Clinical trial results:
A Phase 3 Multi-center, Open-Label Study to Evaluate Pharmacokinetics, Efficacy and Safety of Abatacept Administered Subcutaneously (SC) in Children and Adolescents with Active Polyarticular Juvenile Idiopathic Arthritis (pJIA) and Inadequate Response (IR) to biologic or non biologic Disease Modifying Anti-Rheumatic Drugs (DMARDs)

Summary

EudraCT number	2012-003195-39
Trial protocol	DE BE ES IT Outside EU/EEA FR
Global end of trial date	

Results information

Result version number	v1
This version publication date	12 July 2019
First version publication date	12 July 2019

Trial information

Trial identification

Sponsor protocol code	IM101-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01844518
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Route 206 and Province Line Road, Princeton, United States, NJ 08540-4000
Public contact	Study Director - Bristol-Myers Squibb, Bristol-Myers Squibb, Clinical.Trials@bms.com
Scientific contact	Study Director - Bristol-Myers Squibb, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000118-PIP02-10
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	02 October 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to estimate abatacept steady-state trough serum concentrations (Cminss) at Day 113 in children and adolescents with Polyarticular Juvenile Idiopathic Arthritis (pJIA) aged 6 through 17 years.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 August 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Brazil: 6
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 73
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Mexico: 25
Country: Number of subjects enrolled	Peru: 10
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	South Africa: 19
Country: Number of subjects enrolled	United States: 26
Country: Number of subjects enrolled	Argentina: 26
Worldwide total number of subjects	234
EEA total number of subjects	117

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)	128
Adolescents (12-17 years)	106
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:

Total 234 participants were enrolled, 220 randomized as 14 participants were screen failures. 219 participants were treated as one participant discontinued prior to being dosed, hence not included in analysis.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SC Abatacept Ages 6 to 17

Arm description:

Subcutaneous (SC) abatacept administered by prefilled syringe (PFS) once weekly according to the following weight-tiered dosing regimen: 10 to less than (<) 25 kilogram (kg) (50 milligram [mg] in 0.4 milliliter [mL] PFS), 25 to < 50 kg (87.5 mg in 0.7 mL PFS) and 50 kg (125 mg in 1 mL PFS).

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Abatacept was administered once weekly according to the following weight-tiered dosing regimen: 10 to l< 25 kg (50 mg in 0.4 mL PFS), 25 to < 50 kg (87.5 mg in 0.7 mL PFS) and 50 kg (125 mg in 1 mL PFS).

Arm title	SC Abatacept Ages 2 to 5

Arm description:

All weight-tiered dosing groups receiving SC abatacept administered by prefilled syringe (PFS) once weekly according to weight-tiered dose regimen as follows: 10 to < 25kg (50 mg in 0.4 mL PFS), 25 to < 50 kg (87.5 mg in 0.7 mL PFS) and 50 kg (125 mg in 1 mL PFS).

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Abatacept was administered once weekly according to the following weight-tiered dosing regimen: 10 to l< 25 kg (50 mg in 0.4 mL PFS), 25 to < 50 kg (87.5 mg in 0.7 mL PFS) and 50 kg (125 mg in 1 mL PFS).

Number of subjects in period 1[1]	SC Abatacept Ages 6 to 17	SC Abatacept Ages 2 to 5
Started	173	46
Completed	132	39
Not completed	41	7
Withdrawal of Consent	9	-
Poor/Non-Compliance	1	-
Participant requested to discontinue	4	1
Adverse event, non-fatal	7	1
No Longer Met Study Criteria	2	-
Pregnancy	1	-
Lack of efficacy	17	5

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 234 participants were enrolled, of whom 220 were randomized as 14 participants were screen failures. Of these, 219 participants were treated as one participant discontinued prior to being dosed and was not included in analysis.

Baseline characteristics

Reporting groups	
Reporting group title	SC Abatacept Ages 6 to 17
Reporting group description:	
Subcutaneous (SC) abatacept administered by prefilled syringe (PFS) once weekly according to the following weight-tiered dosing regimen: 10 to less than (<) 25 kilogram (kg) (50 milligram [mg] in 0.4 milliliter [mL] PFS), 25 to < 50 kg (87.5 mg in 0.7 mL PFS) and 50 kg (125 mg in 1 mL PFS).	
Reporting group title	SC Abatacept Ages 2 to 5
Reporting group description:	
All weight-tiered dosing groups receiving SC abatacept administered by prefilled syringe (PFS) once weekly according to weight-tiered dose regimen as follows: 10 to < 25kg (50 mg in 0.4 mL PFS), 25 to < 50 kg (87.5 mg in 0.7 mL PFS) and 50 kg (125 mg in 1 mL PFS).	

Reporting group values	SC Abatacept Ages 6 to 17	SC Abatacept Ages 2 to 5	Total
Number of subjects	173	46	219
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	74	46	120
Adolescents (12-17 years)	99	0	99
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender, Male/Female Units: Subjects			
Female	136	28	164
Male	37	18	55
Race (NIH/OMB) Units: Subjects			
Black or African American	14	1	15
White	144	44	188
Other	15	1	16

End points

End points reporting groups

Reporting group title	SC Abatacept Ages 6 to 17
Reporting group description:	
Subcutaneous (SC) abatacept administered by prefilled syringe (PFS) once weekly according to the following weight-tiered dosing regimen: 10 to less than (<) 25 kilogram (kg) (50 milligram [mg] in 0.4 milliliter [mL] PFS), 25 to < 50 kg (87.5 mg in 0.7 mL PFS) and 50 kg (125 mg in 1 mL PFS).	
Reporting group title	SC Abatacept Ages 2 to 5
Reporting group description:	
All weight-tiered dosing groups receiving SC abatacept administered by prefilled syringe (PFS) once weekly according to weight-tiered dose regimen as follows: 10 to < 25kg (50 mg in 0.4 mL PFS), 25 to < 50 kg (87.5 mg in 0.7 mL PFS) and 50 kg (125 mg in 1 mL PFS).	
Subject analysis set title	10 to <25 kg Dosing Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Weight-tiered dosing group received 50 mg SC abatacept administered to 6 to 17 year old participants by PFS once weekly.	
Subject analysis set title	25 to <50 kg Dosing Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Weight-tiered dosing group received 87.5 mg SC abatacept administered to 6 to 17 year old participants by PFS once weekly.	
Subject analysis set title	>=50 kg Dosing Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Weight-tiered dosing group received 125 mg SC abatacept administered to 6 to 17 year old participants by PFS once weekly.	

Primary: Abatacept Trough Concentration (Cmin) in Subjects Ages 6 to 17

End point title	Abatacept Trough Concentration (Cmin) in Subjects Ages 6 to 17[1][2]
End point description:	
Trough concentration of abatacept (reported as geometric mean of Cmin) in all pharmacokinetic (PK)-evaluable subjects. Cmin is reported in microgram per milliliter (µg/mL). Desired target therapeutic Cmin should be >= 10 µg/mL. Evaluable pharmacokinetic (PK) analysis population at Day 113 included all the subjects whose PK measurements were collected in the 4 to 10 day window after the previous SC dose and prior to Day 113 dose and if 7 consecutive weekly SC abatacept injections of the same dose were administrated prior to Day 113. Here 'N' 'number of subjects analyzed' signifies subjects who were evaluable for this time point. As per planned analysis results were reported for this arm only.	
End point type	Primary
End point timeframe:	
Day 113	

Notes:

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

[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: Only summary statistics were planned for this endpoint.

End point values	SC Abatacept Ages 6 to 17			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cmin	39.7 (± 35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects (ages 6 to 17) Achieving American College of Rheumatology Pediatric 30 Response (ACRp30)

End point title	Percentage of Subjects (ages 6 to 17) Achieving American College of Rheumatology Pediatric 30 Response (ACRp30)[3]

End point description:

ACRp30 is defined as ≥30% improvement in at least 3 of the 6 juvenile idiopathic arthritis (JIA) core set variables [number of active joints, number of joints with limitation of motion (LOM), physician global assessment of disease activity, parent global assessment of patient overall well-being, functional ability as measured by the Children's Health Assessment Questionnaire (CHAQ) and C-reactive protein (CRP)] and ≥30% worsening in not more than 1 of the remaining 6 JIA core set variables. All treated population included all participants who received at least one dose of study medication.

End point type	Secondary

End point timeframe:

Day 113

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: Only summary statistics were planned for this endpoint.

End point values	SC Abatacept Ages 6 to 17			
Subject group type	Reporting group			
Number of subjects analysed	173			
Units: Percentage of subjects				
number (confidence interval 95%)				
ACRp30	80.9 (75.1 to 86.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Abatacept Trough Concentration (Cmin) in Subjects Ages 6 to 17 by Weight Tier Dose

End point title	Abatacept Trough Concentration (Cmin) in Subjects Ages 6 to 17 by Weight Tier Dose

End point description:

Evaluation of the trough concentration of abatacept (reported as geometric mean of Cmin) in all pk-

evaluable subjects at Days 57, 85 and 113 during a 4-month treatment period. Weight-tiered dosing groups are based on the first dose the subject received. Cmin is reported in microgram per milliliter (µg/mL). Evaluable PK analysis population at Days 57 or 85 included all the subjects whose PK measurements were collected in the 4 to 10 day window after the previous SC dose and prior to the Day 57 dose or Day 85 dose, respectively; and for Day 113 included all the subjects whose PK measurements were collected in the 4 to 10 day window after the previous SC dose and prior to Day 113 dose and if 7 consecutive weekly SC abatacept injections of the same dose were administrated prior to Day 113. Here 'n' 'number analyzed' signifies subjects who were evaluable for each time point. As per planned analysis results were reported for this arm only.

End point type	Secondary

End point timeframe:

Days 57, 85 and 113

End point values	10 to <25 kg Dosing Group	25 to <50 kg Dosing Group	>=50 kg Dosing Group	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	18	74	81	
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Day 57 (n =14, 69, 75)	29.5 (± 32)	36.2 (± 35)	33.3 (± 33)	
Day 85 (n= 17, 64, 65)	27.7 (± 38)	42.5 (± 32)	36.0 (± 40)	
Day 113 (n= 14, 62, 59)	34.3 (± 39)	44.2 (± 34)	36.3 (± 31)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects (ages 6 to 17) with Adverse Events (AEs), Deaths, Serious AEs (SAEs) and AEs Leading to Discontinuation in the Short Term Period

End point title	Number of Subjects (ages 6 to 17) with Adverse Events (AEs), Deaths, Serious AEs (SAEs) and AEs Leading to Discontinuation in the Short Term Period[4]

End point description:

An AE is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation subject administered an investigational (medicinal) product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of investigational product, whether or not considered related to the investigational product. A SAE is any untoward medical occurrence that at any dose which results in death, is life threatening, requires inpatient hospitalization or causes prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect. All treated population included all subjects who received at least one dose of study medication. As per planned analysis results were reported for this arm only.

End point type	Secondary

End point timeframe:

Day 1 up to 56 days post last dose in short-term period or first dose in long-term period whichever is first

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary statistics were planned for this endpoint.

End point values	SC Abatacept Ages 6 to 17			
Subject group type	Reporting group			
Number of subjects analysed	173			
Units: Subjects				
Deaths	0			
SAEs	5			
Drug-Related SAEs	1			
Discontinuation due to SAEs	2			
Drug-Related AEs	36			
Discontinuation due to AEs	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Adverse Events (AEs), Deaths, Serious AEs and AEs Leading to Discontinuation in the Cumulative Period

End point title	Number of Subjects with Adverse Events (AEs), Deaths, Serious AEs and AEs Leading to Discontinuation in the Cumulative Period

End point description:

An AE is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation subject administered an investigational (medicinal) product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of investigational product, whether or not considered related to the investigational product. A SAE is any untoward medical occurrence that at any dose which results in death, is life threatening, requires inpatient hospitalization or causes prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect. All treated population included all subjects who received at least one dose of study medication. As per planned analysis results were reported for this arm only.

End point type	Secondary

End point timeframe:

Day 1 up to 56 days after last dose (up to 2 years)

End point values	SC Abatacept Ages 6 to 17	SC Abatacept Ages 2 to 5		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	46		
Units: Subjects				
Deaths	0	0		
SAEs	14	5		
Drug-Related SAEs	1	2		
Discontinuation Due to SAEs	4	0		
Treatment-Related AEs	54	30		
Discontinuation Due to AEs	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects (ages 6 to 17) with Positive Immunogenicity Response in the Short Term Period

End point title	Number of Subjects (ages 6 to 17) with Positive Immunogenicity Response in the Short Term Period[5]

End point description:

Overall number of subjects with either a positive immunogenicity response for 'CTLA4 and possibly Ig' or 'Ig and/or Junction Region' relative to baseline. Sample draws for immunogenicity were scheduled at specific study days while on treatment for all subjects and at follow-up visits 28, 85, and 168 days after the last abatacept dose for those subjects who discontinued from the ST period or completed the ST study without continuing abatacept treatment. Immunogenicity analysis population: who received at least one dose of study medication and who had at least 1 immunogenicity result reported after start of study medication. Here 'N' number of participants analyzed signifies participants who were evaluable for this outcome measure. As per planned analysis results were reported for this arm only.

End point type	Secondary

End point timeframe:

From Day 1 up to start of LT (for those continuing in long-term) or up to 168 days after the lost dose of study medication in the ST period (for those not entering in the long-term)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary statistics were planned for this endpoint.

End point values	SC Abatacept Ages 6 to 17			
Subject group type	Reporting group			
Number of subjects analysed	171			
Units: Subjects				
# of subjects (6-17 yr) with +ve Imm. Resp. in ST	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Positive Immunogenicity Response in the Cumulative Period

End point title	Number of Subjects with Positive Immunogenicity Response in the Cumulative Period

End point description:

Overall number of subjects with either a positive immunogenicity response for 'CTLA4 and possibly Ig' or 'Ig and/or Junction Region' relative to baseline. Sample draws for immunogenicity were scheduled at specific study days while on treatment for all subjects and at follow-up visits 28, 85, and 168 days after the last abatacept dose regardless of whether they discontinued early in the ST or LTE period, elected not to enter the LTE period, or completed both ST and LTE periods. Immunogenicity analysis population included all subjects who received at least one dose of study medication and who had at least 1 immunogenicity result reported after start of study medication.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	SC Abatacept Ages 6 to 17	SC Abatacept Ages 2 to 5		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	46		
Units: Subjects				
# of Subjects with +ve Imm. Resp in Cum. Period	8	7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 up to 56 days after last dose (up to 2 years)	
Adverse event reporting additional description:	
Safety population included all treated population who received at least one dose of study medication.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	SC Abatacept Ages 6 to 17
Reporting group description:	
Subcutaneous (SC) abatacept administered by prefilled syringe (PFS) once weekly according to the following weight-tiered dosing regimen: 10 to less than (<) 25 kilogram (kg) (50 milligram [mg] in 0.4 milliliter [mL] PFS), 25 to < 50 kg (87.5 mg in 0.7 mL PFS) and 50 kg (125 mg in 1 mL PFS).	
Reporting group title	SC Abatacept Ages 2 to 5
Reporting group description:	
All weight-tiered dosing groups receiving SC abatacept administered by prefilled syringe (PFS) once weekly according to weight-tiered dose regimen as follows: 10 to < 25kg (50 mg in 0.4 mL PFS), 25 to < 50 kg (87.5 mg in 0.7 mL PFS) and 50 kg (125 mg in 1 mL PFS).	

Serious adverse events	SC Abatacept Ages 6 to 17	SC Abatacept Ages 2 to 5	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 173 (8.09%)	5 / 46 (10.87%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian germ cell teratoma stage iii			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			

subjects affected / exposed	0 / 173 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autonomic nervous system imbalance			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			
subjects affected / exposed	0 / 173 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Synovitis			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon disorder			
subjects affected / exposed	0 / 173 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonia			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	0 / 173 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 173 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	1 / 173 (0.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	SC Abatacept Ages 6 to 17	SC Abatacept Ages 2 to 5	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	116 / 173 (67.05%)	42 / 46 (91.30%)	
Nervous system disorders			
Headache			
subjects affected / exposed	24 / 173 (13.87%)	6 / 46 (13.04%)	
occurrences (all)	35	11	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	21 / 173 (12.14%)	15 / 46 (32.61%)	
occurrences (all)	35	24	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 173 (2.89%)	3 / 46 (6.52%)	
occurrences (all)	5	3	

Gastrointestinal disorders			
Nausea			
subjects affected / exposed	20 / 173 (11.56%)	6 / 46 (13.04%)	
occurrences (all)	26	7	
Vomiting			
subjects affected / exposed	11 / 173 (6.36%)	6 / 46 (13.04%)	
occurrences (all)	18	9	
Constipation			
subjects affected / exposed	1 / 173 (0.58%)	3 / 46 (6.52%)	
occurrences (all)	1	5	
Diarrhoea			
subjects affected / exposed	5 / 173 (2.89%)	3 / 46 (6.52%)	
occurrences (all)	5	3	
Abdominal pain			
subjects affected / exposed	13 / 173 (7.51%)	4 / 46 (8.70%)	
occurrences (all)	16	5	
Aphthous ulcer			
subjects affected / exposed	3 / 173 (1.73%)	3 / 46 (6.52%)	
occurrences (all)	7	3	
Dental caries			
subjects affected / exposed	7 / 173 (4.05%)	4 / 46 (8.70%)	
occurrences (all)	11	9	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 173 (4.62%)	9 / 46 (19.57%)	
occurrences (all)	9	12	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	52 / 173 (30.06%)	17 / 46 (36.96%)	
occurrences (all)	86	37	
Rhinitis			
subjects affected / exposed	10 / 173 (5.78%)	8 / 46 (17.39%)	
occurrences (all)	16	14	
Pharyngitis			
subjects affected / exposed	11 / 173 (6.36%)	6 / 46 (13.04%)	
occurrences (all)	13	7	

Tonsillitis			
subjects affected / exposed	6 / 173 (3.47%)	4 / 46 (8.70%)	
occurrences (all)	9	7	
Gastroenteritis			
subjects affected / exposed	15 / 173 (8.67%)	6 / 46 (13.04%)	
occurrences (all)	17	6	
Bronchitis			
subjects affected / exposed	6 / 173 (3.47%)	4 / 46 (8.70%)	
occurrences (all)	9	5	
Conjunctivitis			
subjects affected / exposed	7 / 173 (4.05%)	6 / 46 (13.04%)	
occurrences (all)	8	6	
Influenza			
subjects affected / exposed	10 / 173 (5.78%)	3 / 46 (6.52%)	
occurrences (all)	18	4	
Varicella			
subjects affected / exposed	0 / 173 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Scarlet fever			
subjects affected / exposed	0 / 173 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Molluscum contagiosum			
subjects affected / exposed	2 / 173 (1.16%)	3 / 46 (6.52%)	
occurrences (all)	2	3	
Upper respiratory tract infection			
subjects affected / exposed	32 / 173 (18.50%)	10 / 46 (21.74%)	
occurrences (all)	62	15	
Urinary tract infection			
subjects affected / exposed	10 / 173 (5.78%)	1 / 46 (2.17%)	
occurrences (all)	13	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 February 2013	The main reason of this amendment was to eliminate two questionnaires, the requirement of varicella vaccination prior to the enrollment in the study, the modification of the acceptable methods of contraception, and additional minor changes to the protocol.
14 February 2014	The main reason of this amendment was to amend inclusion and exclusion criteria, revise pregnancy testing requirements, and to make additional minor changes to the protocol.
22 January 2015	The main reason of this amendment was to clarify that the 7 days post dose follow up visit is performed as the early termination/final study completion visit, to update objectives/endpoints to align with the current regulatory view on long-term safety analysis, and to make other minor changes to the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported