



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 standard deviation | 33.6 ± 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 \geq 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 \geq 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 \geq 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 \geq 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 \geq 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 \geq 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: | |
| <p>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.</p> <p>For more details on adverse events please see the AE section below.</p> | |
| 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 occurrences (all) | 2 / 28 (7.14%) 2 | | |
| Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | | |
| Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all) Female genital tract fistula subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 | | |
| Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) Blood pressure increased subjects affected / exposed occurrences (all) Blood triglycerides increased subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 1 / 28 (3.57%) 2 1 / 28 (3.57%) 1 | | |
| Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | | |
| Nervous system disorders | | | |

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

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

| | | | |
|-----------------------------------|------------------|--|--|
| 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