Clinical trial results:
Long-Term Extension Study to Evaluate the Safety and Efficacy of Subcutaneous Tocilizumab in Patients with Polyarticular-Course and Systemic Juvenile Idiopathic Arthritis

Summary

EudraCT number	2013-005212-98
Trial protocol	DE IT GB ES FR
Global end of trial date	24 November 2021

Results information

Result version number	v1 (current)
This version publication date	11 June 2022
First version publication date	11 June 2022

Trial information

Trial identification

Sponsor protocol code	WA29231

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02165345
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	
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	24 November 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 November 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This trial was an extension of Roche trials WA28117 and WA28118 and evaluated the long-term safety and efficacy of subcutaneous tocilizumab (SC TCZ) in pediatric participants with polyarticular-course and systemic juvenile idiopathic arthritis (pJIA and sJIA). Efficacy evaluation was performed for up to 3 years, and safety evaluation was done for up to 5 years.

Protection of trial subjects:

All participants (or their parents or guardians) were required to sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 July 2014
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	Argentina: 6
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Brazil: 3
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	82
EEA total number of subjects	33

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)	50
Adolescents (12-17 years)	25
Adults (18-64 years)	7
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Pediatric participants from related Roche studies with polyarticular-course and systemic juvenile idiopathic arthritis (pJIA and sJIA)

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	SC TCZ 162 mg Q3W (< 30 kg) pJIA

Arm description:

Participants received SC TCZ according to body weight and JIA subtype.

Arm type	Experimental
Investigational medicinal product name	Subcutaneous tocilizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

162 mg Q3W

Arm title	SC TCZ 162 mg Q2W (>= 30 kg) pJIA

Arm description:

Participants received SC TCZ according to body weight and JIA subtype.

Arm type	Experimental
Investigational medicinal product name	Subcutaneous tocilizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

162 mg Q2W

Arm title	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA

Arm description:

Participants received SC TCZ according to body weight and JIA subtype.

Arm type	Experimental
Investigational medicinal product name	Subcutaneous tocilizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

162 mg Q10D or Q2W

Arm title	SC TCZ 162 mg QW (>= 30 kg) sJIA

Arm description:

Participants received SC TCZ according to body weight and JIA subtype.

Arm type	Experimental
Investigational medicinal product name	Subcutaneous tocilizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

162 mg QW

Number of subjects in period 1	SC TCZ 162 mg Q3W (< 30 kg) pJIA	SC TCZ 162 mg Q2W (>= 30 kg) pJIA	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA
Started	24	20	19
Completed	13	6	1
Not completed	11	14	18
Consent withdrawn by subject	1	4	2
Physician decision	1	1	2
Adverse event, non-fatal	1	1	-
Commercial Drug Available	3	5	8
Pregnancy	-	1	-
Study Terminated by Sponsor	3	-	4
Lost to follow-up	-	-	1
Lack of efficacy	2	2	1

Number of subjects in period 1	SC TCZ 162 mg QW (>= 30 kg) sJIA
Started	19
Completed	5
Not completed	14
Consent withdrawn by subject	4
Physician decision	2
Adverse event, non-fatal	-
Commercial Drug Available	8
Pregnancy	-
Study Terminated by Sponsor	-
Lost to follow-up	-
Lack of efficacy	-

Baseline characteristics

Reporting groups	
Reporting group title	SC TCZ 162 mg Q3W (< 30 kg) pJIA
Reporting group description:	
Participants received SC TCZ according to body weight and JIA subtype.	
Reporting group title	SC TCZ 162 mg Q2W (>= 30 kg) pJIA
Reporting group description:	
Participants received SC TCZ according to body weight and JIA subtype.	
Reporting group title	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA
Reporting group description:	
Participants received SC TCZ according to body weight and JIA subtype.	
Reporting group title	SC TCZ 162 mg QW (>= 30 kg) sJIA
Reporting group description:	
Participants received SC TCZ according to body weight and JIA subtype.	

Reporting group values	SC TCZ 162 mg Q3W (< 30 kg) pJIA	SC TCZ 162 mg Q2W (>= 30 kg) pJIA	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA
Number of subjects	24	20	19
Age Categorical Units: Subjects			
Children (2-11 years)	24	3	19
Adolescents (12-17 years)	0	14	0
Adults (18-64 years)	0	3	0
Age Continuous Units: years			
arithmetic mean	6.8	14.7	4.9
standard deviation	± 2.1	± 2.8	± 2.3
Gender Categorical Units: Subjects			
Female	18	14	10
Male	6	6	9
Race Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	0	0	0
Black or African American	0	0	1
White	20	19	16
Multiple	0	1	0
Unknown	4	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	6	3	3
Not Hispanic or Latino	14	17	15
Not Stated	2	0	1
Unknown	2	0	0

Reporting group values	SC TCZ 162 mg QW (>= 30 kg) sJIA	Total	

Number of subjects	19	82	
Age Categorical Units: Subjects			
Children (2-11 years)	4	50	
Adolescents (12-17 years)	11	25	
Adults (18-64 years)	4	7	
Age Continuous Units: years			
arithmetic mean	13.9		
standard deviation	± 3.5	-	
Gender Categorical Units: Subjects			
Female	11	53	
Male	8	29	
Race Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	1	1	
Black or African American	0	1	
White	16	71	
Multiple	1	2	
Unknown	1	6	
Ethnicity Units: Subjects			
Hispanic or Latino	0	12	
Not Hispanic or Latino	15	61	
Not Stated	3	6	
Unknown	1	3	

End points

End points reporting groups

Reporting group title	SC TCZ 162 mg Q3W (< 30 kg) pJIA
Reporting group description: Participants received SC TCZ according to body weight and JIA subtype.	
Reporting group title	SC TCZ 162 mg Q2W (>= 30 kg) pJIA
Reporting group description: Participants received SC TCZ according to body weight and JIA subtype.	
Reporting group title	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA
Reporting group description: Participants received SC TCZ according to body weight and JIA subtype.	
Reporting group title	SC TCZ 162 mg QW (>= 30 kg) sJIA
Reporting group description: Participants received SC TCZ according to body weight and JIA subtype.	

Primary: Juvenile Arthritis Disease Activity Score (JADAS-71) - pJIA

End point title	Juvenile Arthritis Disease Activity Score (JADAS-71) - pJIA[1][2]
End point description: The JADAS 71 is a composite score derived from physician's global assessment of disease activity VAS, patient/parent's global assessment of overall well-being VAS, normalized ESR, and the number of joints with active arthritis (0 - 71). The score ranges from 0–101.	
End point type	Primary
End point timeframe: Baseline up to 3 years	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical tests were planned for this study

[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: This end point is specific to the arm reported

End point values	SC TCZ 162 mg Q3W (< 30 kg) pJIA	SC TCZ 162 mg Q2W (>= 30 kg) pJIA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	20		
Units: None				
median (full range (min-max))				
Baseline (n = 22; n = 20)	0.40 (0.0 to 18.4)	2.05 (0.0 to 27.6)		
Week 12 (n = 21; n = 20)	0.20 (0.0 to 15.9)	0.85 (0.0 to 24.9)		
Week 24 (n = 22; n = 19)	0.30 (0.0 to 16.3)	2.30 (0.0 to 11.6)		
Week 36 (n = 22; n = 19)	0.00 (0.0 to 14.6)	1.90 (0.0 to 11.7)		
Week 48 (n = 21; n = 19)	0.20 (0.0 to 14.6)	1.80 (0.0 to 12.0)		
Week 60 (n = 21; n = 19)	0.40 (0.0 to 19.4)	2.20 (0.0 to 42.5)		

Week 72 (n = 21; n = 17)	0.00 (0.0 to 8.2)	1.50 (0.0 to 7.7)		
Week 84 (n = 20; n = 17)	0.05 (0.0 to 13.5)	2.00 (0.0 to 10.0)		
Week 96 (n = 20; n = 17)	0.10 (0.0 to 15.4)	2.00 (0.0 to 4.4)		
Week 108 (n = 19; n = 16)	0.30 (0.0 to 11.3)	2.15 (0.0 to 7.6)		
Week 120 (n = 19; n =16)	0.20 (0.0 to 10.4)	1.40 (0.0 to 4.5)		
Week 132 (n = 19; n = 16)	0.30 (0.0 to 11.5)	0.45 (0.0 to 10.5)		
Week 144 (n = 19; n = 16)	0.30 (0.0 to 11.5)	1.05 (0.1 to 21.0)		
Week 156 (n = 17; n = 15)	0.00 (0.0 to 3.1)	1.70 (0.0 to 21.0)		

Statistical analyses

No statistical analyses for this end point

Primary: JADAS-71 - sJIA

End point title	JADAS-71 - sJIA[3][4]

End point description:

The JADAS-71 is a composite score derived from physician's global assessment of disease activity VAS, patient/parent's global assessment of overall well-being VAS, normalized ESR, and the number of joints with active arthritis (0 - 71). The score ranges from 0 - 101.

End point type	Primary

End point timeframe:

Baseline up to 3 years

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: No statistical tests were planned for this study

[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: No statistical tests were planned for this study

End point values	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA	SC TCZ 162 mg QW (>= 30 kg) sJIA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: None				
median (full range (min-max))				
Baseline (n = 19; n = 18)	0.40 (0.0 to 14.2)	0.25 (0.0 to 11.2)		
Week 8 (n = 19; n = 17)	0.50 (0.0 to 27.5)	0.20 (0.0 to 14.2)		
Week 16 (n = 18; n = 18)	0.05 (0.0 to 3.5)	0.15 (0.0 to 5.8)		
Week 24 (n = 17; n = 18)	0.40 (0.0 to 7.7)	0.35 (0.0 to 7.3)		
Week 32 (n = 17; n = 18)	0.30 (0.0 to 14.1)	0.30 (0.0 to 5.6)		

Week 40 (n = 17; n = 17)	0.40 (0.0 to 7.9)	0.10 (0.0 to 3.6)		
Week 48 (n = 17; n = 16)	0.30 (0.0 to 2.6)	0.15 (0.0 to 7.3)		
Week 56 (n = 17; n = 16)	0.00 (0.0 to 2.6)	0.10 (0.0 to 9.7)		
Week 64 (n = 17; n = 16)	0.00 (0.0 to 12.2)	0.05 (0.0 to 6.1)		
Week 72 (n = 17; n = 16)	0.10 (0.0 to 4.7)	0.15 (0.0 to 1.7)		
Week 80 (n = 17; n = 16)	0.10 (0.0 to 3.2)	0.20 (0.0 to 6.2)		
Week 88 (n = 17; n = 16)	0.00 (0.0 to 5.2)	0.40 (0.0 to 8.6)		
Week 96 (n = 15; n = 16)	0.10 (0.0 to 8.3)	0.45 (0.0 to 3.8)		
Week 104 (n = 13; n = 16)	0.00 (0.0 to 1.6)	0.15 (0.0 to 1.9)		
Week 112 (n = 13; n = 15)	0.00 (0.0 to 1.4)	0.10 (0.0 to 2.4)		
Week 120 (n = 12; n = 15)	0.05 (0.0 to 1.6)	0.10 (0.0 to 1.7)		
Week 128 (n = 12; n = 14)	0.00 (0.0 to 12.8)	0.15 (0.0 to 2.1)		
Week 136 (n = 12; n = 14)	0.10 (0.0 to 1.9)	0.20 (0.0 to 2.1)		
Week 144 (n = 11; n = 14)	0.00 (0.0 to 10.9)	0.10 (0.0 to 1.6)		
Week 152 (n = 11; n = 13)	0.00 (0.0 to 8.3)	0.10 (0.0 to 2.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Adverse Events (AEs), Serious AEs (SAEs), and AEs of Special Interest (AESI)

End point title	Percentage of Participants with Adverse Events (AEs), Serious AEs (SAEs), and AEs of Special Interest (AESI)[5]

End point description:

Hypersensitivity is defined as any AEs occurring during or within 24 hours of TCZ treatment and not deemed unrelated to study medication by the investigator, excluding injection site reactions.

End point type	Primary

End point timeframe:

Baseline up to 5 years

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical tests were planned for this study

End point values	SC TCZ 162 mg Q3W (< 30 kg) pJIA	SC TCZ 162 mg Q2W (>= 30 kg) pJIA	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA	SC TCZ 162 mg QW (>= 30 kg) sJIA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	20	19	19
Units: Percentage of participants				
number (not applicable)				
AEs	100.0	100.0	100.0	100.0
SAEs	12.5	15.0	15.8	10.5
AESI - hypersensitivity	12.5	0	5.3	5.3
AESI - serious infections and infestations	12.5	10.0	5.3	0
AESI - Anaphylactic reactions	0	0	0	0
AESI - anaphylactic reactions (Sampsons Criteria)	0	0	0	0
AESI - serious bleeding	0	0	0	0
AESI - demyelinating AEs	0	0	0	0
AESI - gastrointestinal perforations	0	0	0	0
AESI - serious hepatic adverse events	0	0	0	0
AESI - malignancies	0	0	0	0
AESI - myocardial infarctions	0	0	0	0
AESI - opportunistic infections	0	0	0	0
AESI - stroke (ischaemic or hemorrhagic)	0	0	0	0
AESI - suspected transmission of infectious agent	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Childhood Health Assessment Questionnaire - Disability Index (CHAQ-DI) Score - pJIA

End point title	Childhood Health Assessment Questionnaire - Disability Index (CHAQ-DI) Score - pJIA[6][7]

End point description:

Childhood health assessment questionnaire-disability index (CHAQ-DI) was recorded to evaluate functional ability at a scale of 0 (best) to 3 (worst).

End point type	Primary

End point timeframe:

Baseline up to 3 years

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical tests were planned for this study

[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: This end point is specific to the arm reported

End point values	SC TCZ 162 mg Q3W (< 30 kg) pJIA	SC TCZ 162 mg Q2W (>= 30 kg) pJIA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	20		
Units: None				
median (full range (min-max))				
Baseline (n = 24; n = 20)	0.0000 (0.0000 to 1.750)	0.000 (0.000 to 2.750)		
Week 12 (n = 24; n = 20)	0.1250 (0.000 to 1.875)	0.1250 (0.000 to 2.250)		
Week 24 (n = 24; n = 19)	0.0000 (0.000 to 1.875)	0.1250 (0.000 to 2.000)		
Week 36 (n = 24; n = 19)	0.0000 (0.000 to 1.750)	0.0000 (0.000 to 2.000)		
Week 48 (n = 23; n = 19)	0.0000 (0.000 to 1.750)	0.1250 (0.000 to 2.000)		
Week 60 (n = 23; n = 19)	0.0000 (0.000 to 1.875)	0.0000 (0.000 to 2.000)		
Week 72 (n = 23; n = 17)	0.0000 (0.000 to 1.875)	0.0000 (0.000 to 2.000)		
Week 84 (n = 22; n = 17)	0.0000 (0.000 to 1.500)	0.0000 (0.000 to 2.000)		
Week 96 (n = 22; n = 17)	0.0000 (0.000 to 1.750)	0.0000 (0.000 to 2.000)		
Week 108 (n = 21; n = 16)	0.0000 (0.000 to 1.750)	0.0000 (0.000 to 2.000)		
Week 120 (n = 21; n = 16)	0.0000 (0.000 to 1.875)	0.0000 (0.000 to 2.000)		
Week 132 (n = 21; n = 16)	0.0000 (0.000 to 1.750)	0.0000 (0.000 to 2.000)		
Week 144 (n = 20; n = 16)	0.0000 (0.000 to 1.375)	0.0000 (0.000 to 2.000)		
Week 156 (n = 13; n = 12)	0.0000 (0.000 to 0.250)	0.0000 (0.000 to 0.125)		

Statistical analyses

No statistical analyses for this end point

Primary: CHAQ-DI Score - sJIA

End point title	CHAQ-DI Score - sJIA[8][9]

End point description:

Childhood health assessment questionnaire-disability index (CHAQ-DI) was recorded to evaluate functional ability at a scale of 0 (best) to 3 (worst).

End point type	Primary

End point timeframe:

Baseline up to 3 years

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical tests were planned for this study

[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: This end point is specific to the arm reported

End point values	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA	SC TCZ 162 mg QW (>= 30 kg) sJIA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: None				
median (full range (min-max))				
Baseline (n = 19; n = 19)	0.0000 (0.000 to 0.500)	0.0000 (0.000 to 2.250)		
Week 8 (n = 19; n = 18)	0.0000 (0.000 to 1.125)	0.0000 (0.000 to 1.750)		
Week 16 (n = 18; n = 19)	0.0000 (0.000 to 0.625)	0.0000 (0.000 to 2.000)		
Week 24 (n = 17; n = 19)	0.0000 (0.000 to 0.625)	0.0000 (0.000 to 2.000)		
Week 32 (n = 17; n = 19)	0.0000 (0.000 to 0.500)	0.0000 (0.000 to 1.625)		
Week 40 (n = 16; n = 18)	0.0000 (0.000 to 0.750)	0.0000 (0.000 to 2.000)		
Week 48 (n = 16; n = 17)	0.0000 (0.000 to 0.625)	0.0000 (0.000 to 2.125)		
Week 56 (n = 15; n = 17)	0.0000 (0.000 to 0.500)	0.0000 (0.000 to 2.125)		
Week 64 (n = 16; n = 17)	0.0000 (0.000 to 0.500)	0.0000 (0.000 to 2.000)		
Week 72 (n = 17; n = 17)	0.0000 (0.000 to 0.250)	0.0000 (0.000 to 1.875)		
Week 80 (n = 17; n 17)	0.0000 (0.000 to 0.250)	0.0000 (0.000 to 1.750)		
Week 88 (n = 16; n = 17)	0.0000 (0.000 to 0.375)	0.0000 (0.000 to 1.875)		
Week 96 (n = 14; n = 17)	0.0000 (0.000 to 0.125)	0.0000 (0.000 to 1.750)		
Week 104 (n = 13; n = 17)	0.0000 (0.000 to 0.625)	0.0000 (0.000 to 1.875)		
Week 112 (n = 12; n = 16)	0.0000 (0.000 to 0.125)	0.0000 (0.000 to 2.125)		
Week 120 (n = 11; n = 14)	0.0000 (0.000 to 0.250)	0.0000 (0.000 to 1.375)		
Week 128 (n = 10; n = 14)	0.0000 (0.000 to 0.250)	0.0000 (0.000 to 2.000)		
Week 136 (n = 11; n = 14)	0.0000 (0.000 to 0.125)	0.0000 (0.000 to 1.500)		
Week 144 (n = 9; n = 14)	0.0000 (0.000 to 0.500)	0.0000 (0.000 to 1.375)		
Week 152 (n = 6; n = 13)	0.1875 (0.000 to 0.625)	0.0000 (0.000 to 1.875)		

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of Participants with Protocol-Defined Inactive Disease - pJIA

End point title	Proportion of Participants with Protocol-Defined Inactive Disease - pJIA[10][11]

End point description:

Inactive disease was defined as follows:
- No presence of active joints
- Absence of active uveitis (defined by the AE preferred terms 'uveitis' and 'intermediate uveitis')
- No fever, rash, serositis, splenomegaly, hepatomegaly, or generalized lymphadenopathy attributable to pJIA
- Normal ESR (< 20 mm/hr)
- Physician global VAS </= 10 mm
- Duration of morning stiffness </= 15 minutes

End point type	Primary

End point timeframe:

Baseline up to 3 years

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical tests were planned for this study

[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: This end point is specific to the arm reported

End point values	SC TCZ 162 mg Q3W (< 30 kg) pJIA	SC TCZ 162 mg Q2W (>= 30 kg) pJIA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	20		
Units: Percentage of participants				
number (not applicable)				
Baseline (n = 24; n = 20)	75.0	50.0		
Week 12 (n = 24; n = 20)	79.2	60.0		
Week 24 (n = 24; n = 19)	70.8	52.6		
Week 36 (n = 24; n = 19)	75.0	57.9		
Week 48 (n = 23; n = 19)	78.3	42.1		
Week 60 (n = 23; n = 19)	82.6	42.1		
Week 72 (n = 23; n = 17)	69.6	52.9		
Week 84 (n = 22; n = 17)	77.3	52.9		
Week 96 (n = 22; n = 17)	77.3	58.8		
Week 108 (n = 21; n = 16)	90.5	50.0		
Week 120 (n = 21; n = 16)	81.0	43.8		
Week 132 (n = 21; n = 16)	81.0	81.3		
Week 144 (n = 21; n = 16)	81.0	56.3		
Week 156 (n= 19; n = 15)	89.5	53.3		

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of Participants with Protocol-Defined Inactive Disease - sJIA

End point title	Proportion of Participants with Protocol-Defined Inactive Disease - sJIA[12][13]

End point description:

End point type	Primary

End point timeframe:

Baseline up to 3 years

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical tests were planned for this study

[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: This end point is specific to the arm reported

End point values	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA	SC TCZ 162 mg QW (>= 30 kg) sJIA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: Percentage of participants				
number (not applicable)				
Baseline (n = 19; n = 19)	73.7	78.9		
Week 8 (n = 19; n = 19)	78.9	78.9		
Week 16 (n = 18; n = 19)	88.9	94.7		
Week 24 (n = 17; n = 19)	70.6	89.5		
Week 32 (n = 17; n = 19)	88.2	89.5		
Week 40 (n = 17; n = 18)	76.5	88.9		
Week 48 (n = 17; n = 17)	94.1	88.2		
Week 56 (n = 17; n = 17)	88.2	82.4		
Week 64 (n = 17; n = 17)	82.4	94.1		
Week 72 (n = 17; n = 17)	82.4	88.2		
Week 80 (n = 17; n = 17)	82.4	94.1		
Week 88 (n = 17; n = 17)	82.4	94.1		
Week 96 (n = 15; n = 17)	86.7	76.5		
Week 104 (n = 13; n = 17)	84.6	82.4		
Week 112 (n = 13; n = 16)	84.6	81.3		
Week 120 (n = 12; n = 16)	83.3	87.5		
Week 128 (n = 12; n = 14)	91.7	85.7		
Week 136 (n = 12; n = 14)	83.3	85.7		
Week 144 (n = 11; n = 14)	90.9	78.6		
Week 152 (n = 11; n = 13)	90.9	92.3		

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of Participants with Clinical Remission - pJIA

End point title	Proportion of Participants with Clinical Remission - pJIA[14][15]

End point description:

Clinical remission was defined as inactive disease for a minimum of 6 continuous months irrespective of disease-modifying anti-rheumatic drug, nonsteroidal anti inflammatory drug, or corticosteroid use.

End point type	Primary

End point timeframe:

From Week 24 up to 3 years

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical tests were planned for this study

[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: This end point is specific to the arm reported

End point values	SC TCZ 162 mg Q3W (< 30 kg) pJIA	SC TCZ 162 mg Q2W (>= 30 kg) pJIA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	20		
Units: Percentage of participants				
number (not applicable)				
Week 24 (n = 24; n = 19)	50.0	42.1		
Week 36 (n = 24; n = 19)	58.3	36.8		
Week 48 (n = 23; n = 19)	52.2	21.1		
Week 60 (n = 23; n = 19)	60.9	21.1		
Week 72 (n = 23; n = 17)	60.9	41.2		
Week 84 (n = 22; n = 17)	63.6	35.3		
Week 96 (n = 22; n = 17)	59.1	35.3		
Week 108 (n = 21; n = 16)	66.7	31.3		
Week 120 (n = 21; n = 16)	61.9	31.3		
Week 132 (n = 21; n = 16)	66.7	31.3		
Week 144 (n = 21; n = 16)	66.7	25.0		
Week 156 (n = 19; n = 15)	73.7	33.3		

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of Participants with Clinical Remission - sJIA

End point title	Proportion of Participants with Clinical Remission - sJIA[16][17]

End point description:

Clinical remission was defined as inactive disease for a minimum of 6 continuous months irrespective of disease-modifying anti-rheumatic drug, nonsteroidal anti inflammatory drug, or corticosteroid use.

End point type	Primary

End point timeframe:

From Week 24 up to 3 years

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical tests were planned for this study

[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: This end point is specific to the arm reported

End point values	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA	SC TCZ 162 mg QW (>= 30 kg) sJIA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: Percentage of Participants				
number (not applicable)				
Week 24 (n = 17; n = 19)	70.6	68.4		
Week 32 (n = 17; n= 19)	70.6	68.4		
Week 40 (n = 17; n = 18)	70.6	77.8		
Week 48 (n = 17; n = 17)	58.8	76.5		
Week 56 (n = 17; n= 17)	76.5	76.5		
Week 64 (n = 17;n= 17)	70.6	76.5		
Week 72 (n = 17; n = 17)	76.5	76.5		
Week 80 (n = 17; n = 17)	70.6	76.5		
Week 88 (n = 17; n = 17)	70.6	88.2		
Week 96 (n = 15; n = 17)	66.7	82.4		
Week 104 (n = 13; n = 17)	76.9	76.5		
Week 112 (n = 13; n = 16)	76.9	68.8		
Week 120 (n = 12; n = 16)	83.3	62.5		
Week 128 (n = 12; n = 14)	75.0	64.3		
Week 136 (n = 12; n = 14)	75.0	71.4		
Week 144 (n = 11; n = 14)	72.7	78.6		
Week 152 (n = 11; n = 13)	81.8	76.9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to 5 years	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	SC TCZ 162 mg Q3W (< 30 kg) pJIA
Reporting group description:	
Participants received SC TCZ according to body weight and JIA subtype.	
Reporting group title	SC TCZ 162 mg QW (>= 30 kg) sJIA
Reporting group description:	
Participants received SC TCZ according to body weight and JIA subtype.	
Reporting group title	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA
Reporting group description:	
Participants received SC TCZ according to body weight and JIA subtype.	
Reporting group title	SC TCZ 162 mg Q2W (>= 30 kg) pJIA
Reporting group description:	
Participants received SC TCZ according to body weight and JIA subtype.	

Serious adverse events	SC TCZ 162 mg Q3W (< 30 kg) pJIA	SC TCZ 162 mg QW (>= 30 kg) sJIA	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 24 (12.50%)	2 / 19 (10.53%)	3 / 19 (15.79%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Procedural complication			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral injury			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			

subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Furuncle			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious mononucleosis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	SC TCZ 162 mg Q2W (>= 30 kg) pJIA		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Procedural complication			

subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Craniocerebral injury			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Eye pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Furuncle				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Varicella				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infectious mononucleosis				
subjects affected / exposed	1 / 20 (5.00%)			
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	SC TCZ 162 mg Q3W (< 30 kg) pJIA	SC TCZ 162 mg QW (>= 30 kg) sJIA	SC TCZ 162 mg Q10D or Q2W (< 30 kg) sJIA
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 24 (100.00%)	19 / 19 (100.00%)	19 / 19 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	2 / 24 (8.33%)	3 / 19 (15.79%)	1 / 19 (5.26%)
occurrences (all)	2	3	1
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Sinus operation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Tooth extraction			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
General disorders and administration site conditions			

Peripheral swelling			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Swelling			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Drug intolerance			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Injection site urticaria			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Injection site pruritus			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Injection site warmth			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Chest pain			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	2 / 24 (8.33%)	3 / 19 (15.79%)	0 / 19 (0.00%)
occurrences (all)	3	3	0
Injection site erythema			
subjects affected / exposed	2 / 24 (8.33%)	2 / 19 (10.53%)	0 / 19 (0.00%)
occurrences (all)	2	2	0
Injection site bruising			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Mass			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Injection site swelling			
subjects affected / exposed	0 / 24 (0.00%)	2 / 19 (10.53%)	0 / 19 (0.00%)
occurrences (all)	0	6	0

Asthenia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Injection site pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Illness			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	7 / 24 (29.17%)	3 / 19 (15.79%)	7 / 19 (36.84%)
occurrences (all)	14	5	9
Injection site reaction			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	4	0
Injection site induration			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Swelling face			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 24 (8.33%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
Dust allergy			

subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Allergy to arthropod bite			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Drug hypersensitivity			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	1	3	0
Heavy menstrual bleeding			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Intermenstrual bleeding			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal erythema			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Menstruation irregular			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	4	0	3
Epistaxis			
subjects affected / exposed	2 / 24 (8.33%)	1 / 19 (5.26%)	2 / 19 (10.53%)
occurrences (all)	2	1	2
Laryngeal inflammation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Tonsillolith			

subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	3 / 24 (12.50%)	5 / 19 (26.32%)	3 / 19 (15.79%)
occurrences (all)	5	13	3
Pharyngeal ulceration			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	3 / 24 (12.50%)	1 / 19 (5.26%)	1 / 19 (5.26%)
occurrences (all)	3	3	1
Rhinitis allergic			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	10 / 24 (41.67%)	2 / 19 (10.53%)	7 / 19 (36.84%)
occurrences (all)	19	2	12
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Attention deficit hyperactivity disorder			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Mood swings			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Depression			

subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Suicidal ideation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Learning disorder			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Depressed mood			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Investigations			
Neutrophil count decreased			
subjects affected / exposed	2 / 24 (8.33%)	1 / 19 (5.26%)	2 / 19 (10.53%)
occurrences (all)	3	1	4
Blood triglycerides increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Salivary gland scan abnormal			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			

subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
Haematocrit decreased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Body temperature increased			
subjects affected / exposed	3 / 24 (12.50%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Chlamydia test positive			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Platelet count decreased			
subjects affected / exposed	0 / 24 (0.00%)	2 / 19 (10.53%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Alanine aminotransferase increased			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
Injury, poisoning and procedural complications			
Skin injury			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Injury			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Skin abrasion			
subjects affected / exposed	1 / 24 (4.17%)	2 / 19 (10.53%)	0 / 19 (0.00%)
occurrences (all)	1	3	0
Nail injury			

subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Thermal burn			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Wrist fracture			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Hand fracture			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	2 / 24 (8.33%)	2 / 19 (10.53%)	0 / 19 (0.00%)
occurrences (all)	2	2	0
Induced abortion failed			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Muscle strain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Limb injury			
subjects affected / exposed	4 / 24 (16.67%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	4	0	1
Arthropod bite			
subjects affected / exposed	2 / 24 (8.33%)	3 / 19 (15.79%)	2 / 19 (10.53%)
occurrences (all)	2	4	2
Limb fracture			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Ligament sprain			

subjects affected / exposed	3 / 24 (12.50%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	4	3	0
Traumatic haematoma			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Ear injury			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Skin laceration			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Scratch			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	3
Fall			
subjects affected / exposed	2 / 24 (8.33%)	1 / 19 (5.26%)	3 / 19 (15.79%)
occurrences (all)	3	1	3
Pelvic bone injury			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Arthropod sting			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Upper limb fracture			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Headache			
subjects affected / exposed	4 / 24 (16.67%)	3 / 19 (15.79%)	5 / 19 (26.32%)
occurrences (all)	6	10	5
Paraesthesia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

Syncope			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Leukopenia			
subjects affected / exposed	2 / 24 (8.33%)	2 / 19 (10.53%)	2 / 19 (10.53%)
occurrences (all)	3	5	2
Lymphopenia			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Monocytopenia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Lymphadenitis			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Increased tendency to bruise			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	6 / 24 (25.00%)	3 / 19 (15.79%)	2 / 19 (10.53%)
occurrences (all)	23	7	2
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	3 / 24 (12.50%)	2 / 19 (10.53%)	1 / 19 (5.26%)
occurrences (all)	3	2	2
Vertigo			

subjects affected / exposed	0 / 24 (0.00%)	2 / 19 (10.53%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
Ulcerative keratitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Myopia			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Photophobia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Tongue ulceration			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	2 / 19 (10.53%)
occurrences (all)	1	1	2
Dental discomfort			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	2 / 19 (10.53%)
occurrences (all)	1	1	2
Eructation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Oral pain			

subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Odynophagia			
subjects affected / exposed	1 / 24 (4.17%)	2 / 19 (10.53%)	0 / 19 (0.00%)
occurrences (all)	1	5	0
Gastritis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	10 / 24 (41.67%)	1 / 19 (5.26%)	6 / 19 (31.58%)
occurrences (all)	13	1	11
Dental caries			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
Abdominal pain			
subjects affected / exposed	2 / 24 (8.33%)	1 / 19 (5.26%)	2 / 19 (10.53%)
occurrences (all)	2	1	2
Diarrhoea			
subjects affected / exposed	10 / 24 (41.67%)	3 / 19 (15.79%)	4 / 19 (21.05%)
occurrences (all)	15	3	6
Flatulence			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Chapped lips			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Salivary gland mucocoele			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Aphthous ulcer			

subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	2 / 19 (10.53%)
occurrences (all)	0	1	2
Constipation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Papule			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	4 / 24 (16.67%)	4 / 19 (21.05%)	4 / 19 (21.05%)
occurrences (all)	5	15	7
Pseudoporphyria			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dermatitis allergic			
subjects affected / exposed	0 / 24 (0.00%)	2 / 19 (10.53%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Hyperhidrosis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 24 (0.00%)	3 / 19 (15.79%)	2 / 19 (10.53%)
occurrences (all)	0	3	2
Acne			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Angioedema			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Eczema			

subjects affected / exposed	2 / 24 (8.33%)	3 / 19 (15.79%)	2 / 19 (10.53%)
occurrences (all)	2	3	2
Pruritus			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
Blister			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Plantar fasciitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	2 / 19 (10.53%)
occurrences (all)	1	3	3
Kyphosis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Arthralgia			
subjects affected / exposed	11 / 24 (45.83%)	5 / 19 (26.32%)	5 / 19 (26.32%)
occurrences (all)	21	9	13
Fibromyalgia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Lordosis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Arthritis			

subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	2 / 19 (10.53%)
occurrences (all)	1	1	3
Foot deformity			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Juvenile idiopathic arthritis			
subjects affected / exposed	3 / 24 (12.50%)	0 / 19 (0.00%)	2 / 19 (10.53%)
occurrences (all)	3	0	2
Neck pain			
subjects affected / exposed	1 / 24 (4.17%)	3 / 19 (15.79%)	3 / 19 (15.79%)
occurrences (all)	1	3	5
Spinal disorder			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Still's disease			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	3 / 19 (15.79%)
occurrences (all)	0	1	3
Coccydynia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Torticollis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Osteochondrosis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	2 / 24 (8.33%)	2 / 19 (10.53%)	2 / 19 (10.53%)
occurrences (all)	3	3	3
Myalgia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Joint effusion			

subjects affected / exposed	2 / 24 (8.33%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	4	1	0
Costochondritis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Polyarthritis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	3 / 24 (12.50%)	1 / 19 (5.26%)	1 / 19 (5.26%)
occurrences (all)	8	1	3
Osteoarthritis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Pharyngotonsillitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Candida infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	1 / 24 (4.17%)	3 / 19 (15.79%)	2 / 19 (10.53%)
occurrences (all)	1	4	3
Gingivitis			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	1 / 24 (4.17%)	2 / 19 (10.53%)	2 / 19 (10.53%)
occurrences (all)	1	2	2

Paronychia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Otitis media acute			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	2
Furuncle			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Varicella			
subjects affected / exposed	3 / 24 (12.50%)	1 / 19 (5.26%)	1 / 19 (5.26%)
occurrences (all)	4	1	1
Localised infection			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	2 / 19 (10.53%)
occurrences (all)	1	1	2
Gastroenteritis viral			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Skin infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
Pharyngitis bacterial			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Lower respiratory tract infection			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Nasopharyngitis			
subjects affected / exposed	10 / 24 (41.67%)	10 / 19 (52.63%)	5 / 19 (26.32%)
occurrences (all)	18	32	18
Enteritis infectious			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Vulvovaginitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Post procedural infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Viral rash			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Erythema infectiosum			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
Gastroenteritis			
subjects affected / exposed	11 / 24 (45.83%)	1 / 19 (5.26%)	2 / 19 (10.53%)
occurrences (all)	15	1	2
Upper respiratory tract infection			
subjects affected / exposed	4 / 24 (16.67%)	4 / 19 (21.05%)	9 / 19 (47.37%)
occurrences (all)	4	11	20
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Conjunctivitis			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
Sinusitis			
subjects affected / exposed	1 / 24 (4.17%)	4 / 19 (21.05%)	0 / 19 (0.00%)
occurrences (all)	2	6	0
Tonsillitis			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	1 / 19 (5.26%)
occurrences (all)	1	2	2
Otitis media chronic			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0

Urinary tract infection			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Infected cyst			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	2
Respiratory tract infection			
subjects affected / exposed	4 / 24 (16.67%)	2 / 19 (10.53%)	0 / 19 (0.00%)
occurrences (all)	4	3	0
Bronchitis			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	2 / 19 (10.53%)
occurrences (all)	1	1	3
Rhinovirus infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	4 / 24 (16.67%)	2 / 19 (10.53%)	5 / 19 (26.32%)
occurrences (all)	8	2	10
Tooth abscess			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal viral infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	5	0	1
Epstein-Barr virus infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

Oral herpes			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	5	0
Molluscum contagiosum			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	3
Herpangina			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Lice infestation			
subjects affected / exposed	1 / 24 (4.17%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Influenza			
subjects affected / exposed	4 / 24 (16.67%)	2 / 19 (10.53%)	3 / 19 (15.79%)
occurrences (all)	4	10	5
Impetigo			
subjects affected / exposed	3 / 24 (12.50%)	1 / 19 (5.26%)	1 / 19 (5.26%)
occurrences (all)	3	2	1
Otitis media			
subjects affected / exposed	3 / 24 (12.50%)	0 / 19 (0.00%)	3 / 19 (15.79%)
occurrences (all)	3	0	3
Pharyngitis			
subjects affected / exposed	2 / 24 (8.33%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Tooth infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	1 / 24 (4.17%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hypoglycaemia			

subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 19 (5.26%)	1 / 19 (5.26%)
occurrences (all)	0	4	1
Iron deficiency			
subjects affected / exposed	0 / 24 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	SC TCZ 162 mg Q2W (>= 30 kg) pJIA		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Surgical and medical procedures			
Sinus operation			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Tooth extraction			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Swelling			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Drug intolerance			

subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Injection site urticaria				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	15			
Injection site pruritus				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Injection site warmth				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Chest pain				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Fatigue				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	3			
Injection site erythema				
subjects affected / exposed	4 / 20 (20.00%)			
occurrences (all)	38			
Injection site bruising				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Mass				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Injection site swelling				
subjects affected / exposed	3 / 20 (15.00%)			
occurrences (all)	8			
Asthenia				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Injection site pain				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Pain				

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Illness			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Injection site reaction			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Injection site haematoma			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Injection site induration			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Swelling face			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Dust allergy			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Allergy to arthropod bite			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Drug hypersensitivity			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		

Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Heavy menstrual bleeding			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Intermenstrual bleeding			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Vulvovaginal erythema			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Menstruation irregular			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Laryngeal inflammation			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Tonsillolith			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	6 / 20 (30.00%)		
occurrences (all)	8		
Pharyngeal ulceration			

subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Mood swings			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Anxiety			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Suicidal ideation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Learning disorder			

subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Depressed mood			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Blood triglycerides increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Salivary gland scan abnormal			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
White blood cell count decreased			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Haematocrit decreased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
White blood cell count increased			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Body temperature increased			

subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Chlamydia test positive			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Hepatic enzyme increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Platelet count decreased			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Skin injury			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Injury			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Nail injury			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Thermal burn			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Wrist fracture			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Hand fracture			

subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Contusion				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Induced abortion failed				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Joint injury				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Muscle strain				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Limb injury				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Arthropod bite				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences (all)	2			
Limb fracture				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Wound				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Ligament sprain				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Traumatic haematoma				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Ear injury				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Skin laceration				

subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Scratch subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Fall subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Pelvic bone injury subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Arthropod sting subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Upper limb fracture subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Headache subjects affected / exposed occurrences (all)	5 / 20 (25.00%) 14		
Paraesthesia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Syncope subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Leukopenia			

subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Monocytopenia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Lymphadenitis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Increased tendency to bruise			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Tympanic membrane perforation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Ear pain			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Eye disorders			
Ulcerative keratitis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Conjunctivitis allergic			

subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Myopia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Photophobia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Tongue ulceration			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	6		
Dental discomfort			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	14		
Eructation			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Oral pain			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Odynophagia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

Gastritis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Vomiting subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 6		
Dental caries subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Abdominal pain subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 3		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3		
Flatulence subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Mouth ulceration subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Chapped lips subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Salivary gland mucocoele subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Aphthous ulcer subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 5		
Constipation subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Hepatobiliary disorders Hypertransaminasaemia			

subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Papule			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Pseudoporphyria			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Dermatitis allergic			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Acne			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Angioedema			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Blister			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		

Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Plantar fasciitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Kyphosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Musculoskeletal stiffness			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	18		
Fibromyalgia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Lordosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Arthritis			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	4		
Foot deformity			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Juvenile idiopathic arthritis			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	4		
Neck pain			

subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Spinal disorder				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Still's disease				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Coccydynia				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Torticollis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Musculoskeletal pain				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Osteochondrosis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Pain in extremity				
subjects affected / exposed	3 / 20 (15.00%)			
occurrences (all)	5			
Myalgia				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Joint effusion				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Costochondritis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Polyarthritis				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences (all)	2			
Groin pain				

subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	5		
Osteoarthritis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Pharyngotonsillitis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Candida infection			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Gingivitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Viral infection			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Paronychia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Otitis media acute			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Furuncle			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		

Varicella				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Localised infection				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Gastroenteritis viral				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Skin infection				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Cystitis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	2			
Pharyngitis bacterial				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	9 / 20 (45.00%)			
occurrences (all)	22			
Enteritis infectious				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Vulvovaginitis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Post procedural infection				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Viral rash				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			

Erythema infectiosum				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Gastroenteritis				
subjects affected / exposed	3 / 20 (15.00%)			
occurrences (all)	3			
Upper respiratory tract infection				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences (all)	3			
Hand-foot-and-mouth disease				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Conjunctivitis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Sinusitis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	2			
Tonsillitis				
subjects affected / exposed	5 / 20 (25.00%)			
occurrences (all)	5			
Otitis media chronic				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Urinary tract infection				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences (all)	2			
Infected cyst				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Pharyngitis streptococcal				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences (all)	2			

Respiratory tract infection				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Bronchitis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	2			
Rhinovirus infection				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Ear infection				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Tooth abscess				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Gastrointestinal viral infection				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Vulvovaginal candidiasis				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Viral upper respiratory tract infection				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Epstein-Barr virus infection				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Oral herpes				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Molluscum contagiosum				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Herpangina				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			

Lice infestation subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Influenza subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Impetigo subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Otitis media subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 3		
Pharyngitis subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 4		
Tooth infection subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Metabolism and nutrition disorders Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Hypertriglyceridaemia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Hypoglycaemia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Iron deficiency subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 May 2014	Updates to post-trial access, reasons for discontinuation, and exclusion criteria
23 November 2015	Updates to dosing regimen and eligibility criteria
23 June 2017	Updates to treatment period and sample collection

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated 1 year earlier than planned for operational reasons. At the time of termination, 7 patients were remaining, all within the final year of study participation. They were able to continue treatment following study termination.

Notes: