.1 (0.3 to 48.2)			
≥2 attack	0 (0 to 33.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Patient experienced attack during follow-up period

End point title	Patient experienced attack during follow-up period

End point description:

End point type	Secondary

End point timeframe:

2-month follow-up period

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent				
number (not applicable)				
No	44.4			
Yes	55.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to attack during follow-up period

End point title	Time to attack during follow-up period

End point description:

Time between last injection of canakinumab and Familial Mediterranean fever (FMF) attack.

End point type	Secondary

End point timeframe:

Day 87-144 (follow-up)

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: day				
arithmetic mean (standard deviation)	58.8 (± 22.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Attack severity -Severity of FMF attack

End point title	Attack severity -Severity of FMF attack

End point description:

End point type	Secondary

End point timeframe:

Pre-treatment (Visits 2-4); Post-Treatment (Visit 9/Day 86) and Follow-up period

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent				
number (not applicable)				
Pre-treatment: Very mild	0			
Pre-treatment: Mild	0			
Pre-treatment: Moderate	0			
Pre-treatment: Severe	44.4			
Pre-treatment: Very Severe	55.6			
Post-treatment: Very mild	0			
Post-treatment: Mild	0			
Post-treatment: Moderate	0			
Post-treatment: Severe	0			
Post-treatment: Very Severe	100			
Follow-up period: Very mild	20			
Follow-up period: Mild	0			
Follow-up period: Moderate	40			
Follow-up period: Severe	20			
Follow-up period: Very Severe	20			

Statistical analyses

No statistical analyses for this end point

Secondary: Time adjusted attack frequency comparison of attack history before 3 months from the study and pre and post treatment periods

End point title	Time adjusted attack frequency comparison of attack history before 3 months from the study and pre and post treatment periods

End point description:

At each post-treatment time point, only patients with a value at both, pre-treatment and post-treatment time point, are included.

End point type	Secondary

End point timeframe:

Pre-treatment (Visits 2-4) through Post-Treatment (Visit 9/Day 86)

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: attack number				
arithmetic mean (standard deviation)				
Before Study	4.46 (± 1.46)			
Pre-treatment	3.22 (± 0.7)			
Post treatment	0.11 (± 0.33)			
Change from Before Study/Pre-treatment	-1.24 (± 1.97)			
Change from Before Study/Post-treatment	-3.1 (± 0.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Attack Duration at baseline and post-treatment

End point title	Attack Duration at baseline and post-treatment

End point description:

At each post-baseline time point, only patients with a value at both, baseline and post-baseline time point, are included.

End point type	Secondary

End point timeframe:

Pre-treatment, Visit 7 (Day 29), Visit 8 (Day 57), Visit 9 (Day 86)

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: days				
arithmetic mean (standard deviation)				
Pre-treatment period	3.58 (± 3.11)			
Visit 7	0 (± 0)			
Visit 8	0 (± 0)			
Visit 9	3 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Physician's Global Assessment of Familial Mediterranean fever (FMF) control

End point title	Physician's Global Assessment of Familial Mediterranean fever (FMF) control

End point description:

End point type	Secondary

End point timeframe:

Visit 4 (Day 1), Visit 11 (Day 144), Visit 11 (Day 144) - [(RtT) Response to Treatment]

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent				
number (not applicable)				
Visit 4 - Very good	0			
Visit 4 - Good	0			
Visit 4 - Fair	11.1			
Visit 4 - Poor	88.9			
Visit 4 - Very poor	0			
Visit 11 - Very good	77.8			
Visit 11 - Good	11.1			
Visit 11 - Fair	11.1			
Visit 11 - Poor	0			
Visit 11 - Very poor	0			
Visit 11 RtT - Very good	100			
Visit 11 RtT - Good	0			
Visit 11 RtT - Fair	0			
Visit 11 RtT - Poor	0			
Visit 11 RtT - Very poor	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's Global Assessment of Familial Mediterranean fever (FMF) control

End point title	Patient's Global Assessment of Familial Mediterranean fever (FMF) control

End point description:

End point type	Secondary

End point timeframe:

Visit 4 (Day 1), Visit 11 (Day 144), Visit 11 (Day 144) - [(RtT) Response to Treatment]

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent				
number (not applicable)				
Visit 4 - Very good	0			
Visit 4 - Good	11.1			
Visit 4 - Fair	22.2			
Visit 4 - Poor	22.2			
Visit 4 - Very poor	44.4			
Visit 11 - Very good	37.5			
Visit 11 - Good	37.5			
Visit 11 - Fair	12.5			
Visit 11 - Poor	12.5			
Visit 11 - Very poor	0			
Visit 11 RtT - Very good	77.8			
Visit 11 RtT - Good	22.2			
Visit 11 RtT - Fair	0			
Visit 11 RtT - Poor	0			
Visit 11 RtT - Very poor	0			

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 questionnaire results

End point title	SF-36 questionnaire results

End point description:

At each post-baseline timepoint, only patients with a value at both, baseline and post-baseline timepoint, are included.

End point type	Secondary

End point timeframe:

Visit 4 (Day 1) and Visit 11 (Day 144)

End point values	Canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: scores on a scale				
arithmetic mean (standard deviation)				
Physical Component - Summary Scores Visit 4	38 (± 21.25)			
Physical Component - Summary Scores Visit 11	71.25 (± 17.1)			
Physical Component - Difference from baseline	29.88 (± 12.52)			
Mental Component - Summary Scores Visit 4	45.89 (± 22.53)			
Mental Component - Summary Scores Visit 11	69.88 (± 20.07)			
Mental Component - Difference from baseline	21.13 (± 20.54)			

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	unk

Reporting groups

Reporting group title	ACZ885

Reporting group description: -

Serious adverse events	ACZ885		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	ACZ885		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 9 (88.89%)		
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	4		
Pregnancy, puerperium and perinatal conditions			
Pregnancy			

subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Gastrointestinal disorders Vomitting subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1		
Skin and subcutaneous tissue disorders Hidradenitis subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1		
Infections and infestations Tooth infection subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1 2 / 9 (22.22%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported