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PROPRIETARY DRUG NAME® / GENERIC DRUG NAME: Enbrel® / Etanercept

PROTOCOL NO.: 0881A3-403 (B1801005)

PROTOCOL TITLE: A Multicentre, Double-Blind, Placebo-Controlled, Randomised Study of Etanercept in the Treatment of Adult Patients With Active, Severe and Advanced Axial Ankylosing Spondylitis

Study Centers: A total of 21 centers took part in the study and enrolled subjects; 16 in France, 2 in Germany, 2 in Hungary and 1 in Netherlands.

Study Initiation Date and Final Completion Date: January 2007 to May 2009

Phase of Development: Phase 4

Study Objectives:

The primary objective of the study was to compare the efficacy of etanercept (50 mg, once weekly) with that of placebo in adults with active, severe and advanced ankylosing spondylitis (AS, as defined by the Modified New York criteria) at Week 12.

The secondary objectives of the study were to determine:

- The efficacy of etanercept compared with that of placebo at Weeks 2, 4, and 8.
- The efficacy of the original etanercept group from Baseline to Week 24.
- The change in efficacy of the original placebo group from Week 12 to Week 24 (the efficacy of the original etanercept group was analyzed separately from the original placebo group even though both groups were treated with etanercept for the second 12 weeks).
- The safety of etanercept in this subject population by analyzing safety data for all subjects receiving at least 1 dose of test article.

METHODS

Study Design: This multicenter, double-blind, placebo-controlled, randomized study evaluated the efficacy of etanercept 50 mg once weekly in the treatment of adult subjects with active, severe and advanced axial AS. Eligible subjects were randomly assigned to receive either etanercept 50 mg or placebo, subcutaneously (SC), once weekly. Evaluations were performed at Screening, Baseline, and Weeks 2, 4, 8, and 12. The use of placebo as a

control was necessary to allow a valid comparison and to provide a quantitative assessment of effect. Subjects participated in the study for approximately 30 weeks, beginning with a screening period lasting up to 6 weeks. Following the 12-week randomized controlled period (12-week randomized controlled trial [RCT]), all subjects who completed this study period were proposed to continue with etanercept in a 12-week open-label extension (12-week OLE). Subjects who discontinued from the study during the first 12 weeks were not eligible for the 12-week OLE. Evaluations in this second part of the study were performed at Weeks 14, 18, and 24 for all subjects. A follow-up telephone call was required approximately 15 days after completing study treatment to assess for adverse events (AEs). The study flowchart is presented in Table 1.

Table 1. Study Flowchart

Study Procedures	Double-blind Placebo Controlled Period				Open Period	
	Screening[a]	Baseline Week 0	Weeks 2, 4, 8[b]	Week 12 or Early Discontinuation Visit[b]	Week 14, 18, 24 or Early Discontinuation Visit[b]	Follow-Up Visit[c]
Visit window			±3 days	±3 days	±3 days	
Signed informed consent	X					
Medical history	X	X				
Inclusion/exclusion	X	X				
Record prior/concomitant medications	X	X	X	X	X	
Adverse events	X	X	X	X	X	X
General physical examination	X	X	X	X	X	
Vital signs	X	X	X	X	X	
Subject assessment of extra-spinal and extra-articular involvement	X					
Chest x-ray film[d]	X					
Spinal x-ray film[d] (AP and lateral)/pelvic x-ray film[d]	X					
Score mSASSS, score SASSS, BASRI-hip index		X				
Patient global assessment		X	X	X	X	
Physician global assessment		X	X	X	X	
Nocturnal and total back pain		X	X	X	X	
BASFI		X	X	X	X	
BASDAI	X	X	X	X	X	
BAS-G		X	X	X	X	
BASMI and chest expansion test		X	X	X	X	
Respiratory function tests		X		X		
ASQoL questionnaire		X		X		
Patient physical demanding activities assessment		X	X	X	X	
MCII/PASS			X	X	X	
HLA B27[e]		X				
Serum or urinary pregnancy test[f]	X	X				
Chemistry/haematology/urinalysis	X	X	X	X	X	
C-reactive protein, ESR	X	X	X	X	X	
Dispense test article/diary card		X	X[g]	X[h]	X[i]	

Table 1. Study Flowchart

AP = antero posterior; ASQoL = ankylosing spondylitis quality of life; BASDAI = Bath Ankylosing Spondylitis Disease Activities Index; BASFI = Bath Ankylosing Spondylitis Functional Index; BAS-G = Bath Ankylosing Spondylitis – Global Score; BASMI = Bath Ankylosing Spondylitis Metrology Index; BASRI-hip = Bath Ankylosing Spondylitis Radiological Hip Index; HLA = human leukocyte antigen; ESR = erythrocyte sedimentation rate; MCII = minimum clinically important improvement; mSASSS = modified Stoke Ankylosing Spondylitis Spine Score; PASS = Patient Acceptable Symptom State; SASSS = Stoke Ankylosing Spondylitis Spinal Score.

a. Not >6 weeks before the Baseline Visit.
b. Visits could be scheduled up to 3 days before or after Prescheduled Visit.
c. Evaluations performed to follow-up on adverse events, approximately 15 days after last dose.
d. Chest x-ray film within 1 month of prestudy screening. Spinal and pelvic x-ray films within 1 year of prestudy screening.
e. Waived if results were known and copy of laboratory report was in source documents.
f. If woman of childbearing potential. A serum pregnancy test was to be performed at Screening and a urinary pregnancy test was to be performed at Baseline. If any urinary pregnancy test was positive, a serum pregnancy test was to be performed.
g. Not needed at Week 2.
h. Not needed for early Termination Visit.
i. Not needed at Week 14 and at Week 24 or in case of early termination.

Number of Subjects (Planned and Analyzed): A total of 80 subjects were planned (40 in the etanercept group and 40 in the placebo group). Ninety-five (95) subjects were screened, 13 subjects were not randomized and 82 subjects (42 in France, 23 in Germany, 16 in Hungary and 1 in the Netherlands) were randomly assigned to receive test article in the study for a 12-week double-blind RCT (39 subjects received etanercept and 43 subjects received placebo). Five subjects (1 in the etanercept group and 4 in the placebo group) discontinued from the study during the 12-week RCT and the remaining 77 subjects who completed this 12-week period (38 subjects in the etanercept group and 39 in the placebo group) were included in the 12-week OLE with etanercept only.

Diagnosis and Main Criteria for Inclusion: Subjects between the age of 18 and 70 years with active and severe axial ankylosing spondylitis having ankylosing spondylitis refractory to standard anti-rheumatic treatment were enrolled in the study. Subjects with prior exposure to any tumor necrosis factor (TNF)-inhibitor, including etanercept, or disease-modifying anti-rheumatic drugs (DMARDs, other than hydroxychloroquine, methotrexate and sulphasalazine) within 4 weeks of study drug initiation, or whose dose of non-steroidal anti-inflammatory drugs (NSAIDs) was changed within 2 weeks of study drug initiation were excluded from the study. All women of childbearing potential had to have a negative serum β-human chorionic gonadotropin (β-HCG) pregnancy test at Screening. Sexually active men and women had to use a reliable form of contraception during the study.

Study Treatment: Etanercept was supplied in vials as a sterile lyophilized powder containing 50-mg of etanercept. Matching placebo injections were used to maintain the integrity of the double-blind design. The diluent for rehydratation of etanercept/placebo was sterile water for injection provided in pre-filled syringes.

Subjects were randomly assigned to 1 of the 2 treatment groups for 12 weeks in the RCT; Group A received etanercept 50-mg SC injections once weekly and Group B received placebo SC injections once weekly. All subjects who completed the 12-week RCT were proposed to continue with etanercept 50 mg once weekly in the 12-week OLE.

Test article SC injections were administered at approximately the same time of the day (±4 hours) and the same day of the week. Each dose of test article was administered as 1 SC injection. Alternate sites (arms, thighs, abdomen, or left/right) were used with each administration. Site personnel instructed the subject (or designee) on proper sterile technique and on the reconstitution and administration of test article. The first dose of test article was reconstituted and administered by site personnel while the subject (or designee) observed.

Efficacy Endpoints:

The primary efficacy endpoint was the normalized net incremental area under the curve (AUC) between randomization and Week 12 for the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). The BASDAI consists of six 100 mm horizontal visual analog scales (VAS) to measure severity of fatigue, spinal and peripheral joint pain, localized tenderness, and morning stiffness. The final BASDAI score (computed BASDAI score in statistical tables) has a range of 0 to 100.

The secondary efficacy endpoints were:

- The response at Weeks 2, 4, 8 and 12 (RCT), and at Weeks 14, 18 and 24 (OLE), defined as at least a 50% improvement (decrease) from Baseline in the BASDAI (measured on a 100 mm VAS).

- The Assessment in Ankylosing Spondylitis (ASAS) 20, ASAS 50 and ASAS 70 responses at Weeks 2, 4, 8, and 12 (RCT), and at Weeks 14, 18 and 24 (OLE).

- Partial remission at Weeks 2, 4, 8, and 12 (RCT), and at Weeks 14, 18 and 24 (OLE), defined as: value <20 (on a scale of 0 to 100 mm) in each of the following 4 domains:

  - VAS patient global assessment;

  - VAS pain score;

  - Bath Ankylosing Spondylitis Functional Index (BASFI) score;

  - BASDAI-two morning stiffness-related scores.

- Patient Global Assessment (VAS), Physician Global Assessment, nocturnal and total back pain, BASFI score and its independent components, BASDAI score and its independent components, and the Bath Ankylosing Spondylitis Global score (BAS-G) and its individual components at Baseline, Weeks 2, 4, 8, and 12 (RCT), and at Weeks 14, 18 and 24 (OLE).

- Respiratory function tests vital capacity (VC), forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), the ratio FEV_1/FVC, and the percentage of predicted values of VC, FVC and FEV_1 at Baseline and Week 12.

- Spinal mobility measured with the Bath Ankylosing Spondylitis Metrology Index (BASMI-10), its independent components and with the chest expansion test at Baseline, Weeks 2, 4, 8, and 12 (RCT), and at Weeks 14, 18 and 24 (OLE).

- The ability or/and the easiness to perform physically demanding activities evaluated by a self-assessment instrument at Baseline, Weeks 2, 4, 8, and 12 (RCT), and at Weeks 14, 18 and 24 (OLE).

- Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level at Baseline, and the percentage of subjects with normal and abnormal CRP, at Weeks 2, 4, 8, and 12 (RCT), and at Weeks 14, 18 and 24 (OLE).

- The minimum clinically important improvement (MCII) and the Patient Acceptable Symptom State (PASS) at Weeks 2, 4, 8 and 12 (RCT), and at Weeks 14, 18 and 24 (OLE).

Safety Evaluations: The safety of etanercept was determined using the following assessments: monitoring of AEs, withdrawal due to AEs, concomitant medications, laboratory test results, vital signs, and physical examinations.

Statistical Methods:

Populations For the First 12-Week RCT: The population of primary interest for efficacy analyses was the modified intent-to-treat (mITT) population, which included all randomized subjects who received at least 1 dose of blinded test article. In addition, analyses were performed on the intent-to-treat (ITT) population, which included all randomized subjects. The population of interest for safety analyses of the first 12 week RCT was the mITT population.

Populations For the 12-Week OLE: The population of interest for the efficacy and safety analyses was the "open label population", which included all subjects who received at least 1 dose of open test article (etanercept).

The normalized net incremental AUC between randomization and Week 12 was computed and analyzed using an analysis of covariance (ANCOVA) with treatment as a factor and Baseline as a covariate.

The absolute change from Baseline to Week 12 was computed and analyzed using a mixed model ANCOVA and an auto-regressive correlation structure, with treatment groups, visits and their interaction as fixed factors and Baseline value as a covariate.

For binary efficacy criteria, a generalized estimating equations model, using a logit link, a binomial distribution and an auto-regressive correlation structure, with treatment groups, visits and their interaction as fixed factors, was used.

For all continuous efficacy criteria, the absolute changes from Baseline to Week 24 were computed and described for subjects originally in the etanercept group and subjects originally in the placebo group. For all binary efficacy criteria, a descriptive analysis was performed.

RESULTS

Subject Disposition and Demography: Ninety-five (95) subjects were screened and 13 of these subjects were not randomized. Of the 82 subjects randomly assigned to receive test article in the 12-week RCT, 39 subjects received etanercept and 43 subjects received placebo. Five (5) subjects (1 in the etanercept group and 4 in the placebo group) discontinued from the study during the 12-week RCT. Seventy-seven (77) subjects who completed this 12 week period (38 subjects in the etanercept group and 39 in the placebo group) were included in the 12-week OLE with etanercept only. During the 12 week OLE, 3 subjects discontinued from the study (2 in the original etanercept group and 1 in the original placebo group). All 82 randomized subjects were included in the ITT, mITT and safety populations. The disposition of subjects is presented in Table 2.

Table 2. Disposition of Subjects

Conclusion Status Reason	50 mg/week Etanercept n (%)	Placebo n (%)	Total n (%)
12-Week Randomized Controlled Trial			
Total	39 (100%)	43 (100%)	82 (100%)
Completed	38 (97.4%)	39 (90.7%)	77 (93.9%)
Discontinued	1 (2.6%)	4 (9.3%)	5 (6.1%)
Adverse event	1 (2.6%)	1 (2.3%)	1 (1.2%)
Investigator request: lack of efficacy	0 (0.0%)	1 (2.3%)	2 (2.4%)
Investigator request: subject lost to follow up	0 (0.0%)	1 (2.3%)	1 (1.2%)
Withdrawal of consent	0 (0.0%)	1 (2.3%)	1 (1.2%)
12-Week Open-Label Extension			
Total	38 (47.6%)	39 (52.4%)	77 (100%)
Completed	36 (94.7%)	38 (97.4%)	74 (96.1%)
Discontinued	2 (5.3%)	1 (2.6%)	3 (3.9%)
Investigator request: subject failed to return to visit	1 (2.6%)	0 (0.0%)	1 (1.3%)
Withdrawal of consent	1 (2.6%)	1 (2.6%)	2 (2.6%)

n = number of subjects meeting criteria.

Demography: The study population consisted of subjects with active, severe, and advanced AS with a mean age of 47.3 years. Most subjects were men (93%). A summary of the subject demography is presented in Table 3.

Table 3. Demographic and Baseline Characteristics, mITT Population

Characteristic	50 mg/week Etanercept N=39	Placebo N=43	Total N=82
Age, years			
Mean (±SD)	46.2 (±10.8)	48.2 (±10.0)	47.3 (±10.4)
Gender, n (%)			
Male	37 (94.87%)	39 (90.70%)	76 (92.68%)
Female	2 (5.13%)	4 (9.30%)	6 (7.32%)

mITT = modified intent-to-treat; N = number of subjects; n = number of subject with specified criteria; SD = standard deviation.

Enrolled subjects had AS and the mean AS duration (± standard deviation [SD]) since diagnosis was 15.9 years (±10.4 years). Human leukocyte antigen (HLA)-B27 was positive in 67 subjects (82.7%). The mean number (±SD) of different NSAIDs received since diagnosis of AS was 3.8 (±2.6). A summary of the medical history related to AS is presented in Table 4 and Table 5.

Table 4. Medical History Related to Ankylosing Spondylitis (1/2), mITT Population

Characteristic	p-value[a]	50 mg/week Etanercept N=39	Placebo N=43	Total N=82
Duration[b] since first symptoms of axial involvement, years				
N		39	42	81
Mean (±SD)	0.079	18.8 (±9.8)	23.0 (±11.1)	21.0 (±10.6)
Median		16.0	23.0	20.1
Min; max		2.5; 42.0	3.0; 49.0	2.5; 49.0
Duration[b] since first symptoms of peripheral arthritis, years				
N		18	19	37
Mean (±SD)	0.438	11.0 (±8.9)	14.0 (±13.5)	12.5 (±11.4)
Median		10.0	6.0	10.0
Min; max		1.1; 34.0	0.6; 38.0	0.6; 38.0
Duration[b] since first symptoms of enthesiopathy, years				
N		11	18	29
Mean (±SD)	0.119	9.4 (±7.7)	17.0 (±14.2)	14.1 (±12.6)
Median		11.0	11.0	11.0
Min; max		0.5; 29.0	0.7; 39.0	0.5; 39.0
Duration[b] since first symptoms of extra-articular features, years				
N		13	19	32
Mean (±SD)	0.145	11.7 (±9.0)	17.4 (±11.7)	15.1 (±10.9)
Median		8.7	20.0	12.5
Min; max		0.9; 26.0	0.3; 35.9	0.3; 35.9
Duration[b] since first symptoms of axial involvement, or peripheral arthritis, or enthesiopathy or extra-articular features, years				
N		39	42	81
Mean (±SD)	0.118	19.9 (±10.0)	23.6 (±10.9)	21.9 (±10.5)
Median		19.0	23.0	22.0
Min; max		2.5; 42.0	5.0; 49.0	2.5; 49.0
Duration[b] since diagnostic of AS, years				
N		39	43	82
Mean (±SD)	0.082	13.8 (±9.9)	17.8 (±10.6)	15.9 (±10.4)
Median		13.0	16.0	14.2
Min; max		0.1; 36.0	1.2; 44.0	0.1; 44.0
HLA-B27				
Positive	0.561	31 (79.49%)	36 (85.71%)	67 (82.72%)
Negative		8 (20.51%)	6 (14.29%)	14 (17.28%)
Number of different NSAIDs received by subjects since diagnosis of AS, n (%)				
N		39	43	82
Mean (±SD)	0.093	3.31 (±1.62)	4.26 (±3.12)	3.80 (±2.55)
Median		3.00	4.00	3.00
Min; max		2.00; 10.00	2.00; 20.00	2.00; 20.00
2		15 (38.46%)	12 (27.91%)	27 (32.93%)
3		11 (28.21%)	9 (20.93%)	20 (24.39%)
4		6 (15.38%)	8 (18.60%)	14 (17.07%)
5		4 (10.26%)	8 (18.60%)	12 (14.63%)

Table 4. Medical History Related to Ankylosing Spondylitis (1/2), mITT Population

Characteristic	p-value[a]	50 mg/week Etanercept N=39	Placebo N=43	Total N=82
6		2 (5.13%)	1 (2.33%)	3 (3.66%)
7		0	1 (2.33%)	1 (1.22%)
8		0	1 (2.33%)	1 (1.22%)
9		0	1 (2.33%)	1 (1.22%)
10		1 (2.56%)	1 (2.33%)	2 (2.44%)
20		0	1 (2.33%)	1 (1.22%)

AS = ankylosing spondylitis; HLA = human leukocyte antigen; mITT = modified intent-to-treat; N = number of subjects; n = number of subject with specified criteria; NSAIDs = non-steroidal anti-inflammatory drugs; SD = standard deviation.
a. Analysis of variance (ANOVA) for continuous criteria. Fisher Exact Test for qualitative criteria.
b. Duration from the date of event to the date of Screening Visit.

Fifty-two (52; 63.4%) subjects had at least 1 medical history related to AS. Thirty-one (31; 37.8%) subjects had a peripheral arthritis. A summary of the medical history related to AS is presented in Table 5.

Table 5. Medical History Related to Ankylosing Spondylitis (2/2), mITT Population

Characteristic	p-value[a]	50 mg/week Etanercept N=39	Placebo N=43	Total N=82
Medical history related to AS	0.820	24 (61.54%)	28 (65.12%)	52 (63.41%)
Cutaneous psoriasis	1.000	4 (10.26%)	5 (11.63%)	9 (10.98%)
Ungueal psoriasis	1.000	1 (2.56%)	2 (4.65%)	3 (3.66%)
Crohn's disease	1.000	1 (2.56%)	1 (2.33%)	2 (2.44%)
Colitis	0.362	1 (2.56%)	4 (9.30%)	5 (6.10%)
Uveitis	0.637	13 (33.33%)	12 (27.91%)	25 (30.49%)
Heel pain	0.806	10 (25.64%)	13 (30.23%)	23 (28.05%)
Peripheral arthritis	0.497	13 (33.33%)	18 (41.86%)	31 (37.80%)
Urethritis, colpitis/cervicitis	0.476	1 (2.56%)	0 (0.00%)	1 (1.22%)
Reiter's syndrome	NA	0 (0.00%)	0 (0.00%)	0 (0.00%)
'Sausage-like' finger or toe	1.000	2 (5.13%)	3 (6.98%)	5 (6.10%)
Other medical history related to AS[b]	1.000	1 (2.56%)	1 (2.33%)	2 (2.44%)

AS = ankylosing spondylitis; mITT = modified intent-to-treat; N = number of subjects; NA = not applicable.
a. Analysis of variance (ANOVA) for continuous criteria, Fisher Exact Test for qualitative criteria.
b. One subject (etanercept group) had a rectocolitis (resolved) and another subject (placebo group) had an enthesitis of ischium (resolved).

Efficacy Results:

In this report, the term “adjusted mean” makes reference to a mean derived from any ANCOVA or repeated measure model. The term “adjusted change from Baseline” makes reference to an adjusted mean coming from an analysis on change from Baseline and the term “adjusted difference” makes reference to the difference between two adjusted means.

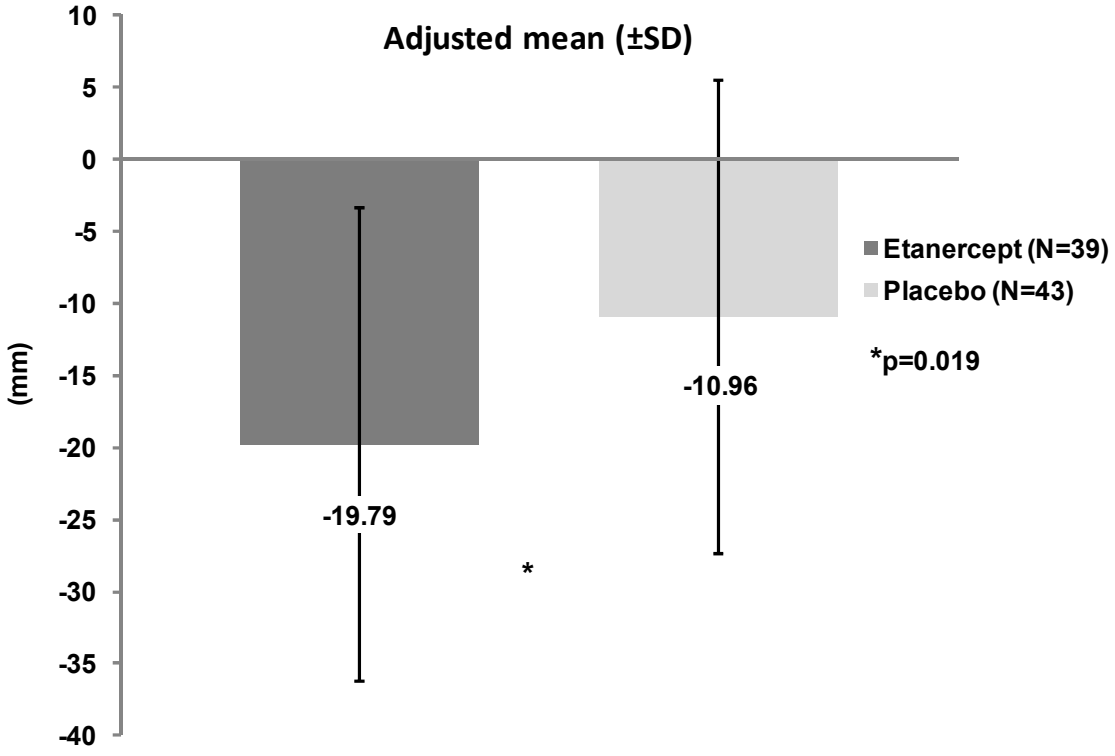
Primary Efficacy Parameter:

The primary endpoint of this study was the normalized net incremental AUC between randomization and Week 12 for the BASDAI.

The BASDAI decrease observed from Baseline to Week 12 was statistically higher in the etanercept group in comparison to the placebo group (adjusted means: -19.79 mm; 95% confidence interval [CI]=[-25.03; -14.54] versus -10.96 mm; 95% CI=[-15.95; -5.97]; adjusted difference: -8.83 mm; 95% CI=[-16.15; -1.51]; p=0.019).

Results of the normalized net incremental AUC for BASDAI are summarized in Figure 1.

Figure 1. Normalized Net Incremental AUC for BASDAI, mITT Population



*: From a mixed model ANCOVA.
ANCOVA = analysis of covariance; AUC = area under the curve; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; mITT = modified intent-to-treat; N = number of subjects; SD = standard deviation.

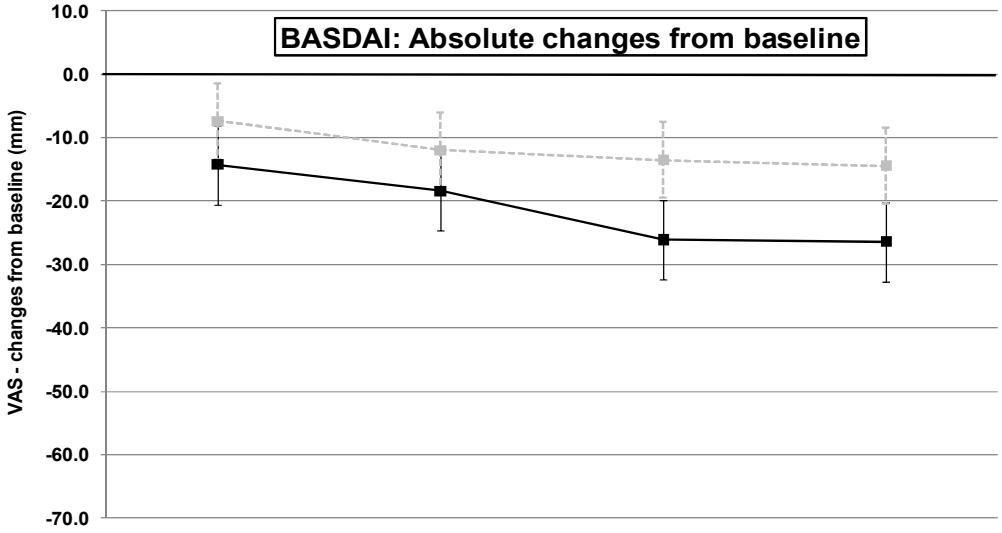
Secondary Efficacy Endpoints:

Changes from Baseline of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI):

The absolute change from Baseline to Week 12 was statistically higher in the etanercept group (adjusted means: -26.38 mm; 95% CI=[-32.64; -20.12]) than in the placebo group (-14.43 mm; 95% CI=[-20.39; -8.47]) (p=0.008). The absolute change from Baseline to Week 8 was also statistically higher in etanercept group (adjusted means: -26.06 mm;

95% CI=[-32.31; -19.80]) than in placebo group (-13.51 mm; 95% CI=[-19.46; -7.55]) (p=0.005). No statistically significant difference between treatment groups was observed before Week 8 (at Week 2 and Week 4 Evaluation Visits). Mean BASDAI changes from Baseline are summarized in Figure 2.

Figure 2. Changes From Baseline of BASDAI, mITT Population



Adjusted mean [95% CI]	W2-baseline	W4-baseline	W8-baseline	W12-baseline
— Etanercept (N=39)	-14.25 [-20.51;-7.99]	-18.41 [-24.67;-12.15]	-26.06 [-32.31;-19.8]	-26.38 [-32.64;-20.12]
---- Placebo (N=43)	-7.39 [-13.34;-1.43]	-11.97 [-17.92;-6.01]	-13.51 [-19.46;-7.55]	-14.43 [-20.39;-8.47]
p-value[a]	0.122	0.145	0.005	0.008

BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; CI = confidence interval; mITT = modified intent-to-treat; N = number of subjects; VAS = Visual Analog Scale; W = week.
a From a mixed model analysis of covariance.

The change from Baseline in the BASDAI during the RCT and OLE (unadjusted) is summarized by visit in Table 6.

Table 6. Changes From Baseline of BASDAI During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
Baseline, mm		
Mean (±SD)	63.7 (±11.8)	59.3 (±14.3)
Median	64.5	55.3
Min; max	37.4; 89.2	40.4; 88.4
Absolute changes from Baseline, mm		
Week 2 - Baseline		
Mean (±SD)	-14.91 (±18.88)	-8.19 (±18.06)
Median	-9.82	-4.36
Min; max	-58.80; 19.40	-52.40; 26.34
Week 4 - Baseline		
Mean (±SD)	-19.19 (±19.84)	-12.13 (±18.68)
Median	-18.13	-8.53
Min; max	-59.24; 11.70	-57.78; 32.40
Week 8 - Baseline		
Mean (±SD)	-27.03 (±20.62)	-14.00 (±20.57)
Median	-26.69	-10.54
Min; max	-65.18; 10.13	-61.57; 26.90
Week 12 - Baseline		
Mean (±SD)	-27.37 (±23.81)	-15.02 (±19.96)
Median	-27.41	-9.95
Min; max	-70.17; 18.01	-59.50; 14.92
Week 14 - Baseline		
Mean (±SD)	-29.26 (±24.59)	-27.41 (±21.64)
Median	-30.22	-22.20
Min; max	-74.22; 18.01	-75.11; 15.07
Week 18 - Baseline		
Mean (±SD)	-34.20 (±23.39)	-28.21 (±23.87)
Median	-37.23	-25.42
Min; max	-71.28; 16.97	-78.29; 12.76
Week 24 - Baseline		
Mean (±SD)	-37.62 (±22.37)	-28.62 (±24.26)
Median	-40.94	-30.58
Min; max	-75.48; 16.97	-75.49; 12.52

BASDAI = Bath Ankylosing Spondylitis Disease Activities Index; max = maximum; min = minimum; n = number of subjects; SD = standard deviation.

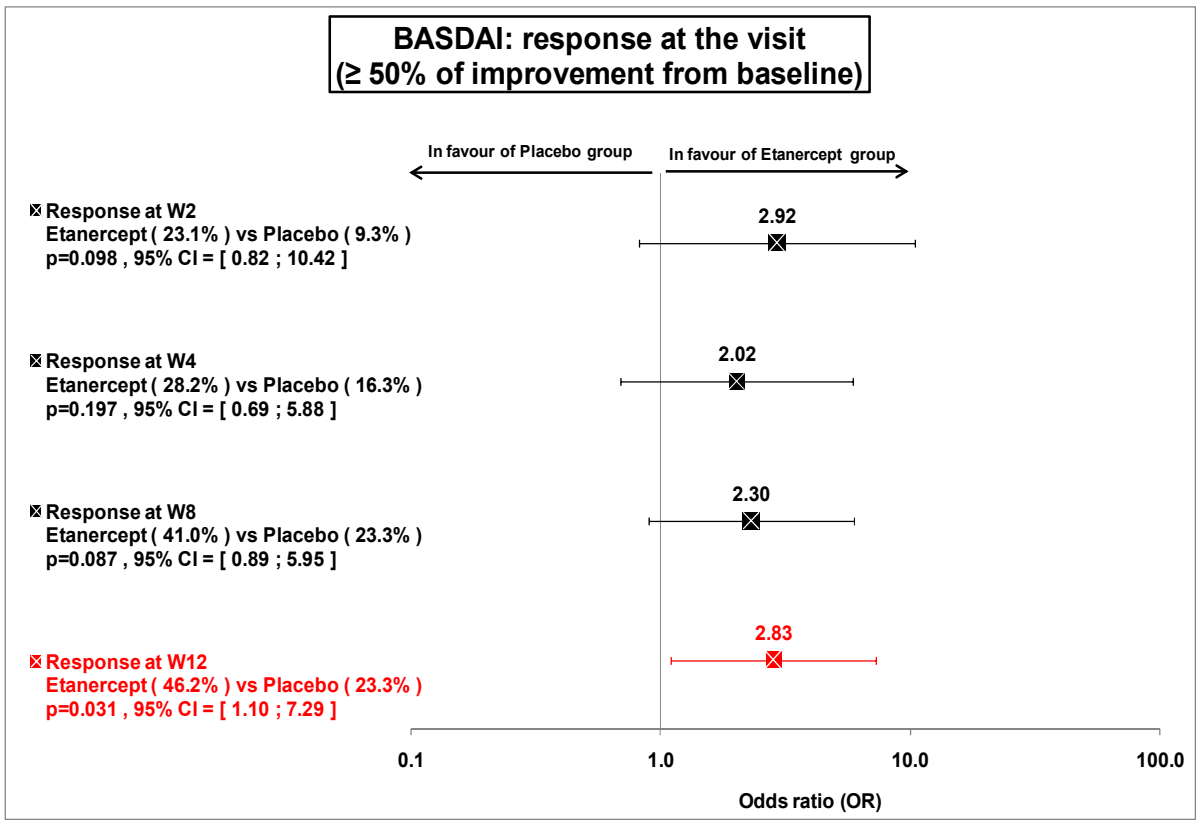
a. Subjects received etanercept 50 mg/week for 24 weeks.

b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

Response Rates of the BASDAI:

The 50% response rate at Week 12 was statistically higher in etanercept group (46.2% of subjects) than in placebo group (22.3% of subjects) (odds ratio [OR]=2.83; 95% CI=[1.10; 7.29]; p=0.031). No statistically significant difference between treatment groups was observed before Week 12 (Weeks 2, 4, and 8). Results of the BASDAI 50% response rates during the 12-week RCT are summarized in Figure 3.

Figure 3. Response Rates of the BASDAI: At Least 50% Improvement From Baseline, mITT Population



p-value: From a generalized estimated equations model.
BASDAI = Bath Ankylosing Spondylitis Disease Activities Index; CI=confidence interval of the odds ratio; mITT = modified intent-to-treat; SD = standard deviation; vs = versus; W = week.

The 50% response rate of the BASDAI during the RCT and OLE (unadjusted) is summarized by visit in Table 7.

Table 7. Response Rates of the BASDAI During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
BASDAI, mm		
Response rates (50% improvement from Baseline), n (%)		
Week 2	9 (23.68%)	4 (10.26%)
Week 4	11 (28.95%)	7 (17.95%)
Week 8	16 (42.11%)	10 (25.64%)
Week 12	18 (47.37%)	10 (25.64%)
Week 14	20 (52.63%)	17 (44.74%)
Week 18	25 (65.79%)	21 (53.85%)
Week 24	25 (65.79%)	19 (48.72%)

BASDAI = Bath Ankylosing Spondylitis Disease Activities Index; N = number of subjects; n = number of subject with specified criteria.
a. Subjects received etanercept 50 mg/week for 24 weeks.
b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

BASDAI independent components at Baseline and Weeks 2, 4, 8 and 12 are presented in Table 8. Subject rating was done on a VAS mm. Components 1-5: 0= none, 100= extreme; Component 6: 0=0 hour 100=2 hours or more.

Table 8. Bath Ankylosing Spondylitis Disease Activities Index (BASDAI): Independent Components at Weeks 2, 4, 8 and 12 (No LOCF)

Components	Treatment		Total (N=82)
	Etanercept (N=39)	Placebo (N=43)	
How would you describe the overall level of fatigue / tiredness you have experienced?: BASDAI 1			
Baseline (LOCF)			
n	39	43	82
Mean (±SD)	68.2 (±17.5)	61.9 (±15.7)	64.9 (±16.8)
95% CI	62.5; 73.8	57.1; 66.8	61.2; 68.6
Week 2			
n	38	40	78
Mean (±SD)	56.6 (±24.0)	55.8 (±20.9)	56.2 (±22.3)
95% CI	48.7; 64.5	49.1; 62.5	51.2; 61.2
Week 4			
n	38	42	80
Mean (±SD)	51.4 (±25.0)	54.2 (±23.1)	52.8 (±23.9)
95% CI	43.1; 59.6	47.0; 61.4	47.5; 58.2
Week 8			
n	38	39	77
Mean (±SD)	44.4 (±25.2)	50.9 (±23.6)	47.7 (±24.4)
95% CI	36.2; 52.7	43.3; 58.5	42.2; 53.2
Week 12			
n	38	39	77
Mean (±SD)	43.9 (±30.4)	48.5 (±25.8)	46.3 (±28.1)
95% CI	33.9; 53.9	40.1; 56.9	39.9; 52.6
How would you describe the overall level of AS neck, back or hip pain you have had?: BASDAI 2			
Baseline (LOCF)			
n	39	43	82
Mean (±SD)	73.0 (±13.3)	68.1 (±15.3)	70.5 (±14.5)
95% CI	68.7; 77.3	63.4; 72.9	67.3; 73.7
Week 2			
n	38	40	78
Mean (±SD)	53.9 (±25.0)	57.6 (±23.2)	55.8 (±24.0)
95% CI	45.7; 62.1	50.2; 65.0	50.4; 61.2
Week 4			
n	38	42	80
Mean (±SD)	51.5 (±26.0)	55.0 (±25.3)	53.4 (±25.5)
95% CI	43.0; 60.0	47.2; 62.9	47.7; 59.0
Week 8			
n	38	39	77
Mean (±SD)	41.4 (±26.4)	52.1 (±21.9)	46.8 (±24.7)
95% CI	32.8; 50.1	45.0; 59.2	41.2; 52.4
Week 12			
n	38	39	77
Mean (±SD)	41.0 (±28.1)	52.0 (±23.1)	46.6 (±26.1)
95% CI	31.8; 50.2	44.5; 59.5	40.7; 52.5
How would you describe the overall level of pain / swelling in joints other than neck, back or hips you have had?: BASDAI 3			
Baseline (LOCF)			
n	39	43	82
Mean (±SD)	49.3 (±25.4)	45.3 (±29.8)	47.2 (±27.7)
95% CI	41.1; 57.5	36.1; 54.4	41.1; 53.3
Week 2			

Table 8. Bath Ankylosing Spondylitis Disease Activities Index (BASDAI): Independent Components at Weeks 2, 4, 8 and 12 (No LOCF)

Components	Treatment		Total (N=82)
	Etanercept (N=39)	Placebo (N=43)	
n	38	40	78
Mean (±SD)	39.2 (±29.6)	41.7 (±31.2)	40.5 (±30.3)
95% CI	29.5; 48.9	31.7; 51.7	33.7; 47.3
Week 4			
n	38	42	80
Mean (±SD)	37.3 (±28.8)	38.2 (±26.3)	37.8 (±27.4)
95% CI	27.8; 46.8	30.0; 46.5	31.7; 43.9
Week 8			
n	38	39	77
Mean (±SD)	30.1 (±28.5)	40.4 (±26.0)	35.3 (±27.5)
95% CI	20.8; 39.5	32.0; 48.8	29.1; 41.6
Week 12			
n	38	39	77
Mean (±SD)	31.8 (±30.7)	37.9 (±25.6)	34.9 (±28.2)
95% CI	21.7; 41.8	29.6; 46.2	28.5; 41.3
How would you describe the overall level of discomfort you have had from any areas tender to touch or pressure?: BASDAI 4			
Baseline (LOCF)			
n	39	43	82
Mean (±SD)	62.3 (±21.2)	57.2 (±23.5)	59.6 (±22.5)
95% CI	55.5; 69.2	49.9; 64.4	54.7; 64.6
Week 2			
n	38	40	78
Mean (±SD)	42.1 (±29.1)	51.9 (±26.6)	47.1 (±28.1)
95% CI	32.5; 51.6	43.3; 60.4	40.7; 53.4
Week 4			
n	38	42	80
Mean (±SD)	38.3 (±28.1)	41.5 (±26.8)	40.0 (±27.3)
95% CI	29.0; 47.5	33.2; 49.9	33.9; 46.0
Week 8			
n	38	39	77
Mean (±SD)	31.2 (±26.3)	40.7 (±25.1)	36.0 (±26.0)
95% CI	22.6; 39.9	32.5; 48.8	30.1; 41.9
Week 12			
n	38	39	77
Mean (±SD)	28.8 (±27.0)	38.0 (±23.0)	33.4 (±25.3)
95% CI	19.9; 37.7	30.5; 45.4	27.7; 39.2
How would you describe the overall level of morning stiffness you have had from the time you wake up?: BASDAI 5			
Baseline) (LOCF)			
n	39	43	82
Mean (±SD)	70.8 (±18.5)	66.3 (±15.0)	68.4 (±16.8)
95% CI	64.8; 76.8	61.6; 70.9	64.7; 72.1
Week 2			
n	38	40	78
Mean (±SD)	51.3 (±25.9)	55.6 (±21.4)	53.5 (±23.6)
95% CI	42.9; 59.8	48.7; 62.4	48.2; 58.8
Week 4			
n	38	42	80

Table 8. Bath Ankylosing Spondylitis Disease Activities Index (BASDAI): Independent Components at Weeks 2, 4, 8 and 12 (No LOCF)

Components	Treatment		Total (N=82)
	Etanercept (N=39)	Placebo (N=43)	
Mean (±SD)	46.5 (±28.1)	50.7 (±22.7)	48.7 (±25.3)
95% CI	37.2; 55.7	43.6; 57.8	43.0; 54.3
Week 8			
n	38	39	77
Mean (±SD)	38.1 (±27.5)	44.7 (±22.5)	41.5 (±25.1)
95% CI	29.1; 47.2	37.4; 52.0	35.8; 47.2
Week 12			
n	38	39	77
Mean (±SD)	37.8 (±31.1)	44.8 (±22.2)	41.4 (±27.0)
95% CI	27.6; 48.1	37.7; 52.0	35.3; 47.5
How long does your morning stiffness last from the time you wake up?: BASDAI 6			
Baseline (LOCF)			
n	39	43	82
Mean (±SD)	62.1 (±25.3)	52.4 (±25.5)	57.0 (±25.7)
95% CI	53.9; 70.3	44.5; 60.3	51.4; 62.7
Week 2			
n	37	40	77
Mean (±SD)	46.8 (±30.7)	44.0 (±25.9)	45.3 (±28.1)
95% CI	36.6; 57.0	35.7; 52.3	39.0; 51.7
Week 4			
n	38	42	80
Mean (±SD)	42.2 (±31.4)	43.0 (±25.2)	42.7 (±28.2)
95% CI	31.9; 52.6	35.2; 50.9	36.4; 48.9
Week 8			
n	38	39	77
Mean (±SD)	34.6 (±31.5)	43.7 (±23.6)	39.2 (±28.0)
95% CI	24.2; 44.9	36.1; 51.4	32.9; 45.5
Week 12			
n	38	39	77
Mean (±SD)	34.9 (±33.2)	44.7 (±26.6)	39.9 (±30.2)
95% CI	24.0; 45.8	36.1; 53.3	33.0; 46.7
Subscore for morning stiffness (BASDAI subscore)			
Baseline (LOCF)			
n	39	43	82
Mean (±SD)	66.45 (±18.60)	59.34 (±16.72)	62.72 (±17.89)
95% CI	60.42; 72.48	54.19; 64.48	58.79; 66.65
Week 2			
n	38	40	78
Mean (±SD)	49.72 (±26.06)	49.78 (±21.58)	49.75 (±23.71)
95% CI	41.16; 58.29	42.88; 56.68	44.41; 55.10
Week 4			
n	38	42	80
Mean (±SD)	44.34 (±26.67)	46.87 (±22.59)	45.67 (±24.49)
95% CI	35.58; 53.11	39.83; 53.91	40.22; 51.12
Week 8			
n	38	39	77
Mean (±SD)	36.34 (±27.82)	44.22 (±21.66)	40.33 (±25.04)
95% CI	27.19; 45.48	37.20; 51.24	34.64; 46.01

Table 8. Bath Ankylosing Spondylitis Disease Activities Index (BASDAI): Independent Components at Weeks 2, 4, 8 and 12 (No LOCF)

Components	Treatment		Total (N=82)
	Etanercept (N=39)	Placebo (N=43)	
Week 12			
n	38	39	77
Mean (±SD)	36.39 (±30.37)	44.77 (±22.71)	40.63 (±26.92)
95% CI	26.41; 46.37	37.41; 52.13	34.52; 46.74

BASDAI = Bath Ankylosing Spondylitis Disease Activities Index; CI = confidence interval; LOCF = last observation carried forward; N = total number of subjects; n = number of subject analyzed; SD = standard deviation.

BASDAI independent components at Baseline and Weeks 14, 18 and 24 are presented in Table 9.

Table 9. Bath Ankylosing Spondylitis Disease Activities Index (BASDAI): Independent Components at Weeks 14, 18 and 24 (No LOCF)

Components	Treatment	
	Etanercept (N=38)	Placebo (N=39)
How would you describe the overall level of fatigue / tiredness you have experienced?: BASDAI 1		
Baseline (LOCF)		
n	38	39
Mean (±SD)	68.6 (±17.5)	63.2 (±15.8)
95% CI	62.9; 74.3	58.0; 68.3
Week 14		
n	36	38
Mean (±SD)	41.7 (±30.5)	38.3 (±26.6)
95% CI	31.4; 52.0	29.5; 47.0
Week 18		
n	35	38
Mean (±SD)	33.1 (±26.4)	38.9 (±30.4)
95% CI	24.0; 42.2	28.9; 48.9
Week 24		
n	35	37
Mean (±SD)	28.0 (±22.9)	35.3 (±29.4)
95% CI	20.1; 35.9	25.5; 45.1
How would you describe the overall level of AS neck, back or hip pain you have had?: BASDAI 2		
Baseline (LOCF)		
n	38	39
Mean (±SD)	73.2 (±13.4)	67.9 (±15.7)
95% CI	68.8; 77.6	62.8; 73.0
Week 14		
n	36	38
Mean (±SD)	39.9 (±30.4)	35.0 (±25.0)
95% CI	29.6; 50.1	26.8; 43.3
Week 18		
n	35	38
Mean (±SD)	35.1 (±26.0)	35.0 (±28.4)
95% CI	26.2; 44.0	25.7; 44.3
Week 24		
n	35	37
Mean (±SD)	28.2 (±25.2)	30.0 (±26.1)
95% CI	19.5; 36.8	21.3; 38.7
How would you describe the overall level of pain / swelling in joints other than neck, back or hips you have had?: BASDAI 3		
Baseline (LOCF)		
n	38	39
Mean (±SD)	49.9 (±25.4)	47.2 (±29.7)
95% CI	41.6; 58.3	37.5; 56.8
Week 14		
n	36	38
Mean (±SD)	27.0 (±28.8)	28.4 (±24.0)
95% CI	17.3; 36.8	20.5; 36.3
Week 18		
n	35	38
Mean (±SD)	23.8 (±27.0)	26.4 (±27.4)
95% CI	14.5; 33.1	17.4; 35.4
Week 24		

Table 9. Bath Ankylosing Spondylitis Disease Activities Index (BASDAI): Independent Components at Weeks 14, 18 and 24 (No LOCF)

Components	Treatment	
	Etanercept (N=38)	Placebo (N=39)
n	35	37
Mean (±SD)	21.0 (±24.6)	24.9 (±25.1)
95% CI	12.5; 29.4	16.5; 33.3
How would you describe the overall level of discomfort you have had from any areas tender to touch or pressure?: BASDAI 4		
Baseline (LOCF)		
n	38	39
Mean (±SD)	61.3 (±20.5)	57.1 (±23.3)
95% CI	54.6; 68.1	49.5; 64.6
Week 14		
n	36	38
Mean (±SD)	30.0 (±29.7)	29.1 (±24.0)
95% CI	19.9; 40.0	21.2; 36.9
Week 18		
n	35	38
Mean (±SD)	24.1 (±25.3)	28.7 (±27.9)
95% CI	15.4; 32.8	19.6; 37.9
Week 24		
n	35	37
Mean (±SD)	19.3 (±21.7)	25.6 (±24.6)
95% CI	11.9; 26.8	17.5; 33.8
How would you describe the overall level of morning stiffness you have had from the time you wake up?: BASDAI 5		
Baseline (LOCF)		
n	38	39
Mean (±SD)	70.1 (±18.2)	67.5 (±13.9)
95% CI	64.2; 76.1	63.0; 72.0
Week 14		
n	36	38
Mean (±SD)	35.8 (±30.3)	28.5 (±25.0)
95% CI	25.6; 46.1	20.3; 36.7
Week 18		
n	35	38
Mean (±SD)	31.4 (±28.9)	28.6 (±25.7)
95% CI	21.5; 41.4	20.2; 37.0
Week 24		
n	34	37
Mean (±SD)	26.4 (±25.6)	24.7 (±20.8)
95% CI	17.5; 35.4	17.8; 31.7
How long does your morning stiffness last from the time you wake up?: BASDAI 6		
Baseline (LOCF)		
n	38	39
Mean (±SD)	61.1 (±24.9)	54.4 (±25.2)
95% CI	52.9; 69.2	46.2; 62.5
Week 14		
n	36	38
Mean (±SD)	31.3 (±30.5)	27.7 (±25.4)
95% CI	20.9; 41.6	19.4; 36.0

Table 9. Bath Ankylosing Spondylitis Disease Activities Index (BASDAI): Independent Components at Weeks 14, 18 and 24 (No LOCF)

Components	Treatment	
	Etanercept (N=38)	Placebo (N=39)
Week 18		
n	35	38
Mean (±SD)	31.3 (±30.3)	25.7 (±24.9)
95% CI	20.9; 41.7	17.6; 33.9
Week 24		
n	35	37
Mean (±SD)	24.9 (±27.6)	24.4 (±21.6)
95% CI	15.4; 34.4	17.2; 31.6
Subscore for morning stiffness (BASDAI subscore)		
Baseline (LOCF)		
n	38	39
Mean (±SD)	65.61 (±18.09)	60.93 (±15.81)
95% CI	59.67; 71.56	55.80; 66.06
Week 14		
n	36	38
Mean (±SD)	33.55 (±28.12)	28.09 (±24.19)
95% CI	24.03; 43.06	20.14; 36.04
Week 18		
n	35	38
Mean (±SD)	31.38 (±28.30)	27.17 (±24.80)
95% CI	21.66; 41.10	19.02; 35.32
Week 24		
n	35	37
Mean (±SD)	25.40 (±25.38)	24.55 (±20.34)
95% CI	16.69; 34.12	17.77; 31.34

BASDAI = Bath Ankylosing Spondylitis Disease Activities Index; CI = confidence interval; LOCF = last observation carried forward; N = total number of subjects; n = number of subject analyzed; SD = standard deviation.

Patient Global Assessment:

Normalized net incremental AUC between randomization and Week 12: The PGA decrease evaluated using the normalized net incremental AUC was statistically higher in the etanercept group than in the placebo group (p=0.018).

Changes from Baseline to Weeks 2, 4, 8, and 12: No statistically significant difference between treatment groups was observed in the changes from Baseline to Weeks 2, 4 and 12. A statistically significant difference between treatment groups was observed in the changes from Baseline to Week 8 (p=0.004). Results of PGA are summarized in Table 10.

Table 10. Results of the Patient Global Assessment, mITT Population

Characteristic	50 mg/week Etanercept N=39	Placebo N=43	Adjusted Difference	p-value[a]
Normalized net incremental AUC, mm				
Adjusted mean (±SD)	-20.35 (±18.44)	-10.39 (±18.44)	-9.95	0.018
95% CI	-26.23; -14.47	-16.13; -4.66	-18.19; -1.72	
Absolute changes from Baseline, mm				
Week 2 - Baseline				
Adjusted mean (±SD)	-16.90 (±22.29)	-8.36 (±22.29)	-8.54	0.089
95% CI	-23.96; -9.85	-15.24; -1.49	-18.40; 1.33	
Week 4 - Baseline				
Adjusted mean (±SD)	-19.06 (±22.29)	-11.04 (±22.29)	-8.02	0.110
95% CI	-26.11; -12.01	-17.92; -4.16	-17.89; 1.85	
Week 8 - Baseline				
Adjusted mean (±SD)	-25.29 (±22.29)	-10.56 (±22.29)	-14.73	0.004
95% CI	-32.35; -18.24	-17.44; -3.68	-24.60; -4.86	
Week 12 - Baseline				
Adjusted mean (±SD)	-25.79 (±22.29)	-16.52 (±22.29)	-9.27	0.065
95% CI	-32.84; -18.74	-23.40; -9.64	-19.14; 0.59	

AUC = area under the curve; CI = confidence interval; mITT = modified intent-to-treat; N = number of subjects; SD = standard deviation.
a. From a mixed model analysis of covariance.

The change from Baseline in the Patient Global Assessment during the RCT and OLE (unadjusted) is summarized by visit in Table 11.

Table 11. Changes From Baseline of Patient Global Assessment During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
Baseline, mm		
Mean (±SD)	69.1 (±13.8)	66.0 (±14.8)
Median	69.3	66.2
Min; max	37.7; 93.8	41.6; 96.0
Absolute changes from Baseline, mm		
Week 2 - baseline		
Mean (±SD)	-18.03 (±24.72)	-9.15 (±20.94)
Median	-11.03	-3.50
Min; max	-80.95; 18.65	-58.85; 27.50
Week 4 - Baseline		
Mean (±SD)	-20.24 (±26.16)	-11.35 (±23.98)
Median	-14.25	-4.68
Min; max	-80.95; 32.10	-70.20; 23.80
Week 8 - Baseline		
Mean (±SD)	-26.64 (±23.28)	-10.83 (±23.33)
Median	-27.20	-3.95
Min; max	-72.95; 11.45	-58.25; 26.60
Week 12 - Baseline		
Mean (±SD)	-27.15 (±25.40)	-17.26 (±22.09)
Median	-28.13	-13.55
Min; max	-75.05; 33.70	-66.20; 21.75
Week 14 - Baseline		
Mean (±SD)	-31.26 (±27.63)	-31.20 (±28.11)
Median	-33.48	-28.85
Min; max	-91.05; 26.60	-88.65; 15.45
Week 18 - Baseline		
Mean (±SD)	-35.50 (±26.41)	-31.92 (±28.96)
Median	-42.60	-30.18
Min; max	-87.15; 26.60	-88.65; 19.95
Week 24 - Baseline		
Mean (±SD)	-40.70 (±25.79)	-34.19 (±26.36)
Median	-44.80	-29.15
Min; max	-87.15; 26.60	-88.65; 16.85

max = maximum; min = minimum; N = number of subjects; SD = standard deviation.
a. Subjects received etanercept 50 mg/week for 24 weeks.
b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

Physician Global Assessment:

Normalized net incremental AUC between randomization and Week 12: The physician global assessment decrease evaluated using the normalized net incremental AUC was statistically higher in the etanercept group than in the placebo group (p=0.002).

Changes from Baseline to Weeks 2, 4, 8, and 12: The physician global assessment absolute change from Baseline to Week 2 was not statistically significant between both groups. After 4 weeks of treatment, the difference became statistically significant in favor of the etanercept group (p=0.011) and was sustained until the end of the 12-week RCT (Week 8: p=0.003, Week 12: p<0.001). Results of the Physician Global Assessment are summarized in Table 12.

Table 12. Results of the Physician Global Assessment, mITT Population

Characteristic	50 mg/week Etanercept N=39	Placebo N=43	Adjusted Difference	p-value[a]
Normalized net incremental AUC, mm				
Adjusted mean (±SD)	-24.14 (±15.14)	-13.15 (±15.14)	-10.99	0.002
95% CI	-28.97; -19.32	-17.80; -8.50	-17.70; -4.28	
Absolute changes from Baseline, mm				
Week 2 - Baseline				
Adjusted mean (±SD)	-15.77 (±19.29)	-7.43 (±19.29)	-8.33	0.054
95% CI	-21.87; -9.67	-13.31; -1.55	-16.81; 0.15	
Week 4 - Baseline				
Adjusted mean (±SD)	-26.25 (±19.29)	-15.23 (±19.29)	-11.02	0.011
95% CI	-32.35; -20.15	-21.11; -9.35	-19.50; -2.54	
Week 8 - Baseline				
Adjusted mean (±SD)	-28.80 (±19.29)	-16.05 (±19.29)	-12.75	0.003
95% CI	-34.90; -22.70	-21.93; -10.17	-21.23; -4.27	
Week 12 - Baseline				
Adjusted mean (±SD)	-32.62 (±19.29)	-17.32 (±19.29)	-15.29	<0.001
95% CI	-38.72; -26.52	-23.20; -11.44	-23.77; -6.82	

ANCOVA = analysis of covariance; AUC = area under the curve; CI = confidence interval; mITT = modified intent-to-treat; N = number of subjects; SD = standard deviation.
a. From a mixed model ANCOVA.

The change from Baseline for the Physician Global Assessment during the RCT and OLE (unadjusted) is summarized by visit in Table 13.

Table 13. Changes From Baseline of Physician Global Assessment During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
Baseline, mm		
Mean (±SD)	64.3 (±14.8)	62.6 (±11.4)
Median	62.3	65.5
Min; max	34.7; 95.1	35.2; 85.3
Absolute changes from Baseline, mm		
Week 2 - Baseline		
Mean (±SD)	-16.73 (±21.31)	-7.94 (±14.09)
Median	-13.00	-6.88
Min; max	-66.05; 19.60	-41.70; 18.70
Week 4 - Baseline		
Mean (±SD)	-27.49 (±25.47)	-14.84 (±15.77)
Median	-26.23	-11.62
Min; max	-86.35; 18.60	-55.25; 23.85
Week 8 - Baseline		
Mean (±SD)	-30.11 (±23.11)	-16.67 (±18.75)
Median	-32.18	-12.95
Min; max	-75.00; 17.30	-51.45; 10.10
Week 12 - Baseline		
Mean (±SD)	-34.03 (±26.03)	-18.08 (±22.33)
Median	-32.65	-14.67
Min; max	-80.60; 18.00	-63.55; 26.10
Week 14 - Baseline		
Mean (±SD)	-37.66 (±25.78)	-35.57 (±20.51)
Median	-37.88	-33.80
Min; max	-80.00; 25.10	-70.20; 11.00
Week 18 - Baseline		
Mean (±SD)	-43.22 (±19.98)	-37.05 (±21.57)
Median	-42.23	-38.28
Min; max	-78.65; 13.45	-82.65; 11.00
Week 24 - Baseline		
Mean (±SD)	-42.68 (±23.05)	-40.41 (±22.01)
Median	-40.95	-43.10
Min; max	-86.05; 4.85	-81.45; 16.85

max = maximum; min = minimum; N = number of subjects; SD = standard deviation.
a. Subjects received etanercept 50 mg/week for 24 weeks.
b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

Nocturnal Back Pain:

Normalized net incremental AUC between randomization and Week 12: The nocturnal back pain decrease evaluated using the normalized net incremental AUC was statistically higher in the etanercept group than in the placebo group (p=0.039).

Changes from Baseline to Weeks 2, 4, 8, and 12: The nocturnal back pain absolute changes from Baseline to Week 2 and Week 4 were not statistically significant between both groups. After 8 weeks of treatment, the difference became statistically significant in favor of the etanercept group (p=0.014) and was sustained until 12 weeks of treatment (p<0.001).

Results of nocturnal back pain are summarized in Table 14.

Table 14. Results of the Nocturnal Back Pain, mITT Population

Characteristic	50 mg/week Etanercept N=39	Placebo N=43	Adjusted Difference	p-value[a]
Normalized net incremental AUC, mm				
Adjusted mean (±SD)	-23.23 (±20.14)	-13.64 (±20.12)	-9.59	0.039
95% CI	-29.65; -16.81	-19.89; -7.38	-18.69; -0.49	
Absolute changes from Baseline, mm				
Week 2 - Baseline				
Adjusted mean (±SD)	-19.41 (±24.26)	-13.12 (±24.25)	-6.28	0.254
95% CI	-27.09; -11.72	-20.61;- 5.63	-17.13; 4.57	
Week 4 - Baseline				
Adjusted mean (±SD)	-20.90 (±24.26)	-15.72 (±24.25)	-5.17	0.348
95% CI	-28.58; -13.21	-23.21; -8.23	-16.02; 5.68	
Week 8 - Baseline				
Adjusted mean (±SD)	-29.27 (±24.26)	-15.54 (±24.25)	-13.72	0.014
95% CI	-36.95; -21.58	-23.03; -8.05	-24.57; -2.88	
Week 12 - Baseline				
Adjusted mean (±SD)	-32.07 (±24.26)	-12.38 (±24.25)	-19.69	<0.001
95% CI	-39.75; -24.38	-19.87; -4.89	-30.54; -8.84	

ANCOVA = analysis of covariance; AUC = area under the curve; CI = confidence interval; mITT = modified intent-to-treat; N = number of subjects; SD = standard deviation.
a. From a mixed model ANCOVA.

The change from Baseline in nocturnal back pain during the RCT and OLE (unadjusted) is summarized by visit in Table 15.

Table 15. Changes From Baseline of Nocturnal Back Pain During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
Baseline, mm		
Mean (±SD)	68.6 (±20.7)	56.5 (±24.4)
Median	71.3	59.7
Min; max	0.0; 99.2	7.5; 98.4
Absolute changes from Baseline, mm		
Week 2 - Baseline		
Mean (±SD)	-22.26 (±24.41)	-11.50 (±26.30)
Median	-17.40	-6.15
Min; max	-86.35; 11.30	-80.30; 43.90
Week 4 - Baseline		
Mean (±SD)	-23.79 (±27.10)	-13.56 (±29.51)
Median	-20.98	-7.22
Min; max	-88.00; 21.70	-82.90; 55.10
Week 8 - Baseline		
Mean (±SD)	-32.38 (±21.96)	-13.36 (±30.76)
Median	-35.73	-13.23
Min; max	-71.90; 3.65	-84.25; 58.75
Week 12 - Baseline		
Mean (±SD)	-35.26 (±26.93)	-9.95 (±29.58)
Median	-38.45	-9.00
Min; max	-86.35; 10.35	-82.70; 61.00
Week 14 - Baseline		
Mean (±SD)	-36.92 (±29.07)	-27.76 (±28.31)
Median	-39.48	-25.13
Min; max	-96.20; 22.35	-82.80; 57.00
Week 18 - Baseline		
Mean (±SD)	-41.73 (±26.95)	-27.89 (±30.50)
Median	-49.95	-26.18
Min; max	-99.15; 1.85	-95.05; 70.55
Week 24 - Baseline		
Mean (±SD)	-45.26 (±27.34)	-28.44 (±30.46)
Median	-51.75	-27.78
Min; max	-99.15; 20.10	-88.85; 68.35

max = maximum; min = minimum; N = number of subjects; SD = standard deviation.
a. Subjects received etanercept 50 mg/week for 24 weeks.
b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

Total Back Pain:

Normalized net incremental AUC between randomization and Week 12: The total back pain decrease evaluated using the normalized net incremental AUC was not statistically higher in the etanercept group than in the placebo group (p=0.071).

Changes from Baseline to Weeks 2, 4, 8, and 12: The total back pain absolute changes from Baseline to Week 2 and Week 4 were not statistically significant between both groups. After 8 weeks of treatment, the difference became statistically significant in favor of the etanercept group (p=0.023) and was sustained until 12 weeks of treatment (p=0.010).

Results of total back pain are summarized in Table 16.

Table 16. Results of the Total Back Pain, mITT Population

Characteristic	50 mg/week Etanercept N=39	Placebo N=43	Adjusted Difference	p-value[a]
Normalized net incremental AUC, mm				
Adjusted mean (±SD)	-21.73 (±20.48)	-13.24 (±20.46)	-8.49	0.071
95% CI	-28.26; -15.20	-19.61; -6.88	-17.73; 0.75	
Absolute changes from Baseline, mm				
Week 2 - Baseline				
Adjusted mean (±SD)	-15.37 (±24.02)	-11.80 (±24.01)	-3.57	0.511
95% CI	-22.99; -7.76	-19.22; -4.38	-14.31; 7.17	
Week 4 - Baseline				
Adjusted mean (±SD)	-18.93 (±24.02)	-14.36 (±24.01)	-4.57	0.401
95% CI	-26.54; -11.32	-21.78; -6.94	-15.31; 6.17	
Week 8 - Baseline				
Adjusted mean (±SD)	-28.24 (±24.02)	-15.78 (±24.01)	-12.45	0.023
95% CI	-35.85; -20.62	-23.20; -8.36	-23.19; -1.71	
Week 12 - Baseline				
Adjusted mean (±SD)	-29.18 (±24.02)	-14.93 (±24.01)	-14.25	0.010
95% CI	-36.79; -21.57	-22.35; -7.51	-24.99; -3.51	

ANCOVA = analysis of covariance; AUC = area under the curve; CI = confidence interval; mITT = modified intent-to-treat; N = number of subjects; SD = standard deviation.
a. From a mixed model ANCOVA.

The change from Baseline in total back pain during the RCT and OLE (unadjusted) is summarized by visit in Table 17.

Table 17. Changes From Baseline of Total Back Pain During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
Baseline, mm		
Mean (±SD)	69.7 (±16.6)	61.0 (±21.2)
Median	70.6	61.7
Min; max	0.0; 96.1	10.8; 98.9
Absolute changes from Baseline, mm		
Week 2 - Baseline		
Mean (±SD)	-18.56 (±22.98)	-10.54 (±28.59)
Median	-15.75	-0.65
Min; max	-66.95; 30.25	-81.15; 45.50
Week 4 - Baseline		
Mean (±SD)	-22.21 (±24.15)	-13.14 (±31.63)
Median	-20.50	-7.52
Min; max	-84.05; 27.10	-80.30; 61.80
Week 8 - Baseline		
Mean (±SD)	-31.76 (±21.52)	-14.68 (±28.94)
Median	-31.90	-13.37
Min; max	-70.10; 5.30	-81.60; 64.10
Week 12 - Baseline		
Mean (±SD)	-32.73 (±25.80)	-13.75 (±27.48)
Median	-33.45	-12.32
Min; max	-84.20; 21.80	-80.70; 54.70
Week 14 - Baseline		
Mean (±SD)	-35.21 (±25.88)	-30.29 (±29.94)
Median	-37.38	-25.13
Min; max	-91.40; 8.35	-92.80; 51.15
Week 18 - Baseline		
Mean (±SD)	-40.02 (±25.48)	-31.19 (±33.70)
Median	-40.23	-28.58
Min; max	-93.65; 13.75	-96.75; 67.80
Week 24 - Baseline		
Mean (±SD)	-44.50 (±25.09)	-32.27 (±31.76)
Median	-49.15	-28.85
Min; max	-93.65; 8.90	-95.30; 63.90

max = maximum; min = minimum; N = number of subjects; SD = standard deviation.
a. Subjects received etanercept 50 mg/week for 24 weeks.
b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

Bath Ankylosing Spondylitis Functional Index (BASFI):

Normalized net incremental AUC between randomization and Week 12: There was no statistically significant difference between both groups concerning the normalized net incremental AUC of the BASFI.

Changes from Baseline to Weeks 2, 4, 8, and 12: The BASFI absolute changes from Baseline to Week 2 and Week 4 were not statistically significant between both groups. After 8 weeks of treatment, the difference became statistically significant in favor of the etanercept group (p=0.039) and was sustained until 12 weeks of treatment (p=0.004).

Results of BASFI are summarized in Table 18.

Table 18. Results of the BASFI, mITT Population

Characteristic	50 mg/week Etanercept N=39	Placebo N=43	Adjusted Difference	p-value[a]
Normalized net incremental AUC, mm				
Adjusted mean (±SD)	-14.59 (±15.22)	-9.34 (±15.22)	-5.25	0.127
95% CI	-19.44;-9.74	-14.02; -4.67	-12.03; 1.53	
Absolute changes from Baseline, mm				
Week 2 - Baseline				
Adjusted mean (±SD)	-8.23 (±17.63)	-7.80 (±17.62)	-0.43	0.914
95% CI	-13.82; -2.63	-13.19; -2.41	-8.23; 7.38	
Week 4 - Baseline				
Adjusted mean (±SD)	-12.44 (±17.63)	-10.04 (±17.62)	-2.40	0.544
95% CI	-18.03; -6.85	-15.43; -4.65	-10.21; 5.41	
Week 8 - Baseline				
Adjusted mean (±SD)	-19.75 (±17.63)	-11.54 (±17.62)	-8.21	0.039
95% CI	-25.35; -14.16	-16.93; -6.15	-16.02; -0.40	
Week 12 - Baseline				
Adjusted mean (±SD)	-21.63 (±17.63)	-10.09 (±17.62)	-11.54	0.004
95% CI	-27.22; -16.03	-15.47; -4.70	-19.35; -3.73	

ANCOVA = analysis of covariance; AUC = area under the curve; BASFI = Bath Ankylosing Spondylitis Functional Index; CI = confidence interval; mITT = modified intent-to-treat; N = number of subjects; SD = standard deviation.

a. From a mixed model ANCOVA.

The change from Baseline in the BASFI during the RCT and OLE (unadjusted) is summarized in Table 19.

Table 19. Changes From Baseline of BASFI During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
Baseline, mm		
Mean (±SD)	62.6 (±19.7)	56.9 (±19.1)
Median	62.8	55.0
Min; max	16.1; 96.7	19.8; 98.0
Absolute changes from Baseline, mm		
Week 2 - Baseline		
Mean (±SD)	-8.61 (±16.17)	-8.37 (±16.73)
Median	-6.36	-4.36
Min; max	-58.80; 30.96	-56.30; 13.47
Week 4 - Baseline		
Mean (±SD)	-12.94 (±19.01)	-10.45 (±18.82)
Median	-13.33	-7.71
Min; max	-64.12; 29.12	-76.62; 12.39
Week 8 - Baseline		
Mean (±SD)	-20.44 (±17.38)	-12.29 (±18.36)
Median	-15.63	-9.15
Min; max	-69.20; 4.27	-83.20; 10.95
Week 12 - Baseline		
Mean (±SD)	-22.37 (±19.45)	-10.68 (±18.51)
Median	-18.36	-8.08
Min; max	-72.23; 6.60	-68.78; 15.40
Week 14 - Baseline		
Mean (±SD)	-23.99 (±22.02)	-21.35 (±19.15)
Median	-22.14	-16.50
Min; max	-72.04; 16.69	-82.19; 7.08
Week 18 - Baseline		
Mean (±SD)	-25.49 (±21.68)	-21.09 (±21.73)
Median	-26.28	-17.82
Min; max	-71.85; 16.69	-86.00; 16.54
Week 24 - Baseline		
Mean (±SD)	-28.87 (±20.83)	-21.81 (±20.86)
Median	-27.50	-19.05
Min; max	-73.11; 16.69	-86.97; 9.30

BASFI = Bath Ankylosing Spondylitis Functional Index; max = maximum; min = minimum; N = number of subjects; SD = standard deviation.

a. Subjects received etanercept 50 mg/week for 24 weeks.

b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

BASFI independent components at Baseline and Weeks 2, 4, 8 and 12 are presented in Table 20. Subject rating was done on a 100 mm VAS; range 0= easy to 100= impossible.

Table 20. Bath Ankylosing Spondylitis Functional Index (BASFI): Independent Components at Weeks 2, 4, 8 and 12 (No LOCF)

Components	Treatment		Total (N=82)
	Etanercept (N=39)	Placebo (N=43)	
Putting on Socks or Tights Without Help or Aids (eg, Sock Aid): BASFI 1			
Baseline (LOCF)			
n	38	42	80
Mean (±SD)	51.1 (±25.2)	43.8 (±26.1)	47.3 (±25.8)
95% CI	42.8; 59.4	35.7; 52.0	41.5; 53.0
Week 2			
n	38	39	77
Mean (±SD)	47.6 (±29.6)	36.5 (±28.0)	42.0 (±29.1)
95% CI	37.9; 57.3	27.4; 45.5	35.4; 48.6
Week 4			
n	37	42	79
Mean (±SD)	41.1 (±29.0)	32.7 (±27.9)	36.6 (±28.5)
95% CI	31.4; 50.8	24.0; 41.4	30.2; 43.0
Week 8			
n	38	39	77
Mean (±SD)	32.3 (±25.4)	30.6 (±26.5)	31.4 (±25.8)
95% CI	24.0; 40.7	22.0; 39.1	25.6; 37.3
Week 12			
n	38	39	77
Mean (±SD)	33.2 (±29.8)	36.0 (±29.6)	34.6 (±29.5)
95% CI	23.4; 43.0	26.4; 45.6	27.9; 41.3
Bending Forward From the Waist to Pick up a Pen From the Floor or Without an Aid: BASFI 2			
Baseline (LOCF)			
n	39	42	81
Mean (±SD)	63.4 (±28.6)	61.5 (±28.7)	62.5 (±28.5)
95% CI	54.2; 72.7	52.6; 70.5	56.1; 68.8
Week 2			
n	38	40	78
Mean (±SD)	54.1 (±34.0)	55.7 (±31.8)	54.9 (±32.7)
95% CI	43.0; 65.3	45.5; 65.9	47.6; 62.3
Week 4			
n	38	42	80
Mean (±SD)	51.1 (±36.4)	54.0 (±31.8)	52.6 (±33.9)
95% CI	39.1; 63.0	44.1; 63.9	45.1; 60.2
Week 8			
n	38	39	77
Mean (±SD)	43.3 (±33.5)	54.2 (±32.9)	48.8 (±33.4)
95% CI	32.3; 54.3	43.5; 64.9	41.2; 56.4
Week 12			
n	38	39	77
Mean (±SD)	41.1 (±34.5)	56.2 (±32.5)	48.7 (±34.1)
95% CI	29.8; 52.4	45.6; 66.7	41.0; 56.5
Reaching up to a High Shelf Without Help or Aids (eg, Helping Hand): BASFI 3			
Baseline (LOCF)			
n	39	42	81
Mean (±SD)	61.5 (±27.8)	54.3 (±25.7)	57.8 (±26.8)
95% CI	52.5; 70.6	46.3; 62.3	51.8; 63.7

Table 20. Bath Ankylosing Spondylitis Functional Index (BASFI): Independent Components at Weeks 2, 4, 8 and 12 (No LOCF)

Components	Treatment		Total (N=82)
	Etanercept (N=39)	Placebo (N=43)	
Week 2			
n	38	40	78
Mean (±SD)	52.1 (±30.8)	50.3 (±29.6)	51.2 (±30.0)
95% CI	41.9; 62.2	40.8; 59.7	44.4; 57.9
Week 4			
n	38	41	79
Mean (±SD)	50.2 (±31.9)	43.8 (±27.3)	46.9 (±29.6)
95% CI	39.7; 60.7	35.2; 52.4	40.3; 53.5
Week 8			
n	38	39	77
Mean (±SD)	37.4 (±29.5)	44.1 (±23.8)	40.8 (±26.8)
95% CI	27.7; 47.1	36.4; 51.8	34.7; 46.9
Week 12			
n	38	39	77
Mean (±SD)	37.3 (±32.0)	44.5 (±25.6)	41.0 (±28.9)
95% CI	26.8; 47.9	36.2; 52.8	34.4; 47.6
Getting up out of an Armless Dining Room Chair Without Using Hands or Any Other Help: BASFI 4			
Baseline (LOCF)			
n	39	42	81
Mean (±SD)	55.8 (±30.0)	47.5 (±27.9)	51.5 (±29.1)
95% CI	46.1; 65.5	38.8; 56.2	45.1; 57.9
Week 2			
n	38	40	78
Mean (±SD)	47.2 (±31.9)	38.1 (±28.4)	42.5 (±30.3)
95% CI	36.7; 57.6	29.0; 47.2	35.7; 49.3
Week 4			
n	38	42	80
Mean (±SD)	42.1 (±33.9)	36.1 (±27.2)	39.0 (±30.5)
95% CI	31.0; 53.3	27.7; 44.6	32.2; 45.8
Week 8			
n	38	39	77
Mean (±SD)	33.6 (±28.4)	35.1 (±28.5)	34.4 (±28.3)
95% CI	24.3; 42.9	25.9; 44.3	27.9; 40.8
Week 12			
n	38	39	77
Mean (±SD)	31.7 (±30.5)	36.5 (±30.1)	34.1 (±30.2)
95% CI	21.7; 41.7	26.8; 46.3	27.3; 41.0
Getting up off the Floor Without Help From Lying on Back: BASFI 5			
Baseline (LOCF)			
n	38	42	80
Mean (±SD)	71.8 (±23.5)	60.8 (±25.9)	66.0 (±25.3)
95% CI	64.1; 79.5	52.7; 68.9	60.4; 71.7
Week 2			
n	37	40	77
Mean (±SD)	57.0 (±30.8)	49.4 (±29.3)	53.1 (±30.0)
95% CI	46.7; 67.3	40.1; 58.8	46.2; 59.9

Table 20. Bath Ankylosing Spondylitis Functional Index (BASFI): Independent Components at Weeks 2, 4, 8 and 12 (No LOCF)

Components	Treatment		Total (N=82)
	Etanercept (N=39)	Placebo (N=43)	
Week 4			
n	38	41	79
Mean (±SD)	55.0 (±32.2)	48.5 (±28.7)	51.6 (±30.4)
95% CI	44.5; 65.6	39.4; 57.5	44.8; 58.4
Week 8			
n	38	39	77
Mean (±SD)	43.7 (±32.7)	44.2 (±29.3)	43.9 (±30.8)
95% CI	32.9; 54.4	34.7; 53.7	36.9; 50.9
Week 12			
n	38	39	77
Mean (±SD)	44.5 (±32.6)	46.1 (±28.9)	45.3 (±30.6)
95% CI	33.7; 55.2	36.7; 55.5	38.4; 52.2
Standing Unsupported for 10 Minutes Without Discomfort: BASFI 6			
Baseline (LOCF)			
n	39	42	81
Mean (±SD)	58.9 (±27.7)	49.0 (±29.9)	53.8 (±29.1)
95% CI	49.9; 67.9	39.7; 58.3	47.3; 60.2
Week 2			
n	38	40	78
Mean (±SD)	50.8 (±31.6)	44.9 (±29.4)	47.7 (±30.4)
95% CI	40.4; 61.2	35.5; 54.3	40.9; 54.6
Week 4			
n	38	42	80
Mean (±SD)	46.4 (±32.2)	42.0 (±26.7)	44.1 (±29.4)
95% CI	35.8; 57.0	33.6; 50.3	37.6; 50.6
Week 8			
n	38	39	77
Mean (±SD)	40.8 (±30.0)	40.9 (±28.5)	40.8 (±29.1)
95% CI	30.9; 50.7	31.6; 50.1	34.2; 47.4
Week 12			
n	38	39	77
Mean (±SD)	39.0 (±32.5)	42.2 (±30.1)	40.6 (±31.1)
95% CI	28.3; 49.7	32.5; 51.9	33.5; 47.7
Climbing 12-15 Steps Without Using a Handrail or Walking Aid. One Foot on Each Step: BASFI 7			
Baseline (LOCF)			
n	39	42	81
Mean (±SD)	55.0 (±30.0)	47.5 (±30.8)	51.1 (±30.5)
95% CI	45.3; 64.8	37.9; 57.1	44.4; 57.9
Week 2			
n	38	40	78
Mean (±SD)	47.4 (±32.5)	38.4 (±28.3)	42.8 (±30.6)
95% CI	36.7; 58.1	29.3; 47.4	35.9; 49.7
Week 4			
n	38	42	80
Mean (±SD)	42.3 (±31.9)	37.4 (±28.9)	39.7 (±30.2)
95% CI	31.8; 52.8	28.4; 46.4	33.0; 46.4

Table 20. Bath Ankylosing Spondylitis Functional Index (BASFI): Independent Components at Weeks 2, 4, 8 and 12 (No LOCF)

Components	Treatment		Total (N=82)
	Etanercept (N=39)	Placebo (N=43)	
Week 8			
n	38	39	77
Mean (±SD)	37.4 (±30.2)	35.6 (±30.0)	36.5 (±29.9)
95% CI	27.5; 47.3	25.8; 45.3	29.7; 43.3
Week 12			
n	38	39	77
Mean (±SD)	35.0 (±31.1)	32.9 (±28.8)	33.9 (±29.8)
95% CI	24.7; 45.2	23.6; 42.3	27.2; 40.7
Looking Over Shoulder Without Turning Body: BASFI 8			
Baseline (LOCF)			
n	39	42	81
Mean (±SD)	81.0 (±21.5)	81.9 (±19.7)	81.4 (±20.5)
95% CI	74.0; 87.9	75.7; 88.0	76.9; 86.0
Week 2			
n	38	40	78
Mean (±SD)	72.9 (±26.2)	68.4 (±27.8)	70.6 (±26.9)
95% CI	64.3; 81.5	59.5; 77.2	64.5; 76.6
Week 4			
n	38	42	80
Mean (±SD)	63.7 (±31.2)	71.6 (±28.4)	67.9 (±29.8)
95% CI	53.5; 74.0	62.8; 80.4	61.2; 74.5
Week 8			
n	38	39	77
Mean (±SD)	56.9 (±33.4)	71.1 (±29.4)	64.1 (±32.0)
95% CI	45.9; 67.9	61.6; 80.7	56.8; 71.4
Week 12			
n	38	39	77
Mean (±SD)	54.1 (±33.9)	68.1 (±28.6)	61.2 (±31.9)
95% CI	43.0; 65.2	58.8; 77.4	54.0; 68.4
Doing Physically Demanding Activities (eg, Physiotherapy Exercises, Gardening or Sports): BASFI 9			
Baseline (LOCF)			
n	39	42	81
Mean (±SD)	67.6 (±21.3)	65.4 (±19.9)	66.5 (±20.5)
95% CI	60.7; 74.5	59.2; 71.6	61.9; 71.0
Week 2			
n	38	40	78
Mean (±SD)	60.7 (±27.3)	58.4 (±22.0)	59.5 (±24.6)
95% CI	51.7; 69.6	51.4; 65.4	54.0; 65.1
Week 4			
n	38	42	80
Mean (±SD)	53.0 (±29.1)	53.6 (±23.1)	53.3 (±26.0)
95% CI	43.4; 62.6	46.4; 60.8	47.5; 59.1
Week 8			
n	38	39	77
Mean (±SD)	48.4 (±30.4)	47.8 (±22.6)	48.1 (±26.5)
95% CI	38.4; 58.3	40.5; 55.1	42.1; 54.1

Table 20. Bath Ankylosing Spondylitis Functional Index (BASFI): Independent Components at Weeks 2, 4, 8 and 12 (No LOCF)

Components	Treatment		Total (N=82)
	Etanercept (N=39)	Placebo (N=43)	
Week 12			
n	38	39	77
Mean (±SD)	43.2 (±29.7)	54.9 (±22.2)	49.1 (±26.7)
95% CI	33.4; 52.9	47.7; 62.1	43.1; 55.2
Doing a Full Days Activities Whether at Home or at Work: BASFI 10			
Baseline (LOCF)			
n	39	42	81
Mean (±SD)	66.9 (±23.3)	57.1 (±24.8)	61.8 (±24.4)
95% CI	59.4; 74.5	49.4; 64.8	56.4; 67.2
Week 2			
n	38	40	78
Mean (±SD)	57.2 (±25.7)	49.3 (±22.5)	53.2 (±24.3)
95% CI	48.7; 65.7	42.1; 56.5	47.7; 58.6
Week 4			
n	38	42	80
Mean (±SD)	52.4 (±27.7)	51.6 (±25.3)	52.0 (±26.3)
95% CI	43.3; 61.4	43.7; 59.5	46.1; 57.8
Week 8			
n	38	39	77
Mean (±SD)	47.6 (±31.2)	44.4 (±21.3)	46.0 (±26.5)
95% CI	37.3; 57.8	37.5; 51.3	39.9; 52.0
Week 12			
n	38	39	77
Mean (±SD)	43.1 (±32.9)	49.0 (±25.2)	46.1 (±29.2)
95% CI	32.2; 53.9	40.9; 57.2	39.5; 52.7

CI = confidence interval; LOCF = last observation carried forward; N = total number of subjects; n = number of subject analyzed; SD = standard deviation.

BASFI independent components at Baseline and Weeks 14, 18 and 24 are presented in Table 21.

Table 21. Bath Ankylosing Spondylitis Functional Index (BASFI): Independent Components at Weeks 14, 18 and 24 (No LOCF)

Components	Treatment	
	Etanercept (N=38)	Placebo (N=39)
Putting on Socks or Tights Without Help or Aids (eg, Sock Aid): BASFI 1		
Baseline (LOCF)		
n	37	38
Mean (±SD)	50.2 (±24.9)	44.3 (±26.4)
95% CI	41.9; 58.5	35.6; 53.0
Week 14		
n	36	38
Mean (±SD)	32.7 (±29.9)	25.7 (±27.8)
95% CI	22.6; 42.8	16.6; 34.8
Week 18		
n	34	38
Mean (±SD)	31.3 (±28.6)	26.6 (±28.8)
95% CI	21.3; 41.2	17.1; 36.1
Week 24		
n	35	38
Mean (±SD)	26.7 (±28.7)	24.5 (±27.7)
95% CI	16.8; 36.5	15.4; 33.6
Bending Forward From the Waist to Pick up a Pen From the Floor or Without an Aid: BASFI 2		
Baseline (LOCF)		
n	38	38
Mean (±SD)	62.9 (±28.8)	62.0 (±29.4)
95% CI	53.4; 72.4	52.4; 71.7
Week 14		
n	36	38
Mean (±SD)	42.1 (±36.9)	47.1 (±34.2)
95% CI	29.6; 54.6	35.9; 58.4
Week 18		
n	34	38
Mean (±SD)	36.9 (±34.1)	45.3 (±37.8)
95% CI	25.0; 48.8	32.9; 57.7
Week 24		
n	35	38
Mean (±SD)	36.1 (±35.6)	44.6 (±35.3)
95% CI	23.9; 48.3	33.0; 56.3
Reaching up to a High Shelf Without Help or Aids (eg, Helping Hand): BASFI 3		
Baseline (LOCF)		
n	38	38
Mean (±SD)	61.0 (±28.0)	54.4 (±26.0)
95% CI	51.8; 70.2	45.9; 63.0
Week 14		
n	36	37
Mean (±SD)	37.0 (±32.4)	31.7 (±26.7)
95% CI	26.0; 48.0	22.8; 40.6
Week 18		
n	34	38
Mean (±SD)	32.1 (±29.9)	34.2 (±28.2)
95% CI	21.7; 42.6	25.0; 43.5
Week 24		
n	35	38

Table 21. Bath Ankylosing Spondylitis Functional Index (BASFI): Independent Components at Weeks 14, 18 and 24 (No LOCF)

Components	Treatment	
	Etanercept (N=38)	Placebo (N=39)
Mean (±SD)	27.4 (±27.1)	32.1 (±25.3)
95% CI	18.1; 36.7	23.8; 40.4
Getting up out of an Armless Dining Room Chair Without Using Hands or Any Other Help: BASFI 4		
Baseline (LOCF)		
n	38	38
Mean (±SD)	55.1 (±30.1)	48.2 (±28.1)
95% CI	45.2; 65.0	38.9; 57.4
Week 14		
n	36	38
Mean (±SD)	32.0 (±32.8)	27.9 (±29.4)
95% CI	20.9; 43.2	18.3; 37.6
Week 18		
n	34	38
Mean (±SD)	27.3 (±29.0)	26.5 (±29.3)
95% CI	17.2; 37.4	16.9; 36.1
Week 24		
n	35	38
Mean (±SD)	23.4 (±25.7)	26.2 (±27.8)
95% CI	14.6; 32.3	17.1; 35.3
Getting up off the Floor Without Help From Lying on Back: BASFI 5		
Baseline (LOCF)		
n	37	38
Mean (±SD)	71.5 (±23.8)	60.8 (±26.2)
95% CI	63.5; 79.4	52.2; 69.4
Week 14		
n	36	38
Mean (±SD)	43.6 (±36.8)	36.3 (±29.6)
95% CI	31.1; 56.1	26.6; 46.1
Week 18		
n	34	38
Mean (±SD)	40.0 (±33.9)	36.5 (±30.0)
95% CI	28.1; 51.8	26.6; 46.3
Week 24		
n	35	38
Mean (±SD)	38.2 (±32.6)	34.4 (±31.4)
95% CI	27.0; 49.4	24.1; 44.7
Standing Unsupported for 10 Minutes Without Discomfort: BASFI 6		
Baseline (LOCF)		
n	38	38
Mean (±SD)	58.2 (±27.7)	48.7 (±30.6)
95% CI	49.1; 67.3	38.7; 58.8
Week 14		
n	36	38
Mean (±SD)	38.8 (±34.1)	29.7 (±27.0)
95% CI	27.2; 50.3	20.8; 38.6
Week 18		
n	34	38
Mean (±SD)	32.6 (±30.3)	33.3 (±31.7)

Table 21. Bath Ankylosing Spondylitis Functional Index (BASFI): Independent Components at Weeks 14, 18 and 24 (No LOCF)

Components	Treatment	
	Etanercept (N=38)	Placebo (N=39)
95% CI	22.1; 43.2	22.9; 43.7
Week 24		
n	35	38
Mean (±SD)	30.5 (±28.5)	33.8 (±29.6)
95% CI	20.7; 40.3	24.1; 43.6
Climbing 12-15 Steps Without Using a Handrail or Walking Aid. One Foot on Each Step: BASFI 7		
Baseline (LOCF)		
n	38	38
Mean (±SD)	54.2 (±29.9)	45.4 (±31.1)
95% CI	44.4; 64.1	35.2; 55.6
Week 14		
n	36	38
Mean (±SD)	34.0 (±34.3)	26.7 (±27.5)
95% CI	22.4; 45.6	17.7; 35.7
Week 18		
n	33	38
Mean (±SD)	30.7 (±30.0)	27.4 (±31.0)
95% CI	20.0; 41.3	17.2; 37.6
Week 24		
n	35	38
Mean (±SD)	28.8 (±29.4)	27.1 (±30.7)
95% CI	18.7; 38.9	17.0; 37.2
Looking Over Shoulder Without Turning Body: BASFI 8		
Baseline (LOCF)		
n	38	38
Mean (±SD)	80.5 (±21.6)	82.0 (±18.0)
95% CI	73.4; 87.6	76.0; 87.9
Week 14		
n	36	37
Mean (±SD)	52.4 (±35.9)	58.6 (±33.4)
95% CI	40.2; 64.5	47.5; 69.8
Week 18		
n	34	38
Mean (±SD)	50.7 (±34.5)	57.7 (±32.9)
95% CI	38.6; 62.7	46.9; 68.5
Week 24		
n	35	38
Mean (±SD)	46.4 (±35.5)	55.3 (±32.1)
95% CI	34.2; 58.6	44.8; 65.9
Doing Physically Demanding Activities (eg, Physiotherapy Exercises, Gardening or Sports): BASFI 9		
Baseline (LOCF)		
n	38	38
Mean (±SD)	67.0 (±21.3)	65.1 (±19.3)
95% CI	60.0; 74.0	58.7; 71.4
Week 14		
n	36	38
Mean (±SD)	41.8 (±33.1)	37.3 (±22.5)
95% CI	30.7; 53.0	29.9; 44.7

Table 21. Bath Ankylosing Spondylitis Functional Index (BASFI): Independent Components at Weeks 14, 18 and 24 (No LOCF)

Components	Treatment	
	Etanercept (N=38)	Placebo (N=39)
Week 18		
n	34	38
Mean (±SD)	38.6 (±29.0)	43.5 (±26.2)
95% CI	28.5; 48.8	34.9; 52.1
Week 24		
n	35	38
Mean (±SD)	33.7 (±28.9)	38.5 (±26.2)
95% CI	23.7; 43.6	29.9; 47.1
Doing a Full Days Activities Whether at Home or at Work: BASFI 10		
Baseline (LOCF)		
n	38	38
Mean (±SD)	66.3 (±23.2)	58.5 (±24.0)
95% CI	58.6; 73.9	50.6; 66.4
Week 14		
n	36	38
Mean (±SD)	40.4 (±33.0)	36.1 (±25.3)
95% CI	29.2; 51.6	27.7; 44.4
Week 18		
n	34	38
Mean (±SD)	37.9 (±31.9)	40.0 (±27.5)
95% CI	26.7; 49.0	30.9; 49.0
Week 24		
n	35	38
Mean (±SD)	32.1 (±27.6)	37.5 (±27.4)
95% CI	22.6; 41.6	28.4; 46.5

CI = confidence interval; LOCF = last observation carried forward; N = total number of subjects; n = number of subject analyzed; SD = standard deviation.

Bath Ankylosing Spondylitis - Global score (BAS-G):

Normalized net incremental AUC between randomization and Week 12: There was no statistically significant difference between both groups concerning the normalized net incremental AUC of the BAS-G.

Changes from baseline to Weeks 2, 4, 8, and 12: The BAS-G absolute changes from Baseline to Week 2 and Week 4 were not statistically significant between both groups. After 8 weeks of treatment, the difference became statistically significant in favor of the etanercept group (p=0.047) and was sustained until 12 weeks of treatment (p=0.007).

Results of BAS-G are summarized in Table 22.

Table 22. Results of the BAS-G, mITT Population

Characteristic	50 mg/week Etanercept N=39	Placebo N=43	Adjusted Difference	p-value[a]
Normalized net incremental AUC, mm				
Adjusted mean (±SD)	-21.36 (±17.67)	-15.43 (±17.66)	-5.94	0.139
95% CI	-27.07;-15.66	-20.85; -10.00	-13.84; 1.96	
Absolute changes from Baseline, mm				
Week 2 - Baseline				
Adjusted mean (±SD)	-13.74 (±22.05)	-14.64 (±22.04)	0.89	0.857
95% CI	-20.81; -6.68	-21.36; -7.92	-8.88; 10.67	
Week 4 - Baseline				
Adjusted mean (±SD)	-20.09 (±22.05)	-14.99 (±22.04)	-5.10	0.304
95% CI	-27.16; -13.02	-21.71; -8.27	-14.88; 4.67	
Week 8 - Baseline				
Adjusted mean (±SD)	-28.17 (±22.05)	-18.27 (±22.04)	-9.90	0.047
95% CI	-35.24; -21.11	-24.99; -11.55	-19.68; -0.13	
Week 12 - Baseline				
Adjusted mean (±SD)	-29.78 (±22.05)	-16.12 (±22.04)	-13.65	0.007
95% CI	-36.84; -22.71	-22.84; -9.40	-23.43; -3.88	

ANCOVA = analysis of covariance; AUC = area under the curve; BAS-G = Bath Ankylosing Spondylitis - Global score; CI = confidence interval; mITT = modified intent-to-treat; N = number of subjects; SD = standard deviation.

a. From a mixed model ANCOVA.

The change from Baseline in the BAS-G during the RCT and OLE (unadjusted) is summarized by visit in Table 23.

Table 23. Changes From Baseline of BAS-G During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
Baseline, mm		
Mean (±SD)	72.1 (±16.2)	70.1 (±16.8)
Median	72.7	69.2
Min; max	39.1; 100.0	43.7; 98.6
Absolute changes from Baseline, mm		
Week 2 - Baseline		
Mean (±SD)	-14.40 (±20.04)	-15.14 (±21.86)
Median	-12.15	-9.42
Min; max	-63.20; 26.25	-66.70; 22.80
Week 4 - Baseline		
Mean (±SD)	-20.91 (±22.60)	-16.84 (±23.97)
Median	-17.10	-8.67
Min; max	-82.30; 25.10	-98.15; 26.25
Week 8 - Baseline		
Mean (±SD)	-29.22 (±23.69)	-21.07 (±22.10)
Median	-27.20	-17.97
Min; max	-89.90; 15.35	-57.40; 16.35
Week 12 - Baseline		
Mean (±SD)	-30.86 (±25.05)	-18.69 (±22.65)
Median	-40.60	-14.97
Min; max	-75.50; 29.85	-94.10; 16.60
Week 14 - Baseline		
Mean (±SD)	-34.29 (±27.87)	-34.93 (±28.33)
Median	-40.95	-26.83
Min; max	-93.15; 24.45	-97.75; 21.55
Week 18 - Baseline		
Mean (±SD)	-36.93 (±25.00)	-35.98 (±26.52)
Median	-46.90	-31.25
Min; max	-89.25; 24.45	-87.45; 21.10
Week 24 - Baseline		
Mean (±SD)	-42.35 (±24.66)	-35.89 (±25.58)
Median	-46.50	-36.73
Min; max	-99.90; 24.45	-98.15; 11.85

BAS-G = Bath Ankylosing Spondylitis - Global score; max = maximum; min = minimum; N = number of subjects; SD = standard deviation.

a. Subjects received etanercept 50 mg/week for 24 weeks.

b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

BAS-G independent component: Effect of disease on well-being at Weeks 2, 4, 8, 12 is presented in Table 24. Subject evaluation of the effect of their disease on well-being was done using a 100 mm VAS; range: 0= none to 100= very important.

Table 24. Bath Ankylosing Spondylitis - Global Score (BAS-G): Effect of Disease on Well-Being at Weeks 2, 4, 8, 12

BAS-G (After LOCF)	Treatment		Total (N=82)
	Etanercept (N=39)	Placebo (N=43)	
Baseline (LOCF)			
n	38	42	80
Mean (±SD)	72.1 (±16.0)	68.3 (±18.1)	70.1 (±17.1)
95% CI	66.9; 77.4	62.6; 73.9	66.3; 73.9
Week 2			
n	39	42	81
Mean (±SD)	57.8 (±24.2)	54.4 (±22.4)	56.0 (±23.2)
95% CI	49.9; 65.6	47.4; 61.4	50.9; 61.1
Week 4			
n	39	42	81
Mean (±SD)	51.4 (±24.5)	54.0 (±23.1)	52.8 (±23.7)
95% CI	43.5; 59.4	46.8; 61.3	47.6; 58.0
Week 8			
n	39	43	82
Mean (±SD)	43.3 (±25.8)	50.8 (±19.2)	47.2 (±22.7)
95% CI	34.9; 51.6	44.9; 56.7	42.2; 52.2
Week 12			
n	39	43	82
Mean (±SD)	42.1 (±28.0)	52.9 (±21.3)	47.7 (±25.2)
95% CI	33.0; 51.1	46.3; 59.5	42.2; 53.3

CI = confidence interval; LOCF = last observation carried forward; N = total number of subjects; n = number of subject analyzed; SD = standard deviation.

Bath Ankylosing Spondylitis Metrology Index (BASMI-10):

Normalized net incremental AUC between randomization and Week 12: The BASMI-10 decrease evaluated using the normalized net incremental AUC was statistically higher in the etanercept group than in the placebo group (p=0.035).

Changes from Baseline to Weeks 2, 4, 8, and 12: The BASMI-10 absolute changes from Baseline to Week 2 and Week 4 were not statistically significant between both groups. After 8 weeks of treatment, the difference became statistically significant in favor of the etanercept group (p=0.008) and was sustained until 12 weeks of treatment (p=0.011).

Results of the BASMI-10 are summarized in Table 25.

Table 25. Results of the BASMI-10, mITT Population

Characteristic	50 mg/week Etanercept N=39	Placebo N=43	Adjusted Difference	p-value[a]
Normalized net incremental AUC				
Adjusted mean (±SD)	-0.41 (±0.49)	-0.18 (±0.49)	-0.23	0.035
95% CI	-0.57; -0.26	-0.33; -0.03	-0.45; -0.02	
Absolute changes from Baseline				
Week 2 - Baseline				
Adjusted mean (±SD)	-0.27 (±0.65)	-0.17 (±0.65)	-0.09	0.515
95% CI	-0.47; -0.06	-0.37; 0.02	-0.38; 0.19	
Week 4 - Baseline				
Adjusted mean (±SD)	-0.37 (±0.65)	-0.23 (±0.65)	-0.14	0.316
95% CI	-0.58; -0.17	-0.43; -0.04	-0.43; 0.14	
Week 8 - Baseline				
Adjusted mean (±SD)	-0.57 (±0.65)	-0.18 (±0.65)	-0.39	0.008
95% CI	-0.77; -0.36	-0.38; 0.01	-0.67; -0.10	
Week 12 - Baseline				
Adjusted mean (±SD)	-0.57 (±0.65)	-0.20 (±0.65)	-0.37	0.011
95% CI	-0.77; -0.36	-0.40; -0.01	-0.65; -0.08	

ANCOVA = analysis of covariance; AUC = area under the curve; BASMI = Bath Ankylosing Spondylitis Metrology Index; CI = confidence interval; mITT = modified intent-to-treat; N = number of subjects; SD = standard deviation.

a. From a mixed model ANCOVA.

The change from Baseline in the BASMI-10 during the RCT and OLE (unadjusted) is summarized by visit in Table 26.

Table 26. Changes From Baseline of BASMI-10 During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
Baseline, range 0 to 10		
Mean (±SD)	5.7 (±1.4)	5.7 (±1.3)
Median	6.0	5.6
Min; max	2.5; 7.6	3.0; 8.2
Absolute changes from Baseline, range 0 to 10		
Week 2 - Baseline		
Mean (±SD)	-0.28 (±0.59)	-0.17 (±0.65)
Median	-0.20	0.00
Min; max	-2.00; 0.60	-2.75; 1.00
Week 4 - Baseline		
Mean (±SD)	-0.38 (±0.84)	-0.19 (±0.54)
Median	-0.20	-0.20
Min; max	-3.00; 1.40	-1.40; 1.20
Week 8 - Baseline		
Mean (±SD)	-0.58 (±0.72)	-0.18 (±0.55)
Median	-0.55	-0.20
Min; max	-2.30; 1.20	-1.60; 0.85
Week 12 - Baseline		
Mean (±SD)	-0.58 (±0.78)	-0.20 (±0.58)
Median	-0.55	0.00
Min; max	-2.30; 1.40	-2.00; 0.75
Week 14 - Baseline		
Mean (±SD)	-0.73 (±0.75)	-0.49 (±0.58)
Median	-0.80	-0.40
Min; max	-2.75; 0.60	-2.20; 0.40
Week 18 - Baseline		
Mean (±SD)	-0.65 (±0.88)	-0.49 (±0.62)
Median	-0.60	-0.40
Min; max	-3.00; 1.40	-2.00; 0.60
Week 24 - Baseline		
Mean (±SD)	-0.80 (±0.76)	-0.50 (±0.67)
Median	-0.70	-0.60
Min;max	-3.00; 0.80	-2.00; 1.20

BASMI = Bath Ankylosing Spondylitis Metrology Index; max = maximum; min = minimum; n = number of subjects; SD = standard deviation.

a. Subjects received etanercept 50 mg/week for 24 weeks.

b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

BASMI independent components: Cervical rotation and tragus-to-wall at Weeks 2, 4, 8, 12 are presented in Table 27. Lateral flexion and modified Schober's test at Weeks 2, 4, 8, 12 are presented in Table 28.

Table 27. Bath Ankylosing Spondylitis Metrology Index (BASMI): Cervical Rotation and Tragus-to-Wall at Weeks 2, 4, 8, 12

Components (No LOCF)	Cervical Rotation			Tragus-to-Wall		
	Etanercept (N=39)	Placebo (N=43)	Total (N=82)	Etanercept (N=39)	Placebo (N=43)	Total (N=82)
Baseline (LOCF)						
n	39	43	82	39	43	82
Mean (±SD)	39.85 (±18.74)	37.14 (±22.00)	38.43 (±20.44)	20.18 (±7.02)	19.76 (±6.87)	19.96 (±6.90)
95% CI	33.77; 45.92	30.37; 43.91	33.94; 42.92	17.90; 22.45	17.64; 21.87	18.44; 21.47
Week 2						
n	38	41	79	38	41	79
Mean (±SD)	43.05 (±22.29)	38.34 (±19.84)	40.61 (±21.05)	19.69 (±7.10)	18.81 (±7.63)	19.24 (±7.34)
95% CI	35.73; 50.38	32.08; 44.60	35.89; 45.32	17.36; 22.03	16.40; 21.22	17.59; 20.88
Week 4						
n	38	43	81	38	43	81
Mean (±SD)	42.55 (±21.04)	39.67 (±21.02)	41.02 (±20.95)	19.19 (±7.22)	18.82 (±7.40)	18.99 (±7.27)
95% CI	35.64; 49.47	33.21; 46.14	36.39; 45.66	16.82; 21.56	16.54; 21.09	17.38; 20.60
Week 8						
n	38	39	77	38	39	77
Mean (±SD)	44.34 (±20.59)	39.79 (±22.67)	42.04 (±21.65)	18.70 (±7.03)	20.03 (±9.61)	19.37 (±8.40)
95% CI	37.57; 51.11	32.44; 47.14	37.13; 46.95	16.39; 21.01	16.91; 23.14	17.47; 21.28
Week 12						
n	38	39	77	38	39	77
Mean (±SD)	46.39 (±20.83)	42.67 (±21.86)	44.51 (±21.30)	18.54 (±6.96)	18.45 (±7.36)	18.49 (±7.12)
95% CI	39.55; 53.24	35.58; 49.75	39.67; 49.34	16.25; 20.83	16.06; 20.83	16.87; 20.11

CI = confidence interval; LOCF = last observation carried forward; N = total number of subjects; n = number of subject analyzed; SD = standard deviation.

Table 28. Bath Ankylosing Spondylitis Metrology Index (BASMI): Lateral Flexion and Modified Schober's Test at Weeks 2, 4, 8, 12

Component (No LOCF)	Lateral Flexion			Modified Schober's Test		
	Etanercept (N=39)	Placebo (N=43)	Total (N=82)	Etanercept (N=39)	Placebo (N=43)	Total (N=82)
Baseline (LOCF)						
n	39	42	81	39	43	82
Mean (±SD)	13.79 (±19.90)	9.80 (±14.43)	11.72 (±17.29)	1.63 (±1.20)	1.52 (±1.34)	1.57 (±1.27)
95% CI	7.34; 20.25	5.30; 14.30	7.90; 15.55	1.24; 2.02	1.10; 1.93	1.29; 1.85
Week 2						
n	38	41	79	38	40	78
Mean (±SD)	13.58 (±18.29)	10.62 (±14.84)	12.04 (±16.55)	1.73 (±1.37)	1.57 (±1.30)	1.65 (±1.33)
95% CI	7.57; 19.59	5.94; 15.31	8.34; 15.75	1.28; 2.18	1.15; 1.99	1.35; 1.95
Week 4						
n	38	43	81	38	42	80
Mean (±SD)	13.01 (±16.87)	10.60 (±15.75)	11.73 (±16.23)	1.85 (±1.42)	1.77 (±1.57)	1.81 (±1.50)
95% CI	7.46; 18.55	5.75; 15.45	8.14; 15.32	1.38; 2.32	1.28; 2.26	1.48; 2.14
Week 8						
n	38	39	77	38	39	77
Mean (±SD)	12.19 (±16.56)	10.21 (±14.45)	11.18 (±15.46)	1.95 (±1.45)	1.57 (±1.39)	1.76 (±1.43)
95% CI	6.74; 17.63	5.52; 14.89	7.68; 14.69	1.47; 2.42	1.12; 2.03	1.43; 2.08
Week 12						
n	38	38	76	38	39	77
Mean (±SD)	12.41 (±16.64)	8.56 (±12.61)	10.48 (±14.79)	1.88 (±1.36)	1.51 (±1.42)	1.69 (±1.40)
95% CI	6.94; 17.87	4.41; 12.71	7.10; 13.86	1.43; 2.32	1.05; 1.97	1.38; 2.01

CI = confidence interval; LOCF = last observation carried forward; N = total number of subjects; n = number of subject analyzed; SD = standard deviation.

BASMI independent component: Spinal mobility measured with intermalleolar distance at Baseline and Weeks 2, 4, 8, 12 is presented in Table 29.

Table 29. Bath Ankylosing Spondylitis Metrology Index (BASMI): Intermalleolar Distance Score

Component (No LOCF)	Intermalleolar Distance Score		
	Etanercept (N=39)	Placebo (N=43)	Total (N=82)
Baseline (LOCF)			
n	36	40	76
Mean (±SD)	82.31 (±30.00)	89.30 (±24.07)	85.99 (±27.09)
95% CI	72.15; 92.46	81.60; 97.00	79.80; 92.18
Week 2			
n	35	38	73
Mean (±SD)	87.89 (±26.35)	92.08 (±21.98)	90.07 (±24.10)
95% CI	78.83; 96.94	84.85; 99.31	84.45; 95.69
Week 4			
n	36	40	76
Mean (±SD)	90.86 (±28.54)	91.53 (±26.76)	91.21 (±27.43)
95% CI	81.20; 100.52	82.97; 100.08	84.94; 97.48
Week 8			
n	36	36	72
Mean (±SD)	93.56 (±24.72)	91.58 (±23.53)	92.57 (±23.98)
95% CI	85.19; 101.92	83.62; 99.54	86.93; 98.20
Week 12			
n	35	39	74
Mean (±SD)	94.46 (±22.09)	91.72 (±24.30)	93.01 (±23.17)
95% CI	86.87; 102.05	83.84; 99.60	87.65; 98.38

CI = confidence interval; LOCF = last observation carried forward; N = total number of subjects; n = number of subject analyzed; SD = standard deviation.

Chest Expansion Test:

Normalized net incremental AUC between randomization and Week 12: There was no statistically significant difference between both groups concerning the normalized net incremental AUC of the chest expansion.

Changes from Baseline to Weeks 2, 4, 8, and 12: No statistically significant difference between treatment groups was observed concerning absolute changes of the chest expansion from Baseline to each visit: Weeks 2, 4, 8, and 12.

Results of the chest expansion test are summarized in Table 30.

Table 30. Results of the Chest Expansion Test, mITT Population

Characteristic	50 mg/week Etanercept N=39	Placebo N=43	Adjusted Difference	p-value[a]
Normalized net incremental AUC				
Adjusted mean (±SD)	0.26 (±0.65)	0.19 (±0.65)	0.07	0.613
95% CI	0.05; 0.48	-0.01; 0.39	-0.22; 0.37	
Absolute changes from Baseline				
Week 2 - Baseline				
Adjusted mean (±SD)	0.17 (±0.91)	0.10 (±0.91)	0.07	0.744
95% CI	-0.12; 0.46	-0.17; 0.38	-0.34; 0.47	
Week 4 - Baseline				
Adjusted mean (±SD)	0.09 (±0.91)	0.19 (±0.91)	-0.10	0.625
95% CI	-0.20; 0.39	-0.08; 0.47	-0.50; 0.30	
Week 8 - Baseline				
Adjusted mean (±SD)	0.43 (±0.91)	0.23 (±0.91)	0.20	0.325
95% CI	0.14; 0.73	-0.04; 0.50	-0.20; 0.60	
Week 12 - Baseline				
Adjusted mean (±SD)	0.39 (±0.91)	0.33 (±0.91)	0.06	0.760
95% CI	0.09; 0.68	0.05; 0.60	-0.34; 0.46	

ANCOVA = analysis of covariance; AUC = area under the curve; CI = confidence interval; mITT = modified intent-to-treat; N = number of subjects; SD = standard deviation.
a. From a mixed model ANCOVA.

The change from Baseline in the chest expansion test in the RCT and OLE (unadjusted) is summarized by visit in Table 31.

Table 31. Changes From Baseline of Chest Expansion During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
Baseline, cm		
Mean (±SD)	2.74 (±1.52)	2.93 (±1.47)
Median	2.80	3.00
Min; max	0.00; 7.00	1.00; 7.00
Absolute changes from Baseline, cm		
Week 2 - Baseline		
Mean (±SD)	0.16 (±1.18)	0.05 (±0.78)
Median	0.00	0.00
Min; max	-3.00; 4.00	-1.50; 2.00
Week 4 - Baseline		
Mean (±SD)	0.08 (±0.76)	0.18 (±0.96)
Median	0.00	0.00
Min; max	-2.50; 1.50	-1.30; 4.00
Week 8 - Baseline		
Mean (±SD)	0.43 (±0.95)	0.24 (±1.02)
Median	0.50	0.00
Min; max	-2.50; 2.00	-1.50; 4.00
Week 12 - Baseline		
Mean (±SD)	0.38 (±0.72)	0.35 (±1.02)
Median	0.30	0.00
Min; max	-1.00; 2.00	-1.50; 3.00
Week 14 - Baseline		
Mean (±SD)	0.26 (±1.16)	0.22 (±1.11)
Median	0.50	0.00
Min; max	-3.50; 3.00	-2.50; 4.00
Week 18 - Baseline		
Mean (±SD)	0.22 (±1.12)	0.33 (±1.25)
Median	0.40	0.50
Min; max	-3.50; 3.00	-2.50; 3.50
Week 24 - Baseline		
Mean (±SD)	0.46 (±1.31)	0.44 (±1.12)
Median	0.50	0.50
Min; max	-3.50; 3.50	-2.50; 3.00

max = maximum; min = minimum; N = number of subjects; SD = standard deviation.
a. Subjects received etanercept 50 mg/week for 24 weeks.
b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

Respiratory Function Tests:

In the etanercept group, VC changed from 79.3% (±16.8) to 81.6% (±16.5) of predicted value, whereas in the placebo group, it changed from 80.0% (±19.7) to 79.1% (±17.9). The difference in VC change between groups was 4.32% of predicted value (1.61-7.04; p=0.002). This difference corresponds to 0.19 liters (0.06-0.31; p=0.003). Similar results were observed when FVC was taken into account. With a threshold of FVC ≤80% as an indicator for restrictive defect, 6 subjects in the etanercept group showed improvement as compared with only 1 subject in the placebo group (p=0.032).

Results of the respiratory function tests are summarized in Table 32.

Table 32. Results of the Respiratory Function Tests, mITT Population

Characteristic	50 mg/week Etanercept N=39	Placebo N=43	Adjusted Difference	p-value[a]
Absolute changes from Baseline to Week 12				
Vital capacity (liter)				
Adjusted mean (±SD)	0.14 (±0.26)	-0.05 (±0.26)	0.19	0.003
95% CI	0.05; 0.23	-0.14; 0.04	0.06; 0.31	
Forced vital capacity (liter)				
Adjusted mean (±SD)	0.16 (±0.28)	-0.02 (±0.28)	0.18	0.006
95% CI	0.07; 0.25	-0.11; 0.07	0.05; 0.31	
Forced expiratory volume in 1 second (liter)				
Adjusted mean (±SD)	0.05 (±0.22)	-0.02 (±0.22)	0.06	0.205
95% CI	-0.02; 0.12	-0.09; 0.05	-0.04; 0.17	
Ratio FEV_1/FVC (%)				
Adjusted mean (±SD)	-2.49 (±5.05)	0.10 (±5.05)	-2.59	0.030
95% CI	-4.15; -0.84	-1.53; 1.73	-4.93; -0.26	
Vital capacity (% of predicted value)				
Adjusted mean (±SD)	2.88 (±5.76)	-1.44 (±5.76)	4.32	0.002
95% CI	0.97; 4.80	-3.36; 0.48	1.61; 7.04	
Forced vital capacity (% of predicted value)				
Adjusted mean (±SD)	3.75 (±6.59)	-0.33 (±6.59)	4.08	0.009
95% CI	1.59; 5.91	-2.46; 1.80	1.04; 7.11	
Improvement from Baseline	6 (16.22%)	1 (2.63%)	7 (9.33%)	0.032
No change: >80%	15 (40.54%)	10 (26.32%)	25 (33.33%)	
No change: ≤80%	15 (40.54%)	21 (55.26%)	36 (48.00%)	
Worsening from Baseline	1 (2.70%)	6 (15.79%)	7 (9.33%)	
Forced expiratory volume in 1 second (% of predicted value)				
Adjusted mean (±SD)	1.23 (±6.30)	-0.33 (±6.30)	1.56	0.286
95% CI	-0.83; 3.30	-2.37; 1.71	-1.34; 4.47	

ANCOVA = analysis of covariance; CI = confidence interval; FEV_1 = forced expiratory Volume in 1 second; FVC = Forced vital capacity; mITT = modified intent-to-treat; n = number of subjects; SD = standard deviation.
a. From a mixed model ANCOVA.

Erythrocyte Sedimentation Rate (ESR):

Normalized net incremental AUC between randomization and Week 12: The ESR decrease evaluated using the normalized net incremental AUC was statistically higher in the etanercept group than in the placebo group ($p<0.0001$).

Changes from Baseline to Weeks 2, 4, 8, and 12: From 2 weeks of treatment, the difference between both groups was statistically significant in favor of the etanercept group ($p<0.0001$). This difference was sustained until the end of the 12-week RCT (Week 4: $p<0.0001$, Week 8: $p<0.0001$, Week 12: $p<0.0001$).

Results of the ESR are summarized in Table 33.

Table 33. Results of the ESR, mITT Population

Characteristic	50 mg/week Etanercept N=39	Placebo N=43	Adjusted Difference	p-value[a]
Normalized net incremental AUC, mm/h				
Adjusted mean (±SD)	-16.18 (±10.57)	-1.45 (±10.57)	-14.73	<0.0001
95% CI	-19.55;-12.81	-4.70; 1.80	-19.44; -10.03	
Baseline, mm/h				
Mean (±SD)	32.18 (±26.41)	24.71 (±23.52)		
Median	27.00	16.00		
Min; max	2.00; 109.00	2.00; 103.00		
Absolute changes from Baseline, mm/h				
Week 2 - Baseline				
Adjusted mean (±SD)	-15.00 (±13.17)	-2.62 (±13.17)	-12.37	<0.0001
95% CI	-19.16; -10.84	-6.63; 1.39	-18.17; -6.58	
Week 4 - Baseline				
Adjusted mean (±SD)	-20.05 (±13.17)	-2.60 (±13.17)	-17.45	<0.0001
95% CI	-24.21; -15.89	-6.61; 1.41	-23.25; -11.65	
Week 8 - Baseline				
Adjusted mean (±SD)	-17.02 (±13.17)	-0.07 (±13.17)	-16.95	<0.0001
95% CI	-21.18; -12.86	-4.08; 3.93	-22.75; -11.15	
Week 12 - Baseline				
Adjusted mean (±SD)	-20.33 (±13.17)	-2.17 (±13.17)	-18.16	<0.0001
95% CI	-24.49; -16.17	-6.18; 1.84	-23.96; -12.36	

ANCOVA = analysis of covariance; AUC = area under the curve; ESR = erythrocyte sedimentation rate; CI = confidence interval; h = hour; mITT = modified intent-to-treat; N = number of subjects; SD = standard deviation.

a. From a mixed model ANCOVA.

The change from Baseline for the ESR during the RCT and OLE (unadjusted) is summarized by visit in Table 34.

Table 34. Changes From Baseline of ESR During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
Baseline, mm		
Mean (±SD)	32.63 (±26.61)	23.32 (±20.92)
Median	27.00	16.00
Min; max	2.00; 109.00	2.00; 83.00
Absolute changes from Baseline, mm		
Week 2 - Baseline		
Mean (±SD)	-16.74 (±18.22)	-1.34 (±13.73)
Median	-13.00	0.00
Min; max	-61.00; 20.00	-61.00; 27.00
Week 4 - Baseline		
Mean (±SD)	-21.92 (±20.12)	-1.32 (±12.62)
Median	-17.50	-2.00
Min; max	-71.00; 0.00	-26.00; 41.00
Week 8 - Baseline		
Mean (±SD)	-18.82 (±24.60)	1.45 (±9.01)
Median	-13.50	-0.50
Min; max	-76.00; 41.00	-14.00; 30.00
Week 12 - Baseline		
Mean (±SD)	-22.21 (±21.80)	-0.87 (±13.58)
Median	-17.50	0.00
Min; max	-75.00; 4.00	-42.00; 37.00
Week 14 - Baseline		
Mean (±SD)	-20.32 (±20.83)	-10.21 (±16.30)
Median	-17.00	-7.00
Min; max	-75.00; 4.00	-60.00; 24.00
Week 18 - Baseline		
Mean (±SD)	-17.95 (±22.98)	-12.32 (±15.61)
Median	-13.50	-10.00
Min; max	-82.00; 37.00	-64.00; 12.00
Week 24 - Baseline		
Mean (±SD)	-18.53 (±25.97)	-14.61 (±17.61)
Median	-12.00	-9.00
Min; max	-82.00; 51.00	-66.00; 7.00

ESR = erythrocyte sedimentation rate; max = maximum; min = minimum; N = number of subjects; SD = standard deviation.
a. Subjects received etanercept 50 mg/week for 24 weeks.
b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

C-Reactive Protein (CRP):

Normalized net incremental AUC between randomization and Week 12: The CRP decrease evaluated using the normalized net incremental AUC was statistically higher in the etanercept group than in the placebo group ($p<0.0001$).

Changes from Baseline to Weeks 2, 4, 8, and 12: From 2 weeks of treatment, the difference between both groups was statistically significant in favor of the etanercept group ($p<0.0001$). This difference was sustained until the end of the 12-week RCT (Week 4: $p<0.0001$, Week 8: $p<0.0001$, Week 12: $p<0.0001$).

Results of the CRP are summarized in Table 35.

Table 35. Results of the CRP, mITT Population

Characteristic	50 mg/week Etanercept N=39	Placebo N=43	Adjusted Difference	p-value[a]
Normalized net incremental AUC, mg/L				
Adjusted mean (±SD)	-14.41 (±11.28)	-1.17 (±11.27)	-13.24	<0.0001
95% CI	-18.01; -10.82	-4.59; 2.25	-18.23; -8.25	
Baseline, mg/L				
Mean (±SD)	24.73 (±31.29)	16.99 (±18.51)		
Median	18.00	11.10		
Min; max	1.00; 177.00	0.50; 95.00		
Absolute changes from Baseline, mg/L				
Week 2 - Baseline				
Adjusted mean (±SD)	-15.37 (±14.17)	-1.05 (±14.16)	-14.32	<0.0001
95% CI	-19.86; -10.88	-5.32; 3.23	-20.55; -8.10	
Week 4 - Baseline				
Adjusted mean (±SD)	-16.99 (±14.17)	-2.01 (±14.16)	-14.98	<0.0001
95% CI	-21.48; -12.50	-6.28; 2.26	-21.20; -8.76	
Week 8 - Baseline				
Adjusted mean (±SD)	-16.19 (±14.17)	-1.01 (±14.16)	-15.19	<0.0001
95% CI	-20.68; -11.71	-5.28; 3.27	-21.41; -8.96	
Week 12 - Baseline				
Adjusted mean (±SD)	-15.69 (±14.17)	-1.28 (±14.16)	-14.41	<0.0001
95% CI	-20.18; -11.20	-5.55; 2.99	-20.63; -8.19	

ANCOVA = analysis of covariance; AUC=area under the curve; CI = confidence interval; CRP = C-reactive protein; mITT = modified intent-to-treat; N = number of subjects; SD = standard deviation.
a. From a mixed model ANCOVA.

The change from Baseline for CRP during the RCT and OLE (unadjusted) is summarized by visit in Table 36.

Table 36. Changes From Baseline of CRP During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
Baseline, mm		
Mean (±SD)	24.98 (±31.67)	16.05 (±18.60)
Median	18.85	10.20
Min; max	1.00; 177.00	0.50; 95.00
Absolute changes from Baseline, mm		
Week 2 - Baseline		
Mean (±SD)	-18.13 (±31.52)	1.22 (±7.99)
Median	-7.50	0.00
Min; max	-172.00; 34.40	-12.00; 35.00
Week 4 - Baseline		
Mean (±SD)	-19.79 (±30.74)	0.58 (±10.50)
Median	-10.20	-0.20
Min; max	-175.00; 2.60	-12.70; 58.00
Week 8 - Baseline		
Mean (±SD)	-18.98 (±30.40)	1.69 (±8.01)
Median	-7.40	0.10
Min; max	-169.00; 7.80	-8.10; 33.90
Week 12 - Baseline		
Mean (±SD)	-18.46 (±29.53)	1.38 (±9.20)
Median	-8.50	0.20
Min; max	-161.00; 14.00	-12.60; 36.00
Week 14 - Baseline		
Mean (±SD)	-18.11 (±29.37)	-10.04 (±12.87)
Median	-13.35	-7.75
Min; max	-161.00; 27.00	-46.90; 8.30
Week 18 - Baseline		
Mean (±SD)	-17.15 (±29.13)	-9.47 (±11.49)
Median	-6.20	-6.10
Min; max	-161.00; 14.00	-36.70; 6.10
Week 24 - Baseline		
Mean (±SD)	-16.05 (±33.01)	-9.62 (±13.01)
Median	-7.00	-6.00
Min; max	-170.00; 67.00	-48.00; 16.70

CRP = C-reactive protein; max = maximum; min = minimum; N = number of subjects; SD = standard deviation.

a. Subjects received etanercept 50 mg/week for 24 weeks.

b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

Response rate of normal CRP during the RCT and OLE (unadjusted) are summarized by visit in Table 37.

Table 37. Normal CRP During the Study

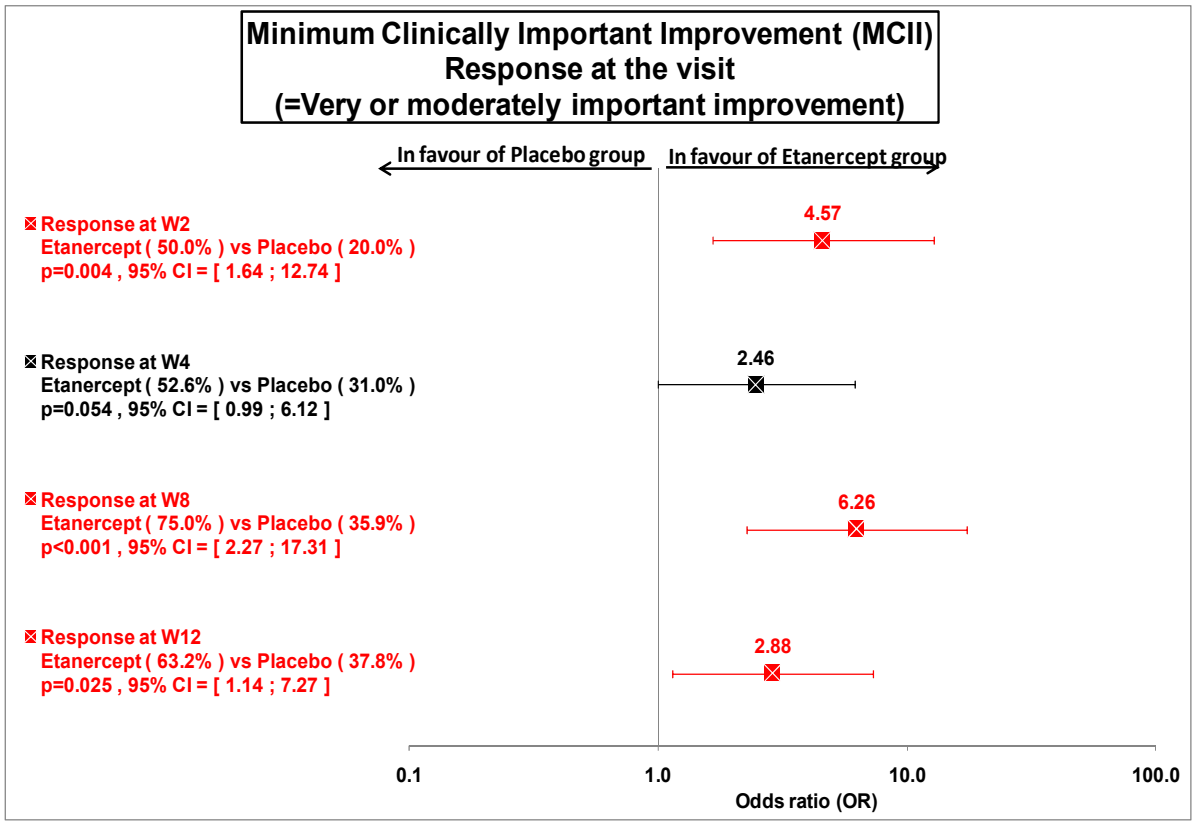
Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
C-reactive protein, mg/L		
Baseline, n (%)		
Normal (<6 mg/L)	13 (34.21%)	13 (33.33%)
Abnormal (≥6 mg/L)	25 (65.79%)	26 (66.67%)
Week 2, n (%)		
Normal (<6 mg/L)	29 (76.32%)	13 (33.33%)
Abnormal (≥6 mg/L)	9 (23.68%)	26 (66.67%)
Week 4, n (%)		
Normal (<6 mg/L)	29 (76.32%)	12 (30.77%)
Abnormal (≥6 mg/L)	9 (23.68%)	27 (69.23%)
Week 8, n (%)		
Normal (<6 mg/L)	28 (73.68%)	13 (33.33%)
Abnormal (≥6 mg/L)	10 (26.32%)	26 (66.67%)
Week 12, n (%)		
Normal (<6 mg/L)	25 (65.79%)	13 (33.33%)
Abnormal (≥6 mg/L)	13 (34.21%)	26 (66.67%)
Week 14, n (%)		
Normal (<6 mg/L)	23 (60.53%)	24 (70.59%)
Abnormal (≥6 mg/L)	15 (39.47%)	10 (29.41%)
Week 18, n (%)		
Normal (<6 mg/L)	24 (63.16%)	26 (66.67%)
Abnormal (≥6 mg/L)	14 (36.84%)	13 (33.33%)
Week 24, n (%)		
Normal (<6 mg/L)	26 (68.42%)	32 (82.05%)
Abnormal (≥6 mg/L)	12 (31.58%)	7 (17.95%)

N = number of subjects; n = number of subject with specified criteria; SD = standard deviation.
a. Subjects received etanercept 50 mg/week for 24 weeks.
b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

Minimum Clinically Important Improvement (MCII):

Percentage of subjects with 'very or moderately important improvement' of the MCII questionnaire: The response rates 'very or moderately important improvement' of the MCII were statistically higher in etanercept group at all Evaluation Visits, except for Week 4 which was also in favor of etanercept but borderline not statistically significant. Results of the MCII are summarized in Figure 4.

Figure 4. Minimum Clinically Important Improvement, mITT Population



p-value: From a generalized estimated equations model.
CI = confidence interval of the odds-ratio; mITT = modified intent-to-treat; vs = versus; W = week.

The change from Baseline for the MCII during the RCT and OLE (unadjusted) is summarized by visit in Table 38.

Table 38. Minimum Clinically Important Improvement During the Study

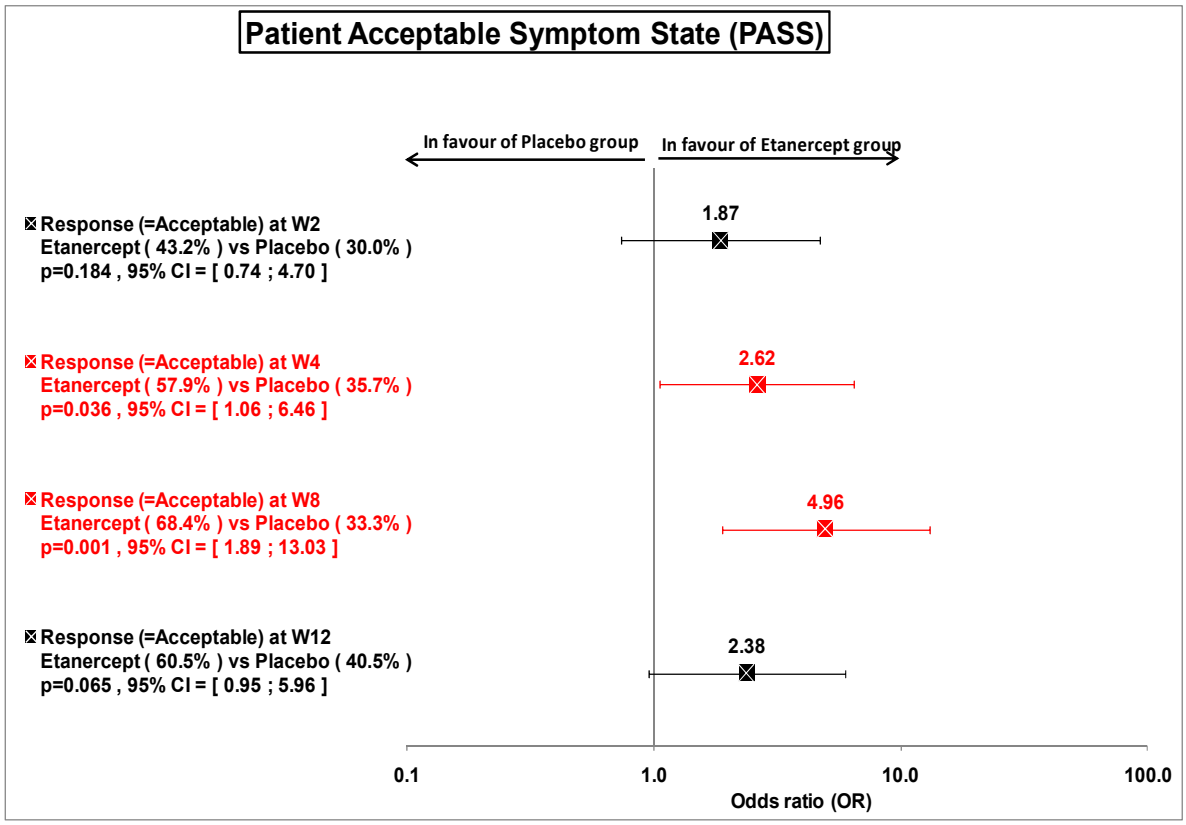
Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
MCII		
Week 2, n (%)		
Improved very or moderately important	18 (51.43%)	8 (21.62%)
Improved slightly or not at all important or no change or worse-more pain	17 (48.57%)	29 (78.38%)
Week 4, n (%)		
Improved very or moderately important	20 (52.63%)	12 (31.58%)
Improved slightly or not at all important or no change or worse-more pain	18 (47.37%)	26 (68.42%)
Week 8, n (%)		
Improved very or moderately important	27 (75.00%)	14 (36.84%)
Improved slightly or not at all important or no change or worse-more pain	9 (25.00%)	24 (63.16%)
Week 12, n (%)		
Improved very or moderately important	24 (63.16%)	14 (37.84%)
Improved slightly or not at all important or no change or worse-more pain	14 (36.84%)	23 (62.16%)
Week 14, n (%)		
Improved very or moderately important	28 (77.78%)	27 (77.14%)
Improved slightly or not at all important or no change or worse-more pain	8 (22.22%)	8 (22.86%)
Week 18, n (%)		
Improved very or moderately important	32 (94.12%)	29 (78.38%)
Improved slightly or not at all important or no change or worse-more pain	2 (5.88%)	8 (21.62%)
Week 24, n (%)		
Improved very or moderately important	32 (91.43%)	31 (86.11%)
Improved slightly or not at all important or no change or worse-more pain	3 (8.57%)	5 (13.89%)

MCII = Minimum Clinically Important Improvement; N = total number of subjects; n = number of subjects with specified criteria.
a. Subjects received etanercept 50 mg/week for 24 weeks
b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

Patient Acceptable Symptom State (PASS):

Percentage of subjects with acceptable state of PASS: No statistically significant difference between treatment groups was observed at Week 2. The response rate 'acceptable' of the PASS questionnaire was statistically higher in the etanercept group than in the placebo group at Week 4 (p=0.036) and Week 8 (p=0.001). At Week 12, the response rate between etanercept and placebo was still in favor of etanercept but was not statistically significant. Results for PASS are summarized in Figure 5.

Figure 5. Patient Acceptable Symptom State, mITT Population



p-value: From a generalized estimated equations model.
CI = confidence interval of the odds-ratio; mITT = modified intent-to-treat; vs = versus; W = week.

The change from Baseline for the PASS during the RCT and OLE (unadjusted) is summarized by visit in Table 39.

Table 39. Patient Acceptable Symptom State During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
PASS		
Week 2, n (%)		
Acceptable	15 (41.67%)	12 (32.43%)
Unacceptable	21 (58.33%)	25 (67.57%)
Week 4, n (%)		
Acceptable	22 (57.89%)	15 (39.47%)
Unacceptable	16 (42.11%)	23 (60.53%)
Week 8, n (%)		
Acceptable	26 (68.42%)	13 (34.21%)
Unacceptable	12 (31.58%)	25 (65.79%)
Week 12, n (%)		
Acceptable	23 (60.53%)	15 (40.54%)
Unacceptable	15 (39.47%)	22 (59.46%)
Week 14, n (%)		
Acceptable	25 (69.44%)	22 (64.71%)
Unacceptable	11 (30.56%)	12 (35.29%)
Week 18, n (%)		
Acceptable	26 (74.29%)	24 (66.67%)
Unacceptable	9 (25.71%)	12 (33.33%)
Week 24, n (%)		
Acceptable	27 (77.14%)	29 (80.56%)
Unacceptable	8 (22.86%)	7 (19.44%)

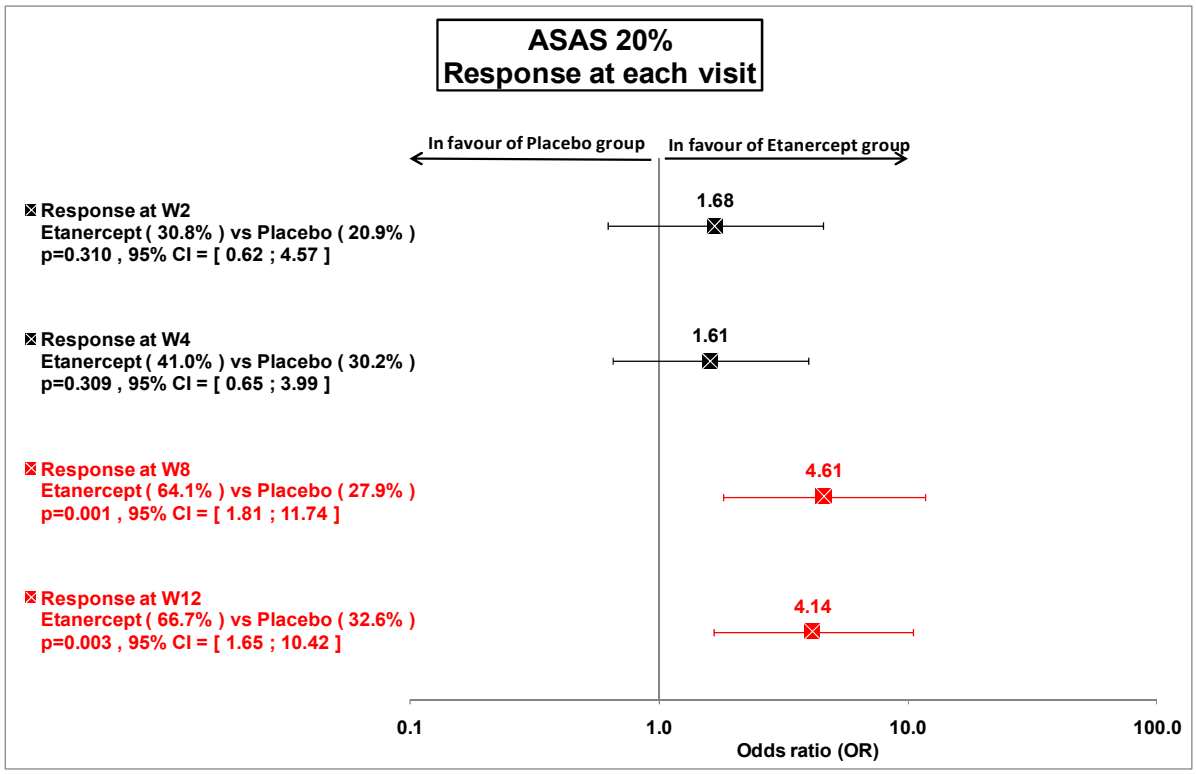
N = total number of subjects; n = number of subjects with specified criteria; PASS = Patient Acceptable Symptom State.
a. Subjects received etanercept 50 mg/week for 24 weeks.
b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

Assessment in Ankylosing Spondylitis (ASAS):

An ASAS20 response requires a 20% and 10 unit improvement in at least 3 of the 4 criteria: Patient Global Assessment, pain, function and inflammation with no deterioration in the remaining criterion. The ASAS50 and ASAS70 responses require a 50% and 70% of improvement, respectively.

Response rates of ASAS 20%: The response rates at Week 8 and Week 12 were statistically higher in etanercept group than in placebo group (Week 8: OR=4.61; 95% CI=[1.81; 11.74]; p=0.001 and Week 12: OR=4.14; 95% CI=[1.65; 10.42]; p=0.003, respectively). No statistically significant difference between treatment groups was observed before Week 8. Results of the ASAS 20% response rates during the 12-week RCT are summarized in Figure 6.

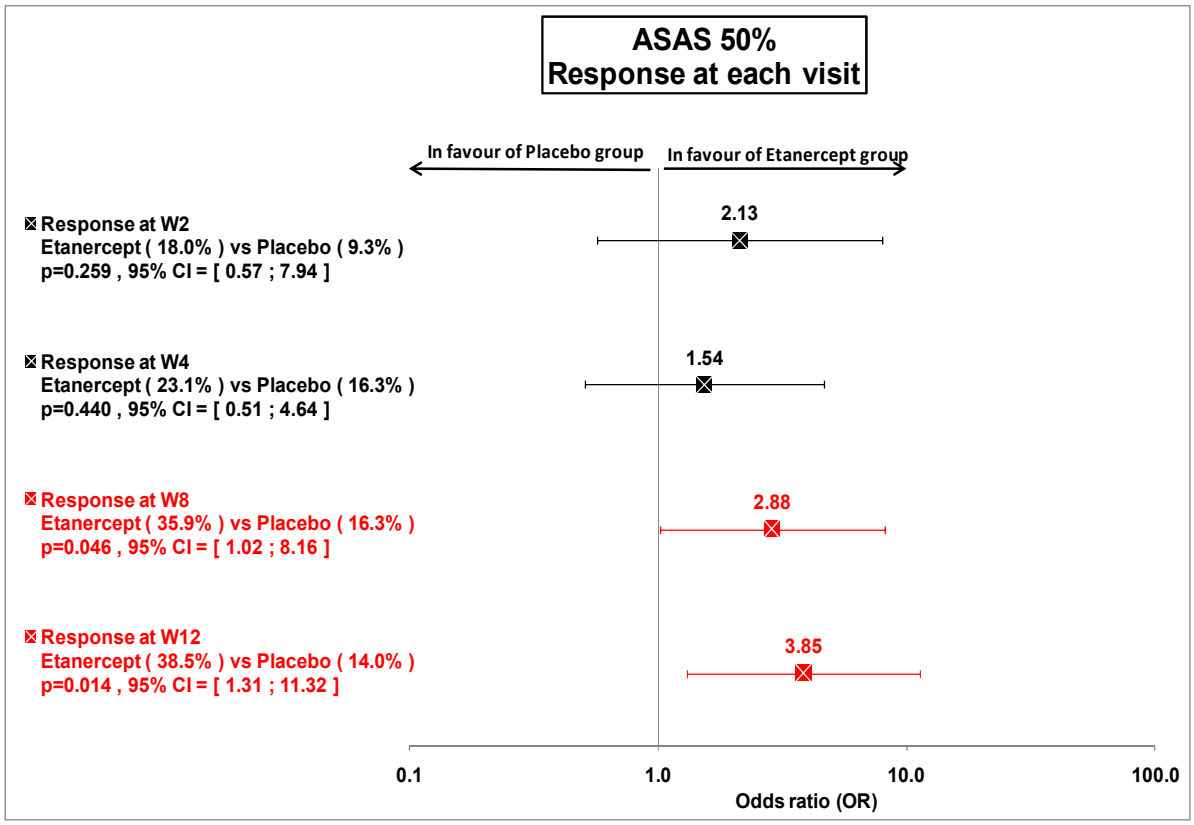
Figure 6. Response Rates of the ASAS 20%, mITT Population



p-value: From a generalized estimated equations model.
ASAS = assessment in ankylosing spondylitis; CI = confidence interval of the odds-ratio; mITT = modified intent-to-treat; vs = versus; W = week.

Response rate of ASAS 50%: The response rates at Week 8 and Week 12 were statistically higher in etanercept group than in placebo group (Week 8: OR=2.88; 95% CI=[1.02; 8.16]; p=0.046 and Week 12: OR=3.85; 95% CI=[1.31; 11.32]; p=0.014, respectively). No statistically significant difference between treatment groups was observed before Week 8. Results of the ASAS 50% response rates during the 12-week RCT are summarized in Figure 7.

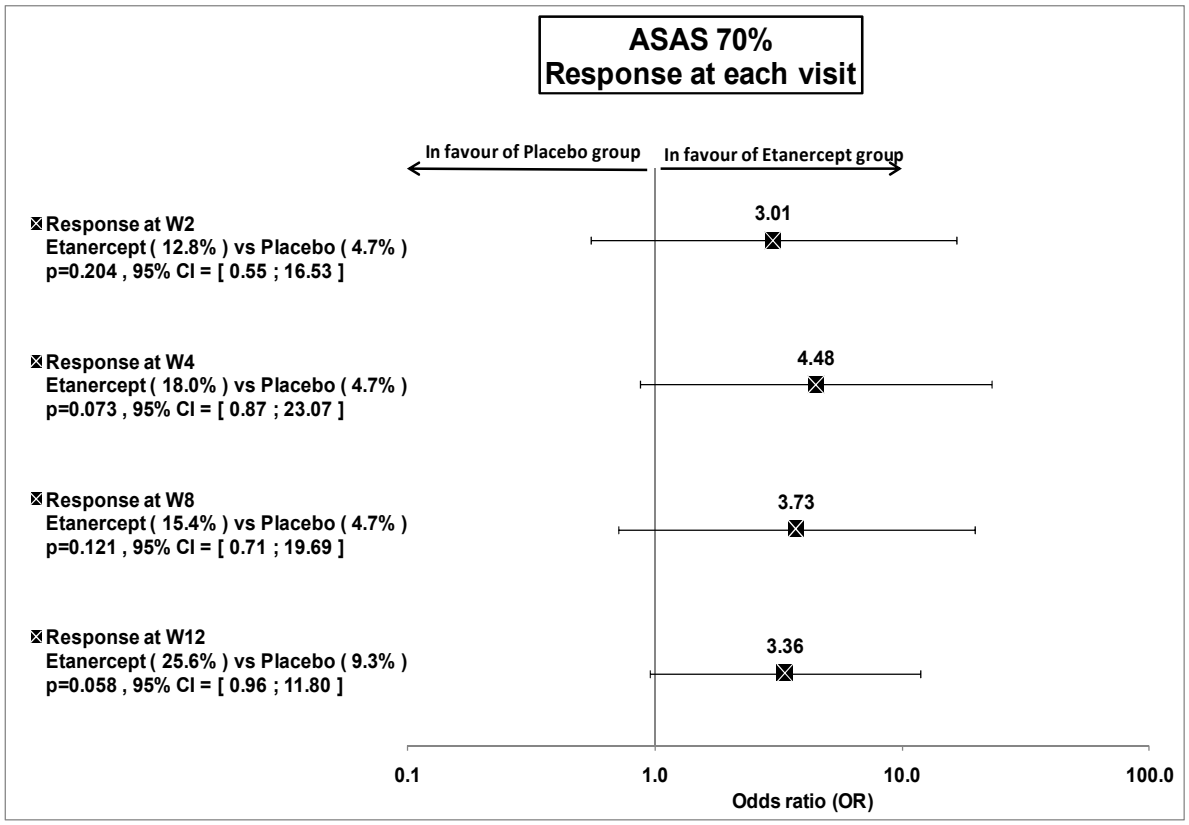
Figure 7. Response Rates of the ASAS 50%, mITT Population



p-value: From a generalized estimated equations model.
ASAS = assessment in ankylosing spondylitis; CI = confidence interval of the odds-ratio; mITT = modified intent-to-treat; vs = versus; W = week.

Response rates of ASAS 70%: There was no statistically significant difference between both groups concerning the response rates of the ASAS 70%. Results of the ASAS 70% response rates during the 12-week RCT are summarized in Figure 8.

Figure 8. Response Rates of the ASAS 70%, mITT Population



p-value: From a generalized estimated equations model.
ASAS = assessment in ankylosing spondylitis; CI = confidence interval of the odds-ratio; mITT = modified intent-to-treat; vs = versus; W = week.

The unadjusted percentage of subjects achieving ASAS20, 50 and 70 during the RCT and OLE is summarized by visit in Table 40.

Table 40. Assessment in Ankylosing Spondylitis During the Study

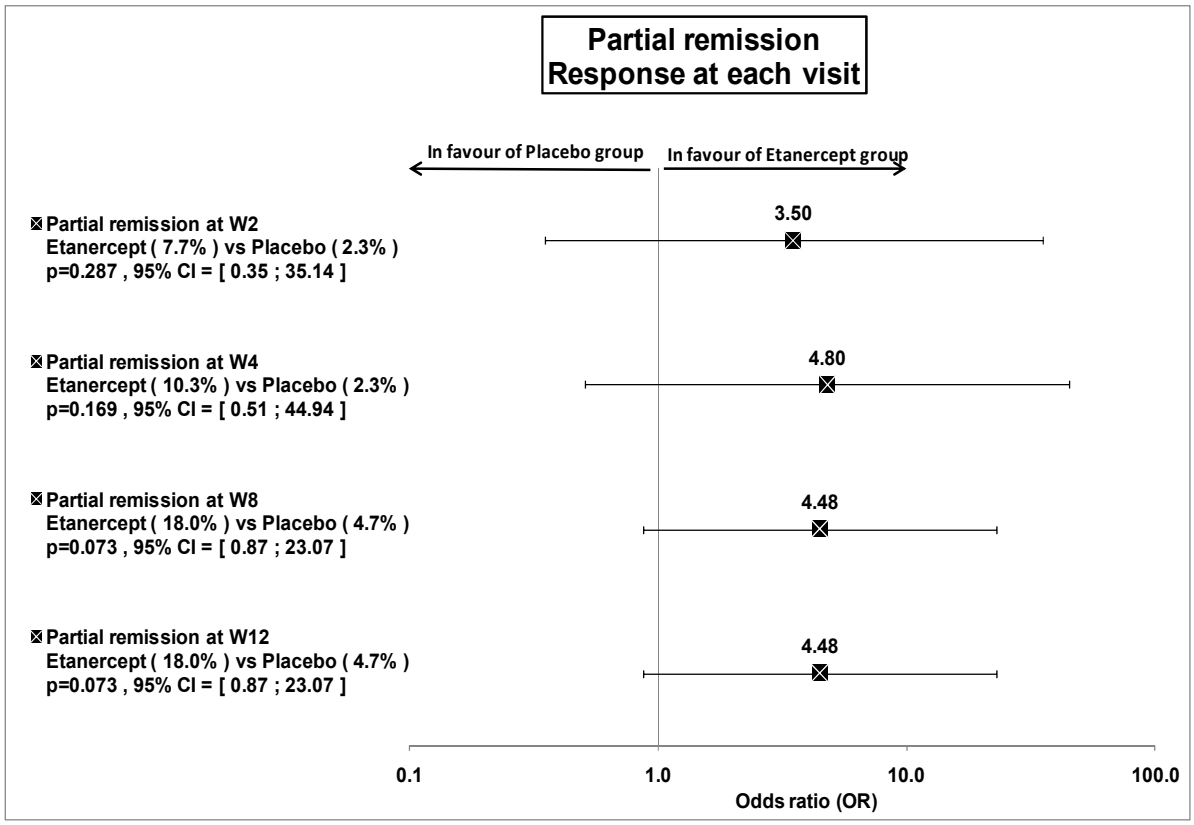
Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
ASAS 20%, n (%) responder		
Week 2	12 (31.58%)	9 (23.08%)
Week 4	16 (42.11%)	13 (33.33%)
Week 8	25 (65.79%)	12 (30.77%)
Week 12	26 (68.42%)	14 (35.90%)
Week 14	27 (71.05%)	21 (53.85%)
Week 18	27 (71.05%)	25 (64.10%)
Week 24	32 (84.21%)	26 (66.67%)
ASAS 50%, n (%) responder		
Week 2	7 (18.42%)	4 (10.26%)
Week 4	9 (23.68%)	7 (17.95%)
Week 8	14 (36.84%)	7 (17.95%)
Week 12	15 (39.47%)	6 (15.38%)
Week 14	17 (44.74%)	17 (43.59%)
Week 18	19 (50.00%)	19 (48.72%)
Week 24	23 (60.53%)	20 (51.28%)
ASAS 70%, n (%) responder		
Week 2	5 (13.16%)	2 (5.13%)
Week 4	7 (18.42%)	2 (5.13%)
Week 8	6 (15.79%)	2 (5.13%)
Week 12	10 (26.32%)	4 (10.26%)
Week 14	12 (31.58%)	13 (33.33%)
Week 18	12 (31.58%)	12 (30.77%)
Week 24	14 (36.84%)	14 (35.90%)

ASAS = Assessment in Ankylosing Spondylitis; N = total number of subjects; n = number of subjects with specified criteria.
a. Subjects received etanercept 50 mg/week for 24 weeks.
b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

Partial Remission:

There was no statistically significant difference between both groups concerning the response rates of partial remission. Results of partial remission response rates during the 12-week RCT are summarized in Figure 9.

Figure 9. Response Rates of a Partial Remission, mITT Population



p-value: From a generalized estimated equations model.
CI = confidence interval of the odds-ratio; mITT = modified intent-to-treat; vs = versus; W = week.

The unadjusted percentage of subjects with partial remission during the RCT and OLE is summarized by visit in Table 41.

Table 41. Partial Remission During the Study

Characteristic	Original Etanercept Group[a] N=38	Original Placebo Group[b] N=39
Partial remission		
Yes, n (%)		
Week 2	3 (7.89%)	1 (2.56%)
Week 4	4 (10.53%)	1 (2.56%)
Week 8	7 (18.42%)	2 (5.13%)
Week 12	7 (18.42%)	2 (5.13%)
Week 14	11 (28.95%)	9 (23.08%)
Week 18	12 (31.58%)	10 (25.64%)
Week 24	11 (28.95%)	9 (23.08%)

N = total number of subjects; n = number of subjects meeting specified criteria.
a. Subjects received etanercept 50 mg/week for 24 weeks.
b. Subjects received placebo for 12 weeks followed by etanercept 50 mg/week for 12 weeks.

Self-Assessment of Ability and/or Easiness to Perform Physically Demanding Activities:

The change from baseline in level of difficulty to perform physically demanding activities due to ankylosing spondylitis at Weeks 2, 4, 8, 12 is shown in Table 42.

Table 42. Change From Baseline in Level of Difficulty to Perform Physically Demanding Activities due to Ankylosing Spondylitis at Weeks 2, 4, 8, 12

Subject Physical Demanding Activity Assessment = Yes	Treatment		Difference (95% CI)	Statistical Significance
	Etanercept (N=19)	Placebo (N=17)		
Week 2 - Baseline				
n	18	16		
Adjusted mean (±SD)	-11.88 (±19.96)	-7.16 (±19.63)	-4.72	p=0.490
95% CI	-21.31; -2.46	-16.99; 2.67	-18.35; 8.91	
Week 4 - Baseline				
n	17	17		
Adjusted mean (±SD)	-15.14 (±19.63)	-12.04 (±20.00)	-3.09	p=0.651
95% CI	-24.67; -5.60	-21.77; -2.32	-16.73; 10.54	
Week 8 - Baseline				
n	16	17		
Adjusted mean (±SD)	-18.65 (±19.33)	-17.25 (±20.00)	-1.39	p=0.840
95% CI	-28.32; -8.98	-26.98; -7.53	-15.12; 12.34	
Week 12 - Baseline				
n	17	16		
Adjusted mean (±SD)	-22.55 (±19.85)	-18.53 (±19.64)	-4.02	p=0.562
95% CI	-32.19; -12.91	-28.37; -8.69	-17.81; 9.77	

CI = confidence interval; N = total number of subjects; n = number of subjects analyzed; SD = standard deviation.

Change from baseline in self-assessment of ability and or easiness to perform physically demanding activities at Weeks 14, 18, 24 is presented in Table 43.

Table 43. Change From Baseline in Self-Assessment of Ability and/or Easiness to Perform Physically Demanding Activities at Weeks 14, 18, 24 (After LOCF)

	Etanercept (N=17)	Placebo (N=17)
Week 14		
n	15	15
Mean (±SD)	-20.01 (±23.07)	-22.95 (±25.00)
95% CI	-32.79; -7.24	-36.79; -9.10
Week 18		
n	15	15
Mean (±SD)	-22.39 (±24.44)	-27.80 (±27.08)
95% CI	-35.92; -8.86	-42.80; -12.81
Week 24		
n	16	14
Mean (±SD)	-24.21 (±24.81)	-25.55 (±27.36)
95% CI	-37.43; -10.99	-41.35; -9.75

CI = confidence interval; LOCF = last observation carried forward; N = total number of subjects; n = number of subject analyzed; SD = standard deviation.

Safety Results:

Randomized Period:

During the 12-week RCT, the most common treatment emergent adverse events (TEAEs) reported in the etanercept group were injection site reaction (injection site erythema, injection site hematoma, injection site pruritus) and rhinitis each reported by 4 (10.3%) subjects, upper respiratory tract infection, transaminase increased and pruritus, each reported by 3 (7.7%) subjects. The most common TEAEs reported in the placebo group were rhinitis and headache, each reported by 3 (7.0%) subjects.

TEAEs in the etanercept group during the 12-week RCT are presented by relationship to study treatment in Table 44.

Table 44. Number (%) of Subjects Reporting Treatment-Emergent Adverse Events During the 12-Week RCT by Drug Relationship (Etanercept Group)

System Organ Class Preferred Term	Etanercept N=39	
	All Causality	Treatment-Related
Any adverse events	24 (61.5)	10 (25.6)
Blood and lymphatic system disorders	1 (2.6)	1 (2.6)
Neutropenia	1 (2.6)[a]	1 (2.6)[a]
Ear and labyrinth disorders	1 (2.6)	-
External ear pain	1 (2.6)	-
Eye disorders	1 (2.6)	-
Iridocyclitis	1 (2.6)	-
Gastrointestinal disorders	4 (10.3)	1 (2.6)
Abdominal pain upper	1 (2.6)	-
Diarrhoea	2 (5.1)	1 (2.6)
Gastric ulcer	1 (2.6)	-
Haematochezia	1 (2.6)	1 (2.6)
Vomiting	1 (2.6)	-
General disorders and administration site conditions	3 (7.7)	2 (5.1)
Asthenia	1 (2.6)	-
Injection site erythema	2 (5.1)	2 (5.1)
Injection site haematoma	1 (2.6)	-
Injection site pruritus	1 (2.6)	1 (2.6)
Oedema peripheral	1 (2.6)	-
Hepatobiliary disorders	1 (2.6)	1 (2.6)
Cytolytic hepatitis	1 (2.6)	1 (2.6)
Infections and infestations	10 (25.6)	4 (10.3)
Bronchitis	2 (5.1)	1 (2.6)
Folliculitis	1 (2.6)	-
Nasopharyngitis	1 (2.6)	-
Rhinitis	4 (10.3)	3 (7.7)
Tracheitis	1 (2.6)	1 (2.6)
Upper respiratory tract infection	3 (7.7)	-
Viral infection	1 (2.6)	-
Injury, poisoning and procedural complications	2 (5.1)	-
Arthropod bite	1 (2.6)	-
Contusion	1 (2.6)	-
Investigations	5 (12.8)	2 (5.1)
Haemoglobin urine present	1 (2.6)	.
Transaminases increased	3 (7.7)	1 (2.6)
Weight increased	1 (2.6)	1 (2.6)
Metabolism and nutrition disorders	1 (2.6)	-
Hypophosphataemia	1 (2.6)	-
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (2.6)	-
Lung neoplasm malignant	1 (2.6)[a]	-
Nervous system disorders	3 (7.7)	-
Headache	2 (5.1)	-
Migraine	1 (2.6)	-
Trigeminal neuralgia	1 (2.6)	-
Psychiatric disorders	2 (5.1)	1 (2.6)
Depression	1 (2.6)	.
Insomnia	1 (2.6)	1 (2.6)
Renal and urinary disorders	1 (2.6)	.

Table 44. Number (%) of Subjects Reporting Treatment-Emergent Adverse Events During the 12-Week RCT by Drug Relationship (Etanercept Group)

System Organ Class Preferred Term	Etanercept N=39	
	All Causality	Treatment-Related
Haematuria	1 (2.6)	-
Reproductive system and breast disorders	1 (2.6)	-
Prostatitis	1 (2.6)	-
Skin and subcutaneous tissue disorders	3 (7.7)	3 (7.7)
Pruritus	3 (7.7)	3 (7.7)
Rash	1 (2.6)	1 (2.6)
Urticaria	1 (2.6)	1 (2.6)
Vascular disorders	2 (5.1)	1 (2.6)
Hot flush	1 (2.6)	1 (2.6)
Hypertension	1 (2.6)	-

AEs and SAEs are not separated out.
AE = adverse event; N = number of subjects in the treatment group; RCT = randomized controlled trial; SAE = serious adverse event.
a. Considered SAEs.

TEAEs in the placebo group during the 12-week RCT are presented by relationship to study treatment in Table 45.

Table 45. Number (%) of Subjects Reporting Treatment-Emergent Adverse Events During the 12-Week RCT by Drug Relationship (Placebo Group)

System Organ Class Preferred Term	Placebo N=43	
	All Causality	Treatment-Related
Any adverse events	28 (65.1)	13 (30.2)
Ear and labyrinth disorders	1 (2.3)	-
Vertigo	1 (2.3)	-
Eye disorders	1 (2.3)	-
Cataract	1 (2.3)	-
Uveitis	1 (2.3)	-
Gastrointestinal disorders	7 (16.3)	1 (2.3)
Abdominal pain	2 (4.7)	-
Abdominal pain upper	1 (2.3)	-
Constipation	1 (2.3)	-
Diarrhoea	2 (4.7)	-
Hiatus hernia	1 (2.3)	-
Nausea	1 (2.3)	1 (2.3)
General disorders and administration site conditions	3 (7.0)	2 (4.7)
Asthenia	1 (2.3)	1 (2.3)
Fatigue	1 (2.3)	1 (2.3)
Malaise	1 (2.3)	-
Immune system disorders	1 (2.3)	-
Seasonal allergy	1 (2.3)	-
Infections and infestations	14 (32.6)	4 (9.3)
Bronchitis	1 (2.3)	1 (2.3)
Gastroenteritis	2 (4.7)	-
Herpes zoster	1 (2.3)	1 (2.3)
Hordeolum	1 (2.3)	-
Nasopharyngitis	2 (4.7)	-
Otitis externa	1 (2.3)	-
Pharyngitis	1 (2.3)	-
Rhinitis	3 (7.0)	1 (2.3)
Upper respiratory tract infection	2 (4.7)	-
Urinary tract infection	1 (2.3)	1 (2.3)
Injury, poisoning and procedural complications	1 (2.3)	-
Skin laceration	1 (2.3)	-
Investigations	5 (11.6)	3 (7.0)
Blood urea increased	1 (2.3)	-
Gamma-glutamyltransferase increased	1 (2.3)	1 (2.3)
Transaminases increased	1 (2.3)	-
Weight decreased	1 (2.3)	1 (2.3)
Weight increased	1 (2.3)	1 (2.3)
Metabolism and nutrition disorders	2 (4.7)	-
Hyperkalaemia	1 (2.3)	-
Hypokalaemia	1 (2.3)	-
Musculoskeletal and connective tissue disorders	3 (7.0)	2 (4.7)
Ankylosing spondylitis	1 (2.3)[a]	1 (2.3)[a]
Joint swelling	1 (2.3)	-
Muscle spasms	1 (2.3)	1 (2.3)
Nervous system disorders	4 (9.3)	2 (4.7)
Carpal tunnel syndrome	1 (2.3)	-
Headache	3 (7.0)	2 (4.7)
Respiratory, thoracic and mediastinal disorders	3 (7.0)	2 (4.7)

Table 45. Number (%) of Subjects Reporting Treatment-Emergent Adverse Events During the 12-Week RCT by Drug Relationship (Placebo Group)

System Organ Class Preferred Term	Placebo N=43	
	All Causality	Treatment-Related
Asthma	1 (2.3)	1 (2.3)
Dyspnoea	1 (2.3)	-
Epistaxis	1 (2.3)	1 (2.3)
Skin and subcutaneous tissue disorders	4 (9.3)	1 (2.3)
Hyperhidrosis	1 (2.3)	1 (2.3)
Pruritus	2 (4.7)	-
Skin inflammation	1 (2.3)	-
Skin lesion	1 (2.3)	-

AEs and SAEs are not separated out.
AE = adverse event; N = number of subjects in the treatment group; RCT = randomized controlled trial; SAE = serious adverse event.
a. Considered SAEs.

Serious Treatment-Related AEs: Three (3) subjects reported serious adverse events (SAEs) during the 12-week RCT:

- One subject in the etanercept group reported a neutropenia.
- One subject in the etanercept group reported a pulmonary nodular lesion (apical right) diagnosed as bronchogenic carcinoma.
- One subject in the placebo group reported an exacerbation of AS.

Safety-Related Discontinuations: Two (2) subjects had a safety-related event that led to discontinuation from the study during the 12-week RCT:

- One subject in the etanercept group discontinued the study at the time of diagnosis (after first injection) of a pulmonary nodular lesion following detailed evaluation of a chest X-rays performed at Screening.
- One subject in the placebo group discontinued the study because of a lack of efficacy.

Deaths: No subject died during the 12-week RCT.

Other Safety Related Observations: Results of each laboratory assessment (eg, blood chemistry, hematology, urinalysis) were examined to identify individual subjects who had laboratory values of potential clinical importance (PCI). After review of each concerned case, it was stated that PCI laboratory values were not of clinical importance. Similarly, vital signs and weight were reviewed for PCI changes during the 12-week RCT. The changes refer to comparisons with baseline values before treatment in each period. After review of each concerned case, it was stated that the PCI vital signs were not of clinical importance.

Open-Label Extension Period:

TEAEs in the original etanercept group during the 12-week OLE are presented by relationship to study treatment in Table 46.

Table 46. Number (%) of Subjects Reporting Treatment-Emergent Adverse Events During the 12-Week OLE by Drug Relationship (Original Etanercept Group)

System Organ Class Preferred Term	Original Etanercept Group N=38	
	All Causality	Treatment-Related
Any adverse events	16 (42.1)	7 (18.4)
Gastrointestinal disorders	2 (5.3)	-
Diarrhoea	1 (2.6)	-
Dyspepsia	1 (2.6)	-
General disorders and administration site conditions	3 (7.9)	1 (2.6)
Injection site pruritus	1 (2.6)	1 (2.6)
Malaise	1 (2.6)	-
Pain	1 (2.6)	-
Infections and infestations	8 (21.1)	4 (10.5)
Bronchitis	1 (2.6)	1 (2.6)
Nasopharyngitis	2 (5.3)	1 (2.6)
Rhinitis	2 (5.3)	1 (2.6)
Sinusitis	1 (2.6)	1 (2.6)
Upper respiratory tract infection	2 (5.3)	-
Injury, poisoning and procedural complications	1 (2.6)	1 (2.6)
Post procedural diarrhoea	1 (2.6)	1 (2.6)
Metabolism and nutrition disorders	2 (5.3)	1 (2.6)
Hypercholesterolaemia	1 (2.6)	-
Hypertriglyceridaemia	1 (2.6)	1 (2.6)
Nervous system disorders	2 (5.3)	-
Carpal tunnel syndrome	1 (2.6)	-
Intercostal neuralgia	1 (2.6)	-
Respiratory, thoracic and mediastinal disorders	2 (5.3)	1 (2.6)
Asthma	1 (2.6)	-
Pharyngolaryngeal pain	1 (2.6)	1 (2.6)
Skin and subcutaneous tissue disorders	1 (2.6)	-
Rash pruritic	1 (2.6)	-
Vascular disorders	1 (2.6)	-
Lymphoedema	1 (2.6)	-

AEs and SAEs are not separated out.
AE = adverse event; N = number of subjects in the treatment group; OLE = open label extension; SAE = serious adverse event.

TEAEs in the original placebo group during the 12-week OLE are presented by relationship to study treatment in Table 47.

Table 47. Number (%) of Subjects Reporting Treatment-Emergent Adverse Events During the 12-Week OLE by Drug Relationship (Original Placebo Group)

System Organ Class Preferred Term	Original Placebo Group (N=39)	
	All Causality	Treatment-Related
Any adverse events	22 (56.4)	8 (20.5)
Blood and lymphatic system disorders	1 (2.6)	-
Leukopenia	1 (2.6)	-
Cardiac disorders	1 (2.6)	-
Tachycardia	1 (2.6)	-
Ear and labyrinth disorders	1 (2.6)	-
Vertigo	1 (2.6)	-
Gastrointestinal disorders	4 (10.3)	-
Abdominal pain upper	1 (2.6)	-
Constipation	1 (2.6)	-
Diarrhoea	1 (2.6)	-
Dysphagia	1 (2.6)	-
General disorders and administration site conditions	4 (10.3)	4 (10.3)
Exercise tolerance decreased	1 (2.6)	1 (2.6)
Fatigue	1 (2.6)	1 (2.6)
Injection site pruritus	2 (5.1)	2 (5.1)
Infections and infestations	7 (18.0)	3 (7.7)
Bronchitis	1 (2.6)	1 (2.6)
Gastroenteritis	1 (2.6)	.
Nasopharyngitis	2 (5.1)	1 (2.6)
Otitis externa	1 (2.6)	1 (2.6)
Rhinitis	1 (2.6)	-
Upper respiratory tract infection	1 (2.6)	-
Viral pharyngitis	1 (2.6)	-
Injury, poisoning and procedural complications	1 (2.6)	-
Road traffic accident	1 (2.6)	-
Skeletal injury	1 (2.6)	-
Investigations	1 (2.6)	-
Aspartate aminotransferase increased	1 (2.6)	-
Metabolism and nutrition disorders	2 (5.1)	-
Hypercholesterolaemia	1 (2.6)	-
Hyperkalaemia	1 (2.6)[a]	-
Musculoskeletal and connective tissue disorders	2 (5.1)	-
Muscle spasms	1 (2.6)	-
Tendonitis	1 (2.6)	-
Nervous system disorders	1 (2.6)	-
Syncope vasovagal	1 (2.6)	-
Psychiatric disorders	1 (2.6)	1 (2.6)
Insomnia	1 (2.6)	1 (2.6)
Respiratory, thoracic and mediastinal disorders	1 (2.6)	-
Cough	1 (2.6)	-
Skin and subcutaneous tissue disorders	3 (7.7)	1 (2.6)
Eczema	1 (2.6)	-
Psoriasis	2 (5.1)	1 (2.6)
Surgical and medical procedures	2 (5.1)	-
Tooth extraction	2 (5.1)	-
Vascular disorders	1 (2.6)	-
Hypertension	1 (2.6)	-

Table 47. Number (%) of Subjects Reporting Treatment-Emergent Adverse Events During the 12-Week OLE by Drug Relationship (Original Placebo Group)

AEs and SAEs are not separated out.
AE = adverse event; N = number of subject in the treatment group; OLE = open label extension; SAE = serious adverse event.
a. Considered SAE.

Serious Treatment-Related AEs: One subject reported an SAE during the 12-week OLE. The subject was in placebo/etanercept group and reported a hyperkalemia without possible relationship to study drug.

Safety-Related Discontinuations: No subject had a safety-related event that led to discontinuation from the study during the 12-week OLE.

Deaths: No subject died during the 12-week OLE.

Other Safety Related Observations: Results of each laboratory assessment (eg, blood chemistry and hematology) were examined to identify individual subjects who had PCI laboratory values. After review of each concerned case, it was stated that PCI laboratory values were not of clinical importance. Similarly, vital signs and weight were reviewed for PCI changes during the 12-week OLE. The changes refer to comparisons with baseline values before treatment in each period. After review of each concerned case, it was stated that the PCI vital signs were not of clinical importance.

CONCLUSIONS: In summary, this study is the first prospective, randomized, placebo-controlled study specifically designed to evaluate etanercept in active, advanced and severe AS disease and demonstrating symptomatic clinically relevant and statistically significant benefit during the RCT period. This efficacy is observed for the main symptoms (pain) and on markers of inflammation (CRP) as well as disease severity in terms of spinal mobility and pulmonary capacity. The maintenance of etanercept treatment during the OLE period shows a sustained efficacy while its delayed administration shows symptomatic clinical benefit.

There were no unexpected AEs during the RCT phase as well as during the OLE of this study.