Clinical trial results:
A Phase IV Study to Evaluate Decreased Dose Frequency in Patients with Systemic Juvenile Arthritis (SJIA) who Experience Laboratory Abnormalities During Treatment with Tocilizumab

Summary

EudraCT number	2012-000444-10
Trial protocol	GB ES NO DE SE IT
Global end of trial date	09 October 2019

Results information

Result version number	v1 (current)
This version publication date	25 April 2020
First version publication date	25 April 2020

Trial information

Trial identification

Sponsor protocol code	WA28029

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01734382
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to explore the efficacy of tocilizumab (TCZ) in reduced dosing frequency regimens (every 3 weeks [Q3W] and every 4 weeks [Q4W], as appropriate) using Juvenile Arthritis Disease Activity Score (JADAS)-71, JIA flare, and fever (attributable to sJIA) and to describe the pharmacodynamics, using soluble interleukin-6 receptor (sIL-6R) and C-reactive protein (CRP), and immunogenicity of TCZ in reduced dosing frequency regimens.

Protection of trial subjects:

All participants or their guardians signed informed consent form (ICF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 June 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	35
EEA total number of subjects	12

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)	25
Adolescents (12-17 years)	10
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with systemic juvenile idiopathic arthritis (sJIA) were recruited at study sites in 8 countries. The study consisted of two parts: Part 1 was a 24-week Run-in period and Part 2 was a 52-week Main study.

Pre-assignment

Screening details:

Part 1 enrolled 19. Patients treated with tocilizumab (TCZ) every other week (Q2W) either during Part 1 or prior to the study, who experienced laboratory abnormalities and which had resolved, were allowed to enroll into Part 2. Part 2 enrolled 22 with 6 from Part 1 and 16 directly enrolled into Part 2.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Part 1: Tocilizumab (TCZ) Q2W

Arm description:

Participants received tocilizumab intravenous (IV) infusions (12 mg/kg for participants < 30 kg; 8 mg/kg for participants >/= 30 kg) once every other week (Q2W) up to 24 weeks or until occurrence of a protocol defined laboratory abnormality in Part 1 of the study.

Arm type	Experimental
Investigational medicinal product name	Tocilizumab (TCZ)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

TCZ dosed by body weight (12 mg/kg for participants < 30 kg; 8 mg/kg for participants ≥ 30 kg) by IV infusion Q2W for
up to 24 weeks or until they experience a laboratory abnormality of neutropenia, thrombocytopenia, or liver enzyme abnormality as per the protocol criteria.

Arm title	Part 2: TCZ IV 12 mg/kg Q3W/Q4W

Arm description:

Participants with weight < 30 kg received tocilizumab IV infusions of 12 mg/kg once every three weeks (Q3W) up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality as per protocol criteria. Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switched to tocilizumab IV infusions of 12 mg/kg once every four weeks (Q4W) up to Week 52 in Part 2 of the study.

Arm type	Experimental
Investigational medicinal product name	Tocilizumab (TCZ)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switiched to tocilizumab IV infusions of 12 mg/kg Q4W up to 52 weeks.

Arm title	Part 2: TCZ IV 8 mg/kg Q3W/Q4W

Arm description:

Participants with weight >/= 30 kg received tocilizumab IV infusions of 8 mg/kg Q3W up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality as per protocol criteria. Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switched to tocilizumab IV infusions of 8 mg/kg Q4W up to Week 52 in Part 2 of the study.

Arm type	Experimental
Investigational medicinal product name	Tocilizumab (TCZ)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switiched to tocilizumab IV infusions of 8 mg/kg Q4W up to 52 weeks.

Number of subjects in period 1	Part 1: Tocilizumab (TCZ) Q2W	Part 2: TCZ IV 12 mg/kg Q3W/Q4W	Part 2: TCZ IV 8 mg/kg Q3W/Q4W
Started	19	7	15
Completed	17	5	8
Not completed	2	2	7
Physician decision	-	-	3
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	2	-	1
Not Specified	-	-	1
Lack of efficacy	-	1	1
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: Tocilizumab (TCZ) Q2W
Reporting group description:	
Participants received tocilizumab intravenous (IV) infusions (12 mg/kg for participants < 30 kg; 8 mg/kg for participants >/= 30 kg) once every other week (Q2W) up to 24 weeks or until occurrence of a protocol defined laboratory abnormality in Part 1 of the study.	
Reporting group title	Part 2: TCZ IV 12 mg/kg Q3W/Q4W
Reporting group description:	
Participants with weight < 30 kg received tocilizumab IV infusions of 12 mg/kg once every three weeks (Q3W) up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality as per protocol criteria. Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switched to tocilizumab IV infusions of 12 mg/kg once every four weeks (Q4W) up to Week 52 in Part 2 of the study.	
Reporting group title	Part 2: TCZ IV 8 mg/kg Q3W/Q4W
Reporting group description:	
Participants with weight >/= 30 kg received tocilizumab IV infusions of 8 mg/kg Q3W up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality as per protocol criteria. Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switched to tocilizumab IV infusions of 8 mg/kg Q4W up to Week 52 in Part 2 of the study.	

Reporting group values	Part 1: Tocilizumab (TCZ) Q2W	Part 2: TCZ IV 12 mg/kg Q3W/Q4W	Part 2: TCZ IV 8 mg/kg Q3W/Q4W
Number of subjects	19	7	15
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	8.5	6.7	11.7
standard deviation	± 3.6	± 1.8	± 2.8
Sex: Female, Male			
Units: participants			
Female	9	4	10
Male	10	3	5

Reporting group values	Total		
Number of subjects	41		
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: participants			
Female	23		

Male	18		

End points

End points reporting groups

Reporting group title	Part 1: Tocilizumab (TCZ) Q2W

Reporting group description:

Participants received tocilizumab intravenous (IV) infusions (12 mg/kg for participants < 30 kg; 8 mg/kg for participants >/= 30 kg) once every other week (Q2W) up to 24 weeks or until occurrence of a protocol defined laboratory abnormality in Part 1 of the study.

Reporting group title	Part 2: TCZ IV 12 mg/kg Q3W/Q4W

Reporting group description:

Participants with weight < 30 kg received tocilizumab IV infusions of 12 mg/kg once every three weeks (Q3W) up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality as per protocol criteria. Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switched to tocilizumab IV infusions of 12 mg/kg once every four weeks (Q4W) up to Week 52 in Part 2 of the study.

Reporting group title	Part 2: TCZ IV 8 mg/kg Q3W/Q4W

Reporting group description:

Participants with weight >/= 30 kg received tocilizumab IV infusions of 8 mg/kg Q3W up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality as per protocol criteria. Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switched to tocilizumab IV infusions of 8 mg/kg Q4W up to Week 52 in Part 2 of the study.

Subject analysis set title	Part 2: TCZ IV 12 mg/kg Q3W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received tocilizumab 12 mg/kg IV infusions Q3W up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality as per protocol criteria.

Subject analysis set title	Part 2: TCZ IV 8 mg/kg Q3W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received tocilizumab 8 mg/kg IV infusions Q3W up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality as per protocol criteria.

Subject analysis set title	Part 2: TCZ IV 12 mg/kg Q4W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switiched to tocilizumab IV infusions of 12 mg/kg Q4W up to Week 52 in Part 2 of the study.

Subject analysis set title	Part 2: TCZ IV 8 mg/kg Q4W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switiched to tocilizumab IV infusions of 8 mg/kg Q4W up to Week 52 in Part 2 of the study.

Subject analysis set title	Part 2: TCZ 12 mg/kg Q3W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received tocilizumab 12 mg/kg IV infusions Q3W up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality as per protocol criteria.

Subject analysis set title	Part 2: TCZ IV 12 mg/kg Q4W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of

neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switiched to tocilizumab IV infusions of 12 mg/kg Q4W up to Week 52 in Part 2 of the study.

Subject analysis set title	Part 2: TCZ IV 12 mg/kg Q3W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received tocilizumab 12 mg/kg IV infusions Q3W up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality as per protocol criteria.

Subject analysis set title	Part 2: TCZ IV 8 mg/kg Q3W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received tocilizumab 8 mg/kg IV infusions Q3W up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality.

Subject analysis set title	Part 2: TCZ IV 12 mg/kg Q4W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switiched to tocilizumab IV infusions of 12 mg/kg Q4W up to Week 52 in Part 2 of the study.

Subject analysis set title	Part 2: TCZ IV 8 mg/kg Q4W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switiched to tocilizumab IV infusions of 8 mg/kg Q4W up to Week 52 in Part 2 of the study.

Subject analysis set title	Part 2: TCZ IV 8 mg/kg Q4W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switiched to tocilizumab IV infusions of 8 mg/kg Q4W up to Week 52 in Part 2 of the study.

Subject analysis set title	Part 2: TCZ IV 12 mg/kg Q4W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switiched to tocilizumab IV infusions of 12 mg/kg Q4W up to Week 52 in Part 2 of the study.

Subject analysis set title	Part 2: TCZ IV 12 mg/kg Q4W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switiched to tocilizumab IV infusions of 12 mg/kg Q4W up to Week 52 in Part 2 of the study.

Subject analysis set title	Part 2: TCZ IV 8 mg/kg Q4W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switiched to tocilizumab IV infusions of 8 mg/kg Q4W up to Week 52 in Part 2 of the study.

Subject analysis set title	Part 2: TCZ IV 8 mg/kg Q4W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switiched to tocilizumab IV infusions of 8 mg/kg Q4W up to 52 weeks.

Subject analysis set title	TCZ Q2W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

IV infusions of tocilizumab once every other week (Q2W). Participants weighing < 30 kg received 8 mg/kg and participants weighing >/= 30 kg received 12 mg/kg.

Subject analysis set title	TCZ Q3W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

IV infusions of tocilizumab once every three weeks (Q3W). Participants weighing < 30 kg received 8 mg/kg and participants weighing >/= 30 kg received 12 mg/kg.

Subject analysis set title	TCZ Q4W
Subject analysis set type	Sub-group analysis

Subject analysis set description:

IV infusions of tocilizumab once every four weeks (Q4W). Participants weighing < 30 kg received 8 mg/kg and participants weighing >/= 30 kg received 12 mg/kg.

Primary: Juvenile Arthritis Disease Activity Score (JADAS-71) at the End of Part 2 of the Study

End point title	Juvenile Arthritis Disease Activity Score (JADAS-71) at the End of Part 2 of the Study[1]

End point description:

JADAS-71 has 4 components:Physician global assessment of disease activity on visual analog scale (VAS) (range=0-10, 0=arthritis inactive, 10=very poor), patient/parent global assessment of overall well-being on VAS (range=0-10, 0=very well, 10=very poor), normalized erythrocyte sedimentation rate (ESR) (range=0-10, If ESR is ≤20 mm/h, set to 0. If ≥120 mm/h, set to 10 mm/h. If > 20 mm/h and < 120 mm/h, apply formula:[ESR−20 mm/h]/10 mm/h), count of active arthritis (swelling present/pain present and limitation of motion) in 71 selected joints (range=0-71). Total score=sum of 4 component scores,range=0-101. Higher score=more arthritis. Data was collected: Part 2:Q3W Baseline, Weeks 3,6,9,12,24,36,48 and 51; Q4W-Baseline, Weeks 0,4,8,12,24,36 and 40. All TCZ population, participants who received at least 1 dose of study drug. n=participants with data at given timepoint. 9999=Not available; No participant analysed at given timepoint. 99999=SD was not estimable for 1 participant.

End point type	Primary

End point timeframe:

Part 2: Up to 52 weeks

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: Only descriptive statistics were planned to be reported for this endpoint. No formal assessment of treatment group comparability was planned to be performed.

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=7,15,1,6)	0.60 (± 0.839)	0.21 (± 0.247)	0.00 (± 99999)	0.35 (± 0.295)
Week 0 (n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	0.00 (± 99999)	0.13 (± 0.242)
Week 3 (n=7,15,0,0)	1.60 (± 2.474)	0.61 (± 0.913)	9999 (± 9999)	9999 (± 9999)
Week 4 (n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	0.00 (± 99999)	0.17 (± 0.266)
Week 6 (n=7,15,0,0)	0.54 (± 0.812)	0.39 (± 0.498)	9999 (± 9999)	9999 (± 9999)
Week 8 (n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	0.00 (± 99999)	0.20 (± 0.490)
Week 9 (n=7,15,0,0)	2.59 (± 5.402)	0.33 (± 0.420)	9999 (± 9999)	9999 (± 9999)

Week 12 (n=6,14,1,6)	0.30 (± 0.600)	0.84 (± 2.318)	0.00 (± 99999)	0.13 (± 0.327)
Week 24 (n=5,6,1,5)	0.42 (± 0.576)	0.05 (± 0.084)	0.00 (± 99999)	0.20 (± 0.346)
Week 36 (n=4,4,1,4)	0.48 (± 0.950)	0.08 (± 0.150)	0.00 (± 99999)	0.00 (± 0.000)
Week 40 (n=0,0,0,4)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	0.00 (± 0.000)
Week 48 (n=4,3,0,0)	0.00 (± 0.000)	0.17 (± 0.289)	9999 (± 9999)	9999 (± 9999)
Week 51 (n=4,3,0,0)	0.00 (± 0.000)	0.17 (± 0.208)	9999 (± 9999)	9999 (± 9999)

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Juvenile Idiopathic Arthritis (JIA) Disease Flare as Determined by JIA Core Variables in Part 2 of the Study

End point title	Number of Participants With Juvenile Idiopathic Arthritis (JIA) Disease Flare as Determined by JIA Core Variables in Part 2 of the Study[2]

End point description:

JIA flare was defined as any 3 of 6 core outcome variables worsening by at least 30% relative to baseline visit of Part 2, with no >1 of remaining variables improving by >30%. For number of joints with active arthritis/limitation of motion a minimum worsening of at least 2 joints had to be present. If physician global assessment (PGA)/parent/patient global assessment were used a minimum worsening of at least 2 units on a scale=0-10 had to be present. For ESR, a worsening of at least 30% was not considered if within normal ranges. The 6 core outcome variables: PGA of disease activity, parent/patient global assessment of overall well-being, number of joints with active arthritis/limitation of movement, ESR (measure of acute phase reaction) and functional ability determined by CHAQ Disability Index. All TCZ population, all participants who received at least one dose of study drug. Number of participants analyzed=participants with data available for analyses.

End point type	Primary

End point timeframe:

Part 2: Up to 52 weeks

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: Only descriptive statistics were planned to be reported for this endpoint. No formal assessment of treatment group comparability was planned to be performed.

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: participants	3	1	0	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Fever Attributable to Systemic Juvenile Idiopathic Arthritis (sJIA) in Part 2 of the Study

End point title	Number of Participants With Fever Attributable to Systemic Juvenile Idiopathic Arthritis (sJIA) in Part 2 of the Study[3]

End point description:

Absence of fever at screening visit was defined as a temperature measurement < 38 degree centigrades (C). Presence of fever at each study visit was defined as a temperature measurement ≥ 38 C. All TCZ population, all participants who have received at least one dose of study drug

End point type	Primary

End point timeframe:

Part 2: Up to 52 weeks

Notes:

[3] - 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: Only descriptive statistics were planned to be reported for this endpoint. No formal assessment of treatment group comparability was planned to be performed.

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With at Least One Adverse Event

End point title	Number of Participants With at Least One Adverse Event

End point description:

An adverse event is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events. Safety population, all participants who have received at least one dose of study drug and who have at least one post-baseline assessment of safety.

End point type	Secondary

End point timeframe:

Part 1 - Baseline up to 24 weeks plus 12 weeks of safety follow up; Part 2 - Baseline up to 52 weeks plus 12 weeks of safety follow up

End point values	Part 1: Tocilizumab (TCZ) Q2W	Part 2: TCZ IV 12 mg/kg Q3W/Q4W	Part 2: TCZ IV 8 mg/kg Q3W/Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	7	15	
Units: participants	16	7	14	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Interleukin-6 (IL-6) Protein Concentration in Part 2 of the Study

End point title	Serum Interleukin-6 (IL-6) Protein Concentration in Part 2 of the Study

End point description:

Pharmacodynamic (PD) population, all participants who have received at least one dose of study drug and who have at least one post-baseline assessment of PD. 'n' is the number of participants with data available at the given timepoint. 9999=0 participants. 99999=Not available (NA) i.e. SD was not estimable for 1 participant.

End point type	Secondary

End point timeframe:

Part 2: Q3W arms - Pre-dose at Baseline, Weeks 3, 6, 9, 12, 24, 36, 48 and 51; Q4W arms - Pre-dose at Baseline, Weeks 0, 4, 8, 12, 24, 36 and 40

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: pg/mL				
arithmetic mean (standard deviation)				
Baseline (n=5,14,1,6)	36.340 (± 19.2413)	23.453 (± 12.1440)	51.500 (± 99999)	25.415 (± 15.0174)
Week 0 (n=0,0,0,4)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	33.000 (± 23.3195)
Week 3 (n=6,11,0,0)	61.617 (± 75.5724)	22.727 (± 7.0321)	9999 (± 9999)	9999 (± 9999)
Week 4 (n=0,0,1,5)	9999 (± 9999)	9999 (± 9999)	13.700 (± 99999)	28.364 (± 24.8937)
Week 6 (n=6,13,0,0)	46.698 (± 50.7148)	82.995 (± 216.2854)	9999 (± 9999)	9999 (± 9999)
Week 8 (n=0,0,1,5)	9999 (± 9999)	9999 (± 9999)	14.300 (± 99999)	30.580 (± 22.0335)
Week 9 (n=5,11,0,0)	45.231 (± 46.2539)	47.582 (± 37.2259)	9999 (± 9999)	9999 (± 9999)
Week 12 (n=4,12,1,5)	84.100 (± 57.8972)	71.867 (± 156.4710)	11.600 (± 99999)	29.662 (± 26.0053)
Week 24 (n=3,5,1,3)	79.200 (± 44.8853)	23.420 (± 14.5520)	45.000 (± 99999)	29.393 (± 19.2760)
Week 36 (n=3,4,1,2)	67.467 (± 84.7317)	30.025 (± 16.5470)	14.100 (± 9999)	21.500 (± 15.8392)
Week 40 (n=0,0,0,2)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	22.820 (± 24.0133)
Week 48 (n=3,3,0,0)	14.533 (± 1.4154)	15.400 (± 10.0936)	9999 (± 9999)	9999 (± 9999)
Week 51 (n=3,1,0,0)	17.523 (± 9.2077)	5.060 (± 99999)	9999 (± 9999)	9999 (± 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Soluble IL-6 Receptor (sIL-6R) Protein Concentration in Part 2 of the Study

End point title	Soluble IL-6 Receptor (sIL-6R) Protein Concentration in Part 2 of the Study

End point description:

PD population, all participants who have received at least one dose of study drug and who have at least one post-baseline assessment of PD. 'n' is the number of participants with data available at the given timepoint. 9999=0 participants. 99999= NA i.e. SD was not estimable for 1 participant.

End point type	Secondary

End point timeframe:

Part 2: Q3W arms - Pre-dose at Baseline, Weeks 3, 6, 9, 12, 24, 36, 48 and 51; Q4W arms - Pre-dose at Baseline, Weeks 0, 4, 8, 12, 24, 36 and 40

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: ngEq/mL				
arithmetic mean (standard deviation)				
Baseline (n=7,14,1,6)	621.04 (± 443.779)	735.16 (± 310.983)	447.00 (± 99999)	855.00 (± 325.572)
Week 0 (n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	72.50 (± 99999)	722.83 (± 229.530)
Week 3 (n=7,14,0,0)	632.43 (± 261.172)	707.73 (± 291.228)	9999 (± 9999)	9999 (± 9999)
Week 4 (n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	379.00 (± 99999)	653.00 (± 143.386)
Week 6 (n=6,15,0,0)	518.67 (± 272.217)	721.73 (± 253.114)	9999 (± 9999)	9999 (± 9999)
Week 8 (n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	434.00 (± 99999)	628.50 (± 145.891)
Week 9 (n=6,13,0,0)	596.58 (± 318.685)	646.92 (± 174.932)	9999 (± 9999)	9999 (± 9999)
Week 12 (n=5,12,1,6)	656.80 (± 123.611)	666.75 (± 144.510)	411.00 (± 99999)	645.33 (± 106.952)
Week 24 (n=5,6,1,4)	574.54 (± 347.127)	554.33 (± 124.498)	519.00 (± 99999)	546.25 (± 330.265)
Week 36 (n=4,4,1,4)	492.50 (± 258.445)	646.00 (± 198.499)	439.00 (± 99999)	599.75 (± 122.200)
Week 40 (n=0,0,0,4)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	609.50 (± 115.613)
Week 48 (n=3,3,0,0)	551.00 (± 91.000)	391.00 (± 220.293)	9999 (± 9999)	9999 (± 9999)
Week 51 (n=2,2,0,0)	651.00 (± 135.765)	517.00 (± 140.007)	9999 (± 9999)	9999 (± 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: C-reactive Protein (CRP) Concentration in Part 2 of the Study

End point title	C-reactive Protein (CRP) Concentration in Part 2 of the Study

End point description:

PD population, all participants who have received at least one dose of study drug and who have at least one post-baseline assessment of PD. 'n' is the number of participants with data available at the given timepoint. 9999=0 participants. 99999=NA i.e. SD was not estimable for 1 participant.

End point type	Secondary

End point timeframe:

Part 2: Q3W arms - Baseline, Weeks 3, 6, 9, 12, 24, 36, 48 and 51; Q4W arms - Baseline, Weeks 0, 4, 8, 12, 24, 36 and 40

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: mg/L				
arithmetic mean (standard deviation)				
Baseline (n=7,15,1,6)	4.844 (± 12.2832)	2.309 (± 6.9847)	0.200 (± 99999)	0.958 (± 1.8575)
Week 0 (n=0,0,1,4)	9999 (± 9999)	9999 (± 9999)	0.610 (± 99999)	0.200 (± 0.0000)
Week 3 (n=7,13,1,2)	0.223 (± 0.0427)	0.216 (± 0.0407)	0.200 (± 99999)	0.200 (± 0.0000)
Week 4 (n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	0.200 (± 99999)	0.200 (± 0.0000)
Week 6 (n=7,14,0,0)	0.291 (± 0.1499)	0.526 (± 1.0163)	9999 (± 9999)	9999 (± 9999)
Week 8 (n=0,0,1,5)	9999 (± 9999)	9999 (± 9999)	0.200 (± 99999)	0.200 (± 0.0000)
Week 9 (n=5,11,1,3)	0.208 (± 0.0179)	0.255 (± 0.1250)	0.200 (± 99999)	0.200 (± 0.0000)
Week 12 (n=5,11,1,6)	0.200 (± 0.0000)	0.238 (± 0.1201)	0.200 (± 99999)	0.203 (± 0.0082)
Week 24 (n=5,5,1,5)	0.280 (± 0.1789)	0.254 (± 0.1207)	0.200 (± 99999)	4.040 (± 8.5865)
Week 36 (n=4,4,1,4)	0.225 (± 0.0500)	0.200 (± 0.0000)	0.200 (± 99999)	0.200 (± 0.0000)
Week 40 (n=0,0,0,4)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	0.200 (± 0.0000)
Week 48 (n=4,3,0,0)	0.200 (± 0.0000)	0.820 (± 1.0739)	9999 (± 9999)	9999 (± 9999)
Week 51 (n=4,3,0,0)	0.318 (± 0.2350)	0.200 (± 0.0000)	9999 (± 9999)	9999 (± 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Erythrocyte Sedimentation Rate (ESR) in Part 2 of the Study

End point title	Erythrocyte Sedimentation Rate (ESR) in Part 2 of the Study

End point description:

PD population, all participants who have received at least one dose of study drug and who have at least one post-baseline assessment of PD. 'n' is the number of participants with data available at the given timepoint. 9999=0 participants. 99999=NA i.e. SD was not estimable for 1 participant.

End point type	Secondary

End point timeframe:

Part 2: Q3W arms - Baseline, Weeks 3, 6, 9, 12, 24, 36, 48 and 51; Q4W arms - Baseline, Weeks 0, 4, 8, 12, 24, 36 and 40

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: mm/h				
arithmetic mean (standard deviation)				
Baseline (n=7,15,1,6)	3.43 (± 5.192)	3.00 (± 1.852)	1.00 (± 99999)	3.17 (± 1.602)
Week 0 (n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	4.00 (± 99999)	2.67 (± 1.633)
Week 3 (n=7,14,1,4)	2.86 (± 2.035)	3.57 (± 2.709)	2.00 (± 99999)	2.75 (± 0.957)
Week 4 (n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	1.00 (± 99999)	3.17 (± 1.722)
Week 6 (n=7,15,0,0)	4.14 (± 4.598)	4.13 (± 3.681)	9999 (± 9999)	9999 (± 9999)
Week 8 (n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	1.00 (± 99999)	3.33 (± 2.160)
Week 9 (n=6,13,1,4)	2.50 (± 2.510)	3.23 (± 2.204)	3.00 (± 99999)	2.25 (± 0.957)
Week 12 (n=5,12,1,6)	2.20 (± 1.789)	3.92 (± 3.315)	1.00 (± 99999)	4.50 (± 3.209)
Week 24 (n=5,6,1,5)	2.80 (± 1.304)	3.17 (± 2.137)	1.00 (± 99999)	2.80 (± 1.789)
Week 36 (n=4,4,1,4)	2.25 (± 2.217)	4.50 (± 2.646)	1.00 (± 99999)	2.25 (± 1.893)
Week 40 (n=0,0,0,4)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	2.25 (± 1.893)
Week 48 (n=4,3,0,0)	3.00 (± 0.816)	4.67 (± 1.528)	9999 (± 9999)	9999 (± 9999)
Week 51 (n=4,3,0,0)	1.75 (± 1.708)	6.00 (± 3.000)	9999 (± 9999)	9999 (± 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-TCZ Antibodies in Part 2 of the Study

End point title	Number of Participants With Anti-TCZ Antibodies in Part 2 of the Study

End point description:

Safety population, all participants who have received at least one dose of study drug and who have at least one post-baseline assessment of safety.

End point type	Secondary

End point timeframe:

Part 2: Up to Week 52

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Serum TCZ Concentration in Part 2 of the Study

End point title	Serum TCZ Concentration in Part 2 of the Study

End point description:

All TCZ population in Part 2, all participants who have received at least one dose of study drug in Part 2. 'n' analyzed is the number of participants with data available at the given timepoint. 9999=0 participants. 99999=NA, i.e. SD was not estimable for 1 participant.

End point type	Secondary

End point timeframe:

Part 2: Q3W arms - Baseline, Weeks 3, 6, 9, 12, 24, 36, 48 and 51; Q4W arms - Baseline, Weeks 0, 4, 8, 12, 24, 36 and 40

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: ug/mL				
arithmetic mean (standard deviation)				
Baseline (n=6,13,1,6)	29.916 (± 35.8002)	44.210 (± 33.2547)	9.520 (± 99999)	53.622 (± 48.5163)
Week 0 (n=0,0,0,6)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	24.212 (± 13.1659)
Week 3 (n=7,13,0,0)	26.420 (± 21.1844)	37.239 (± 21.8192)	9999 (± 9999)	9999 (± 9999)
Week 4 (n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	11.100 (± 99999)	17.718 (± 11.1580)
Week 6 (n=5,14,1,0)	28.636 (± 13.5744)	30.482 (± 19.2402)	9999 (± 9999)	9999 (± 9999)
Week 8 (n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	22.800 (± 99999)	17.578 (± 13.0611)
Week 9 (n=5,13,0,0)	32.020 (± 6.3739)	26.962 (± 17.9122)	9999 (± 9999)	9999 (± 9999)
Week 12 (n=4,12,1,6)	37.600 (± 20.5254)	44.763 (± 77.1798)	23.800 (± 99999)	15.442 (± 11.0714)
Week 24 (n=4,5,1,3)	24.363 (± 20.3686)	20.842 (± 25.9417)	30.300 (± 99999)	16.030 (± 14.2124)
Week 36 (n=3,4,1,4)	30.517 (± 18.6058)	19.733 (± 8.2218)	19.800 (± 99999)	12.903 (± 11.1808)
Week 40 (n=0,0,0,4)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	28.778 (± 16.0031)
Week 48 (n=3,2,0,0)	25.433 (± 34.3053)	22.950 (± 0.9192)	9999 (± 9999)	9999 (± 9999)

Week 51 (n=3,2,0,0)	12.207 (± 8.5862)	10.945 (± 14.6449)	9999 (± 9999)	9999 (± 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Childhood Health Assessment Questionnaire (CHAQ) Disability Index in Part 2 of the Study

End point title	Baseline Childhood Health Assessment Questionnaire (CHAQ) Disability Index in Part 2 of the Study

End point description:

CHAQ- Disability Index consists of 30 questions in 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities-distributed, among a total of 30 items. Each question was rated on 4-point scale with range 0=no difficulty to 3=unable to do. To calculate overall score, participant must have a domain score in at least 6 of 8 domains. Scores were averaged to calculate CHAQ disability index, range is 0=no/minimal physical dysfunction)-3=very severe physical dysfunction, higher score indicates more disability. All TCZ population, all participants who received at least one dose of study drug. 99999=NA i.e. SD was not estimable for 1 participant.

End point type	Secondary

End point timeframe:

Baseline of Part 2

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: score on a scale				
arithmetic mean (standard deviation)	0.0000 (± 0.00000)	0.0417 (± 0.09047)	0.0000 (± 99999)	0.0000 (± 0.00000)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Childhood Health Assessment Questionnaire (CHAQ) Disability Index in Part 2 of the Study

End point title	Change from Baseline in Childhood Health Assessment Questionnaire (CHAQ) Disability Index in Part 2 of the Study

End point description:

CHAQ- Disability Index consists of 30 questions in 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities-distributed, among a total of 30 items. Each question was rated on 4-point scale with range 0=no difficulty to 3=unable to do. To calculate overall score, participant must have a domain score in at least 6 of 8 domains. Scores were averaged to calculate CHAQ disability index, range is 0=no/minimal physical dysfunction)-3=very severe physical dysfunction, higher score indicates more disability. Negative change from baseline indicates an improvement. All TCZ population, all participants who received at least 1 dose of study.'n'= participants with data available at given timepoint. 9999=0 participants. 99999=NA i.e. SD was not estimable for 1 participant.

End point type	Secondary

End point timeframe:

Baseline; Part 2: Q3W arms - Weeks 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48 and 51; Q4W arms - Weeks 0, 4, 8, 12, 16, 20, 24, 28, 32, 36 and 40

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 0(n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	0.0000 (± 99999)	0.0000 (± 0.00000)
Change from Baseline at Week 3(n=7,15,0,0)	0.2500 (± 0.66144)	0.0167 (± 0.25384)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 4(n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	0.0000 (± 99999)	0.0000 (± 0.00000)
Change from Baseline at Week 6(n=7,15,0,0)	0.1071 (± 0.28347)	-0.0083 (± 0.07420)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 8(n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	0.0000 (± 99999)	0.0000 (± 0.00000)
Change from Baseline at Week 9(n=7,14,0,0)	0.2500 (± 0.51539)	-0.0268 (± 0.10022)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 12(n=5,13,1,6)	0.1250 (± 0.27951)	-0.0481 (± 0.09599)	0.0000 (± 99999)	0.0000 (± 0.00000)
Change from Baseline at Week 15(n=6,12,0,0)	0.1458 (± 0.35722)	0.1771 (± 0.54994)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 16(n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	0.0000 (± 99999)	0.0000 (± 0.00000)
Change from Baseline at Week 18(n=5,9,0,0)	0.1000 (± 0.22361)	0.2500 (± 0.85009)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 20(n=0,0,1,5)	9999 (± 9999)	9999 (± 99999999)	0.0000 (± 99999)	0.0000 (± 0.00000)
Change from Baseline at Week 21(n=4,8,0,0)	0.0000 (± 0.00000)	0.2656 (± 0.90740)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 24(n=5,5,1,5)	0.1250 (± 0.27951)	-0.0750 (± 0.11180)	0.0000 (± 99999)	0.0000 (± 0.00000)
Change from Baseline at Week 27(n=4,4,0,0)	0.0000 (± 0.00000)	0.0000 (± 0.10206)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 28(n=0,0,1,5)	9999 (± 9999)	9999 (± 9999)	0.0000 (± 99999)	0.0000 (± 0.00000)
Change from Baseline at Week 30(n=4,3,0,0)	0.0000 (± 0.00000)	0.0000 (± 0.00000)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 32(n=0,0,1,5)	9999 (± 9999)	9999 (± 9999)	0.0000 (± 99999)	0.0000 (± 0.00000)
Change from Baseline at Week 33(n=4,3,0,0)	0.0000 (± 0.00000)	-0.0417 (± 0.07217)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 36(n=4,3,1,4)	0.0000 (± 0.00000)	0.0417 (± 0.07217)	0.0000 (± 99999)	0.0000 (± 0.00000)
Change from Baseline at Week 39(n=4,3,0,0)	0.0000 (± 0.00000)	-0.0417 (± 0.07217)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 40(n=0,0,0,3)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	0.0000 (± 0.00000)
Change from Baseline at Week 42(n=3,3,0,0)	0.0000 (± 0.00000)	-0.0417 (± 0.07217)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 45(n=4,3,0,0)	0.0000 (± 0.00000)	-0.0417 (± 0.07217)	9999 (± 9999)	9999 (± 9999)

Change from Baseline at Week 48(n=4,3,0,0)	0.0000 (± 0.00000)	-0.0417 (± 0.07217)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 51(n=4,3,0,0)	0.0000 (± 0.00000)	-0.0417 (± 0.07217)	9999 (± 9999)	9999 (± 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Participant's/Parent's Global Assessment of Overall Well-being Score in Part 2 of the Study

End point title	Baseline Participant's/Parent's Global Assessment of Overall Well-being Score in Part 2 of the Study

End point description:

Participant's/parent's global assessment of overall well-being was determined on a VAS (range = 0-100, left end of the line = very well, i.e., symptom-free and no arthritis disease activity; right end = very poor, i.e., maximum arthritis disease activity). All TCZ population, all participants who have received at least one dose of study drug. 99999=NA i.e. SD was not estimable for 1 participant.

End point type	Secondary

End point timeframe:

Baseline of Part 2

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: score on a scale				
arithmetic mean (standard deviation)	2.3 (± 3.95)	1.6 (± 2.29)	0.0 (± 99999)	2.5 (± 3.21)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Participant's/Parent's Global Assessment of Overall Well-being Score in Part 2 of the Study

End point title	Change from Baseline in Participant's/Parent's Global Assessment of Overall Well-being Score in Part 2 of the Study

End point description:

Participant's/Parent's global assessment of overall well-being was determined on a VAS (range = 0-100, left end of the line = very well, i.e., symptom-free and no arthritis disease activity; right end = very poor, i.e., maximum arthritis disease activity). Reported is the change from baseline in VAS score with a negative change from baseline indicating an improvement. All TCZ population, all participants who have received at least one dose of study drug.'n' is the number of participants with data available at the given timepoint. 9999=0 participants. 99999=NA i.e. SD was not estimable for 1 participant.

End point type	Secondary

End point timeframe:

Baseline; Part 2: Q3W arms - Weeks 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48 and 51; Q4W arms - Weeks 0, 4, 8, 12, 16, 20, 24, 28, 32, 36 and 40

End point values	Part 2: TCZ IV 12 mg/kg Q3W	Part 2: TCZ IV 8 mg/kg Q3W	Part 2: TCZ IV 12 mg/kg Q4W	Part 2: TCZ IV 8 mg/kg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	15	1	6
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 0(n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	0.0 (± 99999)	-1.2 (± 1.60)
Change from Baseline at Week 3(n=7,15,0,0)	-0.3 (± 2.36)	2.0 (± 6.12)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 4(n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	0.0 (± 99999)	-1.2 (± 1.26)
Change from Baseline at Week 6(n=7,15,0,0)	-1.6 (± 3.51)	2.2 (± 4.55)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 8(n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	0.0 (± 99999)	-0.5 (± 3.56)
Change from Baseline at Week 9(n=7,14,0,0)	8.4 (± 26.48)	0.1 (± 2.62)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 12(n=5,13,1,6)	-1.6 (± 3.58)	-0.7 (± 2.32)	0.0 (± 99999)	-1.2 (± 2.56)
Change from Baseline at Week 15(n=6,12,0,0)	-1.5 (± 3.67)	7.1 (± 29.34)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 16(n=0,0,1,6)	9999 (± 9999)	9999 (± 9999)	0.0 (± 99999)	-1.5 (± 1.97)
Change from Baseline at Week 18(n=5,9,0,0)	-1.4 (± 3.71)	6.9 (± 23.26)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 20(n=0,0,1,5)	9999 (± 9999)	9999 (± 9999)	0.0 (± 99999)	-1.6 (± 2.61)
Change from Baseline at Week 21(n=4,8,0,0)	0.0 (± 0.00)	9.9 (± 30.02)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 24(n=5,5,1,5)	-1.8 (± 4.02)	-0.8 (± 2.17)	0.0 (± 99999)	-1.0 (± 2.00)
Change from Baseline at Week 27(n=4,4,0,0)	0.0 (± 0.00)	0.3 (± 2.87)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 28(n=0,0,1,5)	9999 (± 9999)	9999 (± 9999)	0.0 (± 99999)	-1.2 (± 2.39)
Change from Baseline at Week 30(n=4,3,0,0)	0.0 (± 0.00)	-0.3 (± 2.52)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 32(n=0,0,1,5)	9999 (± 9999)	9999 (± 9999)	0.0 (± 99999)	5.4 (± 14.35)
Change from Baseline at Week 33(n=4,3,0,0)	25.0 (± 50.00)	0.0 (± 3.00)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 36(n=4,3,1,4)	0.3 (± 0.50)	0.0 (± 3.00)	0.0 (± 99999)	-2.0 (± 2.83)
Change from Baseline at Week 39(n=4,3,0,0)	0.3 (± 0.50)	-1.0 (± 1.73)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 40(n=0,0,0,3)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	-2.7 (± 3.06)
Change from Baseline at Week 42(n=3,3,0,0)	0.0 (± 0.00)	-0.7 (± 2.08)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 45(n=4,3,0,0)	0.0 (± 0.00)	0.3 (± 3.51)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 48(n=4,3,0,0)	0.0 (± 0.00)	0.7 (± 4.04)	9999 (± 9999)	9999 (± 9999)
Change from Baseline at Week 51(n=4,3,0,0)	0.0 (± 0.00)	0.3 (± 3.51)	9999 (± 9999)	9999 (± 9999)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part 1 - Baseline up to 24 weeks plus 12 weeks of safety follow up; Part 2 - Baseline up to 52 weeks plus 12 weeks of safety follow up

Adverse event reporting additional description:

Safety population, all participants who received at least one dose of study drug and who had at least one post-baseline assessment of safety.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Part 1: Tocilizumab (TCZ) Q2W

Reporting group description:

Participants received tocilizumab intravenous (IV) infusions (12 mg/kg for participants < 30 kg; 8 mg/kg for participants >/= 30 kg) once every other week (Q2W) up to 24 weeks or until occurrence of laboratory abnormalities in Part 1 of the study.

Reporting group title	Part 2: TCZ IV 12 mg/kg Q3W/Q4W

Reporting group description:

Participants with weight < 30 kg received tocilizumab IV infusions of 12 mg/kg once every three weeks (Q3W) up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality as per protocol criteria. Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switched to tocilizumab IV infusions of 12 mg/kg once every four weeks (Q4W) up to Week 52 in Part 2 of the study.

Reporting group title	Part 2: TCZ IV 8 mg/kg Q3W/Q4W

Reporting group description:

Participants with weight >/= 30 kg received tocilizumab IV infusions of 8 mg/kg Q3W up to 52 weeks or until occurrence of neutropenia, thrombocytopenia, or liver enzyme abnormality as per protocol criteria. Participants who completed 5 consecutive infusions of Q3W and had a laboratory abnormality of neutropenia, thrombocytopenia or elevated liver enzymes as per protocol criteria, after resolution of this laboratory abnormality switched to tocilizumab IV infusions of 8 mg/kg Q4W up to Week 52 in Part 2 of the study.

Serious adverse events	Part 1: Tocilizumab (TCZ) Q2W	Part 2: TCZ IV 12 mg/kg Q3W/Q4W	Part 2: TCZ IV 8 mg/kg Q3W/Q4W
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 19 (5.26%)	1 / 7 (14.29%)	1 / 15 (6.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Immune system disorders			
HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

HYPERTRANSAMINASAEMIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
PNEUMONIA			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Part 1: Tocilizumab (TCZ) Q2W	Part 2: TCZ IV 12 mg/kg Q3W/Q4W	Part 2: TCZ IV 8 mg/kg Q3W/Q4W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 19 (84.21%)	7 / 7 (100.00%)	14 / 15 (93.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SKIN PAPILLOMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
NO CODING AVAILABLE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
PYREXIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
FATIGUE			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
SEASONAL ALLERGY			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
HYPERSENSITIVITY			

subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
DYSMENORRHOEA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
CATARRH			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
COUGH			
subjects affected / exposed	2 / 19 (10.53%)	1 / 7 (14.29%)	2 / 15 (13.33%)
occurrences (all)	3	1	2
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
RHINORRHOEA			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
TONSILLAR HYPERTROPHY			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
FEAR OF INJECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Investigations			
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 19 (10.53%)	0 / 7 (0.00%)	2 / 15 (13.33%)
occurrences (all)	2	0	2
COMPLEMENT FACTOR C4 DECREASED			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	2 / 15 (13.33%)
occurrences (all)	0	1	2
EOSINOPHIL COUNT INCREASED			

subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	1 / 19 (5.26%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
LYMPHOCYTE MORPHOLOGY ABNORMAL			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 19 (10.53%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
LIVER FUNCTION TEST ABNORMAL			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
ROSEOLOVIRUS TEST POSITIVE			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
VITAMIN D DECREASED			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	3 / 19 (15.79%)	2 / 7 (28.57%)	0 / 15 (0.00%)
occurrences (all)	4	2	0
CONTUSION			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
FALL			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
HEAD INJURY			

subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
JOINT INJURY			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
LIGAMENT SPRAIN			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
RADIUS FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
SKIN ABRASION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
TRAUMATIC HAEMATOMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nervous system disorders			
HEADACHE			
subjects affected / exposed	1 / 19 (5.26%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
SYNCOPE			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
LEUKOPENIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	7
NEUTROPENIA			
subjects affected / exposed	1 / 19 (5.26%)	1 / 7 (14.29%)	3 / 15 (20.00%)
occurrences (all)	1	1	4
THROMBOCYTOPENIA			

subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
EAR SWELLING			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
VERTIGO			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
CATARACT SUBCAPSULAR			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
EYE PAIN			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
VISION BLURRED			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
DIARRHOEA			
subjects affected / exposed	2 / 19 (10.53%)	1 / 7 (14.29%)	1 / 15 (6.67%)
occurrences (all)	2	1	1
VOMITING			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
ANAL FISSURE			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
NAUSEA			

subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
BLISTER			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
INGROWING NAIL			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
PETECHIAE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
PRURITUS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
RASH			
subjects affected / exposed	3 / 19 (15.79%)	2 / 7 (28.57%)	0 / 15 (0.00%)
occurrences (all)	3	2	0
RASH PAPULAR			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
SKIN EXFOLIATION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
PRURIGO			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
POLYARTHRITIS			

subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
STILL'S DISEASE			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	2 / 15 (13.33%)
occurrences (all)	0	1	2
SYNOVIAL CYST			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
CONJUNCTIVITIS			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
CYSTITIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	3	0	1
EAR INFECTION			
subjects affected / exposed	1 / 19 (5.26%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
ENTEROBIASIS			
subjects affected / exposed	2 / 19 (10.53%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
INFLUENZA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
MYCOPLASMA INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
NASOPHARYNGITIS			

subjects affected / exposed	1 / 19 (5.26%)	1 / 7 (14.29%)	3 / 15 (20.00%)
occurrences (all)	2	1	7
PARONYCHIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
PHARYNGITIS			
subjects affected / exposed	0 / 19 (0.00%)	2 / 7 (28.57%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
PNEUMONIA			
subjects affected / exposed	2 / 19 (10.53%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	3	1	0
RHINITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 7 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
TONSILLITIS			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	3 / 19 (15.79%)	0 / 7 (0.00%)	3 / 15 (20.00%)
occurrences (all)	4	0	5
URINARY TRACT INFECTION			
subjects affected / exposed	2 / 19 (10.53%)	2 / 7 (28.57%)	2 / 15 (13.33%)
occurrences (all)	2	3	2
VIRAL RASH			
subjects affected / exposed	0 / 19 (0.00%)	1 / 7 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
ASYMPTOMATIC BACTERIURIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
FUNGAL SKIN INFECTION			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
GASTROENTERITIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0

IMPETIGO			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
OTITIS EXTERNA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
OTITIS MEDIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
PNEUMONIA MYCOPLASMAL			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
TONSILLITIS STREPTOCOCCAL			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
IRON DEFICIENCY			
subjects affected / exposed	1 / 19 (5.26%)	0 / 7 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 March 2013	In Protocol WA28029 version 2 the Patient-reported outcome measures section was updated to use Child Health Assessment Questionnaire (CHAQ) instead of Juvenile Arthritis Multidimensional Assessment Report (JAMAR). Physician global assessment of disease activity and parent/patient global assessment of overall well-being were updated to use 100 mm horizontal visual analogue scale (VAS).
07 January 2016	Protocol WA28029 version 3 included the addition of a preliminary screening assessment (Screening Evaluation 1) and a run-in phase of ≤ 24 weeks (Part 1). The proposed modifications were intended to increase enrollment by helping to identify participants with resolved laboratory abnormalities as per protocol criteria in Part 1 on the TCZ Q2W regimen who were eligible to participate in the decreased dose frequency phase (Part 2).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported