Clinical trial results:
An Open-label, Sequential, Ascending, Repeated Dose-finding Study of Sarilumab, Administered with Subcutaneous (SC) Injection, in Children and Adolescents, Aged 2 to 17 Years, with Polyarticular-course Juvenile Idiopathic Arthritis (pcJIA) Followed by an Extension Phase

Summary

EudraCT number	2015-003999-79
Trial protocol	GB IT CZ ES Outside EU/EEA EE FI NL PL DE FR
Global end of trial date	28 December 2023

Results information

Result version number	v1
This version publication date	10 July 2024
First version publication date	10 July 2024

Trial information

Trial identification

Sponsor protocol code	DRI13925

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02776735
WHO universal trial number (UTN)	U1111-1177-3487

Notes:

Sponsors

Sponsor organisation name	Sanofi-Aventis Recherche & Développement
Sponsor organisation address	82 Avenue Raspail, Gentilly, France, 94250
Public contact	Trial Transparency Team, Sanofi-Aventis Recherche & Developpement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi-Aventis Recherche & Developpement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001045-PIP01-10
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the Pharmacokinetic (PK) profile of sarilumab in participants aged 2 to 17 years with polyarticular-course Juvenile Idiopathic Arthritis (pcJIA) in order to identify the dose and regimen for adequate treatment of this population.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric patients. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parents(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 9
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	Finland: 1
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 15
Country: Number of subjects enrolled	Russian Federation: 25
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 2

Worldwide total number of subjects	102
EEA total number of subjects	52

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)	63
Adolescents (12-17 years)	39
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 29 centers in 15 countries. A total of 118 participants were screened from 06 September 2016 and 20 December 2021, of which 16 were screen failures. The main reasons for screen failure were based on criteria for exclusion from the study.

Pre-assignment

Screening details:

A total of 102 participants were enrolled in the study. The dose was capped at 150 milligram (mg) and 200 mg for Cohorts 1 and 3 and Cohort 2, respectively. Cohort 2 was selected dose treatment regimen and participants enrolled directly in selected dose (portions 2 and 3) didn't have upper body weight limit.

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	Cohort 1: >= 30 kg and <= 60 kg

Arm description:

Participants with body weight >= 30 kilograms (kg) and <= 60 kg received sarilumab 2 mg/kg subcutaneous (SC) injection once every other week (q2w) for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

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

Dosage and administration details:

Sarilumab 2 mg/kg q2w was administered SC in 1 of the 4 quadrants of the abdomen or thigh when self injected or also in the upper arm (lateral side) if administered by a professional or a nonprofessional caregiver.

Arm title	Cohort 1: < 30 kg and >= 10 kg

Arm description:

Participants with body weight < 30 kg and >= 10 kg received sarilumab 2.5 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

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

Dosage and administration details:

Sarilumab 2.5 mg/kg q2w was administered SC in 1 of the 4 quadrants of the abdomen or thigh when self injected or also in the upper arm (lateral side) if administered by a professional or a nonprofessional caregiver.

Arm title	Cohort 2: >= 30 kg and <= 60 kg

Arm description:

Participants with body weight >= 30 kg and <= 60 kg received sarilumab 3 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

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

Dosage and administration details:

Sarilumab 3 mg/kg q2w was administered SC in 1 of the 4 quadrants of the abdomen or thigh when self injected or also in the upper arm (lateral side) if administered by a professional or a nonprofessional caregiver.

Arm title	Cohort 2: < 30 kg and >= 10 kg

Arm description:

Participants with body weight < 30 kg and >= 10 kg received sarilumab 4 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 4 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

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

Dosage and administration details:

Sarilumab 4 mg/kg q2w was administered SC in 1 of the 4 quadrants of the abdomen or thigh when self injected or also in the upper arm (lateral side) if administered by a professional or a nonprofessional caregiver.

Arm title	Cohort 3: >= 30 kg and <= 60 kg

Arm description:

Participants with body weight >= 30 kg and <= 60 kg received sarilumab 2 mg/kg SC injection once every week (qw) for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

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

Dosage and administration details:

Sarilumab 2 mg/kg qw was administered SC in 1 of the 4 quadrants of the abdomen or thigh when self injected or also in the upper arm (lateral side) if administered by a professional or a nonprofessional caregiver.

Arm title	Cohort 3: < 30 kg and >= 10 kg

Arm description:

Participants with body weight < 30 kg and >= 10 kg received sarilumab 2.5 mg/kg SC injection qw for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

Arm type	Experimental

Investigational medicinal product name	Sarilumab
Investigational medicinal product code	
Other name	Kevzara®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Sarilumab 2.5 mg/kg qw was administered SC in 1 of the 4 quadrants of the abdomen or thigh when self injected or also in the upper arm (lateral side) if administered by a professional or a nonprofessional caregiver.

Number of subjects in period 1[1]	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 2: >= 30 kg and <= 60 kg
Started	7	6	42
Completed	6	6	38
Not completed	1	0	4
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	-	-	-
Unspecified	-	-	2
Lost to follow-up	-	-	-
Withdrawal by parent/guardian	-	-	2

Number of subjects in period 1[1]	Cohort 2: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Started	31	6	9
Completed	27	6	7
Not completed	4	0	2
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	1	-	1
Unspecified	-	-	-
Lost to follow-up	1	-	-
Withdrawal by parent/guardian	2	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Only treated participants included.

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: >= 30 kg and <= 60 kg
Reporting group description:	
Participants with body weight >= 30 kilograms (kg) and <= 60 kg received sarilumab 2 mg/kg subcutaneous (SC) injection once every other week (q2w) for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).	
Reporting group title	Cohort 1: < 30 kg and >= 10 kg
Reporting group description:	
Participants with body weight < 30 kg and >= 10 kg received sarilumab 2.5 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).	
Reporting group title	Cohort 2: >= 30 kg and <= 60 kg
Reporting group description:	
Participants with body weight >= 30 kg and <= 60 kg received sarilumab 3 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).	
Reporting group title	Cohort 2: < 30 kg and >= 10 kg
Reporting group description:	
Participants with body weight < 30 kg and >= 10 kg received sarilumab 4 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 4 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).	
Reporting group title	Cohort 3: >= 30 kg and <= 60 kg
Reporting group description:	
Participants with body weight >= 30 kg and <= 60 kg received sarilumab 2 mg/kg SC injection once every week (qw) for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).	
Reporting group title	Cohort 3: < 30 kg and >= 10 kg
Reporting group description:	
Participants with body weight < 30 kg and >= 10 kg received sarilumab 2.5 mg/kg SC injection qw for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).	

Reporting group values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 2: >= 30 kg and <= 60 kg
Number of subjects	7	6	42
Age categorical			
Units:			

Age Continuous			
Units: years			
arithmetic mean	12.3	6.5	12.6
standard deviation	± 3.3	± 3.2	± 3.0
Sex: Female, Male			
Units: participants			
Female	5	5	35
Male	2	1	7

Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	6	3	39
Not Reported	0	1	2
Unknown	1	2	0

Reporting group values	Cohort 2: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Number of subjects	31	6	9
Age categorical Units:			

Age Continuous Units: years			
arithmetic mean	5.4	13.7	4.8
standard deviation	± 3.1	± 3.0	± 2.4
Sex: Female, Male Units: participants			
Female	23	3	6
Male	8	3	3
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	28	4	8
Not Reported	3	0	1
Unknown	0	2	0

Reporting group values	Total		
Number of subjects	101		
Age categorical Units:			

Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: participants			
Female	77		
Male	24		
Race Units: Subjects			
American Indian or Alaska Native	0		

Asian	1		
Black or African American	0		
Native Hawaiian or Other Pacific Islander	0		
White	88		
Not Reported	7		
Unknown	5		

End points

End points reporting groups

Reporting group title	Cohort 1: >= 30 kg and <= 60 kg

Reporting group description:

Participants with body weight >= 30 kilograms (kg) and <= 60 kg received sarilumab 2 mg/kg subcutaneous (SC) injection once every other week (q2w) for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

Reporting group title	Cohort 1: < 30 kg and >= 10 kg

Reporting group description:

Participants with body weight < 30 kg and >= 10 kg received sarilumab 2.5 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

Reporting group title	Cohort 2: >= 30 kg and <= 60 kg

Reporting group description:

Participants with body weight >= 30 kg and <= 60 kg received sarilumab 3 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

Reporting group title	Cohort 2: < 30 kg and >= 10 kg

Reporting group description:

Participants with body weight < 30 kg and >= 10 kg received sarilumab 4 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 4 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

Reporting group title	Cohort 3: >= 30 kg and <= 60 kg

Reporting group description:

Participants with body weight >= 30 kg and <= 60 kg received sarilumab 2 mg/kg SC injection once every week (qw) for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

Reporting group title	Cohort 3: < 30 kg and >= 10 kg

Reporting group description:

Participants with body weight < 30 kg and >= 10 kg received sarilumab 2.5 mg/kg SC injection qw for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

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

End point title	Maximum Serum Concentration (Cmax) at Steady State of Sarilumab[1]

End point description:

The Cmax was defined as maximum serum concentration. The PK analysis set included all participants in the safety population with at least 1 post-dose, non-missing serum concentration value. Only participants with data collected are reported.

End point type	Primary

End point timeframe:

Pre-dose on Days 1, 3, 5, 8, 12 and Weeks 2, 4, 8 and 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	39	24
Units: milligram per liter (mg/L)				
arithmetic mean (standard deviation)	11.1 (± 4.82)	14.0 (± 2.97)	27.1 (± 11.6)	40.4 (± 7.77)

End point values	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: milligram per liter (mg/L)				
arithmetic mean (standard deviation)	37.6 (± 8.52)	28.9 (± 5.32)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Serum Concentration Versus Time Curve Using the Trapezoidal Method During a Dose Interval (AUC0-t) at Steady State of Sarilumab

End point title	Area Under the Serum Concentration Versus Time Curve Using the Trapezoidal Method During a Dose Interval (AUC0-t) at Steady State of Sarilumab[2]

End point description:

The AUC0-t was defined as area under the concentration in serum versus time curve calculated using the trapezoidal method during a dose interval (tau). The PK analysis set included all participants in the safety population with at least 1 post-dose, non-missing serum concentration value. Only participants with data collected are reported.

End point type	Primary

End point timeframe:

Pre-dose on Days 1, 3, 5, 8, 12 and Weeks 2, 4, 8 and 12

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	39	24
Units: day*mg/L				
arithmetic mean (standard deviation)	90.7 (± 30.8)	110 (± 40.9)	276 (± 121)	395 (± 101)

End point values	Cohort 3: >= 30 kg and <=	Cohort 3: < 30 kg and >= 10		

	60 kg	kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: day*mg/L				
arithmetic mean (standard deviation)	235 (± 60.9)	176 (± 32.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentration Before Treatment Administration During Repeated Dosing (Ctrough) at Steady State of Sarilumab

End point title	Concentration Before Treatment Administration During Repeated Dosing (Ctrough) at Steady State of Sarilumab[3]

End point description:

The Ctrough was defined as concentration observed before treatment administration during repeated dosing from baseline to Week 12. The PK analysis set included all participants in the safety population with at least 1 post-dose, non-missing serum concentration value. Only participants with data collected are reported.

End point type	Primary

End point timeframe:

Pre-dose on Days 1, 3, 5, 8, 12 and Weeks 2, 4, 8 and 12

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	39	24
Units: mg/L				
arithmetic mean (standard deviation)	1.36 (± 0.872)	1.39 (± 1.44)	9.57 (± 5.84)	14.4 (± 9.81)

End point values	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: mg/L				
arithmetic mean (standard deviation)	28.0 (± 9.06)	21.6 (± 5.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Change From Baseline in High-Sensitivity C-reactive Protein (hs-CRP) at Week 12

End point title	Cohorts 1 and 3: Change From Baseline in High-Sensitivity C-reactive Protein (hs-CRP) at Week 12[4]

End point description:

Serum concentrations of hs-CRP was determined to assess the Pharmacodynamic (PD) effects of sarilumab. All treated population included participants who signed informed consent and received at least 1 dose of the study treatment. Only participants analyzed at baseline and Week 12 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	6	9
Units: mg/L				
arithmetic mean (standard deviation)	-1.00 (± 2.53)	-0.52 (± 3.64)	-5.71 (± 8.90)	-6.83 (± 11.74)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Change From Baseline in High-Sensitivity C-reactive Protein at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Change From Baseline in High-Sensitivity C-reactive Protein at Weeks 12, 24, 48, 96, and 156[5]

End point description:

Serum concentrations of hs-CRP was determined to assess the PD effects of sarilumab. All treated population included participants who signed informed consent and received at least 1 dose of the study treatment. Here, n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	29		
Units: mg/L				
arithmetic mean (standard deviation)				
Week 12 (n= 40,29)	-3.54 (± 33.57)	-20.66 (± 48.35)		

Week 24 (n= 37,29)	-8.54 (± 19.17)	-11.72 (± 23.54)		
Week 48 (n= 38,27)	-9.93 (± 21.60)	-12.57 (± 24.23)		
Week 96 (n= 36,23)	-9.39 (± 21.65)	-13.88 (± 25.96)		
Week 156 (n= 16,16)	-5.10 (± 14.68)	-12.30 (± 26.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Interleukin-6 (IL-6) at Week 12

End point title	Change From Baseline in Interleukin-6 (IL-6) at Week 12

End point description:

Serum concentrations of IL-6 was determined to assess the PD effects of sarilumab. All treated population included participants who signed informed consent and received at least 1 dose of the study treatment. Only participants with data collected at Baseline and Week 12 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	30	20
Units: nanogram (ng)/L				
arithmetic mean (standard deviation)	1.27 (± 9.79)	13.65 (± 18.20)	43.71 (± 113.42)	11.36 (± 35.81)

End point values	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: nanogram (ng)/L				
arithmetic mean (standard deviation)	66.21 (± 86.21)	9.20 (± 26.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Soluble Interleukin-6 Receptor (sIL-6R) at Week 12

End point title	Change From Baseline in Total Soluble Interleukin-6 Receptor (sIL-6R) at Week 12

End point description:

Serum concentrations of sIL-6R was determined to assess the PD effects of sarilumab. All treated population included participants who signed informed consent and received at least 1 dose of the study treatment. Only participants with data collected at Baseline and Week 12 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	33	28
Units: ng/mL				
arithmetic mean (standard deviation)	40.09 (± 49.75)	101.50 (± 129.59)	316.77 (± 129.29)	388.33 (± 185.82)

End point values	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: ng/mL				
arithmetic mean (standard deviation)	535.76 (± 98.12)	582.95 (± 149.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology (JIA ACR) 30 Response at Week 12

End point title	Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology (JIA ACR) 30 Response at Week 12[6]

End point description:

JIA ACR30 response was defined as a participant with at least 3 out of the 6 JIA core set variables with >= 30% improvement from baseline with no more than 1 of the remaining variables worsened by >= 30%. The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	5
Units: percentage of participants with response				
number (not applicable)	100	100	100	100

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 30 Response at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 30 Response at Weeks 12, 24, 48, 96, and 156[7]

End point description:

JIA ACR30 response was defined as a participant with at least 3 out of the 6 JIA core set variables with >= 30% improvement from baseline with no more than 1 of the remaining variables worsened by >= 30%. The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 48, 96, and 156

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	29		
Units: percentage of participants with response				
number (not applicable)				
Week 12 (n= 39,29)	100	100		
Week 24 (n= 39,27)	100	100		
Week 48 (n= 38,26)	100	100		
Week 96 (n= 36,24)	97.2	100		
Week 156 (n= 17,16)	94.1	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 50 Response at Week 12

End point title	Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 50 Response at Week 12[8]

End point description:

JIA ACR50 response was defined as a participant with at least 3 out of the 6 JIA core set variables with >= 50% improvement from baseline with no more than 1 of the remaining variables worsened by >= 30%. The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	5
Units: percentage of participants with response				
number (not applicable)	80.0	100	100	100

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 50 Response at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 50 Response at Weeks 12, 24, 48, 96, and 156[9]

End point description:

JIA ACR50 response was defined as a participant with at least 3 out of the 6 JIA core set variables with >= 50% improvement from baseline with no more than 1 of the remaining variables worsened by >= 30%. The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 48, 96, and 156

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	29		
Units: percentage of participants with response				
number (not applicable)				
Week 12 (n= 39,29)	94.9	96.6		
Week 24 (n= 39,27)	100	100		
Week 48 (n= 38,26)	100	100		
Week 96 (n= 36,24)	97.2	100		
Week 156 (n= 17,16)	94.1	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 70 Response at Week 12

End point title	Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 70 Response at Week 12[10]

End point description:

JIA ACR70 response was defined as a participant with at least 3 out of the 6 JIA core set variables with >= 70% improvement from baseline with no more than 1 of the remaining variables worsened by >= 30%. The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	5
Units: percentage of participants with response				
number (not applicable)	60.0	40.0	100	100

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 70 Response at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 70 Response at Weeks 12, 24, 48, 96, and 156[11]

End point description:

JIA ACR70 response was defined as a participant with at least 3 out of the 6 JIA core set variables with >= 70% improvement from baseline with no more than 1 of the remaining variables worsened by >= 30%. The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 48, 96, and 156

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	29		
Units: percentage of participants with response				
number (not applicable)				
Week 12 (n= 39,29)	74.4	89.7		
Week 24 (n= 39,27)	87.2	96.3		
Week 48 (n= 38,26)	89.5	100		
Week 96 (n= 36,24)	97.2	100		
Week 156 (n= 17,16)	94.1	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 90 Response at Week 12

End point title	Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 90 Response at Week 12[12]

End point description:

JIA ACR90 response was defined as a participant with at least 3 out of the 6 JIA core set variables with >= 90% improvement from baseline with no more than 1 of the remaining variables worsened by >= 30%. The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	5
Units: percentage of participants with response				
number (not applicable)	60.0	20.0	66.7	60.0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 90 Response at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 90 Response at Weeks 12, 24, 48, 96, and 156[13]

End point description:

JIA ACR90 response was defined as a participant with at least 3 out of the 6 JIA core set variables with >= 90% improvement from baseline with no more than 1 of the remaining variables worsened by >= 30%. The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 48, 96, and 156

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	29		
Units: percentage of participants with response				
number (not applicable)				
Week 12 (n= 39,29)	43.6	48.3		
Week 24 (n= 39,27)	64.1	74.1		
Week 48 (n= 38,26)	68.4	88.5		
Week 96 (n= 36,24)	80.6	95.8		
Week 156 (n= 17,16)	76.5	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopatic

Arthritis American College of Rheumatology 100 Response at Week 12

End point title	Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 100 Response at Week 12[14]

End point description:

JIA ACR100 response was defined as a participant with at least 3 out of the 6 JIA core set variables with >= 100% improvement from baseline with no more than 1 of the remaining variables worsened by >= 30%. The efficacy analysis set included all participants who received at least 1dose of sarilumab.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	5
Units: percentage of participants with response				
number (not applicable)	0	0	33.3	40.0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 100 Response at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Percentage of Participants With Juvenile Idiopatic Arthritis American College of Rheumatology 100 Response at Weeks 12, 24, 48, 96, and 156[15]

End point description:

JIA ACR100 response was defined as a participant with at least 3 out of the 6 JIA core set variables with >= 100% improvement from baseline with no more than 1 of the remaining variables worsened by >= 30%. The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 48, 96, and 156

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	29		
Units: percentage of participants with response				
number (not applicable)				
Week 12 (n= 39,29)	12.8	24.1		
Week 24 (n= 39,27)	23.1	48.1		
Week 48 (n= 38,26)	42.1	53.8		
Week 96 (n= 36,24)	47.2	70.8		
Week 156 (n= 17,16)	52.9	87.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Activity Joint Count-71, at Week 12

End point title	Cohorts 1 and 3: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Activity Joint Count-71, at Week 12[16]

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using visual analog scale (VAS), Childhood Health Questionnaire Disability Index (CHAQ-DI) and hs-CRP. Activity joint count-71 was calculated as sum (joints with active arthritis)*(71/number of joints with assessment). The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	5
Units: joint				
arithmetic mean (standard error)	-14.40 (± 2.159)	-11.20 (± 2.871)	-16.50 (± 4.137)	-14.40 (± 5.573)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Activity Joint Count-71, at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Activity Joint Count-71, at Weeks 12, 24, 48, 96, and 156[17]

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Activity joint count-71 was calculated as sum (joints with active arthritis)*(71/number of joints with assessment). The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	29		
Units: joint				
arithmetic mean (standard error)				
Week 12 (n= 39,29)	-15.15 (± 1.511)	-12.38 (± 1.519)		
Week 24 (n= 39,27)	-16.66 (± 1.497)	-13.26 (± 1.575)		
Week 48 (n= 38,26)	-17.24 (± 1.547)	-13.73 (± 1.618)		
Week 96 (n= 36,24)	-16.47 (± 1.682)	-13.79 (± 1.751)		
Week 156 (n= 17,16)	-18.65 (± 2.334)	-13.88 (± 2.495)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Limited Motion Joint Count, at Week 12

End point title	Cohorts 1 and 3: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Limited Motion Joint Count, at Week 12[18]

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Limited motion joint count was calculated as sum (joints with limited motion)*(67/number of joints with assessment). The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[18] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	5
Units: joint				
arithmetic mean (standard error)	-7.80 (± 2.083)	-5.80 (± 2.267)	-7.83 (± 2.600)	-13.00 (± 4.219)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Limited Motion Joint Count, at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Limited Motion Joint Count, at Weeks 12, 24, 48, 96, and 156[19]

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Limited motion joint count was calculated as sum (joints with limited motion)*(67/number of joints with assessment). The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

Notes:

[19] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	29		
Units: joint				
arithmetic mean (standard error)				
Week 12 (n= 39,29)	-9.71 (± 1.249)	-9.21 (± 1.540)		
Week 24 (n= 39,27)	-10.40 (± 1.330)	-10.63 (± 1.559)		

Week 48 (n= 38,26)	-10.99 (± 1.498)	-10.73 (± 1.525)		
Week 96 (n= 36,24)	-11.14 (± 1.661)	-10.42 (± 1.493)		
Week 156 (n= 17,16)	-11.29 (± 2.203)	-11.81 (± 2.550)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Childhood Health Assessment Questionnaire Disability Index, at Week 12

End point title	Cohorts 1 and 3: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Childhood Health Assessment Questionnaire Disability Index, at Week 12[20]

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. CHAQ questionnaire consists of 30 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities. Each domain is scored on a 4-point scale ranges from 0 to 3: 0 (without any difficulty), 1 (with some difficulty), 2 (with much difficulty) and 3 (unable to do). An additional response of "not applicable" is available to indicate participant is unable to perform activities. CHAQ-DI total score is sum of domain scores divided by number of domains that have a non-missing score. This overall score ranges from 0 (best) to 3 (worst). Higher scores indicate worse outcome. Efficacy population.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[20] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	5
Units: units on a scale				
arithmetic mean (standard error)	-0.80 (± 0.242)	-1.08 (± 0.239)	-0.42 (± 0.173)	-0.75 (± 0.213)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Childhood Health Assessment Questionnaire Disability Index, at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Childhood Health Assessment Questionnaire Disability Index, at Weeks 12, 24, 48, 96, and 156[21]

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. CHAQ questionnaire consists of 30 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities. Each domain is scored on a 4-point scale ranges from 0 to 3: 0 (without any difficulty), 1 (with some difficulty), 2 (with much difficulty) and 3 (unable to do). An additional response of "not applicable" is available to indicate participant is unable to perform activities. CHAQ-DI total score is sum of domain scores divided by number of domains that have a non-missing score. This overall score ranges from 0 (best) to 3 (worst). Higher scores indicate worse outcome. Efficacy population. n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

Notes:

[21] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	29		
Units: units on a scale				
arithmetic mean (standard error)				
Week 12 (n= 39,29)	-0.77 (± 0.092)	-0.74 (± 0.113)		
Week 24 (n= 39,27)	-0.90 (± 0.096)	-0.95 (± 0.132)		
Week 48 (n= 38,27)	-0.88 (± 0.084)	-1.08 (± 0.119)		
Week 96 (n= 36,24)	-0.92 (± 0.109)	-1.13 (± 0.136)		
Week 156 (n= 17,16)	-1.07 (± 0.163)	-1.20 (± 0.169)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, C-Reactive Protein, at Week 12

End point title	Cohorts 1 and 3: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, C-Reactive Protein, at Week 12[22]

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Serum concentrations of hs-CRP was determined to assess the PD effects of sarilumab. The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[22] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	5
Units: mg/L				
arithmetic mean (standard error)	-1.00 (± 1.130)	-1.67 (± 1.139)	-5.71 (± 3.633)	-2.54 (± 1.845)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, C-Reactive Protein, at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, C-Reactive Protein, at Weeks 12, 24, 48, 96, and 156[23]

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Serum concentrations of hs-CRP was determined to assess the PD effects of sarilumab. The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

Notes:

[23] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	29		
Units: mg/L				
arithmetic mean (standard error)				
Week 12 (n= 39,27)	-3.84 (± 5.437)	-20.66 (± 9.304)		
Week 24 (n= 37,29)	-8.54 (± 3.151)	-11.72 (± 4.371)		

Week 48 (n= 38,27)	-9.93 (± 3.505)	-12.57 (± 4.664)		
Week 96 (n= 36,23)	-9.39 (± 3.608)	-13.88 (± 5.414)		
Week 156 (n= 16,16)	-5.10 (± 3.671)	-12.30 (± 6.672)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Physician Global Assessment of Disease Activity, at Week 12

End point title	Cohorts 1 and 3: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Physician Global Assessment of Disease Activity, at Week 12[24]

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Physician global assessment of disease activity was assessed on an anchored 100 mm horizontal VAS score ranging from 0 to 100 where 0 is considered the best disease activity (no disease activity) and 100 the worst (most disease activity). Higher scores indicate worse outcome. The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[24] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	5
Units: units on a scale				
arithmetic mean (standard error)	-3.56 (± 0.969)	-6.30 (± 0.397)	-4.55 (± 0.509)	-5.68 (± 1.163)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Physician Global Assessment of Disease Activity, at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Physician Global Assessment of Disease Activity, at Weeks 12, 24, 48,

	96, and 156[25]

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Physician global assessment of disease activity was assessed on an anchored 100 mm horizontal VAS score ranging from 0 to 100 where 0 is considered the best disease activity (no disease activity) and 100 the worst (most disease activity). Higher scores indicate worse outcome. The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

Notes:

[25] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	29		
Units: units on a scale				
arithmetic mean (standard error)				
Week 12 (n= 39,29)	-4.50 (± 0.248)	-4.09 (± 0.367)		
Week 24 (n= 39,27)	-4.99 (± 0.237)	-5.01 (± 0.341)		
Week 48 (n= 38,26)	-5.27 (± 0.263)	-5.25 (± 0.321)		
Week 96 (n= 36,24)	-5.30 (± 0.306)	-5.35 (± 0.347)		
Week 156 (n= 17,16)	-5.66 (± 0.396)	-5.73 (± 0.437)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Participant/Parent Assessment of Overall Well-Being, at Week 12

End point title	Cohorts 1 and 3: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Participant/Parent Assessment of Overall Well-Being, at Week 12[26]

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Participant/parent assessment of overall well-being was rated on an anchored 100 mm horizontal VAS score ranging from 0 to 100 where 0 is considered the best disease activity (no disease activity) and 100 the worst (most disease activity). Higher scores indicate worse outcome. The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[26] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	5
Units: units on a scale				
arithmetic mean (standard error)	-3.30 (± 1.014)	-3.16 (± 1.364)	-3.05 (± 0.992)	-5.00 (± 0.969)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Participant/Parent Assessment of Overall Well-Being, at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Change From Baseline in Juvenile Idiopatic Arthritis American College of Rheumatology Component, Participant/Parent Assessment of Overall Well-Being, at Weeks 12, 24, 48, 96, and 156[27]

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Participant/parent assessment of overall well-being was rated on an anchored 100 mm horizontal VAS score ranging from 0 to 100 where 0 is considered the best disease activity (no disease activity) and 100 the worst (most disease activity). Higher scores indicate worse outcome. The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

Notes:

[27] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	29		
Units: units on a scale				
arithmetic mean (standard error)				
Week 12 (n= 39,29)	-3.73 (± 0.335)	-4.01 (± 0.435)		

Week 24 (n= 39,27)	-4.38 (± 0.313)	-4.39 (± 0.475)		
Week 48 (n= 38,27)	-4.21 (± 0.356)	-4.64 (± 0.510)		
Week 96 (n= 36,23)	-4.36 (± 0.387)	-5.09 (± 0.521)		
Week 156 (n= 17,16)	-4.19 (± 0.738)	-5.01 (± 0.636)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1 and 3: Mean Change From Baseline in Juvenile Arthritis Disease Activity Score (JADAS-27) at Week 12

End point title	Cohorts 1 and 3: Mean Change From Baseline in Juvenile Arthritis Disease Activity Score (JADAS-27) at Week 12[28]

End point description:

The JADAS is used for assessment of disease activity and it includes 4 measures (physician global assessment of disease activity, parent/participant global assessment of well-being, count of joints with active disease and index of inflammation). JADAS total score is calculated as sum of scores of its 4 components. Total score ranges from 0 to 10 where 0= no activity and 10= maximum activity. Higher scores indicate better outcome. JADAS-27 count includes a count of 27 joints (cervical spine, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints, hips, knees and ankles). Index of inflammation is determined by ESR or hs-CRP level. ESR normalized to 0-10 scale according to following formula: (ESR [mm/hour]20)/10. hs-CRP normalized to 0-10 scale according to following formula: (CRP [mg/L]10)/10. Clinical JADAS-27 is without CRP or ESR component. Efficacy population. Here, n= number of participants analyzed at baseline and Week 12 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[28] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	9
Units: units on a scale				
number (not applicable)				
JADAS-27-ESR: Week 12 (n=5,5,6,4)	-15.4	-19.1	-20.0	-19.4
JADAS-27-CRP: Week 12 (n=7,6,6,9)	-16.04	-18.06	-18.48	-21.08
Clinical JADAS-27: Week 12 (n=7,6,6,9)	-16.06	-18.06	-18.27	-21.08

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Mean Change From Baseline in Juvenile Arthritis Disease Activity Score at Weeks 12, 24, 48, 96, and 156

End point title	Cohort 2: Mean Change From Baseline in Juvenile Arthritis Disease Activity Score at Weeks 12, 24, 48, 96, and 156[29]

End point description:

The JADAS is used for assessment of disease activity and it includes 4 measures (physician global assessment of disease activity, parent/participant global assessment of well-being, count of joints with active disease and index of inflammation). JADAS total score is calculated as sum of scores of its 4 components. Total score ranges from 0 to 10 where 0= no activity and 10= maximum activity. Higher scores indicate better outcome. JADAS-27 count includes a count of 27 joints (cervical spine, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints, hips, knees and ankles). Index of inflammation is determined by ESR or hs-CRP level. ESR normalized to 0-10 scale according to following formula: (ESR [mm/hour]20)/10. hs-CRP normalized to 0-10 scale according to following formula: (CRP [mg/L]10)/10. Clinical JADAS-27 is without CRP or ESR component. Efficacy population. Here, n= number of participants analyzed at specific timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

Notes:

[29] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

End point values	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	31		
Units: units on a scale				
number (not applicable)				
JADAS-27-ESR: Week 12 (n= 37,29)	-18.9	-16.9		
JADAS-27-ESR: Week 24 (n= 39,24)	-21.9	-18.3		
JADAS-27-ESR: Week 48 (n= 38,26)	-22.3	-19.4		
JADAS-27-ESR: Week 96 (n= 36,22)	-22.4	-20.4		
JADAS-27-ESR: Week 156 (n= 16,14)	-23.2	-20.6		
JADAS-27-CRP: Week 12 (n= 42,31)	-18.23	-16.31		
JADAS-27-CRP: Week 24 (n= 42,31)	-20.92	-18.84		
JADAS-27-CRP: Week 48 (n= 42,31)	-21.65	-19.44		
JADAS-27-CRP: Week 96 (n= 42,31)	-21.90	-20.06		
JADAS-27-CRP: Week 156 (n= 42,31)	-21.79	-20.21		
Clinical JADAS-27: Week 12 (n= 42,31)	-17.93	-15.99		
Clinical JADAS-27: Week 24 (n= 42,31)	-20.47	-17.96		
Clinical JADAS-27: Week 48 (n= 42,31)	-20.98	-18.77		
Clinical JADAS-27: Week 96 (n= 42,31)	-21.21	-19.46		
Clinical JADAS-27: Week 156 (n= 42,31)	-21.21	-19.31		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events

(TEAEs) and Treatment Emergent Serious Adverse Events (SAEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (SAEs)

End point description:

An adverse events (AEs) is any untoward medical occurrence in a participant or in a clinical investigation participant administered a medicinal product and which does not necessarily have a causal relationship with the study treatment. An SAE is any untoward medical occurrence that at any dose results in death or is life-threatening or requires inpatient hospitalization or prolongation of existing hospitalization or results in persistent or significant disability/incapacity or is a congenital anomaly/birth defect or is an important medical event. TEAEs are defined as AEs that develop or worsen during the on-treatment period [that is, from the time of first dose of study treatment up to 6 weeks after the last administration of the study treatment]. The Safety analysis set included all participants who received at least 1 dose or part of a dose of the study treatment, analyzed according to the treatment actually received.

End point type	Secondary

End point timeframe:

From the first administration of study treatment (Day 1) up to end of treatment period, maximum of 156 weeks for portions 1 and 2 and 96 weeks for portion 3

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	42	31
Units: participants				
Any TEAE	7	6	40	30
Any treatment emergent SAE	2	0	3	3

End point values	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	9		
Units: participants				
Any TEAE	5	9		
Any treatment emergent SAE	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Local Site Reactions

End point title	Number of Participants With Local Site Reactions

End point description:

Participants were observed for at least 30 minutes after each study treatment administration either on site or at home and any local reactions were noted in the diary regardless of being clinically significant. The Safety analysis set included all participants who received at least 1 dose or part of a dose of the study treatment, analyzed according to the treatment actually received.

End point type	Secondary

End point timeframe:

From the first administration of study treatment (Day 1) up to end of treatment period, maximum of 156 weeks for portions 1 and 2 and 96 weeks for portion 3

End point values	Cohort 1: >= 30 kg and <= 60 kg	Cohort 1: < 30 kg and >= 10 kg	Cohort 2: >= 30 kg and <= 60 kg	Cohort 2: < 30 kg and >= 10 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	42	31
Units: participants	1	0	21	19

End point values	Cohort 3: >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	9		
Units: participants	3	1		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

From the first administration of study treatment (Day 1) up to end of treatment period, maximum of 156 weeks for portions 1 and 2 and 96 weeks for portion 3.

Adverse event reporting additional description:

Analysis was performed on the safety analysis set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Cohort 1: >= 30 kg and <= 60 kg

Reporting group description:

Participants with body weight >= 30 kg and <= 60 kg received sarilumab 2 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

Reporting group title	Cohort 2 (from Baseline): >= 30 kg and <= 60 kg

Reporting group description:

Participants with body weight >= 30 kg and <= 60 kg received sarilumab 3 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1).

Reporting group title	Cohort 3: < 30 kg and >= 10 kg

Reporting group description:

Participants with body weight < 30 kg and >= 10 kg received sarilumab 2.5 mg/kg SC injection qw for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

Reporting group title	Cohort 1: < 30 kg and >= 10 kg

Reporting group description:

Participants with body weight < 30 kg and >= 10 kg received sarilumab 2.5 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

Reporting group title	Cohort 2 (from Baseline): < 30 kg and >= 10 kg

Reporting group description:

Participants with body weight < 30 kg and >= 10 kg received sarilumab 4 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1).

Reporting group title	Cohort 2(Post dose-adjustment from Dose 1): <30 kg and >=10 kg

Reporting group description:

Participants with body weight < 30 kg and >= 10 kg received sarilumab 4 mg/kg SC injection q2w for 144 weeks in portion 2.

Reporting group title	Cohort 2(Post dose-adjustment from Dose 3): <30 kg and >=10 kg

Reporting group description:

Participants with body weight < 30 kg and >= 10 kg received sarilumab 4 mg/kg SC injection q2w for 84 weeks in portion 3.

Reporting group title	Cohort 2(Post dose-adjustment from Dose 3):>=30 kg and <=60 kg

Reporting group description:

Participants with body weight >= 30 kg and <= 60 kg received sarilumab 3 mg/kg SC injection q2w for 84 weeks in portion 3.

Reporting group title	Cohort 2(Post dose-adjustment from Dose 1):>=30 kg and <=60 kg

Reporting group description:

Participants with body weight >= 30 kg and <= 60 kg received sarilumab 3 mg/kg SC injection q2w for 144 weeks in portion 2.

Reporting group title	Cohort 3: >= 30 kg and <= 60 kg

Reporting group description:

Participants with body weight >= 30 kg and <= 60 kg received sarilumab 2 mg/kg SC injection qw for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

Serious adverse events	Cohort 1: >= 30 kg and <= 60 kg	Cohort 2 (from Baseline): >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	3 / 42 (7.14%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Ligament Rupture			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (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
Meniscus Injury			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (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			
Syncope			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (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
Gastrointestinal disorders			
Inguinal Hernia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (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
Pancreatic Pseudocyst			

subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (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
Pancreatitis Acute			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (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
Respiratory, thoracic and mediastinal disorders			
Tonsillar Hypertrophy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (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
Musculoskeletal and connective tissue disorders			
Juvenile Idiopathic Arthritis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (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
Infections and infestations			
Acute Sinusitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (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
Infectious Mononucleosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (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
Bone Tuberculosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (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	Cohort 1: < 30 kg and >= 10 kg	Cohort 2 (from Baseline): < 30 kg and >= 10 kg	Cohort 2(Post dose-adjustment from Dose 1): <30 kg and >=10 kg
Total subjects affected by serious			

adverse events			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Ligament Rupture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (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
Meniscus Injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (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
Gastrointestinal disorders			
Inguinal Hernia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (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
Pancreatic Pseudocyst			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (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
Pancreatitis Acute			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (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
Respiratory, thoracic and mediastinal disorders			
Tonsillar Hypertrophy			

subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (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
Musculoskeletal and connective tissue disorders			
Juvenile Idiopathic Arthritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (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			
Acute Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (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
Infectious Mononucleosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (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
Bone Tuberculosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (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

Serious adverse events	Cohort 2(Post dose-adjustment from Dose 3): <30 kg and >=10 kg	Cohort 2(Post dose-adjustment from Dose 3):>=30 kg and <=60 kg	Cohort 2(Post dose-adjustment from Dose 1):>=30 kg and <=60 kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Ligament Rupture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Meniscus Injury			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Gastrointestinal disorders			
Inguinal Hernia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Pancreatic Pseudocyst			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Pancreatitis Acute			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Respiratory, thoracic and mediastinal disorders			
Tonsillar Hypertrophy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Musculoskeletal and connective tissue disorders			
Juvenile Idiopathic Arthritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (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			
Acute Sinusitis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Infectious Mononucleosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Bone Tuberculosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (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	Cohort 3: >= 30 kg and <= 60 kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Ligament Rupture			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meniscus Injury			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Inguinal Hernia			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic Pseudocyst			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis Acute			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Tonsillar Hypertrophy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Juvenile Idiopathic Arthritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Acute Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infectious Mononucleosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone Tuberculosis			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 1: >= 30 kg and <= 60 kg	Cohort 2 (from Baseline): >= 30 kg and <= 60 kg	Cohort 3: < 30 kg and >= 10 kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	39 / 42 (92.86%)	9 / 9 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin Papilloma			
subjects affected / exposed	1 / 7 (14.29%)	1 / 42 (2.38%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Vascular disorders			
Essential Hypertension			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Administration Site Erythema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gait Disturbance			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injection Site Haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Injection Site Erythema			
subjects affected / exposed	1 / 7 (14.29%)	4 / 42 (9.52%)	0 / 9 (0.00%)
occurrences (all)	1	20	0
Injection Site Pruritus			

subjects affected / exposed	0 / 7 (0.00%)	3 / 42 (7.14%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Injection Site Urticaria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Injection Site Reaction			
subjects affected / exposed	0 / 7 (0.00%)	2 / 42 (4.76%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Immune system disorders			
Allergy To Arthropod Bite			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)	2 / 42 (4.76%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
Increased Bronchial Secretion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rhinitis Allergic			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	2 / 9 (22.22%)
occurrences (all)	0	1	3
Psychiatric disorders			
Affective Disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Major Depression			

subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood Pressure Systolic Decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood Bilirubin Increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 7 (0.00%)	2 / 42 (4.76%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 7 (14.29%)	5 / 42 (11.90%)	1 / 9 (11.11%)
occurrences (all)	1	6	1
Eosinophil Count Increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Lymphocyte Count Increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Monocyte Count Decreased			
subjects affected / exposed	0 / 7 (0.00%)	2 / 42 (4.76%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Mean Cell Volume Decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Transaminases Increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Neutrophil Count Decreased			

subjects affected / exposed	0 / 7 (0.00%)	2 / 42 (4.76%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Monocyte Count Increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 7 (0.00%)	4 / 42 (9.52%)	0 / 9 (0.00%)
occurrences (all)	0	5	0
Arthropod Bite			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Ligament Sprain			
subjects affected / exposed	1 / 7 (14.29%)	2 / 42 (4.76%)	0 / 9 (0.00%)
occurrences (all)	1	4	0
Hand Fracture			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	0 / 7 (0.00%)	3 / 42 (7.14%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Contusion			
subjects affected / exposed	1 / 7 (14.29%)	3 / 42 (7.14%)	0 / 9 (0.00%)
occurrences (all)	1	4	0
Thermal Burn			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Traumatic Haematoma			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Cardiovascular Disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 7 (0.00%)	2 / 42 (4.76%)	1 / 9 (11.11%)
occurrences (all)	0	4	2
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	3 / 7 (42.86%)	10 / 42 (23.81%)	6 / 9 (66.67%)
occurrences (all)	3	23	9
Lymphopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 7 (0.00%)	3 / 42 (7.14%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Eye disorders			
Keratitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Uveitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 7 (0.00%)	4 / 42 (9.52%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	3 / 42 (7.14%)	2 / 9 (22.22%)
occurrences (all)	0	3	2

Dental Discomfort			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Constipation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Aphthous Ulcer			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 7 (0.00%)	3 / 42 (7.14%)	0 / 9 (0.00%)
occurrences (all)	0	5	0
Pulpless Tooth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	3 / 42 (7.14%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
Mouth Ulceration			
subjects affected / exposed	1 / 7 (14.29%)	2 / 42 (4.76%)	0 / 9 (0.00%)
occurrences (all)	1	4	0
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	2 / 42 (4.76%)	1 / 9 (11.11%)
occurrences (all)	0	3	1
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pityriasis Alba			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dermatitis Allergic			

subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ingrowing Nail			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Acne			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Rash Pruritic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rash Papular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Skin Reaction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urticaria Chronic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Juvenile Idiopathic Arthritis			
subjects affected / exposed	1 / 7 (14.29%)	3 / 42 (7.14%)	0 / 9 (0.00%)
occurrences (all)	1	3	0
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 42 (4.76%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Pain In Extremity			

subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Acute Sinusitis			
subjects affected / exposed	0 / 7 (0.00%)	2 / 42 (4.76%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)	4 / 42 (9.52%)	2 / 9 (22.22%)
occurrences (all)	0	4	5
Covid-19			
subjects affected / exposed	0 / 7 (0.00%)	4 / 42 (9.52%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
Cellulitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis Bacterial			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	4	0	0
Dengue Fever			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ear Infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Eczema Impetiginous			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Gastritis Viral			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	1 / 7 (14.29%)	4 / 42 (9.52%)	0 / 9 (0.00%)
occurrences (all)	1	5	0
Gastrointestinal Bacterial Infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infected Bite			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal Infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Groin Abscess			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infectious Mononucleosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Molluscum Contagiosum			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Otitis Externa			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Oral Herpes			
subjects affected / exposed	1 / 7 (14.29%)	1 / 42 (2.38%)	1 / 9 (11.11%)
occurrences (all)	1	4	2
Oral Candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	11 / 42 (26.19%)	3 / 9 (33.33%)
occurrences (all)	0	21	6
Otitis Media			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pharyngitis Bacterial			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	1 / 7 (14.29%)	6 / 42 (14.29%)	0 / 9 (0.00%)
occurrences (all)	1	6	0
Paronychia			
subjects affected / exposed	0 / 7 (0.00%)	4 / 42 (9.52%)	0 / 9 (0.00%)
occurrences (all)	0	5	0
Otitis Media Acute			
subjects affected / exposed	0 / 7 (0.00%)	2 / 42 (4.76%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Pharyngitis Streptococcal			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pharyngotonsillitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Scarlet Fever			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Rhinitis			
subjects affected / exposed	2 / 7 (28.57%)	4 / 42 (9.52%)	3 / 9 (33.33%)
occurrences (all)	2	7	3
Respiratory Syncytial Virus Infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pyelonephritis Acute			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Sinobronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tinea Pedis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 7 (0.00%)	2 / 42 (4.76%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Tonsillitis			
subjects affected / exposed	1 / 7 (14.29%)	2 / 42 (4.76%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Varicella			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urinary Tract Infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection Bacterial			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	4 / 7 (57.14%)	6 / 42 (14.29%)	2 / 9 (22.22%)
occurrences (all)	10	10	3
Tracheitis			

subjects affected / exposed	0 / 7 (0.00%)	1 / 42 (2.38%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 7 (14.29%)	1 / 42 (2.38%)	1 / 9 (11.11%)
occurrences (all)	2	1	2
Viral Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Vitamin D Deficiency			
subjects affected / exposed	0 / 7 (0.00%)	0 / 42 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 1: < 30 kg and >= 10 kg	Cohort 2 (from Baseline): < 30 kg and >= 10 kg	Cohort 2(Post dose-adjustment from Dose 1): <30 kg and >=10 kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	29 / 31 (93.55%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin Papilloma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Essential Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Administration Site Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Gait Disturbance			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injection Site Haemorrhage			

subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injection Site Erythema			
subjects affected / exposed	0 / 6 (0.00%)	5 / 31 (16.13%)	0 / 5 (0.00%)
occurrences (all)	0	7	0
Injection Site Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	6	0
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injection Site Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injection Site Reaction			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	0	8	0
Immune system disorders			
Allergy To Arthropod Bite			
subjects affected / exposed	1 / 6 (16.67%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 6 (33.33%)	5 / 31 (16.13%)	0 / 5 (0.00%)
occurrences (all)	2	9	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Increased Bronchial Secretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rhinitis Allergic			

subjects affected / exposed	2 / 6 (33.33%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Psychiatric disorders			
Affective Disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Major Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood Pressure Systolic Decreased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Blood Bilirubin Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Eosinophil Count Increased			
subjects affected / exposed	0 / 6 (0.00%)	6 / 31 (19.35%)	0 / 5 (0.00%)
occurrences (all)	0	9	0
Lymphocyte Count Increased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Monocyte Count Decreased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Mean Cell Volume Decreased			

subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Transaminases Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Neutrophil Count Decreased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	0	6	0
Monocyte Count Increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	1 / 5 (20.00%)
occurrences (all)	0	6	1
Arthropod Bite			
subjects affected / exposed	1 / 6 (16.67%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Ligament Sprain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hand Fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Thermal Burn			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Traumatic Haematoma			

subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cardiovascular Disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	15 / 31 (48.39%)	2 / 5 (40.00%)
occurrences (all)	1	78	2
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Keratitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Uveitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)	4 / 31 (12.90%)	0 / 5 (0.00%)
occurrences (all)	2	6	0
Dental Discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Aphthous Ulcer			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Pulpless Tooth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Mouth Ulceration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	2 / 5 (40.00%)
occurrences (all)	0	4	2
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Pityriasis Alba			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dermatitis Allergic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	2 / 5 (40.00%)
occurrences (all)	0	1	2
Ingrowing Nail			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash Pruritic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash Papular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	8	0
Skin Reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urticaria Chronic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			

Juvenile Idiopathic Arthritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 31 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	2
Arthralgia			
subjects affected / exposed	2 / 6 (33.33%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	2	3	0
Pain In Extremity			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	6 / 31 (19.35%)	0 / 5 (0.00%)
occurrences (all)	0	8	0
Acute Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	1 / 6 (16.67%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	1	5	0
Covid-19			
subjects affected / exposed	0 / 6 (0.00%)	5 / 31 (16.13%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis Bacterial			
subjects affected / exposed	1 / 6 (16.67%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dengue Fever			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ear Infection			

subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Eczema Impetiginous			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastritis Viral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	9 / 31 (29.03%)	0 / 5 (0.00%)
occurrences (all)	0	11	0
Gastrointestinal Bacterial Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infected Bite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal Infection			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Groin Abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Infectious Mononucleosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Laryngitis			

subjects affected / exposed	1 / 6 (16.67%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Molluscum Contagiosum			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Otitis Externa			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oral Herpes			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Oral Candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	17 / 31 (54.84%)	0 / 5 (0.00%)
occurrences (all)	1	38	0
Otitis Media			
subjects affected / exposed	0 / 6 (0.00%)	4 / 31 (12.90%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Pharyngitis Bacterial			
subjects affected / exposed	1 / 6 (16.67%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	2 / 6 (33.33%)	1 / 31 (3.23%)	2 / 5 (40.00%)
occurrences (all)	3	1	4
Paronychia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Otitis Media Acute			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	0	7	0
Pharyngitis Streptococcal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pharyngotonsillitis			

subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	6	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Scarlet Fever			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	1 / 6 (16.67%)	3 / 31 (9.68%)	1 / 5 (20.00%)
occurrences (all)	3	3	1
Respiratory Syncytial Virus Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pyelonephritis Acute			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sinobronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tinea Pedis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 31 (6.45%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Varicella			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	1 / 5 (20.00%)
occurrences (all)	0	3	1
Urinary Tract Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			

Bacterial			
subjects affected / exposed	1 / 6 (16.67%)	0 / 31 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 6 (33.33%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	2	6	0
Tracheitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 31 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Viral Pharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 31 (3.23%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
Vitamin D Deficiency			
subjects affected / exposed	0 / 6 (0.00%)	3 / 31 (9.68%)	0 / 5 (0.00%)
occurrences (all)	0	3	0

Non-serious adverse events	Cohort 2(Post dose-adjustment from Dose 3): <30 kg and >=10 kg	Cohort 2(Post dose-adjustment from Dose 3):>=30 kg and <=60 kg	Cohort 2(Post dose-adjustment from Dose 1):>=30 kg and <=60 kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	5 / 6 (83.33%)	4 / 4 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin Papilloma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Essential Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Administration Site Erythema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gait Disturbance			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection Site Haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection Site Erythema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection Site Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection Site Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection Site Reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergy To Arthropod Bite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Epistaxis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Increased Bronchial Secretion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Rhinitis Allergic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Affective Disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Major Depression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood Pressure Systolic Decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood Bilirubin Increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Eosinophil Count Increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lymphocyte Count Increased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Monocyte Count Decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Mean Cell Volume Decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Transaminases Increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neutrophil Count Decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Monocyte Count Increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Arthropod Bite			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Ligament Sprain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
Hand Fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Contusion			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Thermal Burn			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Traumatic Haematoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cardiovascular Disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Lymphopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Keratitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Uveitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dental Discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Aphthous Ulcer			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulpless Tooth			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Mouth Ulceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vomiting			

subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pityriasis Alba			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dermatitis Allergic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ingrowing Nail			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash Pruritic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Rash Papular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Skin Reaction			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Urticaria Chronic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Juvenile Idiopathic Arthritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain In Extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Acute Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Covid-19			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis Bacterial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cystitis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dengue Fever			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Ear Infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eczema Impetiginous			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Gastritis Viral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal Bacterial Infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Infected Bite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Impetigo			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal Infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Groin Abscess			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infectious Mononucleosis			

subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Molluscum Contagiosum			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Otitis Externa			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Oral Herpes			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	11	1	0
Oral Candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	3 / 5 (60.00%)	4 / 6 (66.67%)	0 / 4 (0.00%)
occurrences (all)	5	6	0
Otitis Media			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pharyngitis Bacterial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Otitis Media Acute			

subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pharyngitis Streptococcal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pharyngotonsillitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Scarlet Fever			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Respiratory Syncytial Virus Infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pyelonephritis Acute			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Sinobronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tinea Pedis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	1	1	1
Varicella			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary Tract Infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection Bacterial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	3 / 4 (75.00%)
occurrences (all)	1	2	5
Tracheitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Viral Pharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Vitamin D Deficiency			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 3: >= 30 kg and <= 60 kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin Papilloma			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Vascular disorders			
Essential Hypertension			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Administration Site Erythema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gait Disturbance			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection Site Haemorrhage			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injection Site Erythema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection Site Pruritus			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injection Site Urticaria			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injection Site Reaction			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Immune system disorders			

Allergy To Arthropod Bite			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Increased Bronchial Secretion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rhinitis Allergic			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Affective Disorder			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Major Depression			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Investigations			
Blood Pressure Systolic Decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood Bilirubin Increased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Aspartate Aminotransferase Increased			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Eosinophil Count Increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Lymphocyte Count Increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Monocyte Count Decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Mean Cell Volume Decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Transaminases Increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Neutrophil Count Decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Monocyte Count Increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Arthropod Bite			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Ligament Sprain			

subjects affected / exposed occurrences (all) Hand Fracture subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all) Contusion subjects affected / exposed occurrences (all) Thermal Burn subjects affected / exposed occurrences (all) Traumatic Haematoma subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0		
Cardiac disorders Cardiovascular Disorder subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1 1 / 6 (16.67%) 1		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) Lymphopenia subjects affected / exposed occurrences (all) Lymphadenopathy	1 / 6 (16.67%) 2 1 / 6 (16.67%) 1		

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Leukopenia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eye disorders			
Keratitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Uveitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dental Discomfort			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Aphthous Ulcer			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Abdominal Pain Upper			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pulpless Tooth			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Mouth Ulceration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	3		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Pityriasis Alba			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Alopecia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dermatitis Allergic			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ingrowing Nail			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Acne			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rash Pruritic			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rash Papular			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin Reaction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Urticaria Chronic			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Juvenile Idiopathic Arthritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pain In Extremity			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Acute Sinusitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Covid-19			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Cellulitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Conjunctivitis Bacterial				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Cystitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Dengue Fever				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Ear Infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Eczema Impetiginous				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Escherichia Urinary Tract Infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastritis Viral				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastroenteritis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Gastrointestinal Bacterial Infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Infected Bite				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Impetigo				

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastrointestinal Infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Groin Abscess				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Infectious Mononucleosis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Influenza				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Laryngitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Molluscum Contagiosum				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Otitis Externa				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Oral Herpes				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Oral Candidiasis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	5			
Otitis Media				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Pharyngitis Bacterial				

subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Paronychia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Otitis Media Acute				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Pharyngitis Streptococcal				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Pharyngotonsillitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	2			
Scarlet Fever				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Rhinitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Respiratory Syncytial Virus Infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Pyelonephritis Acute				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Sinobronchitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Tinea Pedis				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Varicella			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Urinary Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Upper Respiratory Tract Infection Bacterial			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Tracheitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Viral Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Vitamin D Deficiency			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 April 2018	• To modify the study design to implement the amended Pediatric Investigations Plan approved by the European Medicines Agency. • To split the 12-week core treatment phase of the study into 2 portions: a dose-finding portion corresponding to the 12-week core treatment phase of the initial protocol where 3 ascending dose regimens will be tested in 36 participants; and a second portion where additional participants will receive the dose regimen selected from data of the first portion of the study in order to provide sufficient precision for PK parameters and PK-PD relationship assessments at that selected dose regimen. • To prolong the extension phase of the study from 92 weeks to 144 weeks for a total study duration of 166 weeks (per participant). • To increase the number of enrolled participants from 36 to 60 evaluable participants by 24 additional participants enrolled in the second portion of the study. • To revise the secondary efficacy endpoints. • To update the exclusion criteria section to better define the study population. • To incorporate several local protocol amendments that have already been approved, which address local health authorities and/or IRB requests related to the initial protocol.
13 December 2018	To update the stopping rules for Grade 4 neutropenia: The stopping rules for Grade 4 neutropenia was updated during the study after analysis of the 12-week core phase of the Portion 1 in order to provide the best chance for participants to benefit from treatment while continuously monitoring for safety events. Prior to the amendment, sarilumab had to be discontinued in case of Grade 4 neutropenia (absolute neutrophil count <0.5 Giga/liter) whether or not associated with signs of infection. Per the amendment, any Grade 4 neutropenia without infection led to temporary hold of treatment and the decision to resume sarilumab could be considered by the Investigator when absolute neutrophil count returned to >1.0 Giga/liter and based upon medical benefit-to-risk assessment. The rule stayed unchanged for any Grade 3 and 4 neutropenia associated with signs of infection (discontinuation) and Grade 3 neutropenia without infection (absolute neutrophil count ≥0.5 Giga/liter and <1.0 Giga/liter) (temporary hold).
12 September 2019	To increase the planned total number of enrolled participants (28 additional participants) to achieve a total of approximately 100 treated participants (based on health authority recommendations).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported