Clinical trial results:
A Multicenter Open-label Study of the Human Anti-TNF Monoclonal Antibody Adalimumab to Investigate Efficacy, Safety and Pharmacokinetics after Dose Escalation in Japanese Subjects with Crohn's Disease

Summary

EudraCT number	2015-004121-13
Trial protocol	Outside EU/EEA
Global end of trial date	01 October 2015

Results information

Result version number	v1 (current)
This version publication date	09 April 2016
First version publication date	09 April 2016

Trial information

Trial identification

Sponsor protocol code	M13-687

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01958827
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	Morio Ozawa, MS, AbbVie GK, morio.ozawa@abbvie.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	01 October 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to investigate the efficacy, safety and pharmacokinetics after dose escalation in Japanese subjects with Crohn's Disease.

Protection of trial subjects:

Subject and/or representative and/or legal guardian (if subject was < 20 years old) read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2013
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	Japan: 28
Worldwide total number of subjects	28
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)	0
Adolescents (12-17 years)	1
Adults (18-64 years)	27
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included a 21-day screening period. A total of 28 subjects were enrolled and were included in the Full Analysis Set (FAS: All enrolled subjects who received at least one dose of study drug and had at least one post-treatment efficacy assessment).

Period 1

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

Arms

Arm title	Adalimumab 80 mg

Arm description:

All subjects were to receive subcutaneous injections of open-label adalimumab 80 mg every other week from Week 0 to Week 50.

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 pre-filled syringe, administered by subcutaneous injection.

Number of subjects in period 1	Adalimumab 80 mg
Started	28
Completed	18
Not completed	10
Concomitant prohibited medicine for AE	1
Adverse event	3
Lack of efficacy	6

Baseline characteristics

Reporting groups	
Reporting group title	Adalimumab 80 mg
Reporting group description:	
All subjects were to receive subcutaneous injections of open-label adalimumab 80 mg every other week from Week 0 to Week 50.	

Reporting group values	Adalimumab 80 mg	Total	
Number of subjects	28	28	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	33.6		
standard deviation	± 10.09	-	
Gender categorical			
Units: Subjects			
Female	12	12	
Male	16	16	

End points

End points reporting groups

Reporting group title	Adalimumab 80 mg

Reporting group description:

All subjects were to receive subcutaneous injections of open-label adalimumab 80 mg every other week from Week 0 to Week 50.

Primary: Percentage of Subjects Who Achieved Clinical Response 50 (CR50; Crohn's Disease Activity Index [CDAI] Decrease ≥ 50 From Week 0) at Week 8

End point title	Percentage of Subjects Who Achieved Clinical Response 50 (CR50; Crohn's Disease Activity Index [CDAI] Decrease ≥ 50 From Week 0) at Week 8[1]

End point description:

CDAI is used to quantify the signs and symptoms of patients with Crohn's Disease. A score below 150 indicates remission and a score above 450 indicates severe disease. Non-responder imputation (NRI) for missing CDAI observations was used.

End point type	Primary

End point timeframe:

Week 8

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 are summarized for this end point per protocol.

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[2]			
Units: percentage of subjects				
number (confidence interval 95%)	75 (55.1 to 89.3)			

Notes:

[2] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved Clinical Remission (CDAI < 150) Every 4 Weeks up to Week 52

End point title	Percentage of Subjects Who Achieved Clinical Remission (CDAI < 150) Every 4 Weeks up to Week 52

End point description:

CDAI is used to quantify the signs and symptoms of patients with Crohn's Disease. A score below 150 indicates remission and a score above 450 indicates severe disease. Non-responder imputation (NRI) for missing CDAI observations was used.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[3]			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4	14.3 (4 to 32.7)			
Week 8	25 (10.7 to 44.9)			
Week 12	28.6 (13.2 to 48.7)			
Week 16	32.1 (15.9 to 52.4)			
Week 20	35.7 (18.6 to 55.9)			
Week 24	42.9 (24.5 to 62.8)			
Week 28	35.7 (18.6 to 55.9)			
Week 32	42.9 (24.5 to 62.8)			
Week 36	39.3 (21.5 to 59.4)			
Week 40	39.3 (21.5 to 59.4)			
Week 44	42.9 (24.5 to 62.8)			
Week 48	39.3 (21.5 to 59.4)			
Week 52	35.7 (18.6 to 55.9)			

Notes:

[3] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved Clinical Response 50 (CR50; Crohn's Disease Activity Index [CDAI] Decrease ≥ 50 From Week 0) Every 4 Weeks up to Week 52

End point title	Percentage of Subjects Who Achieved Clinical Response 50 (CR50; Crohn's Disease Activity Index [CDAI] Decrease ≥ 50 From Week 0) Every 4 Weeks up to Week 52

End point description:

CDAI is used to quantify the signs and symptoms of patients with Crohn's Disease. A score below 150 indicates remission and a score above 450 indicates severe disease. Non-responder imputation (NRI) for missing CDAI observations was used. Week 8 was the primary outcome measure.

End point type	Secondary

End point timeframe:

Weeks 4, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[4]			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4	67.9 (47.6 to 84.1)			
Week 12	67.9 (47.6 to 84.1)			
Week 16	67.9 (47.6 to 84.1)			
Week 20	67.9 (47.6 to 84.1)			
Week 24	71.4 (51.3 to 86.8)			
Week 28	64.3 (44.1 to 81.4)			
Week 32	71.4 (51.3 to 86.8)			
Week 36	67.9 (47.6 to 84.1)			
Week 40	64.3 (44.1 to 81.4)			
Week 44	60.7 (40.6 to 78.5)			
Week 48	64.3 (44.1 to 81.4)			
Week 52	57.1 (37.2 to 75.5)			

Notes:

[4] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved Clinical Response 70 (CR70; Crohn's Disease Activity Index [CDAI] Decrease ≥ 70 From Week 0) Every 4 Weeks up to Week 52

End point title	Percentage of Subjects Who Achieved Clinical Response 70 (CR70; Crohn's Disease Activity Index [CDAI] Decrease ≥ 70 From Week 0) Every 4 Weeks up to Week 52

End point description:

CDAI is used to quantify the signs and symptoms of patients with Crohn's Disease. A score below 150 indicates remission and a score above 450 indicates severe disease. Non-responder imputation (NRI) for missing CDAI observations was used.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[5]			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4	46.4 (27.5 to 66.1)			
Week 8	57.1 (37.2 to 75.5)			
Week 12	64.3 (44.1 to 81.4)			
Week 16	64.3 (44.1 to 81.4)			
Week 20	64.3 (44.1 to 81.4)			
Week 24	67.9 (47.6 to 84.1)			
Week 28	64.3 (44.1 to 81.4)			
Week 32	67.9 (47.6 to 84.1)			
Week 36	64.3 (44.1 to 81.4)			
Week 40	60.7 (40.6 to 78.5)			
Week 44	57.1 (37.2 to 75.5)			
Week 48	60.7 (40.6 to 78.5)			
Week 52	57.1 (37.2 to 75.5)			

Notes:

[5] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved Clinical Response 100 (CR100; Crohn's Disease Activity Index [CDAI] Decrease of 100 From Week 0) Every 4 Weeks up to Week 52

End point title	Percentage of Subjects Who Achieved Clinical Response 100 (CR100; Crohn's Disease Activity Index [CDAI] Decrease of 100 From Week 0) Every 4 Weeks up to Week 52

End point description:

CDAI is used to quantify the signs and symptoms of patients with Crohn's Disease. A score below 150 indicates remission and a score above 450 indicates severe disease. Non-responder imputation (NRI) for missing CDAI observations was used.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[6]			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 4	32.1 (15.9 to 52.4)			
Week 8	35.7 (18.6 to 55.9)			
Week 12	39.3 (21.5 to 59.4)			
Week 16	46.4 (27.5 to 66.1)			
Week 20	50 (30.6 to 69.4)			
Week 24	50 (30.6 to 69.4)			
Week 28	42.9 (24.5 to 62.8)			
Week 32	50 (30.6 to 69.4)			
Week 36	50 (30.6 to 69.4)			
Week 40	57.1 (37.2 to 75.5)			
Week 44	46.4 (27.5 to 66.1)			
Week 48	50 (30.6 to 69.4)			
Week 52	46.4 (27.5 to 66.1)			

Notes:

[6] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: C-reactive Protein (CRP): Mean Change From Baseline (Week 0) to Week 52

End point title	C-reactive Protein (CRP): Mean Change From Baseline (Week 0) to Week 52

End point description:

C-reactive protein (CRP) was measured from blood samples as a marker for inflammation. Higher levels are indicative of more inflammation. Normal concentration in healthy human serum is usually lower than 0.3 mg/dL, slightly increasing with age. Last Observation Carried Forward (LOCF) was used for missing data.

End point type	Secondary

End point timeframe:

Baseline (Week 0) and Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[7]			
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 4	-0.57 (± 1.4902)			
Week 8	-0.426 (± 1.6072)			
Week 12	-0.71 (± 1.6769)			
Week 16	-0.923 (± 1.6981)			
Week 20	-0.907 (± 1.7532)			
Week 24	-0.813 (± 1.7924)			
Week 28	-0.833 (± 1.882)			
Week 32	-0.853 (± 2.0507)			
Week 36	-0.586 (± 2.3271)			
Week 40	-1.008 (± 2.0471)			
Week 44	-0.915 (± 2.2324)			
Week 48	-0.649 (± 2.5734)			
Week 52	-0.57 (± 2.7635)			

Notes:

[7] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potentially Significant Hematology Parameters

End point title	Number of Subjects With Potentially Significant Hematology Parameters

End point description:

Blood was collected for analysis at designated study visits; hematology results were provided by each site laboratory. The number of subjects with an abnormal laboratory result (higher than upper limit of normal [ULN] or lower than lower limit of normal [LLN]) meeting Common Toxicity Criteria (CTC) of Grade 3 or higher is summarized. Increase is signified by . n=the number of participants with CTC Grade <3 at baseline and a post-baseline value for each parameter.

End point type	Secondary

End point timeframe:

52 weeks

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[8]			
Units: subjects				
Haemoglobin <8 g/dL (n=27)	1			
Haemoglobin >4.0 g/dL (n=28)	0			
Platelet Count <5.0x10^4/mcL (n=28)	0			
White Blood Cells <2.0x10^3/mcL (n=28)	0			
Neutrophils <1.0x10^3/mcL(n=28)	0			
Lymphocytes <0.5x10^3/mcL (n=28)	4			

Notes:

[8] - Safety Analysis Set: All enrolled subjects who received at least one dose of study drug

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potentially Significant Clinical Chemistry Parameters

End point title	Number of Subjects With Potentially Significant Clinical Chemistry Parameters

End point description:

Blood was collected for analysis at designated study visits; chemistry results were provided by a central laboratory. The number of subjects with an abnormal laboratory result (higher than upper limit of normal [ULN] or lower than lower limit of normal [LLN]) meeting Common Toxicity Criteria (CTC) of Grade 3 or higher is summarized. n=the number of participants with CTC Grade <3 at baseline and a post-baseline value for each parameter.

End point type	Secondary

End point timeframe:

52 weeks

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[9]			
Units: subjects				
Alanine Aminotransferase >5xULN (n=28)	0			
Aspartate Aminotransferase >5xULN (n=28)	0			
Gamma-glutamyl Transpeptidase >5x ULN (n=28)	0			
Alkaline Phosphatase >5xU/L (n=28)	0			
Total Bilirubin >3xULN (n=28)	0			
Creatine Phosphokinase >5x ULN (n=28)	1			

Creatinine >3xULN or >3xBL (n=28)	0			
Uric Acid >10.0 mg/dL (n=28)	0			
Inorganic Phosphate <2.0 mg/dL (n=28)	3			
Calcium <7.0 mg/dL (n=28)	1			
Calcium >12.5 mg/dL (n=28)	0			
Sodium <130 mEq/L (n=28)	0			
Sodium >155 mEq/L (n=28)	0			
Potassium <3.0 mEq/L (n=27)	0			
Potassium >6.0 mEq/L (n=28)	0			
Non-fasting Glucose <40 mg/dL (n=28)	0			
Non-fasting Glucose >250 mg/dL (n=28)	0			
Albumin <2.0 g/dL (n=28)	0			
Cholesterol >400 mg/dL (n=28)	0			
Triglycerides >500 mg/dL (n=28)	0			
Magnesium <0.9 mg/dL (n=28)	0			
Magnesium >3.0 mg/dL (n=28)	0			

Notes:

[9] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Systolic Blood Pressure: Mean Change From Baseline (Week 0) to Each Visit

End point title	Systolic Blood Pressure: Mean Change From Baseline (Week 0) to Each Visit

End point description:

Blood pressure was measured while the subject was sitting. n=the number of subjects with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0) and Weeks 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[10]			
Units: mm Hg				
arithmetic mean (standard deviation)				
Week 2 (n=28)	-3.9 (± 11.98)			
Week 4 (n=28)	-2.5 (± 9.41)			
Week 8 (n=25)	-1.1 (± 9.98)			
Week 12 (n=21)	-1.3 (± 9.34)			
Week 16 (n=21)	-0.2 (± 11.72)			
Week 20 (n=20)	1.9 (± 12.64)			
Week 24 (n=20)	2 (± 8.89)			
Week 28 (n=20)	0.8 (± 8.91)			

Week 32 (n=20)	-1.7 (± 7.41)			
Week 36 (n=20)	-0.5 (± 10.79)			
Week 40 (n=20)	2.3 (± 9.55)			
Week 44 (n=19)	1.9 (± 14.12)			
Week 48 (n=19)	4.6 (± 11.66)			
Week 52 (n=18)	-0.3 (± 9.41)			

Notes:

[10] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Diastolic Blood Pressure: Mean Change From Baseline (Week 0) to Each Visit

End point title	Diastolic Blood Pressure: Mean Change From Baseline (Week 0) to Each Visit

End point description:

Blood pressure was measured while the subject was sitting. n=the number of subjects with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0) and Weeks 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[11]			
Units: mm Hg				
arithmetic mean (standard deviation)				
Week 2 (n=28)	-0.6 (± 9.53)			
Week 4 (n=28)	0.2 (± 8.56)			
Week 8 (n=25)	0.7 (± 8.13)			
Week 12 (n=21)	1.1 (± 7.12)			
Week 16 (n=21)	0.1 (± 7.78)			
Week 20 (n=20)	0.8 (± 9.38)			
Week 24 (n=20)	0.8 (± 8.72)			
Week 28 (n=20)	-0.5 (± 7.81)			
Week 32 (n=20)	-0.8 (± 9.27)			
Week 36 (n=20)	-0.4 (± 10.27)			
Week 40 (n=20)	0.7 (± 10.66)			
Week 44 (n=19)	-1.2 (± 8.57)			
Week 48 (n=19)	1.3 (± 8.48)			
Week 52 (n=18)	3 (± 11.97)			

Notes:

[11] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Heart Rate: Mean Change From Baseline (Week 0) to Each Visit

End point title	Heart Rate: Mean Change From Baseline (Week 0) to Each Visit

End point description:

Heart rate was measured while the subject was sitting. n=the number of subjects with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0) and Weeks 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[12]			
Units: bpm				
arithmetic mean (standard deviation)				
Week 2 (n=28)	-0.3 (± 11.94)			
Week 4 (n=28)	0.7 (± 12.78)			
Week 8 (n=25)	-1.1 (± 9.48)			
Week 12 (n=21)	-1.1 (± 11.59)			
Week 16 (n=21)	-1.9 (± 9.56)			
Week 20 (n=20)	-3 (± 8.68)			
Week 24 (n=20)	-0.9 (± 13.15)			
Week 28 (n=20)	-1.6 (± 11.3)			
Week 32 (n=20)	-5.6 (± 11.95)			
Week 36 (n=20)	-4.7 (± 12.88)			
Week 40 (n=20)	-3.7 (± 13.88)			
Week 44 (n=19)	-2 (± 10.78)			
Week 48 (n=19)	-1.3 (± 15.53)			
Week 52 (n=18)	-2.8 (± 11.8)			

Notes:

[12] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Body Temperature: Mean Change From Baseline (Week 0) to Each Visit

End point title	Body Temperature: Mean Change From Baseline (Week 0) to Each Visit

End point description:

n=the number of subjects with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0) and Weeks 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[13]			
Units: degrees Celsius				
arithmetic mean (standard deviation)				
Week 2 (n=28)	-0.03 (± 0.558)			
Week 4 (n=28)	-0.02 (± 0.571)			
Week 8 (n=25)	-0.08 (± 0.569)			
Week 12 (n=21)	-0.14 (± 0.606)			
Week 16 (n=21)	-0.11 (± 0.558)			
Week 20 (n=20)	-0.16 (± 0.545)			
Week 24 (n=20)	-0.2 (± 0.701)			
Week 28 (n=20)	-0.23 (± 0.716)			
Week 32 (n=20)	-0.26 (± 0.762)			
Week 36 (n=20)	-0.36 (± 0.476)			
Week 40 (n=20)	-0.16 (± 0.555)			
Week 44 (n=19)	-0.24 (± 0.472)			
Week 48 (n=19)	-0.03 (± 0.781)			
Week 52 (n=18)	-0.13 (± 0.717)			

Notes:

[13] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events (AEs)

End point title	Number of Subjects With Adverse Events (AEs)

End point description:

An AE is any untoward medical occurrence in a subject which does not necessarily have a causal relationship with this treatment. A serious AE (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent events (TEAEs or TESAE) are defined as any event that began or worsened in severity after the first dose of study drug. The investigator assessed the relationship of each event to the use of study drug as either Reasonable possibility or No reasonable possibility of being related to study drug.
For more details on adverse events please see the AE section below.

End point type	Secondary

End point timeframe:

60 weeks

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[14]			
Units: subjects				
Any TEAE	24			
TEAEs with reasonable possibility of being related	5			
Any severe TEAE	2			
TESAE	8			
Any TEAE Leading to Discontinuation of Study	4			
Death	0			

Notes:

[14] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in Mean Serum Adalimumab Concentration From Baseline (Week 0) to Week 52

End point title	Change in Mean Serum Adalimumab Concentration From Baseline (Week 0) to Week 52

End point description:

Blood samples were drawn prior to drug administration. Adalimumab concentrations in serum were determined using a validated heterogeneous electrochemiluminescence (ECL)-immunoassay method. The assay captures adalimumab via biotinylated anti-idiotypic antibody, and detects it via sulfo-tagged TNF-alpha. n=the number of subjects with available data at each time point.

End point type	Other pre-specified

End point timeframe:

Baseline (Week 0) to Week 52

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[15]			
Units: µg/mL				
arithmetic mean (standard deviation)				
Baseline (Week 0) (n=28)	3.06 (± 2.19)			
Week 52 (n=18)	9.47 (± 5.34)			

Notes:

[15] - All subjects in the FAS with available data at both time points

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in Number of Subjects Positive for Anti-Adalimumab Antibodies (AAA) From Baseline to Week 52

End point title	Change in Number of Subjects Positive for Anti-Adalimumab Antibodies (AAA) From Baseline to Week 52

End point description:

Serum samples with adalimumab concentration below 2 µg/mL were selected for AAA analyses. Samples were considered AAA positive if the measured AAA concentration was above 20 ng/mL. A subject was considered to be AAA positive if the subject had at least one AAA positive sample observed within 30 days following the subject's last adalimumab dose.

End point type	Other pre-specified

End point timeframe:

Baseline (Week 0) to Week 52

End point values	Adalimumab 80 mg			
Subject group type	Reporting group			
Number of subjects analysed	28[16]			
Units: subjects				
Baseline (Week 0)	3			
Week 52	4			

Notes:

[16] - FAS

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from the time of study drug administration until 70 days after last dose of study drug (60 weeks); SAEs were also collected from the time that informed consent was obtained until 70 days after last dose of study drug (up to 63 weeks).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Adalimumab 80 mg

Reporting group description:

All subjects were to receive subcutaneous injections of open-label adalimumab 80 mg every other week from Week 0 to Week 50.

Serious adverse events	Adalimumab 80 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 28 (28.57%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal ulcer haemorrhage			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	1 / 28 (3.57%)		
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	Adalimumab 80 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 28 (75.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pyrexia			

subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Female genital tract fistula			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Blood pressure increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Blood triglycerides increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nervous system disorders			

Headache			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Migraine			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Radiculopathy			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Leukopenia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Aphthous stomatitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Cheilitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Dental caries			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Ileus paralytic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Stomatitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	4		
Urticaria			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		

Bronchitis			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Candida infection			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Infection			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Mycoplasma infection			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	13 / 28 (46.43%)		
occurrences (all)	19		
Otitis externa			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Periodontitis			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Postoperative abscess			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pulpitis dental			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		

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