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

Summary

EudraCT number	2009-010643-14
Trial protocol	FR DE GB CZ ES BE NL
Global end of trial date	08 August 2013

Results information

Result version number	v1 (current)
This version publication date	20 April 2016
First version publication date	14 June 2015

Trial information

Trial identification

Sponsor protocol code	M10-791

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00939003
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	Aileen L. Pangan, MD, AbbVie, aileen.pangan@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	08 August 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate how well adalimumab works in the short and long term in patients with axial spondyloarthritis who are not diagnosed as having either ankylosing spondylitis or psoriatic arthritis.

Protection of trial subjects:

Participant and/or legal guardian read and understood information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 August 2009
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	Netherlands: 5
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Belgium: 30
Country: Number of subjects enrolled	Czech Republic: 52
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	United States: 18
Country: Number of subjects enrolled	Australia: 21
Country: Number of subjects enrolled	Canada: 14
Worldwide total number of subjects	192
EEA total number of subjects	139

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)	189
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 192 participants were enrolled at 37 study sites in Australia, Belgium, Canada, the Czech Republic, France, Germany, the Netherlands, Spain, the United Kingdom, and the US. Due to Investigator non-compliance with protocol requirements, 1 study site was closed; the 7 participants enrolled at this site were excluded from efficacy analyses.

Period 1

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

Arms

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

Arm description:

Participants received placebo every other week (eow) for 12 weeks during the double-blind period and then received adalimumab 40 mg subcutaneously every other week for up to 144 weeks during the open-label period.

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

Dosage and administration details:

Placebo every other week up to Week 12.

Arm title	Double-blind Adalimumab

Arm description:

Participants received adalimumab 40 mg subcutaneously every other week for 12 weeks during the double-blind period and then received adalimumab 40 mg subcutaneously every other week for up to 144 weeks during the open-label period.

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

Dosage and administration details:

40 mg every other week up to Week 12.

Number of subjects in period 1[1]	Double-blind Placebo	Double-blind Adalimumab
Started	94	91
Completed	92	87
Not completed	2	4
MRI Not Diagnostic	1	1
Pregnancy	-	1
Adverse event	1	1
Lack of efficacy	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Full analysis set (FAS), defined as all participants who received at least one dose of blinded study drug excluding seven participants from one site due to investigator non-compliance.

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Adalimumab

Arm description:

Participants received placebo every other week for 12 weeks during the double-blind period and then received adalimumab 40 mg subcutaneously every other week for up to 144 weeks during the open-label period.

Arm type	Experimental
Investigational medicinal product name	Open-label Adalimumab
Investigational medicinal product code	
Other name	ABT-D2E7,Humira
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

40 mg every other week, Week 12 through Week 156.

Arm title	Adalimumab/Adalimumab

Arm description:

Participants received adalimumab 40 mg subcutaneously every other week for 12 weeks during the double-blind period and then received adalimumab 40 mg subcutaneously every other week for up to 144 weeks during the open-label period.

Arm type	Experimental
Investigational medicinal product name	Open-label Adalimumab
Investigational medicinal product code	
Other name	ABT-D2E7,Humira
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

40 mg every other week, from Week 12 through Week 144.

Number of subjects in period 2	Placebo/Adalimumab	Adalimumab/Adalimumab
Started	92	87
Completed	66	62
Not completed	26	25
Consent withdrawn by subject	14	7
Pregnancy	1	1
Adverse event	4	8
Exclusion criteria	1	-
Lack of efficacy	6	9

Baseline characteristics

Reporting groups	
Reporting group title	Double-blind Placebo
Reporting group description:	
Participants received placebo every other week (eow) for 12 weeks during the double-blind period and then received adalimumab 40 mg subcutaneously every other week for up to 144 weeks during the open-label period.	
Reporting group title	Double-blind Adalimumab
Reporting group description:	
Participants received adalimumab 40 mg subcutaneously every other week for 12 weeks during the double-blind period and then received adalimumab 40 mg subcutaneously every other week for up to 144 weeks during the open-label period.	

Reporting group values	Double-blind Placebo	Double-blind Adalimumab	Total
Number of subjects	94	91	185
Age categorical			
Units: Subjects			
Age continuous			
Full analysis set, defined as all participants who received at least one dose of blinded study drug excluding seven participants from one site due to investigator non-compliance			
Units: years			
arithmetic mean	38.4	37.6	
standard deviation	± 10.39	± 11.29	-
Gender categorical			
Full analysis set, defined as all participants who received at least one dose of blinded study drug excluding seven participants from one site due to investigator non-compliance			
Units: Subjects			
Female	54	47	101
Male	40	44	84

End points

End points reporting groups

Reporting group title	Double-blind Placebo
Reporting group description:	
Participants received placebo every other week (eow) for 12 weeks during the double-blind period and then received adalimumab 40 mg subcutaneously every other week for up to 144 weeks during the open-label period.	
Reporting group title	Double-blind Adalimumab
Reporting group description:	
Participants received adalimumab 40 mg subcutaneously every other week for 12 weeks during the double-blind period and then received adalimumab 40 mg subcutaneously every other week for up to 144 weeks during the open-label period.	
Reporting group title	Placebo/Adalimumab
Reporting group description:	
Participants received placebo every other week for 12 weeks during the double-blind period and then received adalimumab 40 mg subcutaneously every other week for up to 144 weeks during the open-label period.	
Reporting group title	Adalimumab/Adalimumab
Reporting group description:	
Participants received adalimumab 40 mg subcutaneously every other week for 12 weeks during the double-blind period and then received adalimumab 40 mg subcutaneously every other week for up to 144 weeks during the open-label period.	
Subject analysis set title	Double-blind Placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
Double-blind placebo every other week for 12 weeks. Safety analysis set, defined as all participants who received at least 1 dose of study drug.	
Subject analysis set title	Double-blind Adalimumab
Subject analysis set type	Safety analysis
Subject analysis set description:	
Double-blind adalimumab 40 mg subcutaneously every other week for 12 weeks. Safety analysis set, defined as all participants who received at least 1 dose of study drug.	

Primary: Number of Participants Achieving an Assessment of Spondyloarthritis International Society (ASAS) 40 Response

End point title	Number of Participants Achieving an Assessment of Spondyloarthritis International Society (ASAS) 40 Response
End point description:	
ASAS40 response was defined as improvement of ≥ 40% relative to Baseline and absolute improvement of ≥ 20 units (on a scale from 0 to 100) in ≥ 3 of the following 4 domains with no deterioration (defined as a net worsening of > 0 units on a scale from 0 to 100) in the potential remaining domain: • Patient's Global Assessment of disease activity, measured on a visual analog scale (VAS) from 0 (none) to 100 (severe); • Pain, measured by the total back pain VAS from 0 (no pain) to 100 (most severe); • Function, measured by the Bath Ankylosing Spondylitis Functional Index (BASFI) which consists of 10 items assessing participants' ability to perform activities on a VAS ranging from 0 (easy) to 100 (impossible); • Inflammation, measured by the mean of the 2 morning stiffness-related Bath AS Disease Activity Index (BASDAI) VAS scores (items 5 [level of stiffness] and 6 [duration of stiffness]) each on a scale from 0 (none/0 hours) to 10 (very severe/2 hours or more duration).	
End point type	Primary
End point timeframe:	
Baseline and Week 12	

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94[1]	91[2]		
Units: Participants	14	33		

Notes:

[1] - FAS. Subjects with missing data at week 12 were counted as non-responders (non-responder imputation)
[2] - FAS. Subjects with missing data at week 12 were counted as non-responders (non-responder imputation)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo v Double-blind Adalimumab
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Chi-squared

Secondary: Number of Participants Achieving an Assessment of Spondyloarthritis International Society (ASAS) 20 Response

End point title	Number of Participants Achieving an Assessment of Spondyloarthritis International Society (ASAS) 20 Response

End point description:

ASAS20 response was defined as improvement of ≥ 20% relative to Baseline and absolute improvement of ≥ 10 units (on a scale from 0 to 100) in ≥ 3 of the following 4 domains with no deterioration (defined as a change for the worse of ≥ 20% and net worsening of ≥ 10 units) in the potential remaining domain:
• Patient's Global Assessment of disease activity, measured on a visual analog scale (VAS) from 0 (none) to 100 (severe);
• Pain, measured by the total back pain VAS from 0 (no pain) to 100 (most severe);
• Function, measured by the Bath Ankylosing Spondylitis Functional Index (BASFI) which consists of 10 items assessing participants' ability to perform activities on a VAS ranging from 0 (easy) to 100 (impossible);
• Inflammation, measured by the mean of the 2 morning stiffness-related Bath AS Disease Activity Index (BASDAI) VAS scores (items 5 [level of stiffness] and 6 [duration of stiffness]) each on a scale from 0 (none/0 hours) to 10 (very severe/2 hours or more duration).

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94[3]	91[4]		
Units: Participants	29	47		

Notes:

[3] - Full analysis set; Non-responder imputation performed.

[4] - Full analysis set; Non-responder imputation performed.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo v Double-blind Adalimumab
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	Chi-squared

Secondary: Number of Participants Achieving a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50 Response

End point title	Number of Participants Achieving a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50 Response

End point description:

The Bath Ankylosing Spondylitis (AS) Disease Activity Index assesses disease activity by asking the participant to answer 6 questions (each on a 10 cm VAS) pertaining to symptoms experienced for the past week. For 5 questions (level of fatigue/tiredness, level of AS neck, back or hip pain, level of pain/swelling in joints, other than neck, back or hips, level of discomfort from any areas tender to touch or pressure, and level of morning stiffness), the response is from 0 (none) to 10 (very severe); for Question 6 (duration of morning stiffness), the response is from 0 (0 hours) to 10 (≥ 2 hours). The overall BASDAI score ranges from 0 to 10 cm. Lower scores indicate less disease activity. BASDAI50 is a 50% improvement from Baseline in BASDAI score.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94[5]	91[6]		
Units: Participants	14	32		

Notes:

[5] - Full analysis set; Non-responder imputation performed.

[6] - Full analysis set; Non-responder imputation performed.

Statistical analyses

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

Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	Chi-squared

Secondary: Change From Baseline in Short Form-36 (SF-36) Physical Component Summary Score

End point title	Change From Baseline in Short Form-36 (SF-36) Physical Component Summary Score

End point description:

The Medical Outcome Study Short Form 36-Item Health Survey, Version 2 (SF-36) is a self-administered instrument that measures the impact of disease on overall quality of life. The SF-36 consists of 36 questions in 8 domains (limitations in physical functioning due to health problems; limitations in usual role because of physical health problems; bodily pain; general health perceptions; vitality; limitations in social functioning because of physical or emotional problems; limitations in usual role due to emotional problems; and general mental health). Two component scores can be summarized: physical and mental; domains 1-4 comprise the physical component summary of the SF-36. A transformed summary score is calculated ranging from 0 to 100 where higher scores indicate a higher level of functioning. A positive change from Baseline score indicates an improvement.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93[7]	91[8]		
Units: units on a scale				
arithmetic mean (standard deviation)	2 (± 7.04)	5.5 (± 8.98)		

Notes:

[7] - Full analysis set with available data

[8] - Full analysis set with available data

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

ANCOVA model adjusting for Baseline value with treatment as a factor.

Comparison groups	Double-blind Placebo v Double-blind Adalimumab
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	ANCOVA

Secondary: Number of Participants Achieving ASAS Partial Remission

End point title	Number of Participants Achieving ASAS Partial Remission

End point description:

ASAS partial remission is an absolute score of < 20 units on a 0 to 100 scale for each of the four following domains:
• Patient's Global Assessment of disease activity, measured on a visual analog scale (VAS) from 0 (none) to 100 (severe);
• Pain, measured by the total back pain VAS from 0 (no pain) to 100 (most severe);
• Function, measured by the Bath Ankylosing Spondylitis Functional Index (BASFI) which consists of 10 items assessing participants' ability to perform activities on a VAS ranging from 0 (easy) to 100 (impossible);
• Inflammation, measured by the mean of the 2 morning stiffness-related Bath AS Disease Activity Index (BASDAI) VAS scores (items 5 [level of stiffness] and 6 [duration of stiffness]) each on a scale from 0 (none/0 hours) to 10 (very severe/2 hours or more duration).

End point type	Secondary

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	94[9]	91[10]		
Units: Participants	5	15		

Notes:

[9] - Full analysis set; Non-responder imputation performed

[10] - Full analysis set; Non-responder imputation performed

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo v Double-blind Adalimumab
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.014
Method	Chi-squared

Secondary: Number of Participants Achieving an ASAS5/6 Response

End point title	Number of Participants Achieving an ASAS5/6 Response

End point description:

ASAS5/6 response is a 20% improvement in five out of the following six domains:
• Patient's Global Assessment of disease activity, measured on a visual analog scale (VAS) from 0 (none) to 100 (severe);
• Pain, measured by the total back pain VAS from 0 (no pain) to 100 (most severe);
• Function, measured by the Bath Ankylosing Spondylitis Functional Index (BASFI) which consists of 10 items assessing participants' ability to perform activities on a VAS ranging from 0 (easy) to 100 (impossible);
• Inflammation, measured by the mean of the 2 morning stiffness-related Bath AS Disease Activity Index (BASDAI) VAS scores (items 5 [level of stiffness] and 6 [duration of stiffness]) each on a scale from 0 (none) to 10 (very severe/2 hours or more duration).
• Spinal mobility, measured from the lateral lumbar flexion score of the Bath AS Metrology Index (BASMI) on a scale from 0 (best mobility) to 10 (worst mobility);
• C-reactive protein level (lower levels indicate less inflammation).

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94[11]	91[12]		
Units: Participants	6	28		

Notes:

[11] - Full analysis set; Non-responder imputation performed

[12] - Full analysis set; Non-responder imputation performed

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Double-blind Placebo v Double-blind Adalimumab
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Chi-squared

Secondary: Change From Baseline in Disability Index of Health Assessment Questionnaire Modified for the Spondyloarthropathies (HAQ-S)

End point title	Change From Baseline in Disability Index of Health Assessment Questionnaire Modified for the Spondyloarthropathies (HAQ-S)

End point description:

Health Assessment Questionnaire modified for spondyloarthropathies (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.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94[13]	91[14]		
Units: units on a scale				
arithmetic mean (standard deviation)	-0.1 (± 0.42)	-0.3 (± 0.49)		

Notes:

[13] - FAS: non-missing Baseline and ≥1 non-missing post-baseline value; Last observation carried forward
[14] - FAS: non-missing Baseline and ≥1 non-missing post-baseline value; Last observation carried forward

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

ANCOVA model adjusting for Baseline value with treatment as a factor.

Comparison groups	Double-blind Placebo v Double-blind Adalimumab
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.027
Method	ANCOVA

Secondary: Change From Baseline in High-Sensitivity C-Reactive Protein (hsCRP)

End point title	Change From Baseline in High-Sensitivity C-Reactive Protein (hsCRP)

End point description:

C-reactive protein (CRP) is considered an efficacy variable for the axial spondyloarthritis indication. It is a general marker of inflammation that is sensitive to acute changes in inflammatory response. Higher levels indicate more inflammation.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73[15]	70[16]		
Units: mg/L				
arithmetic mean (standard deviation)	-0.3 (± 6.39)	-4.7 (± 12.32)		

Notes:

[15] - FAS: non-missing Baseline and ≥1 non-missing post-baseline value; Last observation carried forward
[16] - FAS: non-missing Baseline and ≥1 non-missing post-baseline value; Last observation carried forward

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

ANCOVA model adjusting for Baseline value with treatment as a factor.

Comparison groups	Double-blind Placebo v Double-blind Adalimumab

Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA

Secondary: Change From Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Magnetic Resonance Imaging (MRI) Score for Sacroiliac Joints

End point title	Change From Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Magnetic Resonance Imaging (MRI) Score for Sacroiliac Joints

End point description:

Six consecutive sacroiliac (SI) joint image coronal slices representing the largest proportion of the synovial compartment of the SI joints were assessed for edema, intensity and depth of edema using SPARCC scoring.
Each SI joint (left and right) was divided into quadrants for a total of 8 SI scoring locations. Each quadrant was scored for the presence (1) or absence (0) of edema; the maximum score is 8 per slice and maximum score for 6 SI joint slices is 48.
Intensity of edema: A score of 1 was assigned for each SI joint (left and right) if an intense signal was seen in any quadrant of that joint for each slice. The maximum score is 2 per slice and 12 for 6 slices.
A lesion was graded as deep (score of 1) if there was homogeneous and unequivocal increase in signal extending over a depth of at least 1 cm from the articular surface of the SI joint in any quadrant.
The maximum score per slice is 2 and for 6 slices 12. The total maximum score for all SI joints across 6 slices is 72.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84[17]	84[18]		
Units: units on a scale				
arithmetic mean (standard deviation)	-0.6 (± 6.19)	-3.2 (± 8.34)		

Notes:

[17] - FAS; participants with non-missing Baseline and non-missing post-baseline value were included

[18] - FAS; participants with non-missing Baseline and non-missing post-baseline value were included

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

ANCOVA model adjusting for Baseline value with treatment as a factor.

Comparison groups	Double-blind Placebo v Double-blind Adalimumab
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	ANCOVA

Secondary: Change From Baseline in SPARCC MRI Score for the Spine

End point title	Change From Baseline in SPARCC MRI Score for the Spine

End point description:

Six discovertebral units (DVU) representing the 6 most abnormal DVUs, and 3 consecutive sagittal slices at each DVU representing the most abnormal slices for that DVU were selected for scoring. Each DVU was divided into 4 quadrants and scored for the presence (1) or absence (0) of edema. The maximum score is 12 per DVU. The maximum score is 72 for 6 DVUs.
If edema was present in at least 1 quadrant of a DVU slice, it was scored for intensity and depth of the edema representing that slice:
A score of 1 was assigned if an intense signal was seen in any quadrant on a DVU slice. The maximum score for intensity per slice is 1, per DVU is 3 and for 6 DVUs is 18.
A lesion was graded as deep (score of 1) if there was homogeneous and unequivocal increase in signal extending over a depth of at least 1 cm from the surface of the endplate in any quadrant. The maximum score per slice is 1, for a DVU is 3 and for 6 DVUs is 18.
The total maximum SPARCC score for all 6 DVUs is 108.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82[19]	85[20]		
Units: units on a scale				
arithmetic mean (standard deviation)	-0.2 (± 3.35)	-1.8 (± 4.51)		

Notes:

[19] - FAS; FAS; participants with non-missing Baseline and non-missing post-baseline value were included
[20] - FAS; FAS; participants with non-missing Baseline and non-missing post-baseline value were included

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

ANCOVA model adjusting for Baseline value with treatment as a factor.

Comparison groups	Double-blind Placebo v Double-blind Adalimumab
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	ANCOVA

Other pre-specified: Number of Participants Reporting Adverse Events

End point title	Number of Participants Reporting Adverse Events

End point description:

Adverse events were collected at designated study visits for all participants who received at least 1 dose

of study drug. The number of participants experiencing any adverse event (serious and non-serious) is summarized. For the double-blind phase of the study, adverse events are reported through Week 12.

End point type	Other pre-specified

End point timeframe:

Through Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97[21]	95[22]		
Units: participants	57	55		

Notes:

[21] - All participants who received at least 1 dose of study drug

[22] - All participants who received at least 1 dose of study drug

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Participants With Blood Hematology or Chemistry Values Common Toxicity Criteria Grade ≥ 3

End point title	Number of Participants With Blood Hematology or Chemistry Values Common Toxicity Criteria Grade ≥ 3

End point description:

Blood was collected for analysis at designated study visits; hematology and chemistry results were provided by a central laboratory. The number of participants with an abnormal laboratory result (higher then upper normal limit or lower than lower normal limit) meeting Common Toxicity Criteria (CTC) of Grade 3 or higher is summarized. Results for the double-blind phase phase of the study are reported through Week 12.

End point type	Other pre-specified

End point timeframe:

Through Week 12

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97[23]	95[24]		
Units: Participants	6	4		

Notes:

[23] - All participants who received at least 1 dose of study drug

[24] - All participants who received at least 1 dose of study drug

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Participants Achieving an ASAS20 Response During the Open-label Period

End point title	Number of Participants Achieving an ASAS20 Response During

	the Open-label Period

End point description:

ASAS20 response was defined as improvement of ≥ 20% relative to Baseline and absolute improvement of ≥ 10 units (on a scale from 0 to 100) in ≥ 3 of the following 4 domains with no deterioration (defined as a change for the worse of ≥ 20% and net worsening of ≥ 10 units) in the potential remaining domain:
• Patient's Global Assessment of disease activity, measured on a visual analog scale (VAS) from 0 (none) to 100 (severe);
• Pain, measured by the total back pain VAS from 0 (no pain) to 100 (most severe);
• Function, measured by the Bath Ankylosing Spondylitis Functional Index (BASFI) which consists of 10 items assessing participants' ability to perform activities on a VAS ranging from 0 (easy) to 100 (impossible);
• Inflammation, measured by the mean of the 2 morning stiffness-related Bath AS Disease Activity Index (BASDAI) VAS scores (items 5 [level of stiffness] and 6 [duration of stiffness]) each on a scale from 0 (none/0 hours) to 10 (very severe/2 hours or more duration).

End point type	Other pre-specified

End point timeframe:

Baseline and Weeks 52, 104, and 156

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94[25]	91[26]		
Units: Participants				
Week 52 (N=78, 72)	59	57		
Week 104 (N=74, 64)	59	53		
Week 156 (N=64, 58)	53	48		

Notes:

[25] - Full analysis set participants with available data at each time point (indicated by N)

[26] - Full analysis set participants with available data at each time point (indicated by N)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Participants Achieving an ASAS40 Response During the Open-label Period

End point title	Number of Participants Achieving an ASAS40 Response During the Open-label Period

End point description:

ASAS40 response was defined as improvement of ≥ 40% relative to Baseline and absolute improvement of ≥ 20 units (on a scale from 0 to 100) in ≥ 3 of the following 4 domains with no deterioration (defined as a net worsening of > 0 units on a scale of 0 to 100) in the potential remaining domain:
• Patient's Global Assessment of disease activity, measured on a visual analog scale (VAS) from 0 (none) to 100 (severe);
• Pain, measured by the total back pain VAS from 0 (no pain) to 100 (most severe);
• Function, measured by the Bath Ankylosing Spondylitis Functional Index (BASFI) which consists of 10 items assessing participants' ability to perform activities on a VAS ranging from 0 (easy) to 100 (impossible);
• Inflammation, measured by the mean of the 2 morning stiffness-related Bath AS Disease Activity Index (BASDAI) VAS scores (items 5 [level of stiffness] and 6 [duration of stiffness]) each on a scale from 0 (none/0 hours) to 10 (very severe/2 hours or more duration).

End point type	Other pre-specified

End point timeframe:

Baseline and Weeks 52, 104, and 156

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94[27]	91[28]		
Units: participants				
Week 52 (N=78, 72)	50	42		
Week 104 (N=74, 64)	51	38		
Week 156 (N=64, 58)	44	37		

Notes:

[27] - Full analysis set participants with available data at each time point (indicated by N).

[28] - Full analysis set participants with available data at each time point (indicated by N).

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Participants Achieving a BASDAI50 Response During the Open-label Period

End point title	Number of Participants Achieving a BASDAI50 Response During the Open-label Period

End point description:

The Bath Ankylosing Spondylitis (AS) Disease Activity Index assesses disease activity by asking the participant to answer 6 questions (each on a 10 cm VAS) pertaining to symptoms experienced for the past week. For 5 questions (level of fatigue/tiredness, level of AS neck, back or hip pain, level of pain/swelling in joints, other than neck, back or hips, level of discomfort from any areas tender to touch or pressure, and level of morning stiffness), the response is from 0 (none) to 10 (very severe); for Question 6 (duration of morning stiffness), the response is from 0 (0 hours) to 10 (≥ 2 hours). The overall BASDAI score ranges from 0 to 10 cm. Lower scores indicate less disease activity. BASDAI50 is a 50% improvement from Baseline in BASDAI score.

End point type	Other pre-specified

End point timeframe:

Baseline and Weeks 52, 104, and 156

End point values	Double-blind Placebo	Double-blind Adalimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94[29]	91[30]		
Units: participants				
Week 52 (N=78, 72)	52	42		
Week 104 (N=74, 64)	50	40		
Week 156 (N=64, 58)	46	39		

Notes:

[29] - Full analysis set participants with available data at each time point (indicated by N).

[30] - Full analysis set participants with available data at each time point (indicated by N).

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Twelve weeks during the double blind period and up to Week 156 during the open-label period.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups	
Reporting group title	Double-blind Placebo
Reporting group description: Participants received placebo every other week for 12 weeks during the double-blind period.	
Reporting group title	Double-blind Adalimumab
Reporting group description: Participants received adalimumab 40 mg subcutaneously every other week for 12 weeks during the double-blind period.	
Reporting group title	Any Adalimumab
Reporting group description: Participants who received any dose of adalimumab during the 12-week double-blind period or during the 144-week open-label period.	

Serious adverse events	Double-blind Placebo	Double-blind Adalimumab	Any Adalimumab
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 97 (1.03%)	3 / 95 (3.16%)	33 / 190 (17.37%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events			
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 97 (0.00%)	1 / 95 (1.05%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	1 / 97 (1.03%)	0 / 95 (0.00%)	0 / 190 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 97 (1.03%)	0 / 95 (0.00%)	0 / 190 (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
Reproductive system and breast disorders			
Breast dysplasia			
subjects affected / exposed	0 / 97 (0.00%)	1 / 95 (1.05%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menorrhagia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal prolapse			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
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			
Cough			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary embolism			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Suicide attempt			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
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			
Fall			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiopulmonary failure			

subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 97 (1.03%)	0 / 95 (0.00%)	0 / 190 (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
Headache			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	2 / 190 (1.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Macular degeneration			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oscillopsia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
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 lower			

subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 97 (1.03%)	0 / 95 (0.00%)	0 / 190 (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
Stomatitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 97 (1.03%)	0 / 95 (0.00%)	0 / 190 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis acute			
subjects affected / exposed	0 / 97 (0.00%)	1 / 95 (1.05%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
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			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus-like syndrome			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periarthritis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon calcification			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
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			
Bursitis infective			

subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	2 / 190 (1.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated tuberculosis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
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 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal cyst			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	1 / 190 (0.53%)
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	32 / 97 (32.99%)	42 / 95 (44.21%)	152 / 190 (80.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 97 (2.06%)	0 / 95 (0.00%)	9 / 190 (4.74%)
occurrences (all)	2	0	11
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 97 (2.06%)	3 / 95 (3.16%)	7 / 190 (3.68%)
occurrences (all)	2	3	12
Fatigue			
subjects affected / exposed	0 / 97 (0.00%)	3 / 95 (3.16%)	14 / 190 (7.37%)
occurrences (all)	0	3	16
Injection site erythema			
subjects affected / exposed	0 / 97 (0.00%)	3 / 95 (3.16%)	6 / 190 (3.16%)
occurrences (all)	0	3	7
Injection site pain			
subjects affected / exposed	3 / 97 (3.09%)	1 / 95 (1.05%)	2 / 190 (1.05%)
occurrences (all)	3	1	2
Injection site reaction			
subjects affected / exposed	0 / 97 (0.00%)	4 / 95 (4.21%)	11 / 190 (5.79%)
occurrences (all)	0	4	11
Pyrexia			
subjects affected / exposed	0 / 97 (0.00%)	2 / 95 (2.11%)	8 / 190 (4.21%)
occurrences (all)	0	2	9
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 97 (1.03%)	1 / 95 (1.05%)	8 / 190 (4.21%)
occurrences (all)	1	1	11
Oropharyngeal pain			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	9 / 190 (4.74%)
occurrences (all)	0	0	10

Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	11 / 190 (5.79%)
occurrences (all)	0	0	11
Depression			
subjects affected / exposed	0 / 97 (0.00%)	2 / 95 (2.11%)	7 / 190 (3.68%)
occurrences (all)	0	2	7
Insomnia			
subjects affected / exposed	0 / 97 (0.00%)	2 / 95 (2.11%)	9 / 190 (4.74%)
occurrences (all)	0	3	11
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 97 (1.03%)	1 / 95 (1.05%)	6 / 190 (3.16%)
occurrences (all)	1	1	6
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	7 / 190 (3.68%)
occurrences (all)	0	0	7
Fall			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	6 / 190 (3.16%)
occurrences (all)	0	0	7
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 97 (3.09%)	6 / 95 (6.32%)	19 / 190 (10.00%)
occurrences (all)	3	6	21
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	6 / 190 (3.16%)
occurrences (all)	0	0	6
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 97 (0.00%)	2 / 95 (2.11%)	9 / 190 (4.74%)
occurrences (all)	0	2	10
Constipation			
subjects affected / exposed	3 / 97 (3.09%)	1 / 95 (1.05%)	2 / 190 (1.05%)
occurrences (all)	3	1	2
Diarrhoea			

subjects affected / exposed	7 / 97 (7.22%)	4 / 95 (4.21%)	18 / 190 (9.47%)
occurrences (all)	9	5	23
Nausea			
subjects affected / exposed	7 / 97 (7.22%)	7 / 95 (7.37%)	13 / 190 (6.84%)
occurrences (all)	7	7	17
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 97 (1.03%)	1 / 95 (1.05%)	6 / 190 (3.16%)
occurrences (all)	1	1	11
Rash			
subjects affected / exposed	2 / 97 (2.06%)	2 / 95 (2.11%)	6 / 190 (3.16%)
occurrences (all)	2	2	6
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 97 (1.03%)	1 / 95 (1.05%)	11 / 190 (5.79%)
occurrences (all)	1	1	12
Back pain			
subjects affected / exposed	1 / 97 (1.03%)	0 / 95 (0.00%)	13 / 190 (6.84%)
occurrences (all)	1	0	15
Bursitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	9 / 190 (4.74%)
occurrences (all)	0	0	13
Muscle spasms			
subjects affected / exposed	1 / 97 (1.03%)	0 / 95 (0.00%)	6 / 190 (3.16%)
occurrences (all)	1	0	6
Myalgia			
subjects affected / exposed	1 / 97 (1.03%)	1 / 95 (1.05%)	7 / 190 (3.68%)
occurrences (all)	1	1	8
Spondylitis			
subjects affected / exposed	2 / 97 (2.06%)	2 / 95 (2.11%)	37 / 190 (19.47%)
occurrences (all)	2	2	55
Spondyloarthropathy			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	8 / 190 (4.21%)
occurrences (all)	0	0	9
Synovial cyst			

subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	6 / 190 (3.16%)
occurrences (all)	0	0	6
Tendonitis			
subjects affected / exposed	0 / 97 (0.00%)	1 / 95 (1.05%)	6 / 190 (3.16%)
occurrences (all)	0	1	6
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 97 (2.06%)	1 / 95 (1.05%)	31 / 190 (16.32%)
occurrences (all)	2	1	38
Cystitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	7 / 190 (3.68%)
occurrences (all)	0	0	12
Gastroenteritis			
subjects affected / exposed	3 / 97 (3.09%)	2 / 95 (2.11%)	11 / 190 (5.79%)
occurrences (all)	3	2	15
Influenza			
subjects affected / exposed	0 / 97 (0.00%)	2 / 95 (2.11%)	9 / 190 (4.74%)
occurrences (all)	0	2	9
Nasopharyngitis			
subjects affected / exposed	3 / 97 (3.09%)	11 / 95 (11.58%)	52 / 190 (27.37%)
occurrences (all)	4	11	81
Oral herpes			
subjects affected / exposed	0 / 97 (0.00%)	2 / 95 (2.11%)	6 / 190 (3.16%)
occurrences (all)	0	3	15
Pharyngitis			
subjects affected / exposed	0 / 97 (0.00%)	3 / 95 (3.16%)	15 / 190 (7.89%)
occurrences (all)	0	3	18
Rhinitis			
subjects affected / exposed	2 / 97 (2.06%)	2 / 95 (2.11%)	9 / 190 (4.74%)
occurrences (all)	3	2	15
Sinusitis			
subjects affected / exposed	2 / 97 (2.06%)	1 / 95 (1.05%)	18 / 190 (9.47%)
occurrences (all)	2	1	25
Tonsillitis			
subjects affected / exposed	2 / 97 (2.06%)	1 / 95 (1.05%)	9 / 190 (4.74%)
occurrences (all)	2	1	15

Upper respiratory tract infection			
subjects affected / exposed	4 / 97 (4.12%)	3 / 95 (3.16%)	19 / 190 (10.00%)
occurrences (all)	4	3	33
Urinary tract infection			
subjects affected / exposed	1 / 97 (1.03%)	0 / 95 (0.00%)	7 / 190 (3.68%)
occurrences (all)	1	0	16
Vaginal infection			
subjects affected / exposed	1 / 97 (1.03%)	0 / 95 (0.00%)	6 / 190 (3.16%)
occurrences (all)	1	0	7
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 97 (0.00%)	0 / 95 (0.00%)	7 / 190 (3.68%)
occurrences (all)	0	0	9
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 97 (1.03%)	0 / 95 (0.00%)	6 / 190 (3.16%)
occurrences (all)	1	0	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 August 2011	Extended open-label treatment to 144 weeks; added the QuantiFERON®-TB Gold Test; added yearly testing of subjects negative for purified protein derivative (PPD) at screening; added a confirmatory human leukocyte antigen-B27 (HLA-B27) test if the initial test was reported as equivocal; added an antero-posterior (AP) pelvis x-ray at week 104 for monitoring progression of disease; added tuberculosis (TB) prophylaxis non-compliance as a reason for subject discontinuation; and added clarifications and additional explanations for better understanding by the sites.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported