Clinical trial results:
A Multicenter Double-blind, Randomized Controlled Study of Etanercept and Methotrexate in Combination or as Monotherapy in Subjects With Psoriatic Arthritis

Summary

EudraCT number	2014-004869-24
Trial protocol	LV GR GB PT HU CZ BG PL ES FR
Global end of trial date	06 July 2018

Results information

Result version number	v1 (current)
This version publication date	15 July 2019
First version publication date	15 July 2019

Trial information

Trial identification

Sponsor protocol code	20130207

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02376790
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, 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)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 July 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of etanercept plus methotrexate therapy and etanercept monotherapy compared to methotrexate monotherapy, in subjects with psoriatic arthritis (PsA) as measured by the proportion of subjects achieving an American College of Rheumatology (ACR) 20 response at week 24.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.
A copy of the protocol, proposed informed consent form, other written subject information, and any proposed advertising material were submitted to the institutional IRB/IEC for written approval. A copy of the written approval of the protocol and informed consent form were received by Amgen before subjects were recruited into the study and before shipment of Amgen investigational product.
The investigator or his/her designee informed the subject of all aspects pertaining to the subject's participation in the study before any screening procedures were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 March 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 45
Country: Number of subjects enrolled	Argentina: 10
Country: Number of subjects enrolled	Canada: 25
Country: Number of subjects enrolled	Chile: 53
Country: Number of subjects enrolled	Czech Republic: 32
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Greece: 18
Country: Number of subjects enrolled	Hungary: 31
Country: Number of subjects enrolled	Latvia: 12
Country: Number of subjects enrolled	Mexico: 73
Country: Number of subjects enrolled	Poland: 61
Country: Number of subjects enrolled	Portugal: 16
Country: Number of subjects enrolled	Russian Federation: 77
Country: Number of subjects enrolled	South Africa: 32
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	United Kingdom: 9

Country: Number of subjects enrolled	United States: 347
Worldwide total number of subjects	851
EEA total number of subjects	234

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	754
From 65 to 84 years	96
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 124 centers in Europe, Latin America, North America, and South Africa. Participants were enrolled from 03 March 2015 to 07 July 2017.

Pre-assignment

Screening details:

The study consisted of a 30-day screening period, a 48-week randomized double blind treatment period, and a 30-day safety follow-up period.
Participants were randomly assigned in a 1:1:1 ratio to 1 of 3 treatment groups.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Methotrexate Monotherapy

Arm description:

Participants received oral methotrexate 20 mg weekly plus placebo to etanercept subcutaneous injection once a week for 48 weeks.

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

Dosage and administration details:

Placebo to etanercept was administered by subcutaneous injection once a week.

Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Methotrexate capsules taken orally once a week. Dosing was initiated at 10 mg weekly and titrated up to a final dose of 20 mg weekly over a 4-week period.

Arm title	Etanercept Monotherapy

Arm description:

Participants received etanercept 50 mg weekly by subcutaneous injection plus oral placebo to methotrexate for 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Etanercept
Investigational medicinal product code	
Other name	Enbrel
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:	
Etanercept was administered by subcutaneous injection once a week.	
Investigational medicinal product name	Placebo to Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Placebo to methotrexate capsules taken orally once a week.	
Arm title	Etanercept + Methotrexate
Arm description:	
Participants received etanercept 50 mg a week by subcutaneous injection and oral methotrexate 20 mg a week for 48 weeks.	
Arm type	Experimental
Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Methotrexate capsules taken orally once a week. Dosing was initiated at 10 mg weekly and titrated up to a final dose of 20 mg weekly over a 4-week period.	
Investigational medicinal product name	Etanercept
Investigational medicinal product code	
Other name	Enbrel
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
Etanercept was administered by subcutaneous injection once a week.	

Number of subjects in period 1	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate
Started	284	284	283
Received Treatment	282	284	282
Completed	224	237	230
Not completed	60	47	53
Consent withdrawn by subject	43	36	37
Decision by Sponsor	2	1	4
Lost to follow-up	15	10	12

Baseline characteristics

Reporting groups	
Reporting group title	Methotrexate Monotherapy
Reporting group description:	
Participants received oral methotrexate 20 mg weekly plus placebo to etanercept subcutaneous injection once a week for 48 weeks.	
Reporting group title	Etanercept Monotherapy
Reporting group description:	
Participants received etanercept 50 mg weekly by subcutaneous injection plus oral placebo to methotrexate for 48 weeks.	
Reporting group title	Etanercept + Methotrexate
Reporting group description:	
Participants received etanercept 50 mg a week by subcutaneous injection and oral methotrexate 20 mg a week for 48 weeks.	

Reporting group values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate
Number of subjects	284	284	283
Age, Customized Units: Subjects			
≤ 65 years	257	251	259
> 65 years	27	33	24
Age Continuous Units: years			
arithmetic mean	48.7	48.5	48.1
standard deviation	± 13.1	± 13.5	± 12.7
Sex: Female, Male Units: Subjects			
Female	160	133	139
Male	124	151	144
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	11	11	8
Asian	3	1	1
Black (or African American)	4	0	3
Mixed Race	0	1	0
Native Hawaiian or Other Pacific Islander	1	1	0
Other	10	18	6
White	255	252	265
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	58	70	69
Not Hispanic or Latino	226	214	214
Unknown or Not Reported	0	0	0
Body Mass Index (BMI) Units: Subjects			
≤ 30 kg/m²	146	153	160
> 30 kg/m²	138	130	123
Missing	0	1	0

Prior Use of Non-biologic Disease Modifying Antirheumatic Drugs (DMARDs) Units: Subjects			
Yes	38	26	43
No	246	258	240
Duration of Psoriatic Arthritis Disease			
Data are provided for participants with available data (N = 231, 222, 231)			
Units: years			
arithmetic mean	3.64	3.10	2.96
standard deviation	± 6.85	± 5.96	± 5.99
Swollen Joint Count			
A total of 66 joints were scored for presence or absence of swelling. Data are provided for all participants with available data (N = 284, 283, 282).			
Units: joints			
arithmetic mean	12.9	11.5	11.2
standard deviation	± 9.9	± 9.6	± 9.1
Tender Joint Count			
A total of 68 joints were scored for presence or absence of tenderness. Data are provided for all participants with available data (N = 284, 283, 282).			
Units: joints			
arithmetic mean	20.9	18.8	20.0
standard deviation	± 15.0	± 14.5	± 15.3
Physician Global Assessment of Disease Activity			
Assessed by the physician on a 100 mm visual analog scale (VAS), where 0 mm = No activity at all and 100 mm = Worst activity imaginable. Data are provided for all participants with available data (N = 284, 284, 282).			
Units: mm			
arithmetic mean	58.6	58.3	58.0
standard deviation	± 19.4	± 18.2	± 17.8
Patient Global Assessment of Disease Activity			
Assessed by the participant on a 100 mm VAS, where 0 mm = No arthritis activity at all and 100 mm = Worst arthritis activity imaginable. Data are provided for all participants with available data (N = 283, 284, 282).			
Units: mm			
arithmetic mean	60.7	62.9	61.0
standard deviation	± 22.5	± 22.1	± 20.8
Patient Global Assessment of Joint Pain			
Participants assessed their joint pain on a 100 mm VAS, where 0 mm = No pain at all and 100 mm = Worst pain imaginable. Data are provided for all participants with available data (N = 283, 284, 282).			
Units: mm			
arithmetic mean	56.1	56.5	55.7
standard deviation	± 21.7	± 22.3	± 21.6
Disability Index of the Health Assessment Questionnaire (HAQ-DI)			
The HAQ-DI is a patient-reported questionnaire consisting of 20 questions in 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and usual activities. Participants assessed their ability to do each task in the past week using the following responses: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores were summed and averaged to provide an overall score ranging from 0 (no disability) to 3 (very severe, high-dependency disability). Data are provided for all participants with available data (N = 283, 284, 282).			
Units: units on a scale			
arithmetic mean	1.3	1.1	1.2

standard deviation	± 0.6	± 0.6	± 0.6
C-reactive Protein (CRP) Concentration			
C-reactive protein (CRP) is a protein found in blood. CRP levels rise in response to inflammation. Data are provided for all participants with available data (N = 284, 282, 283).			
Units: mg/L			
arithmetic mean	10.52	10.72	8.70
standard deviation	± 16.29	± 15.59	± 11.65
Psoriatic Arthritis Disease Activity Score (PASDAS)			
PASDAS is a measure of disease activity derived from: • Physician and patient global assessment of disease activity (0-100 VAS) • 68 tender joint count • 66 swollen joint count • Short Form-36 Questionnaire (SF-36) physical component summary (score 0-100) • Tender dactylitis count (each digit assessed for tender dactylitis; total score 0-20) • Leeds enthesitis index (enthesitis assessed at 6 sites; total score 0-6) • CRP The composite score is a weighted index with higher scores indicating more severe disease. Data are provided for subjects with available data (N = 282, 279, 280).			
Units: units on a scale			
median	6.10	6.02	5.95
full range (min-max)	2.2 to 9.1	2.5 to 10.2	3.0 to 9.4
Clinical Disease Activity Index (CDAI)			
The Clinical Disease Activity Index (CDAI) is a composite index that is calculated as the sum of the following items: - 28 tender joint count, - 28 swollen joint count, - Patient's Global Assessment of Disease Activity measured on a 10 cm VAS, where 0 = lowest disease activity and 10 = highest; - Physician's Global Assessment of Disease Activity measured on a 10 cm VAS, where 0 = lowest disease activity and 10 cm highest. The CDAI score ranges from 0-76 where lower scores indicate less disease activity. Data are provided for subjects with available data (N = 283, 283, 281).			
Units: units on a scale			
arithmetic mean	30.51	28.45	28.55
standard deviation	± 13.26	± 12.89	± 12.71
Simplified Disease Activity Index (SDAI)			
The Simplified Disease Activity Index (SDAI) is a composite index that is calculated as the sum of the following items: - 28 tender joint count, - 28 swollen joint count, - Patient's Global Assessment of Disease Activity measured on a 10 cm VAS, where 0 = lowest disease activity and 10 = highest; - Physician's Global Assessment of Disease Activity -measured on a 10 VAS, where 0 = lowest disease activity and 10 cm = highest. - CRP The SDAI score ranges from 0 to 86 with higher scores representing worse disease. Data are provided for subjects with available data (N = 283, 281, 281).			
Units: units on a scale			
arithmetic mean	31.56	29.52	29.43
standard deviation	± 13.52	± 13.19	± 12.90
Disease Activity Score 28 (DAS28)			
The DAS28 measures the severity of disease at a specific time and is derived from the following variables: - 28 tender joint count - 28 swollen joint count - C-reactive protein (CRP) concentration - Patient's global assessment of disease activity, measured on a 100 mm VAS, where 0 = lowest disease activity and 100 = highest. DAS28(CRP) scores range from 0 to approximately 10, with the upper bound dependent on the highest possible level of CRP. Higher scores indicate higher disease activity. Data are provided for subjects with available data (N = 283, 281, 281).			

Units: units on a scale			
arithmetic mean	4.93	4.80	4.75
standard deviation	± 1.11	± 1.13	± 1.12
Medical Outcomes Health Survey Short Form 36 Item (SF-36) Version 2 Physical Component Summary Score			
The SF-36 is a health-related survey that assesses participant's quality of life and consists of 36 questions covering 8 health domains. Two summary component scores are calculated: mental component summary score (MCS) and physical component summary score (PCS). Each domain is scored by summing the individual items and transforming the scores into a 0 to 100 scale with higher scores indicating better health status or functioning. Data are provided for participants with available data (N = 282, 284, 282).			
Units: units on a scale			
arithmetic mean	35.587	37.835	37.353
standard deviation	± 8.411	± 8.381	± 9.243
Medical Outcomes Health Survey Short Form 36 Item(SF-36) Version 2 Mental Component Summary Score			
The SF-36 is a health-related survey that assesses participant's quality of life and consists of 36 questions covering 8 health domains. Two summary component scores are calculated: mental component summary score (MCS) and physical component summary score (PCS). Each domain is scored by summing the individual items and transforming the scores into a 0 to 100 scale with higher scores indicating better health status or functioning. Data are provided for participants with available data (N = 282, 284, 282)			
Units: units on a scale			
arithmetic mean	45.174	45.107	46.256
standard deviation	± 12.073	± 12.496	± 11.236
Leeds Dactylitis Index (LDI)			
The Leeds dactylitis index quantitatively measures dactylitis using the circumference of involved digits and control digits and tenderness of involved digits (on a scale from 0-3). The ratio of circumference between an affected digit and the control digit is multiplied by the tenderness score for the affected digit. The results from each involved digit are summed to provide the LDI; higher LDI indicates worse dactylitis. Data are provided for subjects with available data (N = 284, 283, 282).			
Units: units on a scale			
arithmetic mean	56.89	50.07	44.11
standard deviation	± 174.56	± 137.20	± 143.17
Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index			
The SPARCC enthesitis index assesses enthesitis at 18 sites for palpitation with a resultant total score of 0 to 16 (for scoring purposes, the inferior patella and tibial tuberosity are considered 1 site because of their anatomical proximity). Tenderness at each site is quantified on a dichotomous basis (0 = non-tender, 1 = tender). A higher count represents greater enthesitis burden. Data are provided for subjects with available data (N = 284, 283, 282).			
Units: units on a scale			
arithmetic mean	3.9	3.7	4.1
standard deviation	± 4.3	± 4.3	± 4.5
Percentage of Body Surface Area (BSA) Involved in Psoriasis			
The physician’s assessment of the percentage of the participant’s total body surface area involved with psoriasis.			
Units: percent body surface area			
arithmetic mean	12.68	10.76	10.74
standard deviation	± 18.78	± 14.66	± 15.58
Static Physician Global Assessment (sPGA)			
The static Physician Global Assessment of psoriasis (sPGA) evaluates the physician’s global assessment of the participant’s psoriasis based on severity of induration, scaling, and erythema. The sPGA is assessed on a scale from 0 to 5: 0 = clear (no evidence of plaque elevation, erythema or scaling) 1 = almost clear			

2 = mild 3 = moderate 4 = marked 5 = severe Data are provided for subjects with available data (N = 281, 284, 283).			
Units: units on a scale			
arithmetic mean	2.6	2.6	2.5
standard deviation	± 1.1	± 1.0	± 1.0

Reporting group values	Total		
Number of subjects	851		
Age, Customized Units: Subjects			
≤ 65 years	767		
> 65 years	84		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	432		
Male	419		
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	30		
Asian	5		
Black (or African American)	7		
Mixed Race	1		
Native Hawaiian or Other Pacific Islander	2		
Other	34		
White	772		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	197		
Not Hispanic or Latino	654		
Unknown or Not Reported	0		
Body Mass Index (BMI) Units: Subjects			
≤ 30 kg/m²	459		
> 30 kg/m²	391		
Missing	1		
Prior Use of Non-biologic Disease Modifying Antirheumatic Drugs (DMARDs) Units: Subjects			
Yes	107		
No	744		
Duration of Psoriatic Arthritis Disease			
Data are provided for participants with available data (N = 231, 222, 231)			
Units: years			
arithmetic mean			

standard deviation	-		
Swollen Joint Count			
A total of 66 joints were scored for presence or absence of swelling. Data are provided for all participants with available data (N = 284, 283, 282).			
Units: joints arithmetic mean standard deviation	- -		
Tender Joint Count			
A total of 68 joints were scored for presence or absence of tenderness. Data are provided for all participants with available data (N = 284, 283, 282).			
Units: joints arithmetic mean standard deviation	- -		
Physician Global Assessment of Disease Activity			
Assessed by the physician on a 100 mm visual analog scale (VAS), where 0 mm = No activity at all and 100 mm = Worst activity imaginable. Data are provided for all participants with available data (N = 284, 284, 282).			
Units: mm arithmetic mean standard deviation	- -		
Patient Global Assessment of Disease Activity			
Assessed by the participant on a 100 mm VAS, where 0 mm = No arthritis activity at all and 100 mm = Worst arthritis activity imaginable. Data are provided for all participants with available data (N = 283, 284, 282).			
Units: mm arithmetic mean standard deviation	- -		
Patient Global Assessment of Joint Pain			
Participants assessed their joint pain on a 100 mm VAS, where 0 mm = No pain at all and 100 mm = Worst pain imaginable. Data are provided for all participants with available data (N = 283, 284, 282).			
Units: mm arithmetic mean standard deviation	- -		
Disability Index of the Health Assessment Questionnaire (HAQ-DI)			
The HAQ-DI is a patient-reported questionnaire consisting of 20 questions in 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and usual activities. Participants assessed their ability to do each task in the past week using the following responses: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores were summed and averaged to provide an overall score ranging from 0 (no disability) to 3 (very severe, high-dependency disability). Data are provided for all participants with available data (N = 283, 284, 282).			
Units: units on a scale arithmetic mean standard deviation	- -		
C-reactive Protein (CRP) Concentration			
C-reactive protein (CRP) is a protein found in blood. CRP levels rise in response to inflammation. Data are provided for all participants with available data (N = 284, 282, 283).			
Units: mg/L arithmetic mean standard deviation	- -		
Psoriatic Arthritis Disease Activity Score (PASDAS)			
PASDAS is a measure of disease activity derived from: • Physician and patient global assessment of disease activity (0-100 VAS)			

• 68 tender joint count
• 66 swollen joint count
• Short Form-36 Questionnaire (SF-36) physical component summary (score 0-100)
• Tender dactylitis count (each digit assessed for tender dactylitis; total score 0-20)
• Leeds enthesitis index (enthesitis assessed at 6 sites; total score 0-6)
• CRP
The composite score is a weighted index with higher scores indicating more severe disease.
Data are provided for subjects with available data (N = 282, 279, 280).

Units: units on a scale median full range (min-max)	-		
Clinical Disease Activity Index (CDAI)			

The Clinical Disease Activity Index (CDAI) is a composite index that is calculated as the sum of the following items:
- 28 tender joint count,
- 28 swollen joint count,
- Patient's Global Assessment of Disease Activity measured on a 10 cm VAS, where 0 = lowest disease activity and 10 = highest;
- Physician's Global Assessment of Disease Activity measured on a 10 cm VAS, where 0 = lowest disease activity and 10 cm highest.
The CDAI score ranges from 0-76 where lower scores indicate less disease activity.
Data are provided for subjects with available data (N = 283, 283, 281).

Units: units on a scale arithmetic mean standard deviation	-		
Simplified Disease Activity Index (SDAI)			

The Simplified Disease Activity Index (SDAI) is a composite index that is calculated as the sum of the following items:
- 28 tender joint count,
- 28 swollen joint count,
- Patient's Global Assessment of Disease Activity measured on a 10 cm VAS, where 0 = lowest disease activity and 10 = highest;
- Physician's Global Assessment of Disease Activity -measured on a 10 VAS, where 0 = lowest disease activity and 10 cm = highest.
- CRP
The SDAI score ranges from 0 to 86 with higher scores representing worse disease.
Data are provided for subjects with available data (N = 283, 281, 281).

Units: units on a scale arithmetic mean standard deviation	-		
Disease Activity Score 28 (DAS28)			

The DAS28 measures the severity of disease at a specific time and is derived from the following variables:
- 28 tender joint count
- 28 swollen joint count
- C-reactive protein (CRP) concentration
- Patient's global assessment of disease activity, measured on a 100 mm VAS, where 0 = lowest disease activity and 100 = highest.
DAS28(CRP) scores range from 0 to approximately 10, with the upper bound dependent on the highest possible level of CRP. Higher scores indicate higher disease activity.
Data are provided for subjects with available data (N = 283, 281, 281).

Units: units on a scale arithmetic mean standard deviation	-		
Medical Outcomes Health Survey Short Form 36 Item (SF-36) Version 2 Physical Component Summary Score			

The SF-36 is a health-related survey that assesses participant's quality of life and consists of 36 questions covering 8 health domains. Two summary component scores are calculated: mental component summary score (MCS) and physical component summary score (PCS). Each domain is scored by summing the individual items and transforming the scores into a 0 to 100 scale with higher scores indicating better health status or functioning.
Data are provided for participants with available data (N = 282, 284, 282).

Units: units on a scale arithmetic mean standard deviation	-		
Medical Outcomes Health Survey Short Form 36 Item(SF-36) Version 2 Mental Component Summary Score			
The SF-36 is a health-related survey that assesses participant's quality of life and consists of 36 questions covering 8 health domains. Two summary component scores are calculated: mental component summary score (MCS) and physical component summary score (PCS). Each domain is scored by summing the individual items and transforming the scores into a 0 to 100 scale with higher scores indicating better health status or functioning. Data are provided for participants with available data (N = 282, 284, 282)			
Units: units on a scale arithmetic mean standard deviation	-		
Leeds Dactylitis Index (LDI)			
The Leeds dactylitis index quantitatively measures dactylitis using the circumference of involved digits and control digits and tenderness of involved digits (on a scale from 0-3). The ratio of circumference between an affected digit and the control digit is multiplied by the tenderness score for the affected digit. The results from each involved digit are summed to provide the LDI; higher LDI indicates worse dactylitis. Data are provided for subjects with available data (N = 284, 283, 282).			
Units: units on a scale arithmetic mean standard deviation	-		
Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index			
The SPARCC enthesitis index assesses enthesitis at 18 sites for palpitation with a resultant total score of 0 to 16 (for scoring purposes, the inferior patella and tibial tuberosity are considered 1 site because of their anatomical proximity). Tenderness at each site is quantified on a dichotomous basis (0 = non-tender, 1 = tender). A higher count represents greater enthesitis burden. Data are provided for subjects with available data (N = 284, 283, 282).			
Units: units on a scale arithmetic mean standard deviation	-		
Percentage of Body Surface Area (BSA) Involved in Psoriasis			
The physician’s assessment of the percentage of the participant’s total body surface area involved with psoriasis.			
Units: percent body surface area arithmetic mean standard deviation	-		
Static Physician Global Assessment (sPGA)			
The static Physician Global Assessment of psoriasis (sPGA) evaluates the physician’s global assessment of the participant’s psoriasis based on severity of induration, scaling, and erythema. The sPGA is assessed on a scale from 0 to 5: 0 = clear (no evidence of plaque elevation, erythema or scaling) 1 = almost clear 2 = mild 3 = moderate 4 = marked 5 = severe Data are provided for subjects with available data (N = 281, 284, 283).			
Units: units on a scale arithmetic mean standard deviation	-		

End points

End points reporting groups

Reporting group title	Methotrexate Monotherapy
Reporting group description:	
Participants received oral methotrexate 20 mg weekly plus placebo to etanercept subcutaneous injection once a week for 48 weeks.	
Reporting group title	Etanercept Monotherapy
Reporting group description:	
Participants received etanercept 50 mg weekly by subcutaneous injection plus oral placebo to methotrexate for 48 weeks.	
Reporting group title	Etanercept + Methotrexate
Reporting group description:	
Participants received etanercept 50 mg a week by subcutaneous injection and oral methotrexate 20 mg a week for 48 weeks.	

Primary: Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 24

End point title	Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 24

End point description:

A positive ACR20 response is defined if the following 3 criteria for improvement from baseline were met:
- ≥ 20% improvement in 68 tender joint count;
- ≥ 20% improvement in 66 swollen joint count; and
- ≥ 20% improvement in at least 3 of the 5 following parameters:
  - Patient's assessment of joint pain (measured on a 100 mm visual analog scale [VAS]);
  - Patient's global assessment of disease activity (measured on a 100 mm VAS);
  - Physician's global assessment of disease activity (measured on a 100 mm VAS);
  - Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index [HAQ-DI]);
  - C-reactive protein concentration.

Participants with missing postbaseline data were counted as non-responders.

End point type	Primary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: percentage of participants				
number (not applicable)	50.7	60.9	65.0	

Statistical analyses

Statistical analysis title	Analysis of ACR 20 at Week 24

Statistical analysis description:

The primary hypothesis of this study is that etanercept plus methotrexate therapy and etanercept

monotherapy are more efficacious than methotrexate monotherapy as measured by the percentage of participants with psoriatic arthritis achieving ACR 20 response at week 24.

Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.005 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	13.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.8
upper limit	22

Notes:

[1] - Adjusted p-value was obtained by applying a Bonferroni-based testing procedure for multiplicity adjustment to control the family-wise, two-sided type one error rate at 0.05.
[2] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.

Statistical analysis title	Analysis of ACR 20 at Week 24

Statistical analysis description:

The primary hypothesis of this study is that etanercept plus methotrexate therapy and etanercept monotherapy are more efficacious than methotrexate monotherapy as measured by the percentage of participants with psoriatic arthritis achieving ACR 20 response at week 24.

Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	568
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.029 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	9.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	17.3

Notes:

[3] - Adjusted p-value was obtained by applying a Bonferroni-based testing procedure for multiplicity adjustment to control the family-wise, two-sided type one error rate at 0.05.
[4] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.

Secondary: Percentage of Participants With a Minimal Disease Activity (MDA) Response at Week 24

End point title	Percentage of Participants With a Minimal Disease Activity (MDA) Response at Week 24

End point description:

Minimal Disease Activity (MDA) is a measure of low disease activity specific for psoriatic arthritis (PsA) that incorporates measures of joint and entheseal inflammation, skin disease, patient reported outcomes and functional disability to assess disease activity. Participants were classified as achieving MDA if they fulfilled 5 of the following 7 outcome measures:
- Tender joint count (0-68) ≤ 1
- Swollen joint count (0-66) ≤ 1
- Body surface area (BSA) involvement with psoriasis (0% to 100%) ≤ 3%

- Patient global assessment of joint pain VAS (0-100) ≤ 15
- Patient global assessment of disease activity VAS (0-100) ≤ 20
- HAQ-DI (0-3) ≤ 0.5
- Spondyloarthritis Research Consortium of Canada (SPARCC) enthesitis index (18 sites assessed for enthesitis with an overall score of 0 - 16) ≤ 1
Participants with missing data were counted as non-responders.

End point type	Secondary

End point timeframe:

Week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: percentage of participants				
number (not applicable)	22.9	35.9	35.7	

Statistical analyses

Statistical analysis title	Analysis of MDA at Week 24

Statistical analysis description:

The secondary hypothesis of this study was that etanercept plus methotrexate therapy and etanercept monotherapy are more efficacious than methotrexate monotherapy as measured by the percentage of participants with PsA achieving MDA response at week 24.

Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.005 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	12.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.9
upper limit	19.6

Notes:

[5] - Adjusted p-value was obtained by applying a Bonferroni-based testing procedure for multiplicity adjustment to control the family-wise, two-sided type one error rate at 0.05.
[6] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.

Statistical analysis title	Analysis of MDA at Week 24

Statistical analysis description:

The secondary hypothesis of this study was that etanercept plus methotrexate therapy and etanercept monotherapy are more efficacious than methotrexate monotherapy as measured by the percentage of participants with PsA achieving MDA response at week 24.

Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy

Number of subjects included in analysis	568
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.005 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	11.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.2
upper limit	18.9

Notes:

[7] - Adjusted p-value was obtained by applying a Bonferroni-based testing procedure for multiplicity adjustment to control the family-wise, two-sided type one error rate at 0.05.
[8] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.

Secondary: Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response Over Time

End point title	Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response Over Time

End point description:

A positive ACR20 response is defined if the following 3 criteria for improvement from baseline were met:
- ≥ 20% improvement in 68 tender joint count;
- ≥ 20% improvement in 66 swollen joint count; and
- ≥ 20% improvement in at least 3 of the 5 following parameters:
  - Patient's assessment of joint pain (measured on a 100 mm visual analog scale [VAS]);
  - Patient's global assessment of disease activity (measured on a 100 mm VAS);
  - Physician's global assessment of disease activity (measured on a 100 mm VAS);
  - Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index [HAQ-DI]);
  - C-reactive protein.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: percentage of participants				
number (not applicable)				
Week 4 (N = 280, 280, 276)	25.0	44.3	46.4	
Week 8 (N = 271, 274, 268)	46.5	60.2	60.8	
Week 12 (N = 267, 267, 263)	46.8	65.5	70.3	
Week 16 (N = 253, 256, 248)	58.5	69.5	71.8	
Week 24 (N = 253, 256, 256)	56.9	67.6	71.9	
Week 36 (N = 243, 248, 240)	66.3	77.0	74.2	
Week 48 (N = 229, 237, 230)	70.7	83.1	80.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With an American College of Rheumatology 50% (ACR50) Response Over Time

End point title	Percentage of Participants With an American College of Rheumatology 50% (ACR50) Response Over Time

End point description:

A positive ACR50 response is defined if the following 3 criteria for improvement from baseline were met:
- ≥ 50% improvement in 68 tender joint count;
- ≥ 50% improvement in 66 swollen joint count; and
- ≥ 50% improvement in at least 3 of the 5 following parameters:
  - Patient's assessment of joint pain (measured on a 100 mm visual analog scale [VAS]);
  - Patient's global assessment of disease activity (measured on a 100 mm VAS);
  - Physician's global assessment of disease activity (measured on a 100 mm VAS);
  - Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index [HAQ-DI]);
  - C-reactive protein.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: percentage of participants				
number (not applicable)				
Week 4 (N = 281, 279, 276)	6.0	16.5	18.8	
Week 8 (N = 272, 275, 269)	15.1	31.3	30.1	
Week 12 (N = 267, 267, 263)	16.9	40.4	39.2	
Week 16 (N = 253, 256, 251)	29.2	43.8	43.4	
Week 24 (N = 252, 257, 256)	30.6	44.4	45.7	
Week 36 (N = 244, 246, 241)	41.8	57.3	56.0	
Week 48 (N = 229, 238, 231)	49.3	63.0	60.2	

Statistical analyses

Statistical analysis title	Analysis of ACR50 Response at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	14.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	6.4
upper limit	23

Notes:

[9] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of ACR50 Response at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	568
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	11.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.4
upper limit	20.2

Notes:

[10] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.
P-value is unadjusted and considered descriptive.

Secondary: Percentage of Participants With an American College of Rheumatology 70% (ACR70) Response Over Time

End point title	Percentage of Participants With an American College of Rheumatology 70% (ACR70) Response Over Time

End point description:

A positive ACR70 response is defined if the following 3 criteria for improvement from baseline were met:
- ≥ 70% improvement in 68 tender joint count;
- ≥ 70% improvement in 66 swollen joint count; and
- ≥ 70% improvement in at least 3 of the 5 following parameters:
  - Patient's assessment of joint pain (measured on a 100 mm visual analog scale [VAS]);
  - Patient's global assessment of disease activity (measured on a 100 mm VAS);
  - Physician's global assessment of disease activity (measured on a 100 mm VAS);
  - Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index [HAQ-DI]);
  - C-reactive protein.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: percentage of participants				
number (not applicable)				
Week 4 (N = 281, 280, 276)	2.8	3.6	5.1	
Week 8 (N = 272, 277, 269)	4.4	15.2	14.5	
Week 12 (N = 267, 268, 264)	5.2	24.3	22.3	
Week 16 (N = 252, 256, 251)	10.7	24.2	25.5	
Week 24 (N = 253, 257, 256)	13.8	29.2	27.7	
Week 36 (N = 245, 247, 242)	19.6	38.5	33.5	
Week 48 (N = 230, 237, 232)	25.2	39.7	39.7	

Statistical analyses

Statistical analysis title	Analysis of ACR70 Response at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	13.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.5
upper limit	20.4

Notes:

[11] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of ACR70 Response at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	568
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [12]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	13.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.7
upper limit	20.7

Notes:

[12] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.
P-value is unadjusted and considered descriptive.

Secondary: Change From Baseline in Tender Joint Count Over Time

End point title	Change From Baseline in Tender Joint Count Over Time

End point description:

The tender joint count is an assessment of the pain and/or tenderness of 68 joints using a 0 to 1 point scale (0 = none, 1 = present). The total tender joint count is calculated by summing the number of joints with present tenderness.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: tender joints				
arithmetic mean (standard error)				
Week 4 (N = 280, 279, 277)	-5.7 (± 0.6)	-6.4 (± 0.6)	-7.4 (± 0.6)	
Week 8 (N = 271, 276, 269)	-7.8 (± 0.7)	-8.9 (± 0.6)	-9.4 (± 0.7)	
Week 12 (N = 266, 267, 264)	-9.7 (± 0.7)	-9.8 (± 0.7)	-10.8 (± 0.7)	
Week 16 (N = 253, 257, 251)	-10.0 (± 0.7)	-10.9 (± 0.7)	-11.9 (± 0.8)	
Week 24 (N = 253, 257, 257)	-10.8 (± 0.8)	-10.9 (± 0.8)	-11.0 (± 0.9)	
Week 36 (N = 245, 248, 243)	-13.5 (± 0.8)	-12.7 (± 0.8)	-12.9 (± 0.9)	
Week 48 (N = 230, 239, 232)	-14.5 (± 0.8)	-13.9 (± 0.8)	-12.9 (± 0.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Swollen Joint Count Over Time

End point title	Change From Baseline in Swollen Joint Count Over Time

End point description:

The swollen joint count is an assessment of the swelling of 66 joints using a 0 to 1 point scale (0 = none, 1 = present). The total swollen joint count is calculated by summing the number of joints with present swelling.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: swollen joints				
arithmetic mean (standard error)				
Week 4 (N = 280, 279, 277)	-4.1 (± 0.4)	-4.8 (± 0.3)	-4.7 (± 0.4)	
Week 8 (N = 271, 276, 269)	-5.4 (± 0.5)	-6.2 (± 0.4)	-6.5 (± 0.4)	
Week 12 (N = 266, 267, 264)	-6.6 (± 0.5)	-6.8 (± 0.4)	-7.2 (± 0.4)	
Week 16 (N = 253, 257, 251)	-7.0 (± 0.5)	-7.3 (± 0.4)	-7.8 (± 0.4)	
Week 24 (N = 253, 257, 257)	-7.0 (± 0.5)	-7.6 (± 0.5)	-7.7 (± 0.5)	
Week 36 (N = 245, 248, 243)	-9.2 (± 0.5)	-9.0 (± 0.5)	-8.4 (± 0.5)	
Week 48 (N = 230, 239, 232)	-9.6 (± 0.5)	-9.2 (± 0.5)	-8.7 (± 0.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physician Global Assessment of Disease Activity Over Time

End point title	Change From Baseline in Physician Global Assessment of Disease Activity Over Time

End point description:

A global assessment of the participant’s arthritis assessed by the physician on a 100 mm visual analog scale (VAS) where 0 mm = No activity at all and 100 mm = Worst activity imaginable.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: mm				
arithmetic mean (standard error)				
Week 4 (N = 278, 278, 277)	-16.8 (± 1.2)	-23.1 (± 1.2)	-22.8 (± 1.3)	
Week 8 (N = 271, 277, 269)	-25.0 (± 1.4)	-29.7 (± 1.4)	-30.4 (± 1.4)	
Week 12 (N = 266, 267, 264)	-26.8 (± 1.6)	-32.7 (± 1.6)	-33.9 (± 1.3)	
Week 16 (N = 251, 257, 252)	-30.3 (± 1.7)	-34.9 (± 1.5)	-36.2 (± 1.4)	
Week 24 (N = 250, 257, 257)	-29.6 (± 1.8)	-35.7 (± 1.7)	-35.8 (± 1.6)	
Week 36 (N = 241, 246, 241)	-37.1 (± 1.7)	-42.8 (± 1.5)	-39.9 (± 1.5)	
Week 48 (N = 229, 239, 232)	-41.4 (± 1.5)	-43.8 (± 1.4)	-41.5 (± 1.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient Global Assessment of Disease Activity Over Time

End point title	Change From Baseline in Patient Global Assessment of Disease Activity Over Time

End point description:

A global assessment of the participant's arthritis, assessed by the participant on a 100 mm VAS where 0 mm = No arthritis activity at all and 100 mm = Worst arthritis activity imaginable.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: mm				
arithmetic mean (standard error)				
Week 4 (N = 280, 281, 277)	-11.0 (± 1.5)	-21.9 (± 1.6)	-21.0 (± 1.5)	
Week 8 (N = 271, 277, 269)	-15.6 (± 1.6)	-27.3 (± 1.6)	-26.4 (± 1.6)	
Week 12 (N = 266, 268, 264)	-18.6 (± 1.6)	-29.9 (± 1.7)	-28.0 (± 1.7)	
Week 16 (N = 252, 257, 250)	-22.7 (± 1.7)	-30.9 (± 1.7)	-29.3 (± 1.7)	
Week 24 (N = 252, 258, 257)	-23.0 (± 1.8)	-32.3 (± 1.7)	-29.6 (± 1.8)	
Week 36 (N = 243, 248, 241)	-26.0 (± 1.8)	-36.4 (± 1.8)	-32.4 (± 1.8)	
Week 48 (N = 228, 238, 232)	-28.9 (± 1.9)	-38.8 (± 1.7)	-33.3 (± 1.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient Global Assessment of Joint Pain Over Time

End point title	Change From Baseline in Patient Global Assessment of Joint Pain Over Time

End point description:

A global assessment of the severity of the participant's joint pain, assessed by the participant on a 100 mm VAS where 0 mm = No pain at all and 100 mm = Worst pain imaginable.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: mm				
arithmetic mean (standard error)				
Week 4 (N = 280, 281, 277)	-8.9 (± 1.4)	-18.4 (± 1.5)	-18.5 (± 1.6)	
Week 8 (N = 271, 277, 269)	-14.5 (± 1.5)	-23.5 (± 1.5)	-24.0 (± 1.5)	
Week 12 (N = 266, 268, 264)	-16.0 (± 1.6)	-24.1 (± 1.7)	-24.9 (± 1.6)	
Week 16 (N = 252, 257, 250)	-20.9 (± 1.7)	-25.9 (± 1.7)	-25.6 (± 1.7)	
Week 24 (N = 252, 258, 257)	-20.6 (± 1.7)	-26.4 (± 1.7)	-26.9 (± 1.7)	
Week 36 (N = 243, 248, 241)	-23.9 (± 1.7)	-31.5 (± 1.7)	-28.8 (± 1.8)	
Week 48 (N = 228, 238, 232)	-27.2 (± 1.8)	-32.5 (± 1.7)	-31.1 (± 1.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health Assessment Questionnaire- Disability Index (HAQ-DI) Over Time

End point title	Change From Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Over Time

End point description:

The Health Assessment Questionnaire - Disability Index is a patient-reported questionnaire consisting of 20 questions referring to eight domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and usual activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task are summed and averaged to provide an overall score ranging from 0 to 3, where zero represents no disability and three very severe, high-dependency disability. Negative mean changes from Baseline in the overall score indicate improvement in functional ability.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: units on a scale				
arithmetic mean (standard error)				
Week 4 (N = 280, 281, 277)	-0.188 (± 0.024)	-0.266 (± 0.024)	-0.306 (± 0.029)	
Week 8 (N = 271, 276, 269)	-0.277 (± 0.029)	-0.365 (± 0.031)	-0.403 (± 0.032)	
Week 12 (N = 266, 268, 264)	-0.310 (± 0.030)	-0.404 (± 0.029)	-0.450 (± 0.033)	
Week 16 (N = 252, 257, 250)	-0.378 (± 0.036)	-0.454 (± 0.033)	-0.483 (± 0.036)	
Week 24 (N = 252, 258, 257)	-0.412 (± 0.036)	-0.444 (± 0.035)	-0.468 (± 0.038)	

Week 36 (N = 243, 248, 241)	-0.452 (± 0.038)	-0.496 (± 0.039)	-0.548 (± 0.040)	
Week 48 (N = 228, 238, 232)	-0.526 (± 0.041)	-0.557 (± 0.038)	-0.554 (± 0.041)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in C-reactive Protein Concentration Over Time

End point title	Change From Baseline in C-reactive Protein Concentration Over Time

End point description:

C-reactive protein (CRP) is a specific measure of inflammatory activity.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: mg/L				
arithmetic mean (standard error)				
Week 4 (N = 275, 265, 256)	-0.93 (± 0.93)	-5.91 (± 1.01)	-5.49 (± 0.74)	
Week 8 (N = 270, 265, 257)	-2.31 (± 0.90)	-7.51 (± 0.94)	-5.19 (± 0.88)	
Week 12 (N = 262, 255, 247)	-3.36 (± 0.84)	-7.38 (± 0.99)	-5.71 (± 0.82)	
Week 16 (N = 248, 246, 241)	-2.81 (± 0.82)	-7.40 (± 1.03)	-5.59 (± 0.85)	
Week 24 (N = 246, 249, 247)	-2.60 (± 0.91)	-6.91 (± 1.15)	-5.82 (± 0.70)	
Week 36 (N = 236, 234, 230)	-4.16 (± 0.96)	-7.36 (± 1.13)	-5.82 (± 0.80)	
Week 48 (N = 223, 226, 219)	-4.88 (± 1.03)	-7.45 (± 1.10)	-5.81 (± 0.95)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a American Minimal Disease Activity (MDA) Response Over Time

End point title	Percentage of Participants With a American Minimal Disease Activity (MDA) Response Over Time

End point description:

Minimal Disease Activity (MDA) is a measure of low disease activity specific for psoriatic arthritis (PsA) that incorporates measures of joint and entheseal inflammation, skin disease, patient reported outcomes and functional disability to assess disease activity. Participants were classified as achieving MDA if they fulfilled 5 of the following 7 outcome measures:
• Tender joint count (0-68) ≤ 1
• Swollen joint count (0-66) ≤ 1

• Body surface area (BSA) involvement with psoriasis (0% to 100%) ≤ 3%
• Patient global assessment of joint pain VAS (0-100) ≤ 15
• Patient global assessment of disease activity VAS (0-100) ≤ 20
• HAQ-DI (0-3) ≤ 0.5
• Spondyloarthritis Research Consortium of Canada (SPARCC) enthesitis index (18 sites assessed for enthesitis with an overall score of 0 - 16) ≤ 1

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: percentage of participants				
number (not applicable)				
Week 4 (N = 281, 280, 278)	5.7	11.1	12.6	
Week 8 (N = 271, 276, 270)	3.0	9.4	7.4	
Week 12 (N = 267, 268, 265)	11.6	29.9	29.1	
Week 24 (N = 253, 258, 258)	25.7	39.5	39.1	
Week 36 (N = 244, 248, 242)	30.3	43.5	46.7	
Week 48 (N = 229, 238, 233)	35.8	51.3	53.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Psoriatic Arthritis Disease Activity Score (PASDAS) Over Time

End point title	Change From Baseline in Psoriatic Arthritis Disease Activity Score (PASDAS) Over Time

End point description:

PASDAS is a measure of disease activity derived from the following variables:
• Physician and patient global assessment of disease activity (assessed on a 0-100 VAS)
• 68 tender joint count
• 66 swollen joint count
• Short Form-36 Questionnaire (SF-36) physical component summary (general health status on a scale from 0-100)
• Tender dactylitis count (each digit assessed for tender dactylitis; total score 0-20)
• Leeds enthesitis index (enthesitis assessed at 6 sites; total score of 0-6)
• CRP level (mg/L)
The composite score is a weighted index where higher scores indicate more severe disease.

End point type	Secondary

End point timeframe:

Baseline and weeks 12, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: units on a scale				
arithmetic mean (standard error)				
Week 12 (N = 261, 263, 261)	-1.63 (± 0.08)	-2.32 (± 0.09)	-2.37 (± 0.09)	
Week 24 (N = 246, 250, 255)	-1.98 (± 0.10)	-2.64 (± 0.10)	-2.63 (± 0.11)	
Week 36 (N = 234, 238, 232)	-2.46 (± 0.10)	-3.10 (± 0.10)	-2.95 (± 0.11)	
Week 48 (N = 226, 232, 229)	-2.70 (± 0.10)	-3.23 (± 0.09)	-3.10 (± 0.11)	

Statistical analyses

Statistical analysis title	Analysis of Change in PASDAS at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [13]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	-0.34
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[13] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Change in PASDAS at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	568
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [14]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	-0.34
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[14] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD use. P-value is unadjusted and considered descriptive

Secondary: Change From Baseline in Clinical Disease Activity Index (CDAI) Over Time

End point title	Change From Baseline in Clinical Disease Activity Index (CDAI) Over Time

End point description:

The Clinical Disease Activity Index (CDAI) is a composite index that is calculated as the sum of the following items:
- 28 tender joint count,
- 28 swollen joint count,
- Patient's Global Assessment of Disease Activity measured on a 10 cm VAS, where 0 cm = lowest disease activity and 10 cm = highest;
- Physician's Global Assessment of Disease Activity -measured on a 10 cm VAS, where 0 cm = lowest disease activity and 10 cm = highest.

The CDAI score ranges from 0-76 where lower scores indicate less disease activity.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: units on a scale				
arithmetic mean (standard error)				
Week 4 (N = 276, 277, 276)	-8.38 (± 0.62)	-10.59 (± 0.61)	-10.68 (± 0.60)	
Week 8 (N = 270, 276, 268)	-11.56 (± 0.73)	-14.13 (± 0.66)	-14.56 (± 0.65)	
Week 12 (N = 265, 266, 263)	-13.93 (± 0.74)	-15.61 (± 0.75)	-16.12 (± 0.71)	
Week 16 (N = 250, 256, 248)	-15.20 (± 0.80)	-16.49 (± 0.70)	-17.37 (± 0.76)	
Week 24 (N = 249, 257, 256)	-15.74 (± 0.85)	-17.12 (± 0.78)	-16.43 (± 0.85)	
Week 36 (N = 240, 246, 239)	-18.90 (± 0.76)	-19.79 (± 0.76)	-18.86 (± 0.79)	
Week 48 (N = 228, 238, 231)	-20.16 (± 0.80)	-20.78 (± 0.75)	-19.35 (± 0.83)	

Statistical analyses

Statistical analysis title	Analysis of Change in CDAI at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate

Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.59 [15]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.93
upper limit	1.68
Variability estimate	Standard error of the mean
Dispersion value	1.18

Notes:

[15] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Change in CDAI at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	568
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.26 [16]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.63
upper limit	0.99
Variability estimate	Standard error of the mean
Dispersion value	1.18

Notes:

[16] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD use. P-value is unadjusted and considered descriptive.

Secondary: Change From Baseline in Simplified Disease Activity Index (SDAI) Over Time

End point title	Change From Baseline in Simplified Disease Activity Index (SDAI) Over Time

End point description:

The Simplified Disease Activity Index (SDAI) is a composite index that is calculated as the sum of the following items:
- 28 tender joint count,
- 28 swollen joint count,
- Patient's Global Assessment of Disease Activity measured on a 10 cm VAS, where 0 cm = lowest disease activity and 10 cm = highest;
- Physician's Global Assessment of Disease Activity measured on a 10 cm VAS, where 0 cm = lowest disease activity and 10 cm = highest.
- CRP

The SDAI score ranges from 0 to 86 with higher scores representing worse disease.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: units on a scale				
arithmetic mean (standard error)				
Week 4 (N = 275, 273, 273)	-8.38 (± 0.62)	-11.12 (± 0.62)	-11.18 (± 0.61)	
Week 8 (N = 270, 272, 267)	-11.77 (± 0.72)	-14.92 (± 0.69)	-15.14 (± 0.66)	
Week 12 (N = 264, 264, 263)	-14.32 (± 0.75)	-16.44 (± 0.77)	-16.67 (± 0.73)	
Week 16 (N = 248, 253, 246)	-15.55 (± 0.81)	-17.25 (± 0.72)	-17.79 (± 0.78)	
Week 24 (N = 248, 253, 256)	-15.96 (± 0.86)	-17.75 (± 0.81)	-17.01 (± 0.87)	
Week 36 (N = 239, 242, 235)	-19.27 (± 0.77)	-20.50 (± 0.78)	-19.46 (± 0.82)	
Week 48 (N = 228, 234, 229)	-20.65 (± 0.81)	-21.61 (± 0.77)	-19.94 (± 0.87)	

Statistical analyses

Statistical analysis title	Analysis of Change in SDAI at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.41 [17]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.35
upper limit	1.38
Variability estimate	Standard error of the mean
Dispersion value	1.2

Notes:

[17] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive

Statistical analysis title	Analysis of Change in SDAI at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy

Number of subjects included in analysis	568
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.15 [18]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-1.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.09
upper limit	0.65
Variability estimate	Standard error of the mean
Dispersion value	1.21

Notes:

[18] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Secondary: Change From Baseline in the Disease Activity Score 28 (DAS28) Over Time

End point title	Change From Baseline in the Disease Activity Score 28 (DAS28) Over Time

End point description:

The DAS28 measures the severity of disease at a specific time and is derived from the following variables:
- 28 tender joint count
- 28 swollen joint count
- C-reactive protein (CRP)
- Patient's global assessment of disease activity, measured on a 100 mm VAS, where 0 mm = lowest disease activity and 100 mm = highest.

DAS28(CRP) scores range from 0 to approximately 10, with the upper bound dependent on the highest possible level of CRP. A DAS28 score higher than 5.1 indicates high disease activity, a DAS28 score less than 3.2 indicates low disease activity, and a DAS28 score less than 2.6 indicates clinical remission.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 8, 12, 16, 24, 36, and 48

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	284	283	
Units: units on a scale				
arithmetic mean (standard error)				
Week 4 (N = 278, 275, 273)	-0.73 (± 0.05)	-1.18 (± 0.06)	-1.21 (± 0.06)	
Week 8 (N = 270, 272, 267)	-1.05 (± 0.06)	-1.64 (± 0.07)	-1.61 (± 0.07)	
Week 12 (N = 264, 265, 263)	-1.34 (± 0.06)	-1.78 (± 0.08)	-1.80 (± 0.08)	
Week 16 (N = 250, 253, 246)	-1.47 (± 0.07)	-1.90 (± 0.08)	-1.92 (± 0.08)	
Week 24 (N = 251, 253, 256)	-1.55 (± 0.08)	-1.97 (± 0.08)	-1.86 (± 0.08)	
Week 36 (N = 242, 244, 236)	-1.88 (± 0.07)	-2.25 (± 0.08)	-2.20 (± 0.09)	
Week 48 (N = 228, 234, 229)	-2.04 (± 0.07)	-2.38 (± 0.08)	-2.23 (± 0.09)	

Statistical analyses

Statistical analysis title	Analysis of Change in DAS28 at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01 [19]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[19] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Change in DAS28 at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	568
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [20]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	-0.17
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[20] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Secondary: Change From Baseline in Health Assessment Questionnaire- Disability Index (HAQ-DI) at Week 24

End point title	Change From Baseline in Health Assessment Questionnaire-

	Disability Index (HAQ-DI) at Week 24

End point description:

The Health Assessment Questionnaire - Disability Index is a patient-reported questionnaire consisting of 20 questions referring in 8 functional areas: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and usual activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task are summed and averaged to provide an overall score ranging from 0 to 3, where zero represents no disability and three very severe, high-dependency disability. Negative mean changes from Baseline in the overall score indicate improvement in functional ability.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	252	258	257	
Units: units on a scale				
arithmetic mean (standard error)	-0.412 (± 0.036)	-0.444 (± 0.035)	-0.468 (± 0.038)	

Statistical analyses

Statistical analysis title	Analysis of Change in HAQ-DI at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	509
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34 [21]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.05

Notes:

[21] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Change in HAQ-DI at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy

Number of subjects included in analysis	510
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.67 [22]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.05

Notes:

[22] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Secondary: Change From Baseline in Medical Outcomes Health Survey Short Form 36 Items Version 2 (SF-36 v2) at Week 24

End point title	Change From Baseline in Medical Outcomes Health Survey Short Form 36 Items Version 2 (SF-36 v2) at Week 24

End point description:

The SF-36 is a health-related survey that assesses participant's quality of life and consists of 36 questions covering 8 health domains. Two summary component scores are calculated: mental component summary score (MCS) and physical component summary score (PCS). The MCS consists of social functioning, vitality, mental health, and role-emotional scales and the PCS consists of physical functioning, bodily pain, role-physical, and general health scales. Each domain is scored by summing the individual items and transforming the scores into a 0 to 100 scale with higher scores indicating better health status or functioning.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	256	257	
Units: units on a scale				
arithmetic mean (standard error)				
Physical Component Summary	5.952 (± 0.550)	7.808 (± 0.546)	8.011 (± 0.598)	
Mental Component Summary	3.259 (± 0.589)	2.835 (± 0.624)	3.321 (± 0.572)	

Statistical analyses

Statistical analysis title	Analysis of Change in PCS at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate

Number of subjects included in analysis	510
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015 [23]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	1.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	3.51
Variability estimate	Standard error of the mean
Dispersion value	0.8

Notes:

[23] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Change in PCS at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	509
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.033 [24]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	3.28
Variability estimate	Standard error of the mean
Dispersion value	0.8

Notes:

[24] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Change in MCS at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	510
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.97 [25]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.03

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	1.63
Variability estimate	Standard error of the mean
Dispersion value	0.84

Notes:

[25] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Change in MCS at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	509
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.56 [26]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.16
upper limit	1.16
Variability estimate	Standard error of the mean
Dispersion value	0.85

Notes:

[26] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Secondary: Change From Baseline in Modified Nail Psoriasis Severity Index (mNAPSI) at Week 24

End point title	Change From Baseline in Modified Nail Psoriasis Severity Index (mNAPSI) at Week 24

End point description:

The modified NAPSI scale is a grading system for nail psoriasis that incorporates the following 7 clinical features:
• pitting (scores 0-3, depending on the number of pits)
• nail plate crumbling (scores 0-3, depending on the % of nail involvement)
• onycholysis and oil drop dyschromia (scores 0-3, depending on the % of nail involvement)
• leukonychia (0 = absent, 1 = present)
• red spots in lunula (0 = absent, 1 = present)
• nail bed hyperkeratosis (0 = absent, 1 = present)
• splinter hemorrhages (0 = absent, 1 = present)
In participants with fingernails involved with psoriasis, each fingernail was scored at baseline to determine the worst fingernail (ie, the fingernail with the highest mNAPSI score). This fingernail was followed for the remainder of the study. mNAPSI scores range from 0-13 where higher scores represent worse nail disease.
The analysis includes participants with non-zero mNAPSI score at baseline and available data at week 24.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	121	115	123	
Units: units on a scale				
arithmetic mean (standard error)	-1.1 (± 0.2)	-1.5 (± 0.2)	-1.7 (± 0.2)	

Statistical analyses

Statistical analysis title	Analysis of Change in mNAPSI at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	244
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02 [27]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	-0.09
Variability estimate	Standard error of the mean
Dispersion value	0.24

Notes:

[27] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Change in mNAPSI at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1 [28]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.24

Notes:

[28] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Secondary: Percentage of Participants With Clear mNAPSI at Week 24

End point title	Percentage of Participants With Clear mNAPSI at Week 24

End point description:

The modified NAPSI scale is a grading system for nail psoriasis that incorporates the following 7 clinical features:
• pitting (scores 0-3, depending on the number of pits)
• nail plate crumbling (scores 0-3, depending on the % of nail involvement)
• onycholysis and oil drop dyschromia (scores 0-3, depending on the % of nail involvement)
• leukonychia (0 = absent, 1 = present)
• red spots in lunula (0 = absent, 1 = present)
• nail bed hyperkeratosis (0 = absent, 1 = present)
• splinter hemorrhages (0 = absent, 1 = present)
In participants with fingernails involved with psoriasis, each fingernail was scored at baseline to determine the worst fingernail (ie, with the highest mNAPSI score). This fingernail was followed for the remainder of the study. mNAPSI scores range from 0-13 where higher scores represent worse nail disease. Clear mNAPSI is defined as a score = 0.
The analysis includes participants with non-zero mNAPSI score at baseline and available data at week 24.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	121	115	123	
Units: percentage of participants				
number (not applicable)	0.0	0.0	0.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Leeds Dactylitis Index (LDI) at Week 24

End point title	Change from Baseline in Leeds Dactylitis Index (LDI) at Week 24

End point description:

The Leeds dactylitis index quantitatively measures dactylitis using the circumference of involved digits and control digits and tenderness of involved digits. Digits affected by dactylitis are defined as those with a 10% difference in the ratio of circumference of the affected digit to the contralateral digit. The control digit is either the contralateral digit (digit on opposite hand or foot), or if the contralateral digit is also affected, values from a standard reference table. Tenderness of affected digits is assessed on a scale from 0 [none] to 3 [worst]. The ratio of circumference between an affected digit and the control digit is multiplied by the tenderness score for the affected digit. The results from each involved digit are summed to provide the final LDI. A higher LDI indicates worse dactylitis.
The analysis includes participants with non-zero LDI score at baseline and available data at week 24.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	89	87	
Units: units on a scale				
arithmetic mean (standard error)	-128.80 (± 26.76)	-119.09 (± 20.66)	-110.15 (± 22.70)	

Statistical analyses

Statistical analysis title	Analysis of Change in LDI at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.68 [29]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	13.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.52
upper limit	79.36
Variability estimate	Standard error of the mean
Dispersion value	33.23

Notes:

[29] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Change in LDI at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.85 [30]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	6.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.75
upper limit	71.42
Variability estimate	Standard error of the mean
Dispersion value	33.05

Notes:

[30] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Secondary: Percentage of Participants With Clear LDI at Week 24

End point title	Percentage of Participants With Clear LDI at Week 24

End point description:

The Leeds dactylitis index quantitatively measures dactylitis using the circumference of involved digits and control digits and tenderness of involved digits. Digits affected by dactylitis are defined as those with a 10% difference in the ratio of circumference of the affected digit to the contralateral digit. The control digit is either the contralateral digit (digit on opposite hand or foot), or if the contralateral digit is also affected, values from a standard reference table. Tenderness of affected digits is assessed on a scale from 0 [none] to 3 [worst]. The ratio of circumference between an affected digit and the control digit is multiplied by the tenderness score for the affected digit. The results from each involved digit are summed to provide the final LDI. A higher LDI indicates worse dactylitis. Clear LDI is defined as a score = 0.
The analysis includes participants with non-zero LDI score at baseline and available data at week 24.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	89	87	
Units: percentage of participants				
number (not applicable)	65.2	76.4	79.3	

Statistical analyses

Statistical analysis title	Analysis of Clear LDI at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.057 [31]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	12.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	26.2

Notes:

[31] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Clear LDI at Week 24

Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12 [32]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	10.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	24.4

Notes:

[32] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.
P-value is unadjusted and considered descriptive.

Secondary: Change from Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index at Week 24

End point title	Change from Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index at Week 24

End point description:

The SPARCC enthesitis index assesses enthesitis at 18 sites for palpitation with a resultant total score of 0 to 16 (for scoring purposes, the inferior patella and tibial tuberosity are considered 1 site because of their anatomical proximity). Tenderness at each site is quantified on a dichotomous basis (0 = non-tender, 1 = tender). Entheses assessed are medial epicondyle (left and right), lateral epicondyle (left and right), supraspinatus insertion into greater tuberosity of humerus (left and right), greater trochanter (left and right), quadriceps insertion into superior border of patella (left and right), patellar ligament insertion into inferior pole of patella or tibial tubercle (left and right), Achilles tendon insertion into calcaneum (left and right), plantar fascia insertion into calcaneum (left and right). A higher count represents greater enthesitis burden.
The analysis includes participants with non-zero SPARCC enthesitis index at baseline and available data at week 24.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	167	173	179	
Units: units on a scale				
arithmetic mean (standard error)	-3.1 (± 0.3)	-3.0 (± 0.3)	-2.9 (± 0.3)	

Statistical analyses

Statistical analysis title	Analysis of Change in SPARCC Enthesitis at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate

Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7 [33]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	0.98
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[33] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Change in SPARCC Enthesitis at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	340
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.93 [34]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.86
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[34] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Secondary: Percentage of Participants With Clear SPARCC Enthesitis Index Score at Week 24

End point title	Percentage of Participants With Clear SPARCC Enthesitis Index Score at Week 24

End point description:

The SPARCC enthesitis index assesses enthesitis at 18 sites with a resultant total score of 0 to 16 (for scoring purposes, the inferior patella and tibial tuberosity are considered 1 site due to their anatomical proximity). Tenderness at each site is scored as either 0 (non-tender) or 1 (tender). Entheses assessed are medial epicondyle, lateral epicondyle, supraspinatus insertion into greater tuberosity of humerus, greater trochanter, quadriceps insertion into superior border of patella, patellar ligament insertion into inferior pole of patella or tibial tubercle, Achilles tendon insertion into calcaneum, plantar fascia insertion into calcaneum.
A higher count represents greater enthesitis burden. Clear SPARCC enthesitis is defined as a score = 0. The analysis includes participants with non-zero SPARCC enthesitis index at baseline and available data at week 24.

End point type	Secondary

End point timeframe:
Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	167	173	179	
Units: percentage of participants				
number (not applicable)	43.1	52.6	47.8	

Statistical analyses

Statistical analysis title	Analysis of Clear SPARCC Enthesitis at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.55 [35]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.3
upper limit	13.7

Notes:
[35] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Clear SPARCC Enthesitis at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	340
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.11 [36]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	8.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	19.4

Notes:

[36] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.
P-value is unadjusted and considered descriptive.

Secondary: Percent Improvement from Baseline in the Percentage of Body Surface Area (BSA) Involved in Psoriasis at Week 24

End point title	Percent Improvement from Baseline in the Percentage of Body Surface Area (BSA) Involved in Psoriasis at Week 24

End point description:

The physician's assessment of the percentage of the participant's total body surface area involved with psoriasis. Percent improvement from baseline = (Baseline Value – Post-baseline Value) / Baseline * 100
The analysis includes participants with ≥ 3% body surface area (BSA) psoriasis involvement at baseline and available data at week 24.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	179	166	163	
Units: percent change				
arithmetic mean (standard error)	66.12 (± 2.76)	69.80 (± 2.73)	75.53 (± 3.71)	

Statistical analyses

Statistical analysis title	Analysis of Change in BSA Involvement at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.031 [37]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	9.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	17.87
Variability estimate	Standard error of the mean
Dispersion value	4.33

Notes:

[37] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of Change in BSA Involvement at Week 24
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy

Number of subjects included in analysis	345
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.49 [38]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	3.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.49
upper limit	11.54
Variability estimate	Standard error of the mean
Dispersion value	4.33

Notes:

[38] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or >30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Secondary: Percent Improvement from Baseline in the Percentage of Body Surface Area (BSA) Involved in Psoriasis by Baseline BSA Involvement Subgroups

End point title	Percent Improvement from Baseline in the Percentage of Body Surface Area (BSA) Involved in Psoriasis by Baseline BSA Involvement Subgroups

End point description:

The physician's assessment of the percentage of the participant's total body surface area involved with psoriasis. Percent improvement from baseline = (Baseline Value – Post-baseline Value) / Baseline * 100

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	254	259	259	
Units: percent change				
arithmetic mean (standard error)				
< 3% BSA involvement (N = 75, 93, 96)	-24.49 (± 46.71)	-92.18 (± 108.54)	17.66 (± 51.97)	
≥ 3% to < 10% BSA involvement (N = 87, 75, 77)	66.61 (± 4.18)	64.42 (± 4.43)	68.76 (± 7.26)	
≥ 10% BSA involvement (N = 92, 91, 86)	65.66 (± 3.66)	74.23 (± 3.32)	81.61 (± 2.55)	

Statistical analyses

Statistical analysis title	Analysis of BSA Improvement in BSA ≥ 10% Subgroup

Statistical analysis description:

Analysis of percent improvement from baseline in the percentage of BSA involved in psoriasis in the subgroup of participants with ≥ 10% BSA involvement at baseline.

Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	513
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [39]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	15.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.99
upper limit	24.9
Variability estimate	Standard error of the mean
Dispersion value	4.55

Notes:

[39] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of BSA Improvement in BSA ≥ 10% Subgroup

Statistical analysis description:

Analysis of percent improvement from baseline in the percentage of BSA involved in psoriasis in the subgroup of participants with ≥ 10% BSA involvement at baseline.

Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	513
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12 [40]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	6.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.89
upper limit	15.83
Variability estimate	Standard error of the mean
Dispersion value	4.5

Notes:

[40] - ANCOVA model adjusted for baseline BMI status (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD use.
P-value is unadjusted and considered descriptive.

Secondary: Static Physician Global Assessment (sPGA) at Week 24

End point title	Static Physician Global Assessment (sPGA) at Week 24

End point description:

The static Physician Global Assessment of psoriasis (sPGA) evaluates the physician's global assessment of the participant's psoriasis based on severity of induration, scaling, and erythema. The sPGA is assessed on a scale from 0 to 5:
0 = clear (no evidence of plaque elevation, erythema or scaling)
1 = almost clear (minimal plaque elevation, erythema or scaling)
2 = mild (mild plaque elevation or scaling, light red coloration)
3 = moderate (moderate plaque elevation, scaling, light red coloration)
4 = marked (marked plaque elevation, thick, non-tenacious scale predominates, bright red coloration)
5 = severe (severe plaque elevation, very thick tenacious scaling, dusky to deep red coloration).

The analysis includes participants with ≥ 3% body surface area (BSA) psoriasis involvement at baseline and available sPGA data at week 24.

End point type	Secondary

End point timeframe:

Week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	178	166	161	
Units: participants				
0 (clear)	38	36	63	
1 (almost clear)	80	84	62	
2 (mild)	34	28	25	
3 (moderate)	22	12	10	
4 (marked)	3	6	1	
5 (severe)	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Static Physician Global Assessment (sPGA) at Week 24 by Baseline BSA Involvement Subgroups

End point title	Static Physician Global Assessment (sPGA) at Week 24 by Baseline BSA Involvement Subgroups

End point description:

The static Physician Global Assessment of psoriasis (sPGA) evaluates the physician's global assessment of the participant's psoriasis based on severity of induration, scaling, and erythema. The sPGA is assessed on a scale from 0 to 5:
0 = clear (no evidence of plaque elevation, erythema or scaling)
1 = almost clear (minimal plaque elevation, erythema or scaling)
2 = mild (mild plaque elevation or scaling, light red coloration)
3 = moderate (moderate plaque elevation, scaling, light red coloration)
4 = marked (marked plaque elevation, thick, non-tenacious scale predominates, bright red coloration)
5 = severe (severe plaque elevation, very thick tenacious scaling, dusky to deep red coloration).

End point type	Secondary

End point timeframe:

Week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	258	257	
Units: participants				
< 3% BSA involvement at baseline: Total	75	92	96	

< 3% BSA involvement: 0 (clear)	26	29	52	
< 3% BSA involvement: 1 (almost clear)	28	37	32	
< 3% BSA involvement: 2 (mild)	15	19	9	
< 3% BSA involvement: 3 (moderate)	4	6	3	
< 3% BSA involvement: 4 (marked)	2	1	0	
< 3% BSA involvement: 5 (severe)	0	0	0	
≥ 3% to < 10% BSA involvement at baseline: Total	87	75	76	
≥ 3% to < 10% BSA involvement: 0 (clear)	23	16	35	
≥ 3% to < 10% BSA involvement: 1 (almost clear)	41	32	23	
≥ 3% to < 10% BSA involvement: 2 (mild)	13	18	12	
≥ 3% to < 10% BSA involvement: 3 (moderate)	10	7	5	
≥ 3% to < 10% BSA involvement: 4 (marked)	0	2	1	
≥ 3% to < 10% BSA involvement: 5 (severe)	0	0	0	
≥ 10% BSA involvement at baseline: Total	91	91	85	
≥ 10% BSA involvement at baseline: 0 (clear)	15	20	28	
≥ 10% BSA involvement: 1 (almost clear)	39	52	39	
≥ 10% BSA involvement at baseline: 2 (mild)	21	10	13	
≥ 10% BSA involvement at baseline: 3 (moderate)	12	5	5	
≥ 10% BSA involvement at baseline: 4 (marked)	3	4	0	
≥ 10% BSA involvement at baseline: 5 (severe)	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Static Physician Global Assessment (sPGA) Score at Week 24

End point title	Mean Static Physician Global Assessment (sPGA) Score at Week 24

End point description:

The static Physician Global Assessment of psoriasis (sPGA) evaluates the physician's global assessment of the participant's psoriasis based on severity of induration, scaling, and erythema. The sPGA is assessed on a scale from 0 to 5:
0 = clear (no evidence of plaque elevation, erythema or scaling)
1 = almost clear (minimal plaque elevation, erythema or scaling)
2 = mild (mild plaque elevation or scaling, light red coloration)
3 = moderate (moderate plaque elevation, scaling, light red coloration)
4 = marked (marked plaque elevation, thick, non-tenacious scale predominates, bright red coloration)
5 = severe (severe plaque elevation, very thick tenacious scaling, dusky to deep red coloration).
The analysis includes participants with ≥ 3% body surface area (BSA) psoriasis involvement at baseline and available sPGA data at week 24.

End point type	Secondary

End point timeframe:
Week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	178	166	161	
Units: units on a scale				
arithmetic mean (standard error)	1.3 (± 0.1)	1.2 (± 0.1)	0.9 (± 0.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Static Physician Global Assessment (sPGA) Score at Week 24 by Baseline BSA Involvement Subgroups

End point title	Mean Static Physician Global Assessment (sPGA) Score at Week 24 by Baseline BSA Involvement Subgroups

End point description:

The static Physician Global Assessment of psoriasis (sPGA) evaluates the physician's global assessment of the participant's psoriasis based on severity of induration, scaling, and erythema. The sPGA is assessed on a scale from 0 to 5:
0 = clear (no evidence of plaque elevation, erythema or scaling)
1 = almost clear (minimal plaque elevation, erythema or scaling)
2 = mild (mild plaque elevation or scaling, light red coloration)
3 = moderate (moderate plaque elevation, scaling, light red coloration)
4 = marked (marked plaque elevation, thick, non-tenacious scale predominates, bright red coloration)
5 = severe (severe plaque elevation, very thick tenacious scaling, dusky to deep red coloration).

End point type	Secondary

End point timeframe:
Week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	258	257	
Units: units on a scale				
arithmetic mean (standard error)				
< 3% BSA involvement (N = 75, 92, 96)	1.0 (± 0.1)	1.1 (± 0.1)	0.6 (± 0.1)	
≥ 3% to < 10% BSA involvement (N = 87, 75, 76)	1.1 (± 0.1)	1.3 (± 0.1)	0.9 (± 0.1)	
≥ 10% BSA involvement (N = 91, 91, 85)	1.5 (± 0.1)	1.1 (± 0.1)	0.9 (± 0.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With an sPGA Score of 0 (Clear) or 1 (Almost Clear) at Week 24

End point title	Percentage of Participants With an sPGA Score of 0 (Clear) or 1 (Almost Clear) at Week 24

End point description:

The static Physician Global Assessment of psoriasis (sPGA) evaluates the physician's global assessment of the participant's psoriasis based on severity of induration, scaling, and erythema. The sPGA is assessed on a scale from 0 to 5:
0 = clear (no evidence of plaque elevation, erythema or scaling)
1 = almost clear (minimal plaque elevation, erythema or scaling)
2 = mild (mild plaque elevation or scaling, light red coloration)
3 = moderate (moderate plaque elevation, scaling, light red coloration)
4 = marked (marked plaque elevation, thick, non-tenacious scale predominates, bright red coloration)
5 = severe (severe plaque elevation, very thick tenacious scaling, dusky to deep red coloration).
The analysis included participants with ≥ 3% body surface area (BSA) psoriasis involvement at baseline and available sPGA data at week 24.

End point type	Secondary

End point timeframe:

Week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	178	166	161	
Units: percentage of participants				
number (not applicable)	66.3	72.3	77.6	

Statistical analyses

Statistical analysis title	Analysis of sPGA Clear or Almost Clear
Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	339
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019 [41]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	11.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	20.8

Notes:

[41] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of sPGA Clear or Almost Clear
Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4 [42]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	14

Notes:

[42] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.
P-value is unadjusted and considered descriptive.

Secondary: Percentage of Participants With an sPGA Score of 0 (Clear) or 1 (Almost Clear) at Week 24 by Baseline BSA Involvement Subgroups

End point title	Percentage of Participants With an sPGA Score of 0 (Clear) or 1 (Almost Clear) at Week 24 by Baseline BSA Involvement Subgroups

End point description:

The static Physician Global Assessment of psoriasis (sPGA) evaluates the physician's global assessment of the participant's psoriasis based on severity of induration, scaling, and erythema. The sPGA is assessed on a scale from 0 to 5:
0 = clear (no evidence of plaque elevation, erythema or scaling)
1 = almost clear (minimal plaque elevation, erythema or scaling)
2 = mild (mild plaque elevation or scaling, light red coloration)
3 = moderate (moderate plaque elevation, scaling, light red coloration)
4 = marked (marked plaque elevation, thick, non-tenacious scale predominates, bright red coloration)
5 = severe (severe plaque elevation, very thick tenacious scaling, dusky to deep red coloration).

End point type	Secondary

End point timeframe:

Week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	258	257	
Units: percentage of participants				
number (not applicable)				
< 3% BSA involvement (N = 75, 92, 96)	72.0	71.7	87.5	
≥ 3% to < 10% BSA involvement (N = 87, 75, 76)	73.6	64.0	76.3	
≥ 10% BSA involvement (N = 91, 91, 85)	59.3	79.1	78.8	

Statistical analyses

Statistical analysis title	Analysis of sPGA 0 or 1 in BSA ≥ 10% Subgroup

Statistical analysis description:

Analysis of percentage of participants with an sPGA of 0 or 1 at Week 24 in participants with baseline BSA involvement with psoriasis ≥ 10%.

Comparison groups	Methotrexate Monotherapy v Etanercept + Methotrexate
Number of subjects included in analysis	510
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [43]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	20.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.8
upper limit	33.3

Notes:

[43] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.
P-value is unadjusted and considered descriptive.

Statistical analysis title	Analysis of sPGA 0 or 1 in BSA ≥ 10% Subgroup

Statistical analysis description:

Analysis of percentage of participants with an sPGA of 0 or 1 at Week 24 in participants with baseline BSA involvement with psoriasis ≥ 10%.

Comparison groups	Methotrexate Monotherapy v Etanercept Monotherapy
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012 [44]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	17.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	4
upper limit	30.2

Notes:

[44] - Cochran-Mantel-Haenszel test with baseline body mass index (≤ 30 kg/m² or > 30 kg/m²) and prior non-biologic DMARD treatment as stratification factors.
P-value is unadjusted and considered descriptive.

Secondary: Percentage of Participants With at Least a 1 Grade Improvement in sPGA From Baseline at Week 24

End point title	Percentage of Participants With at Least a 1 Grade Improvement in sPGA From Baseline at Week 24

End point description:

The static Physician Global Assessment of psoriasis (sPGA) evaluates the physician's global assessment of the participant's psoriasis based on severity of induration, scaling, and erythema. The sPGA is assessed on a scale from 0 to 5:
0 = clear (no evidence of plaque elevation, erythema or scaling)
1 = almost clear (minimal plaque elevation, erythema or scaling)
2 = mild (mild plaque elevation or scaling, light red coloration)
3 = moderate (moderate plaque elevation, scaling, light red coloration)
4 = marked (marked plaque elevation, thick, non-tenacious scale predominates, bright red coloration)
5 = severe (severe plaque elevation, very thick tenacious scaling, dusky to deep red coloration).
The analysis includes participants with ≥ 3% body surface area (BSA) psoriasis involvement at baseline and available sPGA data at week 24.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	177	166	161	
Units: percentage of participants				
number (not applicable)	29.9	28.9	18.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With at Least a 1 Grade Improvement in sPGA From Baseline at Week 24 by Baseline BSA Involvement Subgroups

End point title	Percentage of Participants With at Least a 1 Grade Improvement in sPGA From Baseline at Week 24 by Baseline BSA Involvement Subgroups

End point description:

The static Physician Global Assessment of psoriasis (sPGA) evaluates the physician's global assessment of the participant's psoriasis based on severity of induration, scaling, and erythema. The sPGA is assessed on a scale from 0 to 5:
0 = clear (no evidence of plaque elevation, erythema or scaling)
1 = almost clear (minimal plaque elevation, erythema or scaling)
2 = mild (mild plaque elevation or scaling, light red coloration)
3 = moderate (moderate plaque elevation, scaling, light red coloration)
4 = marked (marked plaque elevation, thick, non-tenacious scale predominates, bright red coloration)
5 = severe (severe plaque elevation, very thick tenacious scaling, dusky to deep red coloration).

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	250	258	257	
Units: percentage of participants				
number (not applicable)				
< 3% BSA involvement (N = 73, 92, 96)	37.0	44.6	43.8	
≥ 3% to < 10% BSA involvement (N = 86, 75, 76)	27.9	38.7	21.1	
≥ 10% BSA involvement (N = 91, 91, 85)	31.9	20.9	15.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With at Least a 2 Grade Improvement in sPGA From Baseline at Week 24

End point title	Percentage of Participants With at Least a 2 Grade Improvement in sPGA From Baseline at Week 24

End point description:

The static Physician Global Assessment of psoriasis (sPGA) evaluates the physician's global assessment of the participant's psoriasis based on severity of induration, scaling, and erythema. The sPGA is assessed on a scale from 0 to 5:
0 = clear (no evidence of plaque elevation, erythema or scaling)
1 = almost clear (minimal plaque elevation, erythema or scaling)
2 = mild (mild plaque elevation or scaling, light red coloration)
3 = moderate (moderate plaque elevation, scaling, light red coloration)
4 = marked (marked plaque elevation, thick, non-tenacious scale predominates, bright red coloration)
5 = severe (severe plaque elevation, very thick tenacious scaling, dusky to deep red coloration).
The analysis includes participants with ≥ 3% body surface area (BSA) psoriasis involvement at baseline and available sPGA data at week 24.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	177	166	161	
Units: percentage of participants				
number (not applicable)	30.5	28.9	35.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With at Least a 2 Grade Improvement in

sPGA From Baseline at Week 24 by Baseline BSA Involvement Subgroups

End point title	Percentage of Participants With at Least a 2 Grade Improvement in sPGA From Baseline at Week 24 by Baseline BSA Involvement Subgroups

End point description:

The static Physician Global Assessment of psoriasis (sPGA) evaluates the physician's global assessment of the participant's psoriasis based on severity of induration, scaling, and erythema. The sPGA is assessed on a scale from 0 to 5:
0 = clear (no evidence of plaque elevation, erythema or scaling)
1 = almost clear (minimal plaque elevation, erythema or scaling)
2 = mild (mild plaque elevation or scaling, light red coloration)
3 = moderate (moderate plaque elevation, scaling, light red coloration)
4 = marked (marked plaque elevation, thick, non-tenacious scale predominates, bright red coloration)
5 = severe (severe plaque elevation, very thick tenacious scaling, dusky to deep red coloration).

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	250	258	257	
Units: percentage of participants				
number (not applicable)				
< 3% BSA involvement (N = 73, 92, 96)	15.1	20.7	30.2	
≥ 3% to < 10% BSA involvement (N = 86, 75, 76)	34.9	25.3	32.9	
≥ 10% BSA involvement (N = 91, 91, 85)	26.4	31.9	37.6	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

48-week treatment period plus 30-day safety follow-up

Adverse event reporting additional description:

Two participants randomized to the Etanercept Monotherapy arm also received methotrexate in error, so are counted in the Etanercept + Methotrexate group for safety.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Methotrexate Monotherapy

Reporting group description:

Participants received oral methotrexate 20 mg weekly plus placebo to etanercept subcutaneous injection once a week for 48 weeks.

Reporting group title	Etanercept Monotherapy

Reporting group description:

Participants received etanercept 50 mg weekly by subcutaneous injection plus oral placebo to methotrexate for 48 weeks.

Reporting group title	Etanercept + Methotrexate

Reporting group description:

Participants received etanercept 50 mg a week by subcutaneous injection and oral methotrexate 20 mg a week for 48 weeks.

Serious adverse events	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 282 (5.67%)	19 / 282 (6.74%)	17 / 284 (5.99%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer stage II			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Hodgkin's lymphoma			

subjects affected / exposed	1 / 282 (0.35%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer metastatic			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid neoplasm			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 282 (0.35%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Spinal fusion surgery			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	2 / 284 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			

subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 282 (1.06%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 282 (0.71%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac failure congestive			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachyarrhythmia			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	1 / 282 (0.35%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	1 / 282 (0.35%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 282 (0.00%)	2 / 282 (0.71%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastric ulcer			
subjects affected / exposed	1 / 282 (0.35%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 282 (0.35%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 282 (0.35%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	1 / 282 (0.35%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Psoriasis			
subjects affected / exposed	1 / 282 (0.35%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebral foraminal stenosis			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute pulmonary histoplasmosis			
subjects affected / exposed	1 / 282 (0.35%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	2 / 284 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			

subjects affected / exposed	0 / 282 (0.00%)	2 / 282 (0.71%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 282 (0.00%)	2 / 282 (0.71%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis streptococcal			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia necrotising			

subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural sepsis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 282 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 282 (0.00%)	1 / 282 (0.35%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 282 (0.71%)	0 / 282 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Methotrexate Monotherapy	Etanercept Monotherapy	Etanercept + Methotrexate
Total subjects affected by non-serious adverse events			
subjects affected / exposed	89 / 282 (31.56%)	75 / 282 (26.60%)	109 / 284 (38.38%)
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 282 (5.32%)	12 / 282 (4.26%)	17 / 284 (5.99%)
occurrences (all)	16	17	22
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	17 / 282 (6.03%)	13 / 282 (4.61%)	14 / 284 (4.93%)
occurrences (all)	23	17	15
Nausea			
subjects affected / exposed	37 / 282 (13.12%)	18 / 282 (6.38%)	41 / 284 (14.44%)
occurrences (all)	48	26	57
Vomiting			
subjects affected / exposed	15 / 282 (5.32%)	7 / 282 (2.48%)	10 / 284 (3.52%)
occurrences (all)	28	10	14

Infections and infestations			
Bronchitis			
subjects affected / exposed	9 / 282 (3.19%)	12 / 282 (4.26%)	18 / 284 (6.34%)
occurrences (all)	10	13	20
Nasopharyngitis			
subjects affected / exposed	22 / 282 (7.80%)	21 / 282 (7.45%)	27 / 284 (9.51%)
occurrences (all)	25	23	34
Upper respiratory tract infection			
subjects affected / exposed	21 / 282 (7.45%)	18 / 282 (6.38%)	23 / 284 (8.10%)
occurrences (all)	28	23	30

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 May 2015	- reporting of hepatotoxicity as a serious adverse event was clarified - etanercept indications in US and Canada were updated/clarified - updated inclusion/exclusion criteria regarding tender and swollen joint counts, minimum number of stable dosing for NSAIDS, excluded medications, and minimum number of months since use of excluded medications - clarified joint assessments and allowed for assessment by principal investigators; added folinic acid dosing information and additional information regarding laboratory assessments to determine subject eligibility - Clarified process for inadvertent blinding - Administrative corrections and clarifications were made throughout
09 July 2015	- several secondary endpoints to assess disease activity (DAS-28, SDAI, and CDAI) were added - clarifications to psoriatic arthritis disease assessments were made
30 October 2015	- updated to be consistent with international regulations and requirements, including those regarding tuberculosis screening in the setting of anti-TNF therapy
31 August 2016	- to reflect the most recent version, CTCAE grading was updated to version 4.0 - added language for confirmatory reflex testing by HBV DNA PCR for subjects with Hepatitis-B positive core antibody

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported