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

PROTOCOL NO.: 0881A6-4425 (B1801013)

PROTOCOL TITLE: A Randomized, Double-Blind Trial Assessing the Efficacy and Safety of Etanercept 50 mg Twice Weekly and Etanercept 50 mg Once Weekly for the Treatment of Moderate to Severe Psoriasis

Study Centers: A total of 31 centers took part in the study and randomized subjects; 7 in Germany, 4 in Hungary, 3 each in Argentina and Mexico, 2 each in Belgium, the Czech Republic, the Republic of Korea, Taiwan, and Thailand, and 1 each in Austria, Greece, Italy, and Spain.

Study Initiation and Final Completion Date: 13 June 2008 to 18 January 2010

Phase of Development: Phase 4

Study Objectives:

Primary Objective: To evaluate the effect of etanercept 50 mg once weekly (QW) for 24 weeks and etanercept 50 mg twice weekly (BIW) for 12 weeks followed by etanercept 50 mg QW for 12 weeks in treating the skin manifestations of psoriasis in subjects with moderate to severe psoriasis when used with adjunctive topical therapy as needed.

Secondary Objectives:

- To assess the impact of 2 different treatment regimens of etanercept on quality of life and pharmacoeconomic outcomes through 24 weeks in subjects with moderate to severe plaque psoriasis;
- To assess the cardiovascular risk profile at baseline for subjects with moderate to severe plaque psoriasis;
- To assess the safety of the 2 different treatment regimens of etanercept through 24 weeks in subjects with moderate to severe plaque psoriasis.

METHODS:

Study Design: This was a randomized, multi-center, double-blind trial in subjects with moderate to severe psoriasis. After a screening period of up to 5 weeks, all subjects were treated with etanercept over a 24-week treatment period (12 weeks of double-blind treatment

[Period 1] followed by 12 weeks of open-label treatment [Period 2]) plus a 2-week follow-up telephone call to assess for adverse events (AEs). Eligible subjects were randomized in a 1:1 ratio to 1 of the 2 treatment groups.

Period 1 (Week 1 to Week 12): Etanercept 50 mg QW/QW group received etanercept 50 mg QW for 24 weeks (ie, both Period 1 and Period 2); and etanercept 50 mg BIW/QW group received etanercept 50 mg BIW for 12 weeks (ie, Period 1) followed by etanercept 50 mg QW for 12 weeks (ie, Period 2). During the first 12 weeks, matching placebo for etanercept was to be used to maintain the blinding. Fourteen days prior to the baseline visit through to Week 12, mild topical steroids at a stable dose applied on the scalp, axillae, and groin were only to be allowed at the Investigator's discretion. Other topical agents were not allowed.

Period 2 (Week 13 to Week 24): After Week 12, and until the end of the study (Week 24), all subjects were allowed most topical agents used for the treatment of psoriasis at the Investigator's discretion; these included mild, moderate, potent, or very potent topical steroids (their use must have been according to the approved label for the country in which they were used, and there were no restrictions to the body location or dose), vitamin D analogs, combination products containing topical steroids and vitamin D analogs, and anthralin.

The schedule of activities is provided in Table 1.

Table 1. Schedule of Activities

Study Week[a]	**Days -35 to -1**	**Wk 0 Baseline**	**Wk 2**	**Wk 4**	**Wk 8**	**Wk 12**	**Wk 16**	**Wk 20**	**Wk 24**	**Wk 26**	**Early Discontinuation**
Study Interval	**Screening**[b]	**Baseline**	**Active Phase**							**Follow-Up**	
			Period 1: Weeks 1-12				**Period 2: Weeks 13-24**				
Visit	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**[c]	**99**[c]
Informed consent	X										
Demographics	X										
Medical history	X										
Inclusion/exclusion	X	X									
Family history[d]		X									
Diagnosis history	X										
Substance usage (alcohol and cigarette)	X					X			X		X
Prior medications	X	X									
Concomitant medications			X	X	X	X	X	X	X		X
Vital signs[e]	X	X	X	X	X	X	X	X	X		X
Physical examination	X					X			X		X
Physician Global Assessment of Psoriasis (PGA)[f]	X	X	X	X	X	X	X	X	X		X
Body surface area[f]	X	X	X	X	X	X	X	X	X		X
Psoriasis Area and Severity Index (PASI)[g,h]	X	X	X	X	X	X	X	X	X		X
Subject Global Assessment (SGA)[g]	X	X	X	X	X	X	X	X	X		X
Psoriasis Subject Satisfaction Questionnaire (PSSQ)[g]		X	X	X	X	X	X	X	X		X
Dermatology Life Quality Index (DLQI)[g]		X	X	X	X	X	X	X	X		X
Euro Qol-5D (EQ-5D)[g]		X				X			X		X
Hospital Anxiety and Depression Scale (HADS)[g]		X				X			X		X
Work Productivity and Activity Improvement: Psoriasis (WPAI:PSO)[g]		X				X			X		X
Medical Outcomes Study (MOS) Sleep Scale-12 point[g]		X				X			X		X
Functional assessment of chronic illness therapy-Fatigue (FACIT-Fatigue)[g]		X				X			X		X
Subject Pharmacoeconomic Questionnaire[g,i]		X				X			X		X
Physician Psoriasis Satisfaction Questionnaire		X	X	X	X	X	X	X	X		X
Psoriatic Arthritis Survey Evaluation (PASE)[g]	X					X					X
Pregnancy test (serum)[j]	X										
Pregnancy test (urine)		X									
Blood chemistry, hematology, urine chemistry[k,l]	X	X[m]				X			X		X

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Study Week[a]	Days -35 to -1	Wk 0 Baseline	Wk 2	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 26	Early Discontinuation
Study Interval	**Screening[b]**	**Baseline**	**Active Phase**							**Follow-Up**	
			Period 1: Weeks 1-12				**Period 2: Weeks 13-24**				
Visit	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10[c]**	**99[c]**
Metabolic biomarker labs[k,n]		X				X					X
Cardiovascular labs[k,n]		X		X		X					X
High sensitivity C-reactive protein (hsCRP)[k]		X		X		X			X		X
Chest radiograph/TB testing[o]	X										
Adverse events (AEs)[p]	X----------									----------X	X
Randomization		X									
Photos (if applicable)		X				X			X		X
Collect and review take home diaries			X	X	X	X	X	X	X		X
Drug accountability			X	X	X	X	X	X	X		X
Dispense take home diaries[q]		X	X	X	X	X	X	X			
Dispense test article[r]		X	X	X	X	X	X	X			
Fasting reminder call[s]		X		X		X			X		X

AE = adverse event; eCRF = electronic case report form; PASI = Psoriasis Area and Severity Index; TB = tuberculosis; TNF = tumor necrosis factor; Wk = week.

a. The visit window for Visits 3 through 9 was ±4 days. It was intended all visit procedures should preferably be completed on the same day (with the exception of fasting blood collection, chest radiographs, and possibly purified protein derivative [PPD] testing).

b. Screening visit procedures (Visit 1) were preferred to be occurred on the same day. The screening period was intended for the washout of prohibited medications and tuberculosis screening/prophylactic treatment as necessary per local guidelines. The screening period was a minimum of 4 days but no more than 35 days. Results of all screening procedures were available at the Baseline visit (Visit 2) to determine eligibility.

c. There was a follow-up telephone call to assess new and ongoing adverse events at: approximately 15 days after early discontinuation, if the subject discontinued early from the study; or at Week 26 (Visit 10) that was approximately 15 days after the Week 24 (Visit 9).

d. Family history (parental) questions were used for risk calculations. These data were only recorded at the baseline visit; however, the family history data were used for both the baseline and Week 12 risk calculations.

e. Included sitting blood pressure and pulse rate at each visit; height, weight, hip circumference, and waist circumference were only collected at screening visit. Waist to hip ratio is a predictor of cardiovascular risk and was derived in the database. Additionally, body mass index (BMI) and body surface area (BSA) were not collected in vital signs; however, they were calculated with the appropriate collected data.

f. It was recommended that the same qualified personnel complete these assessments at each visit.

g. Completed only by subjects in regions where valid translations were available.

h. Only at the screening visit, the Investigator or designee was responsible for collecting the PASI data points and calculating the PASI score using a PASI calculator provided. Additionally, at this screening visit, both the PASI data points and the score were entered into the eCRF. At all other visits, only the PASI data points were collected and entered into the eCRF.

i. Question 1a and 1b on the pharmacoeconomic questionnaire were captured on the hospitalization eCRF.

j. For women of childbearing potential only (serum test at screening, urine at baseline).

k. All laboratory tests were collected at the subject's scheduled visit, however, to accommodate rare instances when a subject was unable to fast (or did not fast), all scheduled lab samples for the visit could be drawn within +4 days of the visit.

l. Subject had received isoniazid (INH) therapy during screening and had had the mandatory liver function test (LFT) profile before the baseline visit that was out of the

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Study Week[a]	Days -35 to -1	Wk 0 Baseline	Wk 2	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 26	Early Discontinuation
Study Interval	Screening[b]	Baseline	Active Phase							Follow-Up	
			Period 1: Weeks 1-12				Period 2: Weeks 13-24				
Visit	1	2	3	4	5	6	7	8	9	10[c]	99[c]

normal lab range. (The LFT profile labs had to be drawn after initiating INH therapy at a minimum of 3 weeks and at least 4 days prior to the planned baseline visit).

m. These laboratory tests did not need to be repeated at the Baseline visit (Visit 2) if they were completed at the Screening visit (Visit 1) ≤14 days before baseline, unless the subject was being treated for latent TB in a country where concomitant anti-TB therapy and anti-TNF therapy could be given without delay.

n. At the discontinuation visit, the metabolic biomarker and cardiovascular labs only needed to be completed for those subjects who discontinued on or before Week 12.

o. Chest radiograph was performed at screening visit (Visit 1) only and read locally by a qualified reader. Chest radiograph was not required if it had been done within the past 12 months of screening and the report was available and included in subject's source documents. Local country guidelines were followed for appropriate TB screening and prophylaxis in the setting of anti-TNF therapy including a minimum of a chest radiograph and objective TB testing such as PPD or Quantiferon depending on what was acceptable per local guidelines. If the subject was known to be PPD or Quantiferon positive, the test needed not be repeated if documentation was available to show the subject meets local for criteria for anti-TNF therapy and had not had TB in the last 2 years.

p. AEs were collected from the signing of the informed consent form to approximately 15 days after Visit 9. If an AE was related to infection, this information was captured on the eCRF.

q. Take home diaries collected study medication and nonstudy steroids therapy.

r. The first dose had to be administered in the Investigator site office by study personnel after all baseline evaluations were completed.

s. Phone call had to occur at least 1 day before the subject's Week 0 (baseline), Week 4 (Visit 4), Week 12 (Visit 6), Week 24 (Visit 9), and early discontinuation (Visit 99) (if appropriate) visits to remind the subject that they had to come to the study site fasted.

Number of Subjects (Planned and Analyzed): A total of 250 subjects were planned for enrollment (125 per treatment group) and a total of 273 subjects were randomized (137 subjects in the etanercept 50 mg QW/QW group and 136 subjects in etanercept 50 mg BIW/QW group).

Of the 273 subjects; 66 were randomized in Germany, 50 in Hungary, 34 in Mexico, 28 in Argentina, 25 in Taiwan, 22 in Thailand, 16 in the Republic of Korea, 12 in the Czech Republic, 7 in Belgium, 6 in Austria, 3 in Spain, and 2 each in Greece and Italy.

Diagnosis and Main Criteria for Inclusion: Male and female subjects aged 18 years and older at time of consent with active, moderate to severe chronic plaque psoriasis defined by the following criteria: clinically stable, plaque psoriasis involving ≥10% body surface area (BSA) or Psoriasis Area and Severity Index (PASI) ≥10; and, in the opinion of the Investigator; failure, intolerance, contraindication or not a candidate for the methotrexate , cyclosporine and psoralen plus ultraviolet A radiation therapy, were included in the study.

Exclusion Criteria: Subjects with evidence of skin conditions (eg, eczema) other than psoriasis that would interfere with evaluations of the effect of study medication on psoriasis; with rheumatologic disease such as rheumatoid arthritis, systemic lupus erythematous, systemic vasculitis, scleroderma and polymyositis, or associated syndromes; or subjects with serious infection or active or recent (within 2 years) tuberculosis infection were excluded from the study.

Study Treatment: The subjects were randomly assigned to 1 of the 2 treatment groups:

Etanercept 50 mg QW/QW Group: Subjects received etanercept subcutaneously (SC) at a dose of 50 mg QW and matching placebo QW for the first 12 weeks of the study, followed by etanercept SC at a dose of 50 mg QW for the second 12 weeks of the study. During the first 12 weeks, the first dose of the week was to be etanercept 50 mg and the second dose of the week was to be matching placebo.

Etanercept 50 mg BIW/QW Group: Subjects received etanercept SC at a dose of 50 mg BIW for the first 12 weeks of the study followed by etanercept SC at a dose of 50 mg QW for the second 12 weeks of the study.

During the first 12 weeks, matching placebo for etanercept was used to maintain the blinding. During the second 12 weeks, all subjects received the same treatment of etanercept 50 mg QW in an open-label fashion, although they remained blinded to the original treatment allocation. All subjects were instructed to use the labeled prefilled syringe (PFS).

The injectable study drug was to be administered on approximately the same day of the week. During the first 12 weeks, subjects were to have study medication administered 3 to 4 days apart on the same days of the week (eg, Monday and Thursday, Tuesday and Friday, Wednesday and Saturday, or Sunday and Wednesday). Injections were to be administered in the abdomen, thigh, or upper arm. The location of injection was to be rotated with each dose. If administration of the injectable study drug did not occur on the day that it was scheduled,

the missed dose was to be administered immediately unless it was 1 day before the next scheduled dose.

Efficacy and Outcome Research Endpoints:

Primary Efficacy Endpoint: Proportion of subjects achieving a 75% improvement from baseline in PASI score at Week 24 when used with adjunctive topical therapy as needed.

Secondary Efficacy Endpoints:

- Proportion of subjects achieving a 50%, 75%, 90%, and 100% improvement from baseline in PASI score at each visit through Week 24;
- Proportion of subjects achieving a status on the Physician Global Assessment (PGA) of psoriasis of clear (0), clear/almost clear (0, 1), or clear/almost clear/mild (0, 1, 2) at each visit through Week 24;
- Time to PASI 50, PASI 75, PASI 100, and PGA of clear/almost clear/mild and PGA of clear/almost clear over 24 weeks;
- Change from baseline at each visit in the PGA of psoriasis through 24 weeks;
- Change from baseline at each visit in the PASI through 24 weeks;
- Change from baseline at each visit in the percent BSA involvement of psoriasis through 24 Weeks;
- Change from baseline at each visit in the subject assessments (general health, psoriasis activity, and itching) through 24 weeks;
- Change from baseline at each visit in the Psoriasis Subject Satisfaction Questionnaire (PSSQ) through 24 weeks;
- Change from baseline at each visit in the photographed image of lesions in selected subjects through 24 weeks;
- Proportion of subjects choosing not to use topical preparations at each visit from Week 12 through 24 weeks.

Health Outcomes Assessments: Assessments included:

- Subject Global Assessment (SGA);
- PSSQ;
- Dermatology Life Quality Index (DLQI);
- Euro-Quality of Life 5 diemension (EQ-5D);

- Hospital Anxiety and Depression Scale (HADS);
- Work Productivity and Activity Improvement: Psoriasis Questionnaire (WPAI:PSO);
- Medical Outcomes Study (MOS) Sleep Scale;
- Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Questionnaire;
- Subject Pharmacoeconomic Questionnaire;
- Psoriatic Arthritis Screening and Evaluation (PASE);
- Physician Satisfaction Questionnaire.

Safety Evaluations: Safety was evaluated through assessment of AEs, serious AEs (SAEs), premature withdrawal, vital signs, physical examinations, and results of clinical laboratory tests.

Statistical Methods:

Modified Intent-to-Treat (mITT) Population: The mITT population included all randomly assigned subjects who received at least 1 etanercept dose and had both baseline and on-therapy PASI evaluations. The mITT population was used for all primary and secondary efficacy analyses.

Per-Protocol (PP) Population: The PP population included subjects from the mITT population who had no major protocol violations.

Safety Population: The safety population included all randomly-assigned subjects who took at least 1 dose of test article.

This study assessed the effect of etanercept 50 mg BIW and etanercept 50 mg QW based on the primary endpoint of PASI 75 response at Week 24 when used with adjunctive topical therapy as needed. The primary null hypothesis was that the Week 24 PASI 75 response proportion was ≤50% in the etanercept 50 mg QW/QW group. The conditional primary null hypothesis was that the Week 24 PASI 75 response proportion was ≤60% in the etanercept 50 mg BIW/QW group with adjunctive topical therapy as needed.

The primary statistical hypotheses were tested using the 2-sided 95% confidence interval (CI) on the PASI 75 response proportions at Week 24. If the CI excluded 50% in the etanercept 50 mg QW/QW group, the primary null hypothesis that the proportion is 50% was rejected and the conditional primary hypothesis was tested in the same manner. If the 95% CI excluded 60% in the etanercept 50 mg BIW/QW group, the conditional primary null hypothesis was rejected. Exact binomial CIs were used for proportions.

The primary efficacy analyses used the last observation carried forward (LOCF) approach for missing data imputation; observed cases (OC) results were also summarized for each visit including only those subjects contributing data at each time point. For the primary endpoint

PASI 75 and for key secondary binary endpoints, a third set of analyses were performed; these analyses included the same subjects as the LOCF analyses. However, all subjects who dropped out were treated as non-responders for all subsequent visits; this approach was referred to as non-response imputation (NRI). This methodology was applied to selected binary endpoints.

For continuous health outcome, safety, and secondary efficacy parameters, 1-way analysis of variance or analysis of covariance (ANCOVA) models with treatment group as a factor and baseline measurement as a covariate were used for comparisons between treatment groups of raw scores or change from baseline scores. For dichotomous endpoints, Fisher's exact test or chi-square test was used.

For time to event analyses, estimation used the Kaplan-Meier approach and statistical testing used the log-rank test. For time to event analyses, no imputation was applied; subjects who had not experienced the event were censored at the time of last observation.

RESULTS:

Subject Disposition and Demography: Subject disposition is summarized in Table 2.

Table 2. Subject Disposition and Subjects Analyzed

Number of Subjects	ETN50 BIW/QW N=136 n (%)	ETN50 QW/QW N=137 n (%)	Total N=273 n (%)
Assigned to treatment	136 (100)	137 (100)	273 (100)
Completed	124 (91.2)	127 (92.7)	251 (91.9)
Discontinued[a]	12 (8.8)	10 (7.3)	22 (8.1)
Adverse event	6 (4.4)	3 (2.2)	9 (3.3)
Discontinuation of study by Sponsor[b]	2 (1.5)	0	2 (0.7)
Other	0	1 (0.7)	1 (0.4)
Protocol violation	1 (0.7)	0	1 (0.4)
Subject request	2 (1.5)	5 (3.6)	7 (2.6)
Unsatisfactory response-efficacy	1 (0.7)	1 (0.7)	2 (0.7)
Analyzed for efficacy:			
mITT population	133 (97.79)	137 (100)	270 (98.9)
Anlayzed for safety:			
Adverse events	136 (100)	137 (100)	273 (100)

BIW = twice weekly; ETN50 = etanercept 50 mg; mITT = modified intent-to-treat; N = total number of subjects; n = number of subjects with specified criteria; QW = once weekly.

a. Total discontinued was the sum of individual reasons since they were mutually exclusive by subject.

b. Due to the occurrence of a natural disaster (earthquake in Italy).

Baseline demographic characteristics were similar across both treatment groups as presented in Table 3. The mean age of enrolled subjects was 43.95 years (range, 19-79 years) in the etanercept 50 mg BIW/QW group and 43.85 years in the etanercept 50 mg QW/QW group (range, 18-75 years).

Table 3. Demographic Characteristics

	ETN50 BIW/QW N=136	ETN50 QW/QW N=137	Total N=273
Age (years)			
Mean (SD)	43.95 (12.68)	43.85 (12.69)	43.90 (12.66)
Minimum, Maximum	19.00, 79.00	18.00, 75.00	18.00, 79.00
Median	43.00	44.00	43.00
Sex, n (%)			
Female	47 (34.56)	36 (26.28)	83 (30.40)
Male	89 (65.44)	101 (73.72)	190 (69.60)
Race, n (%)			
White	88 (64.71)	86 (62.77)	174 (63.74)
Asian	31 (22.79)	33 (24.09)	64 (23.44)
Black or African American	0	1 (0.73)	1 (0.37)
Other	17 (12.50)	17 (12.41)	34 (12.45)

BIW = twice weekly; ETN = etanercept; N = number of subjects in each treatment group; n = number of subjects with specified criteria; QW = once weekly; SD = standard deviation.

Efficacy and Outcomes Research Results:

Primary Efficacy Endpoint Results:

Table 4 presents the proportion of subjects achieving a 75% improvement from baseline in PASI score at Week 24.

In the etanercept 50 mg QW/QW group, 59.9% of subjects achieved a PASI 75 response at Week 24, and the lower bound of the 95% CI (51.1% to 68.1%) exceeded the pre-specified criteria of 50%. Therefore, the primary null hypothesis, that the value was <50%, was rejected. In the etanercept 50 mg BIW/QW group, 78.2% of subjects achieved a PASI 75 response at Week 24, and the lower bound of the 95% CI (70.2% to 84.9%) exceeded the pre-specified criteria of 60%, so the conditional primary null hypothesis was also rejected. Thus, both the primary and conditional primary objectives of the trial were met.

The primary efficacy variable was the proportion of subjects achieving a PASI 75 score at Week 24 (LOCF). A significantly greater proportion of subjects in the etanercept 50 mg BIW/QW group achieved a PASI 75 response at Week 24 compared with the etanercept 50 mg QW/QW group (78.2% [95% CI of 70.2 to 84.9] versus 59.9% [95% CI of 51.1 to 68.1] respectively, p-value=0.0015).

In the OC analysis, the difference between the 2 groups in the PASI 75 response rate (95% CI) at Week 24 was significant in favor of the etanercept 50 mg BIW/QW group (79.8% [71.7%, 86.5%] versus 62.1% [52.9%, 70.7%]; p-value=0.0032, Fisher's exact test).

In the NRI analysis, the difference between the 2 groups in the PASI 75 response rate (95% CI) at Week 24 was significant in favor of the etanercept 50 mg BIW/QW group (74.4% [66.2%, 81.6%] versus 56.2% [47.5%, 64.7%]; p-value=0.0021, Fisher's exact test).

Table 4. Number (%) of Subjects Achieving PASI 75 Response at Week 24, mITT Population, LOCF

	ETN50 BIW/QW N=133	ETN50 QW/QW N=137	Proportion Difference	p-Value
PASI 75 at Week 24				
Number of subjects, n (%)	104 (78.2)	82 (59.9)	-	-
95% CI	70.2, 84.9	51.1, 68.1	18.34 (6.80, 29.88)	0.0015

p-value was based on Fisher's exact test.
BIW = twice weekly; CI = confidence interval; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; N = number of subjects in each treatment group; n = number of subjects with specified criteria; PASI = Psoriasis Area and Severity Index; PASI 75 = 75% improvement from baseline in PASI; QW = once weekly.

Secondary Efficacy Endpoints Results:

Proportion of Subjects Achieving a 50%, 75%, 90%, and 100% Improvement From Baseline in PASI Score at Each Visit Through Week 24:

Table 5 presents, for all time points, the results of the between-group analysis of the number (%) of subjects who achieved PASI 50, PASI 75, PASI 90, and PASI 100 responses (LOCF).

The earliest statistically significant difference between treatment groups in PASI response was observed at Week 4 for PASI 50, Week 8 for PASI 75, and Week 12 for PASI 90. The significant differences between treatment groups in those PASI responses continued until Week 24, the final time point. All significant differences in PASI response rates were in favor of the etanercept 50 mg BIW/QW group. At no time during the study was a significant difference observed between treatment groups in PASI 100 response rates.

The results of the OC analysis are similar to the LOCF results except that significance in favor of the etanercept 50 mg BIW/QW group was achieved at Week 20 for the PASI 100 response rate.

The results of the NRI analysis are similar to the LOCF results except that significance in favor of the etanercept 50 mg BIW/QW group was achieved at Week 20 for the PASI 100 response rate.

Table 5. Number (%) of Subjects Achieving PASI 50, PASI 75, PASI 90, and PASI 100 Responses, mITT Population, LOCF

PASI	Time Point	ETN50 BIW/QW n/Total/% (95% CI)	ETN50 QW/QW n/Total/% (95% CI)	Proportion Difference (95% CI)	p-Value
PASI 50					
	Week 2	12/133, 9.0% (4.7%, 15.2%)	8/136, 5.9% (2.6%, 11.3%)	3.14 (-3.88, 10.16)	0.3605
	Week 4	51/133, 38.3% (30.1%, 47.2%)	28/137, 20.4% (14.0%, 28.2%)	17.91 (6.50, 29.32)	0.0013
	Week 8	95/133, 71.4% (63.0%, 78.9%)	71/137, 51.8% (43.1%, 60.4%)	19.60 (7.51, 31.70)	0.0011
	Week 12	117/133, 88.0% (81.2%, 93.0%)	93/137, 67.9% (59.4%, 75.6%)	20.09 (9.77, 30.40)	<.0001
	Week 16	123/133, 92.5% (86.6%, 96.3%)	107/137, 78.1% (70.2%, 84.7%)	14.38 (5.39, 23.37)	0.0010
	Week 20	124/133, 93.2% (87.5%, 96.9%)	113/137, 82.5% (75.1%, 88.4%)	10.75 (2.35, 19.16)	0.0087
	Week 24	123/133, 92.5% (86.6%, 96.3%)	111/137, 81.0% (73.4%, 87.2%)	11.46 (2.77, 20.15)	0.0068
PASI 75					
	Week 2	2/133, 1.5% (0.2%, 5.3%)	0/136, 0.0% (0.0%, 2.7%)	1.50 (-1.31, 4.32)	0.2435
	Week 4	8/133, 6.0% (2.6%, 11.5%)	6/137, 4.4% (1.6%, 9.3%)	1.64 (-4.40, 7.67)	0.5929
	Week 8	47/133, 35.3% (27.3%, 44.1%)	30/137, 21.9% (15.3%, 29.8%)	13.44 (2.02, 24.86)	0.0156
	Week 12	83/133, 62.4% (53.6%, 70.7%)	51/137, 37.2% (29.1%, 45.9%)	25.18 (12.89, 37.47)	<.0001
	Week 16	97/133, 72.9% (64.5%, 80.3%)	70/137, 51.1% (42.4%, 59.7%)	21.84 (9.82, 33.85)	0.0003
	Week 20	104/133, 78.2% (70.2%, 84.9%)	80/137, 58.4% (49.7%, 66.7%)	19.80 (8.23, 31.38)	0.0006
	Week 24	104/133, 78.2% (70.2%, 84.9%)	82/137, 59.9% (51.1%, 68.1%)	18.34 (6.80, 29.88)	0.0015
PASI 90					
	Week 2	0/133, 0.0% (0.0%, 2.7%)	0/136, 0.0% (0.0%, 2.7%)	0.00 (-0.74, 0.74)	-
	Week 4	1/133, 0.8% (0.0%, 4.1%)	1/137, 0.7% (0.0%, 4.0%)	0.02 (-2.77, 2.81)	1.0000
	Week 8	13/133, 9.8% (5.3%, 16.1%)	8/137, 5.8% (2.6%, 11.2%)	3.94 (-3.20, 11.07)	0.2611
	Week 12	39/133, 29.3% (21.8%, 37.8%)	15/137, 10.9% (6.3%, 17.4%)	18.37 (8.30, 28.45)	0.0002
	Week 16	57/133, 42.9% (34.3%, 51.7%)	35/137, 25.5% (18.5%, 33.7%)	17.31 (5.43, 29.19)	0.0031
	Week 20	60/133, 45.1% (36.5%, 54.0%)	40/137, 29.2% (21.7%, 37.6%)	15.92 (3.80, 28.04)	0.0081
	Week 24	66/133, 49.6% (40.8%, 58.4%)	45/137, 32.8% (25.1%, 41.4%)	16.78 (4.46, 29.10)	0.0064
PASI 100					
	Week 2	0/133, 0.0% (0.0%, 2.7%)	0/136, 0.0% (0.0%, 2.7%)	0.00 (-0.74, 0.74)	-
	Week 4	0/133, 0.0% (0.0%, 2.7%)	1/137, 0.7% (0.0%, 4.0%)	-0.73 (-2.90, 1.44)	1.0000
	Week 8	0/133, 0.0% (0.0%, 2.7%)	2/137, 1.5% (0.2%, 5.2%)	-1.46 (-4.21, 1.29)	0.4983
	Week 12	5/133, 3.8% (1.2%, 8.6%)	3/137, 2.2% (0.5%, 6.3%)	1.57 (-3.23, 6.37)	0.4957
	Week 16	10/133, 7.5% (3.7%, 13.4%)	6/137, 4.4% (1.6%, 9.3%)	3.14 (-3.24, 9.52)	0.3115
	Week 20	19/133, 14.3% (8.8%, 21.4%)	10/137, 7.3% (3.6%, 13.0%)	6.99 (-1.13, 15.10)	0.0773
	Week 24	19/133, 14.3% (8.8%, 21.4%)	12/137, 8.8% (4.6%, 14.8%)	5.53 (-2.82, 13.87)	0.1830

p-values were based on Fisher's exact test.
BIW = twice weekly; CI = confidence interval; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; n = number of subjects;
PASI = Psoriasis Area and Severity Index; PASI 50 = 50% improvement from baseline in PASI; PASI 75 = 75% improvement from baseline in PASI;
PASI 90 = 90% improvement from baseline in PASI; PASI 100 = 100% improvement from baseline in PASI; QW = once weekly.

Change From Baseline at Each Visit in the PASI Through 24 Weeks:

Table 6 presents, for all time points, the results of the between-group analysis of change from baseline in PASI score (LOCF).

The adjusted mean change from baseline in PASI score (LOCF) was significantly greater for the etanercept 50 mg BIW/QW group at all time-points (p-values of <0.0001 to 0.0103, ANCOVA). The results of the OC analysis are similar to the LOCF results.

Table 6. Change From Baseline in PASI Score: Comparison Between Treatment Groups, mITT Population, LOCF

Week of Treatment	Treatment Group	Number of Subjects	Adjusted Mean Change (SE)	Difference of Adjusted Mean Change (95% CI) ETN50 BIW/QW-ETN50 QW/QW	p-Value
Week 2	ETN50 BIW/QW	133	-4.5 (0.4)		
	ETN50 QW/QW	136	-3.2 (0.4)	-1.3 (-2.3, -0.3)	0.0103
Week 4	ETN50 BIW/QW	133	-8.7 (0.5)		
	ETN50 QW/QW	137	-6.8 (0.4)	-1.8 (-3.0, -0.6)	0.0031
Week 8	ETN50 BIW/QW	133	-13.6 (0.5)		
	ETN50 QW/QW	137	-10.6 (0.5)	-3.0 (-4.4, -1.7)	<0.0001
Week 12	ETN50 BIW/QW	133	-16.2 (0.5)		
	ETN50 QW/QW	137	-12.6 (0.5)	-3.6 (-5.0, -2.2)	<0.0001
Week 16	ETN50 BIW/QW	133	-17.4 (0.5)		
	ETN50 QW/QW	137	-14.6 (0.5)	-2.8 (-4.0, -1.5)	<0.0001
Week 20	ETN50 BIW/QW	133	-17.5 (0.5)		
	ETN50 QW/QW	137	-15.5 (0.5)	-2.1 (-3.3, -0.8)	0.0012
Week 24	ETN50 BIW/QW	133	-17.4 (0.5)		
	ETN50 QW/QW	137	-15.4 (0.5)	-2.0 (-3.4, -0.7)	0.0042

p-values were based on ANCOVA model: Change from baseline = baseline value + region + treatment group.
ANCOVA = analysis of covariance; BIW = twice weekly; CI = confidence interval; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; PASI = Psoriasis Area and Severity Index; QW = once weekly; SE = standard error.

Table 7 presents, for all time points, the results of the between-group analysis of percent change from baseline in PASI score (LOCF). The mean percent change from baseline is the mean of all of the subjects' individual changes from baseline. The adjusted mean percent change from baseline in PASI score (LOCF) was significantly greater for the etanercept 50 mg BIW/QW group at all time-points (p-values of <0.0001 to 0.0173, ANCOVA). The results of the OC analysis are similar to the LOCF results.

Table 7. Percent Change From Baseline in PASI Score: Comparison Between Treatment Groups, mITT Population, LOCF

Week of Treatment	Treatment Group	Number of Subjects	Adjusted Mean Change (SE)	Difference of Adjusted Mean Change (95% CI) ETN50 BIW/QW- ETN50 QW/QW	p-Value
Week 2	ETN50 BIW/QW	133	-20.0 (1.9)		
	ETN50 QW/QW	136	-13.3 (1.9)	-6.7 (-11.8, -1.6)	0.0099
Week 4	ETN50 BIW/QW	133	-39.4 (2.3)		
	ETN50 QW/QW	137	-32.0 (2.3)	-7.4 (-13.5, -1.3)	0.0173
Week 8	ETN50 BIW/QW	133	-61.9 (2.4)		
	ETN50 QW/QW	137	-49.4 (2.4)	-12.5 (-18.9, -6.2)	0.0001
Week 12	ETN50 BIW/QW	133	-74.1 (2.6)		
	ETN50 QW/QW	137	-58.5 (2.6)	-15.6 (-22.5, -8.8)	<0.0001
Week 16	ETN50 BIW/ QW	133	-80.9 (2.2)		
	ETN50 QW/QW	137	-67.7 (2.1)	-13.3 (-19.0, -7.5)	<0.0001
Week 20	ETN50 BIW/QW	133	-81.8 (2.2)		
	ETN50 QW/QW	137	-71.6 (2.1)	-10.2 (-16.0, -4.4)	0.0006
Week 24	ETN50 BIW/QW	133	-81.3 (2.5)		
	ETN50 QW/QW	137	-70.7 (2.5)	-10.6 (-17.3, -3.9)	0.0021

p-values were based on ANCOVA model: Change from baseline = baseline value + region + treatment group.
ANCOVA = analysis of covariance; BIW = twice weekly; CI = confidence interval; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; PASI = Psoriasis Area and Severity Index; QW = once weekly; SE = standard error.

Time to PASI 50, PASI 75, PASI 100 Reponse:

Table 8 presents the results of the between-group analysis of the Kaplan-Meier estimate of median time to achieve a PASI 50, PASI 75, PASI 90, and PASI 100 response. Times to achieve PASI 50, PASI 75 and PASI 90 responses were significantly shorter in the etanercept 50 mg BIW/QW group compared with the etanercept 50 mg QW/QW group.

Table 8. Kaplan-Meier Estimates of Time to Achieving First PASI 50, PASI 75, PASI 90, and PASI 100 Response, mITT Population, Observed Cases

PASI	ETN50 BIW/QW Median Time in Days (95% CI)	ETN50 QW/QW Median Time in Days (95% CI)	p-Value
PASI 50	57 (56, 57)	57 (57, 85)	<0.0001
PASI 75	85 (84, 85)	113 (110, 141)	<0.0001
PASI 90	141 (113, 170)	171 (169, -)	0.0053
PASI 100	Not estimable	Not estimable	0.0432

p-value was based on log-rank test.
BIW = twice weekly; CI = confidence interval; ETN = etanercept; mITT = modified intent-to-treat; PASI = Psoriasis Area and Severity Index; PASI 50 = 50% improvement from baseline in PASI; PASI 75 = 75% improvement from baseline in PASI; PASI 90 = 90% improvement from baseline in PASI; PASI 100 = 100% improvement from baseline in PASI; QW = once weekly.

Proportion of Subjects Achieving a Status on the PGA of Psoriasis of Clear, Clear/Almost Clear, or Clear/Almost Clear/Mild at Each Visit Through Week 24:

Table 9 presents, for all time points, the results of the between-group analysis of the number (%) of subjects that achieved PGA responses of clear, clear/almost clear, and clear/almost clear/mild (LOCF).

The proportion of subjects achieving a PGA response of clear/almost clear/mild was significantly greater in the etanercept etanercept 50 mg BIW/QW group compared with the etanercept 50 mg QW/QW group from Week 8 onward. All statistically significant differences in PGA responses were in favor of the etanercept 50 mg BIW/QW group.

The results of the OC analysis and the NRI analysis were similar to the LOCF results.

Table 9. Number (%) of Subjects Achieving PGA Responses, mITT Population, LOCF

PGA	Time Point	ETN50 BIW/QW n/Total/% (95% CI)	ETN50 QW/QW n/Total/% (95% CI)	Proportion Difference (95% CI)	p-Value
PGA Clear (0)					
	Baseline	0/133, 0.0% (0.0%, 2.7%)	0/137, 0.0% (0.0%, 2.7%)	0.00 (-0.74, 0.74)	-
	Week 2	0/133, 0.0% (0.0%, 2.7%)	0/136, 0.0% (0.0%, 2.7%)	0.00 (-0.74, 0.74)	-
	Week 4	0/133, 0.0% (0.0%, 2.7%)	1/137, 0.7% (0.0%, 4.0%)	-0.73 (-2.90, 1.44)	1.0000
	Week 8	2/133, 1.5% (0.2%, 5.3%)	2/137, 1.5% (0.2%, 5.2%)	0.04 (-3.58, 3.67)	1.0000
	Week 12	12/133, 9.0% (4.7%, 15.2%)	4/137, 2.9% (0.8%, 7.3%)	6.10 (-0.26, 12.47)	0.0401
	Week 16	17/133, 12.8% (7.6%, 19.7%)	13/137, 9.5% (5.1%, 15.7%)	3.29 (-4.95, 11.54)	0.4415
	Week 20	26/133, 19.5% (13.2%, 27.3%)	15/137, 10.9% (6.3%, 17.4%)	8.60 (-0.67, 17.87)	0.0617
	Week 24	28/133, 21.1% (14.5%, 29.0%)	17/137, 12.4% (7.4%, 19.1%)	8.64 (-0.96, 18.24)	0.0720
PGA Clear/Almost Clear (0,1)					
	Baseline	0/133, 0.0% (0.0%, 2.7%)	1/137, 0.7% (0.0%, 4.0%)	-0.73 (-2.90, 1.44)	1.0000
	Week 2	1/133, 0.8% (0.0%, 4.1%)	3/136, 2.2% (0.5%, 6.3%)	-1.45 (-5.07, 2.16)	0.6223
	Week 4	17/133, 12.8% (7.6%, 19.7%)	9/137, 6.6% (3.0%, 12.1%)	6.21 (-1.56, 13.98)	0.1000
	Week 8	45/133, 33.8% (25.9%, 42.5%)	25/137, 18.2% (12.2%, 25.7%)	15.59 (4.53, 26.65)	0.0037
	Week 12	73/133, 54.9% (46.0%, 63.5%)	45/137, 32.8% (25.1%, 41.4%)	22.04 (9.75, 34.33)	0.0004
	Week 16	81/133, 60.9% (52.1%, 69.2%)	65/137, 47.4% (38.9%, 56.1%)	13.46 (0.94, 25.97)	0.0285
	Week 20	87/133, 65.4% (56.7%, 73.4%)	69/137, 50.4% (41.7%, 59.0%)	15.05 (2.67, 27.43)	0.0139
	Week 24	93/133, 69.9% (61.4%, 77.6%)	69/137, 50.4% (41.7%, 59.0%)	19.56 (7.38, 31.74)	0.0012
PGA Clear/Almost Clear/Mild (0,1,2)					
	Baseline	13/133, 9.8% (5.3%, 16.1%)	17/137, 12.4% (7.4%, 19.1%)	-2.63 (-10.86, 5.59)	0.5633
	Week 2	36/133, 27.1% (19.7%, 35.5%)	30/136, 22.1% (15.4%, 30.0%)	5.01 (-6.01, 16.03)	0.3956
	Week 4	62/133, 46.6% (37.9%, 55.5%)	52/137, 38.0% (29.8%, 46.6%)	8.66 (-3.82, 21.14)	0.1754
	Week 8	97/133, 72.9% (64.5%, 80.3%)	81/137, 59.1% (50.4%, 67.4%)	13.81 (1.90, 25.72)	0.0207
	Week 12	118/133, 88.7% (82.1%, 93.5%)	95/137, 69.3% (60.9%, 76.9%)	19.38 (9.23, 29.53)	<0.0001
	Week 16	118/133, 88.7% (82.1%, 93.5%)	103/137, 75.2% (67.1%, 82.2%)	13.54 (3.79, 23.29)	0.0044
	Week 20	118/133, 88.7% (82.1%, 93.5%)	107/137, 78.1% (70.2%, 84.7%)	10.62 (1.11, 20.13)	0.0223
	Week 24	119/133, 89.5% (83.0%, 94.1%)	107/137, 78.1% (70.2%, 84.7%)	11.37 (1.96, 20.78)	0.0133

p-values were based on Fisher's exact test.
BIW = twice weekly; CI = confidence interval; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; n = number of subjects; PGA = Physician Global Assessment; QW = once weekly.

Time to PGA of Clear/Almost Clear/Mild and Clear/Almost Clear Over 24 Weeks:

Table 10 presents the results of the between-group analysis of the Kaplan-Meier estimates of median time to achieve PGA responses of clear/almost clear and clear/almost clear/mild. Times to achieve PGA responses of clear/almost clear and clear/almost clear/mild were significantly shorter in the etanercept 50 mg BIW/QW group compared with the etanercept 50 mg QW/QW group.

Table 10. Kaplan-Meier Estimates of Time to Achieving First PGA Response, mITT Population, Observed Cases

PGA	ETN50 BIW/QW Median Time in Days (95% CI)	ETN50 QW/QW Median Time in Days (95% CI)	p-Value
PGA clear/almost clear (0,1)	85 (85, 89)	114 (112, 167)	0.0003
PGA clear/almost clear/mild (0,1,2)	53 (29, 57)	57 (56, 57)	0.0022

p-value was based on log-rank test.
BIW = twice weekly; CI = confidence interval; ETN = etanercept; mITT = modified intent-to-treat; PGA = Physician Global Assessment; QW = once weekly.

Change From Baseline at Each Visit in the PGA of Psoriasis Through 24 Weeks:

Table 11 presents, for all time points, the results of the between-group analysis of change from baseline in PGA score (LOCF). The PGA score ranged from 0 to 5, with higher scores indicating worse disease. The mean PGA score at baseline was 3.4 for both the etanercept 50 mg BIW/QW group and the etanercept 50 mg QW/QW group. The adjusted mean change from baseline in PGA score (LOCF) was significantly greater for the etanercept 50 mg BIW/QW group at all time-points (p-values of <0.0001 to 0.0193, ANCOVA). The results of the OC analysis were similar to the LOCF results.

Table 11. Change From Baseline in PGA: Comparison Between Treatment Groups, mITT Population, LOCF

Week of Treatment	Treatment Group	Number of Subjects	Adjusted Mean Change (SE)	Difference of Adjusted Mean Change (95% CI) ETN50 BIW/QW-ETN50 QW/QW	p-Value
Week 2	ETN50 BIW/QW	133	-0.4 (0.0)		
	ETN50 QW/QW	136	-0.3 (0.0)	-0.2 (-0.3, -0.0)	0.0193
Week 4	ETN50 BIW/QW	133	-0.9 (0.1)		
	ETN50 QW/QW	137	-0.7 (0.1)	-0.2 (-0.4, -0.1)	0.0114
Week 8	ETN50 BIW/QW	133	-1.4 (0.1)		
	ETN50 QW/QW	137	-1.1 (0.1)	-0.3 (-0.5, -0.2)	0.0006
Week 12	ETN50 BIW/QW	133	-1.9 (0.1)		
	ETN50 QW/QW	137	-1.4 (0.1)	-0.5 (-0.7, -0.3)	<0.0001
Week 16	ETN50 BIW/QW	133	-2.0 (0.1)		
	ETN50 QW/QW	137	-1.7 (0.1)	-0.3 (-0.5, -0.1)	0.0058
Week 20	ETN50 BIW/QW	133	-2.1 (0.1)		
	ETN50 QW/QW	137	-1.7 (0.1)	-0.4 (-0.6, -0.1)	0.0018
Week 24	ETN50 BIW/QW	133	-2.1 (0.1)		
	ETN50 QW/QW	137	-1.8 (0.1)	-0.4 (-0.6, -0.2)	0.0009

p-values were based on ANCOVA model: Change from baseline = baseline value + region + treatment group.
ANCOVA = analysis of covariance; BIW = twice weekly; CI = confidence interval; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; PGA = Physician Global Assessment; QW = once weekly; SE = standard error.

Change From Baseline at Each Visit in the % BSA Involvement of Psoriasis Through 24 Weeks:

Table 12 presents descriptive statistics and results of the within-group analysis of change from baseline and percent change from baseline in percent BSA involvement of psoriasis at all time-points (LOCF). All of the within-group analyses showed a significant improvement from baseline except for Week 2 in the etanercept 50 mg QW/QW group. The results of the OC analysis were similar to the LOCF results.

Change from baseline in PGA of head, scalp, and neck psoriasis: Table 13 presents, for all time points, the results of the between-group analysis of change from baseline in PGA of head, scalp, and neck (LOCF). The PGA of head, scalp, and neck score ranges from 0 to 5, with higher scores indicating worse disease. The mean PGA score for head, scalp, and neck psoriasis at baseline was 2.8 and 2.7 for the etanercept 50 mg BIW/QW and etanercept 50 mg QW/QW groups, respectively. The adjusted mean change from baseline in PGA score for head, scalp, and neck psoriasis (LOCF) was significantly greater for the etanercept 50 mg BIW/QW group at Weeks 4, 12, 16, and 24. The results of the OC analysis are similar to the LOCF results.

Table 12. BSA of Involvement: Descriptive Statistics and Analysis, mITT Population, LOCF

		Score		Change From Baseline		Percent Change From Baseline		Within Group p-Value	
Week	**Statistics**	**ETN50 BIW/ QW**	**ETN50 QW/QW**	**ETN50 BIW/ QW**	**ETN50 QW/QW**	**ETN50 BIW/ QW**	**ETN50 QW/QW**	**ETN50 BIW/ QW**	**ETN50 QW/QW**
Baseline	N	133	137	-	-	-	-	-	-
	Mean	33.1	32.9	-	-	-	-	-	-
	SD	19.2	21.0	-	-	-	-	-	-
	Median	28.0	28.0	-	-	-	-	-	-
	Min	6.0	9.0	-	-	-	-	-	-
	Max	80.0	92.5	-	-	-	-	-	-
	25 percentile	18.0	15.0	-	-	-	-	-	-
	75 percentile	45.0	41.0	-	-	-	-	-	-
Week 2	N	133	136	133	136	133	136	0.0033	0.6040
	Mean	31.4	32.7	-1.8	-0.3	-3.2	1.7	-	-
	SD	18.4	20.9	7.0	6.7	22.7	39.5	-	-
	Median	30.0	30.0	0.0	0.0	0.0	0.0	-	-
	Min	6.0	5.0	-57.4	-24.0	-80.8	-61.5	-	-
	Max	80.0	91.0	20.0	52.9	166.7	389.0	-	-
	25 percentile	15.0	15.0	-2.1	-1.0	-9.1	-1.5	-	-
	75 percentile	40.0	44.5	0.0	0.0	0.0	0.0	-	-
Week 4	N	133	137	133	137	133	137	<.0001	<.0001
	Mean	27.8	29.8	-5.3	-3.1	-14.1	-11.0	-	-
	SD	18.1	20.8	10.1	7.7	38.7	28.3	-	-
	Median	24.0	25.0	-3.0	-1.0	-12.5	-5.3	-	-
	Min	2.0	0.0	-39.6	-40.0	-93.3	-100.0	-	-
	Max	80.0	90.0	38.0	35.0	316.7	133.3	-	-
	25 percentile	12.0	13.0	-9.0	-6.0	-30.8	-25.0	-	-
	75 percentile	40.0	40.0	0.0	0.0	0.0	0.0	-	-
Week 8	N	133	137	133	137	133	137	<.0001	<.0001
	Mean	19.7	24.6	-13.4	-8.4	-36.1	-28.6	-	-
	SD	15.5	20.5	15.2	11.8	43.6	34.4	-	-
	Median	15.0	20.0	-10.0	-5.0	-33.3	-25.0	-	-
	Min	0.0	0.0	-64.9	-67.0	-100.0	-100.0	-	-
	Max	65.0	90.0	38.0	35.0	316.7	100.0	-	-
	25 percentile	8.0	10.0	-20.0	-15.0	-60.0	-50.0	-	-
	75 percentile	30.0	35.0	-3.0	-1.0	-17.8	-2.9	-	-
Week 12	N	133	137	133	137	133	137	<.0001	<.0001
	Mean	13.1	20.3	-20.0	-12.7	-54.7	-40.9	-	-
	SD	13.1	19.9	19.2	15.7	52.6	36.4	-	-
	Median	8.0	12.0	-15.0	-10.0	-66.7	-50.0	-	-
	Min	0.0	0.0	-72.0	-69.5	-100.0	-100.0	-	-

Table 12. BSA of Involvement: Descriptive Statistics and Analysis, mITT Population, LOCF

		Score		Change From Baseline		Percent Change From Baseline		Within Group p-Value	
Week	**Statistics**	**ETN50 BIW/ QW**	**ETN50 QW/QW**	**ETN50 BIW/ QW**	**ETN50 QW/QW**	**ETN50 BIW/ QW**	**ETN50 QW/QW**	**ETN50 BIW/ QW**	**ETN50 QW/QW**
	Max	62.0	90.0	50.0	35.0	416.7	87.5	-	-
	25 percentile	5.0	6.0	-30.0	-20.0	-85.7	-66.7	-	-
	75 percentile	18.0	30.0	-7.0	-4.0	-38.7	-15.4	-	-
Week 16	N	133	137	133	137	133	137	<.0001	<.0001
	Mean	9.3	17.1	-23.8	-15.9	-66.8	-51.1	-	-
	SD	11.2	19.2	19.7	15.9	40.0	37.0	-	-
	Median	5.0	10.0	-19.0	-12.0	-78.6	-57.1	-	-
	Min	0.0	0.0	-72.0	-69.9	-100.0	-100.0	-	-
	Max	56.0	90.5	28.0	35.0	233.3	87.5	-	-
	25 percentile	2.0	4.0	-38.0	-24.5	-93.9	-80.0	-	-
	75 percentile	10.0	24.0	-8.0	-6.0	-52.4	-24.3	-	-
Week 20	N	133	137	133	137	133	137	<.0001	<.0001
	Mean	7.7	14.8	-25.4	-18.2	-73.1	-57.8	-	-
	SD	10.2	18.2	18.8	16.3	30.6	36.5	-	-
	Median	4.0	8.0	-19.0	-15.0	-82.9	-66.7	-	-
	Min	0.0	0.0	-70.0	-69.9	-100.0	-100.0	-	-
	Max	46.0	90.5	12.0	35.0	66.7	87.5	-	-
	25 percentile	1.0	3.0	-38.0	-26.0	-95.5	-86.7	-	-
	75 percentile	10.0	19.0	-12.0	-9.0	-60.0	-39.1	-	-
Week 24	N	133	137	133	137	133	137	<.0001	<.0001
	Mean	7.2	14.0	-25.9	-19.0	-75.6	-59.9	-	-
	SD	11.2	18.0	19.2	17.2	29.9	38.1	-	-
	Median	3.0	6.0	-20.0	-15.0	-85.0	-69.2	-	-
	Min	0.0	0.0	-70.0	-69.9	-100.0	-100.0	-	-
	Max	76.0	90.5	24.4	35.0	47.3	87.5	-	-
	25 percentile	1.0	2.0	-40.0	-28.0	-96.7	-90.0	-	-
	75 percentile	8.0	20.0	-12.0	-9.0	-69.3	-37.5	-	-

BSA score percent change =100 × (visit score - baseline score) / baseline score.
Within p-value based on paired sample t-test.
BIW = twice weekly; BSA = body surface area; ETN = etanercept; LOCF = last observation carried forward; Max = maximum; Min = minimum; mITT = modified intent-to-treat; QW = once weekly; SD = standard deviation.

Table 13: Change From Baseline in PGA of Head, Scalp, and Neck Psoriasis:Comparison Between Treatment Groups, mITT Population, LOCF

Week of Treatment	Treatment Group	Number of Subjects	Adjusted Mean Change (SE)	Difference of Adjusted Mean Change (95% CI) ETN50 BIW/QW-ETN50 QW/QW	p-Value
Week 2	ETN50 BIW/QW	133	-0.5 (0.1)		
	ETN50 QW/QW	136	-0.3 (0.1)	-0.1 (-0.3, 0.0)	0.0992
Week 4	ETN50 BIW/QW	133	-1.1 (0.1)		
	ETN50 QW/QW	137	-0.8 (0.1)	-0.3 (-0.5, -0.1)	0.0080
Week 8	ETN50 BIW/QW	133	-1.5 (0.1)		
	ETN50 QW/QW	137	-1.3 (0.1)	-0.2 (-0.5, 0.0)	0.0511
Week 12	ETN50 BIW/QW	133	-2.0 (0.1)		
	ETN50 QW/QW	137	-1.5 (0.1)	-0.4 (-0.7, -0.2)	0.0001
Week 16	ETN50 BIW/QW	133	-2.0 (0.1)		
	ETN50 QW/QW	137	-1.8 (0.1)	-0.2 (-0.4, -0.0)	0.0267
Week 20	ETN50 BIW/QW	133	-2.1 (0.1)		
	ETN50 QW/QW	137	-1.9 (0.1)	-0.2 (-0.3, 0.0)	0.0843
Week 24	ETN50 BIW/QW	133	-2.1 (0.1)		
	ETN50 QW/QW	137	-1.9 (0.1)	-0.2 (-0.4, -0.0)	0.0239

p-values were based on ANCOVA model: change from baseline=baseline value + region + treatment group.
ANCOVA=analysis of covariance; BIW=twice weekly; CI=confidence interval; ETN=etanercept; LOCF=last observation carried forward; mITT=modified intent-to-treat; PGA=Physician Global Assessment; QW=once weekly; SE=standard error.

Change From Baseline at Each Visit in the Subject Assessments Through 24 Weeks:

Table 14 presents change from baseline in SGA (itching, joint pain, and psoriasis).

The SGA of itching scale ranged from 0 (no itching) to 5 (severe itching). The adjusted mean change from baseline in SGA of itching score (LOCF) was significantly greater for the etanercept 50 mg BIW/QW group from Week 4 to Week 20 (p-values of <0.0001 to 0.0074, ANCOVA), but not at Weeks 2 or 24. The SGA of joint pain scale ranged from 0 (no pain) to 5 (severe pain). The adjusted mean change from baseline in SGA of joint pain score (LOCF) was not significantly different between treatment groups at any time point. The SGA of psoriasis scale ranged from 0 (good) to 5 (severe). The adjusted mean change from baseline in SGA of psoriasis score (LOCF) was significantly greater for the etanercept 50 mg BIW/QW group from Week 4 to Week 20 (p-values of <0.0001 to 0.0090, ANCOVA), but not at Weeks 2 or 24.

The results of the OC analysis of SGA scores were similar to the LOCF results.

Table 14. Change From Baseline in SGA: Comparison Between Treatment Groups, mITT Population, LOCF

Week of Treatment	Treatment Group	Number of Subjects	Adjusted Mean Change (SE)	Difference of Adjusted Mean Change (95% CI) ETN50 BIW/QW-ETN50 QW/QW	p-Value
SGA of Itching					
Week 2	ETN50 BIW/QW	133	-0.8 (0.1)		
	ETN50 QW/QW	136	-0.7 (0.1)	-0.1 (-0.3, 0.2)	0.6396
Week 4	ETN50 BIW/QW	133	-1.5 (0.1)		
	ETN50 QW/QW	137	-1.1 (0.1)	-0.4 (-0.7, -0.1)	0.0074
Week 8	ETN50 BIW/QW	133	-2.0 (0.1)		
	ETN50 QW/QW	137	-1.4 (0.1)	-0.6 (-0.9, -0.2)	0.0007
Week 12	ETN50 BIW/QW	133	-2.4 (0.1)		
	ETN50 QW/QW	137	-1.6 (0.1)	-0.8 (-1.1, -0.5)	<0.0001
Week 16	ETN50 BIW/QW	133	-2.2 (0.1)		
	ETN50 QW/QW	137	-1.8 (0.1)	-0.5 (-0.8, -0.1)	0.0040
Week 20	ETN50 BIW/QW	133	-2.3 (0.1)		
	ETN50 QW/QW	137	-1.8 (0.1)	-0.6 (-0.9, -0.3)	0.0004
Week 24	ETN50 BIW/QW	133	-2.2 (0.1)		
	ETN50 QW/QW	137	-2.0 (0.1)	-0.2 (-0.5, 0.1)	0.1799
SGA of Joint Pain					
Week 2	ETN50 BIW/QW	133	-0.4 (0.1)		
	ETN50 QW/QW	136	-0.5 (0.1)	0.0 (-0.2, 0.3)	0.7757
Week 4	ETN50 BIW/QW	133	-0.7 (0.1)		
	ETN50 QW/QW	137	-0.5 (0.1)	-0.2 (-0.4, 0.1)	0.2112
Week 8	ETN50 BIW/QW	133	-0.7 (0.1)		
	ETN50 QW/QW	137	-0.6 (0.1)	-0.1 (-0.3, 0.2)	0.5467
Week 12	ETN50 BIW/QW	133	-0.8 (0.1)		
	ETN50 QW/QW	137	-0.6 (0.1)	-0.1 (-0.4, 0.1)	0.3684
Week 16	ETN50 BIW/QW	133	-0.8 (0.1)		
	ETN50 QW/QW	137	-0.6 (0.1)	-0.2 (-0.4, 0.1)	0.2046
Week 20	ETN50 BIW/QW	133	-0.9 (0.1)		
	ETN50 QW/QW	137	-0.6 (0.1)	-0.2 (-0.5, 0.0)	0.0649
Week 24	ETN50 BIW/QW	133	-0.8 (0.1)		
	ETN50 QW/QW	137	-0.8 (0.1)	-0.0 (-0.3, 0.2)	0.8683
SGA of Joint Pain for Subjects With a Baseline Score >0					
Week 2	ETN50 BIW/QW	92	-0.7 (0.1)		
	ETN50 QW/QW	90	-0.9 (0.1)	0.1 (-0.2, 0.5)	0.3735
Week 4	ETN50 BIW/QW	92	-1.1 (0.1)		
	ETN50 QW/QW	91	-0.9 (0.1)	-0.2 (-0.5, 0.2)	0.2861
Week 8	ETN50 BIW/QW	92	-1.2 (0.1)		
	ETN50 QW/QW	91	-1.0 (0.1)	-0.2 (-0.5, 0.2)	0.4201
Week 12	ETN50 BIW/QW	92	-1.2 (0.1)		
	ETN50 QW/QW	91	-1.1 (0.1)	-0.1 (-0.5, 0.2)	0.5019
Week 16	ETN50 BIW/QW	92	-1.3 (0.1)		
	ETN50 QW/QW	91	-1.0 (0.1)	-0.3 (-0.7, 0.1)	0.1101
Week 20	ETN50 BIW/QW	92	-1.4 (0.1)		
	ETN50 QW/QW	91	-1.0 (0.1)	-0.3 (-0.7, 0.0)	0.0717
Week 24	ETN50 BIW/QW	92	-1.3 (0.1)		
	ETN50 QW/QW	91	-1.3 (0.1)	0.0 (-0.3, 0.4)	0.8881
SGA of Psoriasis					
Week 2	ETN50 BIW/QW	133	-1.0 (0.1)		
	ETN50 QW/QW	136	-1.0 (0.1)	-0.0 (-0.3, 0.2)	0.8898
Week 4	ETN50 BIW/QW	133	-1.8 (0.1)		
	ETN50 QW/QW	137	-1.4 (0.1)	-0.4 (-0.7, -0.1)	0.0090
Week 8	ETN50 BIW/QW	133	-2.1 (0.1)		
	ETN50 QW/QW	137	-1.7 (0.1)	-0.4 (-0.7, -0.2)	0.0028
Week 12	ETN50 BIW/QW	133	-2.5 (0.1)		
	ETN50 QW/QW	137	-1.9 (0.1)	-0.6 (-0.9, -0.3)	0.0001
Week 16	ETN50 BIW/QW	133	-2.6 (0.1)		

Table 14. Change From Baseline in SGA: Comparison Between Treatment Groups, mITT Population, LOCF

Week of Treatment	Treatment Group	Number of Subjects	Adjusted Mean Change (SE)	Difference of Adjusted Mean Change (95% CI) ETN50 BIW/QW-ETN50 QW/QW	p-Value
Week 20	ETN50 QW/QW	137	-2.0 (0.1)	-0.6 (-0.9, -0.3)	<0.0001
	ETN50 BIW/QW	133	-2.6 (0.1)		
Week 24	ETN50 QW/QW	137	-2.1 (0.1)	-0.5 (-0.8, -0.2)	0.0016
	ETN50 BIW/QW	133	-2.5 (0.1)		
	ETN50 QW/QW	137	-2.2 (0.1)	-0.3 (-0.6, 0.0)	0.0602

p-values were based on ANCOVA model: change from baseline = baseline value + region + treatment group.
ANCOVA = analysis of covariance; BIW = twice weekly; CI = confidence interval; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; QW = once weekly; SE = standard error; SGA = Subject Global Assessment.

Change From Baseline at Each Visit in the PSSQ Through 24 Weeks:

Table 15 presents a summary of the mean (Standard Deviation [SD]) scores for PSSQ items 1 through 16 at baseline, Week 12, and Week 24, by treatment group. The scores for all items increased significantly from baseline to Week 12 and week 24 in both treatment groups. The magnitude of change from baseline to Week 12 was greater in the etanercept 50 mg BIW/QW group. In the etanercept 50 mg BIW/QW group, little additional improvement was observed from Week 12 to Week 24, whereas in the etanercept 50 mg QW/QW group, item scores generally continued to increase from Week 12 to Week 24. Despite the continued increase in scores from Week 12 to Week 24, the scores in the etanercept 50 mg BIW/QW group at Week 24 were still higher than the scores in the etanercept 50 mg QW/QW group.

Table 15. Summary of Mean (SD) PSSQ Scores at Baseline, Week 12, and Week 24, mITT Population, LOCF

Item (Number) Description Time Point	ETN50 BIW/QW Mean (SD)	ETN50 QW/QW Mean (SD)
(1) Overall appearance of your skin		
Baseline	0.9 (0.8)	0.9 (0.9)
Week 12	3.2 (0.9)*	2.6 (1.2)*
Week 24	3.2 (1.0)*	2.8 (1.2)*
(2) Flaking skin		
Baseline	1.0 (0.9)	1.0 (0.9)
Week 12	3.3 (1.0)*	2.7 (1.2)*
Week 24	3.4 (1.1)*	3.0 (1.3)*
(3) Skin redness		
Baseline	1.1 (0.9)	1.0 (0.9)
Week 12	3.2 (1.0)*	2.5 (1.2)*
Week 24	3.3 (1.1)*	2.9 (1.3)*
(4) Skin tightness		
Baseline	1.2 (0.9)	1.2 (1.0)
Week 12	3.4 (1.1)*	3.0 (1.2)*
Week 24	3.5 (1.1)*	3.2 (1.3)*
(5) Skin bleeding		
Baseline	1.7 (1.0)	1.8 (1.2)
Week 12	3.8 (1.0)*	3.2 (1.3)*
Week 24	3.8 (1.1)*	3.3 (1.4)*
(6) Burning sensation in the skin		
Baseline	1.5 (1.1)	1.5 (1.1)*
Week 12	3.8 (1.1)*	3.0 (1.4)*
Week 24	3.7 (1.1)*	3.3 (1.4)*
(7) Skin pain		
Baseline	1.5 (1.2)	1.5 (1.1)
Week 12	3.8 (1.1)*	3.1 (1.4)*
Week 24	3.7 (1.1)*	3.3 (1.4)*
(8) Joint pain		
Baseline	1.8 (1.3)	1.8 (1.4)
Week 12	3.1 (1.3)*	2.9 (1.4)*
Week 24	3.3 (1.2)*	3.1 (1.5)*
(9) Comfort level with your appearance		
Baseline	1.3 (1.1)	1.2 (1.0)
Week 12	3.2 (1.0)*	2.7 (1.2)*
Week 24	3.2 (1.0)*	2.9 (1.2)*
(10) Anxiety		
Baseline	1.8 (1.1)	1.7 (1.1)
Week 12	3.2 (1.3)*	3.1 (1.3)*
Week 24	3.4 (1.2)*	3.2 (1.5)*
(11) Depression		
Baseline	2.0 (1.1)	1.9 (1.1)
Week 12	3.5 (1.3)*	3.2 (1.4)*
Week 24	3.3 (1.3)*	3.4 (1.4)*
(12) Fatigue		
Baseline	2.0 (1.0)	1.8 (1.0)
Week 12	3.0 (1.1)*	2.9 (1.2)*
Week 24	3.1 (1.1)*	3.0 (1.3)*
(13) How others respond to your appearance		
Baseline	1.6 (1.0)	1.8 (1.0)
Week 12	3.5 (1.1)*	2.9 (1.3)*
Week 24	3.4 (1.0)*	3.2 (1.2)*
(14) How your skin affects your social and leisure activities		
Baseline	1.5 (1.2)	1.3 (1.0)
Week 12	3.1 (1.2)*	2.7 (1.4)*
Week 24	3.4 (1.0)*	3.2 (1.4)*

Table 15. Summary of Mean (SD) PSSQ Scores at Baseline, Week 12, and Week 24, mITT Population, LOCF

Item (Number) Description Time Point	ETN50 BIW/QW Mean (SD)	ETN50 QW/QW Mean (SD)
(15) Satisfaction with psoriasis treatment in general		
Baseline	1.4 (1.2)	1.4 (1.1)
Week 12	3.3 (0.8)*	2.9 (1.0)*
Week 24	3.2 (1.0)*	3.1 (1.0)*
(16) Would like to continue with my current psoriasis treatment		
Baseline	2.0 (1.6)	2.2 (1.6)
Week 12	3.7 (0.6)*	3.5 (0.9)*
Week 24	3.5 (1.0)*	3.4 (1.0)*

*= p-value <0.001.
Within-group change from baseline p-value based on paired sample t-test.
BIW = twice weekly; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; PSSQ = Psoriasis Subject Satisfaction Questionnaire; QW = once weekly; SD = standard deviation.

Table 16 presents, for all time points, the results of the between-group analysis of the number (%) of subjects who were satisfied with their health state (LOCF) and the number (%) of subjects who were satisfied with their primary psoriasis treatment (LOCF). All statistically significant between-group differences in PSSQ responses were in favor of the etanercept 50 mg BIW/QW group.

In the OC analysis, there was no longer a significant difference between groups at Week 24 for the percentage of subjects who were satisfied with their health state, nor at Week 12 for the percentage of subjects who were satisfied with their primary psoriasis treatment.

Table 16. PSSQ (Item 17 and 18): Descriptive Summary and Comparison Between Treatment Groups, mITT Population, LOCF

	Time Point	ETN50 BIW/QW n/Total/% (95% CI)	ETN50 QW/QW n/Total/% (95% CI)	Proportion Difference (95% CI)	p-Value
Satisfaction With Health State					
	Baseline	25/133, 18.8% (12.5%, 26.5%)	28/136, 20.6% (14.1%, 28.4%)	-1.79 (-12.04, 8.45)	0.7603
	Week 2	63/133, 47.4% (38.7%, 56.2%)	60/136, 44.1% (35.6%, 52.9%)	3.25 (-9.39, 15.90)	0.6255
	Week 4	91/133, 68.4% (59.8%, 76.2%)	81/137, 59.1% (50.4%, 67.4%)	9.30 (-2.85, 21.45)	0.1292
	Week 8	108/133, 81.2% (73.5%, 87.5%)	95/137, 69.3% (60.9%, 76.9%)	11.86 (0.94, 22.78)	0.0251
	Week 12	113/133, 85.0% (77.7%, 90.6%)	97/137, 70.8% (62.4%, 78.3%)	14.16 (3.68, 24.64)	0.0055
	Week 16	114/133, 85.7% (78.6%, 91.2%)	101/137, 73.7% (65.5%, 80.9%)	11.99 (1.78, 22.20)	0.0159
	Week 20	113/133, 85.0% (77.7%, 90.6%)	104/137, 75.9% (67.9%, 82.8%)	9.05 (-1.08, 19.18)	0.0672
	Week 24	113/133, 85.0% (77.7%, 90.6%)	102/137, 74.5% (66.3%, 81.5%)	10.51 (0.27, 20.75)	0.0351
Satisfaction With Primary Psoriasis Treatment					
	Baseline	31/132, 23.5% (16.5%, 31.6%)	28/137, 20.4% (14.0%, 28.2%)	3.05 (-7.59, 13.68)	0.5592
	Week 2	110/133, 82.7% (75.2%, 88.7%)	104/136, 76.5% (68.4%, 83.3%)	6.24 (-4.11, 16.58)	0.2283
	Week 4	117/133, 88.0% (81.2%, 93.0%)	113/137, 82.5% (75.1%, 88.4%)	5.49 (-3.68, 14.66)	0.2326
	Week 8	123/133, 92.5% (86.6%, 96.3%)	113/137, 82.5% (75.1%, 88.4%)	10.00 (1.47, 18.52)	0.0165
	Week 12	123/133, 92.5% (86.6%, 96.3%)	113/137, 82.5% (75.1%, 88.4%)	10.00 (1.47, 18.52)	0.0165
	Week 16	121/133, 91.0% (84.8%, 95.3%)	118/137, 86.1% (79.2%, 91.4%)	4.85 (-3.46, 13.15)	0.2536
	Week 20	122/133, 91.7% (85.7%, 95.8%)	118/137, 86.1% (79.2%, 91.4%)	5.60 (-2.59, 13.78)	0.1761
	Week 24	116/133, 87.2% (80.3%, 92.4%)	114/137, 83.2% (75.9%, 89.0%)	4.01 (-5.18, 13.20)	0.3943

p-values were based on Fisher's exact test.
BIW = twice weekly; CI = confidence interval; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; n = number of subjects; PSSQ = Psoriasis Subject Satisfaction Questionnaire; QW = once weekly.

Change From Baseline at Each Visit in the Photographed Image of Lesions in Selected Subjects Through 24 Weeks:

The photographed image of lesions in selected subjects at 12 and 24 weeks was not analyzed. Photographs that were taken were kept at the study site and not sent to the Sponsor.

Proportion of Subjects Using Topical Preparations:

Table 17 presents, for all time points, the results of the between-group analysis of the number (%) of subjects using no topical corticosteroid preparations, the number (%) of subjects using only mild topical corticosteroid preparations, the number (%) of subjects using either no topical corticosteroid preparations or only mild topical corticosteroid preparations, the number (%) of subjects using more than mild topical corticosteroid preparations, the number (%) of subjects using topical vitamin D analogs, and number (%) of subjects using a topical vitamin D analog + corticosteroid preparations.

All observations were LOCF. No statistically significant differences between treatment groups were observed for any of these analyses at any time point. The results of the OC analysis were similar to the LOCF results.

Table 17. Number (%) of Subjects Using Topical Preparations: Descriptive Summary and Comparison Between Treatment Groups, mITT Population, LOCF

	Time Point	ETN50 BIW/QW n/Total/% (95% CI)	ETN50 QW/QW n/Total/% (95% CI)	Proportion Difference (95% CI)	p-Value
Used no Topical Steroid Preparations					
	Baseline	120/133, 90.2% (83.9%, 94.7%)	124/137, 90.5% (84.3%, 94.9%)	-0.29 (-8.07, 7.50)	1.0000
	Week 2	118/133, 88.7% (82.1%, 93.5%)	122/137, 89.1% (82.6%, 93.7%)	-0.33 (-8.57, 7.91)	1.0000
	Week 4	118/133, 88.7% (82.1%, 93.5%)	123/137, 89.8% (83.4%, 94.3%)	-1.06 (-9.19, 7.07)	0.8454
	Week 8	121/133, 91.0% (84.8%, 95.3%)	122/137, 89.1% (82.6%, 93.7%)	1.93 (-5.96, 9.81)	0.6866
	Week 12	119/133, 89.5% (83.0%, 94.1%)	122/137, 89.1% (82.6%, 93.7%)	0.42 (-7.70, 8.55)	1.0000
	Week 16	113/133, 85.0% (77.7%, 90.6%)	111/137, 81.0% (73.4%, 87.2%)	3.94 (-5.75, 13.63)	0.4213
	Week 20	115/133, 86.5% (79.5%, 91.8%)	113/137, 82.5% (75.1%, 88.4%)	3.98 (-5.38, 13.35)	0.4039
	Week 24	114/133, 85.7% (78.6%, 91.2%)	114/137, 83.2% (75.9%, 89.0%)	2.50 (-6.87, 11.88)	0.6168
Used Only Mild Topical Steroid Preparations					
	Baseline	13/133, 9.8% (5.3%, 16.1%)	13/137, 9.5% (5.1%, 15.7%)	0.29 (-7.50, 8.07)	1.0000
	Week 2	15/133, 11.3% (6.5%, 17.9%)	15/137, 10.9% (6.3%, 17.4%)	0.33 (-7.91, 8.57)	1.0000
	Week 4	14/133, 10.5% (5.9%, 17.0%)	14/137, 10.2% (5.7%, 16.6%)	0.31 (-7.71, 8.32)	1.0000
	Week 8	11/133, 8.3% (4.2%, 14.3%)	14/137, 10.2% (5.7%, 16.6%)	-1.95 (-9.59, 5.69)	0.6762
	Week 12	9/133, 6.8% (3.1%, 12.5%)	9/137, 6.6% (3.0%, 12.1%)	0.20 (-6.50, 6.89)	1.0000
	Week 16	5/133, 3.8% (1.2%, 8.6%)	6/137, 4.4% (1.6%, 9.3%)	-0.62 (-6.07, 4.83)	1.0000
	Week 20	3/133, 2.3% (0.5%, 6.5%)	5/137, 3.6% (1.2%, 8.3%)	-1.39 (-6.16, 3.38)	0.7227
	Week 24	3/133, 2.3% (0.5%, 6.5%)	5/137, 3.6% (1.2%, 8.3%)	-1.39 (-6.16, 3.38)	0.7227
Used None or Mild Only Topical Steroid Preparations					
	Baseline	133/133, 100.0% (97.3%, 100.0%)	137/137, 100.0% (97.3%, 100.0%)	0.00 (-0.74, 0.74)	-
	Week 2	133/133, 100.0% (97.3%, 100.0%)	137/137, 100.0% (97.3%, 100.0%)	0.00 (-0.74, 0.74)	-
	Week 4	132/133, 99.2% (95.9%, 100.0%)	137/137, 100.0% (97.3%, 100.0%)	-0.75 (-2.96, 1.46)	0.4926
	Week 8	132/133, 99.2% (95.9%, 100.0%)	136/137, 99.3% (96.0%, 100.0%)	-0.02 (-2.81, 2.77)	1.0000
	Week 12	128/133, 96.2% (91.4%, 98.8%)	131/137, 95.6% (90.7%, 98.4%)	0.62 (-4.83, 6.07)	1.0000
	Week 16	118/133, 88.7% (82.1%, 93.5%)	117/137, 85.4% (78.4%, 90.8%)	3.32 (-5.41, 12.05)	0.4710
	Week 20	118/133, 88.7% (82.1%, 93.5%)	118/137, 86.1% (79.2%, 91.4%)	2.59 (-6.05, 11.23)	0.5842
	Week 24	117/133, 88.0% (81.2%, 93.0%)	119/137, 86.9% (80.0%, 92.0%)	1.11 (-7.54, 9.76)	0.8553
Used More Than Mild Topical Steroid Preparations					
	Baseline	0/133, 0.0% (0.0%, 2.7%)	0/137, 0.0% (0.0%, 2.7%)	0.00 (-0.74, 0.74)	-
	Week 2	0/133, 0.0% (0.0%, 2.7%)	0/137, 0.0% (0.0%, 2.7%)	0.00 (-0.74, 0.74)	-
	Week 4	1/133, 0.8% (0.0%, 4.1%)	0/137, 0.0% (0.0%, 2.7%)	0.75 (-1.46, 2.96)	0.4926
	Week 8	1/133, 0.8% (0.0%, 4.1%)	1/137, 0.7% (0.0%, 4.0%)	0.02 (-2.77, 2.81)	1.0000
	Week 12	5/133, 3.8% (1.2%, 8.6%)	6/137, 4.4% (1.6%, 9.3%)	-0.62 (-6.07, 4.83)	1.0000
	Week 16	15/133, 11.3% (6.5%, 17.9%)	20/137, 14.6% (9.2%, 21.6%)	-3.32 (-12.05, 5.41)	0.4710
	Week 20	15/133, 11.3% (6.5%, 17.9%)	19/137, 13.9% (8.6%, 20.8%)	-2.59 (-11.23, 6.05)	0.5842
	Week 24	16/133, 12.0% (7.0%, 18.8%)	18/137, 13.1% (8.0%, 20.0%)	-1.11 (-9.76, 7.54)	0.8553

Table 17. Number (%) of Subjects Using Topical Preparations: Descriptive Summary and Comparison Between Treatment Groups, mITT Population, LOCF

	Time Point	ETN50 BIW/QW n/Total/% (95% CI)	ETN50 QW/QW n/Total/% (95% CI)	Proportion Difference (95% CI)	p-Value
Vitamin D Analogs					
	Baseline	0/133, 0.0% (0.0%, 2.7%)	0/137, 0.0% (0.0%, 2.7%)	0.00 (-0.74, 0.74)	-
	Week 2	0/133, 0.0% (0.0%, 2.7%)	1/137, 0.7% (0.0%, 4.0%)	-0.73 (-2.90, 1.44)	1.0000
	Week 4	0/133, 0.0% (0.0%, 2.7%)	1/137, 0.7% (0.0%, 4.0%)	-0.73 (-2.90, 1.44)	1.0000
	Week 8	0/133, 0.0% (0.0%, 2.7%)	1/137, 0.7% (0.0%, 4.0%)	-0.73 (-2.90, 1.44)	1.0000
	Week 12	3/133, 2.3% (0.5%, 6.5%)	4/137, 2.9% (0.8%, 7.3%)	-0.66 (-5.19, 3.86)	1.0000
	Week 16	8/133, 6.0% (2.6%, 11.5%)	11/137, 8.0% (4.1%, 13.9%)	-2.01 (-8.84, 4.81)	0.6360
	Week 20	6/133, 4.5% (1.7%, 9.6%)	9/137, 6.6% (3.0%, 12.1%)	-2.06 (-8.24, 4.13)	0.5973
	Week 24	9/133, 6.8% (3.1%, 12.5%)	14/137, 10.2% (5.7%, 16.6%)	-3.45 (-10.82, 3.92)	0.3850
Vitamin D + Steroid					
	Baseline	0/133, 0.0% (0.0%, 2.7%)	0/137, 0.0% (0.0%, 2.7%)	0.00 (-0.74, 0.74)	-
	Week 2	1/133, 0.8% (0.0%, 4.1%)	1/137, 0.7% (0.0%, 4.0%)	0.02 (-2.77, 2.81)	1.0000
	Week 4	0/133, 0.0% (0.0%, 2.7%)	1/137, 0.7% (0.0%, 4.0%)	-0.73 (-2.90, 1.44)	1.0000
	Week 8	0/133, 0.0% (0.0%, 2.7%)	1/137, 0.7% (0.0%, 4.0%)	-0.73 (-2.90, 1.44)	1.0000
	Week 12	0/133, 0.0% (0.0%, 2.7%)	1/137, 0.7% (0.0%, 4.0%)	-0.73 (-2.90, 1.44)	1.0000
	Week 16	6/133, 4.5% (1.7%, 9.6%)	9/137, 6.6% (3.0%, 12.1%)	-2.06 (-8.24, 4.13)	0.5973
	Week 20	7/133, 5.3% (2.1%, 10.5%)	10/137, 7.3% (3.6%, 13.0%)	-2.04 (-8.55, 4.48)	0.6183
	Week 24	9/133, 6.8% (3.1%, 12.5%)	10/137, 7.3% (3.6%, 13.0%)	-0.53 (-7.37, 6.31)	1.0000

p-values were based on Fisher's exact test.
Baseline excluded day -28 or early
BIW = twice weekly; CI = confidence interval; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; QW = once weekly.

DLQI:

The adjusted mean change from baseline in DLQI total score (LOCF) of 10.5 and 9.2 for the etanercept 50 mg BIW/QW and the etanercept 50 mg QW/QW groups, respectively, at Week 24 was well above the clinically meaningful threshold estimated at 3 or 5. The adjusted mean change was significantly greater for the etanercept 50 mg BIW/QW group at Weeks 4, 8, 12, 16, and 20, but not at Weeks 2 or 24 (Table 18).

Table 18: Change From Baseline in DLQI Total Score: Comparison Between Treatment Groups, mITT Population, LOCF

Week of Treatment	Treatment Group	Number of Subjects	Adjusted Mean Change (SE)	Difference of Adjusted Mean Change (95% CI) ETN50 BIW/QW-ETN50 QW/QW	p-Value
Week 2	ETN50 BIW/QW	133	-4.6 (0.4)		
	ETN50 QW/QW	136	-4.3 (0.4)	-0.3 (-1.5, 0.8)	0.5748
Week 4	ETN50 BIW/QW	133	-7.1 (0.5)		
	ETN50 QW/QW	137	-5.9 (0.4)	-1.2 (-2.4, -0.0)	0.0471
Week 8	ETN50 BIW/QW	133	-9.0 (0.5)		
	ETN50 QW/QW	137	-7.0 (0.5)	-2.0 (-3.3, -0.7)	0.0025
Week 12	ETN50 BIW/QW	133	-10.2 (0.5)		
	ETN50 QW/QW	137	-8.1 (0.5)	-2.2 (-3.5, -0.9)	0.0009
Week 16	ETN50 BIW/QW	133	-10.7 (0.4)		
	ETN50 QW/QW	137	-8.8 (0.4)	-1.9 (-3.1, -0.7)	0.0015
Week 20	ETN50 BIW/QW	133	-10.5 (0.5)		
	ETN50 QW/QW	137	-9.0 (0.5)	-1.5 (-2.7, -0.2)	0.0197
Week 24	ETN50 BIW/QW	133	-10.5 (0.5)		
	ETN50 QW/QW	137	-9.2 (0.5)	-1.3 (-2.6, 0.0)	0.0506

p-values were based on ANCOVA model: change from baseline = baseline value + region + treatment group.
ANCOVA = analysis of covariance; BIW = twice weekly; CI = confidence interval; DLQI = Dermatology Life Quality Index; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; QW = once weekly; SE = standard error.

EQ-5D:

The mean EQ-5D utility index at baseline was 0.65 and 0.66 for the etanercept 50 mg BIW/QW and the etanercept 50 mg QW/QW groups, respectively. A significant difference between treatment groups in change from baseline at Weeks 12 and 24 was observed in favor of the etanercept 50 mg BIW/QW group (Table 19).

Table 19: Change From Baseline in EQ-5D Utility Index: Comparison Between Treatment Groups, mITT Population, LOCF

Week of Treatment	Treatment Group	Number of Subjects	Adjusted Mean Change (SE)	Difference of Adjusted Mean Change (95% CI) ETN50 BIW/QW-ETN50 QW/QW	P-Value
Week 12	ETN50 BIW/QW	130	0.21 (0.02)		
	ETN50 QW/QW	134	0.17 (0.02)	0.04 (0.00, 0.09)	0.0435
Week 24	ETN50 BIW/QW	130	0.21 (0.02)		
	ETN50 QW/QW	134	0.15 (0.02)	0.05 (0.01, 0.10)	0.0275

p-values were based on ANCOVA model: change from baseline = baseline value + region + treatment group.
ANCOVA = analysis of covariance; BIW = twice weekly; CI = confidence interval; EQ-5D = EuroQOL 5 Dimension; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; QW = once weekly; SE = standard error.

HADS:

The mean HADS Anxiety Subscale scores and HADS Depression Subscale scores were significantly improved from baseline at Week 12 and Week 24 in both treatment groups (Table 20).

However, the difference between treatment groups for HADS Anxiety Subscale in change from baseline at Weeks 12 (p-value=0.9473) and Week 24 (p-value=0.8217) was not significant. The difference between treatment groups HADS Depression Subscale in change from baseline at Weeks 12 (p-value=0.0539) and Week 24 (p-value=0.1494) was not significant.

Table 20: Summary of Mean (SD) HADS Anxiety and Depression Scores at Baseline, Week 12, and Week 24, mITT Population, LOCF

Item Time Point	ETN50 BIW/QW Mean (SD)	ETN50 QW/QW Mean (SD)
HADS anxiety score		
Baseline	7.2 (4.4)	6.9 (4.1)
Week 12	5.5 (4.0)*	5.3 (3.8)*
Week 24	5.1 (4.1)*	5.0 (3.7)*
HADS depression score		
Baseline	6.0 (4.1)	6.5 (4.1)
Week 12	4.1 (3.5)*	5.1 (3.9)*
Week 24	3.8 (3.3)*	4.6 (3.8)*

*= p<0.001. Within-group change from baseline p-value based on Paired Sample T-test.
BIW = twice weekly; ETN=etanercept; HADS = Hospital Anxiety and Depression Scale; LOCF = last observation carried forward; mITT=modified intent-to-treat; QW=once weekly; SD=standard deviation.

WPAI:

Table 21 presents a summary of the mean (SD) score for each WPAI:PSO item at baseline, Week 12, and Week 24, by treatment group. Percent activity impairment, percent impairment while working, and percent overall work impairment were significantly improved from baseline at Week 12 and Week 24 in both treatment groups. Percent work time missed was significantly improved from baseline at Week 24 in the etanercept 50 mg QW/QW group.

Table 21. Summary of Mean (SD) WPAI Scores at Baseline, Week 12, and Week 24, mITT Population, LOCF

Item Time Point	ETN50 BIW/QW Mean (SD)	ETN50 QW/QW Mean (SD)
Percentage activity impairment due to problem		
Baseline	39.77 (28.96)	40.15 (30.94)
Week 12	16.87 (21.49)*	21.78 (25.65)*
Week 24	13.28 (18.99)*	18.85 (24.58)*
Percentage impairment while working due to problem		
Baseline	24.36 (23.28)	26.09 (27.08)
Week 12	10.25 (14.41)*	13.19 (20.43)*
Week 24	8.00 (11.34)*	13.43 (19.57)*
Percentage overall work impairment due to problem		
Baseline	25.45 (23.53)	29.51 (28.66)
Week 12	14.30 (21.49)*	16.88 (25.24)*
Week 24	12.78 (20.27)*	15.96 (23.05)*
Percentage work time missed		
Baseline	3.60 (16.14)	7.19 (18.92)
Week 12	4.35 (16.86)	4.85 (19.11)
Week 24	5.03 (17.57)	3.10 (13.91)†

*= $p<0.001$; †= $p<0.01$.
Within-group change from baseline p-value based on paired sample t-test.
BIW = twice weekly; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; QW = once weekly; SD = standard deviation; WPAI = Work Productivity and Activity Impairment.

MOS Sleep Scale:

The summary of the mean (SD) scores for the MOS Sleep Scale are presented for baseline, Week 12, and Week 24, by treatment group (Table 22). The difference between groups in the adjusted mean change from baseline to Week 12 and Week 24 in all MOS scores (LOCF), was not significant.

Table 22. Summary of Mean (SD) MOS Scores at Baseline, Week 12, and Week 24, mITT Population, LOCF

Item Time Point	ETN50 BIW/QW Mean (SD)	ETN50 QW/QW Mean (SD)
Sleep snoring		
Baseline	37.9 (29.6)	45.7 (31.0)
Week 12	35.7 (27.8)	45.3 (30.3)
Week 24	38.2 (31.1)	44.0 (31.3)
Sleep somnolence		
Baseline	29.9 (19.9)	30.9 (19.3)
Week 12	27.3 (19.8)	28.8 (20.3)
Week 24	27.0 (18.4)	28.1 (20.3)
Sleep short of breath or headache		
Baseline	13.2 (20.4)	14.3 (20.7)
Week 12	13.6 (20.8)	15.3 (21.2)
Week 24	11.9 (17.3)	13.9 (19.7)
Sleep adequacy		
Baseline	54.6 (25.9)	54.0 (27.3)
Week 12	59.8 (26.4)*	55.6 (24.4)
Week 24	59.8 (25.4)*	60.9 (26.7)†
Sleep disturbance		
Baseline	35.0 (23.6)	34.4 (23.8)
Week 12	30.1 (21.3)†	28.4 (21.1)‡
Week 24	26.7 (19.8)‡	26.6 (21.1)‡
Sleep quantity		
Baseline	6.9 (1.4)	6.9 (1.4)
Week 12	7.2 (1.4)†	6.9 (1.2)
Week 24	7.2 (1.5)†	7.0 (1.3)
Sleep problem index I		
Baseline	32.5 (18.7)	32.9 (19.1)
Week 12	29.3 (17.8)*	30.4 (17.8)
Week 24	27.3 (15.9)‡	27.7 (17.7)‡
Sleep problem index II		
Baseline	33.9 (18.2)	34.2 (19.6)
Week 12	30.1 (17.5)†	30.8 (17.7)*
Week 24	28.2 (15.7)‡	28.4 (17.5)‡

*= p<0.05; †= p<0.01; ‡= p<0.001.
Within-group change from baseline p-value based on paired sample t-test.
BIW = twice weekly; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; MOS = Medical Outcomes Study; QW = once weekly; SD = standard deviation.

FACIT Fatigue Questionnaire:

The mean baseline FACIT score was 37.9 and 36.7 for subjects in the etanercept 50 mg BIW/QW and etanercept 50 mg QW/QW groups, respectively. The mean FACIT score increased significantly from baseline to Week 12 and Week 24 (LOCF) in both treatment groups (Table 23).

Table 23. Summary of Mean (SD) FACIT Total Scores at Baseline, Week 12, and Week 24, mITT Population, LOCF

Item Time Point	ETN50 BIW/QW Mean (SD)	ETN50 QW/QW Mean (SD)
Facit Score		
Baseline	37.9 (10.0)	36.7 (10.8)
Week 12	41.8 (8.1)*	40.1 (8.6)*
Week 24	41.9 (8.3)*	40.8 (9.1)*

*= p<0.001.
Within-group change from baseline p-value based on paired sample t-test.
BIW = twice weekly; ETN = etanercept; FACIT = Functional Assessment of Chronic Illness Therapy; LOCF = last observation carried forward; mITT = modified intent-to-treat; QW = once weekly; SD = standard deviation.

PASE: The mean PASE total score at baseline was 33.0 and 34.4 for the etanercept 50 mg BIW/QW and the etanercept 50 mg QW/QW groups, respectively. No significant difference between treatment groups was observed at Week 12 and Week 24.

Subject Pharmacoeconomic Questionnaire: There was no difference observed between treatment groups at any time point for the percentage of subjects with emergency room visits (yes/no), the mean number of emergency room days, the percentage of subjects with doctor visits (yes/no), or the mean number of doctor visits.

PPSQ: At Week 12 and Week 24, the percentages of subjects whose condition was considered by their Physician to be satisfactory were 87.2% versus 65.7% (p-value <0.0001) and 86.5% versus 75.2% (p-value=0.0209) for the etanercept 50 mg BIW/QW and etanercept 50 mg QW/QW groups, respectively (Table 24).

Table 24. Psoriasis Physician Satisfaction Questionnaire: Descriptive Summary and Comparison Between Treatment Groups, mITT Population, LOCF

	Time Point	ETN50 BIW/QW n/Total/% (95% CI)	ETN50 QW/QW n/Total/% (95% CI)	Proportion Difference (95% CI)	p-Value
Consider Subject's Condition Satisfactory					
	Baseline	16/133, 12.0% (7.0%, 18.8%)	16/137, 11.7% (6.8%, 18.3%)	0.35 (-8.10, 8.81)	1.0000
	Week 2	44/133, 33.1% (25.2%, 41.8%)	37/135, 27.4% (20.1%, 35.7%)	5.68 (-6.05, 17.40)	0.3525
	Week 4	71/133, 53.4% (44.5%, 62.1%)	53/137, 38.7% (30.5%, 47.4%)	14.70 (2.19, 27.20)	0.0202
	Week 8	91/133, 68.4% (59.8%, 76.2%)	74/137, 54.0% (45.3%, 62.6%)	14.41 (2.17, 26.64)	0.0178
	Week 12	116/133, 87.2% (80.3%, 92.4%)	90/137, 65.7% (57.1%, 73.6%)	21.52 (11.02, 32.03)	<0.0001
	Week 16	114/133, 85.7% (78.6%, 91.2%)	103/137, 75.2% (67.1%, 82.2%)	10.53 (0.43, 20.64)	0.0325
	Week 20	116/133, 87.2% (80.3%, 92.4%)	103/137, 75.2% (67.1%, 82.2%)	12.04 (2.10, 21.97)	0.0129
	Week 24	115/133, 86.5% (79.5%, 91.8%)	103/137, 75.2% (67.1%, 82.2%)	11.28 (1.26, 21.30)	0.0209
Consider Primary Psoriasis Therapy Satisfactory					
	Baseline	15/132, 11.4% (6.5%, 18.0%)	17/137, 12.4% (7.4%, 19.1%)	-1.05 (-9.52, 7.43)	0.8518
	Week 2	89/133, 66.9% (58.2%, 74.8%)	74/135, 54.8% (46.0%, 63.4%)	12.10 (-0.24, 24.44)	0.0461
	Week 4	103/133, 77.4% (69.4%, 84.2%)	94/137, 68.6% (60.1%, 76.3%)	8.83 (-2.44, 20.10)	0.1314
	Week 8	111/133, 83.5% (76.0%, 89.3%)	99/137, 72.3% (64.0%, 79.6%)	11.20 (0.65, 21.74)	0.0289
	Week 12	122/133, 91.7% (85.7%, 95.8%)	114/137, 83.2% (75.9%, 89.0%)	8.52 (-0.04, 17.07)	0.0433
	Week 16	122/133, 91.7% (85.7%, 95.8%)	116/137, 84.7% (77.5%, 90.3%)	7.06 (-1.32, 15.43)	0.0902
	Week 20	122/133, 91.7% (85.7%, 95.8%)	115/137, 83.9% (76.7%, 89.7%)	7.79 (-0.68, 16.26)	0.0630
	Week 24	118/133, 88.7% (82.1%, 93.5%)	111/137, 81.0% (73.4%, 87.2%)	7.70 (-1.53, 16.93)	0.0907

p-values were based on Fisher's exact test.
BIW = twice weekly; CI = confidence interval; ETN = etanercept; LOCF = last observation carried forward; mITT = modified intent-to-treat; n = number of evaluated subjects; QW = once weekly.

Safety Results:

Treatment-Emergent Adverse Events (TEAEs): TEAEs (including infections) reported in at least 5% of subjects in either treatment group are presented in Table 25. TEAEs were most frequently associated with the infections and infestations SOC.

Table 25. Treatment-Emergent Adverse Events (All Causality) Reported in ≥5% of Subjects in Any Treatment Group – Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	ETN50 BIW/QW N=136 n (%)	ETN50 QW/QW N=137 n (%)	Total N=273 n (%)
Any TEAE	0.442	94 (69.1)	88 (64.2)	182 (66.7)
Gastrointestinal disorders	0.703	14 (10.3)	17 (12.4)	31 (11.4)
Diarrhoea	0.785	6 (4.4)	8 (5.8)	14 (5.1)
General disorders and administration site conditions	0.249	25 (18.4)	18 (13.1)	43 (15.8)
Fatigue	0.137	8 (5.9)	3 (2.2)	11 (4.0)
Injection site erythema	0.572	7 (5.1)	5 (3.6)	12 (4.4)
Injection site reaction	0.335	3 (2.2)	7 (5.1)	10 (3.7)
Infections and infestations	0.704	49 (36.0)	46 (33.6)	95 (34.8)
Nasopharyngitis	0.347	13 (9.6)	19 (13.9)	32 (11.7)
Pharyngitis	0.769	5 (3.7)	7 (5.1)	12 (4.4)
Investigations	0.867	20 (14.7)	22 (16.1)	42 (15.4)
Blood insulin increased	0.798	7 (5.1)	9 (6.6)	16 (5.9)
Musculoskeletal and connective tissue disorders	0.735	19 (14.0)	22 (16.1)	41 (15.0)
Arthralgia	0.572	7 (5.1)	5 (3.6)	12 (4.4)
Nervous system disorders	1.000	21 (15.4)	21 (15.3)	42 (15.4)
Headache	0.847	15 (11.0)	14 (10.2)	29 (10.6)

AEs and SAEs are not separated out.
Overall p-value: refers to number of subjects data. Fisher's Exact Test p-value (2-Tail).
Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA).
AEs = adverse events; BIW = twice weekly; ETN = etanercept; PBO = placebo; QW = once weekly; SAEs = serious adverse event; TEAE = treatment-emergent adverse event.
a. Totals for the number of subjects at a higher level are not necessarily the sum of those at the lower levels since a subject might report 2 or more different AEs within the higher level category.

Treatment Related TEAEs: Table 26 presents treatment-related TEAEs reported by subjects during the study.

Table 26. Treatment-Emergent Treatment-Related Adverse Events - Safety Population

System Organ Class[a,b] Preferred Term[b]	ETN50 BIW/QW N=136 n (%)	ETN50 QW/QW N=137 n (%)	Total N=273 n (%)
Any adverse event	33 (24.3)	41 (29.9)	74 (27.1)
Ear and labyrinth disorders	1 (0.7)	1 (0.7)	2 (0.7)
Vertigo	1 (0.7)	1 (0.7)	2 (0.7)
Eye disorders	0	1 (0.7)	1 (0.4)
Eye pruritus	0	1 (0.7)	1 (0.4)
Gastrointestinal disorders	1 (0.7)	4 (2.9)	5 (1.8)
Diarrhoea	0	1 (0.7)	1 (0.4)
Dry mouth	0	1 (0.7)	1 (0.4)
Dyspepsia	0	1 (0.7)	1 (0.4)
Gastritis	1 (0.7)	0	1 (0.4)
Glossodynia	0	1 (0.7)	1 (0.4)
Lip dry	0	1 (0.7)	1 (0.4)
General disorders and administration site conditions	12 (8.8)	14 (10.2)	26 (9.5)
Fatigue	1 (0.7)	1 (0.7)	2 (0.7)
Generalised oedema	1 (0.7)	0	1 (0.4)
Influenza like illness	1 (0.7)	0	1 (0.4)
Injection site erythema	6 (4.4)	5 (3.6)	11 (4.0)
Injection site induration	0	1 (0.7)	1 (0.4)
Injection site oedema	0	1 (0.7)	1 (0.4)
Injection site pain	1 (0.7)	1 (0.7)	2 (0.7)
Injection site pruritus	2 (1.5)	1 (0.7)	3 (1.1)
Injection site reaction	3 (2.2)	7 (5.1)	10 (3.7)
Injection site swelling	0	2 (1.5)	2 (0.7)
Malaise	0	1 (0.7)	1 (0.4)
Hepatobiliary disorders	0	1 (0.7)	1 (0.4)
Hepatitis	0	1 (0.7)	1 (0.4)
Infections and infestations	16 (11.8)	15 (10.9)	31 (11.4)
Body tinea	0	1 (0.7)	1 (0.4)
Bronchitis	0	1 (0.7)	1 (0.4)
Cellulitis	1 (0.7)	0	1 (0.4)
Cystitis	1 (0.7)	0	1 (0.4)
Folliculitis	3 (2.2)	0	3 (1.1)
Fungal infection	1 (0.7)	0	1 (0.4)
Furuncle	1 (0.7)	1 (0.7)	2 (0.7)
Influenza	1 (0.7)	0	1 (0.4)
Nasopharyngitis	5 (3.7)	6 (4.4)	11 (4.0)
Oral herpes	2 (1.5)	1 (0.7)	3 (1.1)
Pharyngitis	1 (0.7)	2 (1.5)	3 (1.1)
Rhinitis	1 (0.7)	0	1 (0.4)
Sinusitis	1 (0.7)	0	1 (0.4)
Tinea cruris	0	1 (0.7)	1 (0.4)
Tonsillitis	0	1 (0.7)	1 (0.4)
Upper respiratory tract infection	1 (0.7)	4 (2.9)	5 (1.8)
Investigations	3 (2.2)	5 (3.6)	8 (2.9)
Alanine aminotransferase abnormal	0	1 (0.7)	1 (0.4)
Alanine aminotransferase increased	0	1 (0.7)	1 (0.4)
Blood glucose increased	0	1 (0.7)	1 (0.4)
Liver function test abnormal	1 (0.7)	0	1 (0.4)
Low density lipoprotein increased	1 (0.7)	0	1 (0.4)
Transaminases increased	0	1 (0.7)	1 (0.4)
Weight increased	1 (0.7)	1 (0.7)	2 (0.7)
Metabolism and nutrition disorders	0	1 (0.7)	1 (0.4)
Increased appetite	0	1 (0.7)	1 (0.4)
Musculoskeletal and connective tissue disorders	3 (2.2)	5 (3.6)	8 (2.9)
Arthralgia	2 (1.5)	2 (1.5)	4 (1.5)

Table 26. Treatment-Emergent Treatment-Related Adverse Events - Safety Population

System Organ Class[a,b] Preferred Term[b]	ETN50 BIW/QW N=136 n (%)	ETN50 QW/QW N=137 n (%)	Total N=273 n (%)
Muscle spasms	1 (0.7)	0	1 (0.4)
Muscular weakness	0	1 (0.7)	1 (0.4)
Myalgia	0	1 (0.7)	1 (0.4)
Pain in extremity	0	1 (0.7)	1 (0.4)
Psoriatic arthropathy	0	1 (0.7)	1 (0.4)
Nervous system disorders	4 (2.9)	7 (5.1)	11 (4.0)
Demyelinating polyneuropathy	1 (0.7)	0	1 (0.4)
Dysaesthesia	1 (0.7)	0	1 (0.4)
Headache	2 (1.5)	3 (2.2)	5 (1.8)
Hypersomnia	1 (0.7)	4 (2.9)	5 (1.8)
Hypoaesthesia	0	1 (0.7)	1 (0.4)
Paraesthesia	1 (0.7)	0	1 (0.4)
Psychiatric disorders	4 (2.9)	0	4 (1.5)
Initial insomnia	1 (0.7)	0	1 (0.4)
Insomnia	1 (0.7)	0	1 (0.4)
Libido decreased	1 (0.7)	0	1 (0.4)
Panic attack	1 (0.7)	0	1 (0.4)
Reproductive system and breast disorders	0	1 (0.7)	1 (0.4)
Menstruation irregular	0	1 (0.7)	1 (0.4)
Respiratory, thoracic and mediastinal disorders	1 (0.7)	3 (2.2)	4 (1.5)
Bronchospasm	1 (0.7)	0	1 (0.4)
Cough	0	1 (0.7)	1 (0.4)
Dysphonia	0	1 (0.7)	1 (0.4)
Oropharyngeal pain	0	1 (0.7)	1 (0.4)
Skin and subcutaneous tissue disorders	4 (2.9)	6 (4.4)	10 (3.7)
Acne	1 (0.7)	0	1 (0.4)
Erythema multiforme	0	1 (0.7)	1 (0.4)
Pain of skin	0	1 (0.7)	1 (0.4)
Pruritus	1 (0.7)	4 (2.9)	5 (1.8)
Psoriasis	1 (0.7)	0	1 (0.4)
Skin nodule	1 (0.7)	0	1 (0.4)
Vascular disorders	0	1 (0.7)	1 (0.4)
Hypertension	0	1 (0.7)	1 (0.4)

AE/SAE results are not separated out. Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA).
AE = adverse event; BIW = twice weekly; ETN = etanercept; N = number of subjects in each treatment group; n = number of subjects with adverse events; QW = once weekly; SAE = serious adverse event.
a. Totals for the number of subjects at a higher level are not necessarily the sum of those at the lower levels since a subject may report 2 or more different AEs within the higher level category.
b. Includes all severities of adverse events that were considered related to the study treatment.

SAEs:

Table 27 presents SAEs reported during the study. A total of 3 subjects (2.2%) in the etanercept 50 mg BIW/QW group and 4 subjects (2.9%) in the etanercept 50 mg QW/QW group had an SAE during the study. No individual SAE occurred in more than 1 subject.

Table 27. Number (%) of Subjects Reporting Serious Adverse Events (All Causality)

System Organ Class[a] Preferred Term	Overall p-Value	ETN50 BIW/QW N=136 n (%)	ETN50 QW/QW N=137 n (%)	Total N=273 n (%)
Any SAE	1.000	3 (2.2)	4 (2.9)	7 (2.6)
General disorders and administration site conditions	1.000	0	1 (0.7)	1 (0.4)
Injection site erythema	1.000	0	1 (0.7)	1 (0.4)
Injection site pruritus	1.000	0	1 (0.7)	1 (0.4)
Hepatobiliary disorders	1.000	0	1 (0.7)	1 (0.4)
Hepatitis	1.000	0	1 (0.7)	1 (0.4)
Infections and infestations	1.000	1 (0.7)	1 (0.7)	2 (0.7)
Dengue fever	1.000	0	1 (0.7)	1 (0.4)
Erysipelas	0.498	1 (0.7)	0	1 (0.4)
Investigations	1.000	0	1 (0.7)	1 (0.4)
Transaminases increased	1.000	0	1 (0.7)	1 (0.4)
Musculoskeletal and connective tissue disorders	1.000	1 (0.7)	1 (0.7)	2 (0.7)
Joint swelling	1.000	0	1 (0.7)	1 (0.4)
Muscle spasms	0.498	1 (0.7)	0	1 (0.4)
Nervous system disorders	0.247	2 (1.5)	0	2 (0.7)
Demyelinating polyneuropathy	0.498	1 (0.7)	0	1 (0.4)
Dysaesthesia	0.498	1 (0.7)	0	1 (0.4)
Paraesthesia	0.498	1 (0.7)	0	1 (0.4)
Psychiatric disorders	0.498	1 (0.7)	0	1 (0.4)
Libido decreased	0.498	1 (0.7)	0	1 (0.4)

Overall p-value referred to number of subjects' data. Fisher's Exact Test p-value (2-Tail).
Classifications of AEs are based on the Medical Dictionary for Regulatory Activities (MedDRA).
AE = adverse event; BIW = twice weekly; ETN = etanercept; N = number of subjects in each treatment group; n = number of subjects with adverse events; QW = once weekly; SAE = serious adverse event.
a. Totals for the number of subjects at a higher level were not necessarily the sum of those at the lower levels since a subject might report 2 or more different AEs within the higher level category

Discontinuations due to AEs: A total of 5 subjects (3.7%) in the etanercept 50 mg BIW/QW group and 3 subjects (2.2%) in the etanercept 50 mg QW/QW group were withdrawn from the study due to a TEAE (Table 28).

Table 28. Number (%) of Subjects Reporting Treatment-Emergent Adverse Events Causing Withdrawal

System Organ Class[a] Preferred Term	Overall p-Value	ETN50 BIW/QW N=136 n (%)	ETN50 QW/QW N=137 n (%)	Total N=273 n (%)
Any TEAE causing withdrawal	0.500	5 (3.7)	3 (2.2)	8 (2.9)
General disorders and administration site conditions	1.000	1 (0.7)	1 (0.7)	2 (0.7)
Generalised oedema	0.498	1 (0.7)	0	1 (0.4)
Injection site reaction	1.000	0	1 (0.7)	1 (0.4)
Hepatobiliary disorders	1.000	0	1 (0.7)	1 (0.4)
Hepatitis	1.000	0	1 (0.7)	1 (0.4)
Infections and infestations	1.000	1 (0.7)	1 (0.7)	2 (0.7)
Erysipelas	0.498	1 (0.7)	0	1 (0.4)
Pharyngitis	1.000	0	1 (0.7)	1 (0.4)
Investigations	0.498	1 (0.7)	0	1 (0.4)
Liver function test abnormal	0.498	1 (0.7)	0	1 (0.4)
Nervous system disorders	0.247	2 (1.5)	0	2 (0.7)
Demyelinating polyneuropathy	0.498	1 (0.7)	0	1 (0.4)
Dysaesthesia	0.498	1 (0.7)	0	1 (0.4)

Overall p-value refers to number of subjects' data. Fisher's Exact Test p-value (2-Tail).
Classifications of AEs are based on the Medical Dictionary for Regulatory Activities (MedDRA).
AE = adverse event; BIW = twice weekly; ETN = etanercept; N = number of subjects in each treatment group; n = number of subjects with adverse events; TEAE = treatment emergent adverse event; QW = once weekly.
a. Totals for the number of subjects at a higher level are not necessarily the sum of those at the lower levels since a subject may report 2 or more different AEs within the higher level category

Deaths: No deaths were reported during the study.

Other Safety Related Findings: Three subjects (2.3%) in the etanercept 50 mg BIW/QW group and 1 subject (0.7%) in the etanercept 50 mg QW/QW group had National Cancer Institute (NCI) Grade 3 or 4 hyperbilirubinemia during treatment. One subject (0.8%) in the etanercept 50 mg BIW/QW group and 1 subject (0.7%) in the etanercept 50 mg QW/QW group had NCI Grade 3 or 4 increased serum aspartate aminotransferase level during treatment, and 1 subject (0.8%) in the etanercept 50 mg BIW/QW group and 1 subject (0.7%) in the etanercept 50 mg QW/QW group had NCI Grade 3 or 4 increased serum alanine aminotransferase level during treatment.

CONCLUSIONS:

The purpose of this study was to evaluate the efficacy and safety of etanercept 50 mg administered BIW for 12 weeks followed by QW for 12 weeks with etanercept 50 mg administered QW for 24 weeks in the treatment of psoriasis. Safety was evaluated in 273 subjects and efficacy was evaluated in 270 subjects. A total of 137 subjects were randomized to the etanercept 50 mg QW/QW group and 136 subjects were randomized to the etanercept 50 mg BIW/QW group.

In the etanercept 50 mg QW/QW group, 59.9% of subjects achieved a PASI 75 response at Week 24, and the lower bound of the 95% CI (51.1% to 68.1%) exceeded the prespecified criteria of 50%. Therefore, the primary null hypothesis, that the value was <50%, was rejected. In the etanercept 50 mg BIW/QW group, 78.2% of subjects achieved a PASI 75 response at Week 24, and the lower bound of the 95% CI (70.2% to 84.9%) exceeded the prespecified criteria of 60%, so the conditional primary null hypothesis was also rejected.

Both treatment regimens were effective in the treatment of the skin manifestations of psoriasis in subjects with moderate to severe psoriasis when used with adjunctive topical therapy as needed. The efficacy results are summarized below:

- Mean PASI, PGA, PGA (head, scalp, and neck), SGA (itching), SGA (joint pain), and SGA (psoriasis) scores improved significantly from baseline at all time-points in both treatment groups. Mean percent BSA of involvement by psoriasis decreased significantly from baseline at all time-points in both treatment groups except for Week 2 in the etanercept 50 mg QW/QW group.

- No difference between treatment groups was observed at any time point for emergency room visits (yes/no), the number of emergency room days, doctor visits (yes/no), or the number of doctor visits.

- Overall, 18 of the 185 subjects (9.7%) without a diagnosis of psoriatic arthritis (or 6.7% of all subjects) had a PASE total score ≥47 at baseline, which is a strong indicator for the presence of psoriatic arthritis.

- Baseline DLQI scores suggested a severe quality of life impairment. During treatment, DLQI scores fell by about two-thirds, with a significant difference between treatment groups favoring the etanercept 50 mg BIW/QW group at Week 12, but not at Week 24.

- Baseline EQ-5D utility scores were similar to those observed in subjects with heart disease and stroke in other studies. Scores improved by 3 to 4 times the minimally important difference by Week 12 and remained constant at Week 24. A significant difference between treatment groups in change from baseline at Weeks 12 and 24 was observed in favor of the etanercept 50 mg BIW/QW group.

- HADS Anxiety and Depression subscales, MOS-Sleep Index II, and FACIT-Fatigue Questionnaire scores each saw significant improvements from baseline in both treatment groups.

- PPSQ (physician satisfaction) and PSSQ (subject satisfaction) scores at Week 24 were improved from baseline for both groups.

- Each treatment group at Week 12 improved by almost half on the WPAI questionnaire overall work impairment index.

- There was no difference between treatment groups at any time point during the study in the proportion of subjects using mild topical steroid preparations, more than mild topical steroid preparations, vitamin D topical preparations, or vitamin D + steroid topical preparations. From Week 12 to Week 24, the percentage of subjects in the etanercept 50 mg BIW/QW group who were using more than mild topical steroid preparations increased from 3.8% to 12.0%, and the percentage of subjects in the etanercept 50 mg QW/QW group using same increased from 4.4% to 13.1%. From Week 12 to Week 24, the percentage of subjects in the etanercept 50 mg BIW/QW

group who were using vitamin D topical preparations increased from 2.3% to 6.8%, and the percentage of subjects in the etanercept 50 mg QW/QW group using same increased from 2.9% to 10.2%. From Week 12 to Week 24, the percentage of subjects in the etanercept 50 mg BIW/QW group who were using vitamin D + steroid topical preparations increased from 0% to 6.8%, and the percentage of subjects in the etanercept 50 mg QW/QW group using same increased from 0.7% to 7.3%.

There were no unexpected safety findings in this study population. The following safety results are summarized below:

- TEAEs were reported at a similar incidence in the etanercept 50 mg BIW/QW and etanercept 50 mg QW/QW groups (69.1% and 64.2%, respectively). The most common TEAEs in either treatment group (≥5% of subjects) were nasopharyngitis, headache, diarrhea, injection site erythema, pharyngitis, arthralgia, fatigue, injection site reaction, and blood insulin increased.

- A total of 5 subjects (3.7%) in the etanercept 50 mg BIW/QW group and 3 subjects (2.2%) in the etanercept 50 mg QW/QW group were withdrawn from the study due to a TEAE. No individual TEAE led to the discontinuation of more than 1 subject.

- A total of 3 subjects (2.2%) in the etanercept 50 mg BIW/QW group and 4 subjects (2.9%) in the etanercept 50 mg QW/QW group had an SAE during the study. No individual SAE occurred in more than 1 subject. No deaths were reported during the study.

- Small changes from baseline were reported for most hematology and chemistry laboratory parameters; however, none were considered to be clinically relevant.

In summary, both treatment regimens were effective, with PASI 75 response rates at 24 weeks of 78.2% and 59.9% for the etanercept 50 mg BIW/QW and etanercept 50 mg QW/QW groups, respectively. Safety findings were consistent with previous studies.