Clinical trial results:
An Open-label Extension Study to Evaluate the Safety of Etanercept in Pediatric Subjects With Plaque Psoriasis

Summary

EudraCT number	2012-001186-33
Trial protocol	Outside EU/EEA
Global end of trial date	16 August 2017

Results information

Result version number	v1 (current)
This version publication date	02 March 2018
First version publication date	02 March 2018

Trial information

Trial identification

Sponsor protocol code	20050111

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00141921
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen, Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000299-PIP01-08
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 December 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the long-term safety and efficacy of etanercept in pediatric patients with moderate to severe psoriasis.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/ guidelines.
Written informed consent and verbal/written assent, if applicable, had to be obtained from each subject (if he or she has attained the legal age for consent) or the subject's parents or legal guardian before performing any procedures, including screening.
The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 August 2005
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 56
Country: Number of subjects enrolled	United States: 126
Worldwide total number of subjects	182
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	63
Adolescents (12-17 years)	119
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was designed to evaluate the long-term safety and efficacy of etanercept in pediatric patients with moderate to severe plaque psoriasis who participated in Study 20030211 (2012-001186-33). The study was conducted at 38 sites in the United States and Canada.

Pre-assignment

Screening details:

Results reported below are from the main analysis performed at year 5 (264 weeks). After the final analysis data cutoff date (22 February 2012), 28 subjects continued protocol specified treatment until they reached 18 years of age.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Etanercept

Arm description:

Participants received etanercept 0.8 mg/kg (up to a maximum dose of 50 mg) once weekly by subcutaneous injection for up to 264 weeks.

Arm type	Experimental
Investigational medicinal product name	Etanercept
Investigational medicinal product code	
Other name	Enbrel®
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Open-label at a dose of 0.8 mg/kg (up to an intended dose of 50 mg) given once weekly by subcutaneous injection

Number of subjects in period 1	Etanercept
Started	182
Received Treatment	181
Completed	41
Not completed	141
Consent withdrawn by subject	42
Disease progression	7
Ineligibility Determined	2
Adverse event, non-fatal	5
Administrative decision	2
Other	8
Protocol deviation	7

Pregnancy	4
Lost to follow-up	19
Remained on study	28
Noncompliance	17

Baseline characteristics

Reporting groups	
Reporting group title	Etanercept
Reporting group description:	
Participants received etanercept 0.8 mg/kg (up to a maximum dose of 50 mg) once weekly by subcutaneous injection for up to 264 weeks.	

Reporting group values	Etanercept	Total	
Number of subjects	182	182	
Age Categorical Units: Subjects			
4 - 11 years	63	63	
12 - 17 years	119	119	
Age Continuous Units: years			
arithmetic mean	12.8		
standard deviation	± 3.5	-	
Gender Categorical Units: Subjects			
Female	90	90	
Male	92	92	
Race/Ethnicity Units: Subjects			
White or Caucasian	138	138	
Black or African American	10	10	
Hispanic or Latino	17	17	
Asian	13	13	
Native Hawaiian or Other Pacific Islander	1	1	
Other	3	3	

End points

End points reporting groups

Reporting group title	Etanercept

Reporting group description:

Participants received etanercept 0.8 mg/kg (up to a maximum dose of 50 mg) once weekly by subcutaneous injection for up to 264 weeks.

Primary: Number of Participants With Adverse Events

End point title	Number of Participants With Adverse Events[1]

End point description:

A serious adverse events is any AE that
• is fatal
• is life threatening
• requires in-patient hospitalization or prolongation of existing hospitalization
• results in persistent or significant disability/incapacity
• is a congenital anomaly/birth defect
• other significant medical hazard. The severity assessment for adverse events and infections (except injection site reactions) was done using the Common Toxicity Criteria (CTC) Version 2.0, where Grade 3 indicates a severe toxicity (incapacitating with inability to work or do usual activity).
An infectious event is an event that was considered by the investigator to be an infectious episode. An injection site reaction is a reaction at the site of the subcutaneous injection, commonly characterized, but not limited to symptoms of erythema (redness, usually raised), pruritis (itching), swelling, or pain that is persistent for 4 hours or longer.

End point type	Primary

End point timeframe:

264 Weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A formal hypothesis was not tested in this study, no formal statistical testing was done.

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	181[2]			
Units: participants				
Any adverse event	161			
Non-infectious adverse events	149			
Infections	140			
Grade 3 non-infectious adverse events	14			
Grade 3 infections	5			
Serious non-infectious adverse events	5			
Serious infections	2			
Non-infectious AEs leading to study withdrawal	5			
Infections leading to withdrawal from study	1			
Injection site reactions	16			
Deaths	0			

Notes:

[2] - Participants who received at least one dose of investigational product.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Injection Site Reactions

End point title	Number of Participants With Injection Site Reactions

End point description:

An injection site reaction is a reaction at the site of the subcutaneous injection, commonly characterized, but not limited to symptoms of erythema (redness, usually raised), pruritis (itching), swelling, or pain that is persistent for 4 hours or longer.

End point type	Secondary

End point timeframe:

264 weeks

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	181[3]			
Units: participants				
Any injection site reaction	16			
Injection site erythema	6			
Injection site reaction	4			
Injection site pruritus	3			
Injection site haematoma	2			
Injection site swelling	2			
Injection site discolouration	1			
Injection site irritation	1			
Injection site pain	1			

Notes:

[3] - Participants who received at least one dose of investigational product.

Statistical analyses

No statistical analyses for this end point

Secondary: Exposure-adjusted Adverse Event Rates

End point title	Exposure-adjusted Adverse Event Rates

End point description:

The exposure adjusted event rate for a given event in a given time period is defined as the number of events reported in the given time period divided by total patient-years on investigational product during the period.
Exposure-adjusted event rate per 100 patient years = total number of events / patient years * 100.
Multiple occurrences of the same event for a participant were counted as multiple events.

End point type	Secondary

End point timeframe:

264 weeks

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	181[4]			
Units: events per 100 patient years				
number (not applicable)				
All adverse events	215.8			
Non-infectious Adverse Events	115.9			
Infections	97.3			
Injection Site Reactions	2.6			

Notes:

[4] - Participants who received at least one dose of investigational product.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes in Vital Signs

End point title	Number of Participants With Clinically Significant Changes in Vital Signs

End point description:

End point type	Secondary

End point timeframe:

264 weeks

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	181[5]			
Units: participants	0			

Notes:

[5] - Participants who received at least one dose of investigational product.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Grade 3 and 4 Laboratory Toxicities

End point title	Number of Participants With Grade 3 and 4 Laboratory Toxicities

End point description:

The severity assessment for adverse events and infections (not including injection site reaction) used the Common Toxicity Criteria (CTC) Version 2.0, where Grade 1= Mild - aware of sign or symptom, but easily tolerated; Grade 2= Moderate - discomfort enough to cause interference with usual activity; Grade 3 = Severe - incapacitating with inability to work or do usual activity; Grade 4= Life-threatening - refers to an event in which the patient was, in the view of the investigator, at risk of immediate death at the time of event; Grade 5 = Fatal.

End point type	Secondary

End point timeframe:

264 weeks

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	181[6]			
Units: participants				
Grade 3 high creatinine	1			
Grade 3 high hemoglobin	1			
Grade 3 low hemoglobin	1			
Grade 3 high alanine aminotransferase	1			
Grade 3 high white blood cells	1			
Any grade 4 toxicity	0			

Notes:

[6] - Participants who received at least one dose of investigational product.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Developed Anti-etanercept Antibodies

End point title	Number of Participants Who Developed Anti-etanercept Antibodies

End point description:

Binding antibodies to etanercept were detected using an anti-etanercept immunoassay. The positive samples in the immunoassay were further analyzed for the presence of neutralizing antibodies using a bioassay.
Participants who developed anti-etanercept antibodies are those who were antibody positive post-baseline with a negative or no result at baseline.

End point type	Secondary

End point timeframe:

264 weeks

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	169[7]			
Units: participants				
Binding antibody positive	18			
Neutralizing antibody positive	0			

Notes:

[7] - Subjects who received at least 1 dose of investigational product with post-baseline antibody data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Psoriasis Area and Severity Index 50 Response (PASI 50)

End point title	Percentage of Participants With a Psoriasis Area and Severity Index 50 Response (PASI 50)

End point description:

A PASI 50 response is a 50% or greater improvement (reduction) from baseline in PASI score.
The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis.

End point type	Secondary

End point timeframe:

Baseline and weeks 12, 48, 96, 144, 192, 240 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	181[8]			
Units: percentage of participants				
number (not applicable)				
Week 12 (N = 181)	89.5			
Week 48 (N = 168)	89.3			
Week 96 (N = 138)	89.1			
Week 144 (N = 114)	88.6			
Week 192 (n = 92)	87.0			
Week 240 (N = 74)	91.9			
Week 264 (N = 66)	87.9			

Notes:

[8] - Participants who received at least one dose of investigational product.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a PASI 75 Response

End point title	Percentage of Participants With a PASI 75 Response

End point description:

A PASI 75 response is a 75% or greater improvement (reduction) from baseline in PASI score.
The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis.

End point type	Secondary

End point timeframe:

Baseline and weeks 12, 48, 96, 144, 192, 240 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	181[9]			
Units: percentage of participants				
number (not applicable)				
Week 12 (N = 181)	67.4			
Week 48 (N = 168)	67.3			
Week 96 (N = 138)	60.9			
Week 144 (N = 114)	62.3			
Week 192 (n = 92)	69.6			
Week 240 (N = 74)	64.9			
Week 264 (N = 66)	63.6			

Notes:

[9] - Participants who received at least one dose of investigational product.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a PASI 90 Response

End point title	Percentage of Participants With a PASI 90 Response

End point description:

A PASI 90 response is a 90% or greater improvement (reduction) from baseline in PASI score.

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis.

End point type	Secondary

End point timeframe:

Baseline and weeks 12, 48, 96, 144, 192, 240 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	181[10]			
Units: percentage of participants				
number (not applicable)				
Week 12 (N = 181)	35.4			
Week 48 (N = 168)	32.7			
Week 96 (N = 138)	29.7			
Week 144 (N = 114)	28.1			
Week 192 (N = 92)	35.9			
Week 240 (N = 74)	36.5			
Week 264 (N = 66)	28.8			

Notes:

[10] - Participants who received at least one dose of investigational product.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Improvement From Study 20030211 Baseline in PASI Score

End point title	Percent Improvement From Study 20030211 Baseline in PASI Score

End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis.
Percent improvement from baseline = (Baseline Value – Post-baseline Value) / Baseline Value * 100.

End point type	Secondary

End point timeframe:

Study 20030211 baseline, Study 20050111 baseline and weeks 12, 48, 96, 144, 192, 240 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	181[11]			
Units: percent improvement				
arithmetic mean (standard deviation)				
Study 20050111 baseline (N = 179)	74.429 (± 22.146)			
Week 12 (N = 181)	78.286 (± 21.079)			
Week 48 (N = 168)	77.546 (± 20.682)			
Week 96 (N = 138)	75.355 (± 24.139)			
Week 144 (N = 114)	75.052 (± 23.839)			
Week 192 (N = 92)	77.815 (± 23.965)			
Week 240 (N = 74)	78.924 (± 23.497)			
Week 264 (N = 66)	74.605 (± 29.327)			

Notes:

[11] - Participants who received at least one dose of investigational product.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Static Physician’s Global Assessment (sPGA) of Clear (0) or Almost Clear (1)

End point title	Percentage of Participants With a Static Physician’s Global Assessment (sPGA) of Clear (0) or Almost Clear (1)

End point description:

The sPGA is a 6-point scale ranging from 0 (clear) to 5 (very severe) used to measure the severity of disease (induration, scaling, and erythema). A sPGA response is defined as a sPGA value of clear (score 0) or almost clear (score 1).

End point type	Secondary

End point timeframe:

Weeks 12, 48, 96, 144, 192, 240 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	181[12]			
Units: percentage of participants				
number (not applicable)				
Week 12 (N = 181)	53.6			
Week 48 (N = 168)	48.8			
Week 96 (N = 139)	47.5			
Week 144 (N = 114)	45.6			
Week 192 (N = 92)	47.8			
Week 240 (N = 74)	50.0			
Week 264 (N = 66)	37.9			

Notes:

[12] - Participants who received at least one dose of investigational product.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Improvement From Study 20030211 Baseline in Children's Dermatology Life Quality Index (CDLQI) Total Score

End point title	Percent Improvement From Study 20030211 Baseline in Children's Dermatology Life Quality Index (CDLQI) Total Score

End point description:

The Children's Dermatology Life Quality Index (CDLQI) was used to assess the impact of psoriasis on subject health-related quality of life. The CDLQI has 10 items assessing health-related quality of life (HRQOL) in patients with skin disease each measured on a scale from 0 (Not at all) to 3 (Very much). The total score ranges from 0 to 30, with lower scores indicating better quality of life. If participants were ≥ 13 years old, the text instrument was completed by the participants themselves. Participants ≥ 8 but < 13 years old used the cartoon version of the instrument and participants ≤ 7 years old used the cartoon version of the instrument completed with help from the parents or caregivers.
Percent improvement from baseline = (Baseline Value – Post-baseline Value) / Baseline Value * 100.

End point type	Secondary

End point timeframe:

Study 20030211 baseline, Study 20050111 baseline and weeks 24, 48, 72, 96, 120, 144, 168, 192, 216, 240 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	173[13]			
Units: percent improvement				
arithmetic mean (standard deviation)				
Study 20050111 baseline (N = 164)	59.492 (± 73.501)			

Week 24 (N = 155)	54.978 (± 69.744)			
Week 48 (N = 148)	59.229 (± 65.259)			
Week 72 (N = 136)	57.549 (± 79.389)			
Week 96 (N = 127)	61.084 (± 66.169)			
Week 120 (N = 105)	64.059 (± 75.298)			
Week 144 (N = 103)	69.732 (± 42.008)			
Week 168 (N = 93)	67.531 (± 42.261)			
Week 192 (N = 81)	65.622 (± 53.359)			
Week 216 (N = 70)	76.121 (± 43.217)			
Week 240 (N = 64)	73.631 (± 54.704)			
Week 264 (N = 56)	63.291 (± 63.555)			

Notes:

[13] - Participants who received at least one dose of investigational product with baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Improvement From Study 20030211 Baseline in CDLQI Symptoms and Feelings Score

End point title	Percent Improvement From Study 20030211 Baseline in CDLQI Symptoms and Feelings Score

End point description:

The Children's Dermatology Life Quality Index (CDLQI) was used to assess the impact of psoriasis on subject health-related quality of life. The CDLQI has 10 items assessing health-related quality of life (HRQOL) in patients with skin disease each measured on a scale from 0 (not at all) to 3 (Very much). The CDLQI Symptoms and Feelings Score includes 2 questions and ranges from 0 to 6, with lower scores indicating better quality of life.
Percent improvement from baseline = (Baseline Value – Post-baseline Value) / Baseline Value * 100.

End point type	Secondary

End point timeframe:

Study 20030211 baseline, Study 20050111 baseline and weeks 24, 48, 72, 96, 120, 144, 168, 192, 216, 240 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	173[14]			
Units: percent improvement				
arithmetic mean (standard deviation)				
Study 20050111 baseline (N = 165)	54.869 (± 56.213)			
Week 24 (N = 155)	55.366 (± 64.039)			

Week 48 (N = 149)	53.792 (± 65.857)			
Week 72 (N = 136)	51.005 (± 68.117)			
Week 96 (N = 128)	55.430 (± 57.430)			
Week 120 (N = 105)	53.302 (± 67.555)			
Week 144 (N = 104)	56.250 (± 58.194)			
Week 168 (N = 94)	58.901 (± 49.431)			
Week 192 (N = 81)	55.700 (± 56.352)			
Week 216 (N = 71)	71.056 (± 41.396)			
Week 240 (N = 65)	67.538 (± 43.418)			
Week 264 (N = 57)	56.725 (± 52.965)			

Notes:

[14] - Participants who received at least one dose of investigational product with baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Improvement From Study 20030211 Baseline in CDLQI Leisure Score

End point title	Percent Improvement From Study 20030211 Baseline in CDLQI Leisure Score

End point description:

The Children's Dermatology Life Quality Index (CDLQI) was used to assess the impact of psoriasis on subject health-related quality of life. The CDLQI has 10 items assessing health-related quality of life (HRQOL) in patients with skin disease each measured on a scale from 0 (not at all) to 3 (Very much). The CDLQI Leisure Score includes 3 questions and ranges from 0 to 9, with lower scores indicating better quality of life.
Percent improvement from baseline = (Baseline Value – Post-baseline Value) / Baseline Value * 100.

End point type	Secondary

End point timeframe:

Study 20030211 baseline, Study 20050111 baseline and weeks 24, 48, 72, 96, 120, 144, 168, 192, 216, 240 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	173[15]			
Units: percent improvement				
arithmetic mean (standard deviation)				
Study 20050111 baseline (N = 165)	51.088 (± 52.612)			
Week 24 (N = 156)	50.546 (± 58.606)			
Week 48 (N = 148)	51.792 (± 61.204)			

Week 72 (N = 136)	50.792 (± 70.769)			
Week 96 (N = 129)	48.686 (± 68.482)			
Week 120 (N = 105)	59.031 (± 49.472)			
Week 144 (N = 104)	57.125 (± 54.284)			
Week 168 (N = 94)	55.198 (± 52.141)			
Week 192 (N = 81)	47.989 (± 72.947)			
Week 216 (N = 71)	58.545 (± 60.440)			
Week 240 (N = 64)	55.727 (± 64.420)			
Week 264 (N = 56)	50.072 (± 62.049)			

Notes:

[15] - Participants who received at least one dose of investigational product with baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Improvement From Study 20030211 Baseline in CDLQI School or Holidays Score

End point title	Percent Improvement From Study 20030211 Baseline in CDLQI School or Holidays Score

End point description:

The Children's Dermatology Life Quality Index (CDLQI) was used to assess the impact of psoriasis on subject health-related quality of life. The CDLQI has 10 items assessing health-related quality of life (HRQOL) in patients with skin disease each measured on a scale from 0 (not at all) to 3 (Very much). The CDLQI School or Holidays Score includes 1 question (How much did your skin problem effect your school work/holiday plans over the last week?) and ranges from 0 to 3, with lower scores indicating better quality of life.
Percent improvement from baseline = (Baseline Value – Post-baseline Value) / Baseline Value * 100.

End point type	Secondary

End point timeframe:

Study 20030211 baseline, Study 20050111 baseline and weeks 24, 48, 72, 96, 120, 144, 168, 192, 216, 240 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	173[16]			
Units: percent improvement				
arithmetic mean (standard deviation)				
Study 20050111 baseline (N = 165)	31.616 (± 51.981)			
Week 24 (N = 156)	32.585 (± 52.750)			
Week 48 (N = 148)	36.149 (± 51.778)			
Week 72 (N = 133)	29.825 (± 53.025)			

Week 96 (N = 129)	29.547 (± 55.085)			
Week 120 (N = 105)	32.063 (± 55.166)			
Week 144 (N = 105)	33.333 (± 48.371)			
Week 168 (N = 94)	32.979 (± 50.563)			
Week 192 (N = 81)	31.070 (± 52.886)			
Week 216 (N = 71)	35.211 (± 48.103)			
Week 240 (N = 65)	26.923 (± 56.649)			
Week 264 (N = 57)	27.193 (± 51.815)			

Notes:

[16] - Participants who received at least one dose of investigational product with baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Improvement From Study 20030211 Baseline in CDLQI Personal Relationships Score

End point title	Percent Improvement From Study 20030211 Baseline in CDLQI Personal Relationships Score

End point description:

The Children's Dermatology Life Quality Index (CDLQI) was used to assess the impact of psoriasis on subject health-related quality of life. The CDLQI has 10 items assessing health-related quality of life (HRQOL) in patients with skin disease each measured on a scale from 0 (not at all) to 3 (Very much). The CDLQI Personal Relationships Score includes 2 questions and ranges from 0 to 6, with lower scores indicating better quality of life.
Percent improvement from baseline = (Baseline Value – Post-baseline Value) / Baseline Value * 100.

End point type	Secondary

End point timeframe:

Study 20030211 baseline, Study 20050111 baseline and weeks 24, 48, 72, 96, 120, 144, 168, 192, 216, 240 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	173[17]			
Units: percent improvement				
arithmetic mean (standard deviation)				
Study 20050111 baseline (N = 166)	45.452 (± 65.038)			
Week 24 (N = 156)	49.797 (± 59.328)			
Week 48 (N = 149)	50.895 (± 60.179)			
Week 72 (N = 136)	54.669 (± 54.519)			
Week 96 (N = 129)	48.346 (± 60.414)			

Week 120 (N = 105)	51.206 (± 54.435)			
Week 144 (N = 105)	50.365 (± 49.636)			
Week 168 (N = 94)	44.557 (± 72.287)			
Week 192 (N = 81)	52.284 (± 56.125)			
Week 216 (N = 71)	61.737 (± 48.255)			
Week 240 (N = 65)	56.282 (± 52.042)			
Week 264 (N = 57)	56.140 (± 52.481)			

Notes:

[17] - Participants who received at least one dose of investigational product with baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Improvement From Study 20030211 Baseline in CDLQI Sleep Score

End point title	Percent Improvement From Study 20030211 Baseline in CDLQI Sleep Score

End point description:

The Children's Dermatology Life Quality Index (CDLQI) was used to assess the impact of psoriasis on subject health-related quality of life. The CDLQI has 10 items assessing health-related quality of life (HRQOL) in patients with skin disease each measured on a scale from 0 (not at all) to 3 (Very much). The CDLQI Sleep Score includes 1 question (How much has your sleep been affected by your skin problems over the last week?) and ranges from 0 to 3, with lower scores indicating better quality of life. Percent improvement from baseline = (Baseline Value – Post-baseline Value) / Baseline Value * 100.

End point type	Secondary

End point timeframe:

Study 20030211 baseline, Study 20050111 baseline and weeks 24, 48, 72, 96, 120, 144, 168, 192, 216, 240 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	171[18]			
Units: percent improvement				
arithmetic mean (standard deviation)				
Study 20050111 baseline (N = 161)	36.646 (± 56.851)			
Week 24 (N = 153)	36.057 (± 60.349)			
Week 48 (N = 144)	31.597 (± 56.329)			
Week 72 (N = 132)	34.596 (± 57.390)			
Week 96 (N = 127)	32.940 (± 55.216)			
Week 120 (N = 101)	29.538 (± 61.503)			

Week 144 (N = 102)	41.013 (± 50.229)			
Week 168 (N = 93)	37.814 (± 49.888)			
Week 192 (N = 81)	34.774 (± 54.658)			
Week 216 (N = 71)	35.681 (± 50.811)			
Week 240 (N = 65)	39.231 (± 48.808)			
Week 264 (N = 56)	36.012 (± 57.890)			

Notes:

[18] - Participants who received at least one dose of investigational product with baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Improvement From Study 20030211 Baseline in CDLQI Treatment Satisfaction Score

End point title	Percent Improvement From Study 20030211 Baseline in CDLQI Treatment Satisfaction Score

End point description:

The Children's Dermatology Life Quality Index (CDLQI) was used to assess the impact of psoriasis on subject health-related quality of life. The CDLQI has 10 items assessing health-related quality of life (HRQOL) in patients with skin disease each measured on a scale from 0 (not at all) to 3 (Very much). The CDLQI Treatment Satisfaction Score includes 1 question (How much of a problem has the treatment for your skin been over the last week?) and ranges from 0 to 3, with lower scores indicating better quality of life.
Percent improvement from baseline = (Baseline Value – Post-baseline Value) / Baseline Value * 100.

End point type	Secondary

End point timeframe:

Study 20030211 baseline, Study 20050111 baseline and weeks 24, 48, 72, 96, 120, 144, 168, 192, 216, 240 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	169[19]			
Units: percent improvement				
arithmetic mean (standard deviation)				
Study 20050111 baseline (N = 161)	23.085 (± 64.713)			
Week 24 (N = 152)	13.268 (± 74.987)			
Week 48 (N = 144)	18.634 (± 67.750)			
Week 72 (N = 134)	23.383 (± 73.210)			
Week 96 (N = 128)	17.969 (± 72.561)			
Week 120 (N = 105)	17.778 (± 65.709)			
Week 144 (N = 104)	21.795 (± 62.924)			

Week 168 (N = 93)	20.430 (± 73.849)			
Week 192 (N = 81)	26.955 (± 68.443)			
Week 216 (N = 71)	31.455 (± 59.598)			
Week 240 (N = 65)	30.513 (± 57.703)			
Week 264 (N = 56)	37.500 (± 64.842)			

Notes:

[19] - Participants who received at least one dose of investigational product with baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Improvement From Study 20030211 Baseline in Joint Pain

End point title	Improvement From Study 20030211 Baseline in Joint Pain

End point description:

Participants were asked to indicate how much joint pain they had experienced in the last 7 days on a visual analog scale (VAS) from no pain on the left end of the line (score = 0) to severe pain on the right side of the line (score = 10).
Improvement from baseline = (Baseline Value – Post-baseline Value).

End point type	Secondary

End point timeframe:

Study 20030211 baseline, Study 20050111 baseline and weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252 and 264

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	41[20]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Study 20050111 baseline (N = 31)	1.5 (± 2.7)			
Week 12 (N = 29)	2.3 (± 2.5)			
Week 24 (N = 22)	2.4 (± 3.2)			
Week 36 (N = 22)	1.5 (± 3.2)			
Week 48 (N = 24)	1.5 (± 3.5)			
Week 60 (N = 14)	1.3 (± 3.2)			
Week 72 (N = 16)	2.1 (± 3.6)			
Week 84 (N = 14)	2.9 (± 3.0)			
Week 96 (N = 16)	2.0 (± 2.7)			
Week 108 (N = 14)	2.4 (± 3.4)			
Week 120 (N = 12)	2.4 (± 2.9)			
Week 132 (N = 15)	1.9 (± 3.7)			
Week 144 (N = 12)	1.8 (± 4.3)			
Week 156 (N = 12)	2.5 (± 3.8)			
Week 168 (N = 10)	2.2 (± 4.0)			
Week 180 (N = 11)	2.7 (± 3.3)			
Week 192 (N = 11)	2.5 (± 4.2)			

Week 204 (N = 11)	2.8 (± 3.6)			
Week 216 (N = 9)	2.9 (± 3.4)			
Week 228 (N = 10)	2.8 (± 3.6)			
Week 240 (N = 9)	2.7 (± 3.4)			
Week 252 (N = 8)	3.9 (± 3.7)			
Week 264 (N = 8)	3.9 (± 3.3)			

Notes:

[20] - Participants who received at least one dose of investigational product with baseline data

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Through the End of Treatment (Week 264 or the first quarterly visit after the subject's 18th birthday, whichever comes last) or Early Termination Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Etanercept

Reporting group description:

Participants received etanercept 0.8 mg/kg (up to a maximum dose of 50 mg) once weekly by subcutaneous injection for up to 264 weeks.

Serious adverse events	Etanercept		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 181 (6.08%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Intracranial mass			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Premature separation of placenta			

subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anxiety			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intentional self-injury			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Major depression			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary bladder rupture			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Endocrine disorders			
Thyroid cyst			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteonecrosis			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infectious mononucleosis			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Etanercept		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	149 / 181 (82.32%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	24 / 181 (13.26%)		
occurrences (all)	36		
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	11 / 181 (6.08%)		
occurrences (all)	13		
Procedural pain			

subjects affected / exposed occurrences (all)	12 / 181 (6.63%) 16		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 40 / 181 (22.10%) 65		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	 17 / 181 (9.39%) 28		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 11 / 181 (6.08%) 21 11 / 181 (6.08%) 13 13 / 181 (7.18%) 17		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 22 / 181 (12.15%) 29 17 / 181 (9.39%) 29 20 / 181 (11.05%) 34		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) Dermatitis contact	 33 / 181 (18.23%) 36		

subjects affected / exposed	11 / 181 (6.08%)		
occurrences (all)	17		
Psoriasis			
subjects affected / exposed	14 / 181 (7.73%)		
occurrences (all)	19		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	14 / 181 (7.73%)		
occurrences (all)	18		
Infections and infestations			
Bronchitis			
subjects affected / exposed	18 / 181 (9.94%)		
occurrences (all)	22		
Ear infection			
subjects affected / exposed	12 / 181 (6.63%)		
occurrences (all)	18		
Gastroenteritis			
subjects affected / exposed	14 / 181 (7.73%)		
occurrences (all)	14		
Gastroenteritis viral			
subjects affected / exposed	14 / 181 (7.73%)		
occurrences (all)	15		
Influenza			
subjects affected / exposed	21 / 181 (11.60%)		
occurrences (all)	28		
Pharyngitis			
subjects affected / exposed	15 / 181 (8.29%)		
occurrences (all)	21		
Pharyngitis streptococcal			
subjects affected / exposed	27 / 181 (14.92%)		
occurrences (all)	37		
Sinusitis			
subjects affected / exposed	25 / 181 (13.81%)		
occurrences (all)	36		
Upper respiratory tract infection			

subjects affected / exposed	69 / 181 (38.12%)		
occurrences (all)	154		
Viral upper respiratory tract infection			
subjects affected / exposed	54 / 181 (29.83%)		
occurrences (all)	116		
Urinary tract infection			
subjects affected / exposed	12 / 181 (6.63%)		
occurrences (all)	16		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 July 2005	• Per US Food and Drug Administration request, the discontinuation and dose adjustment criteria were amended to require that subjects with a systemic infection that required intravenous antibiotic use or hospitalization be removed from the study. • Etanercept dose wording was changed to correctly reflect that an exact 0.8 mg/kg dose is not always possible using 2 vials of lyophilized investigational product as the subject's body weight approaches 62 kg.
19 October 2006	• Extended length of study for an additional 18 months • Included the option for investigators to stop treatment with investigational product for subjects with a Static Physician Global Assessment score of clear (0) or almost clear (1) at week 96, 108, 120, 132, 144, or 156
10 September 2008	• Extended length of the study to 5 years • Subjects were no longer required to permanently discontinue treatment if therapy was temporarily withheld more than once because of clearing of psoriasis or if more than 3 consecutive doses were withheld because of an adverse event or surgical procedure • Removed 30 day follow-up visit • Removed collection of Harter's Self-Perception Profile in Children and Adolescents
26 July 2010	• Allowed for the collection of additional safety data (assessments of adverse events and concomitant medication use) on subjects who were under the age of 18. After week 264, only serious adverse events were to be collected. • Subjects were allowed to continue on this study until they reached 18 years of age. • Added a second planned interim analysis (a "week 264 analysis") after all subjects remaining in the study completed the week 264 assessments. This comprises the main comprehensive, integrated analysis of Study 20050111 data.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported