



Clinical trial results:

A 24-Week Randomized Double-Blind, Placebo Controlled Withdrawal Trial With a 16-Week Open-Label Lead-In Phase, and 64-Week Open-Label Follow-Up, to Evaluate the Efficacy and Safety of Tocilizumab in Patients with Active Polyarticular Juvenile Idiopathic Arthritis

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2009-011593-15 |
| Trial protocol | GB DE IT ES BE NL FR |
| Global end of trial date | 28 January 2013 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 01 June 2016 |
| First version publication date | 01 June 2016 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | WA19977 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00988221 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000309-PIP01-08 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 28 January 2013 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 January 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This 3-part study evaluated the efficacy and safety of tocilizumab in patients with active polyarticular-course juvenile idiopathic arthritis who have an inadequate response to, or were intolerant of methotrexate. In Part I of the study, all patients received intravenous (iv) infusions of tocilizumab (8 milligrams per kilogram [mg/kg] for patients greater than or equal to \geq 30 kg, 8 mg/kg or 10 mg/kg for patients less than $<$ 30 kg) every 4 weeks for 16 weeks. In Part II of the study, patients with an adequate response in Part I were randomized to receive either tocilizumab at the same dose as in Part I or placebo every 4 weeks for up to 24 weeks. In Part III of the study, patients received tocilizumab at the same dose as in Part I every 4 weeks for up to another 64 weeks. Standard of care therapy with or without non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or methotrexate was continued throughout the study.

Protection of trial subjects:

The study was conducted in accordance with the principles of the "Declaration of Helsinki" and Good Clinical Practice (GCP) according to the regulations and procedures described in the protocol.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 14 October 2009 |
| 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 | Poland: 23 |
| Country: Number of subjects enrolled | Spain: 10 |
| Country: Number of subjects enrolled | United Kingdom: 6 |
| Country: Number of subjects enrolled | Belgium: 3 |
| Country: Number of subjects enrolled | France: 10 |
| Country: Number of subjects enrolled | Germany: 14 |
| Country: Number of subjects enrolled | Italy: 7 |
| Country: Number of subjects enrolled | Australia: 4 |
| Country: Number of subjects enrolled | Argentina: 19 |
| Country: Number of subjects enrolled | Canada: 10 |
| Country: Number of subjects enrolled | Brazil: 18 |
| Country: Number of subjects enrolled | Mexico: 12 |
| Country: Number of subjects enrolled | Peru: 11 |
| Country: Number of subjects enrolled | Russian Federation: 27 |
| Country: Number of subjects enrolled | United States: 14 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 188 |
| EEA total number of subjects | 73 |

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) | 101 |
| Adolescents (12-17 years) | 87 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In Part I, patients received either tocilizumab 8 or 10 mg/kg. In Part II, eligible patients were randomized to receive placebo or the same dose of tocilizumab as in Part I of the study. In Part III, patients received the same dose of tocilizumab as in Part I of the study, with adjustments based on weight and change in weight from Baseline.

Period 1

| | |
|------------------------------|----------------|
| Period 1 title | Part I |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|----|
| Are arms mutually exclusive? | No |
|------------------------------|----|

| | |
|------------------|--|
| Arm title | Tocilizumab 10 mg/kg in Patients Weighing <30 kg |
|------------------|--|

Arm description:

Patients received tocilizumab 10 mg/kg intravenously every 4 weeks.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tocilizumab |
| Investigational medicinal product code | RO4877533 |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients received tocilizumab intravenously every 4 weeks.

| | |
|------------------|--|
| Arm title | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg |
|------------------|--|

Arm description:

Patients received tocilizumab 8 mg/kg intravenously every 4 weeks.

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

Dosage and administration details:

Patients received tocilizumab 8 mg/kg intravenously every 4 weeks.

| | |
|------------------|--|
| Arm title | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg |
|------------------|--|

Arm description:

Patients received tocilizumab 8 mg/kg intravenously every 4 weeks.

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

Dosage and administration details:

Patients received tocilizumab 8 mg/kg intravenously every 4 weeks.

| | |
|--|---------------------------------|
| Arm title | Tocilizumab 8 or 10 mg/kg |
| Arm description: Patients received tocilizumab 8 or 10 mg/kg intravenously every 4 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Tocilizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients received tocilizumab 8 or 10 mg/kg intravenously every 4 weeks.

| Number of subjects in period 1 | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg |
|---------------------------------------|--|--|--|
| Started | 35 | 34 | 119 |
| Completed | 31 | 24 | 111 |
| Not completed | 4 | 10 | 8 |
| Insufficient therapeutic response | 4 | 6 | 5 |
| Adverse event, non-fatal | - | 1 | 2 |
| Refused treatment | - | 2 | 1 |
| Lost to follow-up | - | 1 | - |

| Number of subjects in period 1 | Tocilizumab 8 or 10 mg/kg |
|---------------------------------------|---------------------------|
| Started | 188 |
| Completed | 166 |
| Not completed | 22 |
| Insufficient therapeutic response | 15 |
| Adverse event, non-fatal | 3 |
| Refused treatment | 3 |
| Lost to follow-up | 1 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Part II |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|----|
| Are arms mutually exclusive? | No |
|------------------------------|----|

| | |
|------------------|---|
| Arm title | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg |
|------------------|---|

Arm description:

Patients received tocilizumab 10 mg/kg intravenously every 4 weeks.

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

Dosage and administration details:

Patients received tocilizumab 10 mg/kg intravenously every 4 weeks.

| | |
|------------------|--|
| Arm title | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg |
|------------------|--|

Arm description:

Patients received tocilizumab 8 mg/kg intravenously every 4 weeks.

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

Dosage and administration details:

Patients received tocilizumab 8 mg/kg intravenously every 4 weeks.

| | |
|------------------|--|
| Arm title | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg |
|------------------|--|

Arm description:

Patients received tocilizumab 8 mg/kg intravenously every 4 weeks.

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

Dosage and administration details:

Patients received tocilizumab 8 mg/kg intravenously every 4 weeks.

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

Dosage and administration details:

Patients received tocilizumab 8 mg/kg intravenously every 4 weeks.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Patients received placebo to tocilizumab intravenously every 4 weeks.

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

Dosage and administration details:

Patients received placebo to tocilizumab intravenously every 4 weeks.

| Number of subjects in period 2 | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg |
|---------------------------------------|---|--|--|
| Started | 16 | 11 | 55 |
| Completed | 15 | 11 | 52 |
| Not completed | 1 | 0 | 3 |
| Consent withdrawn by subject | - | - | 2 |
| Adverse event, non-fatal | 1 | - | - |
| Reason not specified | - | - | 1 |

| Number of subjects in period 2 | Placebo |
|---------------------------------------|---------|
| Started | 84 |
| Completed | 81 |
| Not completed | 3 |
| Consent withdrawn by subject | 1 |
| Adverse event, non-fatal | 2 |
| Reason not specified | - |

Period 3

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

Arms

| | |
|------------------------------|----|
| Are arms mutually exclusive? | No |
|------------------------------|----|

| | |
|--|---|
| Arm title | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg |
| Arm description: Patients received tocilizumab 10 mg/kg intravenously every 4 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Tocilizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: Patients received tocilizumab 10 mg/kg intravenously every 4 weeks. | |
| Arm title | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg |
| Arm description: Patients received tocilizumab 8 mg/kg intravenously every 4 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Tocilizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: Patients received tocilizumab 8 mg/kg intravenously every 4 weeks. | |
| Arm title | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg |
| Arm description: Patients received tocilizumab 8 mg/kg intravenously every 4 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Tocilizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: Patients received tocilizumab 8 mg/kg intravenously every 4 weeks. | |
| Arm title | All Tocilizumab Patients |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Tocilizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: Patients received tocilizumab 8 or 10 mg/kg intravenously every 4 weeks. | |

| Number of subjects in period 3 | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg |
|---------------------------------------|---|--|--|
| Started | 30 | 24 | 106 |
| Completed | 29 | 23 | 103 |
| Not completed | 1 | 1 | 3 |
| Insufficient therapeutic response | - | 1 | 1 |
| Adverse event, non-fatal | 1 | - | 1 |
| Refused treatment | - | - | 1 |

| Number of subjects in period 3 | All Tocilizumab Patients |
|---------------------------------------|--------------------------|
| Started | 160 |
| Completed | 160 |
| Not completed | 0 |
| Insufficient therapeutic response | - |
| Adverse event, non-fatal | - |
| Refused treatment | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | Part I |
|-----------------------|--------|

Reporting group description:

In Part I, patients received either tocilizumab 8 or 10 mg/kg.

| Reporting group values | Part I | Total | |
|------------------------|--------|-------|--|
| Number of subjects | 188 | 188 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 11 | | |
| standard deviation | ± 4.01 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 144 | 144 | |
| Male | 44 | 44 | |

Subject analysis sets

| | |
|----------------------------|------------------------------|
| Subject analysis set title | All Tocilizumab Participants |
|----------------------------|------------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All participants who received 8 or 10 mg/kg of tocilizumab

| | |
|----------------------------|---|
| Subject analysis set title | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg |
|----------------------------|---|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Patients weighing < 30 kg at baseline receiving tocilizumab 10 mg/kg whose body weight increased to ≥ 30 kg and ≥ 5 kg over baseline body weight for 3 consecutive visits had the tocilizumab dose reduced to 8 mg/kg.

| Reporting group values | All Tocilizumab Participants | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | |
|------------------------|------------------------------|---|--|
| Number of subjects | 188 | 7 | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------|--------|---|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 11 | | |
| standard deviation | ± 4.01 | ± | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 144 | | |
| Male | 44 | | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Tocilizumab 10 mg/kg in Patients Weighing <30 kg |
| Reporting group description: Patients received tocilizumab 10 mg/kg intravenously every 4 weeks. | |
| Reporting group title | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg |
| Reporting group description: Patients received tocilizumab 8 mg/kg intravenously every 4 weeks. | |
| Reporting group title | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg |
| Reporting group description: Patients received tocilizumab 8 mg/kg intravenously every 4 weeks. | |
| Reporting group title | Tocilizumab 8 or 10 mg/kg |
| Reporting group description: Patients received tocilizumab 8 or 10 mg/kg intravenously every 4 weeks. | |
| Reporting group title | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg |
| Reporting group description: Patients received tocilizumab 10 mg/kg intravenously every 4 weeks. | |
| Reporting group title | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg |
| Reporting group description: Patients received tocilizumab 8 mg/kg intravenously every 4 weeks. | |
| Reporting group title | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg |
| Reporting group description: Patients received tocilizumab 8 mg/kg intravenously every 4 weeks. | |
| Reporting group title | Placebo |
| Reporting group description: Patients received placebo to tocilizumab intravenously every 4 weeks. | |
| Reporting group title | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg |
| Reporting group description: Patients received tocilizumab 10 mg/kg intravenously every 4 weeks. | |
| Reporting group title | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg |
| Reporting group description: Patients received tocilizumab 8 mg/kg intravenously every 4 weeks. | |
| Reporting group title | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg |
| Reporting group description: Patients received tocilizumab 8 mg/kg intravenously every 4 weeks. | |
| Reporting group title | All Tocilizumab Patients |
| Reporting group description: - | |
| Subject analysis set title | All Tocilizumab Participants |
| Subject analysis set type | Full analysis |
| Subject analysis set description: All participants who received 8 or 10 mg/kg of tocilizumab | |
| Subject analysis set title | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Patients weighing < 30 kg at baseline receiving tocilizumab 10 mg/kg whose body weight increased to ≥ 30 kg and ≥ 5 kg over baseline body weight for 3 consecutive visits had the tocilizumab dose reduced to 8 mg/kg. | |

Primary: Percent of Patients With a Juvenile Idiopathic Arthritis (JIA) American College of Rheumatology 30 (ACR30) Flare in Part II of the Study (Weeks 16-40)

| | |
|-----------------|--|
| End point title | Percent of Patients With a Juvenile Idiopathic Arthritis (JIA) American College of Rheumatology 30 (ACR30) Flare in Part II of the Study (Weeks 16-40) ^{[1][2]} |
|-----------------|--|

End point description:

JIA ACR30 flare is defined as a $\geq 30\%$ worsening of 3 of 6 variables and no more than 1 of the remaining variables improving $> 30\%$. The 6 variables are physician global assessment of disease activity (worsening of 20 units minimum on a 0-100 visual analog scale [VAS]), parent/patient global assessment of overall well-being (worsening of 20 VAS units minimum), number of joints (minimum of 2 worse) with active arthritis (swelling, or pain and limitation of motion), number of joints (minimum of 2 worse) with limitation of movement, erythrocyte sedimentation rate (ESR), and functional ability assessed using the disability index of the Childhood Health Assessment Questionnaire (CHAQ, 30 questions, 8 domains, 0[best]-3[worst]). Patients who withdrew or who took escape medication are classified as flared. The analysis used the Cochran-Mantel-Haenszel test with the stratification variables background use of methotrexate and oral corticosteroids applied at Week 16.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 16 through Week 40

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: This endpoint data were not analyzed for all baseline period arms.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint data were not analyzed for all baseline period arms.

| End point values | Placebo | Tocilizumab 8 or 10 mg/kg | | |
|----------------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 82 | | |
| Units: Percent of patients | | | | |
| number (confidence interval 95%) | 48.1 (37 to 59) | 25.6 (16 to 35) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Patients Achieving JIA ACR30/50/70/90 Responses in Part I of the Study (Baseline to Week 16)

| | |
|-----------------|---|
| End point title | Percent of Patients Achieving JIA ACR30/50/70/90 Responses in Part I of the Study (Baseline to Week 16) |
|-----------------|---|

End point description:

A JIA ACR30/50/70/90 response is defined as a $\geq 30/50/70/90\%$ response on 3 of 6 variables and no more than 1 of the remaining variables worsening $> 30\%$. The 6 variables are physician global assessment of disease activity (20 units minimum on a 0-100 VAS), parent/patient global assessment of overall well-being (20 VAS units minimum), number of joints (minimum of 2 worse) with active arthritis (swelling, or pain and limitation of motion), number of joints (minimum of 2 worse) with limitation of movement, erythrocyte sedimentation rate, and functional ability assessed using the CHAQ, 30 questions, 8 domains, 0[best]-3[worst]).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 16

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|-----------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 34 | 119 | 188 |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| ACR30 response | 88.6 | 76.5 | 93.3 | 89.4 |
| ACR50 response | 80 | 70.6 | 87.4 | 83 |
| ACR70 response | 62.9 | 41.2 | 68.1 | 62.2 |
| ACR90 response | 31.4 | 23.5 | 25.2 | 26.1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in the JIA ACR Component Score Physician Global Assessment of Disease Activity at the End of Part I of the Study (Week 16)

| | |
|-----------------|---|
| End point title | Percent Change From Baseline in the JIA ACR Component Score Physician Global Assessment of Disease Activity at the End of Part I of the Study (Week 16) |
|-----------------|---|

End point description:

The patient's treating physician provides a rating of the patient's arthritis disease activity on a 0 to 100 mm horizontal scale. The extreme left end of the line represents 'arthritis inactive' (ie, symptom-free and no arthritis symptoms) and the extreme right end represents 'arthritis very active'. A higher score indicates more disease activity. A negative change score indicates improvement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 16

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|--------------------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 34 | 119 | 188 |
| Units: percent change | | | | |
| arithmetic mean (standard deviation) | -61.48 (± 48.779) | -65.2 (± 26.17) | -72.61 (± 25.977) | -69.19 (± 31.824) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in the JIA ACR Component Score Patient/Parent Global Assessment of Overall Well-being at the End of Part I of the Study (Week 16)

| | |
|-----------------|--|
| End point title | Percent Change From Baseline in the JIA ACR Component Score Patient/Parent Global Assessment of Overall Well-being at the End of Part I of the Study (Week 16) |
|-----------------|--|

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 16

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|--------------------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 34 | 119 | 188 |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -31.65 (± 120.268) | -55.56 (± 42.092) | -53.34 (± 58.686) | -49.46 (± 72.92) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in the JIA ACR Component Score Number of Joints With Active Arthritis at the End of Part I of the Study (Week 16)

| | |
|-----------------|--|
| End point title | Percent Change From Baseline in the JIA ACR Component Score Number of Joints With Active Arthritis at the End of Part I of the Study (Week 16) |
|-----------------|--|

End point description:

Joints with active arthritis are defined as joints with swelling present or pain present and limitation of motion. The maximum possible number of joints with active arthritis is 71. The joint assessment is performed by an independent assessor who is not the treating physician and who is blinded to all other aspects of the patient's efficacy and safety data. A negative change score indicates improvement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 16

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|--------------------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 34 | 119 | 188 |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -63.36 (± 43.272) | -55.57 (± 44.876) | -72.96 (± 33.915) | -68.15 (± 38.246) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in the JIA ACR Component Score Number of Joints With Limitation of Movement at the End of Part I of the Study (Week 16)

| | |
|-----------------|--|
| End point title | Percent Change From Baseline in the JIA ACR Component Score Number of Joints With Limitation of Movement at the End of Part I of the Study (Week 16) |
|-----------------|--|

End point description:

Joints with limitation of movement are defined as joints with limitation of motion. The maximum possible number of joints with limitation of movement is 67. The joint assessment is performed by an independent assessor who is not the treating physician and who is blinded to all other aspects of the patient's efficacy and safety data. A negative change score indicates improvement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 16

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|--------------------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 34 | 119 | 188 |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -61.83 (± 34.726) | -49.87 (± 48.091) | -65.96 (± 30.134) | -62.42 (± 34.955) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in the JIA ACR Component Score ESR at the End of Part I of the Study (Week 16)

| | |
|-----------------|---|
| End point title | Percent Change From Baseline in the JIA ACR Component Score ESR at the End of Part I of the Study (Week 16) |
|-----------------|---|

End point description:

Erythrocyte sedimentation rate, an acute phase protein, was measured using a kit furnished by the study central laboratory. A negative change score indicates improvement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 16

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|--------------------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 34 | 119 | 188 |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -70.98 (± 24.53) | -21.84 (± 159.592) | -70.87 (± 33.4) | -62.54 (± 73.384) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in the JIA ACR Component Score Functional Ability at the End of Part I of the Study (Week 16)

| | |
|-----------------|--|
| End point title | Percent Change From Baseline in the JIA ACR Component Score Functional Ability at the End of Part I of the Study (Week 16) |
|-----------------|--|

End point description:

Functional ability is assessed with the Childhood Health Assessment Questionnaire disability index (CHAQ-DI) which consists of 30 questions in 8 domains: Dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities. There are 4 possible responses to each question (0=without any difficulty, 1=with some difficulty, 2=with much difficulty, 3=unable to do). A domain score is the highest score in that domain. If aids and devices listed in the questionnaire or assistance from a person are required to perform a task, a domain score of 0 or 1 is increased to 2; if the domain score is 2 or 3, the domain score is not adjusted. To calculate the overall score, the patient must have a domain score in at least 6 of the 8 domains. The CHAQ-DI score is the sum of the domain scores divided by the number of domains that have a non-missing score and ranges from 0 (best) to 3 (worst). A higher score indicates less ability. A negative change score indicates improvement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 16

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|-----------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 34 | 119 | 188 |
| Units: percent change | | | | |

| | | | | |
|--------------------------------------|------------------------|------------------------|------------------------|------------------------|
| arithmetic mean (standard deviation) | -54.48 (\pm 37.214) | -46.16 (\pm 50.961) | -49.07 (\pm 45.048) | -49.62 (\pm 44.573) |
|--------------------------------------|------------------------|------------------------|------------------------|------------------------|

Statistical analyses

No statistical analyses for this end point

Secondary: Juvenile Arthritis Disease Activity Score (JADAS-27) at the End of Part I of the Study (Week 16)

| | |
|--|--|
| End point title | Juvenile Arthritis Disease Activity Score (JADAS-27) at the End of Part I of the Study (Week 16) |
| End point description: | |
| The JADAS-27 is derived from the following components: Physician's global assessment of disease activity on a 0-100 mm visual analog scale (VAS)/10, patient/parent's global assessment of overall well-being on a 0-100 mm VAS/10, normalized erythrocyte sedimentation rate (ESR) (if ESR is \leq 20 then set to 0, if \geq 120 then set to 10, and if $>$ 20 and $<$ 120 then apply formula $[(\text{ESR}-20)/10]$, and number of joints (maximum of 27) with active arthritis (cervical spine, left/right elbow, left/right wrist, left/right metacarpophalangeal (MCP) 1-3, left/right proximal interphalangeal joint (PIP) 1-5, left/right hips, left/right knee and left/right ankle). The scores for the first 3 components range from 0-10; the score for the final component ranges from 0-27. The overall JADAS-27 score ranges from 0-57. A higher score indicates more disease activity. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 16 | |

| End point values | Tocilizumab 10 mg/kg in Patients Weighing $<$ 30 kg | Tocilizumab 8 mg/kg in Patients Weighing $<$ 30 kg | Tocilizumab 8 mg/kg in Patients Weighing \geq 30 kg | Tocilizumab 8 or 10 mg/kg |
|--------------------------------------|---|--|---|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 34 | 119 | 188 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | 9.08 (\pm 8.882) | 12.25 (\pm 10.277) | 7.83 (\pm 7.122) | 8.82 (\pm 8.198) |

Statistical analyses

No statistical analyses for this end point

Secondary: Pain Visual Analogue Scale (VAS) Score at the End of Part I of the Study (Week 16)

| | |
|---|--|
| End point title | Pain Visual Analogue Scale (VAS) Score at the End of Part I of the Study (Week 16) |
| End point description: | |
| The patient or parent/guardian, as appropriate, provides a rating of the patient's pain (also called a discomfort index) on a 0 to 100 mm horizontal scale. The extreme left end of the line represents 'no pain' and the extreme right end represents 'very extreme pain'. A higher score indicates more pain. | |

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 16 | |

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|--------------------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 34 | 119 | 188 |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | 21.9 (± 21.66) | 24.1 (± 23.94) | 20.3 (± 21.13) | 21.2 (± 21.65) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With Inactive Disease at the End of Part I of the Study (Week 16)

| | |
|-----------------|--|
| End point title | Percentage of Patients With Inactive Disease at the End of Part I of the Study (Week 16) |
|-----------------|--|

End point description:

A patient is judged to have inactive disease if all of the following criteria are met: Number of joints with active arthritis = 0; absence of active uveitis, defined by the adverse event preferred terms 'uveitis' and 'intermediate uveitis'; normal erythrocyte sedimentation rate (< 20 mm/hour regardless of age and sex); and physician's global assessment of overall well-being visual analog scale score ≤ 10.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 16

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|-------------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 34 | 119 | 188 |
| Units: Percentage of patients | | | | |
| number (not applicable) | 20 | 8.8 | 18.5 | 17 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With an Elevated C-reactive Protein Concentration at Baseline That Had Normalized at the End of Part I of the Study (Week 16)

| | |
|--|--|
| End point title | Percentage of Patients With an Elevated C-reactive Protein Concentration at Baseline That Had Normalized at the End of Part I of the Study (Week 16) |
| End point description: C-reactive protein (CRP), an acute phase protein, was measured in blood samples with a high-sensitivity CRP (hs-CRP) test using laser nephelometry. CRP levels higher than 10 milligrams per deciliter (mg/dL) are considered to be elevated levels. | |
| End point type | Secondary |
| End point timeframe: Baseline to Week 16 | |

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|-------------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 19 | 46 | 78 |
| Units: Percentage of patients | | | | |
| number (not applicable) | 76.9 | 63.2 | 87 | 79.5 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With an Elevated ESR at Baseline That Had Normalized at the End of Part I of the Study (Week 16)

| | |
|---|---|
| End point title | Percentage of Patients With an Elevated ESR at Baseline That Had Normalized at the End of Part I of the Study (Week 16) |
| End point description: Erythrocyte sedimentation rate, an acute phase protein, was measured using a kit furnished by the study central laboratory. | |
| End point type | Secondary |
| End point timeframe: Baseline to Week 16 | |

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|-----------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 26 | 73 | 122 |
| Units: Percent of patients | | | | |
| number (not applicable) | 82.6 | 57.7 | 87.7 | 80.3 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With an Elevated Platelet Count at Baseline That Had Normalized at the End of Part I of the Study (Week 16)

| | |
|-----------------|--|
| End point title | Percentage of Patients With an Elevated Platelet Count at Baseline That Had Normalized at the End of Part I of the Study (Week 16) |
|-----------------|--|

End point description:

Platelets were measured in blood samples taken from the patients. Platelet counts above 400,00 are considered to be elevated.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 16

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|-------------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 18 | 43 | 74 |
| Units: Percentage of patients | | | | |
| number (not applicable) | 84.6 | 55.6 | 86 | 78.4 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With an Elevated White Blood Count at Baseline That Had Normalized at the End of Part I of the Study (Week 16)

| | |
|-----------------|---|
| End point title | Percentage of Patients With an Elevated White Blood Count at Baseline That Had Normalized at the End of Part I of the Study (Week 16) |
|-----------------|---|

End point description:

White blood cells were measured in blood samples taken from the patients. Counts of more than 10,500 cells per microliter are considered to be elevated levels.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 16

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|-------------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 2 | 8 |
| Units: Percentage of patients | | | | |
| number (not applicable) | 66.7 | 66.7 | 100 | 75 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Patients Achieving JIA ACR30/50/70/90 Responses at the End of Part II of the Study (Week 40)

| | |
|-----------------|--|
| End point title | Percent of Patients Achieving JIA ACR30/50/70/90 Responses at the End of Part II of the Study (Week 40) ^[3] |
|-----------------|--|

End point description:

A JIA ACR30/50/70/90 response is defined as a ≥ 30/50/70/90% response on 3 of 6 variables and no more than 1 of the remaining variables worsening > 30%. The 6 variables are physician global assessment of disease activity (20 units minimum on a 0-100 visual analog scale [VAS]), parent/patient global assessment of overall well-being (20 VAS units minimum), number of joints (minimum of 2 worse) with active arthritis (swelling, or pain and limitation of motion), number of joints (minimum of 2 worse) with limitation of movement, erythrocyte sedimentation rate, and functional ability assessed using the disability index of the Childhood Health Assessment Questionnaire (CHAQ, 30 questions, 8 domains, 0[best]-3[worst]). The analysis used the Cochran-Mantel-Haenszel test with the stratification variables background use of methotrexate and oral corticosteroids applied at Week 16.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 40

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint data were not analyzed for all baseline period arms.

| End point values | Placebo | Tocilizumab 8 or 10 mg/kg | | |
|----------------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 82 | | |
| Units: Percent of patients | | | | |
| number (confidence interval 95%) | | | | |
| ACR30 response | 54.3 (43 to 65) | 74.4 (65 to 84) | | |
| ACR50 response | 51.9 (41 to 63) | 73.2 (64 to 83) | | |
| ACR70 response | 42 (31 to 53) | 64.6 (54 to 75) | | |
| ACR90 response | 23.5 (14 to 33) | 45.1 (34 to 56) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the JIA ACR Component Score Physician Global Assessment of Disease Activity at the End of Part II of the Study (Week 40)

| | |
|-----------------|---|
| End point title | Change From Baseline in the JIA ACR Component Score Physician Global Assessment of Disease Activity at the End of Part II of the Study (Week 40) ^[4] |
|-----------------|---|

End point description:

The patient's treating physician provides a rating of the patient's arthritis disease activity on a 0 to 100 mm horizontal scale. The extreme left end of the line represents 'arthritis inactive' (ie, symptom-free and no arthritis symptoms) and the extreme right end represents 'arthritis very active'. A higher score indicates more disease activity. A negative change score indicates improvement. Change from baseline was calculated using last observation carried forward imputation for missing values.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 40

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: This endpoint data were not analyzed for all baseline period arms.

| End point values | Placebo | Tocilizumab 8 or 10 mg/kg | | |
|--------------------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 82 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -38.2 (± 24.77) | -45.6 (± 21.47) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the JIA ACR Component Score Patient/Parent Global Assessment of Overall Well-being at the End of Part II of the Study (Week 40)

| | |
|-----------------|--|
| End point title | Change From Baseline in the JIA ACR Component Score Patient/Parent Global Assessment of Overall Well-being at the End of Part II of the Study (Week 40) ^[5] |
|-----------------|--|

End point description:

The patient or parent/guardian, as appropriate, provides a rating of the patient's well-being on a 0 to 100 mm horizontal scale. The extreme left end of the line represents 'very well' (ie, symptom-free and no arthritis disease activity) and the extreme right end represents 'very poor' (ie, maximum arthritis disease activity). A higher score indicates poorer well-being. A negative change score indicates improvement. Change from baseline was calculated using last observation carried forward imputation for missing values.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 40

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: This endpoint data were not analyzed for all baseline period arms.

| End point values | Placebo | Tocilizumab 8 or 10 mg/kg | | |
|--------------------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 82 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -32.4 (± 28.57) | -31.1 (± 28.52) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the JIA ACR Component Score Number of Joints With Active Arthritis at the End of Part II of the Study (Week 40)

| | |
|-----------------|--|
| End point title | Change From Baseline in the JIA ACR Component Score Number of Joints With Active Arthritis at the End of Part II of the Study (Week 40) ^[6] |
|-----------------|--|

End point description:

Joints with active arthritis are defined as joints with swelling present or pain present and limitation of motion. The maximum number of joints with active arthritis is 71. The joint assessment is performed by an independent assessor who is not the treating physician and who is blinded to all other aspects of the patient's efficacy and safety data. A negative change score indicates improvement. Change from baseline was calculated using last observation carried forward imputation for missing values.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 40

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: This endpoint data were not analyzed for all baseline period arms.

| End point values | Placebo | Tocilizumab 8 or 10 mg/kg | | |
|--------------------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 82 | | |
| Units: Joints | | | | |
| arithmetic mean (standard deviation) | -11.5 (± 12.77) | -14.5 (± 11.14) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the JIA ACR Component Score Number of Joints With Limitation of Movement at the End of Part II of the Study (Week 40)

| | |
|-----------------|--|
| End point title | Change From Baseline in the JIA ACR Component Score Number of Joints With Limitation of Movement at the End of Part II of the Study (Week 40) ^[7] |
|-----------------|--|

End point description:

Joints with limitation of movement are defined as joints with limitation of motion. The maximum number of joints with limitation of movement is 67. The joint assessment is performed by an independent assessor who is not the treating physician and who is blinded to all other aspects of the patient's efficacy

and safety data. A negative change score indicates improvement. Change from baseline was calculated using last observation carried forward imputation for missing values.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Week 40 | |
| 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: This endpoint data were not analyzed for all baseline period arms.

| End point values | Placebo | Tocilizumab 8 or 10 mg/kg | | |
|--------------------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 82 | | |
| Units: Joints | | | | |
| arithmetic mean (standard deviation) | -8.1 (± 9.9) | -10.2 (± 8.97) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the JIA ACR Component Score ESR at the End of Part II of the Study (Week 40)

| | |
|-----------------|---|
| End point title | Change From Baseline in the JIA ACR Component Score ESR at the End of Part II of the Study (Week 40) ^[8] |
|-----------------|---|

End point description:

Erythrocyte sedimentation rate, an acute phase protein, was measured using a kit furnished by the study central laboratory. A negative change score indicates improvement. Change from baseline was calculated using last observation carried forward imputation for missing values.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Week 40 | |

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: This endpoint data were not analyzed for all baseline period arms.

| End point values | Placebo | Tocilizumab 8 or 10 mg/kg | | |
|--------------------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 82 | | |
| Units: mm/hour | | | | |
| arithmetic mean (standard deviation) | -14 (± 28.46) | -25.2 (± 21.97) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the JIA ACR Component Score CHAQ-DI at the

End of Part II of the Study (Week 40)

| | |
|-----------------|---|
| End point title | Change From Baseline in the JIA ACR Component Score CHAQ-DI at the End of Part II of the Study (Week 40) ^[9] |
|-----------------|---|

End point description:

The Childhood Health Assessment Questionnaire-Disability Index (CHAQ-DI), as a measure of functional ability, consists of 30 questions in 8 domains: Dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities. There are 4 possible responses to each question (0=without any difficulty, 1=with some difficulty, 2=with much difficulty, 3=unable to do). A domain score is the highest score in that domain. To calculate the overall score, the patient must have a domain score in at least 6 of the 8 domains. The CHAQ-DI score is the sum of the domain scores divided by the number of domains that have a non-missing score and ranges from 0 (best) to 3 (worst). A higher score indicates less ability. A negative change score indicates improvement. Change from baseline was calculated using last observation carried forward imputation for missing values.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 40

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: This endpoint data were not analyzed for all baseline period arms.

| End point values | Placebo | Tocilizumab 8 or 10 mg/kg | | |
|--------------------------------------|------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 82 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -0.724 (\pm 0.6905) | -0.804 (\pm 0.6534) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Pain VAS Score at the End of Part II of the Study (Week 40)

| | |
|-----------------|---|
| End point title | Change From Baseline in the Pain VAS Score at the End of Part II of the Study (Week 40) ^[10] |
|-----------------|---|

End point description:

The patient or parent/guardian, as appropriate, provides a rating of the patient's pain (also called a discomfort index) on a 0 to 100 mm horizontal scale. The extreme left end of the line represents 'no pain' and the extreme right end represents 'very extreme pain'. A higher score indicates more pain. A negative change score indicates improvement. Change from baseline was calculated using last observation carried forward (LOCF) imputation for missing values. The analysis was adjusted for the randomization stratification factors background use of methotrexate and background use of oral corticosteroids, and the pain visual analog scale score at Baseline. The adjusted means from the fitted model are presented.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 40

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: This endpoint data were not analyzed for all baseline period arms.

| End point values | Placebo | Tocilizumab 8 or 10 mg/kg | | |
|--------------------------------------|----------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 82 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -30.2 (\pm 27.12) | -31.5 (\pm 31.76) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|-------------------------------------|
| Comparison groups | Placebo v Tocilizumab 8 or 10 mg/kg |
| Number of subjects included in analysis | 163 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0076 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -10.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -17.6 |
| upper limit | -2.7 |

Secondary: Percent of Patients With Inactive Disease at the End of Part II of the Study (Week 40)

| | |
|-----------------|--|
| End point title | Percent of Patients With Inactive Disease at the End of Part II of the Study (Week 40) ^[11] |
|-----------------|--|

End point description:

A patient is judged to have inactive disease if all of the following criteria are met: Number of joints with active arthritis = 0; absence of active uveitis, defined by the adverse event preferred terms 'uveitis' and 'intermediate uveitis'; normal erythrocyte sedimentation rate (< 20 mm/hour regardless of age and sex); and physician's global assessment of overall well-being visual analog scale score \leq 10.

The statistical test is not significant due to a break in the hierarchical chain of significance testing.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 40

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: This endpoint data were not analyzed for all baseline period arms.

| End point values | Placebo | Tocilizumab 8 or 10 mg/kg | | |
|----------------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 82 | | |
| Units: Percent of patients | | | | |
| number (confidence interval 95%) | 17.3 (9 to 26) | 36.6 (26 to 47) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|-------------------------------------|
| Comparison groups | Tocilizumab 8 or 10 mg/kg v Placebo |
| Number of subjects included in analysis | 163 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 1 ^[12] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | weighted difference |
| Point estimate | 18 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5 |
| upper limit | 32 |

Notes:

[12] - 1.000 is used here as the test was considered as not significant due to the break in the hierarchical testing chain.

Secondary: Percent of Patients Achieving JIA ACR30/50/70/90 Responses at Weeks 2, 52, and 104

| | |
|-----------------|--|
| End point title | Percent of Patients Achieving JIA ACR30/50/70/90 Responses at Weeks 2, 52, and 104 |
|-----------------|--|

End point description:

A JIA ACR30/50/70/90 response is defined as a $\geq 30/50/70/90\%$ response on 3 of 6 variables and no more than 1 of the remaining variables worsening $> 30\%$. The 6 variables are physician global assessment of disease activity (20 units minimum on a 0-100 visual analog scale [VAS]), parent/patient global assessment of overall well-being (20 VAS units minimum), number of joints (minimum of 2 worse) with active arthritis (swelling, or pain and limitation of motion), number of joints (minimum of 2 worse) with limitation of movement, erythrocyte sedimentation rate, and functional ability assessed using the disability index of the Childhood Health Assessment Questionnaire (CHAQ, 30 questions, 8 domains, 0[best]-3[worst]).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 2 to Week 104

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Patients |
|-----------------------------|---|--|--|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 11 | 55 | 82 |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| Week 2 - ACR30 Response | 55.6 | 45.5 | 54.5 | 52.4 |
| Week 2 - ACR50 Response | 33.3 | 18.2 | 34.5 | 32.9 |
| Week 2 - ACR70 Response | 11.1 | 9.1 | 12.7 | 11 |
| Week 2 - ACR90 Response | 0 | 0 | 0 | 0 |
| Week 52 - ACR30 Response | 100 | 100 | 96.4 | 97.6 |
| Week 52 - ACR50 Response | 100 | 90.9 | 94.5 | 95.1 |
| Week 52 - ACR70 Response | 100 | 72.7 | 87.3 | 86.6 |
| Week 52 - ACR90 Response | 88.9 | 54.5 | 65.5 | 65.9 |
| Week 104 - ACR30 Response | 100 | 90.9 | 94.5 | 95.1 |
| Week 104 - ACR50 Response | 100 | 90.9 | 87.3 | 90.2 |
| Week 104 - ACR70 Response | 88.9 | 90.9 | 83.6 | 86.6 |
| Week 104 - ACR90 Response | 88.9 | 72.7 | 67.3 | 70.7 |

| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | | | |
|-----------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| Week 2 - ACR30 Response | 42.9 | | | |
| Week 2 - ACR50 Response | 42.9 | | | |
| Week 2 - ACR70 Response | 0 | | | |
| Week 2 - ACR90 Response | 0 | | | |
| Week 52 - ACR30 Response | 100 | | | |
| Week 52 - ACR50 Response | 100 | | | |
| Week 52 - ACR70 Response | 85.7 | | | |
| Week 52 - ACR90 Response | 57.1 | | | |
| Week 104 - ACR30 Response | 100 | | | |
| Week 104 - ACR50 Response | 100 | | | |
| Week 104 - ACR70 Response | 100 | | | |
| Week 104 - ACR90 Response | 71.4 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Patients With 4 Baseline Disease Characteristics Achieving JIA ACR30/50/70/90 Responses at Week 104

| | |
|--|--|
| End point title | Percent of Patients With 4 Baseline Disease Characteristics Achieving JIA ACR30/50/70/90 Responses at Week 104 |
| End point description: | |
| A JIA ACR30/50/70/90 response is defined as a $\geq 30/50/70/90\%$ response on 3 of 6 variables and no more than 1 of the remaining variables worsening $> 30\%$. The 6 variables are physician global assessment of disease activity (20 units minimum on a 0-100 visual analog scale [VAS]), parent/patient global assessment of overall well-being (20 VAS units minimum), number of joints (minimum of 2 worse) with active arthritis (swelling, or pain and limitation of motion), number of joints (minimum of 2 worse) with limitation of movement, erythrocyte sedimentation rate, and functional ability assessed using the disability index of the Childhood Health Assessment Questionnaire (CHAQ, 30 questions, 8 domains, 0[best]-3[worst]). | |
| End point type | Secondary |
| End point timeframe: | |
| Week 2 to Week 104 | |

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Patients |
|--|---|--|---|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 11 | 55 | 82 |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| Previous Biologic Use: Yes - ACR30 (n=1,0,25,27,1) | 100 | 0 | 96 | 96.3 |
| Previous Biologic Use: Yes - ACR50 (n=1,0,25,27,1) | 100 | 0 | 80 | 81.5 |
| Previous Biologic Use: Yes - ACR70 (n=1,0,25,27,1) | 0 | 0 | 72 | 70.4 |
| Previous Biologic Use: Yes - ACR90 (n=1,0,25,27,1) | 0 | 0 | 48 | 48.1 |
| Previous Biologic Use: No - ACR30 (n=8,11,30,55,6) | 100 | 90.9 | 93.3 | 94.5 |
| Previous Biologic Use: No - ACR50 (n=8,11,30,55,6) | 100 | 90.9 | 93.3 | 94.5 |
| Previous Biologic Use: No - ACR70 (n=8,11,30,55,6) | 100 | 90.9 | 93.3 | 94.5 |
| Previous Biologic Use: No - ACR90 (n=8,11,30,55,6) | 100 | 72.7 | 83.3 | 81.8 |
| Methotrexate Use: Yes - ACR30 (n=7,11,42,67,7) | 100 | 90.9 | 95.2 | 95.5 |
| Methotrexate Use: Yes - ACR50 (n=7,11,42,67,7) | 100 | 90.9 | 88.1 | 91 |
| Methotrexate Use: Yes - ACR70 (n=7,11,42,67,7) | 100 | 90.9 | 83.3 | 88.1 |
| Methotrexate Use: Yes - ACR90 (n=7,11,42,67,7) | 100 | 72.7 | 73.8 | 76.1 |
| Methotrexate Use: No - ACR30 (n=2,0,13,15,0) | 100 | 0 | 92.3 | 93.3 |
| Methotrexate Use: No - ACR50 (n=2,0,13,15,0) | 100 | 0 | 84.6 | 86.7 |
| Methotrexate Use: No - ACR70 (n=2,0,13,15,0) | 50 | 0 | 84.6 | 80 |

| | | | | |
|--|------|------|------|------|
| Methotrexate Use: No - ACR90 (n=2,0,13,15,0) | 50 | 0 | 46.2 | 46.7 |
| Oral Corticosteroid Use: Yes - ACR30(n=2,5,23,33,3) | 100 | 80 | 91.3 | 90.9 |
| Oral Corticosteroid Use: Yes - ACR50(n=2,5,23,33,3) | 100 | 80 | 91.3 | 90.9 |
| Oral Corticosteroid Use: Yes - ACR70(n=2,5,23,33,3) | 100 | 80 | 82.6 | 84.8 |
| Oral Corticosteroid Use: Yes - ACR90(n=2,5,23,33,3) | 100 | 80 | 65.2 | 69.7 |
| Oral Corticosteroid Use: No - ACR30(n=7,6,32,49,4) | 100 | 100 | 96.9 | 98 |
| Oral Corticosteroid Use: No - ACR50(n=7,6,32,49,4) | 100 | 100 | 84.4 | 89.8 |
| Oral Corticosteroid Use: No - ACR70(n=7,6,32,49,4) | 85.7 | 100 | 84.4 | 87.8 |
| Oral Corticosteroid Use: No - ACR90(n=7,6,32,49,4) | 85.7 | 66.7 | 68.8 | 71.4 |
| Rheumatoid Factor: Positive - ACR30(n=0,2,23,27,2) | 0 | 100 | 95.7 | 96.3 |
| Rheumatoid Factor: Positive - ACR50(n=0,2,23,27,2) | 0 | 100 | 91.3 | 92.6 |
| Rheumatoid Factor: Positive - ACR70(n=0,2,23,27,2) | 0 | 100 | 91.3 | 92.6 |
| Rheumatoid Factor: Positive - ACR90(n=0,2,23,27,2) | 0 | 100 | 78.3 | 77.8 |
| Rheumatoid Factor: Negative - ACR30(n=9,7,29,50,5) | 100 | 100 | 93.1 | 96 |
| Rheumatoid Factor: Negative - ACR50(n=9,7,29,50,5) | 100 | 100 | 82.8 | 90 |
| Rheumatoid Factor: Negative - ACR70(n=9,7,29,50,5) | 88.9 | 100 | 75.9 | 84 |
| Rheumatoid Factor: Negative - ACR90(n=9,7,29,50,5) | 88.9 | 85.7 | 58.6 | 70 |

| | | | | |
|---|--|--|--|--|
| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| Previous Biologic Use: Yes - ACR30 (n=1,0,25,27,1) | 100 | | | |
| Previous Biologic Use: Yes - ACR50 (n=1,0,25,27,1) | 100 | | | |
| Previous Biologic Use: Yes - ACR70 (n=1,0,25,27,1) | 100 | | | |
| Previous Biologic Use: Yes - ACR90 (n=1,0,25,27,1) | 100 | | | |
| Previous Biologic Use: No - ACR30 (n=8,11,30,55,6) | 100 | | | |
| Previous Biologic Use: No - ACR50 (n=8,11,30,55,6) | 100 | | | |

| | | | | |
|--|------|--|--|--|
| Previous Biologic Use: No - ACR70 (n=8,11,30,55,6) | 100 | | | |
| Previous Biologic Use: No - ACR90 (n=8,11,30,55,6) | 66.7 | | | |
| Methotrexate Use: Yes - ACR30 (n=7,11,42,67,7) | 100 | | | |
| Methotrexate Use: Yes - ACR50 (n=7,11,42,67,7) | 100 | | | |
| Methotrexate Use: Yes - ACR70 (n=7,11,42,67,7) | 100 | | | |
| Methotrexate Use: Yes - ACR90 (n=7,11,42,67,7) | 71.4 | | | |
| Methotrexate Use: No - ACR30 (n=2,0,13,15,0) | 0 | | | |
| Methotrexate Use: No - ACR50 (n=2,0,13,15,0) | 0 | | | |
| Methotrexate Use: No - ACR70 (n=2,0,13,15,0) | 0 | | | |
| Methotrexate Use: No - ACR90 (n=2,0,13,15,0) | 0 | | | |
| Oral Corticosteroid Use: Yes - ACR30(n=2,5,23,33,3) | 100 | | | |
| Oral Corticosteroid Use: Yes - ACR50(n=2,5,23,33,3) | 100 | | | |
| Oral Corticosteroid Use: Yes - ACR70(n=2,5,23,33,3) | 100 | | | |
| Oral Corticosteroid Use: Yes - ACR90(n=2,5,23,33,3) | 66.7 | | | |
| Oral Corticosteroid Use: No - ACR30(n=7,6,32,49,4) | 100 | | | |
| Oral Corticosteroid Use: No - ACR50(n=7,6,32,49,4) | 100 | | | |
| Oral Corticosteroid Use: No - ACR70(n=7,6,32,49,4) | 100 | | | |
| Oral Corticosteroid Use: No - ACR90(n=7,6,32,49,4) | 75 | | | |
| Rheumatoid Factor: Positive - ACR30(n=0,2,23,27,2) | 100 | | | |
| Rheumatoid Factor: Positive - ACR50(n=0,2,23,27,2) | 100 | | | |
| Rheumatoid Factor: Positive - ACR70(n=0,2,23,27,2) | 100 | | | |
| Rheumatoid Factor: Positive - ACR90(n=0,2,23,27,2) | 50 | | | |
| Rheumatoid Factor: Negative - ACR30(n=9,7,29,50,5) | 100 | | | |
| Rheumatoid Factor: Negative - ACR50(n=9,7,29,50,5) | 100 | | | |
| Rheumatoid Factor: Negative - ACR70(n=9,7,29,50,5) | 100 | | | |
| Rheumatoid Factor: Negative - ACR90(n=9,7,29,50,5) | 80 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Juvenile Arthritis Disease Activity Score-71

(JADAS-71) at Week 104

| | |
|-----------------|---|
| End point title | Change From Baseline in the Juvenile Arthritis Disease Activity Score-71 (JADAS-71) at Week 104 |
|-----------------|---|

End point description:

The JADAS-71 is composed of 4 components: Physician global assessment of disease activity on a visual analog scale (VAS) (range = 0-10, left end of the line = arthritis inactive, ie, symptom-free and no arthritis symptoms; right end = arthritis very active), patient/parent global assessment of overall well-being on a VAS (range = 0-10, left end of the line = very well, ie, symptom-free and no arthritis disease activity; right end = very poor, ie, maximum arthritis disease activity), normalized erythrocyte sedimentation rate (ESR) (range = 0-10, If ESR is ≤ 20 mm/h, set to 0. If ≥ 120 mm/h, set to 10 mm/h. If > 20 mm/h and < 120 mm/h, apply formula: $[\text{ESR} - 20 \text{ mm/h}] / 10 \text{ mm/h}$), and a count of active arthritis (swelling present or pain present and limitation of motion) in 71 selected joints (range=0-71). The JADAS-71 is the sum of the 4 component scores and ranges from 0-101. A higher score indicates more arthritis disease activity. A positive change score indicates improvement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 104

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Patients |
|--------------------------------------|---|--|---|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 11 | 51 | 76 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -31.4 (± 17.471) | -25.42 (± 13.142) | -25.7 (± 12.2) | -26.05 (± 12.941) |

| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -24.17 (± 14.856) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in the JIA ACR Component Score Physician Global Assessment of Disease Activity at Week 104

| | |
|-----------------|---|
| End point title | Percent Change From Baseline in the JIA ACR Component Score Physician Global Assessment of Disease Activity at Week 104 |
|-----------------|---|

End point description:

The patient's treating physician provides a rating of the patient's arthritis disease activity on a 0 to 100 mm horizontal scale. The extreme left end of the line represents 'arthritis inactive' (ie, symptom-free and no arthritis symptoms) and the extreme right end represents 'arthritis very active'. A negative change score indicates improvement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 104

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Patients |
|--------------------------------------|---|--|--|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 11 | 51 | 76 |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -97.65 (± 2.689) | -90.42 (± 16.306) | -87.58 (± 27.588) | -89.7 (± 23.747) |

| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -96.01 (± 9.862) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in the JIA ACR Component Score Patient/Parent Global Assessment of Overall Well-being at Week 104

| | |
|-----------------|--|
| End point title | Percent Change From Baseline in the JIA ACR Component Score Patient/Parent Global Assessment of Overall Well-being at Week 104 |
|-----------------|--|

End point description:

The patient or parent/guardian, as appropriate, provides a rating of the patient's well-being on a 0 to 100 mm horizontal scale. The extreme left end of the line represents 'very well' (ie, symptom-free and no arthritis disease activity) and the extreme right end represents 'very poor' (ie, maximum arthritis disease activity). A negative change score indicates improvement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 104

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Patients |
|--------------------------------------|---|--|--|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 11 | 51 | 76 |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -97.01 (± 5.323) | -83.06 (± 25.986) | -75.81 (± 42.143) | -75.35 (± 43.779) |

| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -38.23 (± 75.749) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline the JIA ACR Component Score Number of Joints With Active Arthritis at Week 104

| | |
|---|---|
| End point title | Percent Change From Baseline the JIA ACR Component Score Number of Joints With Active Arthritis at Week 104 |
| End point description: | |
| Joints with active arthritis are defined as joints with swelling present or pain present and limitation of motion. The maximum number of joints with active arthritis is 71. The joint assessment is performed by an independent assessor who is not the treating physician and who is blinded to all other aspects of the patient's efficacy and safety data. A negative change score indicates improvement. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Week 104 | |

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Patients |
|--------------------------------------|---|--|--|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 11 | 52 | 77 |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -98.57 (± 3.78) | -76.43 (± 44.956) | -88.6 (± 24.043) | -87.73 (± 27.088) |

| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -88.22 (± 24.908) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in the JIA ACR Component Score Number of Joints With Limitation of Movement at Week 104

| | |
|-----------------|--|
| End point title | Percent Change From Baseline in the JIA ACR Component Score Number of Joints With Limitation of Movement at Week 104 |
|-----------------|--|

End point description:

Joints with limitation of movement are defined as joints with limitation of motion. The maximum number of joints with limitation of movement is 67. The joint assessment is performed by an independent assessor who is not the treating physician and who is blinded to all other aspects of the patient's efficacy and safety data. A negative change score indicates improvement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 104

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Patients |
|--------------------------------------|---|--|--|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 11 | 52 | 77 |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -98.57 (± | -76.66 (± | -79.88 (± | -81.3 (± |

| | | | |
|-------|---------|---------|---------|
| 3.78) | 55.781) | 26.831) | 31.729) |
|-------|---------|---------|---------|

| | | | | |
|--------------------------------------|---|--|--|--|
| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -81.81 (\pm 32.048) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in the JIA ACR Component Score ESR at Week 104 [Time Frame: Baseline to Week 104]

| | |
|------------------------|--|
| End point title | Percent Change From Baseline in the JIA ACR Component Score ESR at Week 104 [Time Frame: Baseline to Week 104] |
| End point description: | Erythrocyte sedimentation rate, an acute phase protein, was measured using a kit furnished by the study central laboratory. A negative change score indicates improvement. |
| End point type | Secondary |
| End point timeframe: | Baseline to Week 104 |

| | | | | |
|--------------------------------------|---|--|---|--------------------------|
| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing \geq 30 kg | All Tocilizumab Patients |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 11 | 52 | 77 |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -84.42 (\pm 13.141) | -74.06 (\pm 31.967) | -73.85 (\pm 29.073) | -76.24 (\pm 27.263) |

| | | | | |
|-------------------------|---|--|--|--|
| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | | | |
|-------------------------|---|--|--|--|

| | | | | |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -89.21 (\pm 4.682) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in the JIA ACR Component Score Functional Ability at Week 104 [Time Frame: Baseline to Week 104]

| | |
|-----------------|---|
| End point title | Percent Change From Baseline in the JIA ACR Component Score Functional Ability at Week 104 [Time Frame: Baseline to Week 104] |
|-----------------|---|

End point description:

Functional ability is assessed with the Childhood Health Assessment Questionnaire (CHAQ-DI) disability index which consists of 30 questions in 8 domains: Dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities. There are 4 possible responses to each question (0=without any difficulty, 1=with some difficulty, 2=with much difficulty, 3=unable to do). A domain score is the highest score in that domain. If aids and devices listed in the questionnaire or assistance from a person are required to perform a task, a domain score of 0 or 1 is increased to 2; if the domain score is 2 or 3, the domain score is not adjusted. To calculate the overall score, the patient must have a domain score in at least 6 of the 8 domains. The CHAQ-DI score is the sum of the domain scores divided by the number of domains that have a non-missing score and ranges from 0 (best) to 3 (worst). A negative change score indicates improvement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 104

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing \geq 30 kg | All Tocilizumab Patients |
|--------------------------------------|---|--|---|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 11 | 52 | 77 |
| Units: Percent change | | | | |
| arithmetic mean (standard deviation) | -96.03 (\pm 10.499) | -78.58 (\pm 38.745) | -73.34 (\pm 38.745) | -76.71 (\pm 34.696) |

| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | | | |
|-----------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Percent change | | | | |

| | | | | |
|--------------------------------------|------------------|--|--|--|
| arithmetic mean (standard deviation) | -79.5 (± 18.622) | | | |
|--------------------------------------|------------------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Patients With a Minimally Important Improvement in the CHAQ-DI Score at Weeks 16, 40, 52, 80, and 104

| | |
|--|--|
| End point title | Percent of Patients With a Minimally Important Improvement in the CHAQ-DI Score at Weeks 16, 40, 52, 80, and 104 |
| End point description: | |
| <p>The CHAQ-DI consists of 30 questions in 8 domains: Dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities. There are 4 possible responses to each question (0=without any difficulty, 1=with some difficulty, 2=with much difficulty, 3=unable to do). A domain score is the highest score in that domain. If aids and devices listed in the questionnaire or assistance from a person are required to perform a task, a domain score of 0 or 1 is increased to 2; if the domain score is 2 or 3, the domain score is not adjusted. To calculate the overall score, the patient must have a domain score in at least 6 of the 8 domains. The CHAQ-DI score is the sum of the domain scores divided by the number of domains that have a non-missing score and ranges from 0 (best) to 3 (worst). A minimally important improvement is an improvement ≥ 0.13 over Baseline. Patients who withdrew due to non-safety reasons are classified as non-responders.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Week 104 | |

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Patients |
|-----------------------------|---|--|---|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 11 | 55 | 82 |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| Week 16 | 77.8 | 81.8 | 76.4 | 78 |
| Week 40 | 88.9 | 81.8 | 78.2 | 81.7 |
| Week 52 | 88.9 | 81.8 | 80 | 82.9 |
| Week 80 | 88.9 | 90.9 | 80 | 84.1 |
| Week 104 | 88.9 | 100 | 80 | 85.4 |

| | | | | |
|------------------|---|--|--|--|
| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | | | |
|------------------|---|--|--|--|

| | | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| Week 16 | 85.7 | | | |
| Week 40 | 100 | | | |
| Week 52 | 100 | | | |
| Week 80 | 100 | | | |
| Week 104 | 100 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: C-reactive Protein Levels From Baseline to Week 104

| | |
|------------------------|---|
| End point title | C-reactive Protein Levels From Baseline to Week 104 |
| End point description: | C-reactive protein (CRP), an acute phase protein, was measured in blood samples with a high-sensitivity CRP (hs-CRP) test using laser nephelometry. |
| End point type | Secondary |
| End point timeframe: | Baseline to Week 104 |

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Patients |
|--------------------------------------|---|--|--|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 9 | 53 | 78 |
| Units: mg/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 16 (n=9, 7, 53, 75, 6) | 1.726 (± 2.7395) | 1.077 (± 1.1247) | 1.137 (± 3.2472) | 1.129 (± 2.9042) |
| Week 40 (n=7, 11, 51, 76, 7) | 3.709 (± 9.0383) | 1.591 (± 2.6187) | 1.451 (± 5.9168) | 1.756 (± 5.8029) |
| Week 52 (n=8, 10, 52, 77, 7) | 3.405 (± 8.6491) | 4.584 (± 10.4573) | 0.882 (± 2.4335) | 1.569 (± 5.0838) |
| Week 80 (n=8, 10, 51, 76, 7) | 2.329 (± 5.9286) | 4.867 (± 13.0151) | 0.718 (± 1.5474) | 1.425 (± 5.225) |
| Week 104 (n=7, 11, 50, 75, 7) | 0.249 (± 0.0949) | 1.259 (± 2.8519) | 2.032 (± 6.5732) | 1.581 (± 5.4965) |

| | | | | |
|------------------|---|--|--|--|
| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing | | | |
|------------------|---|--|--|--|

| | | | | |
|--------------------------------------|----------------------|--|--|--|
| | <30kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: mg/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 16 (n=9, 7, 53, 75, 6) | 0.22 (± 0.04) | | | |
| Week 40 (n=7, 11, 51, 76, 7) | 2.286 (± 5.5183) | | | |
| Week 52 (n=8, 10, 52, 77, 7) | 0.267 (± 0.1325) | | | |
| Week 80 (n=8, 10, 51, 76, 7) | 0.623 (± 0.6096) | | | |
| Week 104 (n=7, 11, 50, 75, 7) | 0.2 (± 0) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Pain VAS Score at Weeks 2, 40, 52, and 104

| | |
|--|--|
| End point title | Change From Baseline in the Pain VAS Score at Weeks 2, 40, 52, and 104 |
| End point description: | |
| The patient or parent/guardian, as appropriate, provides a rating of the patient's pain (also called a discomfort index) on a 0 to 100 mm horizontal scale. The extreme left end of the line represents 'no pain' and the extreme right end represents 'very extreme pain'. A higher score indicates more pain. A negative change score indicates improvement. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Week 104 | |

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Patients |
|--------------------------------------|---|--|--|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 11 | 55 | 82 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 2 (n=9, 10, 52, 78, 7) | -11.4 (± 13.16) | -6.1 (± 20.98) | -10.3 (± 21.44) | -9.4 (± 19.8) |
| Week 40 (n=8, 11, 52, 78, 7) | -44 (± 12.29) | -27.9 (± 35.85) | -33.9 (± 31.64) | -33.3 (± 30.44) |
| Week 52 (n=8, 1, 52, 78, 7) | -47.8 (± 14.46) | -29.6 (± 28.39) | -35.5 (± 29.07) | -34.9 (± 27.76) |
| Week 104 (n=7, 11, 51, 76, 7) | -48.9 (± 16.71) | -27.1 (± 39.51) | -34.5 (± 34.59) | -34.4 (± 33.72) |

| | | | | |
|--------------------------------------|---|--|--|--|
| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 2 (n=9, 10, 52, 78, 7) | -4.4 (± 13.13) | | | |
| Week 40 (n=8, 11, 52, 78, 7) | -24.7 (± 27.76) | | | |
| Week 52 (n=8, 1, 52, 78, 7) | -24 (± 26.59) | | | |
| Week 104 (n=7, 11, 51, 76, 7) | -30.7 (± 31.63) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Patients With Inactive Disease From Week 16 to Week 104

| | |
|-----------------|--|
| End point title | Percent of Patients With Inactive Disease From Week 16 to Week 104 ^[13] |
|-----------------|--|

End point description:

A patient is judged to have inactive disease if all of the following criteria are met: Number of joints with active arthritis = 0; absence of active uveitis, defined by the adverse event preferred terms 'uveitis' and 'intermediate uveitis'; normal erythrocyte sedimentation rate (< 20 mm/hour regardless of age and sex); and physician's global assessment of overall well-being visual analog scale score ≤ 10. Patients who withdrew due to non-safety reasons are classified as non-responders.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 16 to Week 104

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: This endpoint data were not analyzed for all baseline period arms.

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|-----------------------------|---|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 11 | 55 | 7 |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| Week 16 | 11.1 | 18.2 | 20 | 42.9 |
| Week 40 | 44.4 | 45.5 | 38.2 | 42.9 |
| Week 52 | 66.7 | 45.5 | 50.9 | 57.1 |
| Week 80 | 66.7 | 54.5 | 56.4 | 57.1 |
| Week 104 | 66.7 | 54.5 | 63.6 | 71.4 |

| End point values | All Tocilizumab Patients | | | |
|-----------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 82 | | | |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| Week 16 | 20.7 | | | |
| Week 40 | 40.2 | | | |
| Week 52 | 52.4 | | | |
| Week 80 | 57.3 | | | |
| Week 104 | 63.4 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Patients in Clinical Remission From Week 40 to 104

| | |
|-----------------|---|
| End point title | Percent of Patients in Clinical Remission From Week 40 to |
|-----------------|---|

End point description:

A patient was in clinical remission if they had inactive disease at all visits in the 6 months prior to and including the visit assessment day. A patient was judged to have inactive disease if all of the following criteria were met: Number of joints with active arthritis = 0; absence of active uveitis, defined by the adverse event preferred terms 'uveitis' and 'intermediate uveitis'; normal erythrocyte sedimentation rate (< 20 mm/hour regardless of age and sex); and physician's global assessment of overall well-being visual analog scale score ≤ 10. Patients who withdrew due to non-safety reasons are classified as non-responders.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 40 to Week 104

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: This endpoint data were not analyzed for all baseline period arms.

| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|-----------------------------|---|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 11 | 55 | 7 |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| Week 40 | 0 | 0 | 7.3 | 14.3 |
| Week 52 | 22.2 | 18.2 | 18.2 | 14.3 |
| Week 80 | 55.6 | 36.4 | 25.5 | 42.9 |
| Week 104 | 55.6 | 27.3 | 34.5 | 57.1 |

| | | | | |
|-----------------------------|--------------------------|--|--|--|
| End point values | All Tocilizumab Patients | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 82 | | | |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| Week 40 | 6.1 | | | |
| Week 52 | 18.3 | | | |
| Week 80 | 31.7 | | | |
| Week 104 | 37.8 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Patients Achieving JIA ACR30/50/70/90 Responses at Week 104 by Duration of Disease (< 2 Years, ≥ 2 Years)

| | |
|-----------------|--|
| End point title | Percent of Patients Achieving JIA ACR30/50/70/90 Responses at Week 104 by Duration of Disease (< 2 Years, ≥ 2 Years) ^[15] |
|-----------------|--|

End point description:

A JIA ACR30/50/70/90 response is defined as a ≥ 30/50/70/90% response on 3 of 6 variables and no more than 1 of the remaining variables worsening > 30%. The 6 variables are physician global assessment of disease activity (20 units minimum on a 0-100 visual analog scale [VAS]), parent/patient global assessment of overall well-being (20 VAS units minimum), number of joints (minimum of 2 worse) with active arthritis (swelling, or pain and limitation of motion), number of joints (minimum of 2 worse) with limitation of movement, erythrocyte sedimentation rate, and functional ability assessed using the disability index of the Childhood Health Assessment Questionnaire (CHAQ, 30 questions, 8 domains, 0[best]-3[worst]). Patients who withdrew due to non-safety reasons are classified as non-responders.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 104

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: This endpoint data were not analyzed for all baseline period arms.

| | | | | |
|--|---|--|--|---------------------------|
| End point values | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 11 | 55 | 7 |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| Disease Duration < 2 Years - ACR30 (n=4,4,17,1,26) | 100 | 100 | 88.2 | 100 |
| Disease Duration < 2 Years - ACR50 (n=4,4,17,1,26) | 100 | 100 | 82.4 | 100 |

| | | | | |
|---|-----|------|------|------|
| Disease Duration < 2 Years - ACR70 (n=4,4,17,1,26) | 100 | 100 | 82.4 | 100 |
| Disease Duration < 2 Years - ACR90 (n=4,4,17,1,26) | 100 | 100 | 76.5 | 100 |
| Disease Duration ≥ 2 Years - ACR30 (n=5,7,38,6,56) | 100 | 85.7 | 97.4 | 100 |
| Disease Duration ≥ 2 Years - ACR50 (n=5,7,38,6,56) | 100 | 85.7 | 89.5 | 100 |
| Disease Duration ≥ 2 Years - ACR70 (n=5,7,38,6,56) | 80 | 85.7 | 84.2 | 100 |
| Disease Duration ≥ 2 Years - ACR90 (n=5,7,38,6,56) | 80 | 57.1 | 63.2 | 66.7 |

| End point values | All Tocilizumab Patients | | | |
|---|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 82 | | | |
| Units: Percent of patients | | | | |
| number (not applicable) | | | | |
| Disease Duration < 2 Years - ACR30 (n=4,4,17,1,26) | 92.3 | | | |
| Disease Duration < 2 Years - ACR50 (n=4,4,17,1,26) | 88.5 | | | |
| Disease Duration < 2 Years - ACR70 (n=4,4,17,1,26) | 88.5 | | | |
| Disease Duration < 2 Years - ACR90 (n=4,4,17,1,26) | 84.6 | | | |
| Disease Duration ≥ 2 Years - ACR30 (n=5,7,38,6,56) | 96.4 | | | |
| Disease Duration ≥ 2 Years - ACR50 (n=5,7,38,6,56) | 91.1 | | | |
| Disease Duration ≥ 2 Years - ACR70 (n=5,7,38,6,56) | 85.7 | | | |
| Disease Duration ≥ 2 Years - ACR90 (n=5,7,38,6,56) | 64.3 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Oral Corticosteroid Dose at Baseline, Week 52, and Week 104

| | |
|---|---|
| End point title | Oral Corticosteroid Dose at Baseline, Week 52, and Week |
| End point description: Due to the different types of corticosteroid medications available, the prednisone equivalent was used in the calculation of the oral corticosteroid dose. Values are based on the average daily dose on the study day and if not available the last observation carried forward is used. | |
| End point type | Secondary |
| End point timeframe: Baseline to Week 104 | |

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: This endpoint data were not analyzed for all baseline period arms.

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Participants |
|--------------------------------------|--|--|--|------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 22 | 34 | 119 | 188 |
| Units: mg/kg/day | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=22, 34, 119, 188, 13) | 0.041 (± 0.0704) | 0.079 (± 0.0802) | 0.055 (± 0.0708) | 0.061 (± 0.0743) |
| Week 52 (n=17, 24, 105, 159, 13) | 0.021 (± 0.0474) | 0.037 (± 0.0591) | 0.032 (± 0.049) | 0.034 (± 0.0518) |
| Week 104 (n=16, 23, 103, 155, 13) | 0.014 (± 0.0418) | 0.019 (± 0.0412) | 0.02 (± 0.0558) | 0.02 (± 0.0518) |

| End point values | Tocilizumab 10mg/kg to 8 mg/kg in Patients weighing <30kg | | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 13 | | | |
| Units: mg/kg/day | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=22, 34, 119, 188, 13) | 0.095 (± 0.0836) | | | |
| Week 52 (n=17, 24, 105, 159, 13) | 0.064 (± 0.0599) | | | |
| Week 104 (n=16, 23, 103, 155, 13) | 0.028 (± 0.0497) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Methotrexate Dose at Baseline, Week 52, and Week 104

| | |
|--|--|
| End point title | Methotrexate Dose at Baseline, Week 52, and Week 104 |
| End point description: Values are based on the average daily dose on the study day and if not available the last observation carried forward is used. | |
| End point type | Secondary |
| End point timeframe: Baseline to Week 104 | |

| End point values | Tocilizumab 10 mg/kg in Patients Weighing <30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | Tocilizumab 8 or 10 mg/kg |
|--------------------------------------|--|--|--|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 22 | 34 | 119 | 13 |
| Units: mg/m ² /week | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=22, 34, 118, 13, 187) | 11.304 (± 6.7521) | 12.146 (± 5.2822) | 8.768 (± 5.5387) | 17.562 (± 17.0864) |
| Week 52 (n=17, 24, 105, 13, 159) | 9.247 (± 5.6513) | 11.216 (± 4.689) | 8.326 (± 4.9825) | 15.568 (± 15.2521) |
| Week 104 (n=16, 23, 103, 13, 155) | 8.342 (± 5.2618) | 10.05 (± 4.6316) | 6.855 (± 5.0401) | 11.858 (± 14.3458) |

| End point values | All Tocilizumab Participants | | | |
|--------------------------------------|------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 188 | | | |
| Units: mg/m ² /week | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=22, 34, 118, 13, 187) | 10.292 (± 7.3586) | | | |
| Week 52 (n=17, 24, 105, 13, 159) | 9.453 (± 6.6963) | | | |
| Week 104 (n=16, 23, 103, 13, 155) | 7.902 (± 6.4332) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Height Standard Deviation Score at Baseline, Week 52, and Week 104

| | |
|-----------------|--|
| End point title | Height Standard Deviation Score at Baseline, Week 52, and Week 104 ^[17] |
|-----------------|--|

End point description:

The height Standard Deviation Score was calculated using the following formula: (Observed height - median of the reference population)/standard deviation of the reference population. The reference population was defined as that of the same sex and age to the nearest completed year and month using the World Health Organization norms. A negative score indicates less height than the reference population.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 104

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: This endpoint data were not analyzed for all baseline period arms.

| End point values | Placebo | Tocilizumab 8 or 10 mg/kg | All Tocilizumab Participants | |
|--------------------------------------|-----------------|---------------------------|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 84 | 82 | 187 | |
| Units: Standard deviation score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | -0.57 (± 1.005) | -0.33 (± 1.29) | -0.51 (± 1.219) | |
| Week 52 | -0.51 (± 1.004) | -0.15 (± 1.216) | -0.33 (± 1.125) | |
| Week 104 | -0.34 (± 0.954) | -0.01 (± 1.15) | -0.18 (± 1.066) | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All exposure safety population: All participants randomized into Part I of the study who received at least 1 infusion of tocilizumab and had at least 1 post-baseline safety assessment or event.

Adverse event reporting additional description:

The patients were exposed to weight adjusted doses for the 104 week duration of the study with the exception of those patients randomized in Part II (Weeks 16-40) to receive placebo. Adverse events (AE) are reported for all participants and by the various weight-based dose groups. AEs which occurred in the placebo group in Part II are not included.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 14.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg |
|-----------------------|---|

Reporting group description: -

| | |
|-----------------------|--|
| Reporting group title | Tocilizumab 10 mg/kg to 8 mg/kg in Patients Weighing < 30 kg |
|-----------------------|--|

Reporting group description: -

| | |
|-----------------------|--|
| Reporting group title | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg |
|-----------------------|--|

Reporting group description: -

| | |
|-----------------------|--|
| Reporting group title | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg |
|-----------------------|--|

Reporting group description: -

| | |
|-----------------------|--------------------------|
| Reporting group title | All Tocilizumab Patients |
|-----------------------|--------------------------|

Reporting group description: -

| Serious adverse events | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 10 mg/kg to 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 22 (18.18%) | 1 / 13 (7.69%) | 4 / 34 (11.76%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Neck injury | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Synovial rupture | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Congenital, familial and genetic disorders | | | |
| Familial mediterranean fever | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 | | | |
| Benign intracranial hypertension | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Pregnancy | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Uveitis | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 2 / 34 (5.88%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Hepatobiliary disorders | | | |
| Cholangitis sclerosing | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Hypertransaminaemia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 | | | |
| Asthmatic crisis | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Psychiatric disorders | | | |
| Psychosomatic disease | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Renal and urinary disorders | | | |
| Calculus urinary | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Osteoporosis | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Scleroderma | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 13 (0.00%) | 0 / 34 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 22 (9.09%) | 0 / 13 (0.00%) | 1 / 34 (2.94%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Varicella | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 13 (0.00%) | 1 / 34 (2.94%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Epstein-Barr Virus Infection | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Paronychia | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 0 / 34 (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 |
| Tonsillitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 1 / 34 (2.94%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 1 / 34 (2.94%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Patients | |
|---|--|-----------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 17 / 119 (14.29%) | 26 / 188 (13.83%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Neck injury | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Synovial rupture | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Familial mediterranean fever | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Benign intracranial hypertension | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Pregnancy | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Uveitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 188 (1.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholangitis sclerosing | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertransaminaemia | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthmatic crisis | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Psychosomatic disease | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Calculus urinary | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoporosis | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Scleroderma | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 119 (2.52%) | 4 / 188 (2.13%) | |
| occurrences causally related to treatment / all | 1 / 3 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 188 (1.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 2 / 119 (1.68%) | 2 / 188 (1.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Varicella | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 188 (1.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epstein-Barr Virus Infection | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paronychia | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Tocilizumab 10 mg/kg in Patients Weighing < 30 kg | Tocilizumab 10 mg/kg to 8 mg/kg in Patients Weighing < 30 kg | Tocilizumab 8 mg/kg in Patients Weighing < 30 kg |
|--|--|--|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 19 / 22 (86.36%) | 11 / 13 (84.62%) | 25 / 34 (73.53%) |
| Vascular disorders Hypotension subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 2 | 1 / 34 (2.94%) 1 |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 1 | 2 / 34 (5.88%) 3 |
| Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 34 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Pneumonitis subjects affected / exposed occurrences (all) Nasal obstruction subjects affected / exposed occurrences (all) Productive cough | 4 / 22 (18.18%) 4 1 / 22 (4.55%) 1 2 / 22 (9.09%) 3 1 / 22 (4.55%) 1 0 / 22 (0.00%) 0 0 / 22 (0.00%) 0 1 / 22 (4.55%) 0 | 2 / 13 (15.38%) 3 0 / 13 (0.00%) 0 0 / 13 (0.00%) 0 1 / 13 (7.69%) 1 0 / 13 (0.00%) 0 1 / 13 (7.69%) 1 0 / 13 (0.00%) 0 | 6 / 34 (17.65%) 9 3 / 34 (8.82%) 7 1 / 34 (2.94%) 1 0 / 34 (0.00%) 0 2 / 34 (5.88%) 2 1 / 34 (2.94%) 1 |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 34 (0.00%) 0 |
| Rhinitis allergic subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 34 (0.00%) 0 |
| Sneezing subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 34 (0.00%) 0 |
| Investigations Transaminases increased subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 34 (0.00%) 0 |
| Injury, poisoning and procedural complications Ligament sprain subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 2 | 1 / 13 (7.69%) 1 | 1 / 34 (2.94%) 1 |
| Arthropod bite subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 3 | 1 / 13 (7.69%) 1 | 1 / 34 (2.94%) 1 |
| Contusion subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 2 | 0 / 13 (0.00%) 0 | 0 / 34 (0.00%) 0 |
| Thermal burn subjects affected / exposed occurrences (all) | 1 / 22 (4.55%) 1 | 1 / 13 (7.69%) 1 | 2 / 34 (5.88%) 2 |
| Fall subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 1 | 1 / 34 (2.94%) 1 |
| Tibia fracture subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 34 (0.00%) 0 |
| Foot fracture subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 34 (0.00%) 0 |
| Nervous system disorders | | | |

| | | | |
|--|---------------------|----------------------|----------------------|
| Headache subjects affected / exposed occurrences (all) | 1 / 22 (4.55%) 1 | 3 / 13 (23.08%) 4 | 5 / 34 (14.71%) 6 |
| Dizziness subjects affected / exposed occurrences (all) | 1 / 22 (4.55%) 1 | 0 / 13 (0.00%) 0 | 0 / 34 (0.00%) 0 |
| Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 3 | 0 / 34 (0.00%) 0 |
| Eosinophilia subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 34 (0.00%) 0 |
| Hypochromic anaemia subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 34 (0.00%) 0 |
| Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 0 / 13 (0.00%) 0 | 2 / 34 (5.88%) 2 |
| Eye disorders Conjunctivitis subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 2 | 0 / 13 (0.00%) 0 | 1 / 34 (2.94%) 1 |
| Iridocyclitis subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 0 / 13 (0.00%) 0 | 2 / 34 (5.88%) 2 |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 0 / 13 (0.00%) 0 | 2 / 34 (5.88%) 2 |
| Diarrhoea subjects affected / exposed occurrences (all) | 1 / 22 (4.55%) 1 | 0 / 13 (0.00%) 0 | 2 / 34 (5.88%) 2 |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 22 (4.55%) 1 | 1 / 13 (7.69%) 1 | 3 / 34 (8.82%) 4 |

| | | | |
|--|----------------|----------------|----------------|
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 1 / 13 (7.69%) | 2 / 34 (5.88%) |
| occurrences (all) | 1 | 1 | 2 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 2 / 34 (5.88%) |
| occurrences (all) | 0 | 0 | 5 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Aphthous stomatitis | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 1 | 1 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 13 (0.00%) | 3 / 34 (8.82%) |
| occurrences (all) | 1 | 0 | 4 |
| Ingrowing nail | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eczema | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 2 / 34 (5.88%) |
| occurrences (all) | 0 | 0 | 2 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 2 / 34 (5.88%) |
| occurrences (all) | 0 | 0 | 2 |
| Erythema | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 1 | 1 |
| Prurigo | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 0 / 13 (0.00%) 0 | 2 / 34 (5.88%) 3 |
| Musculoskeletal and connective tissue disorders | | | |
| Juvenile arthritis | | | |
| subjects affected / exposed | 6 / 22 (27.27%) | 3 / 13 (23.08%) | 6 / 34 (17.65%) |
| occurrences (all) | 6 | 3 | 7 |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 22 (13.64%) | 2 / 13 (15.38%) | 0 / 34 (0.00%) |
| occurrences (all) | 3 | 5 | 0 |
| Muscle disorder | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Polyarthrititis | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 7 / 22 (31.82%) | 1 / 13 (7.69%) | 5 / 34 (14.71%) |
| occurrences (all) | 11 | 1 | 15 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 22 (9.09%) | 0 / 13 (0.00%) | 4 / 34 (11.76%) |
| occurrences (all) | 6 | 0 | 4 |
| Pharyngitis | | | |
| subjects affected / exposed | 4 / 22 (18.18%) | 1 / 13 (7.69%) | 3 / 34 (8.82%) |
| occurrences (all) | 7 | 2 | 4 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 2 / 13 (15.38%) | 5 / 34 (14.71%) |
| occurrences (all) | 2 | 2 | 8 |
| Ear infection | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 2 / 13 (15.38%) | 2 / 34 (5.88%) |
| occurrences (all) | 1 | 3 | 3 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 13 (0.00%) | 3 / 34 (8.82%) |
| occurrences (all) | 2 | 0 | 4 |
| Influenza | | | |

| | | | |
|-----------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 2 / 22 (9.09%) | 1 / 13 (7.69%) | 1 / 34 (2.94%) |
| occurrences (all) | 3 | 1 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 2 / 13 (15.38%) | 2 / 34 (5.88%) |
| occurrences (all) | 1 | 2 | 2 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 13 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 2 | 0 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 13 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 1 | 0 | 1 |
| Oral herpes | | | |
| subjects affected / exposed | 2 / 22 (9.09%) | 1 / 13 (7.69%) | 1 / 34 (2.94%) |
| occurrences (all) | 3 | 1 | 1 |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 2 / 34 (5.88%) |
| occurrences (all) | 0 | 0 | 4 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 22 (9.09%) | 0 / 13 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 1 | 1 |
| Laryngitis | | | |
| subjects affected / exposed | 2 / 22 (9.09%) | 0 / 13 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Varicella | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 2 / 13 (15.38%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Infection parasitic | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 1 | 1 |
| Mumps | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 13 (0.00%) | 2 / 34 (5.88%) |
| occurrences (all) | 0 | 0 | 2 |
| Abscess | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin bacterial infection | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 1 | 1 |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 13 (7.69%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| Non-serious adverse events | Tocilizumab 8 mg/kg in Patients Weighing ≥ 30 kg | All Tocilizumab Patients | |
|--|--|-----------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 102 / 119 (85.71%) | 157 / 188 (83.51%) | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 2 / 119 (1.68%) | 4 / 188 (2.13%) | |
| occurrences (all) | 2 | 5 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 119 (3.36%) | 7 / 188 (3.72%) | |
| occurrences (all) | 5 | 9 | |
| Reproductive system and breast disorders | | | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) | |
| occurrences (all) | 0 | 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|--|-------------------|-------------------|--|
| Cough | | | |
| subjects affected / exposed | 13 / 119 (10.92%) | 25 / 188 (13.30%) | |
| occurrences (all) | 16 | 32 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 15 / 119 (12.61%) | 19 / 188 (10.11%) | |
| occurrences (all) | 20 | 28 | |
| Epistaxis | | | |
| subjects affected / exposed | 5 / 119 (4.20%) | 8 / 188 (4.26%) | |
| occurrences (all) | 5 | 9 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 4 / 119 (3.36%) | 6 / 188 (3.19%) | |
| occurrences (all) | 4 | 6 | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 3 / 188 (1.60%) | |
| occurrences (all) | 1 | 3 | |
| Nasal obstruction | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 188 (1.06%) | |
| occurrences (all) | 0 | 2 | |
| Productive cough | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 2 / 188 (1.06%) | |
| occurrences (all) | 1 | 2 | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) | |
| occurrences (all) | 0 | 1 | |
| Sneezing | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) | |
| occurrences (all) | 0 | 1 | |
| Investigations | | | |
| Transaminases increased | | | |
| subjects affected / exposed | 4 / 119 (3.36%) | 5 / 188 (2.66%) | |
| occurrences (all) | 4 | 5 | |
| Injury, poisoning and procedural complications | | | |
| Ligament sprain | | | |
| subjects affected / exposed | 3 / 119 (2.52%) | 7 / 188 (3.72%) | |
| occurrences (all) | 4 | 8 | |
| Arthropod bite | | | |

| | | | |
|--------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed | 2 / 119 (1.68%) | 6 / 188 (3.19%) | |
| occurrences (all) | 2 | 7 | |
| Contusion | | | |
| subjects affected / exposed | 2 / 119 (1.68%) | 4 / 188 (2.13%) | |
| occurrences (all) | 2 | 4 | |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 4 / 188 (2.13%) | |
| occurrences (all) | 0 | 4 | |
| Fall | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 3 / 188 (1.60%) | |
| occurrences (all) | 1 | 3 | |
| Tibia fracture | | | |
| subjects affected / exposed | 2 / 119 (1.68%) | 3 / 188 (1.60%) | |
| occurrences (all) | 2 | 3 | |
| Foot fracture | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 2 / 188 (1.06%) | |
| occurrences (all) | 1 | 2 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 22 / 119 (18.49%) | 31 / 188 (16.49%) | |
| occurrences (all) | 41 | 52 | |
| Dizziness | | | |
| subjects affected / exposed | 7 / 119 (5.88%) | 8 / 188 (4.26%) | |
| occurrences (all) | 11 | 12 | |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 2 / 188 (1.06%) | |
| occurrences (all) | 1 | 4 | |
| Eosinophilia | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) | |
| occurrences (all) | 0 | 1 | |
| Hypochromic anaemia | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) | |
| occurrences (all) | 0 | 1 | |
| Ear and labyrinth disorders | | | |

| | | | |
|--|-------------------------|------------------------|--|
| Ear pain subjects affected / exposed occurrences (all) | 6 / 119 (5.04%) 6 | 8 / 188 (4.26%) 8 | |
| Eye disorders Conjunctivitis subjects affected / exposed occurrences (all) | 6 / 119 (5.04%) 6 | 9 / 188 (4.79%) 9 | |
| Iridocyclitis subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 2 / 188 (1.06%) 2 | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 15 / 119 (12.61%) 26 | 17 / 188 (9.04%) 28 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 14 / 119 (11.76%) 16 | 17 / 188 (9.04%) 19 | |
| Vomiting subjects affected / exposed occurrences (all) | 12 / 119 (10.08%) 14 | 17 / 188 (9.04%) 20 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 12 / 119 (10.08%) 18 | 16 / 188 (8.51%) 22 | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 8 / 119 (6.72%) 9 | 10 / 188 (5.32%) 14 | |
| Mouth ulceration subjects affected / exposed occurrences (all) | 6 / 119 (5.04%) 11 | 7 / 188 (3.72%) 12 | |
| Aphthous stomatitis subjects affected / exposed occurrences (all) | 3 / 119 (2.52%) 5 | 5 / 188 (2.66%) 7 | |
| Dental caries subjects affected / exposed occurrences (all) | 3 / 119 (2.52%) 3 | 4 / 188 (2.13%) 4 | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|-------------------|-------------------|--|
| Rash | | | |
| subjects affected / exposed | 7 / 119 (5.88%) | 11 / 188 (5.85%) | |
| occurrences (all) | 8 | 13 | |
| Ingrowing nail | | | |
| subjects affected / exposed | 6 / 119 (5.04%) | 6 / 188 (3.19%) | |
| occurrences (all) | 7 | 7 | |
| Urticaria | | | |
| subjects affected / exposed | 5 / 119 (4.20%) | 6 / 188 (3.19%) | |
| occurrences (all) | 7 | 8 | |
| Eczema | | | |
| subjects affected / exposed | 3 / 119 (2.52%) | 5 / 188 (2.66%) | |
| occurrences (all) | 4 | 6 | |
| Alopecia | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 3 / 188 (1.60%) | |
| occurrences (all) | 1 | 3 | |
| Erythema | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 3 / 188 (1.60%) | |
| occurrences (all) | 1 | 3 | |
| Prurigo | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 188 (1.06%) | |
| occurrences (all) | 0 | 3 | |
| Musculoskeletal and connective tissue disorders | | | |
| Juvenile arthritis | | | |
| subjects affected / exposed | 37 / 119 (31.09%) | 52 / 188 (27.66%) | |
| occurrences (all) | 49 | 65 | |
| Arthralgia | | | |
| subjects affected / exposed | 5 / 119 (4.20%) | 10 / 188 (5.32%) | |
| occurrences (all) | 7 | 15 | |
| Muscle disorder | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) | |
| occurrences (all) | 0 | 1 | |
| Polyarthrititis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |

| | | |
|-----------------------------------|-------------------|-------------------|
| Nasopharyngitis | | |
| subjects affected / exposed | 32 / 119 (26.89%) | 45 / 188 (23.94%) |
| occurrences (all) | 57 | 84 |
| Upper respiratory tract infection | | |
| subjects affected / exposed | 17 / 119 (14.29%) | 23 / 188 (12.23%) |
| occurrences (all) | 37 | 47 |
| Pharyngitis | | |
| subjects affected / exposed | 18 / 119 (15.13%) | 26 / 188 (13.83%) |
| occurrences (all) | 23 | 36 |
| Rhinitis | | |
| subjects affected / exposed | 7 / 119 (5.88%) | 15 / 188 (7.98%) |
| occurrences (all) | 7 | 19 |
| Ear infection | | |
| subjects affected / exposed | 10 / 119 (8.40%) | 15 / 188 (7.98%) |
| occurrences (all) | 14 | 21 |
| Gastroenteritis | | |
| subjects affected / exposed | 7 / 119 (5.88%) | 11 / 188 (5.85%) |
| occurrences (all) | 11 | 17 |
| Influenza | | |
| subjects affected / exposed | 7 / 119 (5.88%) | 11 / 188 (5.85%) |
| occurrences (all) | 8 | 13 |
| Sinusitis | | |
| subjects affected / exposed | 5 / 119 (4.20%) | 10 / 188 (5.32%) |
| occurrences (all) | 5 | 10 |
| Bronchitis | | |
| subjects affected / exposed | 6 / 119 (5.04%) | 8 / 188 (4.26%) |
| occurrences (all) | 8 | 11 |
| Urinary tract infection | | |
| subjects affected / exposed | 6 / 119 (5.04%) | 8 / 188 (4.26%) |
| occurrences (all) | 6 | 8 |
| Oral herpes | | |
| subjects affected / exposed | 3 / 119 (2.52%) | 7 / 188 (3.72%) |
| occurrences (all) | 3 | 8 |
| Pharyngotonsillitis | | |
| subjects affected / exposed | 6 / 119 (5.04%) | 7 / 188 (3.72%) |
| occurrences (all) | 8 | 9 |

| | | |
|-----------------------------------|-----------------|-----------------|
| Otitis media | | |
| subjects affected / exposed | 3 / 119 (2.52%) | 5 / 188 (2.66%) |
| occurrences (all) | 3 | 7 |
| Pneumonia | | |
| subjects affected / exposed | 3 / 119 (2.52%) | 5 / 188 (2.66%) |
| occurrences (all) | 3 | 5 |
| Respiratory tract infection viral | | |
| subjects affected / exposed | 4 / 119 (3.36%) | 5 / 188 (2.66%) |
| occurrences (all) | 6 | 7 |
| Viral infection | | |
| subjects affected / exposed | 3 / 119 (2.52%) | 4 / 188 (2.13%) |
| occurrences (all) | 3 | 4 |
| Laryngitis | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 3 / 188 (1.60%) |
| occurrences (all) | 1 | 3 |
| Varicella | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 5 / 188 (2.66%) |
| occurrences (all) | 0 | 5 |
| Infection parasitic | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 188 (1.06%) |
| occurrences (all) | 0 | 2 |
| Mumps | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 188 (1.06%) |
| occurrences (all) | 0 | 2 |
| Abscess | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) |
| occurrences (all) | 0 | 1 |
| Skin bacterial infection | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) |
| occurrences (all) | 0 | 1 |
| Respiratory tract infection | | |
| subjects affected / exposed | 2 / 119 (1.68%) | 4 / 188 (2.13%) |
| occurrences (all) | 2 | 4 |
| Abscess limb | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 188 (0.53%) |
| occurrences (all) | 0 | 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported