



Clinical trial results:

A Phase 3 Multicenter Study of the Safety and Efficacy of Adalimumab in Subjects with Moderate to Severe Hidradenitis Suppurativa - PIONEER I Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2011-003400-20 |
| Trial protocol | DE CZ HU |
| Global end of trial date | 16 March 2014 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 20 April 2016 |
| First version publication date | 01 August 2015 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | M11-313 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01468207 |
| 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 | David Williams MD, AbbVie, david.a.williams@abbvie.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000366-PIP04-12 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 16 March 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 March 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and efficacy of treatment with adalimumab in adults with moderate to severe hidradenitis suppurativa (HS).

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 29 November 2011 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Australia: 19 |
| Country: Number of subjects enrolled | Canada: 34 |
| Country: Number of subjects enrolled | United States: 155 |
| Country: Number of subjects enrolled | Czech Republic: 31 |
| Country: Number of subjects enrolled | Germany: 55 |
| Country: Number of subjects enrolled | Hungary: 13 |
| Worldwide total number of subjects | 307 |
| EEA total number of subjects | 99 |

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) | 0 |

| | |
|----------------------|-----|
| Adults (18-64 years) | 304 |
| From 65 to 84 years | 3 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 48 investigative sites in Australia, Canada, Czech Republic, Germany, Hungary, and the United States.

Pre-assignment

Screening details:

Subjects ≥ 18 years of age with hidradenitis suppurativa (HS) for at least 1 year prior to Baseline and HS lesions present in at least 2 distinct anatomical areas (one of which must be at least Hurley Stage II or III) who had experienced inadequate response to ≥ 90 day treatment of oral antibiotics for HS were eligible for enrolment in the study.

Period 1

| | |
|------------------------------|--|
| Period 1 title | Treatment Period 1 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Placebo for 12 weeks.

| | |
|--|------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo pre-filled syringe, administered by subcutaneous injection

| | |
|------------------|----------------------------|
| Arm title | Adalimumab Every Week (EW) |
|------------------|----------------------------|

Arm description:

Adalimumab ew for 12 weeks (160 mg at Week 0; 80 mg at Week 2; and 40 mg ew from Week 4 to Week 12).

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Adalimumab |
| Investigational medicinal product code | |
| Other name | Humira |
| 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 | Placebo | Adalimumab Every Week (EW) |
|--------------------------------|---------|----------------------------|
| Started | 154 | 153 |
| Received study drug | 152 | 153 |
| Completed | 145 | 145 |
| Not completed | 9 | 8 |
| Consent withdrawn by subject | 5 | 4 |
| Other, not specified | - | 2 |
| Adverse event | 1 | - |
| Lost to follow-up | 2 | 1 |
| Protocol deviation | 1 | 1 |

Period 2

| | |
|------------------------------|--|
| Period 2 title | Treatment Period 2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

Arms

| | |
|------------------------------|------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo/Adalimumab Every Week (EW) |

Arm description:

Subjects randomized to receive placebo in Period 1 received adalimumab 160 mg at Week 12, 80 mg at Week 14, and 40 mg ew from Week 16 to Week 35 in Period 2 (up to 24 weeks).

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

Dosage and administration details:

Adalimumab pre-filled syringe, administered by subcutaneous injection

| | |
|--|------------------------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo pre-filled syringe, administered by subcutaneous injection

| | |
|------------------|------------------------------------|
| Arm title | Adalimumab Every Week (EW)/Placebo |
|------------------|------------------------------------|

Arm description:

Subjects randomized to receive adalimumab ew in Period 1 were re-randomized to receive placebo ew from Week 12 to Week 35 in Period 2 (up to 24 weeks).

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|------------------------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo pre-filled syringe, administered by subcutaneous injection

| | |
|--|------------------------|
| Investigational medicinal product name | Adalimumab |
| Investigational medicinal product code | |
| Other name | Humira |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Adalimumab pre-filled syringe, administered by subcutaneous injection

| | |
|------------------|---|
| Arm title | Adalimumab Every Week (EW)/ Adalimumab Every Other Week (EOW) |
|------------------|---|

Arm description:

Subjects randomized to receive adalimumab ew in Period 1 were re-randomized to receive adalimumab 40 mg eow from Week 12 to Week 35 in Period 2; placebo injections were administered eow from Week 13 to Week 35 (up to 24 weeks).

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

Dosage and administration details:

Adalimumab pre-filled syringe, administered by subcutaneous injection

| | |
|------------------|---|
| Arm title | Adalimumab Every Week (EW)/Adalimumab Every Week (EW) |
|------------------|---|

Arm description:

Subjects randomized to receive adalimumab ew in Period 1 were re-randomized to receive 40 mg adalimumab ew from Week 12 to Week 35 in Period 2 (up to 24 weeks).

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Adalimumab |
| Investigational medicinal product code | |
| Other name | Humira |
| 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 2 | Placebo/Adalimumab Every Week (EW) | Adalimumab Every Week (EW)/Placebo | Adalimumab Every Week (EW)/ Adalimumab Every Other Week (EOW) |
|--------------------------------|------------------------------------|------------------------------------|---|
| | | | |
| Started | 145 | 49 | 48 |
| Completed | 93 | 22 | 27 |
| Not completed | 52 | 27 | 21 |
| Consent withdrawn by subject | 5 | - | - |
| Other, not specified | 5 | 1 | 1 |

| | | | |
|--|----|----|----|
| Adverse event | 6 | 1 | 2 |
| Loss or absence of response (per protocol) | 30 | 23 | 18 |
| Lost to follow-up | 5 | 1 | - |
| Lack of efficacy | 1 | 1 | - |

| Number of subjects in period 2 | Adalimumab Every Week (EW)/Adalimumab Every Week (EW) |
|--|---|
| Started | 48 |
| Completed | 28 |
| Not completed | 20 |
| Consent withdrawn by subject | 2 |
| Other, not specified | 2 |
| Adverse event | 1 |
| Loss or absence of response (per protocol) | 13 |
| Lost to follow-up | - |
| Lack of efficacy | 2 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo for 12 weeks.

| | |
|-----------------------|----------------------------|
| Reporting group title | Adalimumab Every Week (EW) |
|-----------------------|----------------------------|

Reporting group description:

Adalimumab ew for 12 weeks (160 mg at Week 0; 80 mg at Week 2; and 40 mg ew from Week 4 to Week 12).

| Reporting group values | Placebo | Adalimumab Every Week (EW) | Total |
|------------------------|---------|----------------------------|-------|
| Number of subjects | 154 | 153 | 307 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------|---------|---------|-----|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 37.8 | 36.2 | |
| standard deviation | ± 11.33 | ± 10.83 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 105 | 91 | 196 |
| Male | 49 | 62 | 111 |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: Placebo for 12 weeks. | |
| Reporting group title | Adalimumab Every Week (EW) |
| Reporting group description: Adalimumab ew for 12 weeks (160 mg at Week 0; 80 mg at Week 2; and 40 mg ew from Week 4 to Week 12). | |
| Reporting group title | Placebo/Adalimumab Every Week (EW) |
| Reporting group description: Subjects randomized to receive placebo in Period 1 received adalimumab 160 mg at Week 12, 80 mg at Week 14, and 40 mg ew from Week 16 to Week 35 in Period 2 (up to 24 weeks). | |
| Reporting group title | Adalimumab Every Week (EW)/Placebo |
| Reporting group description: Subjects randomized to receive adalimumab ew in Period 1 were re-randomized to receive placebo ew from Week 12 to Week 35 in Period 2 (up to 24 weeks). | |
| Reporting group title | Adalimumab Every Week (EW)/ Adalimumab Every Other Week (EOW) |
| Reporting group description: Subjects randomized to receive adalimumab ew in Period 1 were re-randomized to receive adalimumab 40 mg eow from Week 12 to Week 35 in Period 2; placebo injections were administered eow from Week 13 to Week 35 (up to 24 weeks). | |
| Reporting group title | Adalimumab Every Week (EW)/Adalimumab Every Week (EW) |
| Reporting group description: Subjects randomized to receive adalimumab ew in Period 1 were re-randomized to receive 40 mg adalimumab ew from Week 12 to Week 35 in Period 2 (up to 24 weeks). | |
| Subject analysis set title | Placebo - Baseline Hurley Stage II |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects with baseline Hurley Stage II randomized to receive placebo every week (ew) for 12 weeks. | |
| Subject analysis set title | Placebo - Baseline Hurley Stage III |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects with baseline Hurley Stage III randomized to receive placebo every week (ew) for 12 weeks. | |
| Subject analysis set title | Adalimumab Every Week (EW) - Baseline Hurley Stage II |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects with baseline Hurley Stage II randomized to receive adalimumab ew 160 mg at Week 12, 80 mg at Week 14, and 40 mg ew from Week 16 to 35 (up to 24 weeks). | |
| Subject analysis set title | Adalimumab Every Week (ew) - Baseline Hurley Stage III |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects with baseline Hurley Stage III randomized to receive adalimumab ew 160 mg at Week 12, 80 mg at Week 14, and 40 mg ew from Week 16 to 35 (up to 24 weeks). | |
| Subject analysis set title | Placebo - Baseline NRS at Worst ≥ 3 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects with baseline Patient's Global Assessment of Skin Pain Numeric Rating Scale (NRS) ≥ 3 randomized to receive placebo every week (ew) for 12 weeks. | |
| Subject analysis set title | Adalimumab Every Week (EW) - Baseline NRS at Worst ≥ 3 |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Subjects with baseline Patient's Global Assessment of Skin Pain Numeric Rating Scale (NRS) ≥ 3 randomized to receive adalimumab ew 160 mg at Week 12, 80 mg at Week 14, and 40 mg ew from Week 16 to 35 (up to 24 weeks).

Primary: Percentage of Subjects Achieving Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 12

| | |
|-----------------|--|
| End point title | Percentage of Subjects Achieving Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 12 |
|-----------------|--|

End point description:

Hidradenitis Suppurativa Clinical Response (HiSCR) was defined as at least a 50% reduction in abscess and inflammatory nodule (AN) count with no increase in abscess count and no increase in draining fistula count at Week 12 relative to Baseline. Data are presented for all subjects and by baseline Hurley Stage (Stage 1: Abscess formation, single or multiple, without sinus tracts and scarring; Stage II: One or more widely separated recurrent abscesses with tract formation and scars. A subject with at least 1 anatomic region with Hurley Stage II disease and with no anatomic regions with Hurley Stage III disease was classified as Hurley Stage II; and Stage III: Multiple interconnected tracts and abscesses across the entire area, with diffuse or near diffuse involvement. A subject with at least 1 anatomic region with Hurley Stage III disease was classified as Hurley Stage III). Non-responder imputation (NRI): Subjects with missing data were considered non-responders.

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

End point timeframe:

Baseline (Week 0) up to Week 12

| End point values | Placebo | Adalimumab Every Week (EW) | Placebo - Baseline Hurley Stage II | Placebo - Baseline Hurley Stage III |
|-------------------------------|-----------------|----------------------------|------------------------------------|-------------------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 154 | 153 | 84 | 70 |
| Units: percentage of subjects | | | | |
| number (not applicable) | 26 | 41.8 | 29.8 | 21.4 |

| End point values | Adalimumab Every Week (EW) - Baseline Hurley Stage II | Adalimumab Every Week (ew) - Baseline Hurley Stage III | | |
|-------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 83 | 70 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 44.6 | 38.6 | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

The p-value was calculated from the Cochran-Mantel-Haenszel test adjusted for baseline Hurley Stage.

| | |
|-------------------|--------------------------------------|
| Comparison groups | Placebo v Adalimumab Every Week (EW) |
|-------------------|--------------------------------------|

| | |
|---|--------------------------|
| Number of subjects included in analysis | 307 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.003 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted mean difference |
| Point estimate | 15.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.3 |
| upper limit | 26.5 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

The p-value was calculated based on chi-square test.

| | |
|---|--|
| Comparison groups | Placebo - Baseline Hurley Stage II v Adalimumab Every Week (EW) - Baseline Hurley Stage II |
| Number of subjects included in analysis | 167 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.048 |
| Method | Chi-squared |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 14.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.3 |
| upper limit | 29.3 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

The p-value was calculated based on chi-square test.

| | |
|---|--|
| Comparison groups | Adalimumab Every Week (ew) - Baseline Hurley Stage III v Placebo - Baseline Hurley Stage III |
| Number of subjects included in analysis | 140 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.027 |
| Method | Chi-squared |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 17.1 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.2 |
| upper limit | 32.1 |

Secondary: Percentage of Subjects with Baseline Hurley Stage II who Achieved Abscess and Inflammatory Nodule (AN) Count of 0, 1, or 2 at Week 12

| | |
|--|---|
| End point title | Percentage of Subjects with Baseline Hurley Stage II who Achieved Abscess and Inflammatory Nodule (AN) Count of 0, 1, or 2 at Week 12 |
| End point description: The percentage of subjects with AN counts lowered to 0, 1, or 2 at Week 12 among subjects with Hurley Stage II at Baseline. Non-responder imputation (NRI): Subjects with missing data were considered non-responders. | |
| End point type | Secondary |
| End point timeframe: Baseline (Week 0) up to Week 12 | |

| End point values | Placebo - Baseline Hurley Stage II | Adalimumab Every Week (EW) - Baseline Hurley Stage II | | |
|-------------------------------|------------------------------------|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 84 | 83 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 28.6 | 28.9 | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Statistical analysis 1 |
| Statistical analysis description: Secondary end points 1 (AN 0/1/2 counts), 2 (NRS30), and 3 (modified Sartorius score) were ranked analyses. The p-value for the AN 0/1/2 counts end point was calculated from the Chi Squared test. | |
| Comparison groups | Placebo - Baseline Hurley Stage II v Adalimumab Every Week (EW) - Baseline Hurley Stage II |
| Number of subjects included in analysis | 167 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.961 |
| Method | Chi-squared |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.3 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.4 |
| upper limit | 14.1 |

Secondary: Percentage of Subjects Achieving At Least 30% Reduction and At Least 1 Unit Reduction from Baseline in Patient's Global Assessment of Skin Pain (NRS30) – At Worst at Week 12 Among Subjects with Baseline Skin Pain NRS ≥ 3

| | |
|-----------------|---|
| End point title | Percentage of Subjects Achieving At Least 30% Reduction and At Least 1 Unit Reduction from Baseline in Patient's Global Assessment of Skin Pain (NRS30) – At Worst at Week 12 Among Subjects with Baseline Skin Pain NRS ≥ 3 |
|-----------------|---|

End point description:

The Patient's Global Assessment of Skin Pain Numeric Rating Scale (NRS) was used to assess the worst skin pain and the average skin pain due to HS. Ratings for the 2 items range from 0 (no skin pain) to 10 (skin pain as bad as you can imagine). The assessments were completed on a daily diary by subjects before they went to bed and responded to the items based on a recall period of the "last 24 hours." The percentage of subjects who achieved at least 30% reduction and at least 1 unit reduction from Baseline in the Patient's Global Assessment of Skin Pain (NRS30) – at worst at Week 12 among subjects with Baseline NRS ≥ 3 is presented. Weekly averages of daily assessments were analyzed. Non-responder imputation (NRI): Subjects with missing data were considered non-responders.

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

End point timeframe:

Baseline (Week 0) up to Week 12

| End point values | Placebo - Baseline NRS at Worst ≥ 3 | Adalimumab Every Week (EW) - Baseline NRS at Worst ≥ 3 | | |
|-------------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 109 | 122 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 24.8 | 27.9 | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Secondary end points 1 (AN 0/1/2 counts), 2 (NRS30), and 3 (modified Sartorius score) were ranked analyses. The p-value for the NRS30 end point was calculated from the Cochran-Mantel-Haenszel test adjusted for baseline Hurley Stage.

| | |
|-------------------|--|
| Comparison groups | Placebo - Baseline NRS at Worst ≥ 3 v Adalimumab Every Week (EW) - Baseline NRS at Worst ≥ 3 |
|-------------------|--|

| | |
|---|--------------------------|
| Number of subjects included in analysis | 231 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.628 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted mean difference |
| Point estimate | 2.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.6 |
| upper limit | 14.2 |

Secondary: Change from Baseline to Week 12 in Modified Sartorius Score

| | |
|---|---|
| End point title | Change from Baseline to Week 12 in Modified Sartorius Score |
| End point description: | |
| <p>The Sartorius Scale is used to quantify the severity of HS. Points are awarded for 12 body areas (left and right axillae, left and right sub/inframammary areas, intermammary area, left and right buttocks, left and right inguino-crural folds, perianal area, perineal area, and other): points were awarded for nodules (2 points for each); abscesses (4 points); fistulas (4 points); scars (1 point); other findings (1 point); and longest distance between two lesions (2-6 points, 0 if no lesions); and if lesions are separated by normal skin (yes-0 points; No-6 points). The total Sartorius score is the sum of the 12 regional scores. Last Observation Carried Forward (LOCF): The last completed evaluation from the previous visit within the particular period for efficacy measures was carried forward to impute missing data at later visits in the same period. Baseline efficacy evaluations were not carried forward.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Week 0) and Week 12 | |

| End point values | Placebo | Adalimumab Every Week (EW) | | |
|-------------------------------------|-----------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 151 | 153 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -15.7 (± 4) | -24.4 (± 3.97) | | |

Statistical analyses

| | |
|---|--------------------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Statistical analysis description: | |
| <p>Secondary end points 1 (AN 0/1/2 counts), 2 (NRS30), and 3 (modified Sartorius score) were ranked analyses. The p-value for the modified Sartorius score end point was calculated from ANCOVA with stratum, baseline, and treatment as covariates.</p> | |
| Comparison groups | Placebo v Adalimumab Every Week (EW) |

| | |
|---|--------------------|
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.124 |
| Method | ANCOVA |
| Parameter estimate | LS mean difference |
| Point estimate | -8.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -19.7 |
| upper limit | 2.4 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from first dose of study drug until 70 days following last dose of study drug (46 weeks); SAEs were collected from the time that informed consent was obtained (up to 50 weeks).

Adverse event reporting additional description:

AEs with onset in Period 1 were collected from first dose of study drug until prior to the first dose in Period 2, or up to 70 days following last dose of study drug if the subject discontinued during Period 1.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Placebo (Period 1) |
|-----------------------|--------------------|

Reporting group description:

Placebo for 12 weeks

| | |
|-----------------------|--------------------------|
| Reporting group title | Adalimumab EW (Period 1) |
|-----------------------|--------------------------|

Reporting group description:

Adalimumab every week (ew) for 12 weeks (160 mg at Week 0; 80 mg at Week 2; and 40 mg ew from Week 4 to Week 12).

| | |
|-----------------------|----------------------------------|
| Reporting group title | Placebo/Adalimumab EW (Period 2) |
|-----------------------|----------------------------------|

Reporting group description:

Subjects randomized to receive placebo in Period 1 were re-randomized to receive adalimumab 160 mg at Week 12, 80 mg at Week 14, and 40 mg every week (ew) from Week 16 to Week 35 in Period 2 (up to 24 weeks).

| | |
|-----------------------|----------------------------------|
| Reporting group title | Adalimumab EW/Placebo (Period 2) |
|-----------------------|----------------------------------|

Reporting group description:

Subjects randomized to receive adalimumab every week (ew) in Period 1 were re-randomized to receive placebo ew from Week 12 to Week 35 in Period 2 (up to 24 weeks).

| | |
|-----------------------|--|
| Reporting group title | Adalimumab EW/ Adalimumab EOW (Period 2) |
|-----------------------|--|

Reporting group description:

Subjects randomized to receive adalimumab every week (ew) in Period 1 were re-randomized to receive adalimumab 40 mg every other week (eow) from Week 12 to Week 35 in Period 2; placebo injections were administered eow from Week 13 to Week 35 (up to 24 weeks).

| | |
|-----------------------|--|
| Reporting group title | Adalimumab EW/Adalimumab EW (Period 2) |
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Reporting group description:

Subjects randomized to receive adalimumab every week (ew) in Period 1 were re-randomized to receive 40 mg adalimumab ew from Week 12 to Week 35 in Period 2 (up to 24 weeks).

| Serious adverse events | Placebo (Period 1) | Adalimumab EW (Period 1) | Placebo/Adalimumab EW (Period 2) |
|---|--------------------|--------------------------|----------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 152 (3.29%) | 3 / 153 (1.96%) | 5 / 145 (3.45%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Invasive ductal breast carcinoma | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Hepatitis A antibody positive | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver function test abnormal | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Effusion | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 1 / 153 (0.65%) | 0 / 145 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Hidradenitis | | | |
| subjects affected / exposed | 3 / 152 (1.97%) | 1 / 153 (0.65%) | 2 / 145 (1.38%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Intervertebral disc calcification | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendonitis | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 1 / 153 (0.65%) | 0 / 145 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Adalimumab EW/Placebo (Period 2) | Adalimumab EW/ Adalimumab EOW (Period 2) | Adalimumab EW/Adalimumab EW (Period 2) |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 3 / 48 (6.25%) | 1 / 48 (2.08%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |

| | | | |
|---|----------------|----------------|----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Hepatitis A antibody positive | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver function test abnormal | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Effusion | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Hidradenitis | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 2 / 48 (4.17%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Intervertebral disc calcification | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendonitis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events | Placebo (Period 1) | Adalimumab EW (Period 1) | Placebo/Adalimumab EW (Period 2) |
|---|--------------------|--------------------------|----------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 81 / 152 (53.29%) | 64 / 153 (41.83%) | 68 / 145 (46.90%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 152 (1.97%) | 1 / 153 (0.65%) | 2 / 145 (1.38%) |
| occurrences (all) | 3 | 1 | 2 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 152 (2.63%) | 3 / 153 (1.96%) | 2 / 145 (1.38%) |
| occurrences (all) | 6 | 3 | 2 |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 152 (1.97%) | 1 / 153 (0.65%) | 2 / 145 (1.38%) |
| occurrences (all) | 4 | 1 | 2 |
| Chills | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site bruising | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 1 / 153 (0.65%) | 1 / 145 (0.69%) |
| occurrences (all) | 0 | 2 | 1 |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 1 / 153 (0.65%) | 6 / 145 (4.14%) |
| occurrences (all) | 0 | 1 | 16 |
| Injection site pruritus | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 1 / 153 (0.65%) | 3 / 145 (2.07%) |
| occurrences (all) | 0 | 1 | 13 |
| Local swelling | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Xerosis | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |

| | | | |
|--|--|--|--|
| Hypersensitivity subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) Asthma subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Respiratory tract congestion subjects affected / exposed occurrences (all) Sinus congestion subjects affected / exposed occurrences (all) Sneezing subjects affected / exposed occurrences (all) | 4 / 152 (2.63%) 4 0 / 152 (0.00%) 0 3 / 152 (1.97%) 3 0 / 152 (0.00%) 0 1 / 152 (0.66%) 1 0 / 152 (0.00%) 0 | 2 / 153 (1.31%) 3 0 / 153 (0.00%) 0 2 / 153 (1.31%) 2 1 / 153 (0.65%) 1 1 / 153 (0.65%) 1 0 / 153 (0.00%) 0 | 3 / 145 (2.07%) 3 0 / 145 (0.00%) 0 2 / 145 (1.38%) 3 1 / 145 (0.69%) 1 1 / 145 (0.69%) 1 0 / 145 (0.00%) 0 |
| Psychiatric disorders Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 1 / 152 (0.66%) 1 | 3 / 153 (1.96%) 3 1 / 153 (0.65%) 1 | 2 / 145 (1.38%) 2 1 / 145 (0.69%) 1 |
| Investigations Alanine aminotransferase increased | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 2 / 145 (1.38%) |
| occurrences (all) | 0 | 0 | 2 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 1 / 153 (0.65%) | 2 / 145 (1.38%) |
| occurrences (all) | 0 | 1 | 2 |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 3 / 152 (1.97%) | 3 / 153 (1.96%) | 2 / 145 (1.38%) |
| occurrences (all) | 3 | 3 | 2 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 2 / 153 (1.31%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 3 / 152 (1.97%) | 3 / 153 (1.96%) | 2 / 145 (1.38%) |
| occurrences (all) | 3 | 3 | 2 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 2 / 152 (1.32%) | 0 / 153 (0.00%) | 2 / 145 (1.38%) |
| occurrences (all) | 2 | 0 | 2 |
| Excoriation | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fall | | | |

| | | | |
|---|------------------------|------------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 1 / 152 (0.66%) 1 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Ligament sprain subjects affected / exposed occurrences (all) | 1 / 152 (0.66%) 1 | 1 / 153 (0.65%) 1 | 1 / 145 (0.69%) 1 |
| Road traffic accident subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 1 / 153 (0.65%) 1 | 0 / 145 (0.00%) 0 |
| Skin injury subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 15 / 152 (9.87%) 18 | 14 / 153 (9.15%) 19 | 9 / 145 (6.21%) 14 |
| Dizziness subjects affected / exposed occurrences (all) | 2 / 152 (1.32%) 2 | 4 / 153 (2.61%) 4 | 1 / 145 (0.69%) 1 |
| Lethargy subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 1 / 153 (0.65%) 1 | 0 / 145 (0.00%) 0 |
| Nerve compression subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Paraesthesia subjects affected / exposed occurrences (all) | 1 / 152 (0.66%) 1 | 0 / 153 (0.00%) 0 | 1 / 145 (0.69%) 1 |
| Sinus headache subjects affected / exposed occurrences (all) | 1 / 152 (0.66%) 1 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Syncope subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 152 (0.66%) 1 | 1 / 153 (0.65%) 1 | 1 / 145 (0.69%) 1 |
| Leukocytosis subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 2 / 145 (1.38%) 2 |
| Neutrophilia subjects affected / exposed occurrences (all) | 1 / 152 (0.66%) 1 | 0 / 153 (0.00%) 0 | 1 / 145 (0.69%) 1 |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Eye disorders Blepharitis subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Eyelid oedema subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Meibomian gland dysfunction subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Visual impairment subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 4 / 152 (2.63%) 4 | 3 / 153 (1.96%) 3 | 6 / 145 (4.14%) 6 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 3 / 152 (1.97%) 3 | 1 / 153 (0.65%) 1 | 1 / 145 (0.69%) 2 |
| Constipation subjects affected / exposed occurrences (all) | 2 / 152 (1.32%) 2 | 1 / 153 (0.65%) 1 | 1 / 145 (0.69%) 1 |
| Diarrhoea | | | |

| | | | |
|--|-------------------|------------------|------------------|
| subjects affected / exposed | 2 / 152 (1.32%) | 3 / 153 (1.96%) | 3 / 145 (2.07%) |
| occurrences (all) | 2 | 3 | 3 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip swelling | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 2 / 145 (1.38%) |
| occurrences (all) | 1 | 0 | 2 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 152 (1.32%) | 1 / 153 (0.65%) | 1 / 145 (0.69%) |
| occurrences (all) | 2 | 1 | 1 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis contact | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences (all) | 1 | 0 | 2 |
| Hidradenitis | | | |
| subjects affected / exposed | 17 / 152 (11.18%) | 13 / 153 (8.50%) | 14 / 145 (9.66%) |
| occurrences (all) | 23 | 15 | 14 |
| Acne cystic | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermal cyst | | | |

| | | | |
|---|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 2 / 152 (1.32%) 2 | 0 / 153 (0.00%) 0 | 2 / 145 (1.38%) 2 |
| Dermatitis papillaris capillitii subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Dermatitis psoriasiform subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 1 / 145 (0.69%) 1 |
| Eczema subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 1 / 153 (0.65%) 1 | 1 / 145 (0.69%) 1 |
| Eczema asteatotic subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Intertrigo subjects affected / exposed occurrences (all) | 2 / 152 (1.32%) 2 | 1 / 153 (0.65%) 1 | 1 / 145 (0.69%) 1 |
| Keloid scar subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Haematuria subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 145 (0.00%) 0 |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 0 / 153 (0.00%) 0 | 1 / 145 (0.69%) 1 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 0 / 152 (0.00%) 0 | 3 / 153 (1.96%) 3 | 1 / 145 (0.69%) 1 |
| Back pain | | | |

| | | | |
|-----------------------------------|-------------------|-----------------|------------------|
| subjects affected / exposed | 4 / 152 (2.63%) | 3 / 153 (1.96%) | 1 / 145 (0.69%) |
| occurrences (all) | 4 | 3 | 1 |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 2 / 153 (1.31%) | 3 / 145 (2.07%) |
| occurrences (all) | 1 | 2 | 3 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 16 / 152 (10.53%) | 9 / 153 (5.88%) | 11 / 145 (7.59%) |
| occurrences (all) | 16 | 9 | 12 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 152 (2.63%) | 5 / 153 (3.27%) | 5 / 145 (3.45%) |
| occurrences (all) | 4 | 5 | 6 |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 152 (1.97%) | 5 / 153 (3.27%) | 4 / 145 (2.76%) |
| occurrences (all) | 3 | 5 | 4 |
| Body tinea | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 152 (1.32%) | 0 / 153 (0.00%) | 3 / 145 (2.07%) |
| occurrences (all) | 2 | 0 | 3 |
| Cellulitis | | | |
| subjects affected / exposed | 2 / 152 (1.32%) | 2 / 153 (1.31%) | 0 / 145 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Cytolytic vaginosis | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------------|-----------------|-----------------|-----------------|
| Ear infection | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 1 / 153 (0.65%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 2 / 145 (1.38%) |
| occurrences (all) | 1 | 0 | 2 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 3 / 152 (1.97%) | 2 / 153 (1.31%) | 3 / 145 (2.07%) |
| occurrences (all) | 3 | 2 | 4 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 2 / 152 (1.32%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Measles | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences (all) | 1 | 0 | 1 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 1 / 153 (0.65%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 1 / 153 (0.65%) | 2 / 145 (1.38%) |
| occurrences (all) | 1 | 1 | 2 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences (all) | 1 | 0 | 1 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|------------------------------------|-----------------|-----------------|-----------------|
| Rash pustular | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 1 / 153 (0.65%) | 0 / 145 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 3 / 153 (1.96%) | 4 / 145 (2.76%) |
| occurrences (all) | 1 | 3 | 4 |
| Skin candida | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences (all) | 1 | 0 | 1 |
| Tinea infection | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 1 / 153 (0.65%) | 2 / 145 (1.38%) |
| occurrences (all) | 1 | 1 | 2 |
| Tracheitis | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperlipidaemia | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Type 2 diabetes mellitus | | | |

| | | | |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 152 (0.66%) | 0 / 153 (0.00%) | 0 / 145 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 152 (0.00%) | 0 / 153 (0.00%) | 1 / 145 (0.69%) |
| occurrences (all) | 0 | 0 | 1 |

| Non-serious adverse events | Adalimumab EW/Placebo (Period 2) | Adalimumab EW/ Adalimumab EOW (Period 2) | Adalimumab EW/Adalimumab EW (Period 2) |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 30 / 49 (61.22%) | 24 / 48 (50.00%) | 28 / 48 (58.33%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 2 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 3 / 48 (6.25%) | 2 / 48 (4.17%) |
| occurrences (all) | 0 | 3 | 2 |
| Chills | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Injection site bruising | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site pruritus | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Local swelling | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Non-cardiac chest pain | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 48 (2.08%) 1 |
| Xerosis subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 48 (2.08%) 1 |
| Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 48 (0.00%) 0 |
| Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 48 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | 0 / 48 (0.00%) 0 | 0 / 48 (0.00%) 0 |
| Asthma subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | 0 / 48 (0.00%) 0 | 0 / 48 (0.00%) 0 |
| Cough subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 1 / 48 (2.08%) 1 | 2 / 48 (4.17%) 2 |
| Respiratory tract congestion subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 48 (2.08%) 1 |
| Sinus congestion subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 48 (2.08%) 1 |
| Sneezing subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 48 (0.00%) 0 |
| Psychiatric disorders Depression subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | 0 / 48 (0.00%) 0 | 0 / 48 (0.00%) 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Insomnia subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 1 / 48 (2.08%) 1 | 2 / 48 (4.17%) 2 |
| Investigations | | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 2 / 49 (4.08%) 2 | 0 / 48 (0.00%) 0 | 0 / 48 (0.00%) 0 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | 0 / 48 (0.00%) 0 | 0 / 48 (0.00%) 0 |
| Blood glucose increased subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 48 (0.00%) 0 |
| Blood triglycerides increased subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | 0 / 48 (0.00%) 0 | 0 / 48 (0.00%) 0 |
| C-reactive protein increased subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | 0 / 48 (0.00%) 0 | 0 / 48 (0.00%) 0 |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 0 / 48 (0.00%) 0 | 2 / 48 (4.17%) 2 |
| Weight increased subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 48 (2.08%) 1 |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | 0 / 48 (0.00%) 0 | 0 / 48 (0.00%) 0 |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | 0 / 48 (0.00%) 0 | 0 / 48 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | 0 / 48 (0.00%) 0 | 0 / 48 (0.00%) 0 |
| Excoriation | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fall | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Road traffic accident | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin injury | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 49 (8.16%) | 3 / 48 (6.25%) | 2 / 48 (4.17%) |
| occurrences (all) | 9 | 3 | 7 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 2 / 48 (4.17%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Nerve compression | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus headache | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Syncope | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 2 / 48 (4.17%) |
| occurrences (all) | 1 | 0 | 2 |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neutrophilia | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Eye disorders | | | |
| Blepharitis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Eyelid oedema | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Meibomian gland dysfunction | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Visual impairment | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 2 / 48 (4.17%) |
| occurrences (all) | 0 | 0 | 2 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--|-----------------|-----------------|----------------|
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 1 | 0 | 1 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 2 / 48 (4.17%) |
| occurrences (all) | 0 | 0 | 2 |
| Lip swelling | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Toothache | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 48 (2.08%) | 1 / 48 (2.08%) |
| occurrences (all) | 1 | 1 | 1 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 3 / 48 (6.25%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Hidradenitis | | | |
| subjects affected / exposed | 8 / 49 (16.33%) | 7 / 48 (14.58%) | 2 / 48 (4.17%) |
| occurrences (all) | 8 | 7 | 2 |
| Acne cystic | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermal cyst | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis papillaris capillitii | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis psoriasiform | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 1 | 0 | 1 |
| Eczema | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eczema asteatotic | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Intertrigo | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 2 / 48 (4.17%) |
| occurrences (all) | 2 | 0 | 2 |
| Keloid scar | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 1 / 48 (2.08%) | 1 / 48 (2.08%) |
| occurrences (all) | 3 | 1 | 1 |
| Back pain | | | |

| | | | |
|-----------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 1 | 0 | 1 |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint swelling | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 9 / 49 (18.37%) | 1 / 48 (2.08%) | 3 / 48 (6.25%) |
| occurrences (all) | 15 | 2 | 3 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 3 / 48 (6.25%) | 4 / 48 (8.33%) |
| occurrences (all) | 2 | 4 | 4 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 2 / 48 (4.17%) | 2 / 48 (4.17%) |
| occurrences (all) | 1 | 3 | 3 |
| Body tinea | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cytolytic vaginosis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| Ear infection | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 2 / 48 (4.17%) |
| occurrences (all) | 0 | 2 | 2 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Measles | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|------------------------------------|----------------|----------------|----------------|
| Rash pustular | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 2 / 48 (4.17%) |
| occurrences (all) | 1 | 0 | 2 |
| Skin candida | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tinea infection | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Tracheitis | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperlipidaemia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 48 (2.08%) | 0 / 48 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Type 2 diabetes mellitus | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 48 (0.00%) | 0 / 48 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 48 (0.00%) | 1 / 48 (2.08%) |
| occurrences (all) | 0 | 0 | 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 12 April 2012 | Added lesion count assessments at unscheduled visits after Week 12; added waist circumference measurements to assessments; clarified TB testing at screening; revised anti-TB therapy to a minimum of 4 weeks completed prior to starting TNF inhibitors; provided a process of HIV antibody testing where required by country regulatory authorities; added collection of NRS pain and analgesic use using an electronic device; added representative lesion assessments at premature discontinuation visit if the visit occurred prior to Week 12; for the analysis of proportion of subjects achieving at least 30% reduction at least 1 unity reduction from baseline NRS30 - at worst at Week 12, increase baseline requirement from baseline NRS ≥ 1 to ≥ 3 ; classified methods of handling potential confounding effect on pain assessment when medications for HS or pain were used. |
| 07 August 2013 | Added safety monitoring language per AbbVie participation in US FDA-requested TNF inhibitor class wide exploration of the rare appearance of malignancy in patients 30 years of age or younger; provided more details to the risks and benefits of participation; added recently approved biologic therapies as prohibited therapies; clarified that antibiotic rescue therapy dosing regimen must remain stable during the study; added change and percent change from baseline in CRP; added blood samples for biologic marker analysis at Week 36 (or premature discontinuation); replaced pregnancy forms and the pregnancy registry with EDC system entry for pregnancy determination. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported