Clinical trial results:
A French open-label extension study of canakinumab in patients who participated in international phase III studies CACZ885G2301E1 or CACZ885G2306 in Systemic Juvenile Idiopathic Arthritis and CACZ885N2301 in Hereditary Periodic Fevers (TRAPS, HIDS, or crFMF)

Summary

EudraCT number	2014-002872-95
Trial protocol	FR
Global end of trial date	26 December 2018

Results information

Result version number	v1 (current)
This version publication date	08 March 2019
First version publication date	08 March 2019

Trial information

Trial identification

Sponsor protocol code	CACZ885GFR01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02334748
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, Novartis.email@email.com
Scientific contact	Study Director, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 December 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this trial was to collect additional safety data (serious and non serious AEs) and to provide continuous Ilaris® (canakinumab) treatment to patients in France who completed CACZ885G2301E1, CACZ885N2301 or CACZ885G2306 studies.

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	03 November 2014
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	France: 31
Worldwide total number of subjects	31
EEA total number of subjects	31

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)	19
Adolescents (12-17 years)	11
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In total, 31 patients (100%) (24 with SJIA and 7 with periodic fever syndromes [HIDS/MKD and FMF]) were enrolled, of which 23 (74.2%) (16 patients with SJIA and 7 patients with periodic fever syndromes [HIDS/MKD and FMF]) completed the study and the remaining 8 patients (25.8%) prematurely discontinued from the study.

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:

Patients continued same dose as their last dose administered in the study CACZ885G2301E1, CACZ885N2301 or CACZ885G2306. For all indications, the maximum canakinumab dose was 4 mg/kg or 300 mg for patients ≥ 40 kg. Ilaris® dosage may have been adjusted (or interrupted) according to the clinical response and to investigator's judgment.

Arm type	Experimental
Investigational medicinal product name	canakinumab
Investigational medicinal product code	ACZ885G
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

4 mg/kg (maximum 300 mg) q4w

Number of subjects in period 1	canakinumab
Started	31
Completed	23
Not completed	8
Inclusion in the CACZ8852306 study	1
Adverse event, non-fatal	1
Patient no longer required study drug	2
Lack of efficacy	4

Baseline characteristics

Reporting groups	
Reporting group title	canakinumab
Reporting group description:	
Patients continued same dose as their last dose administered in the study CACZ885G2301E1, CACZ885N2301 or CACZ885G2306. For all indications, the maximum canakinumab dose was 4 mg/kg or 300 mg for patients ≥ 40 kg. Ilaris® dosage may have been adjusted (or interrupted) according to the clinical response and to investigator's judgment.	

Reporting group values	canakinumab	Total	
Number of subjects	31	31	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	19	19	
Adolescents (12-17 years)	11	11	
Adults (18-64 years)	1	1	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	9.7		
standard deviation	± 4.07	-	
Sex: Female, Male Units: Subjects			
Female	17	17	
Male	14	14	
Race/Ethnicity, Customized Units: Subjects			
Caucasian	29	29	
Other	2	2	

End points

End points reporting groups

Reporting group title	canakinumab

Reporting group description:

Patients continued same dose as their last dose administered in the study CACZ885G2301E1, CACZ885N2301 or CACZ885G2306. For all indications, the maximum canakinumab dose was 4 mg/kg or 300 mg for patients ≥ 40 kg. Ilaris® dosage may have been adjusted (or interrupted) according to the clinical response and to investigator's judgment.

Primary: Number of adverse events

End point title	Number of adverse events[1]

End point description:

The objective of this protocol was to collect additional safety data (serious and non serious AEs) and to provide continuous Ilaris® (canakinumab) treatment to patients in France who completed CACZ885G2301E1, CACZ885N2301 or CACZ885G2306 studies.

End point type	Primary

End point timeframe:

every 4 weeks up to 1 year

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: No statistical analysis was planned for this study

End point values	canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: participants				
Serious adverse events	13			
Treatment emergent adverse events	29			

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with adverse events

End point title	Number of participants with adverse events[2]

End point description:

End point type	Primary

End point timeframe:

Adverse Events (AEs) were collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All AEs reported in this record are from date of First Patient First Treatment until Last Patient Last Visit) up to approximately one year

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: No statistical analysis was planned for this study

End point values	canakinumab			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: participants				
number (not applicable)				
# Affected by Serious Adverse Events	7			
# Affected by Non Serious Adverse Events	28			
Number of deaths	0			

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 are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	ACZ885

Reporting group description:

ACZ885

Serious adverse events	ACZ885		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 31 (22.58%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Intentional overdose			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 1		
Scar			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Histiocytosis haematophagic			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	2 / 31 (6.45%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 2		
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 1		
Psychiatric disorders			
Hallucination, auditory			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 1		
Suicide attempt			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 1		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 2		
Bone disorder			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Epstein-Barr virus infection			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 1		
Salmonellosis			

subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 1		

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	28 / 31 (90.32%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	0		
Limb injury			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 31 (12.90%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	7 / 31 (22.58%)		
occurrences (all)	0		
Gastrointestinal disorders			

Abdominal pain subjects affected / exposed occurrences (all)	6 / 31 (19.35%) 0		
Abdominal pain upper subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Diarrhoea subjects affected / exposed occurrences (all)	4 / 31 (12.90%) 0		
Mouth ulceration subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Nausea subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Toothache subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 0		
Skin and subcutaneous tissue disorders			
Dermatitis allergic subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Dry skin subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Eczema subjects affected / exposed occurrences (all)	4 / 31 (12.90%) 0		
Rash subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all)	9 / 31 (29.03%) 0		
Arthritis subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Back pain subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 0		
Juvenile idiopathic arthritis subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 0		
Musculoskeletal pain subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Myalgia subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Neck pain subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Pain in extremity subjects affected / exposed occurrences (all)	4 / 31 (12.90%) 0		
Pain in jaw subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Scoliosis subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Tendon pain subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 0		
Infections and infestations Bronchitis			

subjects affected / exposed	3 / 31 (9.68%)			
occurrences (all)	0			
Conjunctivitis				
subjects affected / exposed	4 / 31 (12.90%)			
occurrences (all)	0			
Gastroenteritis				
subjects affected / exposed	7 / 31 (22.58%)			
occurrences (all)	0			
Influenza				
subjects affected / exposed	4 / 31 (12.90%)			
occurrences (all)	0			
Labyrinthitis				
subjects affected / exposed	2 / 31 (6.45%)			
occurrences (all)	0			
Molluscum contagiosum				
subjects affected / exposed	2 / 31 (6.45%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	11 / 31 (35.48%)			
occurrences (all)	0			
Onychomycosis				
subjects affected / exposed	2 / 31 (6.45%)			
occurrences (all)	0			
Oral herpes				
subjects affected / exposed	2 / 31 (6.45%)			
occurrences (all)	0			
Paronychia				
subjects affected / exposed	4 / 31 (12.90%)			
occurrences (all)	0			
Pharyngitis				
subjects affected / exposed	4 / 31 (12.90%)			
occurrences (all)	0			
Rhinitis				
subjects affected / exposed	4 / 31 (12.90%)			
occurrences (all)	0			
Sinusitis				

subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed	4 / 31 (12.90%)		
occurrences (all)	0		
Tracheitis			
subjects affected / exposed	4 / 31 (12.90%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	4 / 31 (12.90%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	0		

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