Clinical trial results:
A Double-blind, Placebo-controlled, Multicenter Study of the Efficacy and Safety of Adalimumab in Pediatric Subjects with Enthesitis Related Arthritis

Summary

EudraCT number	2009-017938-46
Trial protocol	DE FR ES IE SE IT Outside EU/EEA
Global end of trial date	30 December 2015

Results information

Result version number	v1 (current)
This version publication date	15 July 2016
First version publication date	15 July 2016

Trial information

Trial identification

Sponsor protocol code	M11-328

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01166282
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	1 North Waukegan Road, North Chicago, IL, United States, 60064
Public contact	Global Medical Information, AbbVie, 001 800-633-9110,
Scientific contact	Jaclyn Anderson, DO, MS, AbbVie, jaclyn.anderson@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000366-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	30 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy and safety of adalimumab given subcutaneously every other week (eow) as compared to placebo in pediatric subjects with Enthesitis Related Arthritis (ERA).

Protection of trial subjects:

Subject and/or parent or legal guardian read and understood the information provided about the study and gave written informed consent; pediatric subjects provided written verbal and/or informed assent. If a subject became of legal age (according to local regulations) during the course of the study, then that subject signed the informed consent form as well.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 September 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Mexico: 9
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	Canada: 2
Worldwide total number of subjects	46
EEA total number of subjects	31

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)	15
Adolescents (12-17 years)	30
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included a 30-day screening period.

Period 1

Period 1 title	Double-blind Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Double-blind Placebo EOW

Arm description:

Placebo for adalimumab every other week (eow) for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	placebo for adalimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for adalimumab solution for subcutaneous injection.

Arm title	Double-blind Adalimumab EOW

Arm description:

Adalimumab (body surface area dosing 24 mg/m^2 up to a maximum of 40 mg) every other week (eow) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	adalimumab
Investigational medicinal product code	
Other name	ABT-D2E7, Humira
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Adalimumab solution for subcutaneous injection.

Number of subjects in period 1	Double-blind Placebo EOW	Double-blind Adalimumab EOW
Started	15	31
Completed	15	31

Period 2

Period 2 title	Open-label Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Open-label Adalimumab EOW

Arm description:

Adalimumab (body surface area dosing 24 mg/m^2 up to a maximum of 40 mg) every other week (eow) for up to 192 weeks.

Arm type	Experimental
Investigational medicinal product name	adalimumab
Investigational medicinal product code	
Other name	ABT-D2E7, Humira
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Adalimumab solution for subcutaneous injection.

Number of subjects in period 2	Open-label Adalimumab EOW
Started	46
Completed	29
Not completed	17
Adverse event	6
Remission	4
Withdrawal by subject	4
Lack of efficacy	2
Irregular compliance	1

Baseline characteristics

Reporting groups	
Reporting group title	Double-blind Placebo EOW
Reporting group description:	
Placebo for adalimumab every other week (eow) for 12 weeks.	
Reporting group title	Double-blind Adalimumab EOW
Reporting group description:	
Adalimumab (body surface area dosing 24 mg/m^2 up to a maximum of 40 mg) every other week (eow) for 12 weeks.	

Reporting group values	Double-blind Placebo EOW	Double-blind Adalimumab EOW	Total
Number of subjects	15	31	46
Age categorical Units: Subjects			
Age continuous			
Intent-to-treat (ITT) population: All randomized subjects who received at least 1 dose of study drug.			
Units: years			
arithmetic mean	11.9	13.4	
standard deviation	± 2.85	± 2.86	-
Gender categorical			
ITT population			
Units: Subjects			
Female	6	9	15
Male	9	22	31

End points

End points reporting groups

Reporting group title	Double-blind Placebo EOW
Reporting group description:	
Placebo for adalimumab every other week (eow) for 12 weeks.	
Reporting group title	Double-blind Adalimumab EOW
Reporting group description:	
Adalimumab (body surface area dosing 24 mg/m^2 up to a maximum of 40 mg) every other week (eow) for 12 weeks.	
Reporting group title	Open-label Adalimumab EOW
Reporting group description:	
Adalimumab (body surface area dosing 24 mg/m^2 up to a maximum of 40 mg) every other week (eow) for up to 192 weeks.	
Subject analysis set title	Any Adalimumab
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects in this study who received at least 1 dose of adalimumab (body surface area dosing 24 mg/m^2 up to a maximum of 40 mg) every other week (double-blind or open-label) for up to 204 weeks.	

Primary: Percent Change in Number of Active Joints With Arthritis From Baseline to Week 12

End point title	Percent Change in Number of Active Joints With Arthritis From Baseline to Week 12
End point description:	
A joint assessment was recorded at all study visits to assess the number of active joints, with a total possible score of 0 (no active joints) to 72 (all active joints). A total of 72 joints were assessed for swelling not due to deformity or joints with loss of motion (LOM) plus pain and/or tenderness. Baseline is defined as the last nonmissing value prior to the first dose of study drug. Last Observation Carried Forward (LOCF) was used for missing data.	
End point type	Primary
End point timeframe:	
Baseline and Week 12	

End point values	Double-blind Placebo EOW	Double-blind Adalimumab EOW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[1]	31[2]		
Units: percent change				
arithmetic mean (standard deviation)	-11.6 (± 100.5)	-62.6 (± 59.53)		

Notes:

[1] - ITT population

[2] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo EOW v Double-blind Adalimumab EOW

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.039
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-51.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99.69
upper limit	-2.66

Secondary: Number of Sites of Enthesitis: Change From Baseline to Week 12

End point title	Number of Sites of Enthesitis: Change From Baseline to Week 12

End point description:

The presence of enthesitis was assessed by pressure at 35 anatomical locations. Enthesitis was classifed as either present or absent. Scores range from 0 to 35, with higher scores representing higher disease activity. Baseline is defined as the last nonmissing value prior to the first dose of study drug. LOCF was used.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo EOW	Double-blind Adalimumab EOW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[3]	31[4]		
Units: sites of enthesitis				
arithmetic mean (standard deviation)				
Baseline	7.8 (± 7.49)	8.3 (± 8.89)		
Week 12	5.1 (± 8.92)	3.9 (± 6.6)		
Change from Baseline to Week 12	-2.7 (± 4.98)	-4.4 (± 6.2)		

Notes:

[3] - ITT population

[4] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo EOW v Double-blind Adalimumab EOW

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.382
Method	1-way ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.32
upper limit	2.08

Secondary: Tender Joint Count (TJC72): Change From Baseline to Week 12

End point title	Tender Joint Count (TJC72): Change From Baseline to Week 12

End point description:

Seventy-two joints were assessed by pressure on physical examination. Joint tenderness was classified as either present or absent. Scores range from 0 to 72, with higher scores representing higher disease activity. Baseline is defined as the last nonmissing value prior to the first dose of study drug. LOCF was used.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo EOW	Double-blind Adalimumab EOW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[5]	31[6]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	11.9 (± 9.34)	13.4 (± 10.49)		
Week 12	7.5 (± 8.06)	5.5 (± 8.77)		
Change from Baseline to Week 12	-4.5 (± 8.97)	-7.9 (± 8.25)		

Notes:

[5] - ITT population

[6] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo EOW v Double-blind Adalimumab EOW

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.209
Method	1-way ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.78
upper limit	1.97

Secondary: Swollen Joint Count (SJC68): Change From Baseline to Week 12

End point title	Swollen Joint Count (SJC68): Change From Baseline to Week 12

End point description:

Sixty-eight joints were assessed by physical examination. Joint swelling was classified as present or absent. Scores range from 0 to 68, with higher scores representing higher disease activity. Baseline is defined as the last nonmissing value prior to the first dose of study drug. LOCF was used.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo EOW	Double-blind Adalimumab EOW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[7]	31[8]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	5.2 (± 3.69)	6.7 (± 7.3)		
Week 12	2.8 (± 2.83)	3.2 (± 7.27)		
Change from Baseline to Week 12	-2.4 (± 4.66)	-3.5 (± 5.61)		

Notes:

[7] - ITT population

[8] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo EOW v Double-blind Adalimumab EOW

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.509
Method	1-way ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.49
upper limit	2.26

Secondary: Percentage of Subjects Achieving Pediatric American College of Rheumatology Pediatric 30% Response (ACR Pedi30)

End point title	Percentage of Subjects Achieving Pediatric American College of Rheumatology Pediatric 30% Response (ACR Pedi30)

End point description:

The ACR Pedi30 response is defined as ≥30% improvement in at least 3 of 6 juvenile rheumatoid arthritis (JRA) core set criteria with no more than 1 of the 6 criteria with >30% worsening. The 6 variables for the JRA core set criteria are Physician's Global Assessment (PGA) of subject's disease activity, Parent's Global Assessment of subject's overall well-being, number of active joints (joints with swelling not due to deformity or joints LOM plus pain and/or tenderness), number of joints with LOM, Childhood Health Assessment Questionnaire (CHAQ), and high sensitivity C-reactive protein (hs CRP). Baseline is the last value prior to the first dose of study drug. Non-responder imputation (NRI) was used for missing data.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo EOW	Double-blind Adalimumab EOW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[9]	31[10]		
Units: percentage of subjects				
number (not applicable)	60	71		

Notes:

[9] - ITT population

[10] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo EOW v Double-blind Adalimumab EOW

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.514
Method	Fisher exact
Parameter estimate	Mean difference (final values)
Point estimate	11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.5
upper limit	40.5

Secondary: Percentage of Subjects Achieving Pediatric American College of Rheumatology Pediatric 50% Response (ACR Pedi50)

End point title	Percentage of Subjects Achieving Pediatric American College of Rheumatology Pediatric 50% Response (ACR Pedi50)

End point description:

The ACR Pedi50 response is defined as ≥50% improvement in at least 3 of 6 JRA core set criteria with no more than 1 of the 6 criteria with >30% worsening. The 6 variables for the JRA core set criteria are Physician's Global Assessment (PGA) of subject's disease activity, Parent's Global Assessment of subject's overall well-being, number of active joints (joints with swelling not due to deformity or joints LOM plus pain and/or tenderness), number of joints with LOM, Childhood Health Assessment Questionnaire (CHAQ), and high sensitivity C-reactive protein (hs CRP). Baseline is the last value prior to the first dose of study drug. NRI was used.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo EOW	Double-blind Adalimumab EOW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[11]	31[12]		
Units: percentage of subjects				
number (not applicable)	40	67.7		

Notes:

[11] - ITT population

[12] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo EOW v Double-blind Adalimumab EOW

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.111
Method	Fisher exact
Parameter estimate	Mean difference (final values)
Point estimate	27.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	57.5

Secondary: Percentage of Subjects Achieving Pediatric American College of Rheumatology Pediatric 70% Response (ACR Pedi70)

End point title	Percentage of Subjects Achieving Pediatric American College of Rheumatology Pediatric 70% Response (ACR Pedi70)

End point description:

The ACR Pedi70 response is defined as ≥70% improvement in at least 3 of 6 JRA core set criteria with no more than 1 of the 6 criteria with >30% worsening. The 6 variables for the JRA core set criteria are Physician's Global Assessment (PGA) of subject's disease activity, Parent's Global Assessment of subject's overall well-being, number of active joints (joints with swelling not due to deformity or joints LOM plus pain and/or tenderness), number of joints with LOM, Childhood Health Assessment Questionnaire (CHAQ), and high sensitivity C-reactive protein (hs CRP). Baseline is the last value prior to the first dose of study drug. Non-responder imputation NRI was used.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo EOW	Double-blind Adalimumab EOW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[13]	31[14]		
Units: percentage of subjects				
number (not applicable)	20	54.8		

Notes:

[13] - ITT population

[14] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo EOW v Double-blind Adalimumab EOW

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.031
Method	Fisher exact
Parameter estimate	Mean difference (final values)
Point estimate	34.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.1
upper limit	61.6

Secondary: Number of Subjects With Adverse Events (AEs)

End point title	Number of Subjects With Adverse Events (AEs)

End point description:

An AE is any untoward medical occurrence in a subject which does not necessarily have a causal relationship with this treatment. A serious AE (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent events (TEAEs or TESAE) are defined as any event that began or worsened in severity after the first dose of study drug. The investigator assessed the relationship of each event to the use of study drug as either probably related to study drug, possibly related to study drug, probably not related, or not related to study drug.
For more details on adverse events please see the AE section below.

End point type	Secondary

End point timeframe:

Treatment-emergent AEs (TEAEs) were collected from first dose of study drug until 70 days after the last dose of study drug (up to 212 weeks)

End point values	Double-blind Placebo EOW	Double-blind Adalimumab EOW	Any Adalimumab	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	15[15]	31[16]	46	
Units: subjects				
Any TEAE	8	21	46	
TEAEs at least possibly related to study drug	4	9	29	
Any severe TEAE	0	0	7	
TESAE	0	1	10	
Any TEAE Leading to Discontinuation of Study	0	0	7	
Death	0	0	0	

Notes:

[15] - Safety population: All randomized subjects who received at least 1 dose of study drug

[16] - Safety population: All randomized subjects who received at least 1 dose of study drug

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent AEs (TEAEs) were collected from first dose of study drug until 70 days after the last dose of study drug (up to 212 weeks); SAEs were collected from the time informed consent was obtained (up to 216 weeks).

Adverse event reporting additional description:

A TEAE is defined as events with onset or worsening after the first dose of study drug to the first dose of open-label (OL) adalimumab (double blind [DB] period only), or 70 days following the last study drug administration or until the first dose of commercially available Humira after completion of the study, whichever occurs first.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Double-blind Placebo EOW

Reporting group description:

Placebo for adalimumab every other week (eow) for 12 weeks.

Reporting group title	Double-blind Adalimumab EOW

Reporting group description:

Adalimumab (body surface area dosing 24 mg/m^2 up to a maximum of 40 mg) every other week (eow) for 12 weeks.

Reporting group title	Any Adalimumab

Reporting group description:

All subjects in this study who received at least 1 dose of adalimumab (body surface area dosing 24 mg/m^2 up to a maximum of 40 mg) every other week (double-blind or open-label) for up to 204 weeks.

Serious adverse events	Double-blind Placebo EOW	Double-blind Adalimumab EOW	Any Adalimumab
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	10 / 46 (21.74%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Tuberculin test positive			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Burns second degree			

subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burns third degree			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Diffuse vasculitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pain			

subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Joint instability			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Juvenile idiopathic arthritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated tuberculosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Double-blind Placebo EOW	Double-blind Adalimumab EOW	Any Adalimumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 15 (53.33%)	21 / 31 (67.74%)	46 / 46 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Prehypertension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Raynaud's phenomenon			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Vasculitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	2 / 46 (4.35%)
occurrences (all)	0	1	2
Fatigue			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Inflammation			

subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Injection site erythema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	3 / 46 (6.52%)
occurrences (all)	0	1	4
Injection site pain			
subjects affected / exposed	1 / 15 (6.67%)	3 / 31 (9.68%)	5 / 46 (10.87%)
occurrences (all)	1	3	6
Injection site pruritus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	2
Injection site urticaria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences (all)	0	1	1
Pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	2
Peripheral swelling			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	6 / 46 (13.04%)
occurrences (all)	0	0	7
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Penis disorder			

subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Scrotal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Varicocele			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Asthma			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	4 / 46 (8.70%)
occurrences (all)	0	0	4
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	3
Rhinitis allergic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	3
Tonsillar inflammation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	2
Vasomotor rhinitis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	2 / 46 (4.35%)
occurrences (all)	0	1	3
Tic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 15 (0.00%)	3 / 31 (9.68%)	5 / 46 (10.87%)
occurrences (all)	0	3	5
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	2 / 46 (4.35%)
occurrences (all)	0	1	2
Blood pressure increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Bone density increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	3 / 46 (6.52%)
occurrences (all)	0	1	3
Transaminases increased			

subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 15 (6.67%)	0 / 31 (0.00%)	0 / 46 (0.00%)
occurrences (all)	1	0	0
contusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Craniocerebral injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Foot fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Hand fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Joint dislocation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	1	0	1
Joint injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	3
Laceration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Ligament sprain			

subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	4 / 46 (8.70%)
occurrences (all)	0	0	4
Limb injury			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences (all)	0	1	1
Lip injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Post-traumatic pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	3
Radius fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Rib fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	2
Road traffic accident			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Skeletal injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Tooth fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Traumatic haematoma			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Traumatic haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences (all)	0	1	1
Wrist fracture			
subjects affected / exposed	1 / 15 (6.67%)	0 / 31 (0.00%)	0 / 46 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Disturbance in attention			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	2 / 46 (4.35%)
occurrences (all)	0	1	2
Headache			
subjects affected / exposed	0 / 15 (0.00%)	3 / 31 (9.68%)	10 / 46 (21.74%)
occurrences (all)	0	3	16
Migraine			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences (all)	0	1	1
Paraesthesia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 15 (0.00%)	2 / 31 (6.45%)	4 / 46 (8.70%)
occurrences (all)	0	2	4
Tremor			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	3
Blood and lymphatic system disorders			
Bruise			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Iron deficiency anaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences (all)	0	1	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	2 / 46 (4.35%)
occurrences (all)	0	1	2
Vertigo			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	2
Eye disorders			

Astigmatism			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Cataract			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Conjunctivitis allergic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Dry eye			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	2 / 46 (4.35%)
occurrences (all)	0	2	3
Vision blurred			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences (all)	0	1	2
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	6 / 46 (13.04%)
occurrences (all)	0	1	9
Abdominal pain upper			
subjects affected / exposed	1 / 15 (6.67%)	2 / 31 (6.45%)	2 / 46 (4.35%)
occurrences (all)	1	2	3
Anal fissure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	4 / 46 (8.70%)
occurrences (all)	0	0	4
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	8 / 46 (17.39%)
occurrences (all)	0	1	11
Food poisoning			

subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Haematochezia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	1 / 15 (6.67%)	2 / 31 (6.45%)	5 / 46 (10.87%)
occurrences (all)	1	2	6
Odynophagia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	4 / 46 (8.70%)
occurrences (all)	0	1	4
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences (all)	0	1	1
Hyperbilirubinaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Acne			

subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 31 (0.00%)	0 / 46 (0.00%)
occurrences (all)	1	0	0
Dermatitis allergic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 31 (0.00%)	4 / 46 (8.70%)
occurrences (all)	1	0	10
Eczema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Erythema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Keratosis pilaris			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Pityriasis rosea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Psoriasis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Pustular psoriasis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Rash erythematous			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences (all)	0	1	1
Rash maculo-papular			

subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Skin exfoliation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Solar dermatitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Bladder spasm			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
IgA nephropathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Leukocyturia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Back pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	2 / 46 (4.35%)
occurrences (all)	0	1	2
Foot deformity			

subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Growing pains			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Juvenile idiopathic arthritis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 31 (0.00%)	6 / 46 (13.04%)
occurrences (all)	2	0	9
Muscle spasms			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	3
Osteochondrosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Synovial cyst			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Acarodermatitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 31 (0.00%)	0 / 46 (0.00%)
occurrences (all)	1	0	0
Acute sinusitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	5 / 46 (10.87%)
occurrences (all)	0	0	6

Bronchopneumonia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences (all)	0	1	1
Candida infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	2
Cellulitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	4
Cystitis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 31 (3.23%)	1 / 46 (2.17%)
occurrences (all)	1	1	1
Ear infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	6
Folliculitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Fungal skin infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 15 (0.00%)	2 / 31 (6.45%)	8 / 46 (17.39%)
occurrences (all)	0	2	12
Gastrointestinal infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Herpes zoster			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Influenza			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	3

Laryngitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	4
Latent tuberculosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Localised infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 31 (0.00%)	11 / 46 (23.91%)
occurrences (all)	1	0	19
Oral herpes			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	4 / 46 (8.70%)
occurrences (all)	0	0	17
Orchitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	2
Otitis media			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	4 / 46 (8.70%)
occurrences (all)	0	0	7
Otitis media acute			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	4
Otitis media chronic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 31 (3.23%)	3 / 46 (6.52%)
occurrences (all)	1	1	3
Pharyngitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	7 / 46 (15.22%)
occurrences (all)	0	1	16
Pharyngotonsillitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	7 / 46 (15.22%)
occurrences (all)	0	0	11

Pilonidal cyst			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	4
Rhinitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	3
Rotavirus infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Scarlet fever			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	5 / 46 (10.87%)
occurrences (all)	0	1	5
Subcutaneous abscess			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Tinea infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Tinea pedis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Tonsillitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	4 / 46 (8.70%)
occurrences (all)	0	0	4

Tonsillitis bacterial			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Tracheitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 15 (13.33%)	3 / 31 (9.68%)	16 / 46 (34.78%)
occurrences (all)	3	3	38
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	4
Varicella			
subjects affected / exposed	0 / 15 (0.00%)	1 / 31 (3.23%)	2 / 46 (4.35%)
occurrences (all)	0	1	2
Viral infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	3
Viral tonsillitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Hypoglycaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Metabolic syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 31 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 July 2010	The purpose of this amendment was to update the inclusion (birth control timing after last dose of study drug, chest x-ray [CXR] requirements) and exclusion criteria (hepatitis B virus [HBV] screening), update according to new maximum dose for sulfasalazine (3 g/day), and clarify study procedures and timing.
18 January 2011	The purpose of this amendment was to update inclusion criteria (number of active joints and evidence of enthesitis, and CXR dependent on tuberculosis test results) and exclusion criteria (update information pertaining to HBV) testing, clarify time points for assessment of high sensitivity C-reactive protein (hs CRP), and clarify statistical analyses.
02 July 2013	The purpose of this amendment was to add collection requirements for events of malignancy, add prohibited biologic therapies, and update analysis population definition.
10 October 2013	The purpose of this amendment was to extend the study by 1 year (48 weeks).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported