



Clinical trial results:

Long-term, Interventional, Open Label Extension Study Evaluating the Safety of Tocilizumab Treatment in Patients with Polyarticular-Course Juvenile Idiopathic Arthritis From Germany who Completed the Global, Multinational Trial (WA19977)

Summary

EudraCT number	2011-001097-25
Trial protocol	DE
Global end of trial date	14 August 2013

Results information

Result version number	v1 (current)
This version publication date	04 May 2016
First version publication date	07 August 2015

Trial information

Trial identification

Sponsor protocol code	ML25756
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01667471
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	Roche Trial Information Hotline, F. Hoffmann-La Roche AG , 41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG , 41 61 6878333, 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	14 August 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	14 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety of tocilizumab treatment in participants with Polyarticular-Course Juvenile Idiopathic Arthritis (pcJIA) from Germany who completed the WA19977 study and entered this extension.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization (ICH) guideline E6: Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 January 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects**Subjects enrolled per country**

Country: Number of subjects enrolled	Germany: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	1
Adolescents (12-17 years)	4
Adults (18-64 years)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All participants who completed the core study WA19977 were considered for enrollment into this study if they fulfilled the respective requirements of study eligibility. Screening was conducted at Visit 1 during the week prior to enrollment visit.

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	Tocilizumab 8 milligrams per kilogram (mg/kg)
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Arm description:

Participants received tocilizumab 8 mg/kg intravenously (IV) every 4 weeks up to 104 weeks or until tocilizumab was commercially available for polyarticular-course Juvenile Idiopathic Arthritis (pcJIA).

Arm type	Experimental
Investigational medicinal product name	Tocilizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received tocilizumab 8 mg/kg IV every 4 weeks.

Number of subjects in period 1	Tocilizumab 8 milligrams per kilogram (mg/kg)
Started	7
Completed	7

Baseline characteristics

Reporting groups

Reporting group title	Overall Study
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Reporting group description:

All participants who received at least one dose of the study were included in the Safety Analysis Set.

Reporting group values	Overall Study	Total	
Number of subjects	7	7	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	14.4		
standard deviation	± 3.2	-	
Gender categorical			
Units: Subjects			
Female	6	6	
Male	1	1	

End points

End points reporting groups

Reporting group title	Tocilizumab 8 milligrams per kilogram (mg/kg)
Reporting group description: Participants received tocilizumab 8 mg/kg intravenously (IV) every 4 weeks up to 104 weeks or until tocilizumab was commercially available for polyarticular-course Juvenile Idiopathic Arthritis (pcJIA).	

Primary: Number of Participants With Adverse Events of Special Interest and Study-Drug Related Adverse Events

End point title	Number of Participants With Adverse Events of Special Interest and Study-Drug Related Adverse Events ^[1]
End point description: Adverse Events (AEs) and Serious Adverse Events (SAEs) were recorded from the first day of tocilizumab administration until 4 weeks after administration of the last dose of tocilizumab.	
End point type	Primary
End point timeframe: Baseline and every 4 weeks up to Week 108	

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: The primary objective of this study was Safety. No statistical analysis was done for safety endpoints.

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[2]			
Units: participants				
number (not applicable)				
Drug related AEs	6			
Drug related SAEs	0			
AEs of special interest	1			
Drug related AEs of special interest	1			

Notes:

[2] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Number of AEs of Special Interest and Study Drug Related AEs

End point title	Number of AEs of Special Interest and Study Drug Related
End point description: AEs and SAEs were recorded from the first day of tocilizumab administration until 4 weeks after administration of the last dose of tocilizumab.	
End point type	Primary

End point timeframe:

Baseline and every 4 weeks up to Week 108

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: The primary objective of this study was Safety. No statistical analysis was done for safety endpoints.

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[4]			
Units: adverse events				
number (not applicable)				
Drug-related AEs	22			
Drug-related SAEs	0			
AEs of special interest	2			
Drug-related AEs of special interest	2			

Notes:

[4] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Juvenile Idiopathic Arthritis (JIA) American College of Rheumatology (ACR) 30/50/70/90 by Visit

End point title	Percentage of Participants With Juvenile Idiopathic Arthritis (JIA) American College of Rheumatology (ACR) 30/50/70/90 by Visit
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End point description:

The six JIA ACR components comprised of: 1) Physician's global assessment of disease activity, 2) Parent/Participant's global assessment of overall well-being, 3) Maximum number of joints with active arthritis, 4) Number of joints with limitation of movement, 5) Erythrocyte Sedimentation Rate (ESR) and/or C-reactive Protein (CRP), and 6) Childhood Health Assessment Questionnaire - Disease Index (CHAQ-DI).

At an assessment visit a JIA ACR30/50/70/90 response in comparison to Baseline was defined as: At least three of the six JIA ACR core components improving by at least 30 percent (%), 50%, 70%, or 90% and no more than one of the remaining JIA ACR core components worsening by more than 30%.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, 24, 36, 48, 60, 72 and 108

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[5]			
Units: percentage of participants				
number (not applicable)				
Baseline JIA ACR30 (n=7)	85.7			

Week 12 JIA ACR30 (n=7)	100			
Week 24 JIA ACR30 (n=7)	100			
Week 36 JIA ACR30 (n=7)	100			
Week 48 JIA ACR30 (n=6)	100			
Week 60 JIA ACR30 (n=6)	100			
Week 72 JIA ACR30 (n=2)	100			
Week 108 JIA ACR30 (n=7)	100			
Baseline JIA ACR50 (n=7)	85.7			
Week 12 JIA ACR50 (n=7)	100			
Week 24 JIA ACR50 (n=7)	100			
Week 36 JIA ACR50 (n=7)	100			
Week 48 JIA ACR50 (n=6)	100			
Week 60 JIA ACR50 (n=6)	100			
Week 72 JIA ACR50 (n=2)	100			
Week 108 JIA ACR50 (n=7)	100			
Baseline JIA ACR70 (n=6)	85.7			
Week 12 JIA ACR70 (n=7)	100			
Week 24 JIA ACR70 (n=7)	100			
Week 36 JIA ACR70 (n=7)	100			
Week 48 JIA ACR70 (n=6)	100			
Week 60 JIA ACR70 (n=6)	100			
Week 72 JIA ACR70 (n=2)	100			
Week 108 JIA ACR70 (n=7)	100			
Baseline JIA ACR90 (n=6)	85.7			
Week 12 JIA ACR90 (n=7)	85.7			
Week 24 JIA ACR90 (n=7)	85.7			
Week 36 JIA ACR90 (n=7)	71.4			
Week 48 JIA ACR90 (n=6)	83.3			
Week 60 JIA ACR90 (n=6)	66.7			
Week 72 JIA ACR90 (n=2)	100			
Week 108 JIA ACR90 (n=7)	85.7			

Notes:

[5] - n = number of participants analyzed for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Inactive Disease by Visit

End point title	Percentage of Participants With Inactive Disease by Visit
End point description:	
A participant was defined to show inactive disease if all of the following criteria were applied: 1) No joints with active arthritis (no joints with swelling and no joints with lack of motion), 2) No fever, rash, serositis, splenomegaly, or generalized lymphadenopathy attributable to JIA, 3) No active uveitis, 4) ESR and/or CRP within normal range, and 5) Physician's global assessment of disease activity equals (=) 0 millimeters (mm) on a Visual analog scale (VAS).	
End point type	Secondary
End point timeframe:	
Baseline, Weeks 12, 24, 36, 48, 60, 72 and 108	

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[6]			
Units: percentage of participants				
number (not applicable)				
Baseline(n=7)	57.1			
Week 12 (n=7)	42.9			
Week 24 (n=7)	14.3			
Week 36 (n=7)	42.9			
Week 48 (n=6)	16.7			
Week 60 (n=6)	33.3			
Week 72 (n=2)	50			
Week 108 (n=7)	57.1			

Notes:

[6] - n = number of participants analyzed for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Clinical Remission (CR) at Each Visit

End point title	Percentage of Participants Achieving Clinical Remission (CR) at Each Visit
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End point description:

CR was defined as clinical remission with medication (CRem). A participant was in CR if inactive disease was observed for a minimum of 6 consecutive months.

End point type	Secondary
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End point timeframe:

Baseline, Screening, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76 and 108

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[7]			
Units: percentage of participants				
number (not applicable)				
Baseline (n=7)	0			
Screening (n=7)	0			
Week 4 (n=7)	0			
Week 8 (n=7)	0			

Week 12 (n=7)	0			
Week 16 (n=7)	0			
Week 20 (n=7)	0			
Week 24 (n=7)	0			
Week 28 (n=7)	14.3			
Week 32 (n=7)	14.3			
Week 36 (n=7)	14.3			
Week 40 (n=6)	16.7			
Week 44 (n=6)	16.7			
Week 48 (n=6)	16.7			
Week 52 (n=6)	16.7			
Week 56 (n=6)	16.7			
Week 60 (n=6)	0			
Week 64 (n=5)	0			
Week 68 (n=3)	0			
Week 72 (n=2)	0			
Week 76 (n=1)	0			
Week 108 (n=7)	0			

Notes:

[7] - n = number of participants analyzed for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Physicians Assessment of Global Activity (VAS)

End point title	Physicians Assessment of Global Activity (VAS)
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End point description:

The participant's treating physician provided a rating of the participant's arthritis disease activity on a 0 to 100 mm horizontal scale. The extreme left end of the line represented 'arthritis inactive' (ie, symptom-free and no arthritis symptoms) and the extreme right end represented 'arthritis very active'. A higher score indicated more disease activity.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, 24, 28, 32, 36, 48, 60, 72 and 108

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[8]			
Units: mm				
arithmetic mean (standard deviation)				
Baseline (n=7)	12 (± 30.4)			
Week 12 (n=7)	2.3 (± 2.9)			
Week 24 (n=7)	5.4 (± 6.1)			
Week 28 (n=1)	1 (± 0)			
Week 32 (n=2)	29 (± 8.5)			
Week 36 (n=7)	5 (± 7.9)			

Week 48 (n=6)	5.7 (\pm 8.2)			
Week 60 (n=6)	5.7 (\pm 8.7)			
Week 72 (n=2)	1 (\pm 1.4)			
Week 108 (n=7)	5 (\pm 8.7)			

Notes:

[8] - Safety Analysis Set; number (n) = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Parent or Participant's Assessment of Global Activity (VAS)

End point title	Parent or Participant's Assessment of Global Activity (VAS)
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End point description:

The participant or parent/guardian, as appropriate, provided a rating of the participant's well-being on a 0 to 100 mm horizontal scale. The extreme left end of the line represented 'very well' (ie, symptom-free and no arthritis disease activity) and the extreme right end represented 'very poor' (ie, maximum arthritis disease activity). A higher score indicated poorer well-being.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, 24, 28, 32, 36, 48, 60, 72 and 108

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[9]			
Units: mm				
arithmetic mean (standard deviation)				
Baseline (n=7)	10.1 (\pm 20)			
Week 12 (n=7)	7.1 (\pm 8.1)			
Week 24 (n=7)	16.4 (\pm 19.9)			
Week 28 (n=1)	1 (\pm 0)			
Week 32 (n=2)	22.5 (\pm 24.7)			
Week 36 (n=7)	12.1 (\pm 18.4)			
Week 48 (n=6)	11.7 (\pm 13.9)			
Week 60 (n=6)	10.2 (\pm 13.8)			
Week 72 (n=2)	3.5 (\pm 4.9)			
Week 108 (n=7)	9.7 (\pm 16)			

Notes:

[9] - Safety Analysis Set; n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Joints With Active Arthritis

End point title	Number of Joints With Active Arthritis
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End point description:

Joints with active arthritis were defined as joints with swelling or pain, and limited of motion. The maximum number of joints with active arthritis was 71. The joint assessment was performed by an independent assessor who was not the treating physician and who was blinded to all other aspects of the participant's efficacy and safety data.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, 24, 28, 32, 36, 48, 60, 72 and 108

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[10]			
Units: joints				
arithmetic mean (standard deviation)				
Baseline (n=7)	0.9 (± 2.3)			
Week 12 (n=7)	0.3 (± 0.8)			
Week 24 (n=7)	1 (± 2.6)			
Week 28 (n=1)	1 (± 0)			
Week 32 (n=2)	1.5 (± 0.7)			
Week 36 (n=7)	1.1 (± 2.2)			
Week 48 (n=6)	0 (± 0)			
Week 60 (n=6)	0.3 (± 0.8)			
Week 72 (n=2)	0 (± 0)			
Week 108 (n=7)	0.3 (± 0.8)			

Notes:

[10] - Safety Analysis Set; n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Joints With Lack of Motion

End point title	Number of Joints With Lack of Motion
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End point description:

Joints with lack of movement were assessed. The maximum number of joints with lack of movement was 67. The joint assessment was performed by an independent assessor who was not the treating physician and who was blinded to all other aspects of the participant's efficacy and safety data.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, 24, 28, 32, 36, 48, 60, 72 and 108

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[11]			
Units: joints				
arithmetic mean (standard deviation)				
Baseline (n=7)	1.4 (± 2.7)			
Week 12 (n=7)	2.6 (± 5.1)			
Week 24 (n=7)	2.4 (± 3.2)			
Week 28 (n=1)	1 (± 0)			
Week 32 (n=2)	5.5 (± 7.8)			
Week 36 (n=7)	1.7 (± 2.4)			
Week 48 (n=6)	2.7 (± 5.2)			
Week 60 (n=6)	1.8 (± 3)			
Week 72 (n=2)	0 (± 0)			
Week 108 (n=7)	2.9 (± 4.8)			

Notes:

[11] - Safety Analysis Set; n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Erythrocyte Sedimentation Rate (ESR)

End point title	Erythrocyte Sedimentation Rate (ESR)
End point description:	ESR is a marker of inflammation and was measured as millimeters per hour (mm/h).
End point type	Secondary
End point timeframe:	Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76 and 108

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[12]			
Units: mm/h				
arithmetic mean (standard deviation)				
Baseline (n=7)	4.9 (± 5.1)			
Week 4 (n=7)	3 (± 1.9)			
Week 8 (n=7)	2.9 (± 2.3)			
Week 12 (n=7)	3 (± 2)			
Week 16 (n=7)	8.6 (± 16.1)			
Week 20 (n=7)	2.6 (± 0.8)			
Week 24 (n=7)	2.7 (± 1.4)			
Week 28 (n=5)	3.4 (± 3.1)			
Week 32 (n=7)	4.3 (± 4.2)			

Week 36 (n=7)	4.3 (± 2.5)			
Week 40 (n=6)	2 (± 1.8)			
Week 44 (n=6)	2.7 (± 1.5)			
Week 48 (n=6)	3.8 (± 1.5)			
Week 52 (n=6)	3.2 (± 3.6)			
Week 56 (n=6)	2.3 (± 1.6)			
Week 60 (n=6)	10.2 (± 12.7)			
Week 64 (n=5)	3.2 (± 2.4)			
Week 68 (n=3)	10 (± 7.2)			
Week 72 (n=2)	4.5 (± 0.7)			
Week 76 (n=1)	2 (± 0)			
Week 108 (n=7)	4.3 (± 2.8)			

Notes:

[12] - Safety Analysis Set; n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ-DI Score

End point title	CHAQ-DI Score
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End point description:

The CHAQ-DI questionnaire consisted of 30 questions referring to eight domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities. Each domain had at least two component questions and if applicable to the participant there were four possible responses (0 = without any difficulty, 1 = with some difficulty, 2 = with much difficulty, 3 = unable to do). The CHAQ-DI score is the sum of the domain scores divided by the number of domains that have a non-missing score. This overall score ranges from 0 (best) to 3 (worst).

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, 24, 28, 32, 36, 48, 60, 72, and 108

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[13]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=7)	0 (± 0)			
Week 12 (n=7)	0.04 (± 0.09)			
Week 24 (n=7)	0.14 (± 0.2)			
Week 28 (n=1)	0 (± 0)			
Week 32 (n=2)	0.19 (± 0.27)			
Week 36 (n=7)	0.13 (± 0.33)			
Week 48 (n=6)	0 (± 0)			
Week 60 (n=6)	0.21 (± 0.51)			
Week 72 (n=2)	0 (± 0)			
Week 108 (n=7)	0 (± 0)			

Notes:

[13] - Safety Analysis Set; n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Parent or Participant's Assessment of Pain (VAS)

End point title	Parent or Participant's Assessment of Pain (VAS)
End point description: Parents or participants rated participant's pain by placing a horizontal line on a VAS of 0 (no pain)- 100 mm (severe pain).	
End point type	Secondary
End point timeframe: Baseline, Weeks 12, 24, 28, 32, 36, 48, 60, 72, and 108	

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[14]			
Units: mm				
arithmetic mean (standard deviation)				
Baseline (n=7)	10.9 (± 21.8)			
Week 12 (n=7)	7 (± 10)			
Week 24 (n=7)	13.7 (± 16.7)			
Week 28 (n=1)	1 (± 0)			
Week 32 (n=2)	28.5 (± 17.7)			
Week 36 (n=7)	10.6 (± 15.9)			
Week 48 (n=6)	12.3 (± 13.6)			
Week 60 (n=6)	10.2 (± 13.8)			
Week 72 (n=2)	4 (± 5.7)			
Week 108 (n=7)	9.9 (± 15.9)			

Notes:

[14] - Safety Analysis Set; n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: CRP Levels

End point title	CRP Levels
End point description: CRP an acute phase protein, is a marker of inflammation. CRP was measured as milligrams per deciliter (mg/dL).	

End point type	Secondary
End point timeframe:	
Baseline, Weeks 4, 8,12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76 and 108	

End point values	Tocilizumab 8 milligrams per kilogram (mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[15]			
Units: mg/dL				
arithmetic mean (standard deviation)				
Baseline (n=7)	0.03 (± 0.01)			
Week 4 (n=7)	0.05 (± 0.07)			
Week 8 (n=7)	0.02 (± 0.02)			
Week 12 (n=7)	0.03 (± 0.01)			
Week 16 (n=7)	0.23 (± 0.54)			
Week 20 (n=7)	0.05 (± 0.07)			
Week 24 (n=7)	0.03 (± 0.02)			
Week 28 (n=6)	0.02 (± 0.02)			
Week 32 (n=7)	0.03 (± 0.02)			
Week 36 (n=7)	0.02 (± 0.02)			
Week 40 (n=6)	0.03 (± 0.02)			
Week 44 (n=6)	0.03 (± 0.02)			
Week 48 (n=6)	0.03 (± 0.02)			
Week 52 (n=6)	0.02 (± 0.02)			
Week 56 (n=6)	0.03 (± 0.02)			
Week 60 (n=6)	0.38 (± 0.9)			
Week 64 (n=5)	0.03 (± 0.03)			
Week 68 (n=3)	0.09 (± 0.1)			
Week 72 (n=2)	0.04 (± 0.04)			
Week 76 (n=1)	0.05 (± 0)			
Week 108 (n=7)	0.05 (± 0.06)			

Notes:

[15] - Safety Analysis Set; n = number of participants analyzed at the specifies visit.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the date of screening until Week 108.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	Tocilizumab
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Reporting group description:

Participants received tocilizumab 8 mg/kg IV every 4 weeks up to 104 weeks or until tocilizumab was commercially available for pcJIA.

Serious adverse events	Tocilizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Tocilizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)		
Investigations			
Biopsy kidney			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Hepatic enzyme increased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
White blood cell count decreased			

subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Skin papilloma subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Excoriation subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all) Ligament sprain subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1		
Cardiac disorders Aortic valve incompetence subjects affected / exposed occurrences (all) Mitral valve incompetence subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1 1 / 7 (14.29%) 1		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
General disorders and administration site conditions Injection site swelling subjects affected / exposed occurrences (all) Local swelling	1 / 7 (14.29%) 1		

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Vaccination site reaction			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Epigastric discomfort			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Gastritis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	3		
Oropharyngeal pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Tonsillar disorder			

subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 7 (57.14%)		
occurrences (all)	6		
Foot deformity			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Joint effusion			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Juvenile idiopathic arthritis			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	4		
Pain in extremity			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Cystitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Gastroenteritis			

subjects affected / exposed	4 / 7 (57.14%)		
occurrences (all)	4		
Herpes simplex			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Lice infestation			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Otitis externa			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Scarlet fever			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	4		
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2011	Changes were made to the Screening and Exclusion criteria and definition of adverse events of special interest was modified. The amended text included that in case of pregnancy, the treatment must be permanently discontinued.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported