Clinical trial results:
A MULTICENTRE, 12- WEEK DOUBLE BLIND PLACEBO CONTROLLED RANDOMIZED STUDY OF ETANERCEPT ON A BACKGROUND NSAID IN THE TREATMENT OF ADULT SUBJECTS WITH NON RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS WITH A 92-WEEK OPEN LABEL EXTENSION

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2010-020077-16
Trial protocol	ES HU DE BE GB DK NL FI CZ
Global end of trial date	03 October 2014

Results information

Result version number	v1 (current)
This version publication date	05 March 2016
First version publication date	05 March 2016

Trial information

Trial identification

Sponsor protocol code	B1801031

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01258738
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 East 42nd Street,, New York, United States, 10017
Public contact	Pfizer ClinicalTrial.gov Call Center, Pfizer, Inc., +1 800 718 1021,
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 800 718 1021,, ClinicalTrials.gov_Inquiries@pfizer.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	01 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 November 2012
Global end of trial reached?	Yes
Global end of trial date	03 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to compare the efficacy of etanercept (ETN) against placebo in improving symptoms of early non-radiographic axial spondyloarthritis (nr-AxSpA) at 12 weeks when added to a background nonsteroidal anti-inflammatory drugs (NSAID) at the optimal anti-inflammatory dose. The secondary objectives were to assess the efficacy and safety of ETN and background NSAID over 104 weeks, to compare the effect of ETN 50 milligram (mg) once weekly versus placebo on inflammation seen in magnetic resonance imaging (MRI) of the spine at 12 weeks when added to a background NSAID at the optimal inflammatory dose and to compare the quality of life between those participants treated with ETN 50mg once weekly versus placebo over 12 weeks when added to a background NSAID at the optimal anti-inflammatory dose.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines (ICH 1996). In addition, all local regulatory requirements, as well as the general principles set forth in the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences 2002), were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 February 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	21 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hungary: 42
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 20
Country: Number of subjects enrolled	Netherlands: 12
Country: Number of subjects enrolled	Russian Federation: 6
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Taiwan: 29
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Germany: 18
Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Belgium: 26
Country: Number of subjects enrolled	Colombia: 14
Country: Number of subjects enrolled	Czech Republic: 23

Country: Number of subjects enrolled	Finland: 5
Country: Number of subjects enrolled	France: 12
Worldwide total number of subjects	224
EEA total number of subjects	152

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)	224
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicenter study conducted at 48 centers in 14 countries.

Pre-assignment

Screening details:

Eligible participants were randomized to receive etanercept or placebo for 12 week controlled (double-blind) period. Participants completing 12 week period entered a 92 week open-label period.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The study was subject, investigator and Sponsor-blinded in the double-blind period. At the initiation of the study, the study site was instructed on the method for breaking the blind. The method was either a manual or electronic process. Blinding codes were only to be broken in emergency situations for reasons of participant safety.

Arms

Are arms mutually exclusive?	Yes
Arm title	Etanercept

Arm description:

Participants were treated with etanercept subcutaneous injection weekly plus stable background non-steroidal anti-inflammatory drug (NSAID) at optimal anti-inflammatory dose for 12 weeks (double-blind period). All participants who completed the 12-week double-blind period entered into a 92 week open-label period and received etanercept 50 mg once weekly and background NSAID.

Arm type	Active comparator
Investigational medicinal product name	Etanercept
Investigational medicinal product code	
Other name	Enbrel
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were treated with etanercept subcutaneous injection weekly plus stable background NSAID at optimal anti-inflammatory dose for 12 weeks (double-blind period). All participants who completed the 12-week double-blind period entered into a 92 week open-label period and received etanercept 50 mg once weekly and background NSAID.

Arm title	Placebo

Arm description:

Participants were treated with placebo subcutaneous injection weekly plus stable background NSAID at optimal anti-inflammatory dose for 12 weeks (double-blind period). All participants who completed the 12-week double-blind period were eligible to enter into a 92 week open-label period and received etanercept 50 mg once weekly and background NSAID.

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:

Participants were treated with placebo subcutaneous injection weekly plus stable background NSAID at optimal anti-inflammatory dose for 12 weeks (double-blind period). All participants who completed the 12-week double-blind period who were eligible to enter into a 92 week open-label period and received etanercept 50 mg once weekly and background NSAID.

Number of subjects in period 1	Etanercept	Placebo
Started	111	113
Completed	83	86
Not completed	28	27
Did not meet inclusion criteria	3	3
Adverse event not related to study drug	3	1
Pregnancy	1	1
No longer willing to participate in the study	7	8
Lost to follow-up	2	2
Other unspecified reasons	-	1
Adverse event related to study drug	4	5
Insufficient clinical response	5	3
Protocol deviation	3	3

Baseline characteristics

Reporting groups	
Reporting group title	Etanercept
Reporting group description:	
Participants were treated with etanercept subcutaneous injection weekly plus stable background non-steroidal anti-inflammatory drug (NSAID) at optimal anti-inflammatory dose for 12 weeks (double-blind period). All participants who completed the 12-week double-blind period entered into a 92 week open-label period and received etanercept 50 mg once weekly and background NSAID.	
Reporting group title	Placebo
Reporting group description:	
Participants were treated with placebo subcutaneous injection weekly plus stable background NSAID at optimal anti-inflammatory dose for 12 weeks (double-blind period). All participants who completed the 12-week double-blind period were eligible to enter into a 92 week open-label period and received etanercept 50 mg once weekly and background NSAID.	

Reporting group values	Etanercept	Placebo	Total
Number of subjects	111	113	224
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	111	113	224
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous | Units: years			
arithmetic mean	31.7	32	
standard deviation	± 7.8	± 7.8	-
Gender, Male/Female Units: Participants			
Female	41	50	91
Male	70	63	133

End points

End points reporting groups

Reporting group title	Etanercept

Reporting group description:

Participants were treated with etanercept subcutaneous injection weekly plus stable background non-steroidal anti-inflammatory drug (NSAID) at optimal anti-inflammatory dose for 12 weeks (double-blind period). All participants who completed the 12-week double-blind period entered into a 92 week open-label period and received etanercept 50 mg once weekly and background NSAID.

Reporting group title	Placebo

Reporting group description:

Participants were treated with placebo subcutaneous injection weekly plus stable background NSAID at optimal anti-inflammatory dose for 12 weeks (double-blind period). All participants who completed the 12-week double-blind period were eligible to enter into a 92 week open-label period and received etanercept 50 mg once weekly and background NSAID.

Primary: Percentage of participants achieving Ankylosing Spondylitis (ASAS) 40 response at Week 12

End point title	Percentage of participants achieving Ankylosing Spondylitis (ASAS) 40 response at Week 12

End point description:

ASAS measures symptomatic improvement in Ankylosing Spondylitis (AS) in 4 domains: participant global assessment of disease activity, pain, function, inflammation. ASAS 40 = 40% improvement from baseline and an absolute change ≥ 20 units on a 0-100 scale (0 = no disease activity, 100 = high disease activity) for ≥ 3 domains, and no worsening in remaining domain.

End point type	Primary

End point timeframe:

Baseline to Week 12

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	108		
Units: Percentage of participants				
number (not applicable)	32.38	15.74		

Statistical analyses

Statistical analysis title	Statistical analysis 1 at Week 12

Statistical analysis description:

The null hypothesis was that the efficacy of etanercept was not different from placebo as measured by the proportion of subjects achieving an ASAS 40 response after 12 weeks of treatment. The alternative hypothesis was that the efficacy of etanercept was different from placebo. The primary endpoint was tested at 2-sided alpha = 0.05 significance level. Comparative analysis was carried out for Week 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0062 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	16.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.36
upper limit	27.92

Notes:

[1] - P-value <0.05 was required to declare statistical significance. Stratified by positive or negative sacroilitis MRI and geographic region.

Secondary: Percentage of participants achieving ASAS 40 response at time points

End point title	Percentage of participants achieving ASAS 40 response at time points

End point description:

ASAS measures symptomatic improvement in AS in 4 domains: participant global assessment of disease activity, pain, function, inflammation. ASAS 40 = 40% improvement from baseline and an absolute change ≥ 20 units on a 0-100 scale (0 = no disease activity, 100 = high disease activity) for ≥ 3 domains, and no worsening in remaining domain.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	108		
Units: Percentage of participants				
number (not applicable)				
Week 2 (N=105, 106)	15.24	3.77		
Week 4 (N=105, 108)	20	14.81		
Week 8 (N=105, 108)	28.57	15.74		
Week 12 (N= 105, 108)	33.33	14.81		
Week 16 (N= 100, 105)	42	38.1		
Week 24 (N= 100, 105)	44	51.43		
Week 32 (N= 100, 105)	47	52.38		
Week 40 (N= 100, 105)	55	53.33		
Week 48 (N= 100, 105)	52	53.33		
Week 56 (N= 100, 105)	52	59.05		
Week 68 (N= 100, 105)	54	58.1		
Week 80 (N= 100, 105)	49	58.1		
Week 92 (N= 100, 105)	57	61.9		
Week 104 (N= 100, 105)	56	61.9		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 2
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0059
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	11.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.69
upper limit	19.24

Statistical analysis title	Statistical analysis at Week 4
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3786
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	5.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.98
upper limit	15.35

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0304
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	12.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.79
upper limit	23.87

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0023
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	18.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.29
upper limit	29.75

Secondary: Percentage of participants achieving ASAS 20 response at time points

End point title	Percentage of participants achieving ASAS 20 response at time points

End point description:

ASAS measures symptomatic improvement in AS in 4 domains: participant global assessment of disease activity, pain, function, inflammation. ASAS 20 = 20% improvement from baseline and an absolute change ≥ 10 units on a 0-100 scale (0=no disease activity; 100 = high disease activity) for ≥ 3 domains, and no worsening in remaining domain.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	109		
Units: Percentage of participants				
number (not applicable)				
Week 2 (N = 105, 106)	30.48	16.04		
Week 4 (N = 105, 108)	37.14	26.85		
Week 8 (N = 105, 108)	48.57	37.96		
Week 12 (N = 105, 109)	52.38	36.7		
Week 16 (N= 100, 105)	64	65.71		
Week 24 (N = 100, 105)	65	71.43		
Week 32 (N = 100, 105)	64	71.43		
Week 40 (N = 100, 105)	73	73.33		
Week 48 (N = 100, 105)	71	72.38		
Week 56 (N = 100, 105)	70	76.19		
Week 68 (N = 100, 105)	69	76.19		
Week 80 (N = 100, 105)	65	70.48		
Week 92 (N = 100, 105)	71	74.29		
Week 104 (N = 100, 105)	70	79.05		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0189
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	14.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.2
upper limit	25.68

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0867
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	10.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.63
upper limit	23.84

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0983
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	10.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.17
upper limit	22.75

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0195
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	16.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	29.43

Secondary: Percentage of participants achieving ASAS 5/6 response at time points

End point title	Percentage of participants achieving ASAS 5/6 response at time points

End point description:

ASAS 5/6 consists of 6 domains: the 4 used in ASAS 20 (participant global assessment of disease activity, pain, function, inflammation measured on a 0-100 scale, where 0 = no disease activity and 100 = high disease activity) plus spinal mobility and an acute phase reactant, C Reactive Protein (CRP). Achieving ASAS 5/6 requires a 20% improvement compared to baseline in ≥ 5 domains and no worsening in the remaining domain.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	109		
Units: Percentage of participants				
number (not applicable)				
Week 2 (N = 102, 105)	15.69	2.86		
Week 4 (N = 103, 107)	23.3	8.41		
Week 8 (N = 103, 107)	33.01	11.21		
Week 12 (N = 105, 109)	33.01	10.38		
Week 16 (N = 100, 105)	37	34.29		
Week 24 (N = 100, 105)	41	42.86		
Week 32 (N = 100, 105)	40	40.95		
Week 40 (N = 100, 105)	45	40.95		
Week 48 (N = 100, 105)	49	45.71		
Week 56 (N = 100, 105)	42	45.71		
Week 68 (N = 100, 105)	42	43.81		
Week 80 (N = 100, 105)	39	37.14		
Week 92 (N = 100, 105)	46	47.62		
Week 104 (N = 100, 105)	43	40.95		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 12
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	22.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.85
upper limit	33.41

Statistical analysis title	Statistical analysis at Week 2
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0021
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	12.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.09
upper limit	20.57

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	14.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.18
upper limit	24.6

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	21.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.92
upper limit	32.67

Secondary: Mean change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) high sensitivity CRP (hsCRP) score at time points

End point title	Mean change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) high sensitivity CRP (hsCRP) score at time points

End point description:

ASDAS includes CRP (mg/L) or ESR (mm/hr); Apart from the value of CRP or ESR, the four additional self-reported items (rated on 0-10cm VAS or 0-10 numerical rating scale [NRS]) included in this index are back pain, duration of morning stiffness, peripheral pain/swelling and patient global assessment of disease activity. The ASDAS scores are then calculated as follows: ASDAS_CRP = (0.121 x total back pain) + (0.110 x subject global) + (0.073 x peripheral pain/swelling) + (0.058 x duration of morning stiffness) + (0.579 x Ln(CRP+1)). And ASDAS_ESR: (0.079 x total back pain) + (0.113 x subject global) + (0.086 x peripheral pain/swelling) + (0.069 x duration of morning stiffness) + (0.293 x √ESR). In

addition, the proportion of participants who achieve inactive disease based on the ASDAS will be determined for each group. Inactive disease is defined as an ASDAS score <1.3.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	108		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N = 104, 106)	-0.74 (± 0.1)	-0.2 (± 0.1)		
Week 4 (N = 104, 108)	-0.92 (± 0.11)	-0.3 (± 0.1)		
Week 8 (N = 104, 108)	-1.09 (± 0.13)	-0.48 (± 0.12)		
Week 12 (N= 104, 108)	-1.27 (± 0.11)	-0.63 (± 0.08)		
Week 16 (N= 99, 104)	-1.41 (± 0.11)	-1.35 (± 0.11)		
Week 24 (N= 99, 104)	-1.48 (± 0.11)	-1.55 (± 0.11)		
Week 32 (N= 99, 104)	-1.44 (± 0.11)	-1.52 (± 0.11)		
Week 40 (N= 99, 104)	-1.64 (± 0.11)	-1.6 (± 0.12)		
Week 48 (N= 99, 104)	-1.62 (± 0.11)	-1.63 (± 0.12)		
Week 56 (N= 99, 104)	-1.61 (± 0.12)	-1.65 (± 0.11)		
Week 68 (N= 99, 104)	-1.6 (± 0.11)	-1.65 (± 0.11)		
Week 80 (N= 99, 104)	-1.53 (± 0.12)	-1.61 (± 0.12)		
Week 92 (N= 99, 104)	-1.63 (± 0.12)	-1.7 (± 0.12)		
Week 104 (N= 99, 104)	-1.59 (± 0.12)	-1.68 (± 0.12)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	-0.34

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	-0.41

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.61

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	-0.37

Secondary: Percentage of participants achieving ASAS partial remission at time points

End point title	Percentage of participants achieving ASAS partial remission at time points

End point description:

Partial remission defined as a score of 20 units or less (on a scale of 0-100, where 0 = no disease activity and 100 = high disease activity) in each of the 4 Assessment in ASAS domains: participant global assessment of disease activity, pain, function, and inflammation. For scale, 100 = high disease activity.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	109		
Units: Percentage of participants				
number (not applicable)				
Week 2 (N = 105, 108)	11.43	2.78		
Week 4 (N = 105, 109)	10.48	3.67		
Week 8 (N = 105, 109)	21.9	9.17		
Week 12 (N = 105, 109)	24.76	11.93		
Week 16 (N = 100, 105)	29	28.57		
Week 24 (N = 100, 105)	32	42.86		
Week 32 (N = 100, 105)	28	41.9		
Week 40 (N = 100, 105)	40	45.71		
Week 48 (N = 100, 105)	38	37.14		
Week 56 (N = 100, 105)	40	43.81		
Week 68 (N = 100, 105)	37	48.57		
Week 80 (N = 100, 105)	34	49.52		
Week 92 (N = 100, 105)	39	49.52		
Week 104 (N = 100, 105)	40	57.14		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12

data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0209
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	12.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.58
upper limit	23.09

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0179
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	8.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.82
upper limit	15.48

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0611
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	6.81

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	13.65

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0141
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	12.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.14
upper limit	22.32

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Secondary: Time to ASAS partial remission

End point title	Time to ASAS partial remission

End point description:

The median time to partial remission was not reached at Week 12. Hence, we report an estimate of the percentage of participants, estimated using Kaplan-Meier approach.

End point type	Secondary

End point timeframe:

Week 12

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	109		
Units: percentage of participants				
number (confidence interval)	43.3 (30.4 to 59)	22.3 (12.5 to 38.1)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 12
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0022
Method	Logrank

Secondary: Mean Change from Baseline in Visual Analogue Scale (VAS) Physician Global Assessments at time points

End point title	Mean Change from Baseline in Visual Analogue Scale (VAS) Physician Global Assessments at time points
End point description:	
The Investigator estimated the participant's overall disease activity over the previous 48 hours (this was independent of the Subject Assessment of Disease Activity) using a scale between 0 mm (none) and 100 mm (severe).	
End point type	Secondary
End point timeframe:	
Baseline to Week 104	

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	105		
Units: cm				
arithmetic mean (standard error)				
Week 2 (N = 101, 104)	-1.4 (± 0.24)	-0.8 (± 0.23)		
Week 4 (N = 101, 105)	-1.91 (± 0.25)	-1.49 (± 0.24)		
Week 8 (N = 101, 105)	-2.39 (± 0.27)	-2.1 (± 0.25)		
Week 12 (N = 100, 105)	-2.74 (± 0.29)	-2.04 (± 0.28)		

Week 16 (N = 96, 101)	-3.36 (± 0.23)	-2.78 (± 0.23)		
Week 24 (N = 96, 101)	-3.66 (± 0.2)	-3.25 (± 0.23)		
Week 32 (N = 96, 101)	-3.66 (± 0.21)	-3.38 (± 0.22)		
Week 40 (N = 96, 101)	-3.83 (± 0.21)	-3.44 (± 0.21)		
Week 48 (N = 96, 101)	-3.93 (± 0.23)	-3.53 (± 0.21)		
Week 56 (N = 96, 101)	-3.98 (± 0.24)	-3.67 (± 0.22)		
Week 68 (N = 96, 101)	-3.98 (± 0.22)	-3.6 (± 0.22)		
Week 80 (N = 96, 101)	-4.03 (± 0.22)	-3.54 (± 0.24)		
Week 92 (N = 96, 101)	-4 (± 0.22)	-3.43 (± 0.24)		
Week 104 (N = 96, 101)	-4.12 (± 0.23)	-3.78 (± 0.22)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0156
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	-0.13

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0111
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	-0.14

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0936
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	0.07

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2678
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	0.23

Secondary: Mean change from Baseline in VAS score for subject assessment of disease activity at time points

End point title	Mean change from Baseline in VAS score for subject assessment of disease activity at time points

End point description:

Participants to assess their overall disease activity over the last 48 hours using a pain scale between 0 mm (none) and 100 mm (severe), which corresponded to the magnitude of their pain.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: cm				
arithmetic mean (standard error)				
Week 2 (N = 105, 108)	-1 (± 0.27)	-0.08 (± 0.26)		
Week 4 (N = 105, 109)	-1.34 (± 0.29)	-0.55 (± 0.27)		
Week 8 (N = 105, 109)	-1.85 (± 0.32)	-1.02 (± 0.3)		
Week 12 (N = 105, 109)	-2.06 (± 0.31)	-1.26 (± 0.3)		
Week 16 (N = 100, 105)	-2.81 (± 0.27)	-2.65 (± 0.24)		
Week 24 (N = 100, 105)	-2.92 (± 0.28)	-3.21 (± 0.23)		
Week 32 (N = 100, 105)	-2.99 (± 0.27)	-3.23 (± 0.27)		
Week 40 (N = 100, 105)	-3.38 (± 0.27)	-3.33 (± 0.25)		
Week 48 (N = 100, 105)	-3.24 (± 0.28)	-3.36 (± 0.27)		
Week 56 (N = 100, 105)	-3.3 (± 0.28)	-3.45 (± 0.25)		
Week 68 (N = 100, 105)	-3.31 (± 0.28)	-3.57 (± 0.25)		
Week 80 (N = 100, 105)	-3.1 (± 0.27)	-3.49 (± 0.25)		
Week 92 (N = 100, 105)	-3.34 (± 0.28)	-3.65 (± 0.25)		
Week 104 (N = 100, 105)	-3.33 (± 0.3)	-3.75 (± 0.24)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results included unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0102
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.19

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0007
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.92

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.44
upper limit	-0.39

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0057
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.35
upper limit	-0.23

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0077
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.44
upper limit	-0.22

Secondary: Changes from Baseline in VAS score for nocturnal back pain at time

points	
End point title	Changes from Baseline in VAS score for nocturnal back pain at time points

End point description:

The VAS scale was used to assess the level of nocturnal pain during the past 48 hours. For this, participants marked their level of pain on a 100 mm VAS anchored by 0 for "No pain " to 100 mm for "Most Severe Pain."

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: cm				
arithmetic mean (standard error)				
Week 2 (N = 105, 107)	-1.1 (± 0.31)	-0.31 (± 0.29)		
Week 4 (N = 105, 109)	-1.54 (± 0.33)	-0.71 (± 0.31)		
Week 8 (N = 105, 109)	-2.31 (± 0.33)	-1.34 (± 0.31)		
Week 12 (N = 105, 109)	-1.96 (± 0.36)	-1.03 (± 0.34)		
Week 16 (N = 100, 105)	-2.97 (± 0.31)	-2.63 (± 0.26)		
Week 24 (N = 100, 105)	-2.79 (± 0.3)	-3.25 (± 0.26)		
Week 32 (N = 100, 105)	-2.69 (± 0.31)	-3.11 (± 0.29)		
Week 40 (N = 100, 105)	-3.34 (± 0.31)	-3.3 (± 0.26)		
Week 48 (N = 100, 105)	-3.22 (± 0.31)	-3.21 (± 0.27)		
Week 56 (N = 100, 105)	-3.15 (± 0.33)	-3.4 (± 0.27)		
Week 68 (N = 100, 105)	-3.07 (± 0.33)	-3.27 (± 0.26)		
Week 80 (N = 100, 105)	-3.01 (± 0.31)	-3.32 (± 0.27)		
Week 92 (N = 100, 105)	-3.26 (± 0.32)	-3.43 (± 0.27)		
Week 104 (N = 100, 105)	-3.28 (± 0.34)	-3.59 (± 0.27)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0091
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.62
upper limit	-0.23

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0097
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.38
upper limit	-0.19

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0101
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.45
upper limit	-0.2

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0031
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.61
upper limit	-0.33

Secondary: Changes from Baseline in VAS score for total back pain at time points

End point title	Changes from Baseline in VAS score for total back pain at time points

End point description:

The VAS scale was used to assess the level of total back pain during the past 48 hours. For this, participants marked their level of pain on a 100 mm VAS anchored by 0 for "No pain " to 100 mm for "Most Severe Pain."

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: cm				
arithmetic mean (standard error)				
Week 2 (N = 105, 107)	-0.95 (± 0.29)	-0.37 (± 0.27)		
Week 4 (N = 105, 109)	-1.52 (± 0.31)	-0.88 (± 0.29)		
Week 8 (N = 105, 109)	-2.19 (± 0.33)	-1.18 (± 0.31)		
Week 12 (n = 105, 109)	-2.32 (± 0.28)	-1.39 (± 0.21)		
Week 16 (n = 100, 105)	-2.73 (± 0.29)	-2.64 (± 0.25)		
Week 24 (n = 100, 105)	-2.76 (± 0.28)	-2.92 (± 0.24)		
Week 32 (n = 100, 105)	-2.58 (± 0.29)	-2.87 (± 0.26)		
Week 40 (n = 100, 105)	-3.3 (± 0.28)	-3.2 (± 0.24)		
Week 48 (n = 100, 105)	-3.09 (± 0.29)	-3.14 (± 0.25)		
Week 56 (n = 100, 105)	-3.1 (± 0.29)	-3.17 (± 0.26)		
Week 68 (n = 100, 105)	-3.02 (± 0.31)	-3.23 (± 0.26)		
Week 80 (n = 100, 105)	-2.95 (± 0.29)	-3.17 (± 0.26)		
Week 92 (n = 100, 105)	-3.3 (± 0.29)	-3.33 (± 0.27)		
Week 104 (n = 100, 105)	-3.22 (± 0.32)	-3.47 (± 0.26)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0064
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.87

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	-0.25

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0407
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	-0.02

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0349
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	-0.05

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0021
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.65
upper limit	-0.37

Secondary: Changes from Baseline in the Bath Ankylosing Spondylitis Functional Index (BASFI) Total Score at time points

End point title	Changes from Baseline in the Bath Ankylosing Spondylitis Functional Index (BASFI) Total Score at time points

End point description:

BASFI is a validated self assessment tool that determines the degree of functional limitation in AS. Utilizing a VAS of 0-10 (0 = easy, 10 = impossible), participants answered 10 questions assessing their ability in completing normal daily activities or physically demanding activities. The BASFI score is a mean score of the 10 questions.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N = 105, 107)	-0.82 (± 0.21)	-0.27 (± 0.2)		
Week 4 (N = 105, 108)	-0.99 (± 0.22)	-0.44 (± 0.21)		
Week 8 (N = 105, 108)	-1.28 (± 0.23)	-0.73 (± 0.22)		
Week 12 (N = 105, 109)	-1.41 (± 0.24)	-0.84 (± 0.23)		
Week 16 (N = 100, 105)	-1.78 (± 0.23)	-1.75 (± 0.19)		
Week 24 (N = 100, 105)	-1.89 (± 0.22)	-1.85 (± 0.2)		
Week 32 (N = 100, 105)	-1.81 (± 0.22)	-1.98 (± 0.21)		
Week 40 (N = 100, 105)	-2.19 (± 0.23)	-2.13 (± 0.21)		
Week 48 (N = 100, 105)	-2.19 (± 0.23)	-2.1 (± 0.22)		
Week 56 (N = 100, 105)	-2.15 (± 0.22)	-2.3 (± 0.21)		
Week 68 (N = 100, 105)	-2.21 (± 0.21)	-2.31 (± 0.22)		
Week 80 (N = 100, 105)	-2.23 (± 0.21)	-2.19 (± 0.22)		

Week 92 (N = 100, 105)	-2.31 (± 0.23)	-2.35 (± 0.22)		
Week 104 (N = 100, 105)	-2.4 (± 0.23)	-2.36 (± 0.23)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0164
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.04
upper limit	-0.11

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0095
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	-0.13

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0127
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	-0.12

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0166
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.55

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	-0.1

Secondary: Mean change from Baseline in BASFI full day activities at time points

End point title	Mean change from Baseline in BASFI full day activities at time points

End point description:

BASFI is a validated self assessment tool that determines the degree of functional limitation in AS. Utilizing a VAS of 0-10 (0 = easy, 10 = impossible), participants answered 10 questions assessing their ability in completing normal daily activities or physically demanding activities. The BASFI score is a mean score of the 10 questions.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 104, 107)	-0.99 (± 0.26)	-0.21 (± 0.25)		
Week 4 (N= 104, 108)	-1.37 (± 0.28)	-0.7 (± 0.26)		
Week 8 (N= 104, 108)	-1.8 (± 0.27)	-1.05 (± 0.26)		
Week 12 (N = 104, 108)	-2.11 (± 0.29)	-1.16 (± 0.27)		
Week 16 (N = 99, 105)	-2.37 (± 0.25)	-2.03 (± 0.24)		
Week 24 (N = 99, 105)	-2.42 (± 0.25)	-2.13 (± 0.25)		
Week 32 (N = 99, 105)	-2.43 (± 0.23)	-2.38 (± 0.25)		
Week 40 (N = 99, 105)	-2.93 (± 0.26)	-2.3 (± 0.25)		
Week 48 (N = 99, 105)	-2.73 (± 0.25)	-2.34 (± 0.27)		
Week 56 (N = 99, 105)	-2.66 (± 0.25)	-2.59 (± 0.26)		
Week 68 (N = 99, 105)	-2.82 (± 0.25)	-2.71 (± 0.27)		
Week 80 (N = 99, 105)	-2.75 (± 0.25)	-2.58 (± 0.27)		
Week 92 (N = 99, 105)	-2.93 (± 0.27)	-2.7 (± 0.27)		
Week 104 (N = 99, 105)	-3.04 (± 0.27)	-2.66 (± 0.27)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0029
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	-0.27

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0147
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.21
upper limit	-0.13

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0056
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	-0.22

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only. Week 12

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.52
upper limit	-0.39

Secondary: Mean change from Baseline in BASFI bending forward at time points

End point title	Mean change from Baseline in BASFI bending forward at time points

End point description:

BASFI is a validated self assessment tool that determines the degree of functional limitation in AS. Utilizing a VAS of 0-10 (0 = easy, 10 = impossible), participants answered 10 questions assessing their ability in completing normal daily activities or physically demanding activities. The BASFI score is a mean score of the 10 questions.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 107)	-1.05 (± 0.28)	-0.4 (± 0.26)		
Week 4 (N= 105, 108)	-0.96 (± 0.29)	-0.56 (± 0.28)		
Week 8 (N= 105, 108)	-1.34 (± 0.29)	-0.65 (± 0.27)		
Week 12 (N = 105, 109)	-1.34 (± 0.29)	-0.85 (± 0.27)		
Week 16 (N = 100, 105)	-1.76 (± 0.28)	-1.57 (± 0.21)		
Week 24 (N = 100, 105)	-2 (± 0.29)	-1.64 (± 0.23)		
Week 32 (N = 100, 105)	-1.78 (± 0.28)	-1.69 (± 0.23)		
Week 40 (N = 100, 105)	-2.12 (± 0.29)	-1.82 (± 0.24)		
Week 48 (N = 100, 105)	-2.17 (± 0.29)	-1.83 (± 0.25)		
Week 56 (N = 100, 105)	-2.13 (± 0.28)	-2.09 (± 0.25)		
Week 68 (N = 100, 105)	-2.15 (± 0.27)	-1.92 (± 0.25)		
Week 80 (N = 100, 105)	-2.18 (± 0.28)	-1.99 (± 0.26)		
Week 92 (N = 100, 105)	-2.33 (± 0.3)	-2.04 (± 0.26)		
Week 104 (N = 100, 105)	-2.37 (± 0.31)	-2.16 (± 0.27)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0173
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.19
upper limit	-0.12

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1618
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.97
upper limit	0.16

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0153
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.69

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.25
upper limit	-0.13

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0866
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	0.07

Secondary: Mean change from Baseline in BASFI getting out of an arm-less chair at time points

End point title	Mean change from Baseline in BASFI getting out of an arm-less chair at time points

End point description:

BASFI is a validated self assessment tool that determines the degree of functional limitation in AS. Utilizing a VAS of 0-10 (0 = easy, 10 = impossible), participants answered 10 questions assessing their ability in completing normal daily activities or physically demanding activities. The BASFI score is a mean score of the 10 questions.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 107)	-0.94 (± 0.28)	-0.53 (± 0.27)		
Week 4 (N= 105, 108)	-1.44 (± 0.28)	-0.84 (± 0.27)		

Week 8 (N= 105, 108)	-1.54 (± 0.29)	-1.02 (± 0.27)		
Week 12 (N = 105, 108)	-1.79 (± 0.28)	-1.07 (± 0.27)		
Week 16 (N = 100, 105)	-2.04 (± 0.29)	-1.9 (± 0.23)		
Week 24 (N = 100, 105)	-2.2 (± 0.29)	-2.12 (± 0.23)		
Week 32 (N = 100, 105)	-2.04 (± 0.29)	-2.18 (± 0.25)		
Week 40 (N = 100, 105)	-2.4 (± 0.3)	-2.38 (± 0.25)		
Week 48 (N = 100, 105)	-2.4 (± 0.29)	-2.25 (± 0.26)		
Week 56 (N = 100, 105)	-2.27 (± 0.28)	-2.47 (± 0.25)		
Week 68 (N = 100, 105)	-2.45 (± 0.28)	-2.46 (± 0.25)		
Week 80 (N = 100, 105)	-2.52 (± 0.28)	-2.33 (± 0.25)		
Week 92 (N = 100, 105)	-2.6 (± 0.29)	-2.48 (± 0.25)		
Week 104 (N = 100, 105)	-2.65 (± 0.29)	-2.48 (± 0.25)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistcal analysis at Week 2
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1413
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	0.14

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0284
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.14
upper limit	-0.06

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0659
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	0.03

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0098
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	-0.18

Secondary: Mean change from Baseline in BASFI physically demanding activities at time points

End point title	Mean change from Baseline in BASFI physically demanding activities at time points

End point description:

BASFI is a validated self assessment tool that determines the degree of functional limitation in AS. Utilizing a VAS of 0-10 (0 = easy, 10 = impossible), participants answered 10 questions assessing their ability in completing normal daily activities or physically demanding activities. The BASFI score is a mean score of the 10 questions.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 104, 107)	-0.88 (± 0.26)	-0.13 (± 0.25)		
Week 4 (N= 104, 108)	-1.06 (± 0.28)	-0.26 (± 0.27)		
Week 8 (N= 104, 108)	-1.51 (± 0.28)	-0.8 (± 0.26)		
Week 12 (N = 104, 109)	-1.69 (± 0.29)	-0.91 (± 0.27)		
Week 16 (N = 99, 105)	-2.12 (± 0.26)	-1.79 (± 0.25)		
Week 24 (N = 99, 105)	-2.23 (± 0.26)	-2.05 (± 0.26)		
Week 32 (N = 99, 105)	-2.2 (± 0.25)	-2.19 (± 0.24)		
Week 40 (N = 99, 105)	-2.79 (± 0.26)	-2.24 (± 0.27)		
Week 48 (N = 99, 105)	-2.71 (± 0.27)	-2.25 (± 0.26)		
Week 56 (N = 99, 105)	-2.66 (± 0.27)	-2.37 (± 0.28)		
Week 68 (N = 99, 105)	-2.67 (± 0.26)	-2.6 (± 0.29)		
Week 80 (N = 99, 105)	-2.7 (± 0.26)	-2.39 (± 0.28)		
Week 92 (N = 99, 105)	-2.91 (± 0.27)	-2.59 (± 0.28)		
Week 104 (N = 99, 105)	-3.02 (± 0.27)	-2.59 (± 0.3)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0037
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	-0.25

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0044
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.35
upper limit	-0.25

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0104
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	-0.17

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.78

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	-0.22

Secondary: Mean change from Baseline in BASFI reaching up high at time points

End point title	Mean change from Baseline in BASFI reaching up high at time points

End point description:

BASFI is a validated self assessment tool that determines the degree of functional limitation in AS. Utilizing a VAS of 0-10 (0 = easy, 10 = impossible), participants answered 10 questions assessing their ability in completing normal daily activities or physically demanding activities. The BASFI score is a mean score of the 10 questions.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 107)	-0.33 (± 0.26)	-0.02 (± 0.24)		
Week 4 (N= 105, 108)	-0.63 (± 0.27)	-0.21 (± 0.26)		
Week 8 (N= 105, 108)	-0.81 (± 0.26)	-0.31 (± 0.25)		
Week 12 (N = 105, 109)	-0.7 (± 0.27)	-0.2 (± 0.25)		
Week 16 (N = 100, 105)	-1.09 (± 0.26)	-1.34 (± 0.22)		
Week 24 (N = 100, 105)	-1.26 (± 0.26)	-1.46 (± 0.22)		
Week 32 (N = 100, 105)	-1 (± 0.27)	-1.46 (± 0.23)		
Week 40 (N = 100, 105)	-1.3 (± 0.25)	-1.66 (± 0.24)		
Week 48 (N = 100, 105)	-1.38 (± 0.26)	-1.67 (± 0.25)		
Week 56 (N = 100, 105)	-1.34 (± 0.25)	-1.76 (± 0.24)		
Week 68 (N = 100, 105)	-1.42 (± 0.24)	-1.77 (± 0.24)		
Week 80 (N = 100, 105)	-1.37 (± 0.24)	-1.63 (± 0.24)		
Week 92 (N = 100, 105)	-1.55 (± 0.25)	-1.83 (± 0.24)		
Week 104 (N = 100, 105)	-1.62 (± 0.25)	-1.76 (± 0.24)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2268
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.19

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1145
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	0.1

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0512
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0509
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.02
upper limit	0

Secondary: Mean change from Baseline in BASFI climbing steps without aid at time points

End point title	Mean change from Baseline in BASFI climbing steps without aid at time points

End point description:

BASFI is a validated self assessment tool that determines the degree of functional limitation in AS. Utilizing a VAS of 0-10 (0 = easy, 10 = impossible), participants answered 10 questions assessing their ability in completing normal daily activities or physically demanding activities. The BASFI score is a mean score of the 10 questions.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 107)	-0.46 (± 0.26)	-0.16 (± 0.24)		
Week 4 (N= 105, 108)	-0.65 (± 0.28)	-0.09 (± 0.26)		
Week 8 (N= 105, 108)	-0.92 (± 0.28)	-0.44 (± 0.27)		
Week 12 (N = 105, 109)	-0.93 (± 0.29)	-0.58 (± 0.27)		
Week 16 (N = 100, 105)	-1.48 (± 0.28)	-1.64 (± 0.24)		
Week 24 (N = 100, 105)	-1.54 (± 0.27)	-1.65 (± 0.25)		
Week 32 (N = 100, 105)	-1.57 (± 0.28)	-1.97 (± 0.25)		
Week 40 (N = 100, 105)	-1.84 (± 0.28)	-2.19 (± 0.26)		
Week 48 (N = 100, 105)	-1.78 (± 0.28)	-2.05 (± 0.28)		
Week 56 (N = 100, 105)	-1.81 (± 0.27)	-2.26 (± 0.26)		
Week 68 (N = 100, 105)	-1.88 (± 0.28)	-2.34 (± 0.28)		
Week 80 (N = 100, 105)	-1.89 (± 0.28)	-2.16 (± 0.26)		
Week 92 (N = 100, 105)	-1.91 (± 0.29)	-2.38 (± 0.28)		
Week 104 (N = 100, 105)	-2.01 (± 0.29)	-2.42 (± 0.28)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.243
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.2

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0384
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	-0.03

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only. Week 8

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0797
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.48

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	0.06

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2186
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.21

Secondary: Mean change from Baseline in BASFI getting-up off-floor from back at time points

End point title	Mean change from Baseline in BASFI getting-up off-floor from back at time points

End point description:

BASFI is a validated self assessment tool that determines the degree of functional limitation in AS. Utilizing a VAS of 0-10 (0 = easy, 10 = impossible), participants answered 10 questions assessing their ability in completing normal daily activities or physically demanding activities. The BASFI score is a mean score of the 10 questions.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 107)	-0.95 (± 0.28)	-0.53 (± 0.27)		
Week 8 (N= 105, 108)	-1.1 (± 0.28)	-0.77 (± 0.27)		

Week 12 (N = 105, 109)	-1.58 (± 0.31)	-1.18 (± 0.29)		
Week 12 (N= 105, 108)	-1.34 (± 0.3)	-1.05 (± 0.28)		
Week 16 (N = 100, 105)	-1.97 (± 0.28)	-2.18 (± 0.26)		
Week 24 (N = 100, 105)	-2.07 (± 0.26)	-2.18 (± 0.25)		
Week 32 (N = 100, 105)	-2.05 (± 0.27)	-2.31 (± 0.27)		
Week 40 (N = 100, 105)	-2.52 (± 0.27)	-2.59 (± 0.27)		
Week 48 (N = 100, 105)	-2.4 (± 0.28)	-2.51 (± 0.27)		
Week 56 (N = 100, 105)	-2.48 (± 0.27)	-2.81 (± 0.27)		
Week 68 (N = 100, 105)	-2.5 (± 0.27)	-2.75 (± 0.28)		
Week 80 (N = 100, 105)	-2.5 (± 0.26)	-2.63 (± 0.27)		
Week 92 (N = 100, 105)	-2.55 (± 0.29)	-2.84 (± 0.28)		
Week 104 (N = 100, 105)	-2.71 (± 0.29)	-2.9 (± 0.27)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.141
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	0.14

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2299
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	0.21

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3221
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	0.29

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1891
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	0.2

Secondary: Mean change from Baseline in BASFI standing unsupported for 10 minutes at time points

End point title	Mean change from Baseline in BASFI standing unsupported for 10 minutes at time points

End point description:

BASFI is a validated self assessment tool that determines the degree of functional limitation in AS. Utilizing a VAS of 0-10 (0 = easy, 10 = impossible), participants answered 10 questions assessing their ability in completing normal daily activities or physically demanding activities. The BASFI score is a mean score of the 10 questions.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 107)	-0.58 (± 0.26)	-0.17 (± 0.24)		
Week 4 (N= 105, 108)	-0.8 (± 0.27)	-0.25 (± 0.25)		
Week 8 (N= 105, 108)	-1.03 (± 0.28)	-0.6 (± 0.27)		
Week 12 (N = 105, 109)	-1.33 (± 0.3)	-0.97 (± 0.29)		
Week 16 (N = 100, 105)	-1.88 (± 0.26)	-1.93 (± 0.23)		
Week 24 (N = 100, 105)	-1.96 (± 0.26)	-1.98 (± 0.25)		
Week 32 (N = 100, 105)	-1.84 (± 0.26)	-2.19 (± 0.25)		
Week 40 (N = 100, 105)	-2.17 (± 0.27)	-2.44 (± 0.26)		
Week 48 (N = 100, 105)	-2.3 (± 0.28)	-2.41 (± 0.28)		
Week 56 (N = 100, 105)	-2.26 (± 0.25)	-2.63 (± 0.26)		
Week 68 (N = 100, 105)	-2.37 (± 0.27)	-2.64 (± 0.27)		
Week 80 (N = 100, 105)	-2.41 (± 0.26)	-2.56 (± 0.26)		
Week 92 (N = 100, 105)	-2.42 (± 0.27)	-2.72 (± 0.28)		
Week 104 (N = 100, 105)	-2.53 (± 0.27)	-2.74 (± 0.27)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.108
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.09

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0389
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	-0.03

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1181
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	0.11

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2271
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.36

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	0.22

Secondary: Mean change from Baseline in BASFI looking over shoulder at time points

End point title	Mean change from Baseline in BASFI looking over shoulder at time points

End point description:

BASFI is a validated self assessment tool that determines the degree of functional limitation in AS. Utilizing a VAS of 0-10 (0 = easy, 10 = impossible), participants answered 10 questions assessing their ability in completing normal daily activities or physically demanding activities. The BASFI score is a mean score of the 10 questions.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 8 (N= 105, 108)	-1.21 (± 0.28)	-0.84 (± 0.26)		
Week 12 (N = 105, 108)	-1.4 (± 0.28)	-0.82 (± 0.27)		
Week 16 (N = 100, 105)	-1.63 (± 0.28)	-1.69 (± 0.26)		
Week 24 (N = 100, 105)	-1.59 (± 0.28)	-1.84 (± 0.27)		
Week 32 (N = 100, 105)	-1.61 (± 0.29)	-1.92 (± 0.26)		
Week 40 (N = 100, 105)	-1.91 (± 0.28)	-2.03 (± 0.27)		
Week 48 (N = 100, 105)	-1.97 (± 0.28)	-2.08 (± 0.27)		
Week 56 (N = 100, 105)	-1.99 (± 0.27)	-2.27 (± 0.26)		
Week 68 (N = 100, 105)	-2.05 (± 0.27)	-2.25 (± 0.27)		
Week 80 (N = 100, 105)	-2.03 (± 0.27)	-1.94 (± 0.29)		
Week 92 (N = 100, 105)	-1.97 (± 0.28)	-2.19 (± 0.27)		
Week 104 (N = 100, 105)	-2.14 (± 0.27)	-2.16 (± 0.28)		
Week 2 (N= 105, 107)	-0.83 (± 0.27)	-0.07 (± 0.25)		
Week 4 (N= 105, 108)	-0.88 (± 0.28)	-0.33 (± 0.27)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0044
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.27
upper limit	-0.24

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0455
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	-0.01

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.175
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	0.17

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0379
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	-0.03

Secondary: Mean change from Baseline in BASFI putting on socks at time points

End point title	Mean change from Baseline in BASFI putting on socks at time points

End point description:

BASFI is a validated self assessment tool that determines the degree of functional limitation in AS. Utilizing a VAS of 0-10 (0 = easy, 10 = impossible), participants answered 10 questions assessing their ability in completing normal daily activities or physically demanding activities. The BASFI score is a mean score of the 10 questions.

End point type	Secondary

End point timeframe:
Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 107)	-0.94 (± 0.27)	-0.47 (± 0.26)		
Week 4 (N= 105, 108)	-0.74 (± 0.29)	-0.34 (± 0.27)		
Week 8 (N= 105, 108)	-1.04 (± 0.28)	-0.54 (± 0.27)		
Week 12 (N = 105, 108)	-1.02 (± 0.28)	-0.57 (± 0.26)		
Week 16 (N = 100, 105)	-1.52 (± 0.29)	-1.36 (± 0.21)		
Week 24 (N = 100, 105)	-1.65 (± 0.29)	-1.44 (± 0.21)		
Week 32 (N = 100, 105)	-1.55 (± 0.29)	-1.49 (± 0.21)		
Week 40 (N = 100, 105)	-1.92 (± 0.28)	-1.64 (± 0.23)		
Week 48 (N = 100, 105)	-1.95 (± 0.28)	-1.6 (± 0.23)		
Week 56 (N = 100, 105)	-1.85 (± 0.29)	-1.75 (± 0.21)		
Week 68 (N = 100, 105)	-1.8 (± 0.27)	-1.62 (± 0.22)		
Week 80 (N = 100, 105)	-1.92 (± 0.29)	-1.66 (± 0.22)		
Week 92 (N = 100, 105)	-1.93 (± 0.29)	-1.7 (± 0.22)		
Week 104 (N = 100, 105)	-1.95 (± 0.29)	-1.71 (± 0.23)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0826
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	0.06

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1538
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	0.15

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0728
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.04
upper limit	0.05

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0975
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	0.08

Secondary: Changes from Baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Total Score at time points

End point title	Changes from Baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Total Score at time points

End point description:

BASDAI is a validated self assessment tool used to determine disease activity in participant with Ankylosing Spondylitis (AS). Utilizing a VAS of 0-10 (0 = none and 10 = very severe) participant's answered 6 questions measuring discomfort, pain and fatigue. The BASDAI score is obtained by computing the mean score for the 2 questions related to morning stiffness (questions 5 and 6) and then adding that value to the sum of the scores for the first 4 questions and then dividing the total by 5. This can be written as BASDAI=(Q1+Q2+Q3+Q4+(Q5+Q6)/2)/5. The final BASDAI score averages the individual assessments for a final score range of 0-10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N = 105, 108)	-0.96 (± 0.23)	-0.39 (± 0.22)		
Week 4 (N = 105, 109)	-1.63 (± 0.24)	-0.97 (± 0.22)		
Week 8 (N = 105, 109)	-2.05 (± 0.26)	-1.24 (± 0.25)		
Week 12 (N = 105, 109)	-1.96 (± 0.28)	-1.31 (± 0.27)		
Week 16 (N = 100, 105)	-2.7 (± 0.21)	-2.98 (± 0.2)		
Week 24 (N = 100, 105)	-2.86 (± 0.22)	-3.26 (± 0.19)		
Week 32 (N = 100, 105)	-2.72 (± 0.22)	-3.24 (± 0.22)		
Week 40 (N = 100, 105)	-3.22 (± 0.22)	-3.41 (± 0.21)		
Week 48 (N = 100, 105)	-3.18 (± 0.23)	-3.47 (± 0.22)		
Week 56 (N = 100, 105)	-3.21 (± 0.24)	-3.5 (± 0.21)		
Week 68 (N = 100, 105)	-3.17 (± 0.23)	-3.69 (± 0.22)		
Week 80 (N = 100, 105)	-3.12 (± 0.24)	-3.59 (± 0.22)		
Week 92 (N = 100, 105)	-3.35 (± 0.25)	-3.77 (± 0.23)		
Week 104 (N = 100, 105)	-3.41 (± 0.24)	-3.87 (± 0.23)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0186
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.65

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.18
upper limit	-0.11

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0106
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.01
upper limit	-0.13

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0048
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.11
upper limit	-0.2

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0016
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	-0.31

Secondary: Mean change from Baseline in BASDAI level of morning stiffness at time points

End point title	Mean change from Baseline in BASDAI level of morning stiffness at time points

End point description:

BASDAI is a validated self assessment tool used to determine disease activity in participant with Ankylosing Spondylitis (AS). Utilizing a VAS of 0-10 (0 = none and 10 = very severe) participant's answered 6 questions measuring discomfort, pain and fatigue. The BASDAI score is obtained by computing the mean score for the 2 questions related to morning stiffness (questions 5 and 6) and then adding that value to the sum of the scores for the first 4 questions and then dividing the total by 5. This can be written as BASDAI=(Q1+Q2+Q3+Q4+(Q5+Q6)/2)/5. The final BASDAI score averages the individual assessments for a final score range of 0-10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 108)	-1.26 (± 0.29)	-0.45 (± 0.28)		
Week 4 (N= 105, 108)	-1.83 (± 0.31)	-1 (± 0.29)		
Week 8 (N= 101, 106)	-2.46 (± 0.33)	-1.24 (± 0.31)		
Week 12 (N = 101, 106)	-2.26 (± 0.34)	-1.43 (± 0.32)		
Week 16 (N = 100, 105)	-3.5 (± 0.29)	-3.4 (± 0.25)		
Week 24 (N = 100, 105)	-3.71 (± 0.28)	-4 (± 0.25)		
Week 32 (N = 100, 105)	-3.45 (± 0.28)	-3.84 (± 0.26)		
Week 40 (N = 100, 105)	-3.93 (± 0.28)	-4.23 (± 0.24)		
Week 48 (N = 100, 105)	-3.91 (± 0.3)	-4.06 (± 0.25)		
Week 56 (N = 100, 105)	-3.89 (± 0.31)	-4.28 (± 0.25)		

Week 68 (N = 100, 105)	-3.99 (± 0.28)	-4.41 (± 0.26)		
Week 80 (N = 100, 105)	-3.74 (± 0.29)	-4.3 (± 0.26)		
Week 92 (N = 100, 105)	-3.99 (± 0.31)	-4.42 (± 0.25)		
Week 104 (N = 100, 105)	-4.09 (± 0.3)	-4.66 (± 0.24)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0058
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.37
upper limit	-0.24

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0064
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.42
upper limit	-0.24

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.85
upper limit	-0.6

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0134
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.83

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	-0.17

Secondary: Mean change from Baseline in BASDAI level of fatigue/tiredness at time points

End point title	Mean change from Baseline in BASDAI level of fatigue/tiredness at time points

End point description:

BASDAI is a validated self assessment tool used to determine disease activity in participant with Ankylosing Spondylitis (AS). Utilizing a VAS of 0-10 (0 = none and 10 = very severe) participant's answered 6 questions measuring discomfort, pain and fatigue. The BASDAI score is obtained by computing the mean score for the 2 questions related to morning stiffness (questions 5 and 6) and then adding that value to the sum of the scores for the first 4 questions and then dividing the total by 5. This can be written as BASDAI=(Q1+Q2+Q3+Q4+(Q5+Q6)/2)/5. The final BASDAI score averages the individual assessments for a final score range of 0-10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 108)	-0.8 (± 0.27)	-0.23 (± 0.26)		
Week 4 (N= 105, 109)	-1.71 (± 0.28)	-1.26 (± 0.26)		
Week 8 (N= 105, 109)	-1.98 (± 0.3)	-1.29 (± 0.29)		
Week 12 (N = 105, 109)	-1.7 (± 0.34)	-1.32 (± 0.32)		
Week 16 (N = 100, 105)	-2.29 (± 0.24)	-2.89 (± 0.25)		
Week 24 (N = 100, 105)	-2.48 (± 0.27)	-2.95 (± 0.23)		
Week 32 (N = 100, 105)	-2.22 (± 0.26)	-2.74 (± 0.26)		
Week 40 (N = 100, 105)	-2.82 (± 0.26)	-2.93 (± 0.26)		
Week 48 (N = 100, 105)	-2.86 (± 0.25)	-3.19 (± 0.26)		
Week 56 (N = 100, 105)	-3.03 (± 0.26)	-3.2 (± 0.26)		
Week 68 (N = 100, 105)	-2.92 (± 0.27)	-3.48 (± 0.24)		
Week 80 (N = 100, 105)	-3.15 (± 0.28)	-3.36 (± 0.26)		
Week 92 (N = 100, 105)	-3.2 (± 0.27)	-3.68 (± 0.25)		
Week 104 (N = 100, 105)	-3.18 (± 0.27)	-3.63 (± 0.28)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0316
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	-0.05

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0973
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	0.08

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0216
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.27
upper limit	-0.1

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2425
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	0.26

Secondary: Mean change from Baseline in BASDAI level of discomfort at time points

End point title	Mean change from Baseline in BASDAI level of discomfort at time points

End point description:

BASDAI is a validated self assessment tool used to determine disease activity in participant with Ankylosing Spondylitis (AS). Utilizing a VAS of 0-10 (0 = none and 10 = very severe) participant's answered 6 questions measuring discomfort, pain and fatigue. The BASDAI score is obtained by

computing the mean score for the 2 questions related to morning stiffness (questions 5 and 6) and then adding that value to the sum of the scores for the first 4 questions and then dividing the total by 5. This can be written as BASDAI=(Q1+Q2+Q3+Q4+(Q5+Q6)/2)/5. The final BASDAI score averages the individual assessments for a final score range of 0-10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 108)	-0.81 (± 0.31)	-0.48 (± 0.29)		
Week 8 (N= 105, 109)	-1.31 (± 0.33)	-0.77 (± 0.31)		
Week 12 (N= 105, 109)	-1.91 (± 0.33)	-1.2 (± 0.31)		
Week 12 (N = 105, 109)	-1.68 (± 0.34)	-1.29 (± 0.32)		
Week 16 (N = 100, 105)	-2.65 (± 0.3)	-2.82 (± 0.25)		
Week 24 (N = 100, 105)	-2.71 (± 0.31)	-3.07 (± 0.26)		
Week 32 (N = 100, 105)	-2.64 (± 0.31)	-3.25 (± 0.27)		
Week 40 (N = 100, 105)	-3.09 (± 0.3)	-3.25 (± 0.27)		
Week 48 (N = 100, 105)	-2.97 (± 0.33)	-3.27 (± 0.29)		
Week 56 (N = 100, 105)	-3.13 (± 0.34)	-3.24 (± 0.29)		
Week 68 (N = 100, 105)	-3.01 (± 0.32)	-3.49 (± 0.31)		
Week 80 (N = 100, 105)	-2.87 (± 0.33)	-3.5 (± 0.28)		
Week 92 (N = 100, 105)	-3.21 (± 0.33)	-3.57 (± 0.3)		
Week 104 (N = 100, 105)	-3.31 (± 0.34)	-3.72 (± 0.29)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12

data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2688
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	0.26

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0866
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.17
upper limit	0.08

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0277
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.71

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	-0.08

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.239
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.04
upper limit	0.26

Secondary: Mean change from Baseline in BASDAI level of how long stiffness lasts at time points

End point title	Mean change from Baseline in BASDAI level of how long stiffness lasts at time points

End point description:

BASDAI is a validated self assessment tool used to determine disease activity in participant with Ankylosing Spondylitis (AS). Utilizing a VAS of 0-10 (0 = none and 10 = very severe) participant's answered 6 questions measuring discomfort, pain and fatigue. The BASDAI score is obtained by computing the mean score for the 2 questions related to morning stiffness (questions 5 and 6) and then adding that value to the sum of the scores for the first 4 questions and then dividing the total by 5. This can be written as BASDAI=(Q1+Q2+Q3+Q4+(Q5+Q6)/2)/5. The final BASDAI score averages the individual assessments for a final score range of 0-10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 108)	-0.61 (± 0.28)	-0.15 (± 0.26)		
Week 4 (N= 105, 109)	-1.33 (± 0.29)	-0.62 (± 0.28)		
Week 8 (N= 105, 109)	-1.62 (± 0.3)	-0.68 (± 0.29)		
Week 12 (N = 105, 109)	-1.98 (± 0.31)	-0.97 (± 0.29)		
Week 16 (N = 100, 105)	-2.63 (± 0.27)	-2.6 (± 0.26)		
Week 24 (N = 100, 105)	-2.84 (± 0.29)	-3.04 (± 0.29)		
Week 32 (N = 100, 105)	-2.54 (± 0.29)	-3.06 (± 0.3)		
Week 40 (N = 100, 105)	-2.94 (± 0.3)	-3.28 (± 0.3)		
Week 48 (N = 100, 105)	-2.9 (± 0.3)	-3.09 (± 0.32)		
Week 56 (N = 100, 105)	-2.92 (± 0.33)	-3.17 (± 0.3)		
Week 68 (N = 100, 105)	-2.91 (± 0.32)	-3.5 (± 0.32)		
Week 80 (N = 100, 105)	-2.77 (± 0.3)	-3.24 (± 0.31)		
Week 92 (N = 100, 105)	-2.89 (± 0.33)	-3.36 (± 0.31)		
Week 104 (N = 100, 105)	-2.95 (± 0.32)	-3.38 (± 0.31)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0928
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.46

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.08

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0139
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.27
upper limit	-0.15

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0017
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.53
upper limit	-0.36

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.61
upper limit	-0.43

Secondary: Mean change from Baseline in BASDAI level of pain/swelling at time points

End point title	Mean change from Baseline in BASDAI level of pain/swelling at time points

End point description:

BASDAI is a validated self assessment tool used to determine disease activity in participant with Ankylosing Spondylitis (AS). Utilizing a VAS of 0-10 (0 = none and 10 = very severe) participant's answered 6 questions measuring discomfort, pain and fatigue. The BASDAI score is obtained by computing the mean score for the 2 questions related to morning stiffness (questions 5 and 6) and then adding that value to the sum of the scores for the first 4 questions and then dividing the total by 5. This can be written as BASDAI=(Q1+Q2+Q3+Q4+(Q5+Q6)/2)/5. The final BASDAI score averages the individual assessments for a final score range of 0-10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 107)	-0.64 (± 0.32)	-0.41 (± 0.3)		
Week 4 (N= 105, 109)	-1.35 (± 0.32)	-0.68 (± 0.31)		
Week 8 (N= 105, 109)	-1.69 (± 0.33)	-1.01 (± 0.31)		
Week 12 (N = 105, 109)	-1.47 (± 0.33)	-0.87 (± 0.32)		
Week 16 (N = 100, 105)	-2.38 (± 0.28)	-2.66 (± 0.28)		
Week 24 (N = 100, 105)	-2.49 (± 0.29)	-2.92 (± 0.28)		
Week 32 (N = 100, 105)	-2.47 (± 0.3)	-3.1 (± 0.29)		
Week 40 (N = 100, 105)	2.91 (± 0.27)	-3.21 (± 0.28)		
Week 48 (N = 100, 105)	-2.8 (± 0.3)	-3.21 (± 0.3)		
Week 56 (N = 100, 105)	-2.66 (± 0.31)	-3.13 (± 0.29)		

Week 68 (N = 100, 105)	-2.6 (± 0.32)	-3.24 (± 0.32)		
Week 80 (N = 100, 105)	-2.67 (± 0.32)	-3.19 (± 0.31)		
Week 92 (N = 100, 105)	-2.96 (± 0.31)	-3.4 (± 0.32)		
Week 104 (N = 100, 105)	-3.07 (± 0.31)	-3.51 (± 0.31)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4559
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	0.38

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0345
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	-0.05

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.034
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.05

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0634
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	0.03

Secondary: Mean change from Baseline in BASDAI level of neck/back/hip pain at time points

End point title	Mean change from Baseline in BASDAI level of neck/back/hip pain at time points

End point description:

BASDAI is a validated self assessment tool used to determine disease activity in participant with Ankylosing Spondylitis (AS). Utilizing a VAS of 0-10 (0 = none and 10 = very severe) participant's answered 6 questions measuring discomfort, pain and fatigue. The BASDAI score is obtained by computing the mean score for the 2 questions related to morning stiffness (questions 5 and 6) and then adding that value to the sum of the scores for the first 4 questions and then dividing the total by 5. This can be written as BASDAI=(Q1+Q2+Q3+Q4+(Q5+Q6)/2)/5. The final BASDAI score averages the individual assessments for a final score range of 0-10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 108)	-1.34 (± 0.29)	-0.34 (± 0.28)		
Week 4 (N= 105, 109)	-1.91 (± 0.31)	-1.1 (± 0.29)		
Week 8 (N= 105, 109)	-2.32 (± 0.33)	-1.48 (± 0.31)		
Week 12 (N = 105, 109)	-2.44 (± 0.35)	-1.58 (± 0.33)		
Week 16 (N = 100, 105)	-3.13 (± 0.28)	-3.55 (± 0.28)		
Week 24 (N = 100, 105)	-3.32 (± 0.27)	-3.82 (± 0.26)		
Week 32 (N = 100, 105)	-3.27 (± 0.26)	-3.65 (± 0.27)		
Week 40 (N = 100, 105)	-3.81 (± 0.27)	-3.92 (± 0.27)		
Week 48 (N = 100, 105)	-3.85 (± 0.27)	-4.1 (± 0.26)		
Week 56 (N = 100, 105)	-3.82 (± 0.27)	-4.22 (± 0.27)		
Week 68 (N = 100, 105)	-3.83 (± 0.26)	-4.28 (± 0.27)		
Week 80 (N = 100, 105)	-3.6 (± 0.28)	-4.11 (± 0.28)		
Week 92 (N = 100, 105)	-3.88 (± 0.29)	-4.29 (± 0.28)		
Week 104 (N = 100, 105)	-3.96 (± 0.29)	-4.48 (± 0.27)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0007
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.56
upper limit	-0.43

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0073
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	-0.22

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0094
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.48
upper limit	-0.21

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.54
upper limit	-0.19

Secondary: Percentage of participants with BASDAI 50 at time points

End point title	Percentage of participants with BASDAI 50 at time points

End point description:

Response was defined as a 50% improvement of the Baseline BASDAI to 104 weeks of study treatment, respectively. The BASDAI score is obtained by computing the mean score for the 2 questions related to morning stiffness (questions 5 and 6) and then adding that value to the sum of the scores for the first 4 questions and then dividing the total by 5. This can be written as BASDAI=(Q1+Q2+Q3+Q4+(Q5+Q6)

/2)/5.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	109		
Units: Percentage of participants				
number (not applicable)				
Week 2 (N = 105, 108)	17.14	5.56		
Week 4 (N = 105, 109)	24.76	11.01		
Week 8 (N = 105, 109)	37.14	22.02		
Week 12 (N = 105, 109)	43.81	23.85		
Week 16 (N = 100, 105)	45	59.05		
Week 24 (N = 100, 105)	50	62.86		
Week 32 (N = 100, 105)	49	59.05		
Week 40 (N = 100, 105)	58	61.9		
Week 48 (N = 100, 105)	60	64.76		
Week 56 (N = 100, 105)	59	65.71		
Week 68 (N = 100, 105)	61	66.67		
Week 80 (N = 100, 105)	56	66.67		
Week 92 (N = 100, 105)	62	71.43		
Week 104 (N = 100, 105)	64	70.48		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0029
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	19.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.54
upper limit	32.37

Statistical analysis title	Statistical analysis at Week 2
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	11.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.18
upper limit	19.99

Statistical analysis title	Statistical analysis at Week 4
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	13.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.62
upper limit	23.89

Statistical analysis title	Statistical analysis at Week 8
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0213
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	15.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.04
upper limit	27.2

Secondary: Percentage of participants with BASDAI 20 at time points

End point title	Percentage of participants with BASDAI 20 at time points

End point description:

Response was defined as a 20% improvement of the Baseline BASDAI to 104 weeks of study treatment. The BASDAI score is obtained by computing the mean score for the 2 questions related to morning stiffness (questions 5 and 6) and then adding that value to the sum of the scores for the first 4 questions and then dividing the total by 5. This can be written as BASDAI=(Q1+Q2+Q3+Q4+(Q5+Q6)/2)/5.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	109		
Units: Percentage of participants				
number (not applicable)				
Week 2 (N = 105, 108)	41.9	33.33		
Week 4 (N = 105, 109)	56.19	42.2		
Week 8 (N = 105, 109)	66.67	51.38		
Week 12 (N = 105, 109)	64.76	56.88		
Week 16 (N = 100, 105)	73	82.86		
Week 24 (N = 100, 105)	77	86.67		
Week 32 (N = 100, 105)	77	84.76		
Week 40 (N = 100, 105)	86	87.62		
Week 48 (N = 100, 105)	81	87.62		
Week 56 (N = 100, 105)	81	85.71		
Week 68 (N = 100, 105)	80	90.48		
Week 80 (N = 100, 105)	81	88.57		
Week 92 (N = 100, 105)	82	88.57		
Week 104 (N = 100, 105)	84	90.48		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 12
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2755
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	7.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.15
upper limit	20.92

Statistical analysis title	Statistical analysis at Week 2
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.195
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	8.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.39
upper limit	21.54

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0278
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	13.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	27.26

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0174
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	15.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.28
upper limit	28.3

Secondary: Change from Baseline in Bath Ankylosing Spondylitis Global Index (BAS-G) Total Score at time points

End point title	Change from Baseline in Bath Ankylosing Spondylitis Global Index (BAS-G) Total Score at time points

End point description:

The BAS-G was a 2 question assessment evaluating the effect of AS on the participants well-being over the last week and last 6 months. The 2 questions were: How have you been over the last week? and How have you been over the last six months?. Each question is scored by the participant on a 100 mm scale ranging from 0 (Very Good) to 100 (Very Bad). The two values are averaged to obtain the BAS-G score.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 4 (N = 105, 109)	-1.29 (± 0.24)	-0.75 (± 0.22)		
Week 12 (N = 105, 109)	-1.85 (± 0.27)	-1.35 (± 0.25)		
Week 24 (N = 100, 105)	-2.8 (± 0.24)	-2.87 (± 0.19)		
Week 48 (N = 105, 109)	-3.2 (± 0.25)	-3.51 (± 0.22)		
Week 68 (N = 105, 109)	-3.28 (± 0.25)	-3.77 (± 0.23)		
Week 92 (N = 105, 109)	-3.55 (± 0.25)	-3.81 (± 0.23)		
Week 104 (N = 105, 109)	-3.59 (± 0.26)	-3.92 (± 0.24)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4 and 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0558
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.02
upper limit	0.01

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4 and 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0201
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	-0.09

Secondary: Mean change from Baseline in Bath Ankylosing Spondylitis Metrology Index (BASMI) Total Score at time points

End point title	Mean change from Baseline in Bath Ankylosing Spondylitis Metrology Index (BASMI) Total Score at time points

End point description:

BASMI is an objective measure of spinal mobility. The BASMI score is composed of 5 measures: cervical rotation, intermalleolar distance, modified Schober's test, lateral flexion and tragus to wall distance. Each measure was scored 0-2 (0=normal mobility, 2=severe reduction) to give a final score ranging 0 to 10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N = 103, 108)	-0.08 (± 0.12)	-0.13 (± 0.11)		
Week 4 (N = 103, 109)	-0.3 (± 0.12)	-0.2 (± 0.11)		

Week 8 (N = 103, 109)	-0.36 (± 0.14)	-0.41 (± 0.13)		
Week 12 (N = 103, 109)	-0.34 (± 0.14)	-0.19 (± 0.1)		
Week 16 (N = 98, 105)	-0.44 (± 0.14)	-0.35 (± 0.1)		
Week 24 (N = 98, 105)	-0.48 (± 0.13)	-0.34 (± 0.1)		
Week 40 (N = 98, 105)	-0.49 (± 0.14)	-0.49 (± 0.11)		
Week 32 (N = 98, 105)	-0.55 (± 0.14)	-0.47 (± 0.11)		
Week 48 (N = 98, 105)	-0.54 (± 0.13)	-0.44 (± 0.11)		
Week 56 (N = 98, 105)	-0.56 (± 0.13)	-0.49 (± 0.11)		
Week 68 (N = 98, 105)	-0.6 (± 0.13)	-0.58 (± 0.11)		
Week 80 (N = 98, 105)	-0.64 (± 0.14)	-0.62 (± 0.11)		
Week 92 (N = 98, 105)	-0.61 (± 0.13)	-0.62 (± 0.11)		
Week 104 (N = 98, 105)	-0.61 (± 0.14)	-0.55 (± 0.11)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test, after Week 24. For label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6741
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.28

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3896
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.33
upper limit	0.13

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7468
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.31

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6871
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	0.23

Secondary: Mean change from Baseline in BASMI lateral side flexion score by time point

End point title	Mean change from Baseline in BASMI lateral side flexion score by time point

End point description:

BASMI is an objective measure of spinal mobility. The BASMI score is composed of 5 measures: cervical rotation, intermalleolar distance, modified Schober's test, lateral flexion and tragus to wall distance. Each measure was scored 0-2 (0=normal mobility, 2=severe reduction) to give a final score ranging 0 to 10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 100, 105)	1.06 (± 0.49)	0.69 (± 0.46)		
Week 4 (N= 100, 106)	1.49 (± 0.51)	1.49 (± 0.48)		
Week 8 (N= 100, 106)	1.64 (± 0.53)	0.91 (± 0.5)		
Week 12 (N = 100, 106)	1.64 (± 0.62)	0.43 (± 0.58)		
Week 16 (N = 98, 105)	1.35 (± 0.55)	1.02 (± 0.32)		
Week 24 (N = 98, 105)	1.97 (± 0.66)	1.29 (± 0.34)		
Week 32 (N = 98, 105)	2.03 (± 0.57)	1.62 (± 0.35)		
Week 40 (N = 98, 105)	1.86 (± 0.59)	1.57 (± 0.38)		
Week 48 (N = 98, 105)	2.2 (± 0.55)	1.36 (± 0.34)		
Week 56 (N = 98, 105)	1.82 (± 0.54)	1.43 (± 0.36)		
Week 68 (N = 98, 105)	2.24 (± 0.58)	1.54 (± 0.41)		
Week 80 (N = 98, 105)	1.96 (± 0.59)	1.52 (± 0.4)		
Week 92 (N = 98, 105)	2.14 (± 0.6)	1.5 (± 0.38)		
Week 104 (N = 98, 105)	1.97 (± 0.59)	1.65 (± 0.37)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test, after Week 24. For label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4332
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	1.32

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9947
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	0.98

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1558
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	1.75

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0488
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.21

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	2.39

Secondary: Mean change from Baseline in BASMI cervical rotation degree by time point

End point title	Mean change from Baseline in BASMI cervical rotation degree by time point

End point description:

BASMI is an objective measure of spinal mobility. The BASMI score is composed of 5 measures: cervical rotation, intermalleolar distance, modified Schober's test, lateral flexion and tragus to wall distance. Each measure was scored 0-2 (0=normal mobility, 2=severe reduction) to give a final score ranging 0 to 10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 108)	1.35 (± 1.26)	0.98 (± 1.19)		
Week 4 (N= 105, 109)	3.52 (± 1.31)	2.49 (± 1.23)		
Week 8 (N= 105, 109)	4.92 (± 1.42)	3.86 (± 1.34)		
Week 12 (N = 105, 109)	4.46 (± 1.52)	2.07 (± 1.44)		
Week 16 (N = 100, 105)	5.13 (± 1.37)	4.73 (± 1.09)		
Week 24 (N = 100, 105)	5 (± 1.35)	5.1 (± 1.18)		
Week 32 (N = 100, 105)	5.32 (± 1.43)	6 (± 1.25)		
Week 40 (N = 100, 105)	5.56 (± 1.51)	5.61 (± 1.19)		
Week 48 (N = 100, 105)	5.04 (± 1.48)	6.9 (± 1.19)		
Week 56 (N = 100, 105)	5.7 (± 1.44)	6.92 (± 1.31)		
Week 68 (N = 100, 105)	6.47 (± 1.43)	8.1 (± 1.23)		
Week 80 (N = 100, 105)	6.14 (± 1.45)	7.96 (± 1.23)		
Week 92 (N = 100, 105)	6.26 (± 1.5)	8.25 (± 1.24)		
Week 104 (N = 100, 105)	5.92 (± 1.57)	8.55 (± 1.22)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test, after Week 24. For label period results include unadjusted mean changes and standard errors, no covariate adjustments were

applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7645
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.06
upper limit	2.8

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4178
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.48
upper limit	3.55

Statistical analysis title	Statistical analysis at Week 8
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.443
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.67
upper limit	3.79

Statistical analysis title	Statistical analysis at Week 12
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1095
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	5.31

Secondary: Mean change from Baseline in BASMI modified schobers test score by time point

End point title	Mean change from Baseline in BASMI modified schobers test score by time point

End point description:

BASMI is an objective measure of spinal mobility. The BASMI score is composed of 5 measures: cervical rotation, intermalleolar distance, modified Schober's test, lateral flexion and tragus to wall distance.

Each measure was scored 0-2 (0=normal mobility, 2=severe reduction) to give a final score ranging 0 to 10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 89, 90)	0.17 (± 0.24)	0.16 (± 0.23)		
Week 4 (N= 89, 90)	0.02 (± 0.26)	0.2 (± 0.25)		
Week 8 (N= 89, 90)	0.15 (± 0.26)	0.12 (± 0.25)		
Week 12 (N = 89, 90)	0.05 (± 0.31)	0.04 (± 0.3)		
Week 16 (N = 86, 86)	0.71 (± 0.23)	0.37 (± 0.24)		
Week 24 (N = 86, 86)	0.98 (± 0.27)	0.54 (± 0.25)		
Week 32 (N = 86, 86)	0.73 (± 0.3)	0.54 (± 0.28)		
Week 40 (N = 86, 86)	0.68 (± 0.24)	0.77 (± 0.25)		
Week 48 (N = 86, 86)	0.75 (± 0.26)	0.63 (± 0.26)		
Week 56 (N = 86, 86)	1.16 (± 0.36)	0.79 (± 0.32)		
Week 68 (N = 86, 86)	1.34 (± 0.35)	0.89 (± 0.31)		
Week 80 (N = 86, 86)	1.38 (± 0.38)	0.97 (± 0.31)		
Week 92 (N = 86, 86)	1.03 (± 0.35)	0.88 (± 0.29)		
Week 104 (N = 86, 86)	0.99 (± 0.36)	0.92 (± 0.33)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test, after Week 24. For label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9504
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.49

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4971
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.34

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8999
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.03

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.54

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9712
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.62

Secondary: Mean change from Baseline in BASMI intermalleolar distance score by time point

End point title	Mean change from Baseline in BASMI intermalleolar distance score by time point

End point description:

BASMI is an objective measure of spinal mobility. The BASMI score is composed of 5 measures: cervical rotation, intermalleolar distance, modified Schober's test, lateral flexion and tragus to wall distance. Each measure was scored 0-2 (0=normal mobility, 2=severe reduction) to give a final score ranging 0 to 10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 108)	0.75 (± 1.22)	-0.15 (± 1.15)		
Week 4 (N= 105, 109)	4.02 (± 1.5)	1.17 (± 1.42)		

Week 8 (N= 105, 109)	4.25 (± 1.7)	1.99 (± 1.61)		
Week 12 (N = 105, 109)	3.25 (± 1.75)	1.81 (± 1.66)		
Week 16 (N = 100, 105)	6.28 (± 1.44)	3.73 (± 1.27)		
Week 24 (N = 100, 105)	7.48 (± 1.41)	4.76 (± 1.3)		
Week 32 (N = 100, 105)	8.09 (± 1.38)	5.01 (± 1.35)		
Week 40 (N = 100, 105)	8.38 (± 1.38)	5.61 (± 1.34)		
Week 48 (N = 100, 105)	8.35 (± 1.5)	6.32 (± 1.33)		
Week 56 (N = 100, 105)	9.31 (± 1.48)	7.42 (± 1.38)		
Week 68 (N = 100, 105)	9.26 (± 1.55)	7.92 (± 1.37)		
Week 80 (N = 100, 105)	9.17 (± 1.55)	8.73 (± 1.32)		
Week 92 (N = 100, 105)	9.8 (± 1.55)	9.05 (± 1.34)		
Week 104 (N = 100, 105)	8.91 (± 1.57)	8.72 (± 1.35)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test, after Week 24. For label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only. Week 2

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4556
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.46
upper limit	3.24

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0543
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	5.75

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1754
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.02
upper limit	5.53

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3985
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.93
upper limit	4.82

Secondary: Mean change from Baseline in BASMI tragus to wall score by time point

End point title	Mean change from Baseline in BASMI tragus to wall score by time point

End point description:

BASMI is an objective measure of spinal mobility. The BASMI score is composed of 5 measures: cervical rotation, intermalleolar distance, modified Schober's test, lateral flexion and tragus to wall distance. Each measure was scored 0-2 (0=normal mobility, 2=severe reduction) to give a final score ranging 0 to 10.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	109		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N= 105, 108)	0.02 (± 0.21)	-0.2 (± 0.2)		
Week 4 (N= 105, 109)	-0.2 (± 0.21)	-0.37 (± 0.2)		
Week 8 (N= 105, 109)	-0.31 (± 0.2)	-0.44 (± 0.19)		
Week 12 (N = 105, 109)	-0.29 (± 0.23)	-0.41 (± 0.22)		
Week 16 (N = 100, 105)	0.14 (± 0.22)	-0.02 (± 0.16)		
Week 24 (N = 100, 105)	0.28 (± 0.24)	0.01 (± 0.17)		
Week 32 (N = 100, 105)	0.02 (± 0.27)	0.01 (± 0.16)		
Week 40 (N = 100, 105)	-0.07 (± 0.25)	-0.08 (± 0.21)		
Week 48 (N = 100, 105)	-0.16 (± 0.27)	0.03 (± 0.16)		
Week 68 (N = 100, 105)	-0.28 (± 0.27)	0.08 (± 0.18)		
Week 56 (N = 100, 105)	0.01 (± 0.26)	0 (± 0.17)		
Week 80 (N = 100, 105)	-0.24 (± 0.26)	0 (± 0.16)		
Week 92 (N = 100, 105)	-0.17 (± 0.27)	-0.02 (± 0.18)		
Week 104 (N = 100, 105)	-0.39 (± 0.25)	-0.15 (± 0.18)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test, after Week 24. For label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2823
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.62

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4029
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.58

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.511
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.51

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5844
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.56

Secondary: Change from Baseline in Chest Expansion at time points

End point title	Change from Baseline in Chest Expansion at time points

End point description:

Chest expansion, measured in cm, is defined as the difference in thoracic circumference during full expiration versus full inspiration, measured at the fourth intercostal space (nipple line). At maximal inspiration, the chest circumference was measured at nipple line or at the 4th intercostal space (in cm to the nearest 0.1 cm).

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	108		
Units: cm				
arithmetic mean (standard error)				
Week 2 (N = 104, 105)	0.16 (± 0.22)	0.69 (± 0.2)		
Week 4 (N = 104, 108)	0.31 (± 0.25)	0.44 (± 0.23)		
Week 8 (N = 104, 108)	0.2 (± 0.25)	0.61 (± 0.23)		
Week 12 (N = 104, 108)	0.12 (± 0.25)	0.37 (± 0.24)		
Week 16 (N = 99, 104)	0.43 (± 0.19)	0.68 (± 0.19)		
Week 24 (N = 99, 104)	0.38 (± 0.17)	0.69 (± 0.19)		
Week 32 (N = 99, 104)	0.49 (± 0.18)	0.62 (± 0.18)		
Week 40 (N = 99, 104)	0.55 (± 0.17)	0.71 (± 0.17)		
Week 48 (N = 99, 104)	0.63 (± 0.17)	0.8 (± 0.21)		
Week 56 (N = 99, 104)	0.49 (± 0.18)	0.72 (± 0.19)		
Week 68 (N = 99, 104)	0.61 (± 0.17)	0.56 (± 0.18)		
Week 80 (N = 99, 104)	0.32 (± 0.18)	0.74 (± 0.2)		
Week 92 (N = 99, 104)	0.52 (± 0.18)	0.56 (± 0.2)		
Week 104 (N = 99, 104)	0.67 (± 0.18)	0.63 (± 0.2)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Most within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0129
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	-0.11

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6003
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.35

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0911
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	0.07

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3144
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	0.24

Secondary: Mean change from Baseline in Occiput-to-wall test at time points

End point title	Mean change from Baseline in Occiput-to-wall test at time points

End point description:

Occiput-to-wall distance: distance between the occiput (posterior or back portion of the head) and the wall when the participant stood with heels and shoulder against the wall and the back straight.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	108		
Units: cm				
arithmetic mean (standard error)				
Week 2 (N = 104, 106)	-0.21 (± 0.19)	-0.12 (± 0.19)		
Week 4 (N = 104, 108)	-0.37 (± 0.2)	-0.36 (± 0.19)		
Week 8 (N = 104, 108)	-0.09 (± 0.24)	-0.27 (± 0.23)		
Week 12 (N = 104, 108)	-0.28 (± 0.24)	-0.41 (± 0.23)		
Week 16 (N = 99, 104)	-0.24 (± 0.25)	-0.29 (± 0.11)		
Week 24 (N = 99, 104)	-0.11 (± 0.25)	-0.38 (± 0.18)		
Week 32 (N = 99, 104)	-0.2 (± 0.25)	-0.31 (± 0.16)		
Week 40 (N = 99, 104)	-0.34 (± 0.22)	-0.24 (± 0.17)		
Week 48 (N = 99, 104)	-0.25 (± 0.24)	-0.42 (± 0.13)		
Week 56 (N = 99, 104)	-0.42 (± 0.22)	-0.26 (± 0.14)		
Week 68 (N = 99, 104)	-0.42 (± 0.23)	-0.21 (± 0.16)		
Week 80 (N = 99, 104)	-0.34 (± 0.24)	-0.55 (± 0.17)		
Week 92 (N = 99, 104)	-0.29 (± 0.24)	-0.49 (± 0.15)		
Week 104 (N = 99, 104)	-0.73 (± 0.26)	-0.52 (± 0.19)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Most within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12, data only. Week 2

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6476
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.29

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12, data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9777
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.39

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12, data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4453
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.18

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.65

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12, data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5782
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.33
upper limit	0.6

Secondary: Change from Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) - Spine 6 discovertebral units (DVU) Total Score at 12 weeks

End point title	Change from Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) - Spine 6 discovertebral units (DVU) Total Score at 12 weeks

End point description:

The change from baseline in the MRI score of spine was assessed using SPARCC method. The scores of the 6 most severely affected spinal levels (discovertebral units/DVUs) was selected. Each DVU was divided into 4 quadrants. Each quadrant was assigned a score of 0 = no lesion or 1 = increased signal. This was repeated for each of 3 consecutive sagittal slices resulting in a score of up to 12 per DVU. On each slice, the presence of a lesion exhibiting an intense signal in any quadrant was assigned an additional score of 1 for that slice. Additionally, on each slice the presence of a lesion exhibiting depth ≥ 1 cm in any quadrant was given an additional score of 1. The maximum score for 6 DVU Spine Total Score is 108.

End point type	Secondary

End point timeframe:

Week 12

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	105		
Units: units on a scale				
arithmetic mean (standard error)	-2.12 (± 0.72)	-2.12 (± 0.43)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0414
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.88
upper limit	-0.04

Secondary: Mean change from Baseline in SPARCC Score for the Sacroiliac Joint at time points

End point title	Mean change from Baseline in SPARCC Score for the Sacroiliac Joint at time points

End point description:

The change from baseline in the MRI score of sacroiliac joints was assessed using SPARCC method. Scoring was based on 6 consecutive coronal slices from posterior to anterior. Each joint was divided into 4 quadrants. Each quadrant was assigned a score of 0 = no lesion/1 = increased signal. For each slice, the score is increased by 1 for each joint that exhibits an intense signal in any quadrant. Also, for each slice, an additional score of 1 will be given for each joint that includes a lesion demonstrating continuous increased signal of a depth ≥1 cm from the articular surface. The maximum possible score is 72.

End point type	Secondary

End point timeframe:

Weeks 12 and 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	105		
Units: units on a scale				
arithmetic mean (standard error)				
Week 12 (N = 97, 105)	-3.99 (± 0.72)	-0.86 (± 0.43)		
Week 104 (N = 74, 79)	-6 (± 1.15)	-3.36 (± 0.84)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Within group comparisons to baseline were <0.001, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.16
upper limit	-1.7

Secondary: Mean Change from Baseline in SPARCC - Spine 6 discovertebral units (DVU) Total Score at time points

End point title	Mean Change from Baseline in SPARCC - Spine 6 discovertebral units (DVU) Total Score at time points

End point description:

The change from baseline in the MRI score of spine was assessed using SPARCC method. The scores of the 6 most severely affected spinal levels (discovertebral units/DVUs) was selected. Each DVU was

divided into 4 quadrants. Each quadrant was assigned a score of 0 = no lesion or 1 = increased signal. This was repeated for each of 3 consecutive sagittal slices resulting in a score of up to 12 per DVU. On each slice, the presence of a lesion exhibiting an intense signal in any quadrant was assigned an additional score of 1 for that slice. Additionally, on each slice the presence of a lesion exhibiting depth ≥ 1 cm in any quadrant was given an additional score of 1. The maximum score for 6 DVU Spine Total Score is 108.

End point type	Secondary

End point timeframe:

Weeks 12 and 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	105		
Units: units on a scale				
arithmetic mean (standard error)				
Week 12 (N= 95, 105)	-2.12 (± 0.49)	-1.16 (± 0.47)		
Week 104 (N= 74, 80)	-2.08 (± 0.91)	-0.78 (± 0.49)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Within group comparisons to baseline were <0.001, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0414
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.96

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.88
upper limit	-0.04

Secondary: Mean change from Baseline in Ankylosing Spondylitis Spine Magnetic Resonance Imaging-Activity (ASspiMRI-a) Total Score

End point title	Mean change from Baseline in Ankylosing Spondylitis Spine Magnetic Resonance Imaging-Activity (ASspiMRI-a) Total Score

End point description:

ASspiMRI-a measures acute lesion scores as determined by short-tau inversion recovery (STIR) and gadolinium-enhanced T1 (Gd-DTPA). All 23 disco-vertebral units (DVU) of the spine (from C2 to S1), defined as the region between 2 virtual lines through the middle of each vertebra, are scored in a single dimension, which is representing the highest level of inflammation in that particular DVU. Enhancement and bone marrow edema are graded (0-3) for each DVU, with 3 more grades (4-6) if, in addition to the signs of acute inflammation defined for grades 1-3, erosions are visualized, leading to a maximum score of 138 for the entire spine. Acute spinal changes were assessed by using STIR sagittal views of the cervical, thoracic and lumbar spine. The total score ranges from 0 (no inflammation) to 138 (high inflammation).

End point type	Secondary

End point timeframe:

Weeks 12 and 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	105		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 12 (N= 95 105)	-0.73 (± 0.17)	-0.33 (± 0.16)		
Week 104 (N= 73, 80)	-0.79 (± 0.29)	-0.28 (± 0.16)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0132
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	-0.08

Secondary: Mean change from Baseline in number of swollen joints at time points

End point title	Mean change from Baseline in number of swollen joints at time points

End point description:

Forty-four (44) joints were assessed by the Investigator to determine the number of joints that were considered swollen (artificial joints were not assessed). The response to pressure/motion on each joint was assessed using the following scale: Present/Absent/Not Done. The 44 joints to be assessed were:sternoclavicular, acromioclavicular, shoulder, elbow, wrist (includes radiocarpal, carpal and carpometacarpal considered as one unit), metacarpophalangeals (I, II, III, IV, V), thumb interphalangeal (IP), proximal IPs (II, III, IV, V), knee, ankle, metatarsophalangeals (I, II, III, IV, V).

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	105		
Units: Number of joints				
arithmetic mean (standard error)				
Week 2 (N = 100, 102)	-0.27 (± 0.17)	-0.08 (± 0.16)		
Week 4 (N = 100, 105)	-0.62 (± 0.13)	-0.45 (± 0.13)		
Week 8 (N = 101, 105)	-0.71 (± 0.14)	-0.52 (± 0.13)		
Week 12 (N = 101, 105)	-0.6 (± 0.12)	-0.29 (± 0.11)		
Week 16 (N = 96, 102)	-0.76 (± 0.17)	-0.59 (± 0.19)		
Week 24 (N = 96, 102)	-0.8 (± 0.2)	-0.68 (± 0.22)		
Week 32 (N= 96, 102)	-0.75 (± 0.23)	-0.64 (± 0.2)		
Week 40 (N= 96, 102)	-0.8 (± 0.21)	-0.71 (± 0.2)		
Week 48 (N= 96, 102)	-0.83 (± 0.21)	-0.83 (± 0.22)		
Week 56 (N= 96, 102)	-0.86 (± 0.21)	-0.76 (± 0.21)		
Week 68 (N= 96, 102)	-0.86 (± 0.21)	-0.82 (± 0.22)		
Week 80 (N= 96, 102)	-0.85 (± 0.21)	-0.79 (± 0.22)		
Week 92 (N= 96, 102)	-0.83 (± 0.21)	-0.76 (± 0.23)		
Week 104 (N= 96, 102)	-0.89 (± 0.21)	-0.84 (± 0.22)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Within group comparisons to baseline were <0.001, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2438
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	0.13

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1958
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.09

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1624
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.08

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0091
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	-0.08

Secondary: Mean change from Baseline in number of tender joints at time points

End point title	Mean change from Baseline in number of tender joints at time points

End point description:

Forty-four (44) joints were assessed by the Investigator to determine the number of joints that were considered tender or painful. The response to pressure/motion on each joint was assessed using the following scale: Present/Absent/Not Done/Not Aplicable (to be considered for artificial joints). The 44 joints to be assessed were:sternoclavicular, acromioclavicular, shoulder, elbow, wrist (includes radiocarpal, carpal and carpometacarpal considered as one unit), metacarpophalangeals (I, II, III, IV, V), thumb interphalangeal (IP), proximal IPs (II, III, IV, V), knee, ankle, metatarsophalangeals (I, II, III, IV, V).

End point type	Secondary
End point timeframe: Baseline to Week 104	

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	105		
Units: Number of joints				
arithmetic mean (standard error)				
Week 2 (N = 100, 102)	-1.99 (± 0.36)	-1.38 (± 0.35)		
Week 4 (N = 100, 105)	1.52 (± 0.41)	-1.27 (± 0.39)		
Week 8 (N = 101, 105)	-1.93 (± 0.41)	-2.02 (± 0.39)		
Week 12 (N = 101, 105)	-1.55 (± 0.38)	-1.56 (± 0.36)		
Week 16 (N = 96, 102)	-1.93 (± 0.39)	-2.35 (± 0.49)		
Week 24 (N = 96, 102)	-2.46 (± 0.43)	-2.83 (± 0.57)		
Week 32 (N = 96, 102)	-1.96 (± 0.42)	-3.09 (± 0.55)		
Week 40 (N = 96, 102)	-2.42 (± 0.42)	-3.16 (± 0.53)		
Week 48 (N = 96, 102)	-2.65 (± 0.42)	-2.95 (± 0.55)		
Week 56 (N = 96, 102)	-2.44 (± 0.43)	-3.25 (± 0.58)		
Week 68 (N = 96, 102)	-2.43 (± 0.4)	-3.3 (± 0.61)		
Week 80 (N = 96, 102)	-2.6 (± 0.43)	-3.07 (± 0.6)		
Week 92 (N = 96, 102)	-2.45 (± 0.37)	-3.29 (± 0.58)		
Week 104 (N = 96, 102)	-2.72 (± 0.42)	-3.48 (± 0.58)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Within group comparisons to baseline were <0.001, from paired t-test.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2
Statistical analysis description: Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0836
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.32
upper limit	0.08

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5402
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.02
upper limit	0.54

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8167
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	0.87

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9891
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	0.73

Secondary: Mean change from Baseline in dactylitis score at time points

End point title	Mean change from Baseline in dactylitis score at time points

End point description:

Each of the 10 fingers and 10 toes is evaluated for dactylitis. A score of 0, 1, 2 or 3 (where 0 = none, 1= mild, 2 = moderate, 3 = severe) is assigned to each. A total score which can range from 0 to 60 is obtained by adding the scores for the 20 digits

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	108		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N = 105, 107)	0 (± 0.03)	0.02 (± 0.03)		
Week 4 (N = 105, 108)	-0.09 (± 0.03)	-0.05 (± 0.03)		
Week 8 (N = 105, 108)	-0.19 (± 0.02)	-0.16 (± 0.02)		
Week 12 (N = 105, 108)	-0.19 (± 0.08)	-0.21 (± 0.07)		

Week 16 (N = 100, 104)	-0.21 (± 0.13)	-0.2 (± 0.1)		
Week 24 (N = 100, 104)	-0.23 (± 0.13)	-0.2 (± 0.1)		
Week 32 (N = 100, 104)	-0.23 (± 0.13)	-0.21 (± 0.1)		
Week 40 (N = 100, 104)	-0.22 (± 0.13)	-0.23 (± 0.1)		
Week 48 (N = 100, 104)	-0.22 (± 0.13)	-0.22 (± 0.09)		
Week 56 (N = 100, 104)	-0.23 (± 0.13)	-0.22 (± 0.1)		
Week 68 (N = 100, 104)	-0.2 (± 0.11)	-0.23 (± 0.1)		
Week 80 (N = 100, 104)	-0.23 (± 0.13)	-0.23 (± 0.1)		
Week 92 (N = 100, 104)	-0.17 (± 0.1)	-0.23 (± 0.1)		
Week 104 (N = 100, 104)	-0.23 (± 0.13)	-0.23 (± 0.1)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6148
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.05

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No

adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2547
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.03

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1208
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.01

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8291
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.17

Secondary: Changes from Baseline in Maastricht Ankylosing Spondylitis Enthesis Score (MASES) at time points

End point title	Changes from Baseline in Maastricht Ankylosing Spondylitis Enthesis Score (MASES) at time points

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).

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	108		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N = 104, 107)	-0.94 (± 0.23)	-0.74 (± 0.22)		
Week 4 (N = 104, 108)	-1.11 (± 0.27)	-0.65 (± 0.25)		
Week 8 (N = 104, 108)	-1.39 (± 0.27)	-1.2 (± 0.25)		
Week 12 (N = 104, 108)	-1.4 (± 0.28)	-0.74 (± 0.26)		
Week 16 (N = 99, 104)	-1.64 (± 0.24)	-1.5 (± 0.26)		
Week 24 (N = 99, 104)	-1.78 (± 0.25)	-1.34 (± 0.27)		
Week 32 (N = 99, 104)	-1.59 (± 0.26)	-1.66 (± 0.28)		
Week 40 (N = 99, 104)	-1.86 (± 0.26)	-1.62 (± 0.27)		
Week 48 (N = 99, 104)	-1.79 (± 0.27)	-1.73 (± 0.28)		
Week 56 (N = 99, 104)	-2.01 (± 0.28)	-1.63 (± 0.3)		
Week 68 (N = 99, 104)	-1.92 (± 0.27)	-1.73 (± 0.29)		
Week 80 (N = 99, 104)	-1.99 (± 0.28)	-1.72 (± 0.32)		
Week 92 (N = 99, 104)	-2 (± 0.26)	-1.65 (± 0.3)		
Week 104 (N = 99, 104)	-1.87 (± 0.28)	-1.77 (± 0.29)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3536
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	0.23

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0769
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.97
upper limit	0.05

Statistical analysis title	Statistical analysis at Week 8
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4698
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.33

Statistical analysis title	Statistical analysis at Week 12
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0167
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.19
upper limit	-0.12

Secondary: Change from Baseline in C-reactive protein (CRP) concentration time points

End point title	Change from Baseline in C-reactive protein (CRP) concentration time points

End point description:

The test for CRP is a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. A decrease in the level of CRP indicates reduction in

inflammation and therefore improvement.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	108		
Units: mg/L				
arithmetic mean (standard error)				
Week 2 (N = 105, 107)	-4.49 (± 0.71)	-1.46 (± 0.67)		
Week 4 (N = 105, 108)	-3.61 (± 1.16)	0.25 (± 1.1)		
Week 8 (N = 105, 108)	-4.07 (± 1.33)	-0.97 (± 1.27)		
Week 12 (N = 105, 108)	-2.78 (± 1.14)	0.65 (± 1.08)		
Week 16 (N = 100, 104)	-4.84 (± 1.07)	-3.82 (± 1.08)		
Week 24 (N = 100, 104)	-4.62 (± 1.1)	-4.56 (± 1.04)		
Week 32 (N = 100, 104)	-4.97 (± 1.01)	-3.88 (± 1.01)		
Week 40 (N = 100, 104)	-4.88 (± 1.1)	-4.26 (± 1.08)		
Week 48 (N = 100, 104)	-4.94 (± 1.08)	-4.64 (± 1.06)		
Week 56 (N = 100, 104)	-5.2 (± 1.04)	-4.59 (± 1.02)		
Week 68 (N = 100, 104)	-5.03 (± 1.01)	-3.93 (± 1.09)		
Week 80 (N = 100, 104)	-4.29 (± 1.17)	-4.12 (± 0.99)		
Week 92 (N = 100, 104)	-5.1 (± 1.06)	-4.44 (± 1.04)		
Week 104 (N = 100, 104)	-4.28 (± 1.16)	-3.65 (± 1.12)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Most within group comparisons to baseline were <0.001, from paired t-test. For open-label period results include unadjusted mean changes and standard errors, no covariate adjustments were applied.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.39
upper limit	-1.66

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.09
upper limit	-1.62

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0143
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.04

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.47
upper limit	-0.61

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0038
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.23
upper limit	-1.02

Secondary: Change from Baseline in Erythrocyte sedimentation Rate (ESR) at time points

End point title	Change from Baseline in Erythrocyte sedimentation Rate (ESR) at time points

End point description:

ESR is a laboratory test that provides a non-specific measure of inflammation. The test assesses the rate at which red blood cells fall in a test tube. Normal range is 0-30 mm/hr. A higher rate is consistent with inflammation.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	106		
Units: mm/hr				
arithmetic mean (standard error)				
Week 2 (N = 100, 104)	-9.02 (± 1.61)	-1.3 (± 1.53)		
Week 4 (N = 100, 106)	-10 (± 1.57)	-3.98 (± 1.48)		

Week 8 (N = 100, 106)	-10.79 (± 1.84)	-4.81 (± 1.76)		
Week 12 (N = 100, 106)	-11.34 (± 1.8)	-2.68 (± 1.39)		
Week 16 (N = 95, 102)	-12.75 (± 2.03)	-9.77 (± 1.62)		
Week 24 (N = 95, 102)	-14.22 (± 1.96)	-8.82 (± 1.77)		
Week 32 (N = 95, 102)	-12.76 (± 2.04)	-10.13 (± 1.76)		
Week 40 (N = 95, 102)	-11.49 (± 2.22)	-10.48 (± 1.74)		
Week 48 (N = 95, 102)	-12.2 (± 2.05)	-9.91 (± 1.9)		
Week 56 (N = 95, 102)	-13.03 (± 2.18)	-8.91 (± 1.7)		
Week 68 (N = 95, 102)	-10.8 (± 2.17)	-9.48 (± 1.74)		
Week 80 (N = 95, 102)	-10.74 (± 2.14)	-8.15 (± 1.74)		
Week 92 (N = 95, 102)	-10.84 (± 2.28)	-8.79 (± 1.79)		
Week 104 (N = 95, 102)	-10.51 (± 2.15)	-5.73 (± 2.05)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
All within group comparisons to baseline were <0.001, from paired t-test	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.71

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.85
upper limit	-4.58

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-6.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.16
upper limit	-3.09

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only. Week 8

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0009
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-5.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.15
upper limit	-2.41

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.34
upper limit	-3.73

Secondary: Change from Baseline in Euro Quality of Life (EQ)-5D VAS Score time points

End point title	Change from Baseline in Euro Quality of Life (EQ)-5D VAS Score time points

End point description:

EQ-5D: participant rated questionnaire to assess health-related quality of life in terms of a single index value. The VAS component rates current health state on a scale from 0 mm (worst imaginable health state) to 100 mm (best imaginable health state); higher scores indicate a better health state.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	96		
Units: mm				
arithmetic mean (standard error)				
Week 4 (N = 86, 93)	4.76 (± 2.2)	4.77 (± 2.03)		
Week 8 (N = 85, 93)	6.66 (± 2.84)	3.05 (± 2.65)		
Week 12 (N = 84, 92)	9.33 (± 2.97)	3.26 (± 2.77)		
Week 16 (N = 82, 91)	12.72 (± 2.16)	11.56 (± 2.44)		
Week 24 (N = 82, 90)	13.21 (± 2.23)	16.61 (± 2.26)		
Week 40 (N = 79, 86)	16.62 (± 2.13)	14.67 (± 2.64)		
Week 48 (N = 75, 86)	16.29 (± 2.37)	18.72 (± 2.37)		
Week 68 (N = 72, 82)	17.26 (± 2.18)	17.9 (± 2.6)		
Week 92 (N = 69, 77)	16.32 (± 2.33)	21.08 (± 2.73)		
Week 104 (N = 64, 75)	19.81 (± 2.45)	23.69 (± 2.71)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
With the exception of change from Baseline in the placebo group at Week 12, within group comparisons to baseline for all other treatment groups and time points were <0.001, from paired t-test.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.037
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 4
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9965
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.39
upper limit	4.37

Statistical analysis title	Statistical analysis at Week 8
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.197
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.89
upper limit	9.1

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0394
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	6.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	11.84

Secondary: Change from Baseline in EQ-5D Health State Profile Utility Score at time points

End point title	Change from Baseline in EQ-5D Health State Profile Utility Score at time points

End point description:

EQ-5D: participant rated questionnaire to assess health-related quality of life in terms of a single utility score. Health State Profile component assesses level of current health for 5 domains: mobility, self-care, usual activities, pain and discomfort, and anxiety and depression; 1 indicates better health state (no problems); 3 indicates worst health state. Scoring formula developed by EuroQol Group assigns a utility value for each domain in the profile. Score is transformed and results in a total score range -0.594 to 1.000; higher score indicates a better health state.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	96		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 4 (N = 89, 96)	0.14 (± 0.03)	0.09 (± 0.03)		
Week 8 (N = 86, 94)	0.13 (± 0.04)	0.08 (± 0.03)		
Week 12 (N = 85, 93)	0.19 (± 0.04)	0.08 (± 0.03)		
Week 16 (N = 83, 90)	0.19 (± 0.04)	0.17 (± 0.03)		
Week 24 (N = 82, 90)	0.21 (± 0.03)	0.2 (± 0.03)		
Week 40 (N = 79, 86)	0.24 (± 0.04)	0.18 (± 0.03)		
Week 48 (N= 75, 86)	0.23 (± 0.03)	0.22 (± 0.03)		
Week 68 (N= 72, 83)	0.24 (± 0.04)	0.22 (± 0.03)		
Week 92 (N= 69, 78)	0.24 (± 0.04)	0.22 (± 0.03)		
Week 104 (N= 64, 75)	0.29 (± 0.04)	0.25 (± 0.03)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Within group comparisons to baseline were <0.01 at Week 12 and <0.001 thereafter, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.01
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1341
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.21

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0447
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.14

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1345
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.13

Secondary: Change from Baseline in Short Form-36 (SF-36) Physical Component

Summary (PCS) at time points	
End point title	Change from Baseline in Short Form-36 (SF-36) Physical Component Summary (PCS) at time points

End point description:

SF-36 is a standardized survey evaluating 8 aspects of functional health and well being: physical and social functioning, physical and emotional role limitations, bodily pain, general health, vitality, mental health. The score for a section is an average of the individual question scores, which are scaled 0-100 (100 = highest level of functioning).

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	96		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 4 (N = 89, 96)	4.04 (± 0.79)	2.72 (± 0.74)		
Week 12 (N = 85, 94)	6.18 (± 0.97)	3.8 (± 0.91)		
Week 24 (N = 83, 91)	6.67 (± 0.93)	7.29 (± 0.78)		
Week 48 (N = 77, 86)	8.03 (± 0.96)	8.51 (± 0.85)		
Week 68 (N = 72, 83)	8.97 (± 0.98)	9.42 (± 0.94)		
Week 92 (N = 69, 78)	8.35 (± 1.15)	9.28 (± 0.93)		
Week 104 (N = 65, 75)	9.98 (± 1.03)	10.38 (± 1.01)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Within group comparisons to baseline were <0.001, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 12 data only.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1035
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	2.9

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0134
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	4.26

Secondary: Change from Baseline in SF-36 Mental Component Summary (MCS) at time points

End point title	Change from Baseline in SF-36 Mental Component Summary (MCS) at time points

End point description:

SF-36 is a standardized survey evaluating 8 aspects of functional health and well being: physical and social functioning, physical and emotional role limitations, bodily pain, general health, vitality, mental health. The score for a section is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning).

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	96		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 4 (N = 89, 96)	2.65 (± 1.02)	1.47 (± 0.94)		
Week 12 (N = 85, 94)	2.44 (± 1.29)	1.58 (± 1.2)		
Week 24 (N = 83, 91)	3.52 (± 1.3)	4.36 (± 0.99)		
Week 48 (N = 77, 86)	3.47 (± 1.18)	3.54 (± 1.07)		
Week 68 (N = 72, 83)	3.65 (± 1.23)	4.44 (± 1.05)		
Week 92 (N = 69, 78)	4.18 (± 1.48)	4.77 (± 1.19)		
Week 104 (N= 65, 75)	4.9 (± 1.34)	3.74 (± 1.06)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Within group comparisons to baseline were <0.05, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.252
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	3.19

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4981
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.63
upper limit	3.34

Secondary: Change from Baseline in Hospital Anxiety and Depression Scale (HADS) Depression score at time points

End point title	Change from Baseline in Hospital Anxiety and Depression Scale (HADS) Depression score at time points

End point description:

This outcome measure is describing the HADS subscale of depression. HADS is a participant rated questionnaire with 2 subscales. HADS-A assesses state of generalized anxiety (anxious mood, restlessness, anxious thoughts, panic attacks); HADS-D assesses state of lost interest and diminished pleasure response (lowering of hedonic tone). Each subscale comprised of 7 items with range 0 (no presence of anxiety or depression) to 3 (severe feeling of anxiety or depression). Total score 0 to 21 for each subscale; higher score indicates greater severity of anxiety and depression symptoms. There is no Total Score for HADS.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	96		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 4 (N = 89, 96)	-0.63 (± 0.33)	-0.39 (± 0.31)		
Week 12 (N = 85, 94)	-0.45 (± 0.46)	-0.05 (± 0.43)		
Week 24 (N = 83, 91)	-1.22 (± 0.35)	-1.04 (± 0.31)		
Week 48 (N = 77, 85)	-1.42 (± 0.38)	-1.04 (± 0.36)		
Week 68 (N = 72, 82)	-1.61 (± 0.33)	-1.35 (± 0.36)		
Week 92 (N = 69, 78)	-1.29 (± 0.39)	-1.47 (± 0.38)		
Week 104 (N = 65, 74)	-1.91 (± 0.4)	-1.61 (± 0.35)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Within group comparisons to baseline were <0.001, from paired t-test.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 4
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4621
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.41

Statistical analysis title	Statistical analysis at Week 12
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 12 data only.	
Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3842
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	0.5

Secondary: Change from Baseline in HADS Anxiety score at time points

End point title	Change from Baseline in HADS Anxiety score at time points

End point description:

This outcome measure is describing the HADS subscale of anxiety. HADS is a participant rated questionnaire with 2 subscales. HADS-A assesses state of generalized anxiety (anxious mood, restlessness, anxious thoughts, panic attacks); HADS-D assesses state of lost interest and diminished pleasure response (lowering of hedonic tone). Each subscale comprised of 7 items with range 0 (no presence of anxiety or depression) to 3 (severe feeling of anxiety or depression). Total score 0 to 21 for each subscale; higher score indicates greater severity of anxiety and depression symptoms. There is no Total Score for HADS.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	96		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 4 (N = 89, 96)	-0.73 (± 0.35)	-0.89 (± 0.32)		
Week 12 (N = 85, 94)	-1.33 (± 0.45)	-0.81 (± 0.43)		
Week 24 (N = 83, 91)	-0.89 (± 0.4)	-1.66 (± 0.33)		
Week 48 (N = 77, 85)	-1.03 (± 0.38)	-1.4 (± 0.34)		
Week 68 (N = 72, 82)	-1.24 (± 0.39)	-1.76 (± 0.41)		
Week 92 (N = 69, 78)	-0.96 (± 0.46)	-2.24 (± 0.35)		
Week 104 (N = 65, 74)	-1.8 (± 0.4)	-1.74 (± 0.39)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Within group comparisons to baseline were <0.001, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6357
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	0.86

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2439
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	0.36

Secondary: Change from Baseline in Ankylosing Spondylitis Quality of Life (ASQoL) score at time points

End point title	Change from Baseline in Ankylosing Spondylitis Quality of Life (ASQoL) score at time points

End point description:

ASQoL is a questionnaire that assesses disease-specific quality of life (QoL). It consists of 18 statements that are relevant to the physical and mental conditions for a participant with Ankylosing Spondylitis (AS): mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each statement is answered by the participant as a 'Yes' (scored as 1) or 'No' (scored as 0). All item scores are summed to give a total score. Total score can range from 0 (good QoL) to 18 (poor QoL).

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	96		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 12 (N = 88, 94)	-1.93 (± 0.54)	-1.42 (± 0.51)		
Week 24 (N = 83, 91)	-3.12 (± 0.47)	-3.16 (± 0.41)		
Week 48 (N = 77, 86)	-3.74 (± 0.49)	-3.67 (± 0.43)		
Week 68 (N = 72, 83)	-4.04 (± 0.48)	-4.1 (± 0.46)		
Week 92 (N = 69, 77)	-4 (± 0.52)	-4.1 (± 0.53)		
Week 104 (N = 65, 73)	-4.74 (± 0.54)	-3.99 (± 0.54)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Descriptive analysis was carried out for Week 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3286
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.55
upper limit	0.52

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Within group comparisons to baseline were <0.001, from paired t-test.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Secondary: Change from Baseline in Ankylosing Spondylitis Work Instability Index (AS-WIS) score at time points

End point title	Change from Baseline in Ankylosing Spondylitis Work Instability Index (AS-WIS) score at time points
End point description: The AS-WIS is a 20 item questionnaire to assess work disability and risk of unemployment due to AS. Higher scores indicate greater work impairment and instability that results from a mismatch between an individual's ability levels given their AS and their job. Each question is assigned a score of 1 for a response of "True" and 0 for a response of "Not True". All item scores are summed to give a total score that can range from 0 to 20. If a subject has ≥ 5 missing responses (ie more than 20%), then a total score is not calculated. For subjects with ≥ 1 but ≤ 4 missing responses, the total score is calculated as follows: T=20x/(20-m) where: T is the total score, x is the total score for the items answered and n is the number of non-missing items.	
End point type	Secondary
End point timeframe: Baseline to Week 104	

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	91		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 12 (N = 81, 84)	-2.36 (± 0.58)	-1.58 (± 0.55)		
Week 24 (N = 74, 75)	-3.16 (± 0.58)	-2.71 (± 0.6)		
Week 48 (N = 66, 75)	-3.61 (± 0.63)	-4.01 (± 0.59)		
Week 68 (N = 60, 66)	-4.5 (± 0.64)	-5.08 (± 0.71)		
Week 92 (N = 57, 60)	-4.35 (± 0.76)	-5.27 (± 0.71)		
Week 104 (N = 55, 62)	-4.78 (± 0.68)	-5.23 (± 0.74)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Within group comparisons to baseline were <0.001, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1829
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.93
upper limit	0.37

Secondary: Change from Baseline in Work Productivity and Activity Impairment (WPAI): Percent Work Time Missed due to Health Problems at time points

End point title	Change from Baseline in Work Productivity and Activity Impairment (WPAI): Percent Work Time Missed due to Health Problems at time points

End point description:

The WPAI assesses work productivity and impairment. It is a 6-item questionnaire used to assess the degree to which a specified health problem affected work productivity and regular activities over the past 7 days. The questions are: Q1 = currently employed. Q2 = hours missed due to health problems. Q3 = hours missed other reasons. Q4 = hours actually worked. Q5 = degree health affected productivity while working (0-10 scale). Q6 = degree health affected regular activities (0-10 scale). Subscale scores are calculated: Percent work time missed due to health problem: Q2/(Q2+Q4). The computed percentage range for each sub-scale is 0-100, where higher numbers indicate greater impairment and less productivity.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	62		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N = 56, 59)	2.83 (± 3.64)	0.46 (± 3.58)		
Week 4 (N = 57, 59)	1.74 (± 3.35)	0.12 (± 3.25)		
Week 8 (N = 53, 53)	4.19 (± 4.13)	0.67 (± 4.15)		
Week 12 (N = 53, 55)	-0.19 (± 4.36)	-4.93 (± 4.25)		
Week 16 (N = 53, 52)	-1.35 (± 3.34)	-2.03 (± 4.92)		
Week 24 (N = 47, 47)	-0.71 (± 3.4)	-7.39 (± 4.61)		
Week 32 (N = 48, 46)	-4.06 (± 3.02)	-9.76 (± 4.12)		
Week 40 (N= 50, 50)	-2.16 (± 4.15)	-9.23 (± 3.73)		
Week 48 (N= 48, 47)	-5.04 (± 2.33)	-6.12 (± 3.6)		
Week 56 (N= 44, 49)	-3.99 (± 2.77)	-9.11 (± 3.79)		
Week 68 (N= 44, 44)	-2.41 (± 3.19)	-7.51 (± 3.69)		
Week 80 (N= 43, 44)	2.92 (± 2.45)	-9.96 (± 4.21)		
Week 92 (N= 45, 44)	-1.81 (± 3.31)	-8.42 (± 4.29)		
Week 104 (N= 42, 43)	-6.35 (± 3.45)	-10.44 (± 4.74)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Within group comparisons to baseline were <0.05, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5226
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.37

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.95
upper limit	9.68

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6232
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	8.14

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3877
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.53
upper limit	11.57

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2402
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	4.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.22
upper limit	12.69

Secondary: Change from Baseline in WPAI: Percent Impairment While Working Due to Health Problems at time points

End point title	Change from Baseline in WPAI: Percent Impairment While Working Due to Health Problems at time points

End point description:

The WPAI assesses work productivity and impairment. It is a 6-item questionnaire used to assess the degree to which a specified health problem affected work productivity and regular activities over the past 7 days. The questions are: Q1 = currently employed. Q2 = hours missed due to health problems. Q3 = hours missed other reasons. Q4 = hours actually worked. Q5 = degree health affected productivity while working (0-10 scale). Q6 = degree health affected regular activities (0-10 scale). Subscale scores are calculated: Percent impairment while working due to health problem: Q5/10. The computed percentage range for each sub-scale is 0-100, where higher numbers indicate greater impairment and less productivity.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	58		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N = 53, 56)	-11.47 (± 3.71)	-2.28 (± 3.67)		
Week 4 (N = 52, 55)	-8.88 (± 3.66)	-3.81 (± 3.54)		
Week 8 (N = 47, 50)	-12.74 (± 3.94)	-6.48 (± 3.9)		
Week 12 (N = 48, 50)	-21.22 (± 4.74)	-12.09 (± 4.7)		
Week 16 (N = 49, 46)	-16.53 (± 3.69)	-16.09 (± 2.97)		

Week 24 (N = 46, 43)	-16.52 (± 4.66)	-18.84 (± 3.35)		
Week 32 (N = 46, 43)	-18.04 (± 3.76)	-15.81 (± 3.45)		
Week 40 (N = 45, 47)	-22.89 (± 4.04)	-19.36 (± 2.92)		
Week 48 (N = 45, 47)	-22.22 (± 3.55)	-16.6 (± 3.64)		
Week 56 (N = 42, 46)	-23.81 (± 3.9)	-20.43 (± 3.33)		
Week 68 (N = 43, 43)	-22.33 (± 3.96)	-22.09 (± 3.39)		
Week 80 (N = 42, 41)	-24.29 (± 4.06)	-21.95 (± 3.6)		
Week 92 (N = 42, 41)	-23.57 (± 3.47)	-19.27 (± 3.07)		
Week 104 (N = 40, 40)	-25.5 (± 3.69)	-22.5 (± 3.54)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Within group comparisons to baseline were <0.001 at Week 16 and thereafter, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0193
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-9.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.85
upper limit	-1.52

Statistical analysis title	Statistical analysis at Week 4
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.173
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-5.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.41
upper limit	2.26

Statistical analysis title	Statistical analysis at Week 8
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1224
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-6.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.23
upper limit	1.71

Statistical analysis title	Statistical analysis at Week 12
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0461
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-9.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.11
upper limit	-0.16

Secondary: Changes from Baseline in WPAI - Activity Impairment Due to Health Problems at time points

End point title	Changes from Baseline in WPAI - Activity Impairment Due to Health Problems at time points

End point description:

The WPAI assesses work productivity and impairment. It is a 6-item questionnaire used to assess the degree to which a specified health problem affected work productivity and regular activities over the past 7 days. The questions are: Q1 = currently employed. Q2 = hours missed due to health problems. Q3 = hours missed other reasons. Q4 = hours actually worked. Q5 = degree health affected productivity while working (0-10 scale). Q6 = degree health affected regular activities (0-10 scale). Subscale scores are calculated: Percent activity impairment due to health problem: Q6/10. The computed percentage range for each sub-scale is 0-100, where higher numbers indicate greater impairment and less productivity.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	95		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N = 89, 94)	-10.7 (± 2.8)	-4.73 (± 2.61)		
Week 4 (N = 89, 95)	-11.52 (± 2.45)	-8.42 (± 2.28)		
Week 8 (N = 86, 93)	-18.35 (± 3.15)	-11.68 (± 2.96)		
Week 12 (N = 85, 92)	-18.92 (± 3.35)	-12.07 (± 3.14)		
Week 16 (N = 82, 90)	-19.88 (± 2.77)	-22.33 (± 2.69)		
Week 24 (N = 82, 89)	-20.61 (± 3.14)	-23.15 (± 2.31)		
Week 32 (N = 78, 86)	-20.26 (± 2.96)	-22.09 (± 2.58)		
Week 40 (N = 77, 85)	-27.14 (± 2.85)	-24 (± 2.36)		

Week 48 (N = 74, 85)	-24.46 (± 2.93)	-22.12 (± 2.85)		
Week 56 (N = 74, 84)	-25 (± 2.8)	-25.71 (± 2.44)		
Week 68 (N = 72, 82)	-26.53 (± 2.95)	-25.73 (± 2.73)		
Week 80 (N = 69, 77)	-27.39 (± 3.17)	-27.66 (± 2.97)		
Week 92 (N = 69, 77)	-26.96 (± 3.32)	-25.97 (± 2.81)		
Week 104 (N = 65, 73)	-30.77 (± 3.01)	-28.36 (± 2.87)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Within group comparisons to baseline were <0.001, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0372
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-5.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.58
upper limit	-0.36

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No

adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2126
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.98
upper limit	1.79

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only. Week 8

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.033
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-6.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.79
upper limit	-0.54

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0397
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-6.85

Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.38
upper limit	-0.33

Secondary: Changes from Baseline in WPAI - Overall Work Impairment Due to Health Problems at time points

End point title	Changes from Baseline in WPAI - Overall Work Impairment Due to Health Problems at time points

End point description:

The WPAI assesses work productivity and impairment. It is a 6-item questionnaire used to assess the degree to which a specified health problem affected work productivity and regular activities over the past 7 days. The questions are: Q1 = currently employed. Q2 = hours missed due to health problems. Q3 = hours missed other reasons. Q4 = hours actually worked. Q5 = degree health affected productivity while working (0-10 scale). Q6 = degree health affected regular activities (0-10 scale). Subscale scores are calculated: Percent overall work impairment due to health problem: Q2/(Q2+Q4)+[(1-Q2/(Q2+Q4))*(Q5/10)]. The computed percentage range for each sub-scale is 0-100, where higher numbers indicate greater impairment and less productivity.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 2 (N = 51, 56)	-7.43 (± 3.81)	0.86 (± 3.74)		
Week 4 (N = 52, 55)	-7.07 (± 3.72)	-1.82 (± 3.59)		
Week 8 (N = 47, 49)	-10.32 (± 4.04)	-4.35 (± 4.09)		
Week 12 (N = 48, 50)	-20.77 (± 4.94)	-12.09 (± 4.89)		
Week 16 (N = 49, 46)	-16.3 (± 3.83)	-16.39 (± 2.86)		
Week 24 (N = 45, 43)	-14.85 (± 4.52)	-18.59 (± 3.68)		
Week 32 (N = 46, 43)	-17.59 (± 3.79)	-16.53 (± 3.33)		
Week 40 (N = 45, 47)	-23.74 (± 4.15)	-20.52 (± 3.03)		
Week 48 (N = 45, 45)	-23.03 (± 3.61)	-17.54 (± 3.87)		
Week 56 (N = 42, 46)	-23.6 (± 4.1)	-21.39 (± 3.43)		
Week 68 (N = 43, 42)	-21.9 (± 4.26)	-22.27 (± 3.46)		
Week 80 (N = 42, 41)	-20.66 (± 4.15)	-23.1 (± 3.8)		
Week 92 (N = 42, 41)	-24 (± 3.52)	-19.39 (± 3.24)		

Week 104 (N = 40, 40)	-25.76 (± 3.73)	-23.01 (± 3.8)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Within group comparisons to baseline were <0.001 at Week 16 and at Week 32 and thereafter, from paired t test.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 2
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0382
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-8.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.12
upper limit	-0.46

Statistical analysis title	Statistical analysis at Week 4
Statistical analysis description:	
Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.	
Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1648
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-5.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.69
upper limit	2.19

Statistical analysis title	Statistical analysis at Week 8

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1476
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-5.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.11
upper limit	2.15

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 2, 4, 8, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0687
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-8.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.03
upper limit	0.68

Secondary: Change from Baseline in Multidimensional Fatigue Inventory (MFI) score at time points

End point title	Change from Baseline in Multidimensional Fatigue Inventory (MFI) score at time points

End point description:

The MFI is a 20-item questionnaire that evaluates several aspects of fatigue. The General Fatigue Item is disclosed here. The general fatigue item contains four items, two of which are indicative for fatigue and two items contra-indicative for fatigue. Indicative items (eg, "I tire easily") are formulated in such a way that a high score suggests a high degree of fatigue. In case of contra-indicative items (eg, "I feel fit") a high score indicates a low degree of fatigue. Each item is scored on a 5-point numeric rating scale anchored at each end by “Yes, that is true” (scored 1) to “No, that is not true” (scored 5). Scoring for the MFI is done in such a way that higher scores indicate greater fatigue. Therefore, the items indicative for fatigue need to be recoded (1=5, 2=4, 3=3, 4=2, 5=1). For each scale a total score is calculated by summation of the scores of the individual items. Scores can range from the minimum of 4 to the maximum of 20. MFI-20 scale is copyrighted.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	95		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 4 (N = 89, 95)	-1.08 (± 0.38)	-0.64 (± 0.36)		
Week 12 (N = 85, 93)	-1.34 (± 0.42)	-1.08 (± 0.39)		
Week 24 (N = 83, 89)	-1.67 (± 0.37)	-2.69 (± 0.4)		
Week 48 (N = 77, 85)	-2.01 (± 0.39)	-2.84 (± 0.39)		
Week 68 (N = 72, 82)	-1.79 (± 0.42)	-3.01 (± 0.45)		
Week 92 (N = 69, 77)	-2.74 (± 0.4)	-3.18 (± 0.52)		
Week 104 (N = 65, 73)	-3.26 (± 0.46)	-3.04 (± 0.5)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test.

Comparison groups	Etanercept v Placebo

Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2578
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.21
upper limit	0.33

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4334
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.21
upper limit	0.52

Secondary: Change from Baseline in Medical Outcomes Study (MOS) Sleep Scale

score from Baseline to Week 104	
End point title	Change from Baseline in Medical Outcomes Study (MOS) Sleep Scale score from Baseline to Week 104

End point description:

The MOS sleep scale consists of 12 items to measure 6 sleep dimensions: initiation (time to fall asleep), quantity (hours of sleep each night), maintenance, respiratory problems, perceived adequacy, somnolence (the last 4 items reported using a 6-item Likert scale ranging from 1 [all of the time] to 6 [none of the time]). The raw scores ranging from 1 to 6 are transformed to scores ranging from 0 to 100 before the indices are calculated. Therefore the reported scores, consisting of means of converted items, also range from 0 to 100. However, two indexes can be derived: Sleep problems index I (short form) and sleep problems index II (long form). Additional subscales can be derived: sleep disturbance, snoring, awaken shortness of breath or headache, sleep adequacy, sleep somnolence, sleep quantity, and optimal sleep. However, data for two indexes and additional subscales is not reported.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	95		
Units: Units on a scale				
arithmetic mean (standard error)				
Week 4 (N = 89, 94)	-2.35 (± 1.59)	-0.85 (± 1.5)		
Week 12 (N = 85, 93)	-6.01 (± 2)	-4.1 (± 1.88)		
Week 24 (N = 83, 89)	-11.01 (± 2.64)	-14.34 (± 2.28)		
Week 32 (N = 78, 86)	-13.17 (± 2.3)	-17.06 (± 2.42)		
Week 48 (N = 76, 85)	-11.97 (± 2.6)	-17.57 (± 2.23)		
Week 68 (N = 71, 82)	-10.4 (± 2.56)	-15.5 (± 2.49)		
Week 104 (N = 66, 76)	-17.92 (± 2.78)	-15.61 (± 2.66)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

All within group comparisons to baseline were <0.001, from paired t-test.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Statistical analysis at Week 4

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3554
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	1.7

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Comparative analysis was carried out for Week 4, 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.335
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.82
upper limit	1.99

Secondary: Percentage of participants with Minimally Clinically Important Improvement (MCII) at time points

End point title	Percentage of participants with Minimally Clinically Important Improvement (MCII) at time points

End point description:

The MCII asks participants to rate the level of improvement they have experienced in the 48 hours compared to when they started the study. Response options are “Improved - less pain”, “No change”, and “Worse – more pain.” If the participant indicates that improvement has occurred, then they are asked to indicate how important that improvement is to them from “Not at all important” to “Very important’.

End point type	Secondary

End point timeframe:

Weeks 12 and 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	94		
Units: Percentage of participants				
number (not applicable)				
Week 12 (N = 88, 94)	59.09	44.68		
Week 104 (N = 75, 79)	76	81.01		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Descriptive analysis was carried out for Week 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	other
P-value	= 14.41
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	14.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	28.78

Secondary: Percentage of participants Achieving Patient Acceptable Symptom State (PASS) at time points

End point title	Percentage of participants Achieving Patient Acceptable Symptom State (PASS) at time points

End point description:

PASS is defined as a symptom state that the participants consider acceptable.

End point type	Secondary

End point timeframe:

Weeks 12 and 104

End point values	Etanercept	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	94		
Units: Percentage of participants				
number (not applicable)				
Week 12 (N = 88, 94)	72.73	61.7		
Week 104 (N = 74, 80)	79.73	88.75		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 12

Statistical analysis description:

Secondary and supportive analyses were performed at 2-sided alpha = 0.05 significance level. No adjustment for multiple testing was made. Descriptive analysis was carried out for Week 12 data only.

Comparison groups	Etanercept v Placebo
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1285
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	11.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.51
upper limit	24.56

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the signing of the informed consent until Week 104 visit.

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one participant and as nonserious in another participant, or one participant may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants were treated with placebo subcutaneous injection weekly plus stable background NSAID at optimal anti-inflammatory dose for 12 weeks (double-blind period).

Reporting group title	Etanercept

Reporting group description:

Participants were treated with etanercept subcutaneous injection weekly plus stable background NSAID at optimal anti-inflammatory dose for 12 weeks (double-blind period).

Serious adverse events	Placebo	Etanercept	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 113 (7.08%)	9 / 111 (8.11%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 113 (0.00%)	1 / 111 (0.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 113 (0.88%)	0 / 111 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			

subjects affected / exposed	1 / 113 (0.88%)	0 / 111 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	1 / 113 (0.88%)	0 / 111 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	1 / 113 (0.88%)	0 / 111 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 113 (0.88%)	0 / 111 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	1 / 113 (0.88%)	0 / 111 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocarditis			
subjects affected / exposed	0 / 113 (0.00%)	1 / 111 (0.90%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Multiple sclerosis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 111 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 113 (0.88%)	0 / 111 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ear and labyrinth disorders			
Hearing impaired			
subjects affected / exposed	1 / 113 (0.88%)	0 / 111 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	0 / 113 (0.00%)	1 / 111 (0.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 113 (0.00%)	3 / 111 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 113 (0.88%)	0 / 111 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 113 (0.00%)	1 / 111 (0.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondyloarthropathy			
subjects affected / exposed	0 / 113 (0.00%)	2 / 111 (1.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 113 (0.88%)	0 / 111 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Etanercept	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	87 / 113 (76.99%)	86 / 111 (77.48%)	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 113 (7.08%)	9 / 111 (8.11%)	
occurrences (all)	21	9	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	6 / 113 (5.31%)	8 / 111 (7.21%)	
occurrences (all)	14	18	
Injection site reaction			
subjects affected / exposed	6 / 113 (5.31%)	7 / 111 (6.31%)	
occurrences (all)	9	7	
Eye disorders			
Uveitis			
subjects affected / exposed	8 / 113 (7.08%)	13 / 111 (11.71%)	
occurrences (all)	13	18	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 113 (7.96%)	11 / 111 (9.91%)	
occurrences (all)	9	11	
Nausea			
subjects affected / exposed	7 / 113 (6.19%)	2 / 111 (1.80%)	
occurrences (all)	8	2	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 113 (2.65%)	9 / 111 (8.11%)	
occurrences (all)	3	10	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	7 / 113 (6.19%)	2 / 111 (1.80%)	
occurrences (all)	8	3	
Myalgia			

subjects affected / exposed	3 / 113 (2.65%)	6 / 111 (5.41%)	
occurrences (all)	3	7	
Infections and infestations			
Bronchitis			
subjects affected / exposed	7 / 113 (6.19%)	7 / 111 (6.31%)	
occurrences (all)	7	8	
Gastroenteritis			
subjects affected / exposed	7 / 113 (6.19%)	8 / 111 (7.21%)	
occurrences (all)	8	11	
Influenza			
subjects affected / exposed	7 / 113 (6.19%)	7 / 111 (6.31%)	
occurrences (all)	11	10	
Nasopharyngitis			
subjects affected / exposed	23 / 113 (20.35%)	26 / 111 (23.42%)	
occurrences (all)	38	51	
Pharyngitis			
subjects affected / exposed	8 / 113 (7.08%)	5 / 111 (4.50%)	
occurrences (all)	12	7	
Sinusitis			
subjects affected / exposed	4 / 113 (3.54%)	6 / 111 (5.41%)	
occurrences (all)	6	9	
Upper respiratory tract infection			
subjects affected / exposed	14 / 113 (12.39%)	10 / 111 (9.01%)	
occurrences (all)	20	17	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 October 2010	Throughout the protocol, this amendment allowed for the use of historical x-rays in order to comply with local law (as directed by the German Federation of Radiation Control) to limit the use of radiation exposure among the German population. X-rays obtained within 12 months of screening and found to acceptable as determined by central radiologist were permitted.
05 April 2011	In this amendment, under section schedule of activities, added assessment for IBD, psoriasis, uveitis; Clarified timing/order of imaging procedures; added fasting glucose at Baseline, Visits(V) 6, 11, and 16; Clarified visit windows ±4 days for V3-7, ±7 days for V8-17; Clarified collection period for AEs/SAEs and Clarified eligibility regarding Baseline lab values. In the introduction, changed single reference safety document from Core Data Sheet to Investigator Brochure. Under section, objectives/endpoints: Clarified secondary objective is inflammation of MRI of the spine at 12 weeks; Changed primary endpoint from proportion of subjects at 12 weeks who meet ASAS 20 to ASAS 40. Adjusted secondary endpoints to measure ASAS 40 at additional time points, deleted proportion of subjects who achieve ASAS 50 and ASAS 70; Clarified secondary endpoint to measure dactylitis, along with enthesitis; Clarified time points for measurement of exploratory endpoints. Under section for eligibility Criteria: Clarified definition of axial spondyloarthritis diagnosis; Clarified BASDAI 4 required at screening visit; Increased upper age of eligible subjects to less than 50 to coincide with ASAS criteria; Clarified use of tumor necrosis factor alpha inhibitors (added immunosuppressants), for IBD and conditions other than IBD; Clarified timeframes regarding IBD and uveitis episodes; Allowed for the use of historical x-rays (obtained within 4 months of screening) with sacroiliitis grade 0 1 unilaterally or grade 0 bilaterally; Clarified eligibility regarding TB; Clarified timing of active infections; Clarified definition of participation in other studies; Added that when required by Health Authorities, local HIV testing must be performed to determine eligibility. Other changes were made to sections such as study treatments, procedures and adverse event reporting and appendices.
09 May 2011	In this amendment, the final visit (V17) must be an in person visit instead of a telephone call follow up and clarified withdrawal criteria regarding investigator decision.
25 June 2012	In this amendment, global amendment for new protocol template which now included Germany specific requirements and the summary of changes were updated list of abbreviations; clarified eligibility criteria, clarified definition of "legal representative", Added wording to state that medication errors are reportable events and must be documented accordingly in the CRF, Added examples of medication errors, Added language around lack of compliance with protocol, Clarified adverse event information around ongoing safety reviews conducted by the Sponsor, any non-serious adverse event that is determined by the Sponsor to be serious will be reported by the Sponsor as an SAE. Extended investigator reporting SAE requirements to report SAEs if they become aware of them any time after the active reporting period, Added drug abuse and drug dependency to examples of AEs, Added medication error to signs and symptoms of an adverse event, Expanded the bullet in Serious Adverse Event section regarding "results in persistent or significant disability", Clarified the criteria for laboratory abnormalities that require further evaluation in the context of potential cases of drug induced liver injury; Clarified that generally the facts (evidence) or arguments to suggest a causal relationship should be provided by the investigator. Changes to exposure during pregnancy were made to improve clarity. Editorial changes were made to this section were made to data handling and record keeping section, Clarified informed consent process language (changed legally acceptable representative to legal representative) and clarified the communication of results.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported