Clinical trial results:
A long-term, open-label study of TNR-001 in Japanese Juvenile Idiopathic Arthritis Subjects.

Summary

EudraCT number	2014-004103-73
Trial protocol	Outside EU/EEA
Global end of trial date	03 September 2009

Results information

Result version number	v2 (current)
This version publication date	16 March 2016
First version publication date	24 July 2015
Version creation reason	• Correction of full data set MeDRA version correction

Trial information

Trial identification

Sponsor protocol code	0881A1-207

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Alias: B1801001

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 April 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 September 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess the safety of the long-term administration of TNR-001 in subjects with active polyarticular-course Juvenile Idiopathic Arthritis (JIA).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 August 2005
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 32
Worldwide total number of subjects	32
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	6
Adolescents (12-17 years)	22
Adults (18-64 years)	4
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Study was conducted in Japan from 25 August 2005 to 3 September 2009.

Period 1

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

Arms

Arm title	Etanercept

Arm description:

Etanercept administered to subjects subcutaneously by self-injection or by his or her guardian.

Arm type	Experimental
Investigational medicinal product name	Etanercept
Investigational medicinal product code	TNR- 001
Other name	Enbrel
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Etanercept administered at a dose of 0.2 or 0.4 milligram per kilogram (mg/kg) (up to a maximum of 12.5 or 25 mg) twice weekly up to Week 216.

Number of subjects in period 1	Etanercept
Started	32
Completed	18
Not completed	14
Adverse events	2
No efficacy	2
Subject refusal	7
Lack of efficacy	3

Baseline characteristics

Reporting groups	
Reporting group title	Etanercept
Reporting group description:	
Etanercept administered to subjects subcutaneously by self-injection or by his or her guardian.	

Reporting group values	Etanercept	Total	
Number of subjects	32	32	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	13.7		
standard deviation	± 3.6	-	
Gender categorical Units: Subjects			
Female	28	28	
Male	4	4	

End points

End points reporting groups

Reporting group title	Etanercept

Reporting group description:

Etanercept administered to subjects subcutaneously by self-injection or by his or her guardian.

Primary: Physician’s Global Assessment of Disease Activity

End point title	Physician’s Global Assessment of Disease Activity[1]

End point description:

Physician Global Assessment of Disease Activity was measured on a 0 to 10 centimeter (cm) Visual Analog Scale (VAS), with 0 cm = no symptoms and 10 cm = severe symptoms. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 Juvenile Rheumatoid Arthritis (JRA) core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Primary

End point timeframe:

Baseline, Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this end point.

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: cm				
arithmetic mean (standard deviation)				
Baseline (n=32)	6.08 (± 1.82)			
Week 0 (n=32)	1.03 (± 1.86)			
Week 12 (n=32)	1.47 (± 2.25)			
Week 24 (n=31)	1 (± 1.66)			
Week 36 (n=31)	0.53 (± 0.72)			
Week 48 (n=28)	0.47 (± 0.6)			
Week 72 (n=28)	0.52 (± 0.8)			
Week 96 (n=27)	0.57 (± 1.59)			
Week 120 (n=26)	0.67 (± 1.17)			
Week 144 (n=26)	0.71 (± 1.47)			
Week 168 (n=20)	0.53 (± 0.89)			
Week 192 (n=19)	0.57 (± 0.81)			
Week 216 (n=2)	0.05 (± 0.07)			

Statistical analyses

No statistical analyses for this end point

Primary: Subject or Guardians Global Assessment of Overall Well-being

End point title	Subject or Guardians Global Assessment of Overall Well-

End point description:

Face scale composed with 11 check boxes was used to asssess subject's overall well-being. "Laughing face" located left of scale is most good condition as "0", and "Crying face" located right of scale is worst condition as "10". Subject or subject's guardian selected and marked one of eleven check boxes for a question: "How your or his /her usual activities were over the past week on average, considering only those difficulties or limitations that are due to the illness?". Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Primary

End point timeframe:

Baseline, 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this end point.

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=32)	5.3 (± 2.1)			
Week 0 (n=32)	2.4 (± 1.9)			
Week 12 (n=32)	2.2 (± 2.4)			
Week 24 (n=31)	2.3 (± 2.3)			
Week 36 (n=31)	1.8 (± 1.9)			
Week 48 (n=28)	2 (± 2.1)			
Week 72 (n=28)	1.8 (± 2)			
Week 96 (n=27)	1.6 (± 1.8)			
Week 120 (n=26)	1.6 (± 1.6)			
Week 144 (n=26)	1.7 (± 2)			
Week 168 (n=20)	2 (± 2.1)			
Week 192 (n=19)	1.8 (± 1.7)			
Week 216 (n=3)	1.3 (± 1.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Active Joints

End point title	Number of Active Joints[3]

End point description:

Following 73 joints were observed, and presence/absence of swollen joints not due to deformity and of joints with limitation of motion accompanied by pain or tenderness was recorded; 2 jaw joints, 2

shoulder joints, 2 elbow joints, 2 wrist joints, 10 metacarpophalangeal joints, 10 proximal interphalangeal joints, 8 distal interphalangeal joints, 2 sternoclavicular joints, 2 acromioclavicular joints, 1 neck joint, 1 chest joint, 1 lumbar joint, 2 hip joints, 2 knee joints, 2 ankle joints, 2 subtalar joints, 2 tarsal joints, 10 metatarsophalangeal joints, 10 proximal interphalangeal joints of the feet. Efficacy population:subjects who consented to participate in the study except those who violated GCP, never received administration of test article, had no data on 6 JRA core set variables at baseline, had missing data on 3 or more of the 6 JRA core set variables at baseline. Here,'n' signifies subjects evaluable for this end point at specified time points for given arm.

End point type	Primary

End point timeframe:

Baseline, Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this end point.

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Active joints				
arithmetic mean (standard deviation)				
Baseline (n=32)	19 (± 15)			
Week 0 (n=32)	3 (± 5.7)			
Week 12 (n=32)	4.3 (± 9.6)			
Week 24 (n=31)	2.7 (± 6.3)			
Week 36 (n=31)	1.9 (± 4.9)			
Week 48 (n=28)	1 (± 1.6)			
Week 72 (n=28)	0.6 (± 0.8)			
Week 96 (n=27)	0.9 (± 1.6)			
Week 120 (n=26)	0.9 (± 1.8)			
Week 144 (n=26)	0.8 (± 1.9)			
Week 168 (n=20)	1.4 (± 3)			
Week 192 (n=19)	1.4 (± 4)			
Week 216 (n=3)	1 (± 1.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Painful Joints on Pressure or Motion

End point title	Number of Painful Joints on Pressure or Motion[4]

End point description:

Following 71 joints were observed, and presence/absence of a joint with limitation of motion accompanied by pain or tenderness was
recorded; 2 jaw joints, 2 shoulder joints, 2 elbow joints, 2 wrist joints, 10 metacarpophalangeal joints, 10 proximal interphalangeal joints, 8 distal interphalangeal joints, 2 acromioclavicular joints, 1 neck joint, 1 chest joint, 1 lumbar joint, 2 hip joints, 2 knee joints, 2 ankle joint, 2 subtalar joints, 2 tarsal joints, 10 metatarsophalangeal joints, 10 proximal interphalangeal joints of the feet. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Primary

End point timeframe:

Baseline, Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this end point.

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Painful joints				
arithmetic mean (standard deviation)				
Baseline (n=32)	14.4 (± 13.5)			
Week 0 (n=32)	0.9 (± 3.1)			
Week 12 (n=32)	2.9 (± 9.1)			
Week 24 (n=31)	1.4 (± 4.3)			
Week 36 (n=31)	1 (± 4.7)			
Week 48 (n=28)	0.2 (± 0.4)			
Week 72 (n=28)	0.1 (± 0.4)			
Week 96 (n=27)	0.3 (± 1)			
Week 120 (n=26)	0.2 (± 0.5)			
Week 144 (n=26)	0.2 (± 0.8)			
Week 168 (n=20)	0.2 (± 0.4)			
Week 192 (n=19)	0.1 (± 0.2)			
Week 216 (n=3)	1 (± 1.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Childhood Health Assessment Questionnaire (CHAQ) Score

End point title	Childhood Health Assessment Questionnaire (CHAQ) Score[5]

End point description:

Parent-administered,valid assessment of functional disability,discomfort in pediatrics with rheumatic diseases. Parents report subjects's ability to perform activities in 8 domains: dressing and grooming,arising,eating,walking,hygiene, reach,grip,common activities(errands,chores and play). Each item is scored on 4-point Likert scale: 0=no difficulty;1=some difficulty;2=much difficulty;3=unable to do. Highest score reported for domain is score for that domain.Total Score =average of domain scores divided by number of domains answered: 0 = no difficulty to 3 = extreme difficulty. Efficacy population:subjects who consented to participate in study except those who violated GCP,never received administration of test article, had no data on 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here,'n' signifies subjects evaluable for this end point at specified time points for given arm.

End point type	Primary

End point timeframe:

Baseline, Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this end point.

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=32)	1.207 (± 0.906)			
Week 0 (n=32)	0.492 (± 0.62)			
Week 12 (n=32)	0.512 (± 0.693)			
Week 24 (n=31)	0.476 (± 0.615)			
Week 36 (n=31)	0.399 (± 0.574)			
Week 48 (n=28)	0.429 (± 0.589)			
Week 72 (n=28)	0.375 (± 0.575)			
Week 96 (n=27)	0.347 (± 0.627)			
Week 120 (n=26)	0.264 (± 0.555)			
Week 144 (n=26)	0.269 (± 0.492)			
Week 168 (n=20)	0.213 (± 0.391)			
Week 192 (n=19)	0.217 (± 0.365)			
Week 216 (n=3)	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

Primary: Erythrocyte Sedimentation Rate (ESR)

End point title	Erythrocyte Sedimentation Rate (ESR)[6]

End point description:

ESR is a laboratory test that provides a non-specific measure of inflammation. The test assesses the rate at which red blood cells fall in a test tube. Normal range is 0-30 millimeter per hour (mm/hr). A higher rate is consistent with inflammation. ESR was measured using the standard international Westergren method. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Primary

End point timeframe:

Baseline, Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this end point.

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: mm/hr				
arithmetic mean (standard deviation)				
Baseline (n=32)	38.7 (± 27.7)			
Week 0 (n=32)	26.6 (± 27.8)			
Week 12 (n=32)	24.4 (± 25.3)			
Week 24 (n=31)	21.4 (± 15.6)			
Week 36 (n=31)	19.6 (± 16.1)			
Week 48 (n=28)	21.5 (± 14.2)			
Week 72 (n=28)	19.9 (± 14.4)			
Week 96 (n=25)	18.7 (± 13.5)			
Week 120 (n=26)	17.7 (± 14.2)			
Week 144 (n=24)	21.2 (± 18.2)			
Week 168 (n=20)	15.4 (± 10.5)			
Week 192 (n=19)	16.5 (± 11.8)			
Week 216 (n=3)	28.7 (± 31)			

Statistical analyses

No statistical analyses for this end point

Primary: Subject or Guardians Pain Evaluation

End point title	Subject or Guardians Pain Evaluation[7]

End point description:

Face scale composed with 11 check boxes was used for pain evaluation ."Laughing face" located left of scale is most good condition as "0", and "Crying face" located right of scale is worst condition as "10".Subject or guardian answered "How much pain do you think you or your child experienced because of the illness in the past week?" Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Primary

End point timeframe:

Baseline, Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this end point.

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=32)	5.5 (± 2.4)			
Week 0 (n=32)	2.4 (± 2.1)			
Week 12 (n=32)	2.3 (± 2.4)			

Week 24 (n=31)	2.7 (± 2.8)			
Week 36 (n=31)	2.1 (± 2.4)			
Week 48 (n=28)	2.3 (± 2.4)			
Week 72 (n=28)	1.9 (± 2.2)			
Week 96 (n=27)	1.9 (± 2.1)			
Week 120 (n=26)	1.5 (± 1.8)			
Week 144 (n=26)	2.1 (± 2.3)			
Week 168 (n=20)	2 (± 1.9)			
Week 192 (n=19)	1.9 (± 1.9)			
Week 216 (n=3)	1.3 (± 1.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Duration of Morning Stiffness

End point title	Duration of Morning Stiffness[8]

End point description:

Duration of morning stiffness was defined as the time elapsed when subject woke up in the morning and was able to resume normal activities without stiffness in hours. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Primary

End point timeframe:

Baseline, Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this end point.

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: hours				
median (full range (min-max))				
Baseline (n=32)	1 (0 to 5)			
Week 0 (n=32)	0 (0 to 2)			
Week 12 (n=31)	0 (0 to 6)			
Week 24 (n=31)	0 (0 to 5.5)			
Week 36 (n=31)	0 (0 to 3)			
Week 48 (n=28)	0 (0 to 3)			
Week 72 (n=28)	0 (0 to 4)			
Week 96 (n=27)	0 (0 to 2)			
Week 120 (n=26)	0 (0 to 5)			
Week 144 (n=26)	0 (0 to 1)			
Week 168 (n=20)	0 (0 to 2)			
Week 192 (n=19)	0 (0 to 2)			
Week 216 (n=3)	0 (0 to 0.5)			

Statistical analyses

No statistical analyses for this end point

Primary: C-Reactive Protein (CRP)

End point title	C-Reactive Protein (CRP)[9]

End point description:

The test for CRP is a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. A decrease in the level of CRP indicates reduction in inflammation and therefore improvement. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Primary

End point timeframe:

Baseline, Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this end point.

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: milligram per deciliter (mg/dL)				
arithmetic mean (standard deviation)				
Baseline (n=32)	2.223 (± 2.309)			
Week 0 (n=32)	0.846 (± 1.836)			
Week 12 (n=31)	0.585 (± 0.905)			
Week 24 (n=31)	0.632 (± 1.083)			
Week 36 (n=30)	0.593 (± 0.968)			
Week 48 (n=28)	0.856 (± 1.458)			
Week 72 (n=28)	0.585 (± 1.113)			
Week 96 (n=27)	0.33 (± 0.505)			
Week 120 (n=26)	0.403 (± 0.906)			
Week 144 (n=26)	0.502 (± 0.876)			
Week 168 (n=20)	0.282 (± 0.567)			
Week 192 (n=19)	0.353 (± 0.724)			

Week 216 (n=3)	0.98 (± 1.037)			

Statistical analyses

No statistical analyses for this end point

Primary: Rheumatoid factor

End point title	Rheumatoid factor[10]

End point description:

Rheumatoid factor is the auto antibody directed against immunoglobulin G (IgG) and its concentration is observed in human serum or plasma. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Primary

End point timeframe:

Baseline, Week 0, 24, 48, 72, 96, 120, 144, 168, 192, 216

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this end point.

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: IU/mL				
arithmetic mean (standard deviation)				
Baseline (n=32)	427.4 (± 1616.2)			
Week 0 (n=32)	509.7 (± 1897.5)			
Week 24 (n=32)	457.2 (± 1396.7)			
Week 48 (n=30)	367.1 (± 959)			
Week 72 (n=28)	370.4 (± 881.9)			
Week 96 (n=27)	355.5 (± 1004.4)			
Week 120 (n=26)	427.1 (± 1575.7)			
Week 144 (n=26)	377.6 (± 1323.1)			
Week 168 (n=20)	110.6 (± 141.1)			
Week 192 (n=19)	111.4 (± 141)			
Week 216 (n=3)	16.3 (± 20.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Numbers of Subjects Who Achieved Juvenile Rheumatoid Arthritis (JRA) 30 Percent (%) Definition of Improvement (DOI), 50 % DOI And 70 % DOI

End point title	Numbers of Subjects Who Achieved Juvenile Rheumatoid Arthritis (JRA) 30 Percent (%) Definition of Improvement (DOI), 50 % DOI And 70 % DOI

End point description:

JRA 30% DOI, defined as a 30% improvement from baseline in 3 of 6 response variables used to assess disease activity, with no more than 1 variable worsening by more than 30%. JRA 50% DOI, defined as a 50% improvement from baseline in 3 of 6 response variables used to assess disease activity, with no more than 1 variable worsening by more than 50%. JRA 70% DOI, defined as a 70% improvement from baseline in 3 of 6 response variables used to assess disease activity, with no more than 1 variable worsening by more than 70%. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Secondary

End point timeframe:

Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Subjects				
30% DOI: Week 0 (n=32)	31			
30% DOI: Week 12 (n=32)	29			
30% DOI: Week 24 (n=31)	29			
30% DOI: Week 36 (n=31)	30			
30% DOI: Week 48 (n=28)	28			
30% DOI: Week 72 (n=28)	27			
30% DOI: Week 96 (n=27)	26			
30% DOI: Week 120 (n=26)	25			
30% DOI: Week 144 (n=26)	24			
30% DOI: Week 168 (n=20)	20			
30% DOI: Week 192 (n=19)	18			
30% DOI: Week 216 (n=3)	3			
50% DOI: Week 0 (n=32)	30			
50% DOI: Week 12 (n=32)	29			
50% DOI: Week 24 (n=31)	28			
50% DOI: Week 36 (n=31)	30			
50% DOI: Week 48 (n=28)	28			
50% DOI: Week 72 (n=28)	27			
50% DOI: Week 96 (n=27)	26			
50% DOI: Week 120 (n=26)	25			
50% DOI: Week 144 (n=26)	24			
50% DOI: Week 168 (n=20)	20			
50% DOI: Week 192 (n=19)	18			
50% DOI: Week 216 (n=3)	3			

70% DOI: Week 0 (n=32)	27			
70% DOI: Week 12 (n=32)	26			
70% DOI: Week 24 (n=31)	25			
70% DOI: Week 36 (n=31)	29			
70% DOI: Week 48 (n=28)	26			
70% DOI: Week 72 (n=28)	26			
70% DOI: Week 96 (n=27)	24			
70% DOI: Week 120 (n=26)	24			
70% DOI: Week 144 (n=26)	23			
70% DOI: Week 168 (n=20)	20			
70% DOI: Week 192 (n=19)	17			
70% DOI: Week 216 (n=3)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Physicians Global Assessment of Disease Activity at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, and 216

End point title	Percent Change From Baseline in Physicians Global Assessment of Disease Activity at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, and 216

End point description:

Physician Global Assessment of Disease Activity was measured on a 0 to 10 cm VAS, with 0 cm = no symptoms and 10 cm = severe symptoms. Change from baseline was reported in percentage. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Secondary

End point timeframe:

Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percent change				
arithmetic mean (standard deviation)				
Week 0 (n=32)	72.81 (± 72.48)			
Week 12 (n=32)	78.32 (± 31.01)			
Week 24 (n=31)	82.48 (± 30.2)			
Week 36 (n=31)	88.05 (± 20.88)			
Week 48 (n=28)	92.48 (± 9.68)			
Week 72 (n=28)	91.64 (± 12.75)			
Week 96 (n=27)	90.22 (± 25.99)			

Week 120 (n=26)	87.57 (± 22.41)			
Week 144 (n=26)	87.46 (± 26.42)			
Week 168 (n=20)	91.39 (± 15.21)			
Week 192 (n=19)	90.7 (± 12.74)			
Week 216 (n=2)	99.38 (± 0.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Subject or Guardians Global Assessment at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point title	Percent Change From Baseline in Subject or Guardians Global Assessment at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point description:

Face scale composed with 11 check boxes was used to asssess subject's overall well-being. "Laughing face" located left of scale is most good condition as "0", and "Crying face" located right of scale is worst condition as "10". Subject or subject's guardian selected and marked one of eleven check boxes for a question: "How your or his /her usual activities were over the past week on average, considering only those difficulties or limitations that are due to the illness?". Change from baseline was reported in percentage. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Secondary

End point timeframe:

Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percent change				
arithmetic mean (standard deviation)				
Week 0 (n=32)	46.73 (± 43.08)			
Week 12 (n=32)	48.64 (± 82.02)			
Week 24 (n=31)	54.73 (± 39.3)			
Week 36 (n=31)	59.26 (± 57.82)			
Week 48 (n=28)	58.29 (± 37.82)			
Week 72 (n=28)	65.48 (± 35.67)			
Week 96 (n=27)	64.13 (± 36.51)			

Week 120 (n=26)	62.18 (± 39.25)			
Week 144 (n=26)	61.01 (± 48.81)			
Week 168 (n=20)	44.71 (± 87.31)			
Week 192 (n=19)	54.07 (± 49.82)			
Week 216 (n=3)	72.22 (± 25.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Number of Active Joints at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point title	Percent Change From Baseline in Number of Active Joints at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point description:

Following 73 joints were observed, and presence/absence of swollen joints not due to deformity and of joints with limitation of motion accompanied by pain or tenderness was recorded; 2 jaw joints, 2 shoulder joints, 2 elbow joints, 2 wrist joints, 10 metacarpophalangeal joints, 10 proximal interphalangeal joints, 8 distal interphalangeal joints, 2 sternoclavicular joints, 2 acromioclavicular joints, 1 neck joint, 1 chest joint, 1 lumbar joint, 2 hip joints, 2 knee joints, 2 ankle joints, 2 subtalar joints, 2 tarsal joints, 10 metatarsophalangeal joints, 10 proximal interphalangeal joints of the feet. Efficacy population:subjects who consented to participate in the study except those who violated GCP, never received administration of test article, had no data on 6 JRA core set variables at baseline, had missing data on 3 or more of the 6 JRA core set variables at baseline. Here,'n' signifies subjects evaluable for this end point at specified time points for given arm.

End point type	Secondary

End point timeframe:

Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percent change				
arithmetic mean (standard deviation)				
Week 0 (n=32)	85.46 (± 20.24)			
Week 12 (n=32)	84.63 (± 22.83)			
Week 24 (n=31)	86.84 (± 21.4)			
Week 36 (n=31)	91.16 (± 12.08)			
Week 48 (n=28)	91.64 (± 14.2)			
Week 72 (n=28)	93.99 (± 10.67)			
Week 96 (n=27)	91.89 (± 20.28)			
Week 120 (n=26)	93.54 (± 10.98)			

Week 144 (n=26)	91.25 (± 27.89)			
Week 168 (n=20)	94.83 (± 7.7)			
Week 192 (n=19)	95.14 (± 10.76)			
Week 216 (n=3)	91.67 (± 14.43)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Number of Painful Joints on Pressure or Motion at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point title	Percent Change From Baseline in Number of Painful Joints on Pressure or Motion at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point description:

Following 71 joints were observed, and presence/absence of a joint with limitation of motion accompanied by pain or tenderness was
recorded; 2 jaw joints, 2 shoulder joints, 2 elbow joints, 2 wrist joints, 10 metacarpophalangeal joints, 10 proximal interphalangeal joints, 8 distal interphalangeal joints, 2 acromioclavicular joints, 1 neck joint, 1 chest joint, 1 lumbar joint, 2 hip joints, 2 knee joints, 2 ankle joint, 2 subtalar joints, 2 tarsal joints, 10 metatarsophalangeal joints, 10 proximal interphalangeal joints of the feet. Change from baseline was reported in percentage. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at pecified time points for given arm.

End point type	Secondary

End point timeframe:

Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percent change				
arithmetic mean (standard deviation)				
Week 0 (n=32)	91.83 (± 24.45)			
Week 12 (n=32)	88.53 (± 24.13)			
Week 24 (n=31)	87.73 (± 37.74)			
Week 36 (n=31)	96.62 (± 10.08)			
Week 48 (n=28)	97.91 (± 4.87)			
Week 72 (n=28)	98.56 (± 4.24)			
Week 96 (n=27)	96.02 (± 14.08)			
Week 120 (n=26)	98.08 (± 5.92)			
Week 144 (n=26)	97.86 (± 7.71)			

Week 168 (n=20)	98.04 (± 5)			
Week 192 (n=19)	99.12 (± 3.82)			
Week 216 (n=3)	83.33 (± 28.87)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Childhood Health Assessment Questionnaire (CHAQ) at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point title	Percent Change From Baseline in Childhood Health Assessment Questionnaire (CHAQ) at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point description:

Parent-administered,valid assessment of functional disability,discomfort in pediatrics with rheumatic diseases. Parents report subjects's ability to perform activities in 8 domains: dressing,grooming,arising,eating,walking,hygiene, reach,grip,common activities(errands,chores and play). Each item is scored on 4-point Likert scale: 0=no difficulty;1=some difficulty;2=much difficulty;3=unable to do. Highest score reported for domain is score for that domain. Total Score =average of domain scores divided by number of domains answered: 0 = no difficulty to 3 = extreme difficulty. Change from baseline was reported in percentage. Efficacy population:subjects who consented to participate in study except those who violated GCP,never received administration of test article, had no data on 6 JRA core set variables at baseline,had missing data on 3 or more of the 6 JRA core set variables at baseline. Here,'n' signifies subjects evaluable for this end point at specified time points.

End point type	Secondary

End point timeframe:

Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percent change				
arithmetic mean (standard deviation)				
Week 0 (n=28)	58.97 (± 35.47)			
Week 12 (n=28)	63.15 (± 33.65)			
Week 24 (n=27)	61.58 (± 48.6)			
Week 36 (n=27)	69.75 (± 36.44)			
Week 48 (n=25)	71.6 (± 31.42)			
Week 72 (n=25)	73.46 (± 34.85)			
Week 96 (n=24)	73.83 (± 40.51)			
Week 120 (n=23)	84.05 (± 22.49)			
Week 144 (n=23)	81.29 (± 24.82)			
Week 168 (n=17)	85.09 (± 21.1)			

Week 192 (n=16)	84.56 (± 19.75)			
Week 216 (n=3)	100 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Erythrocyte Sedimentation Rate (ESR) at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point title	Percent Change From Baseline in Erythrocyte Sedimentation Rate (ESR) at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point description:

ESR is a laboratory test that provides a non-specific measure of inflammation. The test assesses the rate at which red blood cells fall in a test tube. A higher rate is consistent with inflammation. ESR was measured using the standard international Westergren method. Change from baseline was reported in percentage. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Secondary

End point timeframe:

Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percent change				
arithmetic mean (standard deviation)				
Week 0 (n=32)	26.22 (± 47.99)			
Week 12 (n=32)	34.44 (± 39.68)			
Week 24 (n=31)	32.69 (± 46.3)			
Week 36 (n=31)	28.4 (± 86.21)			
Week 48 (n=28)	8.1 (± 133.23)			
Week 72 (n=28)	24.05 (± 88.16)			
Week 96 (n=27)	36.68 (± 60.57)			
Week 120 (n=26)	42.38 (± 48.48)			
Week 144 (n=24)	42.78 (± 40.44)			
Week 168 (n=20)	47.32 (± 48.24)			
Week 192 (n=19)	41.83 (± 49.2)			
Week 216 (n=3)	45.88 (± 32.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Subject or Guardians Pain Evaluation at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point title	Percent Change From Baseline in Subject or Guardians Pain Evaluation at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point description:

Face scale composed with 11 check boxes was used for pain evaluation ."Laughing face" located left of scale is most good condition as "0", and "Crying face" located right of scale is worst condition as "10". Subject or guardian answered "How much pain do you think you or your child experienced because of the illness in the past week?". Change from baseline was reported in percentage. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Secondary

End point timeframe:

Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percent change				
arithmetic mean (standard deviation)				
Week 0 (n=31)	55.89 (± 37.68)			
Week 12 (n=31)	54.89 (± 47.9)			
Week 24 (n=30)	46.6 (± 50.98)			
Week 36 (n=30)	52.92 (± 67.64)			
Week 48 (n=27)	48.44 (± 54.04)			
Week 72 (n=27)	58.95 (± 46.26)			
Week 96 (n=26)	55.76 (± 51.82)			
Week 120 (n=25)	61.35 (± 54.5)			
Week 144 (n=25)	49.76 (± 55.14)			
Week 168 (n=19)	61.02 (± 35.9)			
Week 192 (n=18)	46.66 (± 70.95)			
Week 216 (n=3)	72.22 (± 25.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Duration of Morning Stiffness at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point title	Percent Change From Baseline in Duration of Morning Stiffness at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point description:

Duration of morning stiffness was defined as the time elapsed when subject woke up in the morning and was able to resume normal activities without stiffness in hours. Change from baseline was reported in percentage. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Secondary

End point timeframe:

Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percent change				
median (full range (min-max))				
Week 0 (n=26)	94.84 (0 to 100)			
Week 12 (n=25)	93.8 (-200 to 100)			
Week 24 (n=25)	94.4 (-100 to 100)			
Week 36 (n=25)	100 (25 to 100)			
Week 48 (n=22)	100 (25 to 100)			
Week 72 (n=22)	100 (0 to 100)			
Week 96 (n=21)	100 (27.3 to 100)			
Week 120 (n=21)	100 (-25 to 100)			
Week 144 (n=21)	100 (0 to 100)			
Week 168 (n=15)	100 (27.3 to 100)			
Week 192 (n=15)	100 (27.3 to 100)			
Week 216 (n=3)	100 (75 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in C-Reactive Protein at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point title	Percent Change From Baseline in C-Reactive Protein at Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192 and 216

End point description:

The test for CRP is a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. A decrease in the level of CRP indicates reduction in inflammation and therefore improvement. Change from baseline was reported in percentage. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Secondary

End point timeframe:

Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percent change				
arithmetic mean (standard deviation)				
Week 0 (n=32)	32.76 (± 143.29)			
Week 12 (n=31)	43.65 (± 81.27)			
Week 24 (n=31)	35.6 (± 115.53)			
Week 36 (n=30)	-112.34 (± 592.41)			
Week 48 (n=28)	-110.2 (± 605.58)			
Week 72 (n=28)	-46.96 (± 444.64)			
Week 96 (n=27)	39.11 (± 107.63)			
Week 120 (n=26)	61.72 (± 61.11)			
Week 144 (n=26)	50.09 (± 89.15)			
Week 168 (n=20)	55.16 (± 71.8)			
Week 192 (n=19)	52.91 (± 85.17)			
Week 216 (n=3)	52.62 (± 54.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Cytokine Concentration

End point title	Serum Cytokine Concentration

End point description:

Serum collected from subjects was analyzed and concentration of cytokines interleukin - 1 beta (IL-1β), interleukin-6 (IL-6) and Tumor Necrosis Factor-alpha (TNF-α) was determined. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Secondary

End point timeframe:

Baseline, Week 0, 12, 24, 36, 48

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: picogram per millilter (pg/mL)				
arithmetic mean (standard deviation)				
IL-1β: Baseline (n=32)	28.7 (± 82)			
IL-1β: Week 0 (n=32)	26.2 (± 65.1)			
IL-1β: Week 12 (n=32)	10.3 (± 1)			
IL-1β: Week 24 (n=31)	11.6 (± 4)			
IL-1β: Week 36 (n=30)	14.7 (± 19.1)			
IL-1β: Week 48 (n=28)	17.8 (± 13.2)			
IL-6: Baseline (n=32)	30.26 (± 41.67)			
IL-6: Week 0 (n=32)	7.5 (± 11.72)			
IL-6: Week 12 (n=32)	7.3 (± 14.63)			
IL-6: Week 24 (n=31)	8.95 (± 22.88)			
IL-6: Week 36 (n=30)	12.37 (± 34.4)			
IL-6: Week 48 (n=28)	7.9 (± 22.7)			
TNF-α: Baseline (n=32)	6.1 (± 5.7)			
TNF-α: Week 0 (n=32)	119.8 (± 47.6)			
TNF-α: Week 12 (n=32)	135.5 (± 53)			
TNF-α: Week 24 (n=31)	153.1 (± 60.7)			
TNF-α: Week 36 (n=30)	162.5 (± 52.1)			
TNF-α: Week 48 (n=28)	160 (± 71.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Soluble TNF Receptor Concentration

End point title	Serum Soluble TNF Receptor Concentration

End point description:

Serum concentrations of soluble tumor necrosis factor receptor 1 (sTNFR I) and receptor II (sTNFR II) was determined over time. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Secondary

End point timeframe:

Baseline, Week 0, 12, 24, 36, 48

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: pg/mL				
arithmetic mean (standard deviation)				
sTNFR I (p55): Baseline (n=32)	1020 (± 302.4)			
sTNFR I (p55): Week 0 (n=32)	942.2 (± 229.9)			
sTNFR I (p55): Week 12 (n=32)	947.8 (± 176.2)			
sTNFR I (p55): Week 24 (n=31)	1003.1 (± 243.3)			
sTNFR I (p55): Week 36 (n=30)	977.7 (± 217.3)			
sTNFR I (p55): Week 48 (n=28)	1099.7 (± 229.9)			
sTNFR II (p75): Baseline (n=32)	2095.9 (± 741.2)			
sTNFR II (p75): Week 0 (n=32)	5000 (± 0)			
sTNFR II (p75): Week 12 (n=32)	5000 (± 0)			
sTNFR II (p75): Week 24 (n=31)	5000 (± 0)			
sTNFR II (p75): Week 36 (n=30)	5000 (± 0)			
sTNFR II (p75): Week 48 (n=28)	4937.9 (± 328.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Activity Score 28 (DAS28)

End point title	Disease Activity Score 28 (DAS28)

End point description:

DAS28 calculated from the number of swollen joints and painful joints using the 28 joints count, the ESR (mm/hour) and Face scale score (subject rated arthritis activity assessment with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity). Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Secondary

End point timeframe:

Baseline, Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=32)	5.73 (± 1.24)			
Week 0 (n=32)	2.96 (± 1.49)			
Week 12 (n=32)	2.95 (± 1.57)			
Week 24 (n=31)	2.74 (± 1.41)			
Week 36 (n=31)	2.47 (± 1.38)			
Week 48 (n=28)	2.52 (± 1.28)			
Week 72 (n=28)	2.33 (± 1.01)			
Week 96 (n=27)	2.17 (± 1.13)			
Week 120 (n=26)	2.22 (± 0.94)			
Week 144 (n=24)	2.33 (± 1.15)			
Week 168 (n=19)	2.48 (± 1.19)			
Week 192 (n=19)	2.35 (± 1.34)			
Week 216 (n=3)	2.55 (± 1.48)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With European League Against Rheumatism (EULAR) Response Based on DAS28

End point title	Percentage of Subjects With European League Against Rheumatism (EULAR) Response Based on DAS28

End point description:

The Disease Activity Score Based on 28-joints Count based (DAS28-based) EULAR response criteria were used to measure individual response as none, good, and moderate, depending on the extent of change from baseline and the level of disease activity reached. Good responders: change from baseline >1.2 with DAS28 =< 3.2; moderate responders: change from baseline >1.2 with DAS28 =>3.2 to =<5.1 or change from baseline >0.6 to =<1.2 with DAS28 =<5.1; non-responders: change from baseline

=< 0.6 or change from baseline >0.6 and =<1.2 with DAS28 >5.1. Efficacy population: population of all the subjects who consented to participate in the study except those who violated the GCP, never received administration of the test article, had no data on the 6 JRA core set variables at baseline and had missing data on 3 or more of the 6 JRA core set variables at baseline. Here, 'n' signifies subjects evaluable for this end point at the specified time points for the given arm.

End point type	Secondary

End point timeframe:

Week 0, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216

End point values	Etanercept			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Percentage of Subjects				
number (not applicable)				
Good Response: Week 0 (n=32)	59.4			
Good Response: Week 12 (n=32)	65.6			
Good Response: Week 24 (n=31)	61.3			
Good Response: Week 36 (n=31)	67.7			
Good Response: Week 48 (n=28)	75			
Good Response: Week 72 (n=28)	75			
Good Response: Week 96 (n=27)	85.2			
Good Response: Week 120 (n=26)	84.6			
Good Response: Week 144 (n=24)	79.2			
Good Response: Week 168 (n=19)	84.2			
Good Response: Week 192 (n=19)	78.9			
Good Response: Week 216 (n=3)	66.7			
Moderate Response: Week 0 (n=32)	37.5			
Moderate Response: Week 12 (n=32)	28.1			
Moderate Response: Week 24 (n=31)	32.3			
Moderate Response: Week 36 (n=31)	25.8			
Moderate Response: Week 48 (n=28)	21.4			
Moderate Response: Week 72 (n=28)	25			
Moderate Response: Week 96 (n=27)	11.1			
Moderate Response: Week 120 (n=26)	15.4			
Moderate Response: Week 144 (n=24)	16.7			
Moderate Response: Week 168 (n=19)	15.8			
Moderate Response: Week 192 (n=19)	15.8			
Moderate Response: Week 216 (n=3)	33.3			
No Response: Week 0 (n=32)	3.1			
No Response: Week 12 (n=32)	6.3			
No Response: Week 24 (n=31)	6.5			
No Response: Week 36 (n=31)	6.5			
No Response: Week 48 (n=28)	3.6			
No Response: Week 72 (n=28)	0			
No Response: Week 96 (n=27)	3.7			
No Response: Week 120 (n=26)	0			
No Response: Week 144 (n=24)	4.2			
No Response: Week 168 (n=19)	0			
No Response: Week 192 (n=19)	5.3			
No Response: Week 216 (n=3)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) and Serious AEs were reported from baseline up to follow-up visit (4 weeks after the last dose of study drug)

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Etanercept

Reporting group description:

Etanercept administered to subjects subcutaneously at a dose of 0.2 or 0.4 mg/kg (up to a maximum of 12.5 or 25 mg) twice weekly up to Week 216.

Serious adverse events	Etanercept		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 32 (18.75%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Feeling abnormal			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Etanercept		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 32 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Haemorrhage			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Internal haemorrhage			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Pallor			

subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
General disorders and administration site conditions			
Administration site pain			
subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	13		
Administration site reaction			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Chest pain			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	4		
Chest discomfort			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	3		
Chills			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Injection site erythema			
subjects affected / exposed	6 / 32 (18.75%)		
occurrences (all)	22		
Injection site pain			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Injection site haemorrhage			
subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	5		
Injection site swelling			
subjects affected / exposed	7 / 32 (21.88%)		
occurrences (all)	21		
Injection site pruritus			

subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	22		
Malaise			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Oedema			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	2		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Breast enlargement			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Menstruation irregular			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Dysmenorrhoea			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Allergic bronchitis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Asthma			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	6		
Cough			

subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Rhinitis allergic			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	4		
Oropharyngeal pain			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Tonsillar hypertrophy			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Vocal cord polyp			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Upper respiratory tract inflammation			
subjects affected / exposed	9 / 32 (28.13%)		
occurrences (all)	10		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Investigations			
Bacterial test			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Blood pressure increased			

subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Blood urea increased				
subjects affected / exposed	2 / 32 (6.25%)			
occurrences (all)	4			
Eosinophil count increased				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Haematocrit decreased				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Granulocyte count decreased				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Lymphocyte count increased				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Haemoglobin decreased				
subjects affected / exposed	2 / 32 (6.25%)			
occurrences (all)	2			
Red blood cell count decreased				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Platelet count increased				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Weight decreased				
subjects affected / exposed	2 / 32 (6.25%)			
occurrences (all)	2			
White blood cell count increased				
subjects affected / exposed	4 / 32 (12.50%)			
occurrences (all)	4			
Weight increased				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
White blood cells urine positive				

subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Chillblains			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Arthropod sting			
subjects affected / exposed	8 / 32 (25.00%)		
occurrences (all)	8		
Contusion			
subjects affected / exposed	10 / 32 (31.25%)		
occurrences (all)	16		
Foot fracture			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Frostbite			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Heat stroke			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Injury			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Injury corneal			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Limb injury			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	5		
Ligament sprain			
subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	5		
Skin abrasion			

subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Sunburn			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Thermal burn			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Congenital, familial and genetic disorders			
Talipes			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	3		
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Cerebral infarction			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Dizziness postural			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	12 / 32 (37.50%)		
occurrences (all)	17		
Hypoaesthesia			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Migraine			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	2		
Iron deficiency anaemia			

subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Lymphadenitis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Eye disorders			
Asthenopia			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Chalazion			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Conjunctivitis allergic			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	4		
Eye pruritus			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Glaucoma			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	2		
Iritis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	2		
Ocular hyperaemia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Papilloedema			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Uveitis			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	3		
Gastrointestinal disorders			
Abdominal discomfort			

subjects affected / exposed	4 / 32 (12.50%)			
occurrences (all)	4			
Abdominal pain				
subjects affected / exposed	9 / 32 (28.13%)			
occurrences (all)	12			
Abdominal pain upper				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Chapped lips				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Constipation				
subjects affected / exposed	5 / 32 (15.63%)			
occurrences (all)	7			
Cheilitis				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Dental caries				
subjects affected / exposed	4 / 32 (12.50%)			
occurrences (all)	5			
Diarrhoea				
subjects affected / exposed	3 / 32 (9.38%)			
occurrences (all)	4			
Faeces soft				
subjects affected / exposed	2 / 32 (6.25%)			
occurrences (all)	2			
Gastric ulcer				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Gastritis				
subjects affected / exposed	3 / 32 (9.38%)			
occurrences (all)	3			
Gastrointestinal disorder				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Lip oedema				

subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Toothache			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	6		
Vomiting			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Alopecia			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Dermatitis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Dermatitis atopic			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	4		
Erythema			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Hyperkeratosis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		

Palmar erythema			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Prurigo			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	10 / 32 (31.25%)		
occurrences (all)	13		
Skin erosion			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	4		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Monarthritis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Intervertebral disc protrusion			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Musculoskeletal stiffness			

subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Musculoskeletal pain			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	6		
Pain in extremity			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	3		
Spinal osteoarthritis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Synovial cyst			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	6		
Tenosynovitis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis bacterial			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	4		
Bronchitis fungal			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Bronchitis viral			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		

Conjunctivitis				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Candida infection				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Gastroenteritis				
subjects affected / exposed	6 / 32 (18.75%)			
occurrences (all)	9			
Gastroenteritis viral				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	2			
Hordeolum				
subjects affected / exposed	2 / 32 (6.25%)			
occurrences (all)	2			
Herpes zoster				
subjects affected / exposed	3 / 32 (9.38%)			
occurrences (all)	3			
Impetigo				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Infection				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	29 / 32 (90.63%)			
occurrences (all)	157			
Influenza				
subjects affected / exposed	7 / 32 (21.88%)			
occurrences (all)	8			
Onychomycosis				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Oral herpes				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	4			

Periodontitis				
subjects affected / exposed	2 / 32 (6.25%)			
occurrences (all)	2			
Otitis media				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	5 / 32 (15.63%)			
occurrences (all)	10			
Pneumonia mycoplasmal				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Skin candida				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Rhinitis				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Skin infection				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Tinea versicolour				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Subcutaneous abscess				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Tonsillitis				
subjects affected / exposed	2 / 32 (6.25%)			
occurrences (all)	3			
Upper respiratory tract infection				
subjects affected / exposed	3 / 32 (9.38%)			
occurrences (all)	4			
Urinary tract infection				
subjects affected / exposed	2 / 32 (6.25%)			
occurrences (all)	2			

Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported