Clinical trial results:
A 12-week randomized, double-blind, placebo-controlled, parallel-group, 2-arm study to evaluate the efficacy and safety of tocilizumab in patients with active systemic juvenile idiopathic arthritis (sJIA); with a 92-week single arm open-label extension to examine the long term use of tocilizumab, followed by a 3 year open-label continuation of the study to examine the long term use of tocilizumab

Summary

EudraCT number	2007-000872-18
Trial protocol	BE SE DE NO CZ ES DK NL GR SK IT GB
Global end of trial date	05 August 2014

Results information

Result version number	v1 (current)
This version publication date	11 May 2016
First version publication date	11 May 2016

Trial information

Trial identification

Sponsor protocol code	WA18221

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00642460
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, CH-4070, Basel, Switzerland,
Public contact	F. Hoffmann-La Roche AG, Roche Trial Information Hotline, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, Roche Trial Information Hotline, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000309-PIP02-14
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 August 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part I: Primary Objectives:
1. To assess the efficacy of tocilizumab versus placebo in combination with stable ongoing therapy at 12 weeks, with regard to signs and symptoms in sJIA patients with persistent activity and an inadequate response to Non-Steroid Anti-Inflammatory Drugs (NSAIDs) and systemic corticosteroids.
Part II: Primary Objectives: 1. To evaluate the safety of tocilizumab in chronic administration and to assess the effect of tocilizumab to enable the reduction or elimination of corticosteroids. Part III: Primary Objective: To assess the long-term safety of 8 mg/kg tocilizumab in children greater than or equal to (≥) 30 kg and 12 mg/kg TCZ in children less than (<) 30 kg with regard to adverse events and laboratory result abnormalities.

Protection of trial subjects:

The study was conducted in accordance with the principals or laws of the country in which the study was conducted to ensure maximum protection to the individual. The study fully adhered to the provisions in "Principles of Good Clinical Practice" in the respective countries.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 May 2008
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	Argentina: 12
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Brazil: 6
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	United States: 18
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	United Kingdom: 8

Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Italy: 13
Worldwide total number of subjects	112
EEA total number of subjects	61

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)	70
Adolescents (12-17 years)	42
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study consists of 3 parts. Part I: a 12 week double-blind placebo controlled study followed by Part II: a 92 week single arm open-label extension study followed by Part III: a 3 year open label continuation study.

Period 1

Period 1 title	Part I: 12 Week Double-Blind
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind[1]
Roles blinded	Subject, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Tocilizumab_8 mg/kg

Arm description:

Tocilizumab 8 milligrams per kilogram (mg/kg) (for patients greater than or equal to [≥] 30 kg) intravenous (iv) every 2 weeks for 12 weeks in Part I
Participants remained on their prescribed standard of care treatment with NSAIDs, methotrexate and corticosteroids if applicable.

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:

Patients weighing≥30 kg received 8 mg/kg iv every 2 weeks for 12 weeks in Part I.

Arm title	Tocilizumab_12 mg/kg

Arm description:

Tocilizumab 12 mg/kg (for patients <30 kg) intravenous (iv) every 2 weeks for 12 weeks in Part I and every 2 weeks for 92 weeks in Part II.

Participants remained on their prescribed standard of care treatment with NSAIDs, methotrexate and corticosteroids if applicable

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:

Patients weighing less than (<) 30 kg received 12 mg/kg iv every 2 weeks for 12 weeks in Part I.

Arm title	Placebo

Arm description:

Placebo iv every 2 weeks for 12 weeks in Part 1. Participants remained on their prescribed standard of care treatment with NSAIDs, methotrexate and corticosteroids if applicable.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients received placebo infusion iv every 2 weeks for 12 weeks.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: Investigator was not blinded in this study.

Number of subjects in period 1	Tocilizumab_8 mg/kg	Tocilizumab_12 mg/kg	Placebo
Started	37	38	37
Completed	36	37	36
Not completed	1	1	1
Adverse event, non-fatal	-	1	1
Refused Treatment	1	-	-

Period 2

Period 2 title	Part II: Open-Label Up to Week 92
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Tocilizumab_8 mg/kg

Arm description:

Tocilizumab 8 mg/kg (for patients ≥30 kg) iv every 2 weeks for 92 weeks.
Participants remained on their prescribed standard of care treatment with (NSAIDs, methotrexate and corticosteroids if applicable.

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

Dosage and administration details:

Patients weighing≥30 kg received 8 mg/kg iv every 2 weeks for 12 weeks in Part I and every 2 weeks for 92 weeks in Part II.

Arm title	Tocilizumab_12 mg/kg

Arm description:

Tocilizumab 12 mg/kg (for patients <30 kg) iv every 2 weeks for 92 weeks.

Participants remained on their prescribed standard of care treatment with NSAIDs, methotrexate and corticosteroids if applicable.

Arm type	Experimental

Investigational medicinal product name	Tocilizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients weighing < 30 kg received 12 mg/kg iv every 2 weeks for 12 weeks in Part I and every 2 weeks for 92 weeks in Part II.

Arm title	Tocilizumab Switchers

Arm description:

Tocilizumab Switchers includes all participants who changed their dose either Tocilizumab 8 mg/kg or 12 mg/kg iv every 2 weeks in Part II.
Participants remained on their prescribed standard of care treatment with NSAIDs, methotrexate and corticosteroids if applicable.

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

Dosage and administration details:

Patients weighing ≥30 kg received 8 mg/kg and those weighing < 30 kg received 12 mg/kg iv every 2 weeks for 92 weeks.

Number of subjects in period 2	Tocilizumab_8 mg/kg	Tocilizumab_12 mg/kg	Tocilizumab Switchers
Started	52	40	20
Completed	43	32	17
Not completed	9	8	3
Adverse event, serious fatal	-	1	2
Insufficient therapeutic response	2	3	-
Adverse event, non-fatal	4	2	-
Refused Treatment	3	1	-
Administrative reasons	-	-	1
Lost to follow-up	-	1	-

Period 3

Period 3 title	Part III Open Label Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No

Arm title	Participants ≥30 kg

Arm description:

Tocilizumab 8 mg/kg iv every 2 weeks for 12 weeks in Part I, every 2 weeks for 92 weeks in Part II and every 2 weeks up to 260 weeks in Part III based on the body weight (BW) recorded at Baseline. The dose of TCZ could be adjusted for non-transient changes in BW (< 30 kg to ≥ 30 kg) over a minimum of 3 consecutive visits.

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

Dosage and administration details:

8 mg/kg (for patients ≥30 kg) iv every 2 weeks for 12 weeks in Part I, every 2 weeks for 92 weeks in Part II and every 2 weeks up to 260 weeks in Part III.

Arm title	Participants <30 kg

Arm description:

Tocilizumab 12 mg/kg iv every 2 weeks for 12 weeks in Part I, every 2 weeks for 92 weeks in Part II and every 2 weeks up to 260 weeks in Part III based on the BW recorded at Baseline. The dose of TCZ could be adjusted for non-transient changes in BW (30 kg to ≥ 30 kg) over a minimum of 3 consecutive visits.

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

Dosage and administration details:

12 mg/kg iv every 2 weeks for 12 weeks in Part I, every 2 weeks for 92 weeks in Part II and every 2 weeks up to 260 weeks in Part III.

Arm title	All Tocilizumab

Arm description:

Tocilizumab either 8 mg/kg (participants ≥ 30 kg) or 12 mg/kg (participants <30 kg) iv every 2 weeks for 12 weeks in Part I, every 2 weeks for 92 weeks in Part II and every 2 weeks for 156 weeks in Part III.
Participants remained on their prescribed standard of care treatment with NSAIDs, methotrexate and corticosteroids if applicable.

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

Dosage and administration details:

8 mg/kg (for patients ≥30 kg) or 12 mg/kg (participants <30 kg) iv every 2 weeks for 12 weeks in Part I and every 2 weeks for 92 weeks in Part II and every 2 weeks for 156 weeks in Part III.

Number of subjects in period 3	Participants ≥30 kg	Participants <30 kg	All Tocilizumab
Started	53	59	112
Completed on Q2W	28	38	66 [2]
Went into Alternative Dosing	23 [3]	22 [4]	39 [5]
Withdrawn from Alternative Dosing	6 [6]	2 [7]	7 [8]
Withdrawn from Q2W	19 [9]	19 [10]	39 [11]
Completed Alternative Dosing	12 [12]	20 [13]	32 [14]
Completed	28	38	73
Not completed	25	21	39
Adverse event, serious fatal	-	3	3
Insufficient therapeutic response	3	4	7
Consent withdrawn by subject	4	1	-
Adverse event, non-fatal	-	6	12
Refused Treatment	8	3	11
Administrative reasons	-	1	-
Adverse event	7	-	-
Unspecified	-	-	4
Lost to follow-up	1	1	2
Unknown reasons	2	2	-

Notes:

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.
[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.
[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.
[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.
[11] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.
[12] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.
[13] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.
[14] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants were allowed to participate in an alternative dosing schedule if a participant had an inactive disease status and was not receiving oral CS for the previous 12 consecutive weeks and met certain protocol-defined criteria. Not all participants entered the alternative dosing schedule.

Baseline characteristics

Reporting groups	
Reporting group title	Part I: 12 Week Double-Blind

Reporting group description:

Patients received either Tocilizumab 8 mg/kg (for patients ≥30 kg) or 12 mg/kg (for patients <30 kg) iv every 2 weeks for 12 weeks or placebo iv every 2 weeks for 12 weeks in Part I of the study. All patients remained on their prescribed standard of care treatment with non-steroidal anti-inflammatory drugs (NSAIDs), methotrexate and corticosteroids if applicable.

Reporting group values	Part I: 12 Week Double-Blind	Total	
Number of subjects	112	112	
Age categorical Units: Subjects			
2 to 5	27	27	
6 to 12	48	48	
13 to 17	37	37	
Gender categorical Units: Subjects			
Female	56	56	
Male	56	56	

End points

End points reporting groups

Reporting group title	Tocilizumab_8 mg/kg

Reporting group description:

Tocilizumab 8 milligrams per kilogram (mg/kg) (for patients greater than or equal to [≥] 30 kg) intravenous (iv) every 2 weeks for 12 weeks in Part I
Participants remained on their prescribed standard of care treatment with NSAIDs, methotrexate and corticosteroids if applicable.

Reporting group title	Tocilizumab_12 mg/kg

Reporting group description:

Tocilizumab 12 mg/kg (for patients <30 kg) intravenous (iv) every 2 weeks for 12 weeks in Part I and every 2 weeks for 92 weeks in Part II.

Participants remained on their prescribed standard of care treatment with NSAIDs, methotrexate and corticosteroids if applicable

Reporting group title	Placebo

Reporting group description:

Placebo iv every 2 weeks for 12 weeks in Part 1. Participants remained on their prescribed standard of care treatment with NSAIDs, methotrexate and corticosteroids if applicable.

Reporting group title	Tocilizumab_8 mg/kg

Reporting group description:

Tocilizumab 8 mg/kg (for patients ≥30 kg) iv every 2 weeks for 92 weeks.
Participants remained on their prescribed standard of care treatment with (NSAIDs, methotrexate and corticosteroids if applicable.

Reporting group title	Tocilizumab_12 mg/kg

Reporting group description:

Tocilizumab 12 mg/kg (for patients <30 kg) iv every 2 weeks for 92 weeks.

Participants remained on their prescribed standard of care treatment with NSAIDs, methotrexate and corticosteroids if applicable.

Reporting group title	Tocilizumab Switchers

Reporting group description:

Tocilizumab Switchers includes all participants who changed their dose either Tocilizumab 8 mg/kg or 12 mg/kg iv every 2 weeks in Part II.
Participants remained on their prescribed standard of care treatment with NSAIDs, methotrexate and corticosteroids if applicable.

Reporting group title	Participants ≥30 kg

Reporting group description:

Tocilizumab 8 mg/kg iv every 2 weeks for 12 weeks in Part I, every 2 weeks for 92 weeks in Part II and every 2 weeks up to 260 weeks in Part III based on the body weight (BW) recorded at Baseline. The dose of TCZ could be adjusted for non-transient changes in BW (< 30 kg to ≥ 30 kg) over a minimum of 3 consecutive visits.

Reporting group title	Participants <30 kg

Reporting group description:

Tocilizumab 12 mg/kg iv every 2 weeks for 12 weeks in Part I, every 2 weeks for 92 weeks in Part II and every 2 weeks up to 260 weeks in Part III based on the BW recorded at Baseline. The dose of TCZ could be adjusted for non-transient changes in BW (30 kg to ≥ 30 kg) over a minimum of 3 consecutive visits.

Reporting group title	All Tocilizumab

Reporting group description:

Tocilizumab either 8 mg/kg (participants ≥ 30 kg) or 12 mg/kg (participants <30 kg) iv every 2 weeks for 12 weeks in Part I, every 2 weeks for 92 weeks in Part II and every 2 weeks for 156 weeks in Part III.
Participants remained on their prescribed standard of care treatment with NSAIDs, methotrexate and corticosteroids if applicable.

Primary: Part I: Percentage of Participants With ≥30 percent (%) Improvement in Juvenile Idiopathic Arthritis (JIA) American College of Rheumatology (ACR) Core Set and Absence of Fever

End point title	Part I: Percentage of Participants With ≥30 percent (%) Improvement in Juvenile Idiopathic Arthritis (JIA) American College of Rheumatology (ACR) Core Set and Absence of Fever[1][2]

End point description:

Percentage of participants with ≥30% improvement in ACR core set consisting of 6 components: 1) Physician's global assessment of disease activity Visual Analog Scale (VAS), 2) Parent/Patient global assessment of overall well-being VAS, 3) Maximum number of joints with active arthritis, 4) Number of joints with limitation of movement, 5) Erythrocyte Sedimentation Rate, and 6) Childhood Health Assessment Questionnaire-Disability Index (CHAQ-DI) consisting of 30 questions in 8 domains. Absence of fever was defined as no diary temperature recording ≥37.5 degrees Celsius in the preceding seven days.
Analysis was performed on Intent-to-treat population which included all participants who had at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline, Week 12

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: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: percentage of participants				
number (not applicable)	24.3	85.3		

Statistical analyses

No statistical analyses for this end point

Primary: Part II: Percentage of Participants With Decreases in Oral Corticosteroid Dose at Week 104

End point title	Part II: Percentage of Participants With Decreases in Oral Corticosteroid Dose at Week 104[3]

End point description:

Percentage of participants with ≥20 percent, ≥50 percent, ≥75 percent and ≥90 percent decreases in oral corticosteroid dose (mg/kg/day) from baseline. Analysis included only participants on oral corticosteroids at baseline.

End point type	Primary

End point timeframe:

Baseline, Week 104

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: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	All Tocilizumab			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (not applicable)				
≥20 percent decrease	76			
≥50 percent decrease	73			
≥75 percent decrease	62			
≥90 percent decrease	47			

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage of Participants With JIA Core Set ACR 30/50/70/90 Response at Week 12

End point title	Part I: Percentage of Participants With JIA Core Set ACR 30/50/70/90 Response at Week 12[4]

End point description:

The six JIA ACR components consist of: 1)Physician's global assessment of disease activity, 2)Parent/Patient 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, and 6) CHAQ-DI.
At an assessment visit a JIA ACR30/50/70/90 response in comparison to Baseline is defined as: At least three of the six JIA ACR core components improving by at least 30%/50%/70%/90% and no more than one of the remaining JIA ACR core components worsening by more than 30%. Analysis was performed on Intent-to-treat population which included all participants who had at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: percentage of participants				
number (not applicable)				
JIA ACR30 response	24.3	90.7		
JIA ACR50 response	10.8	85.3		
JIA ACR70 response	8.1	70.7		
JIA ACR90 response	5.4	37.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage Change From Baseline in JIA Core Set ACR Score Component: Physician's Global Assessment of Disease Activity

End point title	Part I: Percentage Change From Baseline in JIA Core Set ACR Score Component: Physician's Global Assessment of Disease Activity[5]

End point description:

Physician's Global Assessment of disease activity is a Visual Analog Scale. The scale is 0 to 100 mm horizontal scale, the extreme left end of the line represents 'arthritis inactive' (i.e. symptom-free and no arthritis symptoms) and the extreme right end represents 'arthritis very active'. This item is completed by the treating physician. Patients who withdrew, received escape medication, or for whom the endpoint cannot be determined were excluded. LOCF rule applied to missing JIA ACR core set components at Week 12.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	73		
Units: percentage change				
number (not applicable)	-41.1	-69.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage Change From Baseline in JIA Core Set ACR Score Component: Parent/Patient Global Assessment of Overall Well-being

End point title	Part I: Percentage Change From Baseline in JIA Core Set ACR Score Component: Parent/Patient Global Assessment of Overall Well-being[6]

End point description:

The Parent/Patient global assessment of overall well-being is a VAS. The scale is a 0 to 100 mm horizontal scale, the extreme left end of the line represents 'very well' (i.e. symptom-free and no arthritis disease activity) and the extreme right end represents 'very poor' (i.e. maximum arthritis disease activity). This item is completed by the patient or parent/guardian as appropriate.Patients who withdrew, received escape medication, or for whom the endpoint cannot be determined are excluded. LOCF rule applied to missing JIA ACR core set components at Week 12. Analysis was performed on

Intent-to-treat population which included all participants who had at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	73		
Units: percentage change				
number (not applicable)	-1.4	-65.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage Change From Baseline in JIA Core Set ACR Score Component: Maximum Number of Joints With Active Arthritis

End point title	Part I: Percentage Change From Baseline in JIA Core Set ACR Score Component: Maximum Number of Joints With Active Arthritis[7]

End point description:

The maximum number of joints with active arthritis is 71 and these are defined as those in the joint assessment with: swelling present or pain present and limitation of motion. The joint assessment is performed by an independent assessor, who is not the treating physician, blinded to all other aspects of the patient's efficacy and safety data.Patients who withdrew, received escape medication, or for whom the endpoint cannot be determined are excluded. LOCF rule applied to missing JIA ACR core set components at Week 12. Analysis was performed on Intent-to-treat population which included all participants who had at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	73		
Units: percentage change				
number (not applicable)	-37.2	-70.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage Change From Baseline in JIA Core Set ACR Score Component: Number of Joints With Limitation of Movement

End point title	Part I: Percentage Change From Baseline in JIA Core Set ACR Score Component: Number of Joints With Limitation of Movement[8]

End point description:

The maximum number of joints with limitation of movement is 67 and these are defined as those in the joint assessment with 'limitation of motion'. Analysis was performed on Intent-to-treat population which included all participants who had at least one dose of study drug. Patients who withdrew, received escape medication, or for whom the endpoint could not be determined were excluded. LOCF rule applied to missing JIA ACR core set components at Week 12.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	72		
Units: percentage change				
number (not applicable)	-22.5	-51.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage Change From Baseline in JIA Core Set ACR Score Component: Erythrocyte Sedimentation Rate

End point title	Part I: Percentage Change From Baseline in JIA Core Set ACR Score Component: Erythrocyte Sedimentation Rate[9]

End point description:

Erythrocyte Sedimentation Rate (ESR) is an acute phase reactant measured in mm/hour. Analysis was performed on Intent-to-treat population which included all participants who had at least one dose of study drug. Patients who withdrew, received escape medication, or for whom the endpoint could not be determined were excluded. LOCF rule applied to missing JIA ACR core set components at Week 12.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	73		
Units: percentage change				
number (not applicable)	33.6	-88.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage Change From Baseline in JIA Core Set ACR Score Component: Childhood Health Assessment Questionnaire Disability Index (CHAQ-DI)

End point title	Part I: Percentage Change From Baseline in JIA Core Set ACR Score Component: Childhood Health Assessment Questionnaire Disability Index (CHAQ-DI)[10]

End point description:

Functional ability is assessed using the CHAQ-DI. The questionnaire consists of 30 questions referring to eight domains; dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities. Each domain has at least two component questions and if applicable to the patient there are 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). Analysis was performed on Intent-to-treat population which included all participants who had at least one dose of study drug. Patients who withdrew, received escape medication, or for whom the endpoint could not be determined were excluded. LOCF rule applied to missing JIA ACR core set components at Week 12.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	72		
Units: percentage change				
number (not applicable)	-10.3	-45.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage of Participants With Fever Due to Systemic Juvenile Idiopathic Arthritis (sJIA) at Baseline Who Are Free of Fever at Week 12

End point title	Part I: Percentage of Participants With Fever Due to Systemic

	Juvenile Idiopathic Arthritis (sJIA) at Baseline Who Are Free of Fever at Week 12[11]

End point description:

Fever free was defined as no diary temperature recording ≥37.5° Celsius in the preceding fourteen days. Participants from the Intent-to-treat population (all randomized participants who received at least one dose of study drug) who had a fever due to Systemic Juvenile Idiopathic Arthritis at baseline were included in analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	41		
Units: percentage of participants				
number (not applicable)	20.8	85.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage of Participants With Changes in Laboratory Indicators: High-sensitivity C-Reactive Protein (hsCRP), Hemoglobin (Hb), Platelets and Leukocytes From Abnormal at Baseline to Normal at Week 12

End point title	Part I: Percentage of Participants With Changes in Laboratory Indicators: High-sensitivity C-Reactive Protein (hsCRP), Hemoglobin (Hb), Platelets and Leukocytes From Abnormal at Baseline to Normal at Week 12[12]

End point description:

Percentage of participants with a change from an elevated hsCRP value at baseline to a normal hsCRP value at week 12; a change from anemia (low Hemoglobin) at baseline to a normal hemoglobin value at week 12; a change from thrombocytosis (elevated platelets) at baseline to a normal platelet value at week 12; a change from leukocytosis (elevated white blood cell count) at baseline to a normal white blood cell count at week 12.Analysis was performed on Intent-to-treat population which included all participants who had at least one dose of study drug. 'n' in each of the categories is the number of participants with data available at baseline and week 12 for analyses.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: percentage of participants				
number (not applicable)				
hsC-Reactive Protein (n=34,72)	5.9	98.6		
Hemoglobin (n=29,50)	6.9	80		
Platelets (n=26,52)	3.8	90.4		
Leukocytes (n=21,28)	9.5	75		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage of Participants With Concomitant Corticosteroid Reduction

End point title	Part I: Percentage of Participants With Concomitant Corticosteroid Reduction[13]

End point description:

The percentage of participants receiving oral corticosteroids(CS) with a JIA ACR70 response at week 6 or Week 8 who reduced their oral CS dose by at least 20% without subsequent JIA ACR30 flare or occurrence of systemic symptoms at week 12.
At an assessment visit a JIA ACR70 response is defined as: At least three of the six JIA ACR core components improving by at least 70% and no more than one of the remaining JIA ACR core components worsening by more than 30%. Analysis was performed on participants from the Intent-to-treat population (all randomized participants who received at least one dose of study drug) who were taking oral corticosteroids.

End point type	Secondary

End point timeframe:

Week 6 or Week 8, Week 12

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	70		
Units: percentage of participants				
number (not applicable)	3.2	24.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Change From Baseline in the Pain Visual Analog Scale (VAS) at Week 12

End point title	Part I: Change From Baseline in the Pain Visual Analog Scale

	(VAS) at Week 12[14]

End point description:

Participants rated their pain by placing a horizontal line on a Visual Analog Scale on a scale of 0 (no pain)- 100 mm (severe pain). The score at 12 weeks minus the score at baseline. A negative number indicates improvement.
Participants from the Intent-to-treat population who had Pain VAS data available at baseline and week 12. Patients who withdrew, received escape medication, or for whom the endpoint cannot be determined are excluded. LOCF rule applied to missing pain VAS at Week 12.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	73		
Units: mm				
number (not applicable)	-1.1	-41		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage of Patients With Minimally Important Improvement in CHAQ-DI Score at Week 12

End point title	Part I: Percentage of Patients With Minimally Important Improvement in CHAQ-DI Score at Week 12[15]

End point description:

Percentage of patients who had at least a 0.13 improvement in CHAQ-DI score from Baseline to Week 12.
The CHAQ-DI questionnaire consists of 30 questions referring to eight domains; dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities. Each domain has at least two component questions and if applicable to the patient there are four possible responses (0 = without any difficulty, 1 = with some difficulty, 2 = with much difficulty, 3 = unable to do).ntent-to-treat Population. Patients who withdrew, received escape medication, or for whom the endpoint cannot be determined are classified as non-responders.
LOCF rule applied to missing CHAQ-DI Scores at Week 12.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: percentage of participants				
number (not applicable)	18.9	77.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage of Patients With Rash at Baseline Who Are Free From Rash at Week 12

End point title	Part I: Percentage of Patients With Rash at Baseline Who Are Free From Rash at Week 12[16]

End point description:

Percentage of participants who had a rash characteristic of sJIA in the 14 days prior to the baseline visit but no rash characteristic of sJIA in the 14 days preceding the Week 12 visit day. Analysis was performed on participants from the Intent-to-treat population for whom data was available. Patients who withdrew, received escape medication, or for whom the endpoint cannot be determined are classified as non-responders.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	22		
Units: percentage of participants				
number (not applicable)	11.1	63.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Part I: Percentage of Patients With Anemia at Baseline With a ≥10 g/L Increase in Hemoglobin at Week 6 and Week 12

End point title	Part I: Percentage of Patients With Anemia at Baseline With a ≥10 g/L Increase in Hemoglobin at Week 6 and Week 12[17]

End point description:

Part I: Percentage of patients who had anemia (hemoglobin <lower level normal based on sex and age) at Baseline and a ≥10 g/L increase in hemoglobin at Week 6 and at Week 12. Analysis was performed on participants from the Intent-to-treat population for whom hemoglobin data available. Patients who withdrew, received escape medication, or for whom the endpoint cannot be determined are classified as non-responders. LOCF rule applied to missing hemoglobin values at Week 6 and Week 12.

End point type	Secondary

End point timeframe:

Baseline, Week 6 and Week 12

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol the statistical comparison was made between placebo and all participants who received tocilizumab treatment irrespective of the dosage.

End point values	Placebo	All Tocilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	50		
Units: percentage of participants				
number (not applicable)				
Week 6	3.4	88		
Week 12	3.4	88		

Statistical analyses

No statistical analyses for this end point

Secondary: Part II: Percentage of Participants With JIA ACR70 and JIA ACR90 Responses Week 104

End point title	Part II: Percentage of Participants With JIA ACR70 and JIA ACR90 Responses Week 104

End point description:

The six JIA ACR components consist of: 1)Physician's global assessment of disease activity, 2)Parent/Patient 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, and 6) CHAQ-DI.
At an assessment visit a JIA ACR70/90 response in comparison to Baseline is defined as: At least three of the six JIA ACR core components improving by at least 70%/90% and no more than one of the remaining JIA ACR core components worsening by more than 30%. Analysis was performed on participants from the Intent to Treat population who reached the time point plus patients who withdrew because of insufficient therapeutic response and are assumed to have been non-responders.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	All Tocilizumab			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: percentage of participants				
number (not applicable)				
JIA ACR70 response	76			
JIA ACR90 response	61.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Part II: Number of Active Joints at Week 104

End point title	Part II: Number of Active Joints at Week 104

End point description:

Seventy-one joints were assessed for signs of active arthritis. The mean number of joints with signs of active arthritis is reported. Analysis was performed on participants from the Intent to Treat population who reached this time point. No data imputation is applied and patients with missing data are excluded.

End point type	Secondary

End point timeframe:

Week 104

End point values	All Tocilizumab			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: active joints				
arithmetic mean (standard deviation)	1.9 (± 3.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part II: Percentage of Participants With no Active Joints at Week 104

End point title	Part II: Percentage of Participants With no Active Joints at Week 104

End point description:

Seventy-one joints were assessed for signs of active arthritis. The percentage of participants with no signs of active arthritis is reported. The Intent to Treat population in Part II includes 112 participants who received at least one dose of study drug. Only those participants who reached this time point are included in the analyses.

End point type	Secondary

End point timeframe:

Week 104

End point values	All Tocilizumab			
Subject group type	Reporting group			
Number of subjects analysed	76			
Units: percentage of participants				
number (not applicable)	47.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Part II: Percentage of Participants With Inactive Disease at Week 104

End point title	Part II: Percentage of Participants With Inactive Disease at Week 104

End point description:

Criteria for Inactive Disease: 1) No joints with active arthritis, 2) No fever, rash, serositis, splenomegaly, hepatomegaly (by physical exam) or generalized lymphadenopathy attributable to systemic juvenile idiopathic arthritis (sJIA), 3) Normal Erythrocyte Sedimentation Rate (<20 mm/hour), 4) Physician's global assessment of disease activity Visual Analog Scale (VAS) indicates no disease activity (where no disease activity is considered to be a score ≤10 mm on a 100 mm VAS). Participants from the Intent to Treat population who reached time point plus patients who withdrew because of insufficient therapeutic response and are assumed to have been nonresponders.

End point type	Secondary

End point timeframe:

Week 104

End point values	All Tocilizumab			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: percentage of participants				
number (not applicable)	26.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Part II: Childhood Health Assessment Questionnaire-Disability Index (CHAQ-DI) Score at Week 104

End point title	Part II: Childhood Health Assessment Questionnaire-Disability Index (CHAQ-DI) Score at Week 104

End point description:

Functional ability is assessed using the CHAQ-DI. The questionnaire consists of 30 questions referring to eight domains; dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities. Each domain has at least two component questions and if applicable to the patient there are 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). Participants from the Intent to Treat population who withdrew have been excluded at post withdrawal visits. n = number of participants

analyzed at the specified visit.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	All Tocilizumab			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=112)	1.68 (± 0.86)			
Week 104 (n=57)	0.55 (± 0.71)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part II: Percentage of Participants With Oral Corticosteroid Cessation at Week 104

End point title	Part II: Percentage of Participants With Oral Corticosteroid Cessation at Week 104

End point description:

Percentage is based on only those participants who were on oral corticosteroid at baseline and reached a nominal visit day on which dose was calculated. Participants from the Intent to Treat population who withdrew have been excluded at post withdrawal visits.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	All Tocilizumab			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: percentage of participants				
number (not applicable)	60			

Statistical analyses

No statistical analyses for this end point

Secondary: Part II: Rate of Serious Adverse Events (SAEs), Serious Infection Adverse Events (AEs), Related SAEs, Macrophage Activation Syndrome, AEs Leading to Withdrawal and Deaths Per 100 Patient Years to Week 104

End point title	Part II: Rate of Serious Adverse Events (SAEs), Serious Infection Adverse Events (AEs), Related SAEs, Macrophage Activation Syndrome, AEs Leading to Withdrawal and Deaths Per 100 Patient Years to Week 104

End point description:

Rate of SAEs, Rate of Serious Infection AEs, Rate of Related SAEs (remotely, possibly, probably) to Tocilizumab (TCZ), Rate of Macrophage Activation Syndrome, Rate of AEs leading to withdrawal and Rate of deaths per 100 patient years (PY) were calculated using the formula: Number of Patient Events / Duration in study (years) * 100.
Multiple occurrences of the same AE in one individual are counted. Safety Population- all participants who received at least one dose of study drug and had 1 post-baseline safety assessment. Includes all safety data in the database up to the week 104 infusion based on the date of randomization for each patient. (Last date was 31 May 2011)

End point type	Secondary

End point timeframe:

104 Weeks

End point values	All Tocilizumab			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: events per 100 patient years				
number (not applicable)				
SAEs	23.3			
Serious infection AEs	10.9			
SAEs related to TCZ	7.4			
Macrophage activation syndrome	1.5			
AEs leading to withdrawal	3			
Deaths	1.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Part III: Percentage of Participants with at least 30%, 50%, 70%, and 90% improvement in JIA core set according to ACR

End point title	Part III: Percentage of Participants with at least 30%, 50%, 70%, and 90% improvement in JIA core set according to ACR

End point description:

The six JIA ACR components consist of: 1)Physician's global assessment of disease activity, 2)Parent/Patient 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, and 6) CHAQ-DI.
At an assessment visit a JIA ACR30/50/70/90 response in comparison to Baseline is defined as: At least three of the six JIA ACR core components improving by at least 30%/50%/70%/90% and no more than one of the remaining JIA ACR core components worsening by more than 30%. n = number of participants analyzed for the given parameter at the specified visit. The Part III intent-to-treat (ITT3) population consists of all participants who entered into Part III of the study and received at least one administration of tocilizumab during Part III.

End point type	Secondary

End point timeframe:

Weeks 104, 116, 128, 140, 152, 164, 176, 188, 200, 212, 224, 236, 248 and 260

End point values	Participants ≥30 kg	Participants <30 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	47		
Units: percentage of participants				
number (not applicable)				
Week 104 JIA ACR30 (n=42,47)	100	100		
Week 104 JIA ACR50 (n=42,47)	100	100		
Week 104 JIA ACR70 (n=42,47)	92.9	95.7		
Week 104 JIA ACR90 (n=42,47)	81	72.3		
Week 116 JIA ACR30 (n=41,45)	100	100		
Week 116 JIA ACR50 (n=41,45)	100	97.8		
Week 116 JIA ACR70 (n=41,45)	95.1	97.8		
Week 116 JIA ACR90 (n=41,45)	82.9	80		
Week 128 JIA ACR30 (n=39,41)	100	100		
Week 128 JIA ACR50 (n=39,41)	100	100		
Week 128 JIA ACR70 (n=39,41)	97.4	97.6		
Week 128 JIA ACR90 (n=39,41)	79.5	82.9		
Week 140 JIA ACR30 (n=34,37)	100	100		
Week 140 JIA ACR50 (n=34,37)	100	100		
Week 140 JIA ACR70 (n=34,37)	100	94.6		
Week 140 JIA ACR90 (n=34,37)	73.5	75.7		
Week 152 JIA ACR30 (n=27,28)	100	100		
Week 152 JIA ACR50 (n=27,28)	100	100		
Week 152 JIA ACR70 (n=27,28)	100	96.4		
Week 152 JIA ACR90 (n=27,28)	66.7	78.6		
Week 164 JIA ACR30 (n=27,24)	100	100		
Week 164 JIA ACR50 (n=27,24)	100	100		
Week 164 JIA ACR70 (n=27,24)	92.6	95.8		
Week 164 JIA ACR90 (n=27,24)	66.7	75		
Week 176 JIA ACR30 (n=22,22)	100	100		
Week 176 JIA ACR50 (n=22,22)	100	100		
Week 176 JIA ACR70 (n=22,22)	100	95.5		
Week 176 JIA ACR90 (n=22,22)	63.6	63.6		
Week 188 JIA ACR30 (n=20,22)	100	100		
Week 188 JIA ACR50 (n=20,22)	100	100		
Week 188 JIA ACR70 (n=20,22)	95	95.5		
Week 188 JIA ACR90 (n=20,22)	45	72.7		
Week 200 JIA ACR30 (n=19,19)	100	100		
Week 200 JIA ACR50 (n=19,19)	100	94.7		
Week 200 JIA ACR70 (n=19,19)	94.7	89.5		
Week 200 JIA ACR90 (n=19,19)	63.2	78.9		
Week 212 JIA ACR30 (n=18,18)	100	100		
Week 212 JIA ACR50 (n=18,18)	100	94.4		
Week 212 JIA ACR70 (n=18,18)	100	94.4		
Week 212 JIA ACR90 (n=18,18)	72.2	77.8		
Week 224 JIA ACR30 (n=17,18)	100	100		
Week 224 JIA ACR50 (n=17,18)	100	88.9		

Week 224 JIA ACR70 (n=17,18)	100	88.9		
Week 224 JIA ACR90 (n=17,18)	64.7	83.3		
Week 236 JIA ACR30 (n=16,17)	100	100		
Week 236 JIA ACR50 (n=16,17)	100	100		
Week 236 JIA ACR70 (n=16,17)	93.8	100		
Week 236 JIA ACR90 (n=16,17)	68.8	88.2		
Week 248 JIA ACR30 (n=15,17)	100	100		
Week 248 JIA ACR50 (n=15,17)	100	100		
Week 248 JIA ACR70 (n=15,17)	86.7	94.1		
Week 248 JIA ACR90 (n=15,17)	73.3	70.6		
Week 260 JIA ACR30 (n=15,15)	100	93.3		
Week 260 JIA ACR50 (n=15,15)	93.3	93.3		
Week 260 JIA ACR70 (n=15,15)	86.7	93.3		
Week 260 JIA ACR90 (n=15,15)	60	66.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Part III: Percentage of participants who mainitain JIA ACR30, JIA ACR50, JIA ACR70, JIA ACR90 response for 6 months Previous to the specified Week

End point title	Part III: Percentage of participants who mainitain JIA ACR30, JIA ACR50, JIA ACR70, JIA ACR90 response for 6 months Previous to the specified Week

End point description:

The six JIA ACR components consist of: 1)Physician's global assessment of disease activity, 2)Parent/Patient 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, and 6) CHAQ-DI.
At an assessment visit a JIA ACR30/50/70/90 response in comparison to Baseline is defined as: At least three of the six JIA ACR core components improving by at least 30%/50%/70%/90% and no more than one of the remaining JIA ACR core components worsening by more than 30%. n = number of participants analyzed for the given parameter at the specified visit. Analysis was performed on The Part III ITT3 population. 99999 = Data not available.

End point type	Secondary

End point timeframe:

Weeks 104, 116, 128, 140, 152, 164, 176, 188, 200, 212, 224, 236, 248 and 260

End point values	All Tocilizumab			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: percentage of participants				
number (not applicable)				
Week 104 JIA ACR30 (n=89)	99999			
Week 104 JIA ACR50 (n=89)	99999			
Week 104 JIA ACR70 (n=89)	99999			
Week 104 JIA ACR90 (n=89)	99999			
Week 116 JIA ACR 30 (n=86)	99999			
Week 116 JIA ACR 50 (n=86)	99999			

Week 116 JIA ACR 70 (n=86)	99999			
Week 116 JIA ACR 90 (n=86)	99999			
Week 128 JIA ACR 30 (n=80)	100			
Week 128 JIA ACR 50 (n=80)	98.8			
Week 128 JIA ACR 70 (n=80)	91.3			
Week 128 JIA ACR 90 (n=80)	68.8			
Week 140 JIA ACR30 (n=71)	100			
Week 140 JIA ACR50 (n=71)	98.6			
Week 140 JIA ACR70 (n=71)	93			
Week 140 JIA ACR90 (n=71)	66.2			
Week 152 JIA ACR30 (n=55)	100			
Week 152 JIA ACR50 (n=55)	100			
Week 152 JIA ACR70 (n=55)	94.5			
Week 152 JIA ACR90 (n=55)	60			
Week 164 JIA ACR30 (n=51)	100			
Week 164 JIA ACR50 (n=51)	100			
Week 164 JIA ACR70 (n=51)	92.2			
Week 164 JIA ACR90 (n=51)	56.9			
Week 176 JIA ACR30 (n=44)	100			
Week 176 JIA ACR50 (n=44)	100			
Week 176 JIA ACR70 (n=44)	88.6			
Week 176 JIA ACR90 (n=44)	52.3			
Week 188 JIA ACR30 (n=42)	100			
Week 188 JIA ACR50 (n=42)	100			
Week 188 JIA ACR70 (n=42)	88.1			
Week 188 JIA ACR90 (n=42)	50			
Week 200 JIA ACR30 (n=38)	100			
Week 200 JIA ACR50 (n=38)	97.4			
Week 200 JIA ACR70 (n=38)	86.8			
Week 200 JIA ACR90 (n=38)	52.6			
Week 212 JIA ACR30 (n=36)	100			
Week 212 JIA ACR50 (n=36)	97.2			
Week 212 JIA ACR70 (n=36)	88.9			
Week 212 JIA ACR90 (n=36)	55.6			
Week 224 JIA ACR30 (n=35)	100			
Week 224 JIA ACR50 (n=35)	94.3			
Week 224 JIA ACR70 (n=35)	91.4			
Week 224 JIA ACR90 (n=35)	68.6			
Week 236 JIA ACR30 (n=33)	100			
Week 236 JIA ACR50 (n=33)	93.9			
Week 236 JIA ACR70 (n=33)	90.9			
Week 236 JIA ACR90 (n=33)	72.7			
Week 248 JIA ACR30 (n=32)	100			
Week 248 JIA ACR50 (n=32)	93.8			
Week 248 JIA ACR70 (n=32)	87.5			
Week 248 JIA ACR90 (n=32)	65.6			
Week 260 JIA ACR30 (n=30)	96.7			
Week 260 JIA ACR50 (n=30)	93.3			
Week 260 JIA ACR70 (n=30)	80			
Week 260 JIA ACR90 (n=30)	56.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Part III: Doses of Oral Corticosteroids (CS)

End point title	Part III: Doses of Oral Corticosteroids (CS)

End point description:

Oral corticosteroid values summarized are based on average daily dose on the nominal study day. The prednisone equivalent is used in calculation of oral corticosteroid dose. Participants who withdrew are excluded at the visit of withdrawal and all subsequent visits. n=number of participants contributing to the specific statistic.

End point type	Secondary

End point timeframe:

Baseline and Weeks 104, 116, 128, 140, 152, 164, 176, 188, 200, 212, 224, 236, 248 and 260

End point values	Participants ≥30 kg	Participants <30 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	59		
Units: mg/kg/day				
arithmetic mean (standard deviation)				
Baseline (n=53,59)	0.203 (± 0.1572)	0.356 (± 0.1397)		
Week 104 (n=45,48)	0.02 (± 0.0455)	0.047 (± 0.0869)		
Week 116 (n=42,46)	0.022 (± 0.0464)	0.046 (± 0.0831)		
Week 128 (n=41,42)	0.022 (± 0.0449)	0.058 (± 0.1635)		
Week 140 (n=34,38)	0.031 (± 0.0625)	0.051 (± 0.1112)		
Week 152 (n=28,31)	0.021 (± 0.0388)	0.06 (± 0.1125)		
Week 164 (n=28,25)	0.018 (± 0.0349)	0.068 (± 0.1179)		
Week 176 (n=25,23)	0.019 (± 0.0383)	0.073 (± 0.1327)		
Week 188 (n=21,22)	0.02 (± 0.0366)	0.075 (± 0.1275)		
Week 200 (n=20,20)	0.017 (± 0.0284)	0.083 (± 0.1397)		
Week 212 (n=19,19)	0.016 (± 0.0274)	0.077 (± 0.1449)		
Week 224 (n=18,19)	0.017 (± 0.0279)	0.075 (± 0.1399)		
Week 236 (n=17,18)	0.018 (± 0.0283)	0.077 (± 0.1436)		

Week 248 (n=16,18)	0.02 (± 0.029)	0.076 (± 0.1429)		
Week 260 (n=16,18)	0.019 (± 0.0282)	0.079 (± 0.1486)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part III: Percentage of Participants on Corticosteroids at Baseline Able to Discontinue Corticosteroids by Weeks 104,116, 128, 140, 152, 164, 176, 188, 200, 212, 224, 236, 248, and 260

End point title	Part III: Percentage of Participants on Corticosteroids at Baseline Able to Discontinue Corticosteroids by Weeks 104,116, 128, 140, 152, 164, 176, 188, 200, 212, 224, 236, 248, and 260

End point description:

Values summarized are based on average daily dose on the nominal study day. The prednisone equivalent is used in calculation of oral corticosteroid dose. Participants who withdrew are excluded at the timepoint of this event and at all subsequent visits.
Baseline considered first dose of study treatment. Data presented up to entry into the Alternative Dosing Schedule.
ITT3 population; n=number of participants contributing to the specific statistic.

End point type	Secondary

End point timeframe:

Weeks 104,116, 128, 140, 152, 164, 176, 188, 200, 212, 224, 236, 248, and 260

End point values	Participants ≥30 kg	Participants <30 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	46		
Units: percentage of participants				
number (not applicable)				
Week 104 (n=38,46)	66	67		
Week 116 (n=36,44)	67	68		
Week 128 (n=35,40)	69	70		
Week 140 (n=31,36)	68	67		
Week 152 (n=25,30)	64	57		
Week 164 (n=25,24)	68	58		
Week 176 (n=22,22)	68	64		
Week 188 (n=18,21)	61	57		
Week 200 (n=17,20)	59	60		
Week 212 (n=16,19)	56	63		
Week 224 (n=15,19)	53	63		
Week 236 (n=14,18)	50	61		
Week 248 (n=13,18)	46	61		
Week 260 (n=13,18)	46	61		

Statistical analyses

No statistical analyses for this end point

Secondary: Part III: Percentage of Participants with a ≥20/50/75/90% Decrease from Baseline in Oral Corticosteroid Dose at Visits

End point title	Part III: Percentage of Participants with a ≥20/50/75/90% Decrease from Baseline in Oral Corticosteroid Dose at Visits

End point description:

Values summarized are based on average daily dose on the nominal study day. The prednisone equivalent is used in calculation of oral corticosteroid dose. Participants who withdrew are excluded at the timepoint of this event and at all subsequent visits.
Baseline considered first dose of study treatment.
ITT3 population; n=number of participants contributing to the specific statistic.

End point type	Secondary

End point timeframe:

Every 2 weeks from Week 104 to 260

End point values	Participants ≥30 kg	Participants <30 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	46		
Units: percentage of participants				
number (not applicable)				
Week 104 ≥20% decrease (n=38,46)	100	97.8		
Week 104 ≥50% decrease (n=38,46)	94.7	91.3		
Week 104 ≥75% decrease (n=38,46)	84.2	82.6		
Week 104 ≥90% decrease (n=38,46)	71.1	71.7		
Week 106 ≥20% decrease (n=37,46)	100	97.8		
Week 106 ≥50% decrease (n=37,46)	91.9	91.3		
Week 106 ≥75% decrease (n=37,46)	83.8	82.6		
Week 106 ≥90% decrease (n=37,46)	70.3	71.7		
Week 108 ≥20% decrease (n=37,45)	100	100		
Week 108 ≥50% decrease (n=37,45)	89.2	91.1		
Week 108 ≥75% decrease (n=37,45)	81.1	84.4		
Week 108 ≥90% decrease (n=37,45)	70.3	73.3		
Week 110 ≥20% decrease (n=36,44)	100	100		
Week 110 ≥50% decrease (n=36,44)	88.9	93.2		
Week 110 ≥75% decrease (n=36,44)	80.6	84.1		
Week 110 ≥90% decrease (n=36,44)	72.2	75		
Week 112 ≥20% decrease (n=36,44)	100	100		
Week 112 ≥50% decrease (n=36,44)	88.9	95.5		
Week 112 ≥75% decrease (n=36,44)	80.6	81.8		
Week 112 ≥90% decrease (n=36,44)	72.2	75		

Week 114 ≥20% decrease (n=36,44)	100	100		
Week 114 ≥50% decrease (n=36,44)	88.9	95.5		
Week 114 ≥75% decrease (n=36,44)	80.6	79.5		
Week 114 ≥90% decrease (n=36,44)	72.2	72.7		
Week 116 ≥20% decrease (n=35,44)	100	100		
Week 116 ≥50% decrease (n=35,44)	91.4	93.2		
Week 116 ≥75% decrease (n=35,44)	80	79.5		
Week 116 ≥90% decrease (n=35,44)	71.4	72.7		
Week 118 ≥20% decrease (n=35,43)	100	100		
Week 118 ≥50% decrease (n=35,43)	88.6	93		
Week 118 ≥75% decrease (n=35,43)	80	81.4		
Week 118 ≥90% decrease (n=35,43)	71.4	74.4		
Week 120 ≥20% decrease (n=35,43)	100	100		
Week 120 ≥50% decrease (n=35,43)	88.6	93		
Week 120 ≥75% decrease (n=35,43)	80	83.7		
Week 120 ≥90% decrease (n=35,43)	74.3	76.7		
Week 122 ≥20% decrease (n=35,43)	97.1	100		
Week 122 ≥50% decrease (n=35,43)	88.6	93		
Week 122 ≥75% decrease (n=35,43)	77.1	81.4		
Week 122 ≥90% decrease (n=35,43)	74.3	74.4		
Week 124 ≥20% decrease (n=35,43)	100	100		
Week 124 ≥50% decrease (n=35,43)	94.3	93		
Week 124 ≥75% decrease (n=35,43)	80	83.7		
Week 124 ≥90% decrease (n=35,43)	77.1	74.4		
Week 126 ≥20% decrease (n=35,43)	100	100		
Week 126 ≥50% decrease (n=35,43)	94.3	90.7		
Week 126 ≥75% decrease (n=35,43)	80	81.4		
Week 126 ≥90% decrease (n=35,43)	77.1	74.4		
Week 128 ≥20% decrease (n=35,39)	100	97.4		
Week 128 ≥50% decrease (n=35,39)	91.4	89.7		
Week 128 ≥75% decrease (n=35,39)	80	82.1		
Week 128 ≥90% decrease (n=35,39)	77.1	71.8		
Week 130 ≥20% decrease (n=35,39)	100	97.4		
Week 130 ≥50% decrease (n=35,39)	91.4	89.7		
Week 130 ≥75% decrease (n=35,39)	80	87.2		
Week 130 ≥90% decrease (n=35,39)	80	74.4		
Week 132 ≥20% decrease (n=35,39)	100	97.4		
Week 132 ≥50% decrease (n=35,39)	91.4	87.2		
Week 132 ≥75% decrease (n=35,39)	80	84.6		
Week 132 ≥90% decrease (n=35,39)	80	71.8		
Week 134 ≥20% decrease (n=35,39)	94.3	97.4		
Week 134 ≥50% decrease (n=35,39)	88.6	87.2		
Week 134 ≥75% decrease (n=35,39)	77.1	84.6		
Week 134 ≥90% decrease (n=35,39)	77.1	71.8		
Week 136 ≥20% decrease (n=34,39)	97.1	97.4		
Week 136 ≥50% decrease (n=34,39)	91.2	89.7		
Week 136 ≥75% decrease (n=34,39)	76.5	84.6		
Week 136 ≥90% decrease (n=34,39)	76.5	71.8		
Week 138 ≥20% decrease (n=34,39)	94.1	97.4		
Week 138 ≥50% decrease (n=34,39)	88.2	89.7		
Week 138 ≥75% decrease (n=34,39)	76.5	84.6		
Week 138 ≥90% decrease (n=34,39)	76.5	71.8		

Week 140 ≥20% decrease (n=29,36)	93.1	97.2		
Week 140 ≥50% decrease (n=29,36)	86.2	88.9		
Week 140 ≥75% decrease (n=29,36)	72.4	83.3		
Week 140 ≥90% decrease (n=29,36)	72.4	72.2		
Week 142 ≥20% decrease (n=29,36)	93.1	97.2		
Week 142 ≥50% decrease (n=29,36)	86.2	88.9		
Week 142 ≥75% decrease (n=29,36)	72.4	83.3		
Week 142 ≥90% decrease (n=29,36)	69	72.2		
Week 144 ≥20% decrease (n=28,36)	92.9	97.2		
Week 144 ≥50% decrease (n=28,36)	89.3	88.9		
Week 144 ≥75% decrease (n=28,36)	71.4	83.3		
Week 144 ≥90% decrease (n=28,36)	67.9	72.2		
Week 146 ≥20% decrease (n=28,36)	96.4	97.2		
Week 146 ≥50% decrease (n=28,36)	92.9	86.1		
Week 146 ≥75% decrease (n=28,36)	75	80.6		
Week 146 ≥90% decrease (n=28,36)	71.4	66.7		
Week 148 ≥20% decrease (n=27,35)	100	97.1		
Week 148 ≥50% decrease (n=27,35)	96.3	85.7		
Week 148 ≥75% decrease (n=27,35)	77.8	80		
Week 148 ≥90% decrease (n=27,35)	74.1	65.7		
Week 150 ≥20% decrease (n=25,35)	100	97.1		
Week 150 ≥50% decrease (n=25,35)	96	88.6		
Week 150 ≥75% decrease (n=25,35)	76	80		
Week 150 ≥90% decrease (n=25,35)	76	68.6		
Week 152 ≥20% decrease (n=25,27)	100	96.3		
Week 152 ≥50% decrease (n=25,27)	96	85.2		
Week 152 ≥75% decrease (n=25,27)	76	77.8		
Week 152 ≥90% decrease (n=25,27)	76	63		
Week 154 ≥20% decrease (n=25,27)	100	96.3		
Week 154 ≥50% decrease (n=25,27)	96	88.9		
Week 154 ≥75% decrease (n=25,27)	76	77.8		
Week 154 ≥90% decrease (n=25,27)	76	70.4		
Week 156 ≥20% decrease (n=25,27)	100	96.3		
Week 156 ≥50% decrease (n=25,27)	96	85.2		
Week 156 ≥75% decrease (n=25,27)	76	77.8		
Week 156 ≥90% decrease (n=25,27)	76	70.4		
Week 158 ≥20% decrease (n=25,27)	100	96.3		
Week 158 ≥50% decrease (n=25,27)	96	88.9		
Week 158 ≥75% decrease (n=25,27)	76	77.8		
Week 158 ≥90% decrease (n=25,27)	76	70.4		
Week 160 ≥20% decrease (n=25,27)	100	96.3		
Week 160 ≥50% decrease (n=25,27)	96	85.2		
Week 160 ≥75% decrease (n=25,27)	76	77.8		
Week 160 ≥90% decrease (n=25,27)	76	70.4		
Week 162 ≥20% decrease (n=25,27)	100	96.3		
Week 162 ≥50% decrease (n=25,27)	96	81.5		
Week 162 ≥75% decrease (n=25,27)	76	77.8		
Week 162 ≥90% decrease (n=25,27)	76	70.4		
Week 164 ≥20% decrease (n=24,24)	100	95.8		
Week 164 ≥50% decrease (n=24,24)	95.8	83.3		
Week 164 ≥75% decrease (n=24,24)	75	75		
Week 164 ≥90% decrease (n=24,24)	75	70.8		

Week 166 ≥20% decrease (n=24,22)	100	95.5		
Week 166 ≥50% decrease (n=24,22)	95.8	81.8		
Week 166 ≥75% decrease (n=24,22)	75	72.7		
Week 166 ≥90% decrease (n=24,22)	75	68.2		
Week 168 ≥20% decrease (n=24,22)	100	95.5		
Week 168 ≥50% decrease (n=24,22)	95.8	81.8		
Week 168 ≥75% decrease (n=24,22)	75	72.7		
Week 168 ≥90% decrease (n=24,22)	75	68.2		
Week 170 ≥20% decrease (n=22,22)	100	90.9		
Week 170 ≥50% decrease (n=22,22)	95.5	81.8		
Week 170 ≥75% decrease (n=22,22)	77.3	72.7		
Week 170 ≥90% decrease (n=22,22)	77.3	68.2		
Week 172 ≥20% decrease (n=22,22)	100	90.9		
Week 172 ≥50% decrease (n=22,22)	95.5	90.9		
Week 172 ≥75% decrease (n=22,22)	77.3	72.7		
Week 172 ≥90% decrease (n=22,22)	77.3	68.2		
Week 174 ≥20% decrease (n=22,22)	100	90.9		
Week 174 ≥50% decrease (n=22,22)	95.5	90.9		
Week 174 ≥75% decrease (n=22,22)	77.3	72.7		
Week 174 ≥90% decrease (n=22,22)	77.3	68.2		
Week 176 ≥20% decrease (n=19,22)	100	90.9		
Week 176 ≥50% decrease (n=19,22)	94.7	90.9		
Week 176 ≥75% decrease (n=19,22)	73.7	72.7		
Week 176 ≥90% decrease (n=19,22)	73.7	68.2		
Week 178 ≥20% decrease (n=19,22)	100	90.9		
Week 178 ≥50% decrease (n=19,22)	94.7	90.9		
Week 178 ≥75% decrease (n=19,22)	73.7	72.7		
Week 178 ≥90% decrease (n=19,22)	73.7	68.2		
Week 180 ≥20% decrease (n=19,22)	100	90.9		
Week 180 ≥50% decrease (n=19,22)	94.7	90.9		
Week 180 ≥75% decrease (n=19,22)	73.7	68.2		
Week 180 ≥90% decrease (n=19,22)	73.7	63.6		
Week 182 ≥20% decrease (n=18,22)	100	90.9		
Week 182 ≥50% decrease (n=18,22)	94.4	90.9		
Week 182 ≥75% decrease (n=18,22)	72.2	68.2		
Week 182 ≥90% decrease (n=18,22)	72.2	63.6		
Week 184 ≥20% decrease (n=18,22)	100	90.9		
Week 184 ≥50% decrease (n=18,22)	94.4	86.4		
Week 184 ≥75% decrease (n=18,22)	72.2	68.2		
Week 184 ≥90% decrease (n=18,22)	72.2	63.6		
Week 186 ≥20% decrease (n=18,22)	100	90.9		
Week 186 ≥50% decrease (n=18,22)	94.4	90.9		
Week 186 ≥75% decrease (n=18,22)	72.2	68.2		
Week 186 ≥90% decrease (n=18,22)	72.2	63.6		
Week 188 ≥20% decrease (n=18,21)	100	90.5		
Week 188 ≥50% decrease (n=18,21)	94.4	90.5		
Week 188 ≥75% decrease (n=18,21)	72.2	71.4		
Week 188 ≥90% decrease (n=18,21)	72.2	61.9		
Week 190 ≥20% decrease (n=18,21)	100	95.2		
Week 190 ≥50% decrease (n=18,21)	94.4	85.7		
Week 190 ≥75% decrease (n=18,21)	72.2	66.7		
Week 190 ≥90% decrease (n=18,21)	72.2	61.9		

Week 192 ≥20% decrease (n=18,21)	100	95.2		
Week 192 ≥50% decrease (n=18,21)	94.4	81		
Week 192 ≥75% decrease (n=18,21)	72.2	66.7		
Week 192 ≥90% decrease (n=18,21)	72.2	61.9		
Week 194 ≥20% decrease (n=18,20)	100	95		
Week 194 ≥50% decrease (n=18,20)	94.4	80		
Week 194 ≥75% decrease (n=18,20)	72.2	70		
Week 194 ≥90% decrease (n=18,20)	72.2	65		
Week 196 ≥20% decrease (n=18,20)	100	90		
Week 196 ≥50% decrease (n=18,20)	94.4	80		
Week 196 ≥75% decrease (n=18,20)	72.2	70		
Week 196 ≥90% decrease (n=18,20)	72.2	65		
Week 198 ≥20% decrease (n=18,20)	100	90		
Week 198 ≥50% decrease (n=18,20)	94.4	80		
Week 198 >75% decrease (n=18,20)	72.2	75		
Week 198 ≥90% decrease (n=18,20)	72.2	65		
Week 200 ≥20% decrease (n=17,20)	100	90		
Week 200 ≥50% decrease (n=17,20)	94.1	85		
Week 200 ≥75% decrease (n=17,20)	76.5	75		
Week 200 ≥90% decrease (n=17,20)	70.6	65		
Week 202 ≥20% decrease (n=17,20)	100	90		
Week 202 ≥50% decrease (n=17,20)	94.1	85		
Week 202 ≥75% decrease (n=17,20)	76.5	75		
Week 202 ≥90% decrease (n=17,20)	70.6	65		
Week 204 ≥20% decrease (n=17,20)	100	90		
Week 204 ≥50% decrease (n=17,20)	94.1	85		
Week 204 ≥70% decrease (n=17,20)	76.5	75		
Week 204 ≥90% decrease (n=17,20)	70.6	65		
Week 206 ≥20% decrease (n=16,20)	100	85		
Week 206 ≥50% decrease (n=16,20)	93.8	75		
Week 206 ≥75% decrease (n=16,20)	75	75		
Week 206 ≥90% decrease (n=16,20)	68.8	70		
Week 208 ≥20% decrease (n=16,20)	100	90		
Week 208 ≥50% decrease (n=16,20)	93.8	80		
Week 208 ≥75% decrease (n=16,20	75	75		
Week 208 ≥90% decrease (n=16,20)	68.8	70		
Week 210 ≥20% decrease (n=16,19)	100	89.5		
Week 210 ≥50% decrease (n=16,19)	93.8	84.2		
Week 210 ≥75% decrease (n=16,19)	81.3	78.9		
Week 210 ≥90% decrease (n=16,19)	75	73.7		
Week 212 ≥20% decrease (n=15,19)	100	89.5		
Week 212 ≥50% decrease (n=15,19)	93.3	84.2		
Week 212 ≥75% decrease (n=15,19)	73.3	78.9		
Week 212 ≥90% decrease (n=15,19)	73.3	73.7		
Week 214 ≥20% decrease (n=15,19)	100	89.5		
Week 214 ≥50% decrease (n=15,19)	93.3	84.2		
Week 214 ≥75% decrease (n=15,19)	73.3	78.9		
Week 214 ≥90% decrease (n=15,19)	73.3	73.7		
Week 216 ≥20% decrease (n=15,19)	100	94.7		
Week 216 ≥50% decrease (n=15,19)	93.3	84.2		
Week 216 ≥75% decrease (n=15,19)	73.3	78.9		
Week 216 ≥90% decrease (n=15,19)	73.3	73.7		

Week 218 ≥20% decrease (n=15,19)	100	89.5		
Week 218 ≥50% decrease (n=15,19)	93.3	84.2		
Week 218 ≥75% decrease (n=15,19)	80	78.9		
Week 218 ≥90% decrease (n=15,19)	73.3	73.7		
Week 220 ≥20% decrease (n=15,19)	100	89.5		
Week 220 ≥50% decrease (n=15,19)	93.3	84.2		
Week 220 ≥75% decrease (n=15,19)	80	78.9		
Week 220 ≥90% decrease (n=15,19)	73.3	73.7		
Week 222 ≥20% decrease (n=15,19)	100	89.5		
Week 222 ≥50% decrease (n=15,19)	93.3	84.2		
Week 222 ≥75% decrease (n=15,19)	80	78.9		
Week 222 ≥90% decrease (n=15,19)	73.3	73.7		
Week 224 ≥20% decrease (n=15,19)	100	89.5		
Week 224 ≥50% decrease (n=15,19)	93.3	84.2		
Week 224 ≥75% decrease (n=15,19)	80	78.9		
Week 224 ≥90% decrease (n=15,19)	73.3	73.7		
Week 226 ≥20% decrease (n=14,19)	100	89.5		
Week 226 ≥50% decrease (n=14,19)	92.9	84.2		
Week 226 ≥75% decrease (n=14,19)	78.6	78.9		
Week 226 ≥90% decrease (n=14,19)	71.4	73.7		
Week 228 ≥20% decrease (n=14,19)	100	89.5		
Week 228 ≥50% decrease (n=14,19)	92.9	89.5		
Week 228 ≥75% decrease (n=14,19)	78.6	78.9		
Week 228 ≥90% decrease (n=14,19)	71.4	73.7		
Week 230 ≥20% decrease (n=14,19)	100	89.5		
Week 230 ≥50% decrease (n=14,19)	92.9	89.5		
Week 230 ≥75% decrease (n=14,19)	78.6	78.9		
Week 230 ≥90% decrease (n=14,19)	71.4	73.7		
Week 232 ≥20% decrease (n=14,18)	100	88.9		
Week 232 ≥50% decrease (n=14,18)	92.9	88.9		
Week 232 ≥75% decrease (n=14,18)	78.6	77.8		
Week 232 ≥90% decrease (n=14,18)	71.4	72.2		
Week 234 ≥20% decrease (n=14,18)	100	88.9		
Week 234 ≥50% decrease (n=14,18)	92.9	88.9		
Week 234 ≥75% decrease (n=14,18)	78.6	77.8		
Week 234 ≥90% decrease (n=14,18)	71.4	72.2		
Week 236 ≥20% decrease (n=14,18)	100	94.4		
Week 236 ≥50% decrease (n=14,18)	92.9	88.9		
Week 236 ≥75% decrease (n=14,18)	78.6	77.8		
Week 236 ≥90% decrease (n=14,18)	71.4	72.2		
Week 238 ≥20% decrease (n=14,18)	100	94.4		
Week 238 ≥50% decrease (n=14,18)	92.9	88.9		
Week 238 ≥75% decrease (n=14,18)	78.6	77.8		
Week 238 ≥90% decrease (n=14,18)	71.4	72.2		
Week 240 ≥20% decrease (n=13,18)	100	94.4		
Week 240 ≥50% decrease (n=13,18)	92.3	88.9		
Week 240 ≥75% decrease (n=13,18)	76.9	77.8		
Week 240 ≥90% decrease (n=13,18)	69.2	72.2		
Week 242 ≥20% decrease (n=13,18)	100	94.4		
Week 242 ≥50% decrease (n=13,18)	92.3	88.9		
Week 242 ≥75% decrease (n=13,18)	76.9	77.8		
Week 242 ≥90% decrease (n=13,18)	69.2	72.2		

Week 244 ≥20% decrease (n=13,18)	100	94.4		
Week 244 ≥50% decrease (n=13,18)	92.3	88.9		
Week 244 ≥75% decrease (n=13,18)	76.9	77.8		
Week 244 ≥90% decrease (n=13,18)	69.2	72.2		
Week 246 ≥20% decrease (n=13,18)	100	94.4		
Week 246 ≥50% decrease (n=13,18)	92.3	88.9		
Week 246 ≥75% decrease (n=13,18)	76.9	77.8		
Week 246 ≥90% decrease (n=13,18)	69.2	72.2		
Week 248 ≥20% decrease (n=13,18)	100	94.4		
Week 248 ≥50% decrease (n=13,18)	92.3	88.9		
Week 248 ≥75% decrease (n=13,18)	76.9	77.8		
Week 248 ≥90% decrease (n=13,18)	69.2	72.2		
Week 250 ≥20% decrease (n=13,18)	100	94.4		
Week 250 ≥50% decrease (n=13,18)	92.3	83.3		
Week 250 ≥75% decrease (n=13,18)	76.9	77.8		
Week 250 ≥90% decrease (n=13,18)	69.2	72.2		
Week 252 ≥20% decrease (n=13,18)	100	94.4		
Week 252 ≥50% decrease (n=13,18)	92.3	83.3		
Week 252 ≥75% decrease (n=13,18)	76.9	77.8		
Week 252 ≥90% decrease (n=13,18)	69.2	72.2		
Week 254 ≥20% decrease (n=13,18)	100	94.4		
Week 254 ≥50% decrease (n=13,18)	92.3	83.3		
Week 254 ≥75% decrease (n=13,18)	76.9	77.8		
Week 254 ≥90% decrease (n=13,18)	69.2	72.2		
Week 256 ≥20% decrease (n=13,18)	100	94.4		
Week 256 ≥50% decrease (n=13,18)	92.3	83.3		
Week 256 ≥75% decrease (n=13,18)	76.9	77.8		
Week 256 ≥90% decrease (n=13,18)	69.2	72.2		
Week 258 ≥20% decrease (n=13,18)	100	94.4		
Week 258 ≥50% decrease (n=13,18)	92.3	83.3		
Week 258 ≥75% decrease (n=13,18)	76.9	77.8		
Week 258 ≥90% decrease (n=13,18)	69.2	72.2		
Week 260 ≥20% decrease (n=13,18)	100	94.4		
Week 260 ≥50% decrease (n=13,18)	92.3	88.9		
Week 260 ≥75% decrease (n=13,18)	76.9	77.8		
Week 260 ≥90% decrease (n=13,18)	69.2	72.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Part III: Percentage of Participants with Inactive Disease

End point title	Part III: Percentage of Participants with Inactive Disease

End point description:

Participants who previously withdrew are excluded.
Responders are participants who met all of the following criteria for inactive disease at the visit assessment day:
i. Number of active joints = 0. ii. Absence of lymphadenopathy, hepatomegaly or splenomegaly in the nearest non-missing physical examination prior to or after the week assessment day. This could include results outside of the time window.
iii. Absence of symptomatic serositis adverse event. iv. In the 14 days preceding the week assessment

day no fever (temperature >=37.5 degrees C) or rash characteristic of sJIA.
v. Normal ESR as defined by an ESR <20 mm/hr regardless of age and sex. vi. Physician global assessment VAS <=10. LOCF rule applied to missing number of active joints, ESR and Physician global assessment VAS.
Data presented up to the point of entry into the Alternative Dosing Schedule.
ITT3 population; n=number of participants contributing to the specific statistic.

End point type	Secondary

End point timeframe:

Weeks 104, 116, 128, 140, 152, 164, 176, 188, 200, 212, 224, 236, 248, and 260

End point values	Participants ≥30 kg	Participants <30 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	47		
Units: percentage of participants				
number (not applicable)				
Week 104 (n=42,47)	45.2	46.8		
Week 116 (n=41,46)	48.8	43.5		
Week 128 (n=40,43)	55	48.8		
Week 140 (n=38,40)	55.3	45		
Week 152 (n=27,35)	33.3	54.3		
Week 164 (n=27,25)	37	28		
Week 176 (n=24,22)	41.7	36.4		
Week 188 (n=21,22)	23.8	31.8		
Week 200 (n=19,21)	42.1	14.3		
Week 212 (n=18,18)	55.6	44.4		
Week 224 (n=17,18)	47.1	44.4		
Week 236 (n=16,17)	43.8	29.4		
Week 248 (n=15,17)	26.7	41.2		
Week 260 (n=15,15)	46.7	6.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Part III: Percentage of Participants in Clinical Remission

End point title	Part III: Percentage of Participants in Clinical Remission

End point description:

Patients who previously withdrew are excluded. Responders are patients who met all of the following criteria for inactive disease at all visits in 6 months (180 days) prior to and including the visit assessment day: i. Number of active joints = 0. ii. Absence of lymphadenopathy, hepatomegaly or splenomegaly in the nearest non-missing physical examination prior to or after the week assessment day. This could include results outside of the time window. iii. Absence of symptomatic serositis adverse event. iv. In the 14 days preceding the week assessment day no fever (temperature >=37.5 C) or rash characteristic of sJIA. v. Normal ESR as defined by an ESR <20 mm/hr regardless of age and sex. iv. Physician global assessment VAS <=10. LOCF rule applied to missing number of active joints, ESR and Physician global assessment VAS. ESR = Erythrocyte Sedimentation Rate. VAS = Visual Analogue Scale.
Data presented up to the point of entry into the Alternative Dosing Schedule.
ITT3 population.

End point type	Secondary

End point timeframe:

Weeks 116, 128, 140, 152, 164, 176, 188, 200, 212, 224, 236, 248 and 260

End point values	Participants ≥30 kg	Participants <30 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	47		
Units: percentage of participants				
number (not applicable)				
Week 116 (n=41,46)	14.6	17.4		
Week 128 (n=40,43)	32.5	23.3		
Week 140 (n=38,40)	34.2	25		
Week 152 (n=27,35)	25.9	25.7		
Week 164 (n=27,25)	22.2	16		
Week 176 (n=24,22)	16.7	13.6		
Week 188 (n=21,22)	14.3	9.1		
Week 200 (n=19,21)	15.8	4.8		
Week 212 (n=18,18)	16.7	5.6		
Week 224 (n=17,18)	29.4	11.1		
Week 236 (n=16,17)	25	29.4		
Week 248 (n=15,17)	13.3	23.5		
Week 260 (n=15,15)	13.3	6.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Part III: Percentage of Participants on CSs at Baseline in Clinical Remission off all Oral CSs for 6 Months Prior to Specific Weeks

End point title	Part III: Percentage of Participants on CSs at Baseline in Clinical Remission off all Oral CSs for 6 Months Prior to Specific Weeks

End point description:

There were 4 levels of clinical remission defined while the patient remained on tocilizumab as defined below.. After level 1, each successive level required that all the previous level criteria be met:
Level 1: inactive disease criteria have been met at all assessments in the last 6 months (180 days) preceding the timepoint assessment day Level 2: level 1 criteria and no oral corticosteroids received in the last 6 months (180 days) preceding the timepoint assessment day. Level 3: level 2 criteria and no methotrexate received in the last 6 months (180 days) preceding the timepoint assessment day Level 4: level 3 criteria and no NSAIDs received for sJIA in the last 6 months (180 days) preceding the timepoint assessment day. ITT3 population; n=number of participants contributing to the specific statistic.

End point type	Secondary

End point timeframe:

Weeks 116, 128, 140, 152, 164, 188, 200, 212, 224,236,248 and 260

End point values	Participants ≥30 kg	Participants <30 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	46		
Units: percentage of participants				
number (not applicable)				
Week 116 (n=41,46)	12.2	17.4		
Week 128 (n=40,43)	32.5	20.9		
Week 140 (n=38,40)	28.9	20		
Week 152 (n=27,35)	18.5	20		
Week 164 (n=27,25)	18.5	12		
Week 176 (n=24,22)	16.7	9.1		
Week 188 (n=21,22)	14.3	4.5		
Week 200 (n=19,21)	10.5	4.8		
Week 212 (n=18,18)	11.1	5.6		
Week 224 (n=17,18)	23.5	11.1		
Week 236 (n=16,17)	25	23.5		
Week 248 (n=15,17)	6.7	17.6		
Week 260 (n=15,15)	6.7	6.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Part III: Percentage of Participants on Methotrexate (MTX) at Baseline in Clinical Remission off Corticosteroids and MTX for 6 Months Prior to Specified Weeks

End point title	Part III: Percentage of Participants on Methotrexate (MTX) at Baseline in Clinical Remission off Corticosteroids and MTX for 6 Months Prior to Specified Weeks

End point description:

There were 4 levels of clinical remission defined while the patient remained on tocilizumab as defined below.. After level 1, each successive level required that all the previous level criteria be met:
Level 1: inactive disease criteria have been met at all assessments in the last 6 months (180 days) preceding the timepoint assessment day Level 2: level 1 criteria and no oral corticosteroids received in the last 6 months (180 days) preceding the timepoint assessment day Level 3: level 2 criteria and no methotrexate received in the last 6 months (180 days) preceding the timepoint assessment day Level 4: level 3 criteria and no NSAIDs received for sJIA in the last 6 months (180 days) preceding the timepoint assessment day. ITT3 population; n=number of participants contributing to the specific statistic

End point type	Secondary

End point timeframe:

Weeks 116, 128, 140, 152, 164, 188, 200, 212, 224,236,248 and 260

End point values	Participants ≥30 kg	Participants <30 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	46		
Units: percentage of participants				
number (not applicable)				
Week 116 (n=41,46)	7.3	8.7		
Week 128 (n=40,43)	20	11.6		
Week 140 (n=38,40)	18.4	5		
Week 152 (n=27,35)	3.7	2.9		
Week 164 (n=27,25)	3.7	4		
Week 176 (n=24,22)	4.2	0		
Week 188 (n=21,22)	4.8	0		
Week 200 (n=19,21)	5.3	4.8		
Week 212 (n=18,18)	5.6	5.6		
Week 224 (n=17,18)	5.9	5.6		
Week 236 (n=16,17)	12.5	5.9		
Week 248 (n=15,17)	0	5.9		
Week 260 (n=15,15)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part III: Percentage of Participants in Clinical Remission off all Arthritis Medications except TCZ for 6 months Prior to Specified Weeks

End point title	Part III: Percentage of Participants in Clinical Remission off all Arthritis Medications except TCZ for 6 months Prior to Specified Weeks

End point description:

There were 4 levels of clinical remission defined while the patient remained on tocilizumab as defined below.. After level 1, each successive level required that all the previous level criteria be met:
Level 1: inactive disease criteria have been met at all assessments in the last 6 months (180 days) preceding the timepoint assessment day Level 2: level 1 criteria and no oral corticosteroids received in the last 6 months (180 days) preceding the timepoint assessment day Level 3: level 2 criteria and no methotrexate received in the last 6 months (180 days) preceding the timepoint assessment day Level 4: level 3 criteria and no NSAIDs received for sJIA in the last 6 months (180 days) preceding the timepoint assessment day. ITT3 population; n=number of participants contributing to the specific statistic.

End point type	Secondary

End point timeframe:

Weeks 116, 128, 140, 152, 164, 176, 188, 200, 212, 224, 236, 248, and 260

End point values	Participants ≥30 kg	Participants <30 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	46		
Units: percentage of participants				
number (not applicable)				
Week 116 (n=41,46)	4.9	8.7		

Week 128 (n=40,43)	15	9.3		
Week 140 (n=38,40)	15.8	5		
Week 152 (n=27,35)	0	2.9		
Week 164 (n=27,25)	0	0		
Week 176 (n=24,22)	4.2	0		
Week 188 (n=21,22)	4.8	0		
Week 200 (n=19,21)	5.3	0		
Week 212 (n=18,18)	5.6	0		
Week 224 (n=17,18)	5.9	0		
Week 236 (n=16,17)	12.5	0		
Week 248 (n=15,17)	0	0		
Week 260 (n=15,15)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part III: Percentage of Participants Who Develop Anti-TCZ Antibodies

End point title	Part III: Percentage of Participants Who Develop Anti-TCZ Antibodies

End point description:

Human antibodies against human antibodies (HAHA), anti-tocilizumab antibodies were assessed by immunogenicity techniques from blood samples drawn every two weeks during Part III of the study. ITT3 population; n=number of participants contributing to the specific statistic.

End point type	Secondary

End point timeframe:

Every 2 weeks from Week 104 to 260

End point values	Participants ≥30 kg	Participants <30 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: percentage of participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part III: Percentage of Participants who Develop Anti-TCZ Antibodies Associated With Drug Hypersensitivity Reactions

End point title	Part III: Percentage of Participants who Develop Anti-TCZ Antibodies Associated With Drug Hypersensitivity Reactions

End point description:

HAHA, anti-tocilizumab antibodies were assessed by immunogenicity techniques from blood samples drawn every two weeks during Part III of the study. ITT3 population; n=number of participants

contributing to the specific statistic.

End point type	Secondary

End point timeframe:

Every 2 weeks from Week 104 to 260

End point values	Participants ≥30 kg	Participants <30 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: percentage of participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE onset between time of very first drug intake and date of last contact or 30 days after very last drug intake. 30 days after 12 weeks of treatment in Part I, 30 days after up to Week 104 in Part II and 30 days after up to Week 260 in Part III .

Adverse event reporting additional description:

Adverse Events (AEs) reported in the All Tocilizumab (Part I, Part II and Part III) arm are cumulative to Week 260 and include AEs previously reported in the Tocilizumab_8 mg/kg (Part I) and Tocilizumab_12 mg/kg (Part I) arms that occurred in the 12 week treatment period.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	All Tocilizumab (Part I, II and III)

Reporting group description: -

Serious adverse events	All Tocilizumab (Part I, II and III)		
Total subjects affected by serious adverse events			
subjects affected / exposed	48 / 112 (42.86%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Drug intolerance			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Influenza like illness			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Testicular torsion			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pulmonary veno-occlusive disease			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Self injurious behaviour			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Liver function test abnormal			

subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Forearm fracture			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fracture			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tendon rupture			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ulna fracture			

subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Histiocytosis haematophagic			
subjects affected / exposed	5 / 112 (4.46%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 0		
Lymphadenitis			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Vomiting			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Panniculitis			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urticaria			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Juvenile idiopathic arthritis			

subjects affected / exposed	1 / 112 (0.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	1 / 112 (0.89%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Gastroenteritis				
subjects affected / exposed	5 / 112 (4.46%)			
occurrences causally related to treatment / all	2 / 7			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	5 / 112 (4.46%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Varicella				
subjects affected / exposed	5 / 112 (4.46%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	3 / 112 (2.68%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 112 (1.79%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	1 / 1			
Lower respiratory tract infection				
subjects affected / exposed	2 / 112 (1.79%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Arthritis bacterial				

subjects affected / exposed	1 / 112 (0.89%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchopneumonia				
subjects affected / exposed	1 / 112 (0.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related sepsis				
subjects affected / exposed	1 / 112 (0.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	1 / 112 (0.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Kidney infection				
subjects affected / exposed	1 / 112 (0.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis media				
subjects affected / exposed	1 / 112 (0.89%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed	1 / 112 (0.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pharyngotonsillitis				
subjects affected / exposed	1 / 112 (0.89%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				

subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Hyperkalaemia			
subjects affected / exposed	1 / 112 (0.89%)		
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	All Tocilizumab (Part I, II and III)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	112 / 112 (100.00%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	7 / 112 (6.25%)		
occurrences (all)	11		

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	11 / 112 (9.82%)		
occurrences (all)	19		
Influenza like illness			
subjects affected / exposed	10 / 112 (8.93%)		
occurrences (all)	14		
Fatigue			
subjects affected / exposed	6 / 112 (5.36%)		
occurrences (all)	6		
Local swelling			
subjects affected / exposed	5 / 112 (4.46%)		
occurrences (all)	6		
Pain			
subjects affected / exposed	4 / 112 (3.57%)		
occurrences (all)	4		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	3 / 112 (2.68%)		
occurrences (all)	13		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	45 / 112 (40.18%)		
occurrences (all)	70		
Oropharyngeal pain			
subjects affected / exposed	24 / 112 (21.43%)		
occurrences (all)	40		
Nasal congestion			
subjects affected / exposed	10 / 112 (8.93%)		
occurrences (all)	16		
Epistaxis			
subjects affected / exposed	9 / 112 (8.04%)		
occurrences (all)	10		
Rhinorrhoea			

subjects affected / exposed	7 / 112 (6.25%)		
occurrences (all)	8		
Investigations			
Transaminases increased			
subjects affected / exposed	11 / 112 (9.82%)		
occurrences (all)	12		
Neutrophil count decreased			
subjects affected / exposed	5 / 112 (4.46%)		
occurrences (all)	13		
Platelet count decreased			
subjects affected / exposed	5 / 112 (4.46%)		
occurrences (all)	36		
Alanine aminotransferase increased			
subjects affected / exposed	4 / 112 (3.57%)		
occurrences (all)	5		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	17 / 112 (15.18%)		
occurrences (all)	24		
Ligament sprain			
subjects affected / exposed	13 / 112 (11.61%)		
occurrences (all)	16		
Contusion			
subjects affected / exposed	10 / 112 (8.93%)		
occurrences (all)	18		
Excoriation			
subjects affected / exposed	8 / 112 (7.14%)		
occurrences (all)	8		
Limb injury			
subjects affected / exposed	8 / 112 (7.14%)		
occurrences (all)	15		
Fall			
subjects affected / exposed	7 / 112 (6.25%)		
occurrences (all)	7		
Joint injury			

subjects affected / exposed	7 / 112 (6.25%)		
occurrences (all)	8		
Traumatic haematoma			
subjects affected / exposed	7 / 112 (6.25%)		
occurrences (all)	10		
Wound			
subjects affected / exposed	6 / 112 (5.36%)		
occurrences (all)	8		
Hand fracture			
subjects affected / exposed	5 / 112 (4.46%)		
occurrences (all)	5		
Laceration			
subjects affected / exposed	5 / 112 (4.46%)		
occurrences (all)	5		
Infusion related reaction			
subjects affected / exposed	4 / 112 (3.57%)		
occurrences (all)	5		
Muscle strain			
subjects affected / exposed	4 / 112 (3.57%)		
occurrences (all)	4		
Thermal burn			
subjects affected / exposed	4 / 112 (3.57%)		
occurrences (all)	4		
Nervous system disorders			
Headache			
subjects affected / exposed	25 / 112 (22.32%)		
occurrences (all)	53		
Dizziness			
subjects affected / exposed	6 / 112 (5.36%)		
occurrences (all)	11		
Migraine			
subjects affected / exposed	3 / 112 (2.68%)		
occurrences (all)	6		
Blood and lymphatic system disorders			
Neutropenia			

subjects affected / exposed	25 / 112 (22.32%)		
occurrences (all)	143		
Leukopenia			
subjects affected / exposed	11 / 112 (9.82%)		
occurrences (all)	34		
Lymphadenopathy			
subjects affected / exposed	6 / 112 (5.36%)		
occurrences (all)	12		
Lymphadenitis			
subjects affected / exposed	4 / 112 (3.57%)		
occurrences (all)	5		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	11 / 112 (9.82%)		
occurrences (all)	14		
Middle ear effusion			
subjects affected / exposed	4 / 112 (3.57%)		
occurrences (all)	4		
Eye disorders			
Cataract			
subjects affected / exposed	4 / 112 (3.57%)		
occurrences (all)	4		
Chalazion			
subjects affected / exposed	3 / 112 (2.68%)		
occurrences (all)	6		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	29 / 112 (25.89%)		
occurrences (all)	44		
Vomiting			
subjects affected / exposed	29 / 112 (25.89%)		
occurrences (all)	34		
Nausea			
subjects affected / exposed	26 / 112 (23.21%)		
occurrences (all)	37		
Abdominal pain			

subjects affected / exposed occurrences (all)	16 / 112 (14.29%) 22		
Abdominal pain upper subjects affected / exposed occurrences (all)	15 / 112 (13.39%) 21		
Dental caries subjects affected / exposed occurrences (all)	6 / 112 (5.36%) 6		
Gastrointestinal disorder subjects affected / exposed occurrences (all)	6 / 112 (5.36%) 7		
Abdominal discomfort subjects affected / exposed occurrences (all)	3 / 112 (2.68%) 4		
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	22 / 112 (19.64%) 31		
Eczema subjects affected / exposed occurrences (all)	10 / 112 (8.93%) 18		
Prurigo subjects affected / exposed occurrences (all)	8 / 112 (7.14%) 10		
Urticaria subjects affected / exposed occurrences (all)	8 / 112 (7.14%) 14		
Dry skin subjects affected / exposed occurrences (all)	5 / 112 (4.46%) 6		
Pruritus subjects affected / exposed occurrences (all)	4 / 112 (3.57%) 9		
Dermatitis atopic subjects affected / exposed occurrences (all)	3 / 112 (2.68%) 3		

Dermatitis contact			
subjects affected / exposed	3 / 112 (2.68%)		
occurrences (all)	5		
Erythema			
subjects affected / exposed	3 / 112 (2.68%)		
occurrences (all)	4		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	5 / 112 (4.46%)		
occurrences (all)	5		
Musculoskeletal and connective tissue disorders			
Juvenile idiopathic arthritis			
subjects affected / exposed	31 / 112 (27.68%)		
occurrences (all)	72		
Arthralgia			
subjects affected / exposed	25 / 112 (22.32%)		
occurrences (all)	48		
Back pain			
subjects affected / exposed	12 / 112 (10.71%)		
occurrences (all)	19		
Pain in extremity			
subjects affected / exposed	12 / 112 (10.71%)		
occurrences (all)	24		
Musculoskeletal pain			
subjects affected / exposed	11 / 112 (9.82%)		
occurrences (all)	23		
Neck pain			
subjects affected / exposed	9 / 112 (8.04%)		
occurrences (all)	16		
Joint swelling			
subjects affected / exposed	7 / 112 (6.25%)		
occurrences (all)	10		
Arthritis			
subjects affected / exposed	5 / 112 (4.46%)		
occurrences (all)	9		
Musculoskeletal stiffness			

subjects affected / exposed	4 / 112 (3.57%)		
occurrences (all)	6		
Osteoporosis			
subjects affected / exposed	3 / 112 (2.68%)		
occurrences (all)	3		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	53 / 112 (47.32%)		
occurrences (all)	168		
Upper respiratory tract infection			
subjects affected / exposed	49 / 112 (43.75%)		
occurrences (all)	156		
Gastroenteritis			
subjects affected / exposed	28 / 112 (25.00%)		
occurrences (all)	43		
Pharyngitis			
subjects affected / exposed	20 / 112 (17.86%)		
occurrences (all)	26		
Rhinitis			
subjects affected / exposed	19 / 112 (16.96%)		
occurrences (all)	40		
Ear infection			
subjects affected / exposed	18 / 112 (16.07%)		
occurrences (all)	34		
Viral infection			
subjects affected / exposed	16 / 112 (14.29%)		
occurrences (all)	17		
Impetigo			
subjects affected / exposed	14 / 112 (12.50%)		
occurrences (all)	22		
Otitis media			
subjects affected / exposed	14 / 112 (12.50%)		
occurrences (all)	15		
Conjunctivitis			
subjects affected / exposed	12 / 112 (10.71%)		
occurrences (all)	14		

Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	12 / 112 (10.71%) 14			
Bronchitis subjects affected / exposed occurrences (all)	11 / 112 (9.82%) 15			
Sinusitis subjects affected / exposed occurrences (all)	10 / 112 (8.93%) 11			
Urinary tract infection subjects affected / exposed occurrences (all)	10 / 112 (8.93%) 30			
Gastroenteritis viral subjects affected / exposed occurrences (all)	9 / 112 (8.04%) 9			
Influenza subjects affected / exposed occurrences (all)	9 / 112 (8.04%) 12			
Tonsillitis subjects affected / exposed occurrences (all)	9 / 112 (8.04%) 11			
Otitis externa subjects affected / exposed occurrences (all)	8 / 112 (7.14%) 15			
Paronychia subjects affected / exposed occurrences (all)	7 / 112 (6.25%) 10			
Herpes zoster subjects affected / exposed occurrences (all)	6 / 112 (5.36%) 6			
Laryngitis subjects affected / exposed occurrences (all)	6 / 112 (5.36%) 9			
Cellulitis subjects affected / exposed occurrences (all)	5 / 112 (4.46%) 5			

Skin infection			
subjects affected / exposed	5 / 112 (4.46%)		
occurrences (all)	5		
Tinea pedis			
subjects affected / exposed	5 / 112 (4.46%)		
occurrences (all)	8		
Varicella			
subjects affected / exposed	4 / 112 (3.57%)		
occurrences (all)	4		
Otitis media acute			
subjects affected / exposed	3 / 112 (2.68%)		
occurrences (all)	4		
Pneumonia			
subjects affected / exposed	3 / 112 (2.68%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 June 2009	Updated disease definitions including sJIA disease and MAS; Clarified section 4.1.1.2 title to indicate that first open label treatment dose was administered at Week 12 for Part II; Clarified the inclusion and exclusion criteria; Updated treatments allowed and prohibited for sJIA; Updated the withdrawal requirements for patients and discontinuation criteria if patients did not achieve a JIA ACR30 response; Extended the length of the study design from a two-part, 3 year study to a three-part, 5 year study; Clarified the visits and weeks of Part I – the double-blind portion of the study to evaluate efficacy and safety; Changed the day of the Baseline score taken as the pre-dose assessment at Visit 1 (the day of the first infusion of study drug) to Day 1 from Day 0; Updated the timing of reporting to Roche with local serum ferritin results ≥ 3,000 nanograms/milliliter (ng/mL); Clarified the definition of improvement in JIA and Tanner Stage; If at least two consecutive TCZ infusions were missed for safety reasons, quantitative immunoglobulin (Ig) and PK/PD assessments (IL-6, TCZ, sIL-6R and anti-TCZ antibodies) were performed pre-dose at the next scheduled visit and pre-dose 2 weeks later; Clarified responsibility of collaborative groups and the guidance for steroid tapering during and after escape therapy; Added the escape option to allow children with more severe disease at Baseline an opportunity to escape and receive active open-label study drug; To allow varicella zoster immunoglobulin upon exposure to chicken pox in children who had not had chicken pox; Clarified safety parameters and thus improved safety monitoring and reporting.

07 January 2011	The primary goal of this amendment was to introduce an optional, less frequent, dosing schedule in Part III for patients who had achieved inactive disease while off oral CSs and met specific response criteria. Other changes were made to correct ambiguous or incorrect wording and to improve clarity and included the following: Updated secondary and exploratory endpoints for Part II of the study; Updated the sample size of the study; Changes to add clarity to safety parameters, address safety issues seen with TCZ, and modified risk mitigation rules, particularly related to an infusion related reaction; Protocol additions based on the information which was gathered from the current conduct of the protocol. Clarification of the timing of the interim analyses of efficacy and safety data: at study week 12, when the 50th patient completed the 1 year on TCZ in study Part II, at week 104 (end of study Part II), and at week 260 (end of study Part III).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported