Clinical trial results:
Compassionate Use Study of Adalimumab in Children 2 to < 4 Years Old or Age 4 and Above Weighing Less Than 15 kg with Active Juvenile Idiopathic Arthritis (JIA)

Summary

EudraCT number	2009-013091-40
Trial protocol	FR DE SE SK CZ DK Outside EU/EEA
Global end of trial date	21 March 2013

Results information

Result version number	v2 (current)
This version publication date	18 May 2016
First version publication date	22 July 2015
Version creation reason	• Correction of full data set Potential category issues

Trial information

Trial identification

Sponsor protocol code	M10-444

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00775437
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	1 North Waukegan Road, North Chicago, IL, United States, 60064
Public contact	Global Medical Information, AbbVie, 001 800-633-9110,
Scientific contact	Aileen L. Pangan MD, AbbVie, aileen.pangan@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000036-PIP01-08
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 March 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 March 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to evaluate the safety of adalimumab in patients 2 to < 4 years of age or ≥ 4 years of age weighing < 15 kg, with moderately to severely active polyarticular juvenile idiopathic arthritis (JIA) or polyarticular course JIA.

Protection of trial subjects:

Parent or legal guardian read and understood the information provided about the study and gave written permission. An assent form was not used in this study due to the young age of children being studied.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 March 2009
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	Czech Republic: 9
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	32
EEA total number of subjects	17

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)	32
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 14 investigative sites in the Czech Republic, France, Germany, and the United States.

Pre-assignment

Screening details:

Subjects age 2 to < 4 years or ≥ 4 years and under 15 kg with moderately to severely active polyarticular or polyarticular-course JIA with a parent/guardian to administer injections. The screening visit occurred between Day -28 and Day 0.

Period 1

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

Arms

Arm title	Adalimumab

Arm description:

Adalimumab 24 mg/m^2 body surface area (BSA) up to a total dose of 20 mg administered every other week (eow) by parent or designee as a single dose via subcutaneous injection at approximately the same time of day, for a minimum of 24 weeks. Subjects could continue in the study until age 4 and 15 kg (US and Puerto Rico) or for up to 1 additional year after reaching age 4 and 15 kg (EU). Visits beyond Week 24 occurred every 12 weeks for those subjects who continued in the study.

Arm type	Experimental
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	Humira, ABT-D2E7
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Adalimumab administered by parent or designee as a single dose via subcutaneous injection at approximately the same time of day

Number of subjects in period 1	Adalimumab
Started	32
Completed	26
Not completed	6
Consent withdrawn by subject	3
Loss of efficacy	2
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Adalimumab
Reporting group description:	
Adalimumab 24 mg/m^2 body surface area (BSA) up to a total dose of 20 mg administered every other week (eow) by parent or designee as a single dose via subcutaneous injection at approximately the same time of day, for a minimum of 24 weeks. Subjects could continue in the study until age 4 and 15 kg (US and Puerto Rico) or for up to 1 additional year after reaching age 4 and 15 kg (EU). Visits beyond Week 24 occurred every 12 weeks for those subjects who continued in the study.	

Reporting group values	Adalimumab	Total	
Number of subjects	32	32	
Age categorical Units: Subjects			
< 4 years	28	28	
≥ 4 years	4	4	
Age continuous Units: years			
arithmetic mean	3.04		
standard deviation	± 0.723	-	
Gender categorical Units: Subjects			
Female	28	28	
Male	4	4	
Weight Units: kilogram(s)			
arithmetic mean	13.4		
standard deviation	± 1.96	-	

End points

End points reporting groups

Reporting group title	Adalimumab

Reporting group description:

Adalimumab 24 mg/m^2 body surface area (BSA) up to a total dose of 20 mg administered every other week (eow) by parent or designee as a single dose via subcutaneous injection at approximately the same time of day, for a minimum of 24 weeks. Subjects could continue in the study until age 4 and 15 kg (US and Puerto Rico) or for up to 1 additional year after reaching age 4 and 15 kg (EU). Visits beyond Week 24 occurred every 12 weeks for those subjects who continued in the study.

Primary: Number of Subjects with Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Subjects with Treatment-Emergent Adverse Events (TEAEs)[1]

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.
If an AE meets any of the following criteria, it is considered a serious adverse event (SAE): Results in death, is life-threatening, results in hospitalization or the prolongation of hospitalization, is a congenital anomaly or a persistent or significant disability/incapacity, or is an important medical event requiring medical or surgical intervention to prevent a serious outcome.
A treatment-emergent AE (TEAE) is defined as any AE with onset or worsening reported by a subject from the time that the first dose of adalimumab is administered until 5 half-lives (70 days) have elapsed following discontinuation of adalimumab administration (total of 32.5 months).

End point type	Primary

End point timeframe:

TEAEs were collected from first dose of study drug until 70 days after the last dose of study drug and before start of commercial adalimumab or other biologics (32.5 months).

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: Descriptive data were summarized for this endpoint per protocol.

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Subjects				
Any Treatment-emergent AE	29			
Any Treatment-emergent SAE	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Serum Adalimumab Trough Concentrations at Week 0, Week 12, and Week 24

End point title	Mean Serum Adalimumab Trough Concentrations at Week 0, Week 12, and Week 24

End point description:

Adalimumab concentrations in serum were determined using a validated enzyme-linked immunoadsorbent assay (ELISA) method. The lower limit of quantitation (LLOQ) for adalimumab is 3.13 ng/mL.

End point type	Secondary

End point timeframe:

Weeks 0, 12, and 24

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	15[2]			
Units: µg/mL				
arithmetic mean (standard deviation)				
Week 0	0 (± 0)			
Week 12	6.97 (± 5.69)			
Week 24	7.78 (± 5.85)			

Notes:

[2] - All subjects who had samples for pharmacokinetic analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Hemoglobin: Mean Change From Baseline to Each Visit

End point title	Hemoglobin: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: g/L				
arithmetic mean (standard deviation)				
Week 12 (n=29)	6.7 (± 7.32)			
Week 24 (n=29)	6.7 (± 9.76)			
Week 36 (n=25)	5.5 (± 9.31)			
Week 48 (n=24)	5.3 (± 10.68)			
Week 60 (n=21)	6 (± 10.96)			
Week 72 (n=17)	9.5 (± 10.65)			
Week 84 (n=16)	10.5 (± 13.69)			
Week 96 (n=11)	8.6 (± 9.99)			

Week 108 (n=9)	7.7 (± 8.08)			
Week 120 (n=3)	4.7 (± 2.89)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematocrit: Mean Change From Baseline to Each Visit

End point title	Hematocrit: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Fraction				
arithmetic mean (standard deviation)				
Week 12 (n=29)	0.018 (± 0.0206)			
Week 24 (n=29)	0.016 (± 0.0289)			
Week 36 (n=25)	0.017 (± 0.0292)			
Week 48 (n=24)	0.011 (± 0.0288)			
Week 60 (n=21)	0.009 (± 0.0275)			
Week 72 (n=17)	0.024 (± 0.0264)			
Week 84 (n=16)	0.026 (± 0.0366)			
Week 96 (n=11)	0.023 (± 0.0319)			
Week 108 (n=9)	0.018 (± 0.0273)			
Week 120 (n=3)	0.008 (± 0.0082)			

Statistical analyses

No statistical analyses for this end point

Secondary: Red Blood Cell (RBC) Count: Mean Change From Baseline to Each Visit

End point title	Red Blood Cell (RBC) Count: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: x1012/L				
arithmetic mean (standard deviation)				
Week 12 (n=29)	0.15 (± 0.231)			
Week 24 (n=29)	0.08 (± 0.308)			
Week 36 (n=25)	0.098 (± 0.277)			
Week 48 (n=24)	0.05 (± 0.213)			
Week 60 (n=21)	0.07 (± 0.296)			
Week 72 (n=17)	0.1 (± 0.187)			
Week 84 (n=16)	0.06 (± 0.228)			
Week 96 (n=11)	0.08 (± 0.343)			
Week 108 (n=9)	0.1 (± 0.32)			
Week 120 (n=3)	0.03 (± 0.153)			

Statistical analyses

No statistical analyses for this end point

Secondary: Platelets: Mean Change From Baseline to Each Visit

End point title	Platelets: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: x109/L				
arithmetic mean (standard deviation)				
Week 12 (n=29)	-35 (± 145.44)			
Week 24 (n=29)	-57.7 (± 140.82)			
Week 36 (n=25)	-75.2 (± 148.51)			
Week 48 (n=23)	-21 (± 174.17)			
Week 60 (n=21)	-46.7 (± 125.71)			
Week 72 (n=17)	-51.1 (± 111.11)			
Week 84 (n=15)	-58.5 (± 127.29)			
Week 96 (n=11)	-49.2 (± 142.73)			
Week 108 (n=9)	-30.4 (± 137.84)			
Week 120 (n=3)	20 (± 185.95)			

Statistical analyses

No statistical analyses for this end point

Secondary: White Blood Cell (WBC) Count: Mean Change From Baseline to Each Visit

End point title	White Blood Cell (WBC) Count: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: x10^9/L				
arithmetic mean (standard deviation)				
Week 12 (n=29)	0.19 (± 3.959)			
Week 24 (n=29)	-0.25 (± 3.756)			
Week 36 (n=25)	-0.42 (± 4.632)			
Week 48 (n=24)	0.3 (± 4.804)			
Week 60 (n=21)	0.25 (± 2.183)			

Week 72 (n=17)	0.66 (± 3.225)			
Week 84 (n=16)	0.18 (± 2.944)			
Week 96 (n=11)	0.55 (± 2.757)			
Week 108 (n=9)	-0.76 (± 4.166)			
Week 120 (n=3)	1.8 (± 3.651)			

Statistical analyses

No statistical analyses for this end point

Secondary: Neutrophils: Mean Change From Baseline to Each Visit

End point title	Neutrophils: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: x109/L				
arithmetic mean (standard deviation)				
Week 12 (n=29)	-0.138 (± 2.9819)			
Week 24 (n=29)	-0.619 (± 3.0082)			
Week 36 (n=25)	-0.586 (± 3.7363)			
Week 48 (n=24)	0.065 (± 3.4433)			
Week 60 (n=21)	0.222 (± 2.0937)			
Week 72 (n=17)	-0.169 (± 2.6167)			
Week 84 (n=16)	-0.206 (± 2.0077)			
Week 96 (n=11)	0.293 (± 2.511)			
Week 108 (n=9)	-0.39 (± 3.1702)			
Week 120 (n=3)	2.47 (± 3.2658)			

Statistical analyses

No statistical analyses for this end point

Secondary: Lymphocytes: Mean Change From Baseline to Each Visit

End point title	Lymphocytes: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: x109/L				
arithmetic mean (standard deviation)				
Week 12 (n=29)	0.371 (± 2.3523)			
Week 24 (n=29)	0.292 (± 1.9345)			
Week 36 (n=25)	0.176 (± 1.962)			
Week 48 (n=24)	0.186 (± 1.9584)			
Week 60 (n=21)	-0.034 (± 1.6129)			
Week 72 (n=17)	0.636 (± 1.7404)			
Week 84 (n=16)	0.306 (± 1.5143)			
Week 96 (n=11)	0.006 (± 1.9402)			
Week 108 (n=9)	-0.46 (± 2.4315)			
Week 120 (n=3)	-0.67 (± 1.8041)			

Statistical analyses

No statistical analyses for this end point

Secondary: Monocytes: Mean Change From Baseline to Each Visit

End point title	Monocytes: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: x10^9/L				
arithmetic mean (standard deviation)				
Week 12 (n=29)	-0.032 (± 0.3051)			
Week 24 (n=29)	0.081 (± 0.4547)			
Week 36 (n=25)	0.028 (± 0.2978)			
Week 48 (n=24)	-0.006 (± 0.2718)			
Week 60 (n=21)	0.08 (± 0.1831)			
Week 72 (n=17)	0.113 (± 0.2054)			
Week 84 (n=16)	0.061 (± 0.2594)			
Week 96 (n=11)	0.089 (± 0.2295)			
Week 108 (n=9)	0.096 (± 0.3248)			
Week 120 (n=3)	0.057 (± 0.0777)			

Statistical analyses

No statistical analyses for this end point

Secondary: Eosinophils: Mean Change From Baseline to Each Visit

End point title	Eosinophils: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: x10^9/L				
arithmetic mean (standard deviation)				
Week 12 (n=29)	-0.004 (± 0.1771)			
Week 24 (n=29)	-0.006 (± 0.1545)			
Week 36 (n=25)	-0.052 (± 0.1374)			
Week 48 (n=24)	0.056 (± 0.2773)			
Week 60 (n=21)	-0.015 (± 0.1363)			
Week 72 (n=17)	0.069 (± 0.1886)			
Week 84 (n=16)	0.016 (± 0.1631)			
Week 96 (n=11)	0.158 (± 0.3207)			
Week 108 (n=9)	-0.002 (± 0.0864)			
Week 120 (n=3)	-0.063 (± 0.0929)			

Statistical analyses

No statistical analyses for this end point

Secondary: Basophils: Mean Change From Baseline to Each Visit

End point title	Basophils: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: x10^9/L				
arithmetic mean (standard deviation)				
Week 12 (n=29)	-0.012 (± 0.0299)			
Week 24 (n=29)	-0.002 (± 0.0272)			

Week 36 (n=25)	0.003 (± 0.0244)			
Week 48 (n=24)	0.005 (± 0.0412)			
Week 60 (n=21)	-0.003 (± 0.0256)			
Week 72 (n=17)	0.007 (± 0.031)			
Week 84 (n=16)	-0.001 (± 0.0171)			
Week 96 (n=11)	-0.003 (± 0.0205)			
Week 108 (n=9)	-0.001 (± 0.0117)			
Week 120 (n=3)	0.003 (± 0.0306)			

Statistical analyses

No statistical analyses for this end point

Secondary: Alanine Aminotransferase (SGPT/ALT): Mean Change From Baseline to Each Visit

End point title	Alanine Aminotransferase (SGPT/ALT): Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: U/L				
arithmetic mean (standard deviation)				
Week 12 (n=27)	0.5 (± 9.96)			
Week 24 (n=28)	-1.1 (± 17.13)			
Week 36 (n=25)	0 (± 29.82)			
Week 48 (n=24)	-4.5 (± 24.81)			
Week 60 (n=21)	-2 (± 10.25)			
Week 72 (n=16)	-1.8 (± 10.1)			
Week 84 (n=16)	-0.5 (± 14.56)			
Week 96 (n=11)	-3.9 (± 15.4)			
Week 108 (n=9)	-2.4 (± 6.31)			
Week 120 (n=3)	-14.3 (± 23.12)			

Statistical analyses

No statistical analyses for this end point

Secondary: Aspartate Aminotransferase (SGOT/AST): Mean Change From Baseline to Each Visit

End point title	Aspartate Aminotransferase (SGOT/AST): Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: U/L				
arithmetic mean (standard deviation)				
Week 12 (n=26)	2.8 (± 7.56)			
Week 24 (n=28)	-0.6 (± 8.82)			
Week 36 (n=25)	2 (± 23.26)			
Week 48 (n=24)	-0.7 (± 16.13)			
Week 60 (n=21)	-0.4 (± 7.63)			
Week 72 (n=16)	0.3 (± 7.36)			
Week 84 (n=16)	-0.4 (± 6.89)			
Week 96 (n=10)	1.5 (± 11.48)			
Week 108 (n=9)	0.4 (± 6.21)			
Week 120 (n=3)	-8.3 (± 11.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Alkaline Phosphatase (ALP): Mean Change From Baseline to Each Visit

End point title	Alkaline Phosphatase (ALP): Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at

least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: U/L				
arithmetic mean (standard deviation)				
Week 12 (n=27)	15.7 (± 64.65)			
Week 24 (n=28)	10.6 (± 68.75)			
Week 36 (n=25)	23.2 (± 73.28)			
Week 48 (n=24)	21.7 (± 73.03)			
Week 60 (n=21)	17.9 (± 85.55)			
Week 72 (n=16)	17.9 (± 83.52)			
Week 84 (n=16)	31.5 (± 89.3)			
Week 96 (n=11)	59.4 (± 57.65)			
Week 108 (n=9)	-6.3 (± 100.72)			
Week 120 (n=3)	-72.3 (± 169.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Creatine Phosphokinase: Mean Change From Baseline to Each Visit

End point title	Creatine Phosphokinase: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: U/L				
arithmetic mean (standard deviation)				
Week 12 (n=27)	17.2 (± 50.48)			
Week 24 (n=27)	7 (± 30.79)			
Week 36 (n=25)	24.8 (± 44.5)			
Week 48 (n=24)	18.4 (± 54.02)			
Week 60 (n=21)	26.6 (± 65.48)			
Week 72 (n=16)	41.6 (± 40.63)			
Week 84 (n=16)	36.4 (± 53.64)			
Week 96 (n=11)	28.7 (± 41.79)			
Week 108 (n=9)	7.2 (± 22.97)			
Week 120 (n=3)	14 (± 40.73)			

Statistical analyses

No statistical analyses for this end point

Secondary: Total Bilirubin: Mean Change From Baseline to Each Visit

End point title	Total Bilirubin: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: µmol/L				
arithmetic mean (standard deviation)				
Week 12 (n=27)	1.2 (± 2.42)			
Week 24 (n=28)	0.6 (± 1.59)			
Week 36 (n=25)	0.6 (± 1.61)			
Week 48 (n=24)	0.9 (± 2.4)			
Week 60 (n=21)	1 (± 2.09)			
Week 72 (n=16)	0.2 (± 1.25)			
Week 84 (n=16)	0.5 (± 2.36)			
Week 96 (n=11)	0.7 (± 1.62)			
Week 108 (n=9)	1.1 (± 2.71)			
Week 120 (n=3)	2.3 (± 0.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Creatinine: Mean Change From Baseline to Each Visit

End point title	Creatinine: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: µmol/L				
arithmetic mean (standard deviation)				
Week 12 (n=27)	1.7 (± 5.98)			
Week 24 (n=28)	0.5 (± 5.3)			
Week 36 (n=25)	0.3 (± 5.84)			
Week 48 (n=24)	2.5 (± 7.8)			
Week 60 (n=21)	2.8 (± 5.79)			
Week 72 (n=16)	3.4 (± 6.96)			
Week 84 (n=16)	4 (± 6.37)			
Week 96 (n=11)	3.2 (± 5.53)			
Week 108 (n=9)	6.2 (± 6.7)			
Week 120 (n=3)	8.7 (± 5.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Uric Acid: Mean Change From Baseline to Each Visit

End point title	Uric Acid: Mean Change From Baseline to Each Visit

End point description:

Baseline is the last value prior to the first dose of study drug. Subjects with non-missing baseline and at least 1 post-baseline observation are included in the analysis. n=subjects with evaluable data at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: µmol/L				
arithmetic mean (standard deviation)				
Week 12 (n=27)	1.7 (± 48.24)			
Week 24 (n=27)	6.5 (± 47.93)			
Week 36 (n=25)	2.5 (± 41.77)			
Week 48 (n=24)	5.6 (± 45.62)			
Week 60 (n=21)	1.9 (± 30.86)			
Week 72 (n=16)	-0.9 (± 43.53)			
Week 84 (n=16)	-4.5 (± 46.76)			
Week 96 (n=11)	13.3 (± 36.39)			
Week 108 (n=9)	-10.1 (± 33.55)			
Week 120 (n=3)	-7 (± 27.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Pediatric American College of Rheumatology 30% Response (PedACR30)

End point title	Percentage of Subjects Achieving Pediatric American College of Rheumatology 30% Response (PedACR30)

End point description:

The PedACR30 response is defined by the Pediatric American College of Rheumatology as ≥30% improvement in ≥3 of 6 JIA core set criteria, and ≥30% worsening in ≤1 of 6 JIA core set criteria. The 6 variables for the JIA core set criteria are Physician's Global Assessment (PGA) of subject's disease activity, Parent's Global Assessment of subject's disease activity, number of active joints (joints with swelling not due to deformity or joints with loss of passive motion [LOM] and joints with pain on passive motion [POM], tenderness, or both), number of joints with LOM, Disability Index of Child Health Assessment Questionnaire (DICHAQ), and C-reactive protein (CRP). Baseline=last value prior to the first dose of study drug. Missing data were imputed up to Week 60 using last observation carried forward (LOCF) and non-responder imputation (NRI); observed values are presented for timepoints past Week 60. n=number of subjects for either observed or imputed methods at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of subjects				
number (not applicable)				
Week 12 Observed (n=31)	93.5			
Week 12 NRI (n=32)	90.6			
Week 12 LOCF (n=31)	93.5			
Week 24 Observed (n=30)	90			
Week 24 NRI (n=32)	84.4			
Week 24 LOCF (n=31)	90.3			
Week 36 Observed (n=27)	92.6			
Week 36 NRI (n=32)	78.1			
Week 36 LOCF (n=31)	93.5			
Week 48 Observed (n=24)	83.3			
Week 48 NRI (n=32)	62.5			
Week 48 LOCF (n=31)	83.9			
Week 60 Observed (n=20)	90			
Week 60 NRI (n=32)	56.3			
Week 60 LOCF (n=31)	87.1			
Week 72 Observed (n=17)	100			
Week 84 Observed (n=17)	100			
Week 96 Observed (n=13)	92.3			
Week 108 Observed (n=9)	88.9			
Week 120 Observed (n=3)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Pediatric American College of Rheumatology 50% Response (PedACR50)

End point title	Percentage of Subjects Achieving Pediatric American College of Rheumatology 50% Response (PedACR50)

End point description:

The PedACR50 response is defined by the Pediatric American College of Rheumatology as ≥ 50% improvement in at least 3 of 6 JIA core set criteria, and ≥ 30% worsening in not more than 1 of 6 JIA core set criteria. The 6 variables for the JIA core set criteria include PGA of subject's disease activity, Parent's Global Assessment of subject's disease activity, number of active joints (joints with swelling not due to deformity or joints with LOM and joints with POM, tenderness, or both), number of joints with LOM, DICHAQ, and CRP. Baseline is the last value prior to the first dose of study drug. Missing data were imputed up to Week 60 using LOCF and by NRI; observed values are presented for timepoints past Week 60. n=number of subjects for either observed or imputed methods at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of subjects				
number (not applicable)				
Week 12 Observed (n=31)	90.3			
Week 12 NRI (n=32)	87.5			
Week 12 LOCF (n=31)	90.3			
Week 24 Observed (n=30)	83.3			
Week 24 NRI (n=32)	78.1			
Week 24 LOCF (n=31)	83.9			
Week 36 Observed (n=27)	88.9			
Week 36 NRI (n=32)	75			
Week 36 LOCF (n=31)	90.3			
Week 48 Observed (n=24)	79.2			
Week 48 NRI (n=32)	59.4			
Week 48 LOCF (n=31)	80.6			
Week 60 Observed (n=20)	80			
Week 60 NRI (n=32)	50			
Week 60 LOCF (n=31)	80.6			
Week 72 Observed (n=17)	100			
Week 84 Observed (n=17)	94.1			
Week 96 Observed (n=13)	92.3			
Week 108 Observed (n=9)	88.9			
Week 120 Observed (n=3)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Pediatric American College of Rheumatology 70% Response (PedACR70)

End point title	Percentage of Subjects Achieving Pediatric American College of Rheumatology 70% Response (PedACR70)

End point description:

The PedACR70 response is defined by the Pediatric American College of Rheumatology as ≥ 70% improvement in at least 3 of 6 JIA core set criteria, and ≥ 30% worsening in not more than 1 of 6 JIA core set criteria. The 6 variables for the JIA core set criteria include PGA of subject's disease activity, Parent's Global Assessment of subject's disease activity, number of active joints (joints with swelling not due to deformity or joints with LOM and joints with POM, tenderness, or both), number of joints with LOM, DICHAQ, and CRP. Baseline is the last value prior to the first dose of study drug. Missing data were imputed up to Week 60 using LOCF and by NRI; observed values are presented for timepoints past Week 60. n=number of subjects for either observed or imputed methods at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of subjects				
number (not applicable)				
Week 12 Observed (n=31)	61.3			
Week 12 NRI (n=32)	59.4			
Week 12 LOCF (n=31)	61.3			
Week 24 Observed (n=30)	73.3			
Week 24 NRI (n=32)	68.8			
Week 24 LOCF (n=31)	74.2			
Week 36 Observed (n=27)	66.7			
Week 36 NRI (n=32)	56.3			
Week 36 LOCF (n=31)	67.7			
Week 48 Observed (n=24)	75			
Week 48 NRI (n=32)	56.3			
Week 48 LOCF (n=31)	74.2			
Week 60 Observed (n=20)	70			
Week 60 NRI (n=32)	43.8			
Week 60 LOCF (n=31)	71			
Week 72 Observed (n=17)	76.5			
Week 84 Observed (n=17)	82.4			
Week 96 Observed (n=13)	76.9			
Week 108 Observed (n=9)	77.8			
Week 120 Observed (n=3)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Pediatric American College of Rheumatology 90% Response (PedACR90)

End point title	Percentage of Subjects Achieving Pediatric American College of Rheumatology 90% Response (PedACR90)

End point description:

The PedACR90 response is defined by the Pediatric American College of Rheumatology as ≥ 90% improvement in at least 3 of 6 JIA core set criteria, and ≥ 30% worsening in not more than 1 of 6 JIA core set criteria. The 6 variables for the JIA core set criteria include PGA of subject's disease activity, Parent's Global Assessment of subject's disease activity, number of active joints (joints with swelling not due to deformity or joints with LOM and joints with POM, tenderness, or both), number of joints with LOM, DICHAQ, and CRP. Baseline is the last value prior to the first dose of study drug. Missing data were imputed up to Week 60 using LOCF and by NRI; observed values are presented for timepoints past Week 60. n=number of subjects for either observed or imputed methods at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of subjects				
number (not applicable)				
Week 12 Observed (n=31)	38.7			
Week 12 NRI (n=32)	37.5			
Week 12 LOCF (n=31)	38.7			
Week 24 Observed (n=30)	36.7			
Week 24 NRI (n=32)	34.4			
Week 24 LOCF (n=31)	35.5			
Week 36 Observed (n=27)	51.9			
Week 36 NRI (n=32)	43.8			
Week 36 LOCF (n=31)	51.6			
Week 48 Observed (n=24)	62.5			
Week 48 NRI (n=32)	46.9			
Week 48 LOCF (n=31)	58.1			
Week 60 Observed (n=20)	50			
Week 60 NRI (n=32)	31.3			
Week 60 LOCF (n=31)	51.6			
Week 72 Observed (n=17)	64.7			
Week 84 Observed (n=17)	64.7			
Week 96 Observed (n=13)	61.5			
Week 108 Observed (n=9)	66.7			
Week 120 Observed (n=3)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Physician's Global Assessment of Disease Activity: Mean Change from Baseline to Each Visit

End point title	Physician's Global Assessment of Disease Activity: Mean Change from Baseline to Each Visit

End point description:

The physician’s assessment of subject’s overall disease activity on a visual analog scale (VAS). The VAS is a 100 mm scale, with scores ranging from 0 (very good) to 100 (very bad). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=31)	-41.4 (± 21.2)			
Week 24 (n=30)	-45.3 (± 21.32)			
Week 36 (n=28)	-43 (± 23.9)			
Week 48 (n=24)	-46.5 (± 18.35)			
Week 60 (n=21)	-42.7 (± 28.17)			
Week 72 (n=17)	-51.1 (± 19.53)			
Week 84 (n=17)	-50.5 (± 16.77)			
Week 96 (n=13)	-47.5 (± 24.42)			
Week 108 (n=9)	-48.3 (± 28.24)			
Week 120 (n=3)	-56.3 (± 5.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Parent's Global Assessment of Disease Activity: Mean Change from Baseline to Each Visit

End point title	Parent's Global Assessment of Disease Activity: Mean Change from Baseline to Each Visit

End point description:

The parent’s assessment of how the subject’s arthritis is doing overall on a VAS. The VAS is a 100 mm scale, with scores ranging from 0 (very good) to 100 (very bad). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=31)	-28.1 (± 29.91)			
Week 24 (n=30)	-32.2 (± 29.74)			

Week 36 (n=27)	-35.1 (± 27.42)			
Week 48 (n=24)	-35.6 (± 32.19)			
Week 60 (n=21)	-34.5 (± 33.31)			
Week 72 (n=17)	-43.8 (± 25.58)			
Week 84 (n=17)	-42.6 (± 28.62)			
Week 96 (n=13)	-45.8 (± 29.1)			
Week 108 (n=9)	-39.9 (± 37.54)			
Week 120 (n=3)	-47.7 (± 34.96)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disability Index of Child Health Assessment Questionnaire (DICHAQ): Mean Change from Baseline to Each Visit

End point title	Disability Index of Child Health Assessment Questionnaire (DICHAQ): Mean Change from Baseline to Each Visit

End point description:

The DICHAQ is a self-reported subject-oriented outcome measure, calculated as the mean of the following 8 category scores (range: 0 to 3): Dressing and Grooming, Arising, Eating, Walking, Hygiene, Reach, Grip, and Activities. The score of each category is calculated as the maximum of the scores for the questions within that category. If aids and devices and/or help from another person are used for a category, a lower category score is adjusted to 2 for that category. A subject must have scores for at least 6 categories in order to compute the DICHAQ score. Total score is derived as average of all categories: 0 (no disability) to 3 (complete disability). Baseline is the last value prior to the first dose of study drug. Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=31)	-0.5 (± 0.64)			
Week 24 (n=30)	-0.5 (± 0.69)			
Week 36 (n=27)	-0.6 (± 0.7)			
Week 48 (n=24)	-0.6 (± 0.68)			
Week 60 (n=21)	-0.6 (± 0.71)			
Week 72 (n=16)	-0.9 (± 0.64)			
Week 84 (n=17)	-0.9 (± 0.68)			

Week 96 (n=13)	-0.8 (± 0.56)			
Week 108 (n=9)	-0.8 (± 0.63)			
Week 120 (n=3)	-0.8 (± 1.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Active Joint Counts (AJC73): Mean Change from Baseline to Each Visit

End point title	Active Joint Counts (AJC73): Mean Change from Baseline to Each Visit

End point description:

A joint assessment was recorded at all study visits to assess the number of active joints, with a total possible score of 0 (no active joints) to 73 (all active joints). Active joints are defined as joints with positive results for tenderness, swelling, pain on passive motion, or limitation of passive motion. Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 8, 12, 16, 20, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 2 (n=32)	-5 (± 6.58)			
Week 4 (n=32)	-6.1 (± 6.69)			
Week 8 (n=32)	-7 (± 5.24)			
Week 12 (n=31)	-7.3 (± 4.52)			
Week 16 (n=31)	-7.1 (± 5.87)			
Week 20 (n=29)	-8 (± 5.68)			
Week 24 (n=30)	-7.2 (± 5.6)			
Week 36 (n=28)	-7.3 (± 5.21)			
Week 48 (n=24)	-8 (± 5.5)			
Week 60 (n=20)	-9.5 (± 7.5)			
Week 72 (n=17)	-10.2 (± 6.64)			
Week 84 (n=17)	-10.4 (± 7.57)			
Week 96 (n=13)	-8.9 (± 7.04)			
Week 108 (n=9)	-5.9 (± 3.33)			
Week 120 (n=3)	-7.3 (± 2.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: Limitation of Passive Motion (LOM69) Joint Count: Mean Change from Baseline to Each Visit

End point title	Limitation of Passive Motion (LOM69) Joint Count: Mean Change from Baseline to Each Visit

End point description:

Sixty-nine joints were assessed by physical examination. The joints to be examined for LOM were the same as those examined for tenderness, except that the sacroiliac, sternoclavicular, and acromio clavicular joints were excluded. LOM of the joint was classified as present ("1"), absent ("0"), or replaced/injected ("9"). Scores range from 0 to 621, with higher scores representing higher disease activity. Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 8, 12, 16, 20, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 2 (n=32)	-4.5 (± 7.14)			
Week 4 (n=32)	-5.4 (± 6.48)			
Week 8 (n=32)	-5.3 (± 5.02)			
Week 12 (n=31)	-5.6 (± 4.8)			
Week 16 (n=31)	-6.3 (± 6.31)			
Week 20 (n=29)	-6.8 (± 6.63)			
Week 24 (n=30)	-5.6 (± 5.54)			
Week 36 (n=28)	-5.1 (± 5.29)			
Week 48 (n=24)	-5.5 (± 7.06)			
Week 60 (n=20)	-5.5 (± 8.31)			
Week 72 (n=17)	-6.9 (± 7.84)			
Week 84 (n=17)	-8.4 (± 6.9)			
Week 96 (n=13)	-7.5 (± 6.73)			
Week 108 (n=9)	-5.2 (± 3.96)			
Week 120 (n=3)	-6 (± 2.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: C-reactive Protein (CRP): Mean Change from Baseline to Each Visit

End point title	C-reactive Protein (CRP): Mean Change from Baseline to Each Visit

End point description:

CRP is a laboratory parameter and considered as an efficacy variable. CRP is a general marker of

inflammation that is sensitive to acute changes in inflammatory response. CRP is reported using mg/dL. Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 12 (n=28)	-0.6 (± 2.65)			
Week 24 (n=28)	-0.2 (± 3.2)			
Week 36 (n=25)	-0.4 (± 3.08)			
Week 48 (n=23)	0.4 (± 2.68)			
Week 60 (n=20)	-0.3 (± 1.83)			
Week 72 (n=17)	-0.7 (± 1.25)			
Week 84 (n=17)	-0.7 (± 1.47)			
Week 96 (n=12)	0.1 (± 1.6)			
Week 108 (n=9)	0.2 (± 1.93)			
Week 120 (n=3)	0.3 (± 0.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Tender Joint Count (TJC75): Mean Change from Baseline to Each Visit

End point title	Tender Joint Count (TJC75): Mean Change from Baseline to Each Visit

End point description:

Seventy-five joints or regions were assessed by pressure and joint manipulation on physical examination. Joint tenderness was classified as either present ("1"), absent ("0") or replaced/injected ("9"). Scores range from 0 to 675, with higher scores representing higher disease activity. Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 8, 12, 16, 20, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 2 (n=32)	-2.3 (± 4.62)			
Week 4 (n=32)	-2.8 (± 4.48)			
Week 8 (n=32)	-3.1 (± 4.31)			
Week 12 (n=31)	-2.7 (± 5.09)			
Week 16 (n=31)	-3.5 (± 4.77)			
Week 20 (n=29)	-3.9 (± 5.09)			
Week 24 (n=30)	-3 (± 5.54)			
Week 36 (n=28)	-2.9 (± 5.65)			
Week 48 (n=24)	-4.4 (± 4.85)			
Week 60 (n=20)	-4.5 (± 5.85)			
Week 72 (n=17)	-5.3 (± 5.53)			
Week 84 (n=17)	-4.8 (± 5.2)			
Week 96 (n=13)	-4 (± 5.46)			
Week 108 (n=9)	-1.1 (± 4.73)			
Week 120 (n=3)	-1.3 (± 2.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Swollen Joint Count (SJC66): Mean Change from Baseline to Each Visit

End point title	Swollen Joint Count (SJC66): Mean Change from Baseline to Each Visit

End point description:

Sixty-six joints were assessed by physical examination. The joints to be examined for swelling were the same as those examined for tenderness, except that the hip, subtalar, sacroiliac, lumbar spine, thoracic spine, and cervical spine joints were excluded. Joint swelling was classified as present ("1"), absent ("0") or replaced/injected ("9"). Scores range from 0 to 594, with higher scores representing higher disease activity. Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis.
n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 8, 12, 16, 20, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 2 (n=32)	-4.5 (± 6.46)			
Week 4 (n=32)	-5.3 (± 6.63)			
Week 8 (n=32)	-6 (± 5.32)			

Week 12 (n=31)	-6.2 (± 4.24)			
Week 16 (n=31)	-6.1 (± 6.59)			
Week 20 (n=29)	-6.9 (± 5.62)			
Week 24 (n=30)	-6.3 (± 5.83)			
Week 36 (n=28)	-6.2 (± 4.73)			
Week 48 (n=24)	-6.7 (± 5.34)			
Week 60 (n=20)	-8.4 (± 7.15)			
Week 72 (n=17)	-8.9 (± 6.06)			
Week 84 (n=17)	-9.4 (± 7.15)			
Week 96 (n=13)	-8.5 (± 6.89)			
Week 108 (n=9)	-5.8 (± 3.31)			
Week 120 (n=3)	-7.3 (± 2.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pain on Passive Motion (POM75) Joint Count: Mean Change from Baseline to Each Visit

End point title	Pain on Passive Motion (POM75) Joint Count: Mean Change from Baseline to Each Visit

End point description:

Seventy-five joints were assessed by physical examination. The joints to be examined for POM were the same as those examined for tenderness. POM of the joint was classified as present ("1"), absent ("0"), or replaced/injected ("9"). Scores range from 0 to 675, with higher scores representing higher disease activity. Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 8, 12, 16, 20, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 2 (n=32)	-3.3 (± 4.5)			
Week 4 (n=32)	-4 (± 4.01)			
Week 8 (n=32)	-4.6 (± 5.17)			
Week 12 (n=31)	-4.9 (± 4.59)			
Week 16 (n=31)	-4.9 (± 4.6)			
Week 20 (n=29)	-5.4 (± 4.81)			
Week 24 (n=30)	-4.1 (± 7.32)			
Week 36 (n=28)	-4.3 (± 7.34)			
Week 48 (n=24)	-5.8 (± 4.42)			
Week 60 (n=20)	-5.9 (± 5.25)			
Week 72 (n=17)	-6.4 (± 5.41)			

Week 84 (n=17)	-6.1 (± 5.34)			
Week 96 (n=13)	5.7 (± 5.12)			
Week 108 (n=9)	-3.6 (± 5.85)			
Week 120 (n=3)	-5.3 (± 1.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Global Health Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Global Health Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=29)	17.1 (± 29.48)			
Week 24 (n=28)	24.3 (± 25.77)			
Week 36 (n=24)	25 (± 27.27)			
Week 48 (n=22)	30.9 (± 23.79)			
Week 60 (n=19)	21.8 (± 27.35)			
Week 72 (n=17)	31.5 (± 24.86)			
Week 84 (n=17)	26.2 (± 25.89)			
Week 96 (n=11)	32.7 (± 20.66)			
Week 108 (n=8)	36.9 (± 19.99)			
Week 120 (n=3)	45 (± 17.32)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Physical

Functioning Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Physical Functioning Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120.

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=31)	30.6 (± 32.14)			
Week 24 (n=30)	31.6 (± 31.91)			
Week 36 (n=27)	36.4 (± 31.26)			
Week 48 (n=23)	31.5 (± 28.39)			
Week 60 (n=21)	29 (± 32.3)			
Week 72 (n=16)	40.6 (± 27)			
Week 84 (n=17)	40 (± 30.44)			
Week 96 (n=13)	34.3 (± 27.88)			
Week 108 (n=9)	37 (± 27.92)			
Week 120 (n=3)	53.7 (± 8.49)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Role/Social Limitations/Emotional/Behavioral Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Role/Social Limitations/Emotional/Behavioral Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=23)	20.8 (± 32.53)			
Week 24 (n=22)	17.7 (± 29.43)			
Week 36 (n=20)	17.2 (± 25.86)			
Week 48 (n=18)	16 (± 27.28)			
Week 60 (n=16)	20.8 (± 31.91)			
Week 72 (n=13)	26.5 (± 32.25)			
Week 84 (n=13)	20.5 (± 33.29)			
Week 96 (n=9)	30.9 (± 32.76)			
Week 108 (n=7)	23.8 (± 25.2)			
Week 120 (n=2)	33.3 (± 47.14)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Role/Social Limitations – Physical Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Role/Social Limitations – Physical Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120.

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=21)	28.6 (± 32.97)			
Week 24 (n=20)	31.7 (± 35)			
Week 36 (n=18)	30.6 (± 39.3)			

Week 48 (n=17)	27.5 (± 37.24)			
Week 60 (n=15)	34.4 (± 39.07)			
Week 72 (n=12)	36.1 (± 41.34)			
Week 84 (n=12)	34.7 (± 43.5)			
Week 96 (n=8)	41.7 (± 37.8)			
Week 108 (n=6)	47.2 (± 37.14)			
Week 120 (n=1)	66.7 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Bodily Pain/Discomfort Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Bodily Pain/Discomfort Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=30)	35 (± 30.6)			
Week 24 (n=29)	36.2 (± 32.99)			
Week 36 (n=26)	38.8 (± 27.76)			
Week 48 (n=23)	41.7 (± 29.64)			
Week 60 (n=20)	39 (± 34.78)			
Week 72 (n=17)	48.2 (± 20.38)			
Week 84 (n=17)	41.2 (± 25.47)			
Week 96 (n=13)	42.3 (± 23.51)			
Week 108 (n=9)	41.1 (± 37.56)			
Week 120 (n=3)	50 (± 17.32)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Behavior Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Behavior Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=29)	5.6 (± 15.78)			
Week 24 (n=28)	4.2 (± 13.58)			
Week 36 (n=27)	0.4 (± 16.87)			
Week 48 (n=24)	3.6 (± 17.04)			
Week 60 (n=21)	-0.3 (± 13.95)			
Week 72 (n=17)	0.1 (± 16.44)			
Week 84 (n=17)	1.5 (± 13.97)			
Week 96 (n=13)	7.1 (± 11.81)			
Week 108 (n=9)	8.9 (± 10.46)			
Week 120 (n=3)	-6.1 (± 31.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Global Behavior Item: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Global Behavior Item: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=19)	4.5 (± 18.17)			
Week 24 (n=19)	10.8 (± 17.66)			
Week 36 (n=18)	9.2 (± 25.04)			
Week 48 (n=16)	4.1 (± 18.55)			
Week 60 (n=13)	-3.5 (± 20.35)			
Week 72 (n=10)	2 (± 15.31)			
Week 84 (n=11)	-5 (± 14.32)			
Week 96 (n=9)	0 (± 17.68)			
Week 108 (n=6)	-4.2 (± 10.21)			
Week 120 (n=1)	-25 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Mental Health Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Mental Health Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=31)	3.5 (± 11.12)			
Week 24 (n=30)	3.5 (± 10.76)			

Week 36 (n=27)	4.1 (± 14.01)			
Week 48 (n=24)	5.4 (± 11.88)			
Week 60 (n=21)	2.1 (± 14.02)			
Week 72 (n=17)	5 (± 12.37)			
Week 84 (n=17)	2.6 (± 8.5)			
Week 96 (n=13)	4.2 (± 11.88)			
Week 108 (n=9)	-0.8 (± 15)			
Week 120 (n=3)	-3.3 (± 20.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Self Esteem Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Self Esteem Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=23)	10.6 (± 23.91)			
Week 24 (n=22)	10.5 (± 24.75)			
Week 36 (n=19)	16.8 (± 22.02)			
Week 48 (n=16)	15.2 (± 22.6)			
Week 60 (n=14)	10.2 (± 22.53)			
Week 72 (n=13)	-2.8 (± 31.78)			
Week 84 (n=13)	9.4 (± 18.52)			
Week 96 (n=9)	6.9 (± 19.87)			
Week 108 (n=6)	-4.2 (± 10.87)			
Week 120 (n=1)	4.2 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) General Health Perceptions Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) General Health Perceptions Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=26)	0.7 (± 14.27)			
Week 24 (n=25)	3.8 (± 14.98)			
Week 36 (n=22)	6.2 (± 15.99)			
Week 48 (n=19)	7.2 (± 13.36)			
Week 60 (n=18)	0.7 (± 10.65)			
Week 72 (n=15)	9.1 (± 10.1)			
Week 84 (n=15)	7.2 (± 13.03)			
Week 96 (n=11)	10.9 (± 16)			
Week 108 (n=7)	9 (± 16.61)			
Week 120 (n=3)	4.7 (± 12.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Change in Health Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Change in Health Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=30)	1.4 (± 1.75)			
Week 24 (n=29)	1.7 (± 1.67)			
Week 36 (n=25)	1.7 (± 1.8)			
Week 48 (n=22)	1.7 (± 2.4)			
Week 60 (n=20)	1.3 (± 2.57)			
Week 72 (n=16)	1.6 (± 2.13)			
Week 84(n=16)	1.3 (± 1.98)			
Week 96 (n=12)	1.5 (± 2.02)			
Week 108 (n=8)	0.9 (± 2.7)			
Week 120 (n=3)	2.3 (± 0.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Parental Impact - Emotional Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Parental Impact - Emotional Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=30)	11.4 (± 26.12)			
Week 24 (n=28)	19 (± 28.59)			
Week 36 (n=26)	29.2 (± 33.1)			
Week 48 (n=23)	34.1 (± 33.98)			
Week 60 (n=20)	31.7 (± 32.4)			
Week 72 (n=16)	34.4 (± 36.37)			
Week 84 (n=16)	27.6 (± 41.69)			
Week 96 (n=11)	43.9 (± 40.15)			
Week 108 (n=8)	46.9 (± 40.81)			
Week 120 (n=2)	62.5 (± 41.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Parental Impact - Time Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Parental Impact - Time Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=30)	4.6 (± 24.5)			
Week 24 (n=28)	13.5 (± 28.59)			
Week 36 (n=26)	21.8 (± 24.24)			
Week 48 (n=23)	18.4 (± 24.76)			
Week 60 (n=20)	13.3 (± 31.55)			
Week 72 (n=16)	22.2 (± 30.09)			
Week 84 (n=16)	17.4 (± 35.13)			

Week 96 (n=12)	20.4 (± 27.15)			
Week 108 (n=8)	15.3 (± 25.85)			
Week 120 (n=2)	55.6 (± 62.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Family Activities Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Family Activities Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=30)	8.3 (± 28.41)			
Week 24 (n=28)	17.6 (± 24.15)			
Week 36 (n=26)	20 (± 28.5)			
Week 48 (n=23)	16.8 (± 26.43)			
Week 60 (n=20)	14.8 (± 30.9)			
Week 72 (n=16)	17.2 (± 31.43)			
Week 84 (n=16)	18.2 (± 30.27)			
Week 96 (n=12)	19.4 (± 27.6)			
Week 108 (n=8)	20.8 (± 29.38)			
Week 120 (n=2)	68.8 (± 20.62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Child's Health Questionnaire Parent Form (CHQ-PF50) Family Cohesion Category: Mean Change from Baseline to Each Visit

End point title	Child's Health Questionnaire Parent Form (CHQ-PF50) Family Cohesion Category: Mean Change from Baseline to Each Visit

End point description:

The CHQ-PF50 is a subject-reported outcome measure that includes 50 questions related to physical and mental health, social limitations, and impact on parents and family. Scores for each category were converted to a scale from 0 (implies higher disease activity) to 100 (implies lower disease activity). Baseline is defined as the last nonmissing value prior to the first dose of study drug. Subjects with nonmissing Baseline and at least 1 postbaseline observation are included in the analysis. n=subjects with a nonmissing value at baseline and each visit.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, and 120

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=30)	2.5 (± 14)			
Week 24 (n=28)	4.3 (± 23.28)			
Week 36 (n=26)	5.6 (± 20.66)			
Week 48 (n=23)	3.7 (± 15.61)			
Week 60 (n=20)	4.8 (± 16.66)			
Week 72 (n=16)	7.2 (± 29.15)			
Week 84 (n=16)	8.4 (± 39.19)			
Week 96 (n=12)	18.8 (± 35.36)			
Week 108 (n=8)	19.4 (± 35.3)			
Week 120 (n=2)	-27.5 (± 38.89)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs were collected from first dose of study drug until 70 days after the last dose of study drug and before start of commercial adalimumab or other biologics (32.5 months); SAEs were collected from the time informed consent was obtained (33.5 months)

Adverse event reporting additional description:

A treatment-emergent AE (TEAE) is defined as any AE with onset or worsening reported by a subject from the time that the first dose of adalimumab is administered until 5 half-lives (70 days) have elapsed following discontinuation of adalimumab administration. TEAEs were collected whether elicited or spontaneously reported by the subject.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Adalimumab

Reporting group description:

Adalimumab 24 mg/m^2 body surface area (BSA) up to a total dose of 20 mg administered every other week (eow) by parent or designee as a single dose via subcutaneous injection at approximately the same time of day, for a minimum of 24 weeks. Subjects could continue in the study until age 4 and 15 kg (US and Puerto Rico) or for up to 1 additional year after reaching age 4 and 15 kg (EU).Visits beyond Week 24 occurred every 12 weeks for those subjects who continued in the study.

Serious adverse events	Adalimumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 32 (15.63%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Juvenile arthritis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis rotavirus			

subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Varicella			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Adalimumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 32 (84.38%)		
Investigations			
Body temperature increased			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	3		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	7 / 32 (21.88%)		
occurrences (all)	11		
Eye disorders			

Uveitis subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 4 / 32 (12.50%) 4 5 / 32 (15.63%) 5		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	 6 / 32 (18.75%) 11 6 / 32 (18.75%) 7		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 4 / 32 (12.50%) 5		
Musculoskeletal and connective tissue disorders Juvenile arthritis subjects affected / exposed occurrences (all)	 4 / 32 (12.50%) 9		
Infections and infestations Acute tonsillitis subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Cystitis subjects affected / exposed occurrences (all) Ear infection	 2 / 32 (6.25%) 4 6 / 32 (18.75%) 7 2 / 32 (6.25%) 2 		

subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	4		
Gastroenteritis			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	4		
Gastroenteritis viral			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
H1N1 influenza			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	8 / 32 (25.00%)		
occurrences (all)	11		
Otitis media			
subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	9		
Pharyngitis			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	6		
Pharyngitis streptococcal			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Pneumonia			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Rhinitis			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	5		
Sinusitis			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	6 / 32 (18.75%)		
occurrences (all)	11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 August 2008	To add study visits to gather additional safety data and to shorten the intervals between visits, and change study duration from based on age (10 years) to based on age and weight.
08 January 2009	To clarify and update study procedures; include BSA dosing and dosing diaries; and update criteria for JIA diagnosis to include International League of Associations for Rheumatology (ILAR) classification.
06 July 2009	To extend the study population to include children in the EU who meet the study criteria; update the classification of JIA to add back in 'moderately to severely' in the description and to include polyarticular course JIA; revise inclusion exclusion criteria for safety reasons (eg, normal cardiopulmonary and neurological exams, parent/legal guardian responsible for storage and handling of study drug, procedures following positive purified protein derivative [PPD] test, and exclusionary concomitant medications); update conditions in which a subject should be withdrawn; and include (EU) and update (US) injection instructions for adalimumab.
29 October 2009	To extend the study for subjects in the EU who have reached 4 years of age and weight ≥ 15 kg for up to 1 additional year to allow time for transition to an appropriate treatment.
23 August 2010	To add anti-adalimumab antibody (AAA) assay; clarify that subjects beginning commercial adalimumab immediately after the trial will not be required to have a 70-day follow-up call; expand anti-nuclear antibody (ANA)/double-stranded DNA (dsDNA) test to include US subjects; and include previous Disease-Modifying Anti-Rheumatic Drug (DMARD) failure as part of inclusion criteria for subjects in the EU.
01 May 2012	To include annual tuberculosis tests.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported