Clinical trial results:
An open-label, single-arm, active-treatment, efficacy and safety study of canakinumab (ACZ885) administered for at least 48 weeks in Japanese patients with Systemic Juvenile Idiopathic Arthritis (SJIA)

Summary

EudraCT number	2018-002355-15
Trial protocol	Outside EU/EEA
Global end of trial date	01 August 2018

Results information

Result version number	v1 (current)
This version publication date	15 February 2019
First version publication date	15 February 2019

Trial information

Trial identification

Sponsor protocol code	CACZ885G1301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02396212
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@novartis.com
Scientific contact	Clinical Disclosure Office, 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	01 August 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives were:
- to evaluate the efficacy of canakinumab, defined as the proportion of patients who achieved a minimum a ACR ped 30 criteria at Week 8;
- to evaluate the proportion of patients with canakinumab treatment who were able to taper corticosteroids successfully at Week 28.

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	07 May 2015
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	Japan: 19
Worldwide total number of subjects	19
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)	1
Children (2-11 years)	12
Adolescents (12-17 years)	5
Adults (18-64 years)	1
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

It was planned to enroll approximately 20 patients in this study. There were19 patients enrolled and data from all patients were analyzed.

Pre-assignment

Screening details:

It was planned to enroll approximately 20 patients in this stud. There were19 patients enrolled and data from all patients were analyzed.

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 4 mg/kg every 4 weeks

Arm description:

All patients received canakinumab (ACZ885) as open-label study medication. Patients were administered canakinumab 4 mg/kg every 4 weeks. The maximal total single dose of canakinumab allowed was 300 mg.

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:

Canakinumab 4 mg/kg subcutaneously every 4 weeks

Number of subjects in period 1	Canakinumab 4 mg/kg every 4 weeks
Started	19
Completed	16
Not completed	3
Adverse event, non-fatal	1
Lack of efficacy	2

Baseline characteristics

Reporting groups	
Reporting group title	Canakinumab 4 mg/kg every 4 weeks
Reporting group description:	
All patients received canakinumab (ACZ885) as open-label study medication. Patients were administered canakinumab 4 mg/kg every 4 weeks. The maximal total single dose of canakinumab allowed was 300 mg.	

Reporting group values	Canakinumab 4 mg/kg every 4 weeks	Total	
Number of subjects	19	19	
Age categorical			
Units: Subjects			
Infants and toddlers (28 days-23 months)	1	1	
Children (2-11 years)	12	12	
Adolescents (12-17 years)	5	5	
Adults (18-64 years)	1	1	
Age Continuous			
Units: Years			
arithmetic mean	9.9		
standard deviation	± 4.47	-	
Sex: Female, Male			
Units: Subjects			
Female	13	13	
Male	6	6	
Race/Ethnicity, Customized			
Units: Subjects			
Asian	19	19	

End points

End points reporting groups

Reporting group title	Canakinumab 4 mg/kg every 4 weeks

Reporting group description:

All patients received canakinumab (ACZ885) as open-label study medication. Patients were administered canakinumab 4 mg/kg every 4 weeks. The maximal total single dose of canakinumab allowed was 300 mg.

Primary: Percentage of participants who achieved a minimum adapted American College of Rheumatology (ACR) Pediatric 30 criteria

End point title	Percentage of participants who achieved a minimum adapted American College of Rheumatology (ACR) Pediatric 30 criteria[1]

End point description:

To evaluate the efficacy of canakinumab, defined as the percentage of patients who achieved a minimum adapted ACR Pediatric 30 criteria at Week 8

End point type	Primary

End point timeframe:

Week 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: No statistical analysis was planned for this 1-arm study.

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Percentage of participants	19			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with canakinumab treatment who were able to taper corticosteroids successfully

End point title	Percentage of participants with canakinumab treatment who were able to taper corticosteroids successfully[2]

End point description:

To evaluate the percentage of participants with canakinumab treatment who were able to taper corticosteroids successfully at Week 28

End point type	Primary

End point timeframe:

Week 28

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 1-arm study.

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Participants	14			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who met the adapted ACR Pediatric 30/50/70/90/100 criteria of canakinumab over time

End point title	Percentage of participants who met the adapted ACR Pediatric 30/50/70/90/100 criteria of canakinumab over time

End point description:

To evaluate the efficacy (percentage of participants who met the adapted ACR Pediatric 30/50/70/90/100 criteria) of canakinumab over time; EOS means End of study which is performed at study completion

End point type	Secondary

End point timeframe:

Weeks 4, 8, 28, 48, 96, 144, end of study (EOS)

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Percentage of Participants				
number (not applicable)				
Week 4 adapted ACR Pediatric 30	94.7			
Week 4 adapted ACR Pediatric 50	94.7			
Week 4 adapted ACR Pediatric 70	94.7			
Week 4 adapted ACR Pediatric 90	84.2			
Week 4 adapted ACR Pediatric 100	47.4			
Week 8 adapted ACR Pediatric 30	100.0			
Week 8 adapted ACR Pediatric 50	100.0			
Week 8 adapted ACR Pediatric 70	100.0			
Week 8 adapted ACR Pediatric 90	89.5			
Week 8 adapted ACR Pediatric 100	68.4			
Week 28 adapted ACR Pediatric 30	100.0			
Week 28 adapted ACR Pediatric 50	100.0			
Week 28 adapted ACR Pediatric 70	100.0			
Week 28 adapted ACR Pediatric 90	100.0			
Week 28 adapted ACR Pediatric 100	56.3			
Week 48 adapted ACR Pediatric 30	100.0			
Week 48 adapted ACR Pediatric 50	100.0			
Week 48 adapted ACR Pediatric 70	100.0			
Week 48 adapted ACR Pediatric 90	87.5			

Week 48 adapted ACR Pediatric 100	68.8			
Week 96 adapted ACR Pediatric 30	100.0			
Week 96 adapted ACR Pediatric 50	100.0			
Week 96 adapted ACR Pediatric 70	100.0			
Week 96 adapted ACR Pediatric 90	93.8			
Week 96 adapted ACR Pediatric 100	62.5			
Week 144 adapted ACR Pediatric 30	100.0			
Week 144 adapted ACR Pediatric 50	100.0			
Week144 adapted ACR Pediatric 70	100.0			
Week 144 adapted ACR Pediatric 90	100.0			
Week 144 adapted ACR Pediatric 100	80.0			
Week EOS adapted ACR Pediatric 30	89.5			
End of Study (EOS) adapted ACR Pediatric 50	89.5			
EOS adapted ACR Pediatric 70	89.5			
EOS adapted ACR Pediatric 90	84.2			
EOS adapted ACR Pediatric 100	63.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in the adapted ACR pediatric criteria of canakinumab over time: ACR component: Physician's Global Assessment of disease activity

End point title	Absolute change from baseline in the adapted ACR pediatric criteria of canakinumab over time: ACR component: Physician's Global Assessment of disease activity

End point description:

ACR component, Physician's Global Assessment of disease activity on a 0 - 100 mm VAS by visit is the first response variable in the ACR ped criteria. The a ACR ped 30 criteria were used to determine efficacy and were defined as improvement from baseline of at least 30% in at least 3 of response variables 1 to 6 and no intermittent fever (i.e., axillary, oral, or rectal body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 28, 48, 96, 144, EOS

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4	-60.2 (± 32.27)			
Week 8	-62.2 (± 28.23)			

Week 28 (n = 16)	-62.2 (± 28.61)			
Week 48 (n = 16)	-63.9 (± 28.81)			
Week 96 (n = 16)	-63.1 (± 26.99)			
Week 144 (n = 5)	-61.0 (± 37.24)			
EOS	-61.4 (± 31.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in the adapted ACR pediatric criteria of canakinumab over time: ACR component: CHAQ: Parent’s Global Assessment of patient's overall well-being as part of CHAQ

End point title	Absolute change from baseline in the adapted ACR pediatric criteria of canakinumab over time: ACR component: CHAQ: Parent’s Global Assessment of patient's overall well-being as part of CHAQ

End point description:

ACR component, Parent’s Global Assessment of patient's overall well-being as part of CHAQ on a 0 - 100 mm VAS by visit is the second response variable in the ACR ped criteria. The a ACR ped 30 criteria were used to determine efficacy and were defined as improvement from baseline of at least 30% in at least 3 of response variables 1 to 6 and no intermittent fever (i.e., axillary, oral, or rectal body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 28, 48, 96, 144, EOS

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4	-64.4 (± 40.80)			
Week 8	-73.5 (± 24.0)			
Week 28 (n = 16)	-71.9 (± 23.13)			
Week 48 (n = 16)	-68.6 (± 28.67)			
Week 96 (n = 16)	-68.4 (± 27.72)			
Week 144 (n = 5)	-72.8 (± 25.65)			
EOS	-68.1 (± 26.29)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in the adapted ACR pediatric criteria of canakinumab over time: ACR component: CHAQ: Functional Ability Score

End point title	Absolute change from baseline in the adapted ACR pediatric criteria of canakinumab over time: ACR component: CHAQ: Functional Ability Score

End point description:

ACR component, Disability Score as part of CHAQ per functional ability score (range from 0 to 3) is the third response variable in the ACR ped criteria. The a ACR ped 30 criteria were used to determine efficacy and were defined as improvement from baseline of at least 30% in at least 3 of response variables 1 to 6 and no intermittent fever (i.e., axillary, oral, or rectal body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 28, 48, 96, 144, EOS

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4	-0.833 (± 0.7750)			
Week 8	-0.912 (± 0.7338)			
Week 28 (n = 16)	-0.998 (± 0.7871)			
Week 48 (n = 16)	-1.013 (± 0.7963)			
Week 96 (n = 16)	-0.951 (± 0.8381)			
Week 144 (n = 5)	-1.026 (± 0.9465)			
EOS	-0.938 (± 0.7682)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in the adapted ACR pediatric criteria of canakinumab over time: ACR component: Number of joints with active arthritis

End point title	Absolute change from baseline in the adapted ACR pediatric criteria of canakinumab over time: ACR component: Number of joints with active arthritis

End point description:

ACR component, Number of joints with active arthritis is the forth response variable in the ACR ped criteria. The a ACR ped 30 criteria were used to determine efficacy and were defined as improvement from baseline of at least 30% in at least 3 of response variables 1 to 6 and no intermittent fever (i.e., axillary, oral, or rectal body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 28, 48, 96, 144, EOS

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4	-5.2 (± 4.87)			
Week 8	-6.2 (± 7.71)			
Week 28 (n = 16)	-4.4 (± 3.44)			
Week 48 (n = 16)	-4.4 (± 3.44)			
Week 96 (n = 16)	-4.4 (± 3.18)			
Week 144 (n = 5)	-5.2 (± 2.68)			
EOS	-5.6 (± 8.10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in the adapted ACR pediatric criteria of canakinumab over time: ACR component: Number of joints with limitation of motion

End point title	Absolute change from baseline in the adapted ACR pediatric criteria of canakinumab over time: ACR component: Number of joints with limitation of motion

End point description:

ACR component, Number of joints with limitation of motion is the fifth response variable in the ACR ped criteria. The a ACR ped 30 criteria were used to determine efficacy and were defined as improvement from baseline of at least 30% in at least 3 of response variables 1 to 6 and no intermittent fever (i.e., axillary, oral, or rectal body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 28, 48, 96, 144, EOS

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4	-3.9 (± 4.02)			
Week 8	-4.2 (± 4.30)			
Week 28 (n = 16)	-3.4 (± 3.79)			
Week 48 (n = 16)	-3.5 (± 3.78)			
Week 96 (n = 16)	-3.4 (± 3.59)			
Week 144 (n = 5)	-3.8 (± 2.86)			
EOS	-3.7 (± 4.81)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants having fever in the adapted ACR pediatric criteria of canakinumab over time

End point title	Number of participants having fever in the adapted ACR pediatric criteria of canakinumab over time

End point description:

ACR component, Number of participants having fever is the seventh response variable in the ACR ped criteria. The a ACR ped 30 criteria were used to determine efficacy and were defined as improvement from baseline of at least 30% in at least 3 of response variables 1 to 6 and no intermittent fever (i.e., axillary, oral, or rectal body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%.

End point type	Secondary

End point timeframe:

Baseline, Day 3, Weeks 2, 56, 124

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: participants				
Baseline	19			
Day 3	16			
Week 2	2			
Week 8	0			
Week 28 (n = 16)	0			
Week 48 (n = 16)	0			

Week 56 (n = 16)	1			
Week 96 (n = 16)	0			
Week 124 (n = 8)	1			
Week 144 (n = 5)	0			
EOS	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from baseline in the adapted ACR pediatric criteria of canakinumab over time: ACR component: Standardized CRP

End point title	Percentage change from baseline in the adapted ACR pediatric criteria of canakinumab over time: ACR component: Standardized CRP

End point description:

ACR component, Standardized CRP is the sixth response variable in the ACR ped criteria. CRP values were standardized to a normal range of 0 to 10 mg/L. The a ACR ped 30 criteria were used to determine efficacy and were defined as improvement from baseline of at least 30% in at least 3 of response variables 1 to 6 and no intermittent fever (i.e., axillary, oral, or rectal body temperature ≤ 38°C) in the preceding week (variable 7), with no more than one variable 1-6 worsening by more than 30%.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 28, 48, 96, 144, EOS

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Percentage change				
arithmetic mean (standard deviation)				
Baseline	357.79 (± 359.408)			
Week 4	-89.45 (± 41.431)			
Week 8	-96.95 (± 6.915)			
Week 28 (n = 16)	-98.19 (± 2.567)			
Week 48 (n = 16)	-97.64 (± 6.333)			
Week 96 (n = 16)	-97.95 (± 3.730)			
Week 144 (n = 5)	-98.58 (± 1.330)			
EOS	-89.71 (± 20.717)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who had flares with canakinumab treatment over time

End point title	Percentage of participants who had flares with canakinumab treatment over time

End point description:

Flare was defined by at least 1 of the following: Reappearance of SJIA-related (e.g., not due to infection) fever (> 38°C) lasting for at least 2 consecutive days &/OR Flare according to the JIA pediatric criteria for flare (all criteria must be met): ≥ 30% worsening in at least 3 of the 6 response variables and ≥ 30% improvement in at not more than 1 of the 6 response variables if the physician's or parent's global assessment is 1of 3 response variables used to define flare, worsening of ≥ 20 mm must be present, if the number of active joints or joints with limitation of motion is one of 3 response variables used to define flare, worsening in ≥ 2 joints must be present if CRP is used to define flare, CRP must be > 30 mg/L

End point type	Secondary

End point timeframe:

> Day3, to <= Week164

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Percentage of participants				
number (not applicable)				
>Day 3 =<Week 2	5.3			
>Week 2 =<Week 4	5.3			
>Week 4 =<Week 8	5.3			
>Week 8 =<Week 12 (n = 18)	5.6			
>Week 12 =<Week 16 (n = 18)	5.6			
>Week 92 =<Week 96 (n = 16)	6.3			
>Week 104 =<Week 108 (n = 13)	7.7			
>Week 120 =<Week 124 (n = 8)	12.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieved inactive disease (with and without duration of morning stiffness) with canakinumab treatment over time

End point title	Percentage of participants who achieved inactive disease (with and without duration of morning stiffness) with canakinumab treatment over time

End point description:

Inactive disease was defined as meeting all of the following: No joints with active arthritis; No fever (body temperature ≤ 38°C); No rheumatoid rash, serositis, splenomegaly, hepatomegaly or generalized lymphadenopathy attributable to JIA; Normal CRP; Physician's global assessment of disease activity score ≤ 10 mm

End point type	Secondary
End point timeframe:	
Weeks 4, 8, 28, 48, 96, 144, EOS	

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Percentage of participants				
number (not applicable)				
Week 4	63.2			
Week 8	63.2			
Week 28 (n = 16)	75.0			
Week 48 (n = 16)	75.0			
Week 96 (n = 16)	75.0			
Week 144 (n = 5)	80.0			
EOS	68.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with canakinumab treatment who were able to taper corticosteroids successfully over time

End point title	Percentage of participants with canakinumab treatment who were able to taper corticosteroids successfully over time
End point description:	
To evaluate the percentage of participants with canakinumab treatment who were able to taper corticosteroids successfully over time	
End point type	Secondary
End point timeframe:	
Weeks 28, 48, 96, 144, EOS	

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Percentage of perticipants				
number (not applicable)				
Week 28 (n = 16)	87.5			
Week 48 (n = 16)	81.3			
Week 96 (n = 16)	87.5			
Week 144 (n = 5)	100.0			
EOS (n = 18)	66.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline of corticosteroids dose reduction with canakinumab treatment over time

End point title	Absolute change from baseline of corticosteroids dose reduction with canakinumab treatment over time

End point description:

To evaluate corticosteroids dose reduction with canakinumab treatment over time

End point type	Secondary

End point timeframe:

Baseline, Weeks 28, 48, 96, 144, EOS

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: mg/kg/day				
arithmetic mean (standard deviation)				
Week 28 (n = 16)	-0.133 (± 0.1676)			
Week 48 (n = 16)	-0.195 (± 0.2317)			
Week 96 (n = 16)	-0.226 (± 0.2618)			
Week 144 (n = 5)	-0.296 (± 0.2545)			
EOS (n = 18)	-0.171 (± 0.2334)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of canakinumab and total IL-1 beta

End point title	Serum concentration of canakinumab and total IL-1 beta

End point description:

To evaluate serum concentration (mean, standard deviation) of canakinumab and total IL-1 beta

End point type	Secondary

End point timeframe:
Baseline, Weeks 4, 24, 48, 72, 96, end of study

End point values	Canakinumab 4 mg/kg every 4 weeks			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: µg/mL				
arithmetic mean (standard deviation)				
Baseline	0.01 (± 0.05)			
Week 4	15.7 (± 5.9)			
Week 24 (n = 16)	31.3 (± 11.5)			
Week 48 (n = 16)	31.1 (± 9.08)			
Week 72 (n = 16)	30.6 (± 8.95)			
Week 96 (n = 16)	29.5 (± 8.49)			
EOS	28.3 (± 6.41)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse Events are collected fro First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV) up to approximately 39 months.	
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	10 / 19 (52.63%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Histiocytosis haematophagic			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Somatic symptom disorder			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Still's disease			
subjects affected / exposed	6 / 19 (31.58%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Epstein-Barr virus infection			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pharyngitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Varicella			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Viral infection			
subjects affected / exposed	1 / 19 (5.26%)		
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	ACZ885		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 19 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Histiocytic necrotising lymphadenitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Injection site reaction			
subjects affected / exposed	5 / 19 (26.32%)		
occurrences (all)	7		
Malaise			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	5		
Vessel puncture site pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Immune system disorders			

Allergy to arthropod sting subjects affected / exposed occurrences (all) Seasonal allergy subjects affected / exposed occurrences (all)	 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1		
Reproductive system and breast disorders Vulvovaginal pruritus subjects affected / exposed occurrences (all)	 1 / 19 (5.26%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Nasal obstruction subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Pneumomediastinum subjects affected / exposed occurrences (all)	 1 / 19 (5.26%) 1 4 / 19 (21.05%) 19 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1		
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1		
Investigations Alanine aminotransferase increased			

subjects affected / exposed	4 / 19 (21.05%)			
occurrences (all)	4			
Amylase increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Blood cholesterol increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Blood creatine phosphokinase decreased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Blood creatine phosphokinase increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Blood creatinine increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Blood glucose increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Blood lactate dehydrogenase increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Blood uric acid increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Intraocular pressure increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
White blood cell count decreased				

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Arthropod sting			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	4 / 19 (21.05%)		
occurrences (all)	6		
Cardiac disorders			
Ventricular extrasystoles			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 19 (31.58%)		
occurrences (all)	17		
Neuropathy peripheral			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		

Leukopenia subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 2		
Lymphadenitis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1		
Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 2		
Ear and labyrinth disorders Motion sickness subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1		
Eye disorders Chalazion subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1		
Conjunctivitis allergic subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2		
Colitis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1		
Constipation subjects affected / exposed occurrences (all)	6 / 19 (31.58%) 6		
Dental caries subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2		
Enterocolitis			

subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	5 / 19 (26.32%)		
occurrences (all)	13		
Hepatic steatosis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Alopecia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Blister			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Dermatitis atopic			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	3		
Dry skin			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	3		
Eczema			
subjects affected / exposed	4 / 19 (21.05%)		
occurrences (all)	4		
Eczema asteatotic			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Haemorrhage subcutaneous			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Macule			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Purpura			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Urticaria			
subjects affected / exposed	4 / 19 (21.05%)		
occurrences (all)	5		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Joint range of motion decreased			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Limb discomfort			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Musculoskeletal pain			

subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Musculoskeletal stiffness			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	4		
Neck pain			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	3		
Pain in extremity			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Still's disease			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Tenosynovitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Infections and infestations			
Angular cheilitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	4 / 19 (21.05%)		
occurrences (all)	5		
Gastroenteritis			
subjects affected / exposed	6 / 19 (31.58%)		
occurrences (all)	7		
Gastroenteritis viral			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Herpes zoster			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		

Hordeolum				
subjects affected / exposed	4 / 19 (21.05%)			
occurrences (all)	4			
Impetigo				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	4 / 19 (21.05%)			
occurrences (all)	4			
Lice infestation				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	12 / 19 (63.16%)			
occurrences (all)	47			
Otitis media acute				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	3 / 19 (15.79%)			
occurrences (all)	3			
Rhinitis				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Skin infection				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Upper respiratory tract infection				
subjects affected / exposed	4 / 19 (21.05%)			
occurrences (all)	7			
Viral infection				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Viral pharyngitis				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			

Metabolism and nutrition disorders			
Hyperalbuminaemia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Hyperamylasaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hypercholesterolaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	8		
Hyperlipidaemia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Hyperuricaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Hypocalcaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hypoproteinaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		

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