Clinical trial results:
A Phase Ib, Open-Label, Multicenter Study to Investigate the Pharmacokinetics, Pharmacodynamics, and Safety of Tocilizumab Following Subcutaneous Administration to Patients With Polyarticular Juvenile Idiopathic Arthritis

Summary

EudraCT number	2012-003486-18
Trial protocol	DE IT GB ES PL Outside EU/EEA
Global end of trial date	19 May 2016

Results information

Result version number	v1 (current)
This version publication date	09 February 2017
First version publication date	09 February 2017

Trial information

Trial identification

Sponsor protocol code	WA28117

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01904279
WHO universal trial number (UTN)	-
Other trial identifiers	Acronym: JIGSAW 117

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche Ltd, +41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche Ltd, +41 61 6878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the pharmacokinetics of subcutaneous tocilizumab (SC TCZ) in participants with polyarticular juvenile idiopathic arthritis (pJIA).

Protection of trial subjects:

The study was conducted in full conformance with the principles of the "Declaration of Helsinki" or with the laws and regulations of the country in which the research was conducted, whichever affords the greater protection to the individual. The study fully adhered to the principles outlined in "Guideline for Good Clinical Practice (GCP)" International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Tripartite Guideline and ensured compliance with the EU Clinical Trial Directive [2001/20/EC]. Approval from the Institutional Review Board (IRB)/Independent Ethics Committee (IEC) and the relevant Competent Authority was obtained before study start.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 July 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	Argentina: 4
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	52
EEA total number of subjects	24

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	1
Children (2-11 years)	30
Adolescents (12-17 years)	21
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:

A total of 52 participants were enrolled in the study. Study included a 21-day screening period.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	TCZ SC 162 mg Q3W

Arm description:

Participants with body weight less than (<) 30 kilograms (kg) were administered 162 milligrams (mg) of TCZ as an subcutaneous (SC) injection every 3 weeks (Q3W) for 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Tocilizumab (TCZ)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 162 mg of TCZ as SC injection Q3W or Q2W for 52 weeks.

Arm title	TCZ SC 162 mg Q2W

Arm description:

Participants with body weight greater than or equal to (>/=) 30 kg were administered 162 mg of TCZ as an SC injection every 2 weeks (Q2W) for 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Tocilizumab (TCZ)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 162 mg of TCZ as SC injection Q3W or Q2W for 52 weeks.

Number of subjects in period 1	TCZ SC 162 mg Q3W	TCZ SC 162 mg Q2W
Started	27	25
Completed	24	22
Not completed	3	3
Consent withdrawn by subject	1	-
Lack of efficacy	2	3

Baseline characteristics

Reporting groups	
Reporting group title	TCZ SC 162 mg Q3W
Reporting group description:	
Participants with body weight less than (<) 30 kilograms (kg) were administered 162 milligrams (mg) of TCZ as an subcutaneous (SC) injection every 3 weeks (Q3W) for 52 weeks.	
Reporting group title	TCZ SC 162 mg Q2W
Reporting group description:	
Participants with body weight greater than or equal to (>/=) 30 kg were administered 162 mg of TCZ as an SC injection every 2 weeks (Q2W) for 52 weeks.	

Reporting group values	TCZ SC 162 mg Q3W	TCZ SC 162 mg Q2W	Total
Number of subjects	27	25	52
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	5.5	13.9	
standard deviation	± 2.1	± 2.7	-
Gender categorical			
Units: Subjects			
Female	18	18	36
Male	9	7	16

End points

End points reporting groups

Reporting group title	TCZ SC 162 mg Q3W
Reporting group description:	
Participants with body weight less than (<) 30 kilograms (kg) were administered 162 milligrams (mg) of TCZ as an subcutaneous (SC) injection every 3 weeks (Q3W) for 52 weeks.	
Reporting group title	TCZ SC 162 mg Q2W
Reporting group description:	
Participants with body weight greater than or equal to (>/=) 30 kg were administered 162 mg of TCZ as an SC injection every 2 weeks (Q2W) for 52 weeks.	

Primary: Minimum Serum Concentration (Cmin) of TCZ at Steady State

End point title	Minimum Serum Concentration (Cmin) of TCZ at Steady
End point description:	
Detailed timeframe for TCZ SC 162 mg Q3W arm: pre-dose (Hour 0), 96, 504, 1008, 2016, 2022, 2064, 2112, 2160, 2520 hours post Day 1 dose (additionally at 6, 12, 48, 120, 2028 hours post Day 1 dose in participants >/=2 years old). Detailed timeframe for TCZ SC 162 mg Q2W arm: pre-dose (Hour 0), 6, 12, 48, 120, 336, 672, 1008, 2016, 2022, 2028, 2040, 2064, 2112, 2160, 2520 hours post Day 1 dose. The analysis was performed in pharmacokinetic population. Pharmacokinetic population included all enrolled participants who were adherent to the protocol.	
End point type	Primary
End point timeframe:	
Pre-dose (Hour 0) up to 2520 hours post Day 1 dose (detailed timeframe is provided in outcome description section)	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Only descriptive data was planned to be presented for the endpoint.	

End point values	TCZ SC 162 mg Q3W	TCZ SC 162 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Micrograms per milliliter (mcg/mL)				
median (full range (min-max))	13.35 (0.21 to 52.25)	12.71 (0.19 to 23.75)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Curve From Time 0 to 12 Weeks (AUC12weeks) of TCZ Treatment

End point title	Area Under the Curve From Time 0 to 12 Weeks (AUC12weeks) of TCZ Treatment[2]
End point description:	
Detailed timeframe for TCZ SC 162 mg Q3W arm: pre-dose (Hour 0), 96, 504, 1008, 2016 hours post Day 1 dose (additionally at 6, 12, 48, 120 hours post Day 1 dose in participants >/=2 years old).	

Detailed timeframe for TCZ SC 162 mg Q2W arm: pre-dose (Hour 0), 6, 12, 48, 120, 336, 672, 1008, 2016 post Day 1 dose. The analysis was performed in pharmacokinetic population.

End point type	Primary

End point timeframe:

Pre-dose (Hour 0) up to 2016 hours post Day 1 dose (detailed timeframe is provided in outcome description section)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be presented for the endpoint.

End point values	TCZ SC 162 mg Q3W	TCZ SC 162 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Mcg/mL*day				
median (full range (min-max))	2998 (1465 to 7708)	1933 (324 to 3098)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Serum Concentration (Cmax) of TCZ at Steady State

End point title	Maximum Serum Concentration (Cmax) of TCZ at Steady

End point description:

Detailed timeframe for TCZ SC 162 mg Q3W arm: pre-dose (Hour 0), 96, 504, 1008, 2016, 2022, 2064, 2112, ,2160, 2520 hours post Day 1 dose (additionally at 6, 12, 48, 120, 2028 hours post Day 1 dose in participants >/=2 years old). Detailed timeframe for TCZ SC 162 mg Q2W arm: pre-dose (Hour 0), 6, 12, 48, 120, 336, 672, 1008, 2016, 2022, 2028, 2040, 2064, 2112, 2160, 2520 hours post Day 1 dose.The analysis was performed in pharmacokinetic Population.

End point type	Primary

End point timeframe:

Pre-dose (Hour 0) up to 2520 hours post Day 1 dose (detailed timeframe is provided in outcome description section)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be presented for the endpoint.

End point values	TCZ SC 162 mg Q3W	TCZ SC 162 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: mcg/mL				
median (full range (min-max))	62.44 (39.37 to 121.13)	29.74 (7.56 to 50.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Interleukin-6 (IL-6) Levels

End point title	Change From Baseline in Serum Interleukin-6 (IL-6) Levels

End point description:

IL-6 is a cytokine associated with disease activity in juvenile idiopathic arthritis (JIA) including the pJIA subset. It is found in high levels in the synovial fluid and is associated with indicators of inflammatory activity. Here n refers to the number of participants analyzed at specific time point. The analysis was performed in safety population. Safety population included all participants who received at least one dose of treatment and who had at least one post-dose safety assessment. Here number of subjects analyzed represents participants evaluable for this outcome measure and "n" represents participants evaluable for the specified category. 99999 represented data not analysed as no participants were evaluable. 9999 represented data was not available as only single participant was evaluated.

End point type	Secondary

End point timeframe:

Baseline, Days 0.25, 0.5, 2, 4, 5, 84.25, 84.5, 85, 86, 88, 90; Weeks 2, 3, 4, 6, 12, 14, 15, 27, 28, 36, 44, 52

End point values	TCZ SC 162 mg Q3W	TCZ SC 162 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	23		
Units: picograms per milliliter(pg/mL)				
arithmetic mean (standard deviation)				
Baseline (n=18, 23)	77.569 (± 278.376)	10.567 (± 11.24)		
Day 0.25 (n=18, 23)	-15.309 (± 108.157)	4.575 (± 7.555)		
Day 0.5 (n=15, 23)	-16.181 (± 116.587)	11.932 (± 13.33)		
Day 2 (n=18, 23)	17.998 (± 157.295)	23.223 (± 23.935)		
Day 4 (n= 0, 0)	99999 (± 99999)	99999 (± 99999)		
Day 5 (n= 17, 23)	17.265 (± 186.212)	35.263 (± 64.907)		
Week 2 (n= 0, 23)	99999 (± 99999)	21.751 (± 49.964)		
Week 3 (n=18, 0)	-12.801 (± 198.038)	99999 (± 99999)		
Week 4 (n=0, 22)	99999 (± 99999)	15.944 (± 26.322)		
Week 6 (n=18, 23)	-0.412 (± 271.409)	17.841 (± 34.515)		
Week 12 (n=16, 21)	-45.569 (± 294.169)	17.236 (± 28.727)		
Day 84.25 (n= 14, 21)	32.644 (± 65.094)	14.66 (± 24.026)		
Day 84.5 (n=13, 20)	-46.575 (± 318.217)	24.478 (± 31.747)		
Day 85 (n=0, 22)	99999 (± 99999)	27.934 (± 53.23)		
Day 86 (n=16, 21)	-53.35 (± 285.831)	36.06 (± 82.547)		
Day 88 (n=17, 21)	-42.836 (± 280.041)	19.397 (± 22.712)		

Day 90 (n=15, 19)	-51.899 (± 299.59)	20.642 (± 20.247)		
Week 14 (n=0, 23)	99999 (± 99999)	11.958 (± 16.665)		
Week 15 (n=17, 1)	-21.565 (± 312.758)	122.88 (± 9999)		
Week 27 (n=18, 0)	-16.408 (± 293.156)	99999 (± 99999)		
Week 28 (n= 0, 20)	99999 (± 99999)	14.206 (± 20.762)		
Week 36 (n=16, 16)	-38.921 (± 303.851)	13.273 (± 24.814)		
Week 44 (n=0, 20)	99999 (± 99999)	14.765 (± 18.458)		
Week 52 (n=17, 20)	-44.611 (± 289.698)	10.401 (± 18.455)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Soluble IL-6 Receptor Levels

End point title	Change From Baseline in Soluble IL-6 Receptor Levels

End point description:

The analysis was performed in safety population. 99999 represented data not analysed as no participants were evaluable. 9999 represented data was not available as only single participant was evaluated. Here number of subjects analyzed represents participants evaluable for this outcome measure and "n" represents participants evaluable for the specified category.

End point type	Secondary

End point timeframe:

Baseline, Days 0.25, 0.5, 2, 4, 5, 84.25, 84.5, 85, 86, 88, 90; Weeks 2, 3, 4, 6, 12, 14, 15, 27, 28, 36, 44, 52

End point values	TCZ SC 162 mg Q3W	TCZ SC 162 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	23		
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Baseline (n=20, 23)	140.4 (± 225.72)	206.7 (± 241.69)		
Day 0.25 (n= 19, 23)	-4.04 (± 41.14)	1.78 (± 29.68)		
Day 0.5 (n=16, 22)	-1.45 (± 53.39)	4.58 (± 51.71)		
Day 2 (n=19, 23)	89.72 (± 75.29)	68.9 (± 66.75)		
Day 4 (n=1, 0)	323.4 (± 9999)	99999 (± 99999)		
Day 5 (n=19, 23)	194.46 (± 143.28)	124.65 (± 100.58)		
Week 2 (n=0, 23)	99999 (± 99999)	193.25 (± 158.69)		

Week 3 (n=20, 0)	418.54 (± 237.02)	99999 (± 99999)		
Week 4 (n=0, 23)	99999 (± 99999)	239.86 (± 194.47)		
Week 6 (n=20, 23)	407.36 (± 344.44)	233.82 (± 234.92)		
Week 12 (n=17, 21)	464.77 (± 317.77)	286.06 (± 260.33)		
Day 84.25 (n= 17, 23)	461.85 (± 280.99)	245.05 (± 253.45)		
Day 84.5 (17, 22)	482.55 (± 299.43)	274.85 (± 230.86)		
Day 85 (n=0, 22)	99999 (± 99999)	268.72 (± 254.46)		
Day 86 (n=19, 22)	461.19 (± 345.97)	244.53 (± 257.08)		
Day 88 (n=19, 21)	514.89 (± 303.29)	256.47 (± 234.7)		
Day 90 (n=19, 20)	494.05 (± 276.35)	292.29 (± 229.2)		
Week 14 (n=0, 23)	99999 (± 99999)	272.93 (± 241.9)		
Week 15 (n=20, 1)	497.21 (± 295.29)	200 (± 9999)		
Week 27 (n= 20, 0)	532.81 (± 270.07)	99999 (± 99999)		
Week 28 (n=0, 21)	99999 (± 99999)	295.28 (± 286.78)		
Week 36 (n=18, 18)	416.02 (± 305.07)	269.32 (± 276.03)		
Week 44 (n=0, 21)	99999 (± 99999)	243.93 (± 299.72)		
Week 52 (n=20, 22)	470.6 (± 263.38)	209.51 (± 318.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in C-Reactive Protein (CRP) Levels

End point title	Change From Baseline in C-Reactive Protein (CRP) Levels

End point description:

The analysis was performed in safety population. Here "n" represents participants evaluable for the specified category. Here 99999 represented data not analysed as no participants were evaluable.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 6, 9, 12,18, 20, 27, 28, 36, 44, 45, 51, 52

End point values	TCZ SC 162 mg Q3W	TCZ SC 162 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: mg/L				
arithmetic mean (standard deviation)				
Baseline (n=27, 25)	3.391 (± 5.27)	3.356 (± 6.908)		
Week 4 (n=0, 25)	99999 (± 99999)	-2.187 (± 5.27)		
Week 6 (n=27, 25)	-3 (± 5.21)	-2.368 (± 5.735)		
Week 9 (n=27, 0)	-3.069 (± 5.346)	99999 (± 99999)		
Week 12 (n=27, 24)	-3.16 (± 5.285)	-1.783 (± 4.559)		
Week 18 (n=26, 0)	-3.213 (± 5.377)	99999 (± 99999)		
Week 20 (n=0, 25)	99999 (± 99999)	-1.336 (± 6.158)		
Week 27 (n=27, 0)	-3.122 (± 5.279)	99999 (± 99999)		
Week 28 (n=0, 25)	99999 (± 99999)	-2.467 (± 6.455)		
Week 36 (n=25, 22)	-3.254 (± 5.492)	-2.209 (± 5.316)		
Week 44 (n=0, 22)	99999 (± 99999)	-2.039 (± 5.47)		
Week 45 (n=26, 0)	-3.153 (± 5.385)	99999 (± 99999)		
Week 51 (n=25, 0)	-3.344 (± 5.453)	99999 (± 99999)		
Week 52 (n=0, 22)	99999 (± 99999)	-2.225 (± 5.285)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Erythrocyte Sedimentation Rate (ESR)

End point title	Change From Baseline in Erythrocyte Sedimentation Rate (ESR)

End point description:

The ESR is an acute phase reactant and a measure of inflammation. A negative change from baseline indicates improvement. The analysis was performed in safety population. 99999 represented data not analysed as no participants were evaluable. Here "n" represents participants evaluable for the specified category.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 6, 9, 12, 18, 20, 27, 28, 36, 44, 45, 51, 52

End point values	TCZ SC 162 mg Q3W	TCZ SC 162 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: millimeters per hour (mm/h)				
arithmetic mean (standard deviation)				
Baseline (n=27, 25)	15.9 (± 14.2)	13 (± 13.1)		
Week 4 (n=0, 25)	99999 (± 99999)	-7 (± 9)		
Week 6 (n= 26, 25)	-10.6 (± 12.8)	-7.2 (± 10.5)		
Week 9 (n=25, 0)	-9.9 (± 10.9)	99999 (± 99999)		
Week 12 (n=26, 25)	-9.8 (± 12.4)	-6.8 (± 13)		
Week 18 (n=26, 0)	-11.8 (± 12.3)	99999 (± 99999)		
Week 20 (n=0, 25)	99999 (± 99999)	-7.9 (± 11.2)		
Week 27 (n=27,0)	-11.9 (± 12.2)	99999 (± 99999)		
Week 28 (n=0, 23)	99999 (± 99999)	-8 (± 14.2)		
Week 36 (n=26, 21)	-11.8 (± 12.8)	-8 (± 13.1)		
Week 44 (n=0, 21)	99999 (± 99999)	-10.2 (± 13)		
Week 45 (n=26, 0)	-12 (± 12.2)	99999 (± 99999)		
Week 51 (n=25,0)	-12.2 (± 13)	99999 (± 99999)		
Week 52 (n=0, 22)	99999 (± 99999)	-8.5 (± 13.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anti-TCZ Antibodies of Neutralizing Potential

End point title	Percentage of Participants With Anti-TCZ Antibodies of Neutralizing Potential

End point description:

The analysis was performed in safety population.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	TCZ SC 162 mg Q3W	TCZ SC 162 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Percentage of Participants				
number (not applicable)	3.7	8		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to Week 56	
Adverse event reporting additional description:	
Safety population.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	TCZ SC 162 mg Q2W
Reporting group description:	
Participants with body weight >/= 30 kg were administered 162 mg of TCZ as an SC injection Q2W for 52 weeks.	
Reporting group title	TCZ SC 162 mg Q3W
Reporting group description:	
Participants with body weight < 30 kg were administered 162 mg of TCZ as an SC injection Q3W for 52 weeks.	

Serious adverse events	TCZ SC 162 mg Q2W	TCZ SC 162 mg Q3W	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 25 (8.00%)	1 / 27 (3.70%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Varicella			
subjects affected / exposed	0 / 25 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			

subjects affected / exposed	0 / 25 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 25 (4.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	TCZ SC 162 mg Q2W	TCZ SC 162 mg Q3W	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 25 (88.00%)	23 / 27 (85.19%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	2 / 25 (8.00%)	1 / 27 (3.70%)	
occurrences (all)	3	1	
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 25 (8.00%)	1 / 27 (3.70%)	
occurrences (all)	3	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 25 (8.00%)	0 / 27 (0.00%)	
occurrences (all)	6	0	
Injection site erythema			
subjects affected / exposed	6 / 25 (24.00%)	4 / 27 (14.81%)	
occurrences (all)	18	9	
Injection site haematoma			
subjects affected / exposed	2 / 25 (8.00%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Injection site pain			
subjects affected / exposed	2 / 25 (8.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	

Injection site pruritus			
subjects affected / exposed	2 / 25 (8.00%)	0 / 27 (0.00%)	
occurrences (all)	4	0	
Injection site swelling			
subjects affected / exposed	2 / 25 (8.00%)	1 / 27 (3.70%)	
occurrences (all)	5	1	
Pyrexia			
subjects affected / exposed	4 / 25 (16.00%)	2 / 27 (7.41%)	
occurrences (all)	4	2	
Vessel puncture site haematoma			
subjects affected / exposed	2 / 25 (8.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 25 (8.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	3 / 25 (12.00%)	10 / 27 (37.04%)	
occurrences (all)	5	15	
Oropharyngeal pain			
subjects affected / exposed	3 / 25 (12.00%)	1 / 27 (3.70%)	
occurrences (all)	5	2	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 25 (8.00%)	2 / 27 (7.41%)	
occurrences (all)	2	2	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 25 (8.00%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 25 (24.00%)	1 / 27 (3.70%)	
occurrences (all)	9	1	
Blood and lymphatic system disorders			

Neutropenia			
subjects affected / exposed	1 / 25 (4.00%)	3 / 27 (11.11%)	
occurrences (all)	1	9	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 25 (4.00%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 25 (12.00%)	3 / 27 (11.11%)	
occurrences (all)	4	3	
Constipation			
subjects affected / exposed	1 / 25 (4.00%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Aphthous ulcer			
subjects affected / exposed	3 / 25 (12.00%)	1 / 27 (3.70%)	
occurrences (all)	5	2	
Diarrhoea			
subjects affected / exposed	4 / 25 (16.00%)	1 / 27 (3.70%)	
occurrences (all)	4	1	
Nausea			
subjects affected / exposed	5 / 25 (20.00%)	1 / 27 (3.70%)	
occurrences (all)	8	1	
Vomiting			
subjects affected / exposed	5 / 25 (20.00%)	4 / 27 (14.81%)	
occurrences (all)	7	8	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Dermatitis Atopic			
subjects affected / exposed	0 / 25 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Eczema			
subjects affected / exposed	3 / 25 (12.00%)	2 / 27 (7.41%)	
occurrences (all)	3	3	
Rash			

subjects affected / exposed	2 / 25 (8.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 25 (4.00%)	3 / 27 (11.11%)	
occurrences (all)	2	3	
Arthralgia			
subjects affected / exposed	4 / 25 (16.00%)	5 / 27 (18.52%)	
occurrences (all)	10	6	
Joint Swelling			
subjects affected / exposed	2 / 25 (8.00%)	0 / 27 (0.00%)	
occurrences (all)	4	0	
Juvenile idiopathic arthritis			
subjects affected / exposed	3 / 25 (12.00%)	1 / 27 (3.70%)	
occurrences (all)	3	1	
Neck Pain			
subjects affected / exposed	1 / 25 (4.00%)	2 / 27 (7.41%)	
occurrences (all)	3	2	
Pain in extremity			
subjects affected / exposed	4 / 25 (16.00%)	1 / 27 (3.70%)	
occurrences (all)	6	2	
Infections and infestations			
Ear Infection			
subjects affected / exposed	0 / 25 (0.00%)	4 / 27 (14.81%)	
occurrences (all)	0	4	
Bronchitis			
subjects affected / exposed	1 / 25 (4.00%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Impetigo			
subjects affected / exposed	0 / 25 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	3	
Gastrointeritis			
subjects affected / exposed	2 / 25 (8.00%)	4 / 27 (14.81%)	
occurrences (all)	2	7	
Nasopharyngitis			

subjects affected / exposed	7 / 25 (28.00%)	11 / 27 (40.74%)	
occurrences (all)	8	18	
Influenza			
subjects affected / exposed	0 / 25 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Otitis media			
subjects affected / exposed	0 / 25 (0.00%)	3 / 27 (11.11%)	
occurrences (all)	0	3	
Rhinitis			
subjects affected / exposed	3 / 25 (12.00%)	1 / 27 (3.70%)	
occurrences (all)	4	1	
Paronychia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Upper respiratory tract infection			
subjects affected / exposed	4 / 25 (16.00%)	1 / 27 (3.70%)	
occurrences (all)	6	1	
Viral infection			
subjects affected / exposed	0 / 25 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 March 2013	1) Removal of the Juvenile Arthritis Multidimensional Assessment Report (JAMAR) as a patient-reported outcome (PRO) tool and replacement with child health assessment questionnaire (CHAQ) functional ability instrument 2) The immunogenicity testing requirements were updated for participants who withdrew due to hypersensitivity or anaphylaxis 3)The dose interval changes for participants whose body weight increased or decreased above or below the 30 kg threshold were clarified
01 August 2013	The number of participants switching from TCZ intravenous to TCZ SC was limited to no more than 50 percent of the total number of participants and to include the request to collect information on the prior four intravenous infusions for participants switching.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported