Clinical trial results:
A randomized, double-blind, placebo controlled, single-dose study to assess the initial efficacy of canakinumab (ACZ885) with respect to the adapted ACR Paediatric 30 criteria in patients with Systemic Juvenile Idiopathic Arthritis (SJIA) and active systemic manifestations

Summary

EudraCT number	2008-005476-27
Trial protocol	ES NO FR HU DE BE SE IT GB DK GR Outside EU/EEA
Global end of trial date	02 December 2010

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	01 August 2015

Trial information

Trial identification

Sponsor protocol code	CACZ885G2305

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00886769
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000060-PIP02-08
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	02 December 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 December 2010
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to evaluate the efficacy of canakinumab over a 4 week treatment period in subjects with systemic juvenile idiopathic arthritis (sJIA) having a flare. Response to treatment was measured using an adapted American College of Rheumatology (ACR) paediatric 30 criteria at Day 15.

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. Subjects who did not improve with treatment, and did not meet the adapted ACR paediatric 30 at Day 15, or experienced flare between Day 15 and Day 29 were discontinued from the study. The investigator provided follow-up medical care for all subjects who prematurely withdrew from the study, or referred them for appropriate ongoing care as per standard local medical practice. This care included initiating another treatment outside of the study as deemed appropriate by the investigator. No rescue medication was allowed during the course of the study. The investigators were well-informed of additional procedures to be followed in case of early termination of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 July 2009
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	Netherlands: 3
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Peru: 3
Country: Number of subjects enrolled	Israel: 10
Country: Number of subjects enrolled	Turkey: 11

Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Argentina: 2
Country: Number of subjects enrolled	Brazil: 3
Worldwide total number of subjects	84
EEA total number of subjects	45

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)	60
Adolescents (12-17 years)	20
Adults (18-64 years)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 40 centres in 18 countries.

Pre-assignment

Screening details:

A total of 84 subjects were screened and randomized into the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Subject, Assessor

Blinding implementation details:

Randomization data were kept strictly confidential until the time of unblinding, and was accessible only to an independent, unblinded qualified study person at the investigator's site who prepared the study medication. The identity of the treatments were concealed by the use of study drugs in form of syringes filled with reconstituted drug solutions that were all identical in appearance, but the actual vials with lyophilisate were supplied open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Canakinumab

Arm description:

Subjects received a single dose of subcutaneous (s.c.) injection of canakinumab [4 milligrams (mg)/kilograms (kg)] on Day 1 with a maximum allowed daily dose of 300 mg. Any subject who required a dose greater than 150 mg (for subjects with body weight more than 37.5 kg) received two s.c. injections of canakinumab.

Arm type	Experimental
Investigational medicinal product name	Canakinumab
Investigational medicinal product code	ACZ885
Other name	Ilaris
Pharmaceutical forms	Powder for cutaneous solution
Routes of administration	Subcutaneous use

Dosage and administration details:

Canakinumab (4mg/kg) s.c. solution was administered on Day 1. The maximal allowed daily dose of canakinumab was 300 mg.

Arm title	Placebo

Arm description:

Subjects received a single s.c. dose of matching placebo solution to canakinumab on Day 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for cutaneous solution
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo matching to canakinumab s.c. solution was administered on Day 1.

Number of subjects in period 1	Canakinumab	Placebo
Started	43	41
Completed	37	4
Not completed	6	37
Unsatisfactory therapeutic effect	6	37

Baseline characteristics

Reporting groups	
Reporting group title	Canakinumab
Reporting group description:	
Subjects received a single dose of subcutaneous (s.c.) injection of canakinumab [4 milligrams (mg)/kilograms (kg)] on Day 1 with a maximum allowed daily dose of 300 mg. Any subject who required a dose greater than 150 mg (for subjects with body weight more than 37.5 kg) received two s.c. injections of canakinumab.	
Reporting group title	Placebo
Reporting group description:	
Subjects received a single s.c. dose of matching placebo solution to canakinumab on Day 1.	

Reporting group values	Canakinumab	Placebo	Total
Number of subjects	43	41	84
Age categorical Units: Subjects			
Children (2-11 years)	31	29	60
Adolescents (12-17 years)	10	10	20
Adults (18-64 years)	2	2	4
Age continuous Units: years			
arithmetic mean	8.3	9.7	
standard deviation	± 5.08	± 4.32	-
Gender categorical Units: Subjects			
Female	27	23	50
Male	16	18	34

End points

End points reporting groups

Reporting group title	Canakinumab
Reporting group description:	
Subjects received a single dose of subcutaneous (s.c.) injection of canakinumab [4 milligrams (mg)/kilograms (kg)] on Day 1 with a maximum allowed daily dose of 300 mg. Any subject who required a dose greater than 150 mg (for subjects with body weight more than 37.5 kg) received two s.c. injections of canakinumab.	
Reporting group title	Placebo
Reporting group description:	
Subjects received a single s.c. dose of matching placebo solution to canakinumab on Day 1.	

Primary: Percentage of subjects achieving the adapted American College of Rheumatology (ACR) Paediatric 30 criteria at Day 15

End point title	Percentage of subjects achieving the adapted American College of Rheumatology (ACR) Paediatric 30 criteria at Day 15
End point description:	
Adapted ACR Paediatric 30 criteria was assessed based on following 7 variables: 1.Physician’s Global Assessment on a 0-100 millimetres (mm) visual analog scale (VAS); 2.Patient Global Assessment on a 0-100 mm VAS in the Child Health Assessment Questionnaire (CHAQ); 3.Functional ability; 4.Joints count with active arthritis; 5.Joints count with limitation of motion; 6.Laboratory measure of C-reactive protein (CRP) and 7.Absence of intermittent fever due to sJIA during the preceding week. Response was defined as more than or equal to (≥) 30% improvement in at least 3 of the response variables 1 to 6 and no intermittent fever (i.e. body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%. The analysis was performed on Full analysis set (FAS), defined as all randomized subjects who received at least one dose of study drug.	
End point type	Primary
End point timeframe:	
Day 15	

End point values	Canakinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Percentage of subjects				
number (not applicable)	83.7	9.8		

Statistical analyses

Statistical analysis title	Odd's ratio of treatment responders
Statistical analysis description:	
Comparison of treatment groups using exact Cochran-Mantel-Haenszel (CMH) test adjusting for stratification factors.	
Comparison groups	Canakinumab v Placebo

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	62.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.68
upper limit	306.07

Notes:

[1] - Null hypothesis stated odds ratio was equal to 1, i.e. the probability to respond to treatment was same for both groups. While, alternative hypothesis stated odds ratio to be greater than 1, i.e. the probability to respond to treatment was higher for canakinumab.

Secondary: Percentage of subjects achieving the adapted ACR Paediatric 30 criteria at Day 29

End point title	Percentage of subjects achieving the adapted ACR Paediatric 30 criteria at Day 29

End point description:

Adapted ACR Paediatric 30 criteria was assessed based on following 7 variables: 1.Physician's Global Assessment on a 0-100 mm VAS; 2.Patient Global Assessment on a 0-100 mm VAS in the CHAQ; 3.Functional ability; 4.Joints count with active arthritis; 5.Joints count with limitation of motion; 6.Laboratory measure of CRP and 7.Absence of intermittent fever due to sJIA during the preceding week. Response was defined as ≥ 30% improvement from baseline in at least 3 of the response variables 1 to 6 and no intermittent fever (i.e. body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%. The analysis was performed on FAS population.

End point type	Secondary

End point timeframe:

Day 29

End point values	Canakinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: percentage of subjects				
number (not applicable)	81.4	9.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects achieving the adapted ACR Paediatric 50 criteria

End point title	Percentage of subjects achieving the adapted ACR Paediatric 50 criteria

End point description:

Adapted ACR Paediatric 50 criteria was assessed based on following 7 variables: 1.Physician's Global Assessment on a 0-100 mm VAS; 2.Patient Global Assessment on a 0-100 mm VAS in the CHAQ; 3.

Functional ability; 4.Joints count with active arthritis; 5.Joints count with limitation of motion; 6.Laboratory measure of CRP and 7.Absence of intermittent fever due to sJIA during the preceding week. Response was defined as ≥50% improvement from baseline in at least 3 of the response variables 1 to 6 and no intermittent fever (i.e. body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%. The analysis was performed on FAS population.

End point type	Secondary

End point timeframe:

Day 15, Day 29

End point values	Canakinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Percentage of subjects				
number (not applicable)				
Day 15	67.4	4.9		
Day 29	79.1	4.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects achieving the adapted ACR Paediatric 70 criteria

End point title	Percentage of subjects achieving the adapted ACR Paediatric 70 criteria

End point description:

Adapted ACR Paediatric 70 criteria was assessed based on following 7 variables: 1.Physician’s Global Assessment on a 0-100 mm VAS; 2.Patient Global Assessment on a 0-100 mm VAS in the CHAQ; 3.Functional ability; 4.Joints count with active arthritis; 5.Joints count with limitation of motion; 6.Laboratory measure of CRP and 7.Absence of intermittent fever due to sJIA during the preceding week. Response was defined as ≥70% improvement from baseline in at least 3 of the response variables 1 to 6 and no intermittent fever (i.e. body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%. The analysis was performed on FAS population.

End point type	Secondary

End point timeframe:

Day 15, Day 29

End point values	Canakinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Percentage of subjects				
number (not applicable)				
Day 15	60.5	2.4		
Day 29	67.4	2.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects achieving the adapted ACR Paediatric 90 criteria

End point title	Percentage of subjects achieving the adapted ACR Paediatric 90 criteria

End point description:

Adapted ACR Paediatric 90 criteria was assessed based on following 7 variables: 1.Physician's Global Assessment on a 0-100 mm VAS; 2.Patient Global Assessment on a 0-100 mm VAS in the CHAQ; 3.Functional ability; 4.Joints count with active arthritis; 5.Joints count with limitation of motion; 6.Laboratory measure of CRP and 7.Absence of intermittent fever due to sJIA during the preceding week. Response was defined as ≥90% improvement from baseline in at least 3 of the response variables 1 to 6 and no intermittent fever (i.e. body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%. The analysis was performed on FAS population.

End point type	Secondary

End point timeframe:

Day 15, Day 29

End point values	Canakinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Percentage of subjects				
number (not applicable)				
Day 15	41.9	0		
Day 29	46.5	2.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects achieving the adapted ACR Paediatric 100 criteria

End point title	Percentage of subjects achieving the adapted ACR Paediatric 100 criteria

End point description:

Adapted ACR Paediatric 100 criteria was assessed based on following 7 variables: 1.Physician's Global Assessment on a 0-100 mm VAS; 2.Patient Global Assessment on a 0-100 mm VAS in the CHAQ; 3.Functional ability; 4.Joints count with active arthritis; 5.Joints count with limitation of motion; 6.Laboratory measure of CRP and 7.Absence of intermittent fever due to sJIA during the preceding week. Response was defined as 100% improvement from baseline in at least 3 of the response variables 1 to 6 and no intermittent fever (i.e. body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%. The analysis was performed on FAS

population.

End point type	Secondary

End point timeframe:

Day 15, Day 29

End point values	Canakinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Percentage of subjects				
number (not applicable)				
Day 15	32.6	0		
Day 29	32.6	2.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with normal body temperature at Day 3

End point title	Percentage of subjects with normal body temperature at Day 3

End point description:

Subjects who had body temperature of less than or equal to 38 degree Celsius were counted. Body temperature was derived from vital signs evaluation and normal body temperature indicated treatment response. The analysis was performed on FAS population.

End point type	Secondary

End point timeframe:

Day 3

End point values	Canakinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	38[2]		
Units: Percentage of subjects				
number (not applicable)	100	86.8		

Notes:

[2] - Only 38 subjects were evaluable for this measure at specified time point

Statistical analyses

No statistical analyses for this end point

Secondary: Subject's pain intensity at Day 15 and Day 29

End point title	Subject's pain intensity at Day 15 and Day 29

End point description:

Subject's pain intensity was assessed by parents and adult subjects (18-20 years old) as a part of

Childhood Health Assessment Questionnaire (CHAQ). Parents responded to the following question of CHAQ: "How much pain do you think your child has had because of his/her illness in the past week?" on a VAS scale of 0-100 mm (0 mm: no pain to 100: very severe pain). The analysis was performed on 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:

Baseline, Day 15, Day 29

End point values	Canakinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Units on a scale				
least squares mean (standard error)				
Day 15 (n=43, 25)	20.3 (± 5.08)	66.7 (± 6.35)		
Day 29 (n=38,7)	20.6 (± 5.59)	62.5 (± 9.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Health-Related Quality of Life (HRQoL) over time by use of Child Health Questionnaire - Parent Form (CHQ-PF50)

End point title	Change from baseline in Health-Related Quality of Life (HRQoL) over time by use of Child Health Questionnaire - Parent Form (CHQ-PF50)

End point description:

The Child Health Questionnaire – Parent Form (CHQ-PF50) instrument was used to measure HRQoL aged 5 to 18 years from a parent's perspective. This 14-concept questionnaire measured physical and psychosocial health of the subjects on following points: physical functioning, role/social emotional, role/social behavior, role/social physical, bodily pain, general behavior, mental health, self-esteem, general health perception, change in health, parental impact – emotional, parental impact – time, family activities, and family cohesion. Total score ranged from 0-100. Increase in score represented improvement in overall well-being of subjects. The analysis was performed on 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:

Baseline, Day 1 up to Day 29

End point values	Canakinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Units on a scale				
least squares mean (standard error)				
CHQ-PF50 physical score (n=28, 34)	16.9 (± 3.46)	4.9 (± 3.97)		
CHQ-PF50 psychosocial score (n=28, 34)	6.2 (± 2.15)	-1.1 (± 2.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in disability score over time by use of the CHAQ

End point title	Change in disability score over time by use of the CHAQ

End point description:

The disability dimension of CHAQ questionnaire comprised of 20 items concerning difficulty in performing eight common activities of daily living; dressing and grooming, arising, eating, walking, reaching, personal hygiene, gripping and activities. Subjects rated the responses from 0-3 (0: without any difficulty, 1- with some difficulty, 2: with much difficulty and 3: unable to do). Negative change in score indicated improvement. The analysis was performed on FAS population.

End point type	Secondary

End point timeframe:

Baseline, Day 1 up to Day 29

End point values	Canakinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Units on a scale				
least squares mean (standard error)	-0.9 (± 0.15)	-0.2 (± 0.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-canakinumab antibodies at any visit

End point title	Number of subjects with 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:

Day 1 up to Day 29

End point values	Canakinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Number of subjects				
number (not applicable)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with adverse events (AEs), serious adverse events (SAEs)

End point title	Number of subjects with adverse events (AEs), serious adverse events (SAEs)

End point description:

An AE was defined as any undesirable sign, symptom or medical condition occurring after starting study drug even if the event was not considered to be related to study drug. A SAE was defined as an event which was fatal or life threatening, required or prolonged hospitalization, was significantly or permanently disabling or incapacitating, constituted a congenital anomaly or a birth defect, or encompassed any other clinically significant event that could jeopardize the subject or require medical or surgical intervention to prevent one of the aforementioned outcomes. The analysis was performed on the safety set, defined as all subjects who received at least one dose of study drug and had at least one post-baseline safety assessment.

End point type	Secondary

End point timeframe:

Day 1 up to Day 29

End point values	Canakinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Number of subjects				
number (not applicable)				
AEs	24	16		
SAEs	2	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

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received a single s.c. dose of matching placebo solution to canakinumab on Day 1.

Reporting group title	Canakinumab

Reporting group description:

Subjects received a single dose of s.c. injection of canakinumab (4 mg/kg) on Day 1 with a maximum allowed daily dose of 300 mg. Any subject who required a dose greater than 150 mg (for subjects with body weight more than 37.5 kg) received two s.c. injections of canakinumab.

Serious adverse events	Placebo	Canakinumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 41 (4.88%)	2 / 43 (4.65%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Histiocytosis haematophagic			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Varicella			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Canakinumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 41 (4.88%)	8 / 43 (18.60%)	
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	1 / 41 (2.44%)	3 / 43 (6.98%)	
occurrences (all)	1	3	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 41 (2.44%)	3 / 43 (6.98%)	
occurrences (all)	1	3	
Upper respiratory tract infection			
subjects affected / exposed	0 / 41 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2009	The purpose of this amendment was to change the criteria for which a subject would discontinue between Days 15-29 due to declining efficacy after first demonstrating a clinical response (a minimum adapted ACR Pediatric 30 response) at Day 15.
03 November 2009	This amendment addressed the feedback of health authorities to: 1) clarify absence of fever in the secondary objectives, 2) ensure that subjects were on a stable dose of corticosteroids at least 3 days prior to baseline,and 3) clarify the transition of CACZ885G2305 placebo or canakinumab subjects to study CACZ885G2301 (EudraCT number: 2008- 005479-82) or CACZ885G2301E1 (EudraCT number: 2008-008008-42), respectively, if they did not maintain a minimum adapted ACR Pediatric 30 response after Day 15.
04 October 2010	The amendment was introduced to implement an interim analysis by an Data monitoring committee in order to assess the primary efficacy endpoint (Adapted ACR pediatric 30 at Day 15).

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.

An unblinded interim analysis of the primary efficacy endpoint was performed to potentially avoid additional subjects to be treated with placebo. Since the interim results were found to be positive, IDMC recommended to stop the study early.

Notes: