Clinical trial results:
A Multicenter Study of the Efficacy and Safety of the Human Anti-TNF Monoclonal Antibody Adalimumab in Subjects with Peripheral Spondyloarthritis

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2009-014567-39
Trial protocol	DE FR BE IE HU ES CZ GR
Global end of trial date	12 May 2014

Results information

Result version number	v2 (current)
This version publication date	28 July 2016
First version publication date	18 July 2015
Version creation reason	• Correction of full data set potential category issues

Trial information

Trial identification

Sponsor protocol code	M10-883

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01064856
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Abbvie Deutschland GmbH & Co.KG
Sponsor organisation address	Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4XE
Public contact	Global Medical Information, AbbVie, 001 800-633-9110,
Scientific contact	In-Ho Song, AbbVie, in-ho.song@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 May 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to evaluate the efficacy and safety of adalimumab 40 mg administered every other week (eow) subcutaneously (SC) compared to placebo for 12 weeks followed by open label (OL) safety and efficacy assessments in subjects with non-ankylosing spondylitis (AS), non-psoriatic arthritis (PsA) active peripheral spondyloarthritis (SpA) who have had an inadequate response to ≥ 2 non-steroidal anti-inflammatory drugs (NSAIDs), or are intolerant to, or have a contraindication for, NSAIDs.

Protection of trial subjects:

All subjects entering the study had to sign an informed consent that was explained to them and questions encouraged.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	15 March 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	Australia: 32
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	United States: 19
Country: Number of subjects enrolled	Belgium: 21
Country: Number of subjects enrolled	Czech Republic: 35
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Greece: 7
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Ireland: 2
Worldwide total number of subjects	165
EEA total number of subjects	105

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	162
From 65 to 84 years	3
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 (DB) Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Subject

Blinding implementation details:

All subjects were centrally randomized using an Interactive Voice Response System/Interactive Web Response System (IVRS/IWRS). All personnel with direct oversight of the conduct and management of the trial (except the Drug Supply Management Team) investigator, study site personnel, and subject remained blinded to each subject's treatment throughout the 12-week DB period. The IVRS/IWRS provided access to blinded subject treatment information in the case of medical emergency.

Arms

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

Arm description:

Placebo subcutaneous (SC) injection every other week (eow) up to Week 12 in the double-blind period.

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

Dosage and administration details:

Study drug was provided as a sterile SC injection solution in 1 mL pre-filled syringes containing matching placebo for adalimumab. Study drug was SC self-administered eow at approximately the same time of day.

Arm title	Double-blind Adalimumab

Arm description:

Adalimumab 40 mg SC injection eow up to Week 12 in double-blind period.

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

Dosage and administration details:

Study drug was provided as a sterile SC injection solution in 1 mL pre-filled syringes containing adalimumab 40 mg/0.8 mL. Study drug was SC self-administered eow at approximately the same time of day.

Number of subjects in period 1	Double-blind Placebo	Double-blind Adalimumab
Started	81	84
Completed	81	82
Not completed	0	2
Consent withdrawn by subject	-	1
Adverse event	-	1

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Double-blind Placebo / Open-label Adalimumab

Arm description:

Placebo SC injection every other week (eow) up to Week 12 in the double-blind period; adalimumab 40 mg subcutaneous injection eow from Week 12 to Week 156 in the open-label period.

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

Dosage and administration details:

Study drug was provided as a sterile SC injection solution in 1 mL pre-filled syringes containing adalimumab 40 mg/0.8 mL. Study drug was SC self-administered eow at approximately the same time of day.

Arm title	Double-blind Adalimumab / Open-label Adalimumab

Arm description:

Adalimumab 40 mg SC injection eow up to Week 12 in double-blind period and from Week 12 to Week 156 in open-label period.

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

Dosage and administration details:

Study drug was provided as a sterile SC injection solution in 1 mL pre-filled syringes containing adalimumab 40 mg/0.8 mL. Study drug was SC self-administered eow at approximately the same time of day.

Number of subjects in period 2	Double-blind Placebo / Open-label Adalimumab	Double-blind Adalimumab / Open-label Adalimumab
Started	81	82
Completed	61	56
Not completed	20	26
Consent withdrawn by subject	6	5
Not specified	7	7
Adverse event	6	12
Lost to follow-up	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Double-blind Placebo
Reporting group description:	
Placebo subcutaneous (SC) injection every other week (eow) up to Week 12 in the double-blind period.	
Reporting group title	Double-blind Adalimumab
Reporting group description:	
Adalimumab 40 mg SC injection eow up to Week 12 in double-blind period.	

Reporting group values	Double-blind Placebo	Double-blind Adalimumab	Total
Number of subjects	81	84	165
Age categorical Units: Subjects			
< 40 years	50	35	85
40 to 65 years	29	48	77
> 65 years	2	1	3
Age continuous Units: years			
arithmetic mean	38.5	42.5	
standard deviation	± 12.77	± 10.79	-
Gender categorical Units: Subjects			
Female	42	48	90
Male	39	36	75
Tender Joint Count (78 Joints)			
Seventy-eight joints were assessed for tenderness by physical examination. Tenderness of each joint was classified as present (1) or absent (0), for a total possible score of 0 (no tenderness) to 78 (worst possible score/severe tenderness).			
Units: units on a scale			
arithmetic mean	13.62	12.95	
standard deviation	± 16.101	± 12.79	-
Swollen Joint Count (76 Joints)			
Seventy-six joints were assessed for swelling by physical examination. Swelling of each joint was classified as present (1) or absent (0), for a total possible score of 0 (no swelling) to 76 (worst possible score/severe swelling).			
Units: units on a scale			
arithmetic mean	7.31	6.12	
standard deviation	± 7.996	± 5.581	-
Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)			
Assessment of enthesitis was performed in 7 domains. Each domain was graded for the presence (1) and absence (0) of tenderness yielding total MASES ranging from 0 (no tenderness) to 13 (worst possible score; severe tenderness).			
Units: units on a scale			
arithmetic mean	3.59	3.13	
standard deviation	± 3.398	± 3.603	-
Leeds Enthesitis Index			
Assessment of enthesitis was performed in 6 domains. Each domain was graded for the presence (1) and absence (0) of tenderness yielding total Leeds Enthesitis Index scores ranging from 0 (no tenderness) to 6 (worst possible score; severe tenderness).			

Units: units on a scale			
arithmetic mean	1.42	1.49	
standard deviation	± 1.611	± 1.661	-
Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Score			
Assessment of enthesitis was performed in 16 domains. Each domain was graded for the presence (1) and absence (0) of tenderness yielding total SPARCC scores ranging from 0 (no tenderness) to 16 (worst possible score; severe tenderness).			
Units: units on a scale			
arithmetic mean	4.05	3.83	
standard deviation	± 3.785	± 4.038	-
Total Enthesitis Count			
Total enthesitis count in the sum of all unique, individual entheses location included in the Leeds, SPARCC, and MASES entheses indices. Scores range from 0 (no enthesitis) to 29 (most severe enthesitis).			
Units: units on a scale			
arithmetic mean	7.33	6.73	
standard deviation	± 6.69	± 6.958	-
Patient Global Assessment (PTGA) of Disease Activity			
PTGA of Disease Activity as measured by a 100 mm visual analogue scale (VAS) where 0=no symptoms and 100=maximum symptoms.			
Units: mm			
arithmetic mean	66.43	65.24	
standard deviation	± 15.864	± 15.225	-
PTGA – Pain			
PTGA – Pain as measured by a 100 mm VAS where 0=no pain and 100=maximum pain.			
Units: units on a scale			
arithmetic mean	65.6	64.3	
standard deviation	± 15.897	± 14.036	-
Physician Global Assessment (PGA) of Disease Activity			
A VAS was to be used for the PGA of disease activity (current status). The left end of the VAS scale (0 mm) signifies the absence of symptoms and the right end (100 mm) signifies maximum disease activity.			
Units: units on a scale			
arithmetic mean	57.02	60.29	
standard deviation	± 14.987	± 15.537	-
Ankylosing Spondylitis Disease Activity Score (ASDAS)			
The ASDAS is categorized into 4 disease activity states based on score: inactive disease (< 1.3), moderate (≥ 1.3 to < 2.1), high (≥ 2.1 to ≤ 3.5), and very high (> 3.5). One subject in the Placebo arm did not have a baseline ASDAS assessment.			
Units: units on a scale			
arithmetic mean	3.06	2.92	
standard deviation	± 0.804	± 0.844	-
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)			
The BASDAI consisted of a VAS scale used to answer 6 questions pertaining to symptoms experienced by the subject for the past week. Each question on the BASDAI was reported in cm (0 [none] to 10 [very severe] with one question's possible answers being in time increments [0 hours to ≥ 2 hours]). The BASDAI has a maximum value of 10.			
Units: units on a scale			
arithmetic mean	5.57	5.68	
standard deviation	± 1.587	± 1.749	-
Dactylitis Count			
Assessment of the presence or absence of dactylitis as well as grading of tenderness and swelling in all 20 of the subjects' digits was performed. Tenderness at each site was quantified from absent to severe.			

Swelling was quantified from mild to severe. Total Dactylitis Assessment scores ranging from 0 (no dactylitis) to 20 (worst possible score; severe dactylitis). One subject in the Adalimumab arm did not have a baseline dactylitis count.			
Units: units on a scale			
arithmetic mean	0.65	0.35	
standard deviation	± 1.257	± 0.943	-
Short Form-36 Health Status Survey™ Version 2 (SF-36™V2) Physical Component Score (PCS)			
The SF-36™V2 is a 36-item generic health-related quality of life measure to assess the subject's view of their health consisting of 2 components: physical and mental. Scores range from 0 to 100. Higher scores indicate a better health state.			
Units: units on a scale			
arithmetic mean	34.48	34.56	
standard deviation	± 7.629	± 7.936	-

End points

End points reporting groups

Reporting group title	Double-blind Placebo
Reporting group description:	
Placebo subcutaneous (SC) injection every other week (eow) up to Week 12 in the double-blind period.	
Reporting group title	Double-blind Adalimumab
Reporting group description:	
Adalimumab 40 mg SC injection eow up to Week 12 in double-blind period.	
Reporting group title	Double-blind Placebo / Open-label Adalimumab
Reporting group description:	
Placebo SC injection every other week (eow) up to Week 12 in the double-blind period; adalimumab 40 mg subcutaneous injection eow from Week 12 to Week 156 in the open-label period.	
Reporting group title	Double-blind Adalimumab / Open-label Adalimumab
Reporting group description:	
Adalimumab 40 mg SC injection eow up to Week 12 in double-blind period and from Week 12 to Week 156 in open-label period.	

Primary: Percentage of Responders According to the Composite Peripheral SpA Response Criteria (PSpARC 40) at Week 12

End point title	Percentage of Responders According to the Composite Peripheral SpA Response Criteria (PSpARC 40) at Week 12
End point description:	
Percentage of subjects achieving the following composite response at Week 12: ≥ 40% improvement (minimum 20 mm absolute improvement) from Baseline in Patient Global Assessment (PTGA) of Disease Activity as measured by a 100 mm visual analogue scale (VAS) where 0=no symptoms and 100=maximum symptoms; ≥ 40% improvement (minimum 20 mm absolute improvement) from Baseline in PTGA – Pain as measured by a 100 mm VAS where 0=no pain and 100=maximum pain; and ≥ 40% improvement from Baseline in at least 1 of the following 3 criteria: swollen joint count (76 joints) and tender joint count (78 joints); total enthesitis count; or total dactylitis count. Non-responder imputation: missing response was imputed as non-response.	
End point type	Primary
End point timeframe:	
Week 12	

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	84		
Units: percentage of subjects				
number (not applicable)				
Responder	19.8	39.3		
Non-responder	80.2	60.7		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo v Double-blind Adalimumab
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [1]
Method	Pearson's chi-square

Notes:

[1] - Based on Pearson's chi-square test.

Secondary: Change from Baseline in Physician Global Assessment (PGA) of Disease Activity at Week 12

End point title	Change from Baseline in Physician Global Assessment (PGA) of Disease Activity at Week 12

End point description:

A VAS was to be used for the Physician Global Assessment (PGA) of disease activity (current status). The left end of the VAS scale (0 mm) signifies the absence of symptoms and the right end (100 mm) signifies maximum disease activity. Last observation carried forward (LOCF): missing values were imputed using the last non-missing post-baseline value prior to the missing value.

End point type	Secondary

End point timeframe:

Baseline (last measurement prior to first DB dose), Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	84		
Units: units on a scale				
arithmetic mean (standard deviation)	-18.2 (± 22.93)	-32.2 (± 22.52)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo v Double-blind Adalimumab
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [2]
Method	ANCOVA

Notes:

[2] - Based on an ANCOVA model adjusting for baseline with treatment as a factor.

Secondary: Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Week 12

End point title	Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Week 12

End point description:

The BASDAI was to be completed at the designated study visits. The subject was to assess his/her disease activity using the BASDAI which consisted of a VAS scale used to answer 6 questions (Q1 through Q6) pertaining to symptoms experienced by the subject for the past week. Each question on the BASDAI was reported in cm (0 [none] to 10 [very severe] with one question's possible answers being in time increments [0 hours to ≥ 2 hours]). The BASDAI has a maximum value of 10 and was calculated as follows: BASDAI Score = 0.2 × (Q1 + Q2 + Q3 + Q4 + Q5/2 + Q6/2). LOCF: Missing value was imputed using the last non-missing post-baseline value prior to missing value.

End point type	Secondary

End point timeframe:

Baseline (last measurement prior to first DB dose), Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	84		
Units: units on a scale				
arithmetic mean (standard deviation)	-1 (± 2.19)	-2.1 (± 2.32)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo v Double-blind Adalimumab
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003 [3]
Method	ANCOVA

Notes:

[3] - Based on an ANCOVA model adjusting for baseline with treatment as a factor.

Secondary: Change from Baseline in Health Assessment Questionnaire Modified for the Spondyloarthropathies (HAQ-S) Total at Week 12

End point title	Change from Baseline in Health Assessment Questionnaire Modified for the Spondyloarthropathies (HAQ-S) Total at Week 12

End point description:

The HAQ-S is a self-reported measure to assess the physical function and health-related quality of life. The Disability Index (DI) of HAQ-S is calculated as the mean of the following 8 category scores (range: 0 [without any difficulty] to 3 [unable to do]): Dressing and Grooming, Rising, Eating, Walking, Hygiene, Reach, Grip, and Activities. Five additional items in the functional status measure were included in the HAQ-S, including carrying heavy packages, sitting for long periods, able to work at a flat topped table, and (if the participant had a driver's license or a car) able to look in the rear view mirror and able to turn head to drive in reverse. The overall score ranges from 0 (no disability) to 3 (three very severe, high-dependency disability). Negative mean changes from Baseline in the overall score indicate improvement. LOCF: Missing value was imputed using the last non-missing post-baseline value prior to missing value.

End point type	Secondary

End point timeframe:

Baseline (last measurement prior to first DB dose), Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	84		
Units: units on a scale				
arithmetic mean (standard deviation)	-0.2 (± 0.47)	-0.3 (± 0.44)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo v Double-blind Adalimumab
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.051 [4]
Method	ANCOVA

Notes:

[4] - Based on an ANCOVA model adjusting for baseline with treatment as a factor.

Secondary: Change from Baseline in Short Form-36 Health Status Survey™ Version 2 (SF-36™V2) Physical Component Score (PCS) at Week 12

End point title	Change from Baseline in Short Form-36 Health Status Survey™ Version 2 (SF-36™V2) Physical Component Score (PCS) at Week 12

End point description:

The Short Form-36 Health Status Survey™ Version 2 (SF-36™V2) is a 36-item generic health-related quality of life measure to assess the subject's view of their health consisting of 2 components: physical and mental. For each component, a transformed summary score is calculated using 8 sub-domains: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. Scores range from 0 to 100. Higher scores indicate a better health state.

End point type	Secondary

End point timeframe:

Baseline (last measurement prior to first DB dose), Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79[5]	83[6]		
Units: units on a scale				
arithmetic mean (standard deviation)	2.4 (± 6.65)	6.7 (± 7.85)		

Notes:

[5] - subjects with non-missing values

[6] - subjects with non-missing values

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) at Week 12

End point title	Change from Baseline in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) at Week 12

End point description:

Assessment of enthesitis was performed in the following 7 domains: 1) 1st costochondral joint left and right, 2) 7th costochondral joint left and right, 3) posterior superior iliac spine left and right, 4) anterior superior iliac spine left and right, 5) iliac crest left and right, 6) 5th lumbar spinous process and 7) proximal insertion of Achilles tendon left and right. Each domain was graded for the presence (1) and absence (0) of tenderness yielding total MASES ranging from 0 (no tenderness) to 13 (worst possible score; severe tenderness). Subjects with non-missing Baseline and at least 1 non-missing post-Baseline value were included in post-Baseline visits. LOCF: missing value was imputed using the last non-missing post-Baseline value prior to missing value.

End point type	Secondary

End point timeframe:

Baseline (last measurement prior to first DB dose), Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	84		
Units: units on a scale				
arithmetic mean (standard deviation)	-0.8 (± 2.38)	-1.2 (± 2.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Leeds Enthesitis Index at Week 12

End point title	Change from Baseline in Leeds Enthesitis Index at Week 12

End point description:

Assessment of enthesitis was performed in the following 6 domains: left and right lateral epicondyle, left and right medial femoral condyle, left and right Achilles tendon insertion. Tenderness at each site was quantified on a dichotomous basis: Each domain was graded for the presence (1) and absence (0) of tenderness yielding total Leeds Enthesitis Index scores ranging from 0 (no tenderness) to 6 (worst possible score; severe tenderness). Subjects with non-missing Baseline and at least 1 non-missing post-Baseline value were included in post-Baseline visits. LOCF: missing value was imputed using the last non-missing post-Baseline value prior to missing value.

End point type	Secondary

End point timeframe:

Baseline (last measurement prior to first DB dose), Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	84		
Units: units on a scale				
arithmetic mean (standard deviation)	-0.1 (± 1.19)	-0.8 (± 1.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Score at Week 12

End point title	Change from Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Score at Week 12

End point description:

Assessment of enthesitis was performed in the following 16 domains: left and right (L/R) medial epicondyle; L/R lateral epicondyle; L/R supraspinatus insertion into the greater tuberosity of humerus; L/R greater trochanter; L/R quadriceps insertion into superior border of patella; L/R patellar ligament insertion into inferior pole of patella or tibial tubercle; L/R Achilles tendon insertion into calcaneum; L/R plantar fascia insertion into calcaneum. Tenderness at each site was quantified on a dichotomous basis. Each domain was graded for the presence (1) and absence (0) of tenderness yielding total SPARCC scores ranging from 0 (no tenderness) to 16 (worst possible score; severe tenderness). Subjects with non-missing Baseline and at least 1 non-missing post-Baseline value were included in post-Baseline visits. LOCF: missing value was imputed using the last non-missing post-Baseline value prior to missing value.

End point type	Secondary

End point timeframe:

Baseline (last measurement prior to first DB dose), Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	84		
Units: units on a scale				
arithmetic mean (standard deviation)	-0.7 (± 2.21)	-1.7 (± 2.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Dactylitis at Week 12

End point title	Change from Baseline in Dactylitis at Week 12

End point description:

Assessment of the presence or absence of dactylitis as well as grading of tenderness and swelling in all 20 of the subjects' digits was performed. Tenderness at each site was quantified from absent to severe. Swelling was quantified from mild to severe. Total Dactylitis Assessment scores ranging from 0 (no dactylitis) to 20 (worst possible score; severe dactylitis). Subjects with non-missing Baseline and at

least 1 non-missing post-Baseline value were included in post-Baseline visits. LOCF: missing value was imputed using the last non-missing post-Baseline value prior to missing value.

End point type	Secondary

End point timeframe:

Baseline (last measurement prior to first DB dose), Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	83[7]		
Units: units on a scale				
arithmetic mean (standard deviation)	-0.3 (± 0.93)	-0.2 (± 1.05)		

Notes:

[7] - subjects with non-missing values for both Baseline and the post-baseline

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Tender Joint Count 78 (TJC78) and Swollen Joint Count 76 (SJC76) at Week 12

End point title	Change from Baseline in Tender Joint Count 78 (TJC78) and Swollen Joint Count 76 (SJC76) at Week 12

End point description:

Seventy-eight joints were assessed for tenderness by physical examination. Tenderness of each joint was classified as present (1) or absent (0), for a total possible TJC78 score of 0 (no swelling) to 78 (worst possible score). Seventy-six joints were assessed for swelling by physical examination. Swelling of each joint was classified as present (1) or absent (0), for a total possible score SJC76 of 0 (no swelling) to 76 (worst possible score). Subjects with non-missing Baseline and at least 1 non-missing post-Baseline value were included in post-Baseline visits. LOCF: missing value was imputed using the last non-missing post-Baseline value prior to missing value.

End point type	Secondary

End point timeframe:

Baseline (last measurement prior to first DB dose), Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	84		
Units: units on a scale				
arithmetic mean (standard deviation)				
TJC78	-1.8 (± 8.41)	-5.9 (± 8.67)		
SJC76	-3.1 (± 5.64)	-3.6 (± 4.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) at Week 12

End point title	Change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) at Week 12

End point description:

The ASDAS is categorized into 4 disease activity states based on score: inactive disease (< 1.3), moderate (≥ 1.3 to < 2.1), high (≥ 2.1 to ≤ 3.5), and very high (> 3.5). Clinically important and major improvements in ASDAS are defined as a reduction from Baseline of ≥ 1.1 and ≥ 2.0 points, respectively. Subjects with non-missing Baseline and at least 1 non-missing post-Baseline value were included in post-Baseline visits. LOCF: missing value was imputed using the last non-missing post-Baseline value prior to missing value.

End point type	Secondary

End point timeframe:

Baseline (last measurement prior to first DB dose), Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80[8]	84		
Units: units on a scale				
arithmetic mean (standard deviation)	-0.5 (± 0.9)	-1 (± 1.07)		

Notes:

[8] - subjects with non-missing values for both Baseline and post-baseline visit

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline (day of first study drug administration) through Week 156 plus 70 days.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Double-blind Placebo
Reporting group description:	
Placebo SC injection eow up to Week 12 in the double-blind period.	
Reporting group title	Double-blind Adalimumab
Reporting group description:	
Adalimumab 40 mg SC injection eow up to Week 12 in double-blind period.	
Reporting group title	Any Adalimumab
Reporting group description:	
All randomized subjects who had received at least 1 dose of adalimumab (blinded or open-label) at any time during the study (up to Week 156).	

Serious adverse events	Double-blind Placebo	Double-blind Adalimumab	Any Adalimumab
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 81 (1.23%)	1 / 84 (1.19%)	24 / 165 (14.55%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events			
Investigations			
Mycobacterium tuberculosis complex test positive			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign ovarian tumour			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phaeochromocytoma			

subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
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			
Ankle fracture			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fibula fracture			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
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			
Coronary artery disease			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
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			
Brain stem haemorrage			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cervicobrachial syndrome			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis cerebral			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 81 (1.23%)	0 / 84 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			

subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleurisy			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal and urinary disorders			
Cystitis haemorrhagic			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal disorder			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sacroiliitis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondyloarthropathy			

subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	3 / 165 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Double-blind Placebo	Double-blind Adalimumab	Any Adalimumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 81 (40.74%)	30 / 84 (35.71%)	139 / 165 (84.24%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 81 (0.00%)	2 / 84 (2.38%)	12 / 165 (7.27%)
occurrences (all)	0	2	12
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 81 (1.23%)	1 / 84 (1.19%)	14 / 165 (8.48%)
occurrences (all)	1	1	17
Influenza like illness			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	7 / 165 (4.24%)
occurrences (all)	0	0	7
Injection site reaction			

subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	8 / 165 (4.85%)
occurrences (all)	0	1	9
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 81 (2.47%)	2 / 84 (2.38%)	12 / 165 (7.27%)
occurrences (all)	2	2	15
Oropharyngeal pain			
subjects affected / exposed	3 / 81 (3.70%)	3 / 84 (3.57%)	15 / 165 (9.09%)
occurrences (all)	3	3	17
Sinus congestion			
subjects affected / exposed	1 / 81 (1.23%)	1 / 84 (1.19%)	5 / 165 (3.03%)
occurrences (all)	1	1	7
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 81 (2.47%)	0 / 84 (0.00%)	8 / 165 (4.85%)
occurrences (all)	2	0	9
Liver function test abnormal			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	6 / 165 (3.64%)
occurrences (all)	0	0	6
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	6 / 165 (3.64%)
occurrences (all)	0	0	6
Fall			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	8 / 165 (4.85%)
occurrences (all)	0	0	9
Ligament sprain			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	6 / 165 (3.64%)
occurrences (all)	0	0	6
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 81 (3.70%)	4 / 84 (4.76%)	17 / 165 (10.30%)
occurrences (all)	3	8	27
Paraesthesia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	6 / 165 (3.64%)
occurrences (all)	0	1	7

Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 81 (1.23%)	4 / 84 (4.76%)	12 / 165 (7.27%)
occurrences (all)	1	5	15
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	6 / 165 (3.64%)
occurrences (all)	0	1	6
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 81 (1.23%)	1 / 84 (1.19%)	5 / 165 (3.03%)
occurrences (all)	1	1	5
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 81 (4.94%)	1 / 84 (1.19%)	15 / 165 (9.09%)
occurrences (all)	4	1	15
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 81 (1.23%)	0 / 84 (0.00%)	5 / 165 (3.03%)
occurrences (all)	1	0	5
Nausea			
subjects affected / exposed	3 / 81 (3.70%)	2 / 84 (2.38%)	10 / 165 (6.06%)
occurrences (all)	4	4	14
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	6 / 165 (3.64%)
occurrences (all)	0	1	8
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	11 / 165 (6.67%)
occurrences (all)	0	1	11
Back pain			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	7 / 165 (4.24%)
occurrences (all)	0	1	9
Muscle spasms			
subjects affected / exposed	0 / 81 (0.00%)	2 / 84 (2.38%)	9 / 165 (5.45%)
occurrences (all)	0	3	13
Neck pain			

subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	7 / 165 (4.24%)
occurrences (all)	0	0	10
Spondyloarthropathy			
subjects affected / exposed	4 / 81 (4.94%)	6 / 84 (7.14%)	42 / 165 (25.45%)
occurrences (all)	4	6	73
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 81 (2.47%)	1 / 84 (1.19%)	23 / 165 (13.94%)
occurrences (all)	2	1	29
Conjunctivitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	6 / 165 (3.64%)
occurrences (all)	0	1	8
Cystitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	7 / 165 (4.24%)
occurrences (all)	0	1	9
Gastroenteritis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	10 / 165 (6.06%)
occurrences (all)	0	1	15
Gastroenteritis viral			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	5 / 165 (3.03%)
occurrences (all)	0	1	5
Influenza			
subjects affected / exposed	1 / 81 (1.23%)	3 / 84 (3.57%)	8 / 165 (4.85%)
occurrences (all)	1	3	8
Nasopharyngitis			
subjects affected / exposed	11 / 81 (13.58%)	4 / 84 (4.76%)	51 / 165 (30.91%)
occurrences (all)	11	4	75
Oral herpes			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	5 / 165 (3.03%)
occurrences (all)	0	1	6
Pharyngitis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 84 (0.00%)	12 / 165 (7.27%)
occurrences (all)	0	0	13
Rhinitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	13 / 165 (7.88%)
occurrences (all)	0	1	17

Sinusitis			
subjects affected / exposed	1 / 81 (1.23%)	1 / 84 (1.19%)	15 / 165 (9.09%)
occurrences (all)	1	1	26
Tonsillitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 84 (1.19%)	8 / 165 (4.85%)
occurrences (all)	0	1	11
Upper respiratory tract infection			
subjects affected / exposed	4 / 81 (4.94%)	4 / 84 (4.76%)	30 / 165 (18.18%)
occurrences (all)	4	4	69
Urinary tract infection			
subjects affected / exposed	2 / 81 (2.47%)	0 / 84 (0.00%)	7 / 165 (4.24%)
occurrences (all)	2	0	10

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2009	• Updated Table 1 Efficacy and Safety Measurements and Flow Chart to add high-sensitivity C-reactive protein to table for consistency within the protocol. Revised footnote "e" to increase the acceptable time frame for anteroposterior pelvic x-ray, from 90 days to 180 days. • Updated Study Procedures to increase window for prior AP pelvic x-ray from 3 months (90 days) to 6 months (180 days). • Updated Table 2 Clinical Laboratory Tests to clarify the time points of when tests were to be performed. Moved human chorionic gonadotropin to proper laboratory category. • Updated Protocol Appendix B, List of Protocol Signatories. • Corrected minor typographical errors.
10 December 2009	• Updated exclusion criteria to add criterion to clarify maximum dose, stability, and washout requirements for corticosteroids. • Updated exclusion criteria to add criterion to exclude subjects with diagnosis and current symptoms of fibromyalgia.
21 April 2010	• Updated the title page to correct European Union Sponsor address. • Updated Selection of Study Population to add "non-AS" to selection of study population for consistency. • Updated inclusion criteria to modify criterion to specify severity of disease as agreed upon with the Food and Drug Administration (FDA). • Updated exclusion criteria to revise criterion to remove age restriction for early onset arthritis. • Updated Table 1 Efficacy and Safety Measurement and Flow Chart to remove duplicate table note and corrected references within Table 1. Added Week 52 urinalysis and updated corresponding table note. • Updated Study Procedures to clarify acceptable alternative methods for the purified protein derivative skin test for tuberculosis screening and to add the local requirements for the Czech Republic. • Updated Health Outcomes Questionnaires to add tenderness and swelling assessment for dactylitis. • Updated Discussion of Study Design and Choice of Control Groups to add the words "non-AS" and "active" to clarify subject population. • Updated Suitability of Subject Population to add "non-AS" to selection of study population for consistency. • Added applicable reference to Protocol Appendix I. PGA of Disease Activity: VAS. • Revised Protocol Appendix Q. Subject Dosing Sheets – Adalimumab and instruction text as per updated standard protocol text. • Added Protocol Appendix V. Dactylitis Assessment to include clarification on how to capture presence of swelling and tenderness for dactylitis. • Updated Table 2 Clinical Laboratory Tests to add leukocytes and nitrites to remain consistent with the text.
22 November 2010	• Updated Study Procedures to add text to footnote on Table 2. Clinical Laboratory Tests regarding an additional confirmatory human leukocyte antigen-B27 test if the initial test result was reported as equivocal.
22 March 2012	• Extended the study for 1 additional year (from 104 to 156 weeks). • Updated Overall Study Design and Plan as well as the Table 1 Study Activities table to reflect 144 weeks of open-label treatment. • Updated Table 1 Study Activities for TB testing to include acceptability of QuantiFERON-TB Gold test and yearly testing of subjects that were PPD negative at Screening. • Editorial edits to comply with the current protocol template and Humira standards.

27 June 2013	• Update sections of the protocol to incorporate AbbVie's participation in an FDA-requested tumor necrosis factor (TNF) inhibitor class wide exploration of the rare appearance of malignancy in patients who are 30 years of age or younger at the time of diagnosis. • Incorporate Administrative Change 2 into this protocol to update the Sponsor Name Change throughout the document. • Editorial changes to reflect the current protocol template and safety standards.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported