



Clinical trial results:

A Multicenter, Open-label Study of the Safety, Efficacy, and Pharmacokinetics of the Human Anti-TNF Monoclonal Antibody Adalimumab in Children With Polyarticular Juvenile Rheumatoid Arthritis

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2014-004558-33 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 05 September 2011 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 20 April 2016 |
| First version publication date | 13 June 2015 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | M10-240 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00690573 |
| 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 | Shigeki Hashimoto, AbbVie, shigeki.hashimoto@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 | 05 September 2011 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 05 September 2011 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate efficacy, safety and pharmacokinetics of adalimumab in Japanese children with Polyarticular Juvenile Rheumatoid Arthritis

Protection of trial subjects:

Subject and/or legal guardian read and understood information provided about the study and gave written permission. If a subject had an ability to provide an assent to participating in the clinical trial, the subject provided written informed assent. If a subject could not provide his/her signature, the investigator or clinical trial support staff confirmed the subject's willingness and recorded it.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 19 May 2008 |
| 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: 25 |
| Worldwide total number of subjects | 25 |
| 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) | 8 |
| Adolescents (12-17 years) | 17 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adalimumab dose was determined by baseline body weight (20 mg for subjects weighing < 30 kg, 40 mg for subjects weighing 30 kg or more) through Week 14. After Week 16, dose was based on body weight measured at Week 16 and every 12 weeks. Twenty subjects received concomitant methotrexate therapy during the study.

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 administered subcutaneously every other week, with dosage determined by body weight at study entry (20 mg for children weighing less than 30 kg, 40 mg for children weighing 30 kg or more).

| | |
|--|------------------------|
| 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 subcutaneously every other week, with dosage determined by body weight at study entry (20 mg for children weighing less than 30 kg, 40 mg for children weighing 30 kg or more).

| Number of subjects in period 1 | Adalimumab |
|--------------------------------|------------|
| Started | 25 |
| Completed | 16 |
| Not completed | 9 |
| Consent withdrawn by subject | 1 |
| Lack of efficacy | 8 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Adalimumab |
|-----------------------|------------|

Reporting group description:

Adalimumab administered subcutaneously every other week, with dosage determined by body weight at study entry (20 mg for children weighing less than 30 kg, 40 mg for children weighing 30 kg or more).

| Reporting group values | Adalimumab | Total | |
|--|------------|-------|--|
| Number of subjects | 25 | 25 | |
| Age Categorical Units: participants | | | |
| <=18 years | 25 | 25 | |
| Between 18 and 65 years | 0 | 0 | |
| >=65 years | 0 | 0 | |
| Age Continuous Units: years | | | |
| arithmetic mean | 13 | | |
| standard deviation | ± 3.38 | - | |
| Gender, Male/Female Units: participants | | | |
| Female | 20 | 20 | |
| Male | 5 | 5 | |

End points

End points reporting groups

| | |
|---|------------|
| Reporting group title | Adalimumab |
| Reporting group description: | |
| Adalimumab administered subcutaneously every other week, with dosage determined by body weight at study entry (20 mg for children weighing less than 30 kg, 40 mg for children weighing 30 kg or more). | |

Primary: Number of subjects achieving Pediatric American College of Rheumatology 30% (PedACR30) Response at Week 16

| | |
|-----------------|---|
| End point title | Number of subjects achieving Pediatric American College of Rheumatology 30% (PedACR30) Response at Week 16 ^[1] |
|-----------------|---|

End point description:

Response defined as at least 30% improvement in 3 or more of 6 juvenile rheumatoid arthritis (JRA) core set criteria, and at least 30% worsening in not more than 1 JRA criterion, compared with baseline. JRA core set criteria include physician's global assessment of disease severity; parent's/patient's global assessment of overall well-being; number of active joints (joints with swelling or with limitation of motion [LOM] and with pain, tenderness or both); number of joints with LOM; physical function of the Disability Index of Childhood Health Assessment Questionnaire; C-reactive protein. The analysis was conducted using the full analysis set (FAS) population, which was defined as all subjects who received at least one dose of study drug.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 16

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 | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: Participants | | | | |
| number (not applicable) | 23 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects achieving PedACR50 and PedACR70 Responses at Week 16

| | |
|-----------------|---|
| End point title | Number of subjects achieving PedACR50 and PedACR70 Responses at Week 16 |
|-----------------|---|

End point description:

Response defined as at least 50/70% improvement in 3 or more of 6 juvenile rheumatoid arthritis (JRA) core set criteria, and at least 50/70% worsening in not more than 1 JRA criterion compared with baseline. JRA core set criteria include physician's global assessment of disease severity; parent's/patient's global assessment of overall well-being; number of active joints (joints with swelling or with limitation of motion [LOM] and with pain, tenderness or both); number of joints with LOM; physical function of the Disability Index of Childhood Health Assessment Questionnaire; C-reactive protein. The analysis was conducted using the FAS population. Missing values were treated as non-

responders.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 16 | |

| | | | | |
|--|-----------------|--|--|--|
| End point values | Adalimumab | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Number of Subjects Achieving PedACR50 at Week 16 | 22 | | | |
| Number of Subjects Achieving PedACR70 at Week 16 | 15 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Achieving PedACR 30/50/70 Responses

| | |
|--|--|
| End point title | Number of Subjects Achieving PedACR 30/50/70 Responses |
| End point description: | |
| The analysis was conducted using the full analysis set FAS population as observed. N=25 at Weeks 2, 4, and the Final Visit; N=24 at Weeks 8, 24, and 36; N=23 at Week 48; N=22 at Week 60; N=19 at Weeks 72 and 96; N=11 at Week 120; and N=5 at Week 144. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 2, 4, 8, and 24, every 12 weeks from Week 24 to Week 60, and every 24 weeks from Week 72 to the final visit | |

| | | | | |
|--|-----------------|--|--|--|
| End point values | Adalimumab | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Number of subjects achieving PedACR30 at Week 2 | 15 | | | |
| Number of subjects achieving PedACR30 at Week 4 | 16 | | | |
| Number of subjects achieving PedACR30 at Week 8 | 19 | | | |
| Number of subjects achieving PedACR30 at Week 24 | 21 | | | |
| Number of subjects achieving PedACR30 at Week 36 | 22 | | | |

| | | | | |
|--|----|--|--|--|
| Number of subjects achieving PedACR30 at Week 48 | 21 | | | |
| Number of subjects achieving PedACR30 at Week 60 | 20 | | | |
| Number of subjects achieving PedACR30 at Week 72 | 19 | | | |
| Number of subjects achieving PedACR30 at Week 96 | 18 | | | |
| Number of subjects achieving PedACR30 at Week 120 | 11 | | | |
| Number of subjects achieving PedACR30 at Week 144 | 5 | | | |
| Number of subjects achieving PedACR30- Final Visit | 22 | | | |
| Number of subjects achieving PedACR50 at Week 2 | 7 | | | |
| Number of subjects achieving PedACR50 at Week 4 | 13 | | | |
| Number of subjects achieving PedACR50 at Week 8 | 15 | | | |
| Number of subjects achieving PedACR50 at Week 24 | 19 | | | |
| Number of subjects achieving PedACR50 at Week 36 | 22 | | | |
| Number of subjects achieving PedACR50 at Week 48 | 19 | | | |
| Number of subjects achieving PedACR50 at Week 60 | 20 | | | |
| Number of subjects achieving PedACR50 at Week 72 | 18 | | | |
| Number of subjects achieving PedACR50 at Week 96 | 18 | | | |
| Number of subjects achieving PedACR50 at Week 120 | 11 | | | |
| Number of subjects achieving PedACR50 at Week 144 | 5 | | | |
| Number of subjects achieving PedACR50- Final Visit | 20 | | | |
| Number of subjects achieving PedACR70 at Week 2 | 1 | | | |
| Number of subjects achieving PedACR70 at Week 4 | 7 | | | |
| Number of subjects achieving PedACR70 at Week 8 | 8 | | | |
| Number of subjects achieving PedACR70 at Week 24 | 15 | | | |
| Number of subjects achieving PedACR70 at Week 36 | 19 | | | |
| Number of subjects achieving PedACR70 at Week 48 | 17 | | | |
| Number of subjects achieving PedACR70 at Week 60 | 16 | | | |
| Number of subjects achieving PedACR70 at Week 72 | 15 | | | |
| Number of subjects achieving PedACR70 at Week 96 | 14 | | | |
| Number of subjects achieving PedACR70 at Week 120 | 11 | | | |
| Number of subjects achieving PedACR70 at Week 144 | 5 | | | |
| Number of subjects achieving PedACR70- Final Visit | 17 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean serum adalimumab concentration

| | |
|-----------------|-------------------------------------|
| End point title | Mean serum adalimumab concentration |
|-----------------|-------------------------------------|

End point description:

Blood samples were drawn prior to drug administration. Adalimumab concentrations in serum were determined using a validated enzyme-linked immunosorbent assay (ELISA) method based on a double-antigen technique. Concentrations are reported as micrograms per milliliter (mcg/mL). For the 20 mg dose, N = 8 at each timepoint. For the 40 mg dose, N = 17 at Weeks 2 and 4; N = 16 at Weeks 8, 16, and 24; N = 14 at Week 36; N = 15 at Week 48; and N = 14 at Week 60.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 2, 4, 8, 16, and 24, and every 12 weeks up to Week 60

| End point values | Adalimumab | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| 20 mg dose at Week 2 | 5.24 (± 1.74) | | | |
| 20 mg dose at Week 4 | 5.46 (± 5.18) | | | |
| 20 mg dose at Week 8 | 6.15 (± 5.88) | | | |
| 20 mg dose at Week 16 | 5.73 (± 5.26) | | | |
| 20 mg dose at Week 24 | 5.79 (± 6.51) | | | |
| 20 mg dose at Week 36 | 7.6 (± 7.58) | | | |
| 20 mg dose at Week 48 | 7.97 (± 6.69) | | | |
| 20 mg dose at Week 60 | 11.4 (± 9.87) | | | |
| 40 mg dose at Week 2 | 5.03 (± 1.45) | | | |
| 40 mg dose at Week 4 | 5.63 (± 2.71) | | | |
| 40 mg dose at Week 8 | 8.66 (± 4.41) | | | |
| 40 mg dose at Week 16 | 10.8 (± 6.15) | | | |
| 40 mg dose at Week 24 | 11.9 (± 6.8) | | | |
| 40 mg dose at Week 36 | 12.6 (± 6.44) | | | |
| 40 mg dose at Week 48 | 13 (± 8.89) | | | |
| 40 mg dose at Week 60 | 13.1 (± 6.73) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects positive for anti-adalimumab antibodies (AAA)

| | |
|-----------------|--|
| End point title | Number of subjects positive for anti-adalimumab antibodies (AAA) |
|-----------------|--|

End point description:

Serum samples with adalimumab concentration below 2 mcg/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 | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 60

| End point values | Adalimumab | | | |
|--|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Number of subjects with AAA by Week 24 | 4 | | | |
| Number of subjects with AAA by Week 60 | 6 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events reported from the time of first study drug administration until 70 days following discontinuation of study drug administration were collected.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 11.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Adalimumab |
|-----------------------|------------|

Reporting group description:

Adalimumab administered subcutaneously every other week, with dosage determined by body weight at study entry (20 mg for children weighing less than 30 kg, 40 mg for children weighing 30 kg or more).

| Serious adverse events | Adalimumab | | |
|--|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 25 (24.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Nervous system disorders | | | |
| Amnesia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pharyngolaryngeal pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Juvenile arthritis | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Hepatitis B | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Herpes zoster | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pharyngitis | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| alternative assessment type: | | | |
| Systematic | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |

| | | | |
|--|----------------|--|--|
| Dehydration | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 1 / 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 | 25 / 25 (100.00%) | | |
| General disorders and administration site conditions | | | |
| Injection site erythema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 4 / 25 (16.00%) | | |
| occurrences (all) | 4 | | |
| Injection site reaction | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| Malaise | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 3 | | |
| Pyrexia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 5 / 25 (20.00%) | | |
| occurrences (all) | 6 | | |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|----------------------|--|--|
| Cough alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 3 / 25 (12.00%) 3 | | |
| Pharyngolaryngeal pain alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 4 / 25 (16.00%) 5 | | |
| Rhinitis allergic alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 3 / 25 (12.00%) 3 | | |
| Rhinorrhoea alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 3 | | |
| Investigations Antinuclear antibody positive alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 3 | | |
| DNA antibody positive alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | | |
| Injury, poisoning and procedural complications Contusion alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | | |
| Hand fracture alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | | |
| Joint sprain | | | |

| | | | |
|--|--|--|--|
| alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 4 / 25 (16.00%) 5 | | |
| Nervous system disorders Headache alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 3 / 25 (12.00%) 16 | | |
| Blood and lymphatic system disorders Iron deficiency anaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 5 / 25 (20.00%) 6 | | |
| Eye disorders Conjunctivitis alternative assessment type: Systematic subjects affected / exposed occurrences (all) Conjunctivitis allergic alternative assessment type: Systematic subjects affected / exposed occurrences (all) Keratoconjunctivitis sicca alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 4 3 / 25 (12.00%) 3 2 / 25 (8.00%) 2 | | |
| Gastrointestinal disorders Abdominal pain alternative assessment type: Systematic subjects affected / exposed occurrences (all) Abdominal pain upper alternative assessment type: Systematic subjects affected / exposed occurrences (all) Constipation | 3 / 25 (12.00%) 3 2 / 25 (8.00%) 2 | | |

| | | | |
|--|---------------------------------|--|--|
| <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 25 (12.00%)</p> <p>4</p> | | |
| <p>Dental caries</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 25 (12.00%)</p> <p>3</p> | | |
| <p>Diarrhoea</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 25 (12.00%)</p> <p>3</p> | | |
| <p>Nausea</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 25 (12.00%)</p> <p>3</p> | | |
| <p>Stomatitis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 25 (8.00%)</p> <p>2</p> | | |
| <p>Vomiting</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 25 (8.00%)</p> <p>2</p> | | |
| <p>Hepatobiliary disorders</p> <p>Hepatic function abnormal</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 25 (8.00%)</p> <p>2</p> | | |
| <p>Skin and subcutaneous tissue disorders</p> <p>Acne</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dermatitis atopic</p> <p>alternative assessment type: Systematic</p> | <p>2 / 25 (8.00%)</p> <p>2</p> | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| Dermatitis bullous | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 3 | | |
| Eczema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 5 / 25 (20.00%) | | |
| occurrences (all) | 7 | | |
| Rash | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 4 / 25 (16.00%) | | |
| occurrences (all) | 5 | | |
| Urticaria | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 6 / 25 (24.00%) | | |
| occurrences (all) | 7 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| Juvenile arthritis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | | |
| occurrences (all) | 3 | | |
| Myalgia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 6 / 25 (24.00%) | | |
| occurrences (all) | 10 | | |
| Hordeolum | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 5 / 25 (20.00%) | | |
| occurrences (all) | 5 | | |
| Impetigo | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | | |
| occurrences (all) | 4 | | |
| Influenza | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 8 / 25 (32.00%) | | |
| occurrences (all) | 8 | | |
| Nasopharyngitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 14 / 25 (56.00%) | | |
| occurrences (all) | 33 | | |
| Oral herpes | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | | |
| occurrences (all) | 4 | | |
| Pharyngitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 8 / 25 (32.00%) | | |
| occurrences (all) | 12 | | |
| Upper respiratory tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 14 / 25 (56.00%) | | |
| occurrences (all) | 38 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 04 June 2008 | <ul style="list-style-type: none">- Updated the approval status of adalimumab.- Added the procedure to confirm subject's safety after the dose escalation.- Added the detailed explanation about when MTX dose was changed before the enrollment to the procedure for eligibility confirmation.- Changed the timing to conduct chest X-ray.- Changed the contact information of the sponsor. |
| 02 February 2009 | <ul style="list-style-type: none">- Changed the amount of MTX described in inclusion criteria #2 from 10 mg/m²/week to 8 to 10 mg/m²/week to relax this inclusion criterion.- Updated the approval status of adalimumab.- Extended the enrollment period. |
| 22 June 2009 | <ul style="list-style-type: none">- Added the criteria for interruption due to clinical remission.- Changed the procedure of the protocol deviation.- Changed the medical expert and adalimumab concentration assay institution. |
| 10 September 2010 | <ul style="list-style-type: none">- Deleted the section for Dose escalation |
| 27 May 2011 | <ul style="list-style-type: none">- Added the follow-up test at approval. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported