



## Clinical trial results:

### A Phase 3, Open-Label Study of the Safety and Efficacy of Adalimumab in Subjects With Moderate to Severe Hidradenitis Suppurativa - PIONEER (Open-Label Extension)

#### Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2011-003478-98       |
| Trial protocol           | SE NL HU GR DE DK CZ |
| Global end of trial date | 12 August 2016       |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1             |
| This version publication date  | 20 August 2017 |
| First version publication date | 20 August 2017 |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | M12-555 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01635764 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | AbbVie Deutschland GmbH & Co.   |
| Sponsor organisation address | AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB |
| Public contact               | Global Medical Services, AbbVie, 001 800-633-9110,  |
| Scientific contact           | Dawn Carlson, MD, AbbVie, dawn.carlson@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? | No |

Notes:

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**Results analysis stage**

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|  |                |
|--|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 12 August 2016 |
| Is this the analysis of the primary completion data? | No             |

|                                  |                |
|----------------------------------|----------------|
| Global end of trial reached?     | Yes            |
| Global end of trial date         | 12 August 2016 |
| Was the trial ended prematurely? | No             |

Notes:

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**General information about the trial**

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Main objective of the trial:

The purpose of this study to evaluate the long term safety, tolerability and efficacy of adalimumab in subjects with moderate to severe hidradenitis suppurativa (HS).

Protection of trial subjects:

Subject read and understood the information provided about the study and gave written permission

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 12 April 2012 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Australia: 61      |
| Country: Number of subjects enrolled | Canada: 53         |
| Country: Number of subjects enrolled | Czech Republic: 28 |
| Country: Number of subjects enrolled | Denmark: 13        |
| Country: Number of subjects enrolled | France: 37         |
| Country: Number of subjects enrolled | Germany: 44        |
| Country: Number of subjects enrolled | Greece: 39         |
| Country: Number of subjects enrolled | Hungary: 13        |
| Country: Number of subjects enrolled | Netherlands: 16    |
| Country: Number of subjects enrolled | Sweden: 2          |
| Country: Number of subjects enrolled | Switzerland: 16    |
| Country: Number of subjects enrolled | Turkey: 2          |
| Country: Number of subjects enrolled | United States: 184 |
| Worldwide total number of subjects   | 508                |
| EEA total number of subjects         | 192                |

Notes:

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**Subjects enrolled per age group**

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|  |   |
|--|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|  |     |
|--|-----|
| wk                                       |     |
| 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)                     | 502 |
| From 65 to 84 years                      | 6   |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects were evaluated for entry into Study M12-555 at the final study visit of the prior Phase 3 study in which they participated. Therefore, the Study M12-555 Baseline (Week 0) visit and administration of the first dose of study drug in Study M12-555 was performed on the same day as the final or last visit of the prior Phase 3 study.

### Period 1

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

### Arms

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Adalimumab Every Week |
|------------------|-----------------------|

Arm description:

Adalimumab 40 mg every week.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | adalimumab                                   |
| Investigational medicinal product code |  |
| Other name                             | Humira                                       |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Adalimumab pre-filled syringe, administered by subcutaneous injection

| Number of subjects in period 1          | Adalimumab Every Week |
|---|-----------------------|
| Started                                 | 508                   |
| Completed                               | 235                   |
| Not completed                           | 273                   |
| Exceed Protocol-specified Interventions | 2                     |
| Not specified                           | 28                    |
| Adverse event                           | 46                    |
| Withdrew consent                        | 67                    |
| Lost to follow-up                       | 53                    |
| Lack of efficacy                        | 76                    |
| Protocol deviation                      | 1                     |



## Baseline characteristics

### Reporting groups

|  |                       |
|--|-----------------------|
| Reporting group title  | Adalimumab Every Week |
| Reporting group description:<br>Adalimumab 40 mg every week. |                       |

| Reporting group values  | Adalimumab Every Week | Total |  |
|---|-----------------------|-------|--|
| Number of subjects  | 508                   | 508   |  |
| Age categorical   |                       |       |  |
| Units: Subjects   |                       |       |  |
| Age continuous  |                       |       |  |
| Baseline characteristics provided by reporting groups defined by treatment received in prior HS study plus treatment received in M12-555. |                       |       |  |
| Units: years  |                       |       |  |
| arithmetic mean   | 36.8                  |       |  |
| standard deviation  | ± 11.35               | -     |  |
| Gender categorical  |                       |       |  |
| Baseline characteristics provided by reporting groups defined by treatment received in prior HS study plus treatment received in M12-555. |                       |       |  |
| Units: Subjects   |                       |       |  |
| Female  | 328                   | 328   |  |
| Male  | 180                   | 180   |  |

### Subject analysis sets

|  |                    |
|--|--------------------|
| Subject analysis set title   | EW/EW/EW           |
| Subject analysis set type  | Intention-to-treat |
| Subject analysis set description:<br>All participants who received adalimumab 40 mg every week (EW) in both Period A and Period B of the prior Phase 3 studies.                            |                    |
| Subject analysis set title   | EW/EOW/EW          |
| Subject analysis set type  | Intention-to-treat |
| Subject analysis set description:<br>All participants who received adalimumab 40 mg every week (EW) in Period A and 40 mg every other week (EOW) in Period B in the prior Phase 3 studies. |                    |
| Subject analysis set title   | EW/PBO/EW          |
| Subject analysis set type  | Intention-to-treat |
| Subject analysis set description:<br>All participants who received adalimumab 40 mg every week (EW) in Period A and placebo in Period B in the prior Phase 3 studies.                      |                    |
| Subject analysis set title   | PBO/EW/EW          |
| Subject analysis set type  | Intention-to-treat |
| Subject analysis set description:<br>All participants who received placebo in Period A and adalimumab 40 mg every week (EW) in Period B in prior phase 3 study M11-313.                    |                    |
| Subject analysis set title   | PBO/PBO/EW         |
| Subject analysis set type  | Intention-to-treat |

| <b>Reporting group values</b> | EW/EW/EW | EW/EOW/EW | EW/PBO/EW |
|-------------------------------|----------|-----------|-----------|
| Number of subjects            | 88       | 90        | 92        |
| Age categorical               |          |           |           |
| Units: Subjects               |          |           |           |

|   |         |        |         |
|---|---------|--------|---------|
| Age continuous  |         |        |         |
| Baseline characteristics provided by reporting groups defined by treatment received in prior HS study plus treatment received in M12-555. |         |        |         |
| Units: years  |         |        |         |
| arithmetic mean   | 35.5    | 36.1   | 36.5    |
| standard deviation  | ± 10.27 | ± 10.5 | ± 11.06 |
| Gender categorical  |         |        |         |
| Baseline characteristics provided by reporting groups defined by treatment received in prior HS study plus treatment received in M12-555. |         |        |         |
| Units: Subjects   |         |        |         |
| Female  | 56      | 60     | 50      |
| Male  | 32      | 30     | 42      |

| <b>Reporting group values</b> | PBO/EW/EW | PBO/PBO/EW |  |
|-------------------------------|-----------|------------|--|
| Number of subjects            | 115       | 123        |  |
| Age categorical               |           |            |  |
| Units: Subjects               |           |            |  |

|   |         |         |  |
|---|---------|---------|--|
| Age continuous  |         |         |  |
| Baseline characteristics provided by reporting groups defined by treatment received in prior HS study plus treatment received in M12-555. |         |         |  |
| Units: years  |         |         |  |
| arithmetic mean   | 38.5    | 37      |  |
| standard deviation  | ± 11.92 | ± 12.28 |  |
| Gender categorical  |         |         |  |
| Baseline characteristics provided by reporting groups defined by treatment received in prior HS study plus treatment received in M12-555. |         |         |  |
| Units: Subjects   |         |         |  |
| Female  | 79      | 83      |  |
| Male  | 36      | 40      |  |

## End points

### End points reporting groups

|  |                       |
|--|-----------------------|
| Reporting group title  | Adalimumab Every Week |
| Reporting group description:<br>Adalimumab 40 mg every week.   |                       |
| Subject analysis set title   | EW/EW/EW              |
| Subject analysis set type  | Intention-to-treat    |
| Subject analysis set description:<br>All participants who received adalimumab 40 mg every week (EW) in both Period A and Period B of the prior Phase 3 studies.                            |                       |
| Subject analysis set title   | EW/EOW/EW             |
| Subject analysis set type  | Intention-to-treat    |
| Subject analysis set description:<br>All participants who received adalimumab 40 mg every week (EW) in Period A and 40 mg every other week (EOW) in Period B in the prior Phase 3 studies. |                       |
| Subject analysis set title   | EW/PBO/EW             |
| Subject analysis set type  | Intention-to-treat    |
| Subject analysis set description:<br>All participants who received adalimumab 40 mg every week (EW) in Period A and placebo in Period B in the prior Phase 3 studies.                      |                       |
| Subject analysis set title   | PBO/EW/EW             |
| Subject analysis set type  | Intention-to-treat    |
| Subject analysis set description:<br>All participants who received placebo in Period A and adalimumab 40 mg every week (EW) in Period B in prior phase 3 study M11-313.                    |                       |
| Subject analysis set title   | PBO/PBO/EW            |
| Subject analysis set type  | Intention-to-treat    |
| Subject analysis set description:<br>All participants who received placebo in both Period A and Period B in prior phase 3 study M11-810.   |                       |

### **Primary: Percentage of Participants in the EW/EW/EW, EW/EOW/EW, and EW/PBO/EW Analysis Populations Achieving Clinical Response Per Hidradenitis Suppurativa Clinical Response (HiSCR) at Each Visit**

|  |   |
|--|---|
| End point title  | Percentage of Participants in the EW/EW/EW, EW/EOW/EW, and EW/PBO/EW Analysis Populations Achieving Clinical Response Per Hidradenitis Suppurativa Clinical Response (HiSCR) at Each Visit <sup>[1]</sup> |
| End point description:<br>Clinical response per HiSCR defined as percent reduction from baseline of the prior phase 3 study in the abscess and inflammatory nodule $\geq$ 50% (AN50) with no increase in the abscess count and no increase in the draining fistula count. Last Observation Carried Forward (LOCF): The last completed evaluation from the previous visit was carried forward to impute missing data at later visits. n=number of participants at given time point. |   |
| End point type   | Primary   |
| End point timeframe:<br>Weeks 2 (first dose of adalimumab in prior phase 3 study), 4, 8, 12, 16, 20, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216  |   |

#### Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.



| End point values                  | EW/EW/EW             | EW/EOW/EW            | EW/PBO/EW            |  |
|-----------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed       | 88 <sup>[2]</sup>    | 90 <sup>[3]</sup>    | 92 <sup>[4]</sup>    |  |
| Units: percentage of participants |                      |                      |                      |  |
| number (not applicable)           |                      |                      |                      |  |
| Week 2 (n=88,88,91)               | 34.1                 | 39.8                 | 34.1                 |  |
| Week 4 (n=88,90,92)               | 38.6                 | 41.1                 | 40.2                 |  |
| Week 8 (n=88,90,92)               | 51.1                 | 48.9                 | 47.8                 |  |
| Week 12 (n=88,90,92)              | 52.3                 | 55.6                 | 51.1                 |  |
| Week 16 (n=88,90,92)              | 50                   | 56.7                 | 45.7                 |  |
| Week 20 (n=88,90,92)              | 56.8                 | 45.6                 | 45.7                 |  |
| Week 24 (n=88,90,92)              | 48.9                 | 47.8                 | 42.4                 |  |
| Week 36 (n=88,90,92)              | 62.5                 | 54.4                 | 52.2                 |  |
| Week 48 (n=88,90,92)              | 58                   | 55.6                 | 58.7                 |  |
| Week 60 (n=88,90,92)              | 62.5                 | 57.8                 | 58.7                 |  |
| Week 72 (n=88,90,92)              | 59.1                 | 61.1                 | 53.3                 |  |
| Week 84 (n=88,90,92)              | 56.8                 | 56.7                 | 55.4                 |  |
| Week 96 (n=88,90,92)              | 56.8                 | 54.4                 | 53.3                 |  |
| Week 108 (n=88,90,92)             | 60.2                 | 56.7                 | 53.3                 |  |
| Week 120 (n=88,90,92)             | 56.8                 | 52.2                 | 45.7                 |  |
| Week 132 (n=88,90,92)             | 52.3                 | 52.2                 | 50                   |  |
| Week 144 (n=88,90,92)             | 51.1                 | 54.4                 | 52.2                 |  |
| Week 156 (n=88,90,92)             | 48.9                 | 52.2                 | 50                   |  |
| Week 168 (n=88,90,92)             | 52.3                 | 53.3                 | 46.7                 |  |
| Week 180 (n=88,90,92)             | 51.1                 | 54.4                 | 46.7                 |  |
| Week 192 (n=88,90,92)             | 51.1                 | 55.6                 | 46.7                 |  |
| Week 204 (n=88,90,92)             | 50                   | 54.4                 | 46.7                 |  |
| Week 216 (n=88,90,92)             | 50                   | 54.4                 | 46.7                 |  |

Notes:

[2] - All participants with evaluable data at given time point.

[3] - All participants with evaluable data at given time point.

[4] - All participants with evaluable data at given time point.

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants in the PBO/EW/EW Analysis Population Achieving Clinical Response Per HiSCR at Each Visit

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants in the PBO/EW/EW Analysis Population Achieving Clinical Response Per HiSCR at Each Visit <sup>[5]</sup> |
|-----------------|--|

End point description:

Clinical response per HiSCR defined as percent reduction from baseline of the prior phase 3 study in the abscess and inflammatory nodule  $\geq 50\%$  (AN50) with no increase in the abscess count and no increase in the draining fistula count. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits. n=number of participants at given time point.

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

End point timeframe:

Entry of Period B in prior phase 3 study, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, and 204

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                  | PBO/EW/EW            |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 115 <sup>[6]</sup>   |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| Entry of Period B (n=115)         | 26.1                 |  |  |  |
| Week 12 (n=114)                   | 54.4                 |  |  |  |
| Week 24 (n=114)                   | 57.9                 |  |  |  |
| Week 36 (n=114)                   | 57                   |  |  |  |
| Week 48 (n=114)                   | 60.5                 |  |  |  |
| Week 60 (n=114)                   | 57                   |  |  |  |
| Week 72 (n=114)                   | 50                   |  |  |  |
| Week 84 (n=114)                   | 50                   |  |  |  |
| Week 96 (n=114)                   | 53.5                 |  |  |  |
| Week 108 (n=114)                  | 52.6                 |  |  |  |
| Week 120 (n=114)                  | 53.5                 |  |  |  |
| Week 132 (n=114)                  | 56.1                 |  |  |  |
| Week 144 (n=114)                  | 51.8                 |  |  |  |
| Week 156 (n=114)                  | 52.6                 |  |  |  |
| Week 168 (n=114)                  | 55.3                 |  |  |  |
| Week 180 (n=114)                  | 54.4                 |  |  |  |
| Week 192 (n=114)                  | 53.5                 |  |  |  |
| Week 204 (n=114)                  | 53.5                 |  |  |  |

Notes:

[6] - All participants with evaluable data at given time point.

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants in the PBO/PBO/EW Analysis Population Achieving Clinical Response Per HiSCR at Each Visit

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants in the PBO/PBO/EW Analysis Population Achieving Clinical Response Per HiSCR at Each Visit <sup>[7]</sup> |
|-----------------|---|

End point description:

Clinical response per HiSCR defined as percent reduction from baseline of the prior phase 3 study in the abscess and inflammatory nodule  $\geq 50\%$  (AN50) with no increase in the abscess count and no increase in the draining fistula count. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits. n=number of participants at given time point.

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

End point timeframe:

Entry of M12-555, Weeks 4, 8, 12, 18, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, and 192

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                  | PBO/PBO/EW           |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 123 <sup>[8]</sup>   |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| Entry of M12-555 (n=123)          | 19.5                 |  |  |  |
| Week 4 (n=122)                    | 46.7                 |  |  |  |
| Week 8 (n=122)                    | 51.6                 |  |  |  |
| Week 12 (n=122)                   | 48.4                 |  |  |  |
| Week 18 (n=122)                   | 57.4                 |  |  |  |
| Week 24 (n=122)                   | 55.7                 |  |  |  |
| Week 36 (n=122)                   | 60.7                 |  |  |  |
| Week 48 (n=122)                   | 54.9                 |  |  |  |
| Week 60 (n=122)                   | 55.7                 |  |  |  |
| Week 72 (n=122)                   | 54.9                 |  |  |  |
| Week 84 (n=122)                   | 54.9                 |  |  |  |
| Week 96 (n=122)                   | 57.4                 |  |  |  |
| Week 108 (n=122)                  | 54.9                 |  |  |  |
| Week 120 (n=122)                  | 52.5                 |  |  |  |
| Week 132 (n=122)                  | 54.1                 |  |  |  |
| Week 144 (n=122)                  | 51.6                 |  |  |  |
| Week 156 (n=122)                  | 50.8                 |  |  |  |
| Week 168 (n=122)                  | 51.6                 |  |  |  |
| Week 180 (n=122)                  | 51.6                 |  |  |  |
| Week 192 (n=122)                  | 51.6                 |  |  |  |

Notes:

[8] - All participants with evaluable data at given time point.

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Participants in the EW/EW/EW Analysis Population Who Achieved Abscess and Inflammatory Nodule (AN) Count of 0, 1, or 2 at Each Visit

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants in the EW/EW/EW Analysis Population Who Achieved Abscess and Inflammatory Nodule (AN) Count of 0, 1, or 2 at Each Visit <sup>[9]</sup> |
|-----------------|---|

End point description:

The percentage of participants with AN counts lowered to 0, 1, or 2 at each visit. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits.

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

End point timeframe:

Weeks 2 (first dose of adalimumab in prior phase 3 study), 4, 8, 12, 16, 20, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 201, and 216

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                  | EW/EW/EW             |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 88 <sup>[10]</sup>   |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| Week 2                            | 22.7                 |  |  |  |
| Week 4                            | 28.4                 |  |  |  |
| Week 8                            | 38.6                 |  |  |  |
| Week 12                           | 35.2                 |  |  |  |
| Week 16                           | 37.5                 |  |  |  |
| Week 20                           | 42                   |  |  |  |
| Week 24                           | 36.4                 |  |  |  |
| Week 36                           | 48.9                 |  |  |  |
| Week 48                           | 46.6                 |  |  |  |
| Week 60                           | 43.2                 |  |  |  |
| Week 72                           | 50                   |  |  |  |
| Week 84                           | 45.5                 |  |  |  |
| Week 96                           | 44.3                 |  |  |  |
| Week 108                          | 46.6                 |  |  |  |
| Week 120                          | 44.3                 |  |  |  |
| Week 132                          | 44.3                 |  |  |  |
| Week 144                          | 43.2                 |  |  |  |
| Week 156                          | 45.5                 |  |  |  |
| Week 168                          | 46.6                 |  |  |  |
| Week 180                          | 46.6                 |  |  |  |
| Week 192                          | 47.7                 |  |  |  |
| Week 204                          | 47.7                 |  |  |  |
| Week 216                          | 46.6                 |  |  |  |

Notes:

[10] - All participants with evaluable data at given time point.

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants in the EW/EOW/EW, EW/PBO/EW, and PBO/PBO/EW Analysis Populations Who Achieved AN Count of 0, 1, or 2 at Each Visit

|  |   |
|--|---|
| End point title  | Percentage of Participants in the EW/EOW/EW, EW/PBO/EW, and PBO/PBO/EW Analysis Populations Who Achieved AN Count of 0, 1, or 2 at Each Visit <sup>[11]</sup> |
| End point description:<br>The percentage of participants with AN counts lowered to 0, 1, or 2 at each visit. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits. n=number of participants at given time point. |   |
| End point type   | Primary   |
| End point timeframe:<br>Entry of M12-555, Weeks 4, 8, 12, 18, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, and 192   |   |

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                  | EW/EOW/EW            | EW/PBO/EW            | PBO/PBO/EW           |  |
|-----------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed       | 90 <sup>[12]</sup>   | 92 <sup>[13]</sup>   | 123 <sup>[14]</sup>  |  |
| Units: percentage of participants |                      |                      |                      |  |
| number (not applicable)           |                      |                      |                      |  |
| Entry of M12-555 (n=90,92,123)    | 31.1                 | 22.8                 | 21.1                 |  |
| Week 4 (n=87,92,122)              | 35.6                 | 34.8                 | 44.3                 |  |
| Week 8 (n=88,92,122)              | 43.2                 | 42.4                 | 53.3                 |  |
| Week 12 (n=88,92,122)             | 45.5                 | 44.6                 | 45.1                 |  |
| Week 18 (n=88,92,122)             | 50                   | 41.3                 | 50                   |  |
| Week 24 (n=88,92,122)             | 43.2                 | 46.7                 | 57.4                 |  |
| Week 36 (n=88,92,122)             | 54.5                 | 45.7                 | 57.4                 |  |
| Week 48 (n=88,92,122)             | 50                   | 42.4                 | 52.5                 |  |
| Week 60 (n=88,92,122)             | 48.9                 | 43.5                 | 51.6                 |  |
| Week 72 (n=88,92,122)             | 50                   | 43.5                 | 54.1                 |  |
| Week 84 (n=88,92,122)             | 53.4                 | 44.6                 | 50.8                 |  |
| Week 96 (n=88,92,122)             | 51.1                 | 40.2                 | 52.5                 |  |
| Week 108 (n=88,92,122)            | 51.1                 | 40.2                 | 51.6                 |  |
| Week 120 (n=88,92,122)            | 46.6                 | 37                   | 52.5                 |  |
| Week 132 (n=88,92,122)            | 51.1                 | 37                   | 53.3                 |  |
| Week 144 (n=88,92,122)            | 48.9                 | 41.3                 | 52.5                 |  |
| Week 156 (n=88,92,122)            | 47.7                 | 39.1                 | 51.6                 |  |
| Week 168 (n=88,92,122)            | 51.1                 | 35.9                 | 51.6                 |  |
| Week 180 (n=88,92,122)            | 51.1                 | 35.9                 | 51.6                 |  |
| Week 192 (n=88,92,122)            | 51.1                 | 35.9                 | 51.6                 |  |

Notes:

[12] - All participants with evaluable data at given time point.

[13] - All participants with evaluable data at given time point.

[14] - All participants with evaluable data at given time point.

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants in the PBO/EW/EW Analysis Population Who Achieved AN Count of 0, 1, or 2 at Each Visit

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants in the PBO/EW/EW Analysis Population Who Achieved AN Count of 0, 1, or 2 at Each Visit <sup>[15]</sup> |
|-----------------|---|

End point description:

The percentage of participants with AN counts lowered to 0, 1, or 2 at each visit. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits. n=number of participants at given time point.

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

End point timeframe:

Entry of Period B in prior phase 3 study, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, and 204

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                  | PBO/EW/EW            |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 115 <sup>[16]</sup>  |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| Entry of Period B (n=115)         | 20                   |  |  |  |
| Week 12 (n=114)                   | 38.6                 |  |  |  |
| Week 24 (n=114)                   | 43                   |  |  |  |
| Week 36 (n=114)                   | 42.1                 |  |  |  |
| Week 48 (n=114)                   | 43.9                 |  |  |  |
| Week 60 (n=114)                   | 45.6                 |  |  |  |
| Week 72 (n=114)                   | 43.9                 |  |  |  |
| Week 84 (n=114)                   | 43.9                 |  |  |  |
| Week 96 (n=114)                   | 46.5                 |  |  |  |
| Week 108 (n=114)                  | 42.1                 |  |  |  |
| Week 120 (n=114)                  | 45.6                 |  |  |  |
| Week 132 (n=114)                  | 46.5                 |  |  |  |
| Week 144 (n=114)                  | 49.1                 |  |  |  |
| Week 156 (n=114)                  | 45.6                 |  |  |  |
| Week 168 (n=114)                  | 46.5                 |  |  |  |
| Week 180 (n=114)                  | 46.5                 |  |  |  |
| Week 192 (n=114)                  | 45.6                 |  |  |  |
| Week 204 (n=114)                  | 45.6                 |  |  |  |

Notes:

[16] - All participants with evaluable data at given time point.

## Statistical analyses

No statistical analyses for this end point

## Primary: Modified Sartorius Score: Change From Baseline to Each Visit for Participants in the EW/EW/EW Analysis Population

|                 |   |
|-----------------|---|
| End point title | Modified Sartorius Score: Change From Baseline to Each Visit for Participants in the EW/EW/EW Analysis Population <sup>[17]</sup> |
|-----------------|---|

End point description:

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. Higher scores indicate greater severity of HS. A negative change indicates decrease in severity. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits.

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

End point timeframe:

Baseline (in prior phase 3 study) to Weeks 2 (first dose of adalimumab in prior phase 3 study), 4, 8, 12, 16, 20, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                     | EW/EW/EW             |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 88 <sup>[18]</sup>   |  |  |  |
| Units: units on a scale              |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Week 2                               | -18 (± 25.27)        |  |  |  |
| Week 4                               | -21 (± 31.81)        |  |  |  |
| Week 8                               | -22.8 (± 35.45)      |  |  |  |
| Week 12                              | -23.9 (± 48.3)       |  |  |  |
| Week 16                              | -26.6 (± 54.63)      |  |  |  |
| Week 20                              | -32.1 (± 73.69)      |  |  |  |
| Week 24                              | -36.6 (± 74.99)      |  |  |  |
| Week 36                              | -41.6 (± 93.11)      |  |  |  |
| Week 48                              | -42.2 (± 115.22)     |  |  |  |
| Week 60                              | -41.9 (± 119.98)     |  |  |  |
| Week 72                              | -43.2 (± 122.3)      |  |  |  |
| Week 84                              | -42.8 (± 123.18)     |  |  |  |
| Week 96                              | -43.2 (± 126.21)     |  |  |  |
| Week 108                             | -43.2 (± 124.92)     |  |  |  |
| Week 120                             | -43.4 (± 127.65)     |  |  |  |
| Week 132                             | -42.5 (± 128.45)     |  |  |  |
| Week 144                             | -42.4 (± 129.37)     |  |  |  |
| Week 156                             | -40.7 (± 130.3)      |  |  |  |
| Week 168                             | -41.5 (± 130.4)      |  |  |  |
| Week 180                             | -41.8 (± 129.89)     |  |  |  |
| Week 192                             | -41.9 (± 130.46)     |  |  |  |
| Week 204                             | -41.4 (± 130.72)     |  |  |  |
| Week 216                             | -41.4 (± 130.94)     |  |  |  |

Notes:

[18] - All participants with evaluable data at given time point.

## Statistical analyses

No statistical analyses for this end point

**Primary: Modified Sartorius Score: Change From Baseline to Each Visit for Participants in the EW/EOW/EW, EW/PBO/EW, and PBO/PBO/EW Analysis Populations**

|                 |  |
|-----------------|--|
| End point title | Modified Sartorius Score: Change From Baseline to Each Visit for Participants in the EW/EOW/EW, EW/PBO/EW, and PBO/PBO/EW Analysis Populations <sup>[19]</sup> |
|-----------------|--|

End point description:

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. Higher scores indicate greater severity of HS. A negative change indicates decrease in severity. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits. n=number of participants at given time point.

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

End point timeframe:

Baseline (in prior phase 3 study) to Entry of M12-555 and Weeks 4, 8, 12, 18, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, and 192

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                     | EW/EOW/EW            | EW/PBO/EW            | PBO/PBO/EW           |  |
|--------------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type                   | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed          | 90 <sup>[20]</sup>   | 92 <sup>[21]</sup>   | 123 <sup>[22]</sup>  |  |
| Units: units on a scale              |                      |                      |                      |  |
| arithmetic mean (standard deviation) |                      |                      |                      |  |
| Entry of M12-555 (n=90,92,123)       | -23.1 (± 56.94)      | -10.5 (± 56.74)      | 0.2 (± 51.35)        |  |
| Week 4 (n=87,92,122)                 | -30.2 (± 48.99)      | -18.8 (± 56.52)      | -16.2 (± 56.16)      |  |
| Week 8 (n=88,92,122)                 | -34.9 (± 47.42)      | -21.2 (± 63.26)      | -24.8 (± 51.55)      |  |
| Week 12 (n=88,92,122)                | -34.8 (± 55.71)      | -25.5 (± 57.92)      | -26.2 (± 54.58)      |  |
| Week 18 (n=88,92,122)                | -35.9 (± 47.92)      | -26.2 (± 60.59)      | -32.3 (± 48.6)       |  |
| Week 24 (n=88,92,122)                | -37.1 (± 47.39)      | -24.1 (± 61.52)      | -33.5 (± 50.2)       |  |
| Week 36 (n=88,92,122)                | -37.1 (± 46.07)      | -24.7 (± 63.81)      | -33.6 (± 57.58)      |  |
| Week 48 (n=88,92,122)                | -37.5 (± 47.94)      | -24.8 (± 63.21)      | -30.2 (± 64.84)      |  |
| Week 60 (n=88,92,122)                | -34.8 (± 50.17)      | -22.6 (± 65.06)      | -31.7 (± 66.33)      |  |
| Week 72 (n=88,92,122)                | -35.4 (± 55.22)      | -20.1 (± 64.52)      | -31.8 (± 65.26)      |  |
| Week 84 (n=88,92,122)                | -36.6 (± 51.33)      | -20 (± 66.02)        | -29.5 (± 65.79)      |  |
| Week 96 (n=88,92,122)                | -34 (± 49.42)        | -18.3 (± 65.14)      | -29 (± 68.85)        |  |
| Week 108 (n=88,92,122)               | -34 (± 54.41)        | -18.3 (± 66.88)      | -28.4 (± 71.52)      |  |
| Week 120 (n=88,92,122)               | -31.8 (± 60.85)      | -16.2 (± 66.82)      | -28.3 (± 70.37)      |  |
| Week 132 (n=88,92,122)               | -35.1 (± 53.01)      | -16.7 (± 66.87)      | -28.8 (± 69.79)      |  |
| Week 144 (n=88,92,122)               | -35.1 (± 53.94)      | -16.6 (± 67.3)       | -28.6 (± 70.03)      |  |



|                        |                 |                 |                 |  |
|------------------------|-----------------|-----------------|-----------------|--|
| Week 156 (n=88,92,122) | -34.7 (± 53.95) | -15.7 (± 67.09) | -28 (± 69.11)   |  |
| Week 168 (n=88,92,122) | -35.6 (± 53.72) | -15.5 (± 67.4)  | -28.7 (± 69.81) |  |
| Week 180 (n=88,92,122) | -35.6 (± 53.64) | -15.4 (± 67.39) | -28.7 (± 69.81) |  |
| Week 192 (n=88,92,122) | -35.6 (± 53.64) | -15.4 (± 67.39) | -28.7 (± 69.81) |  |

Notes:

[20] - All participants with evaluable data at given time point.

[21] - All participants with evaluable data at given time point.

[22] - All participants with evaluable data at given time point.

## Statistical analyses

No statistical analyses for this end point

## Primary: Modified Sartorius Score: Change From Baseline to Each Visit for Participants in the PBO/EW/EW Analysis Population

|                 |  |
|-----------------|--|
| End point title | Modified Sartorius Score: Change From Baseline to Each Visit for Participants in the PBO/EW/EW Analysis Population <sup>[23]</sup> |
|-----------------|--|

End point description:

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. Higher scores indicate greater severity of HS. A negative change indicates decrease in severity. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits. n=number of participants at given time point.

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

End point timeframe:

Baseline (in prior phase 3 study) to Entry of Period B in prior phase 3 study and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, and 204

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                     | PBO/EW/EW            |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 115 <sup>[24]</sup>  |  |  |  |
| Units: units on a scale              |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Entry of Period B (n=115)            | -18 (± 38.32)        |  |  |  |
| Week 12 (n=114)                      | -43.2 (± 48.07)      |  |  |  |
| Week 24 (n=114)                      | -43 (± 53.08)        |  |  |  |
| Week 36 (n=114)                      | -49.5 (± 57.05)      |  |  |  |
| Week 48 (n=114)                      | -47.1 (± 61.95)      |  |  |  |
| Week 60 (n=114)                      | -46.2 (± 60.94)      |  |  |  |
| Week 72 (n=114)                      | -44.5 (± 67.13)      |  |  |  |

|                  |                 |  |  |  |
|------------------|-----------------|--|--|--|
| Week 84 (n=114)  | -46.8 (± 64.57) |  |  |  |
| Week 96 (n=114)  | -45.5 (± 70.63) |  |  |  |
| Week 108 (n=114) | -45 (± 74.15)   |  |  |  |
| Week 120 (n=114) | -45.9 (± 75.3)  |  |  |  |
| Week 132 (n=114) | -44.4 (± 78.09) |  |  |  |
| Week 144 (n=114) | -45.4 (± 76.53) |  |  |  |
| Week 156 (n=114) | -46 (± 76.17)   |  |  |  |
| Week 168 (n=114) | -46.1 (± 75.84) |  |  |  |
| Week 180 (n=114) | -45.8 (± 75.96) |  |  |  |
| Week 192 (n=114) | -45.8 (± 75.89) |  |  |  |
| Week 204 (n=114) | -45.9 (± 75.96) |  |  |  |

Notes:

[24] - All participants with evaluable data at given time point.

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Participants in the EW/EW/EW Analysis Population Achieving Skin Pain NRS30 - At Worst at Each Visit Among Participants With Baseline Skin Pain NRS At Worst ≥ 3

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants in the EW/EW/EW Analysis Population Achieving Skin Pain NRS30 - At Worst at Each Visit Among Participants With Baseline Skin Pain NRS At Worst ≥ 3 <sup>[25]</sup> |
|-----------------|---|

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 participants before they went to bed and responded to the items based on a recall period of the "last 24 hours." The percentage of participants 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 each visit among participants with baseline skin pain NRS - at worst ≥ 3 are presented. Weekly averages of daily assessments were analyzed. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits.

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

End point timeframe:

Weeks 2 (first dose of adalimumab in prior phase 3 study), 4, 8, 12, 16, 20, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, and 192

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                  | EW/EW/EW             |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 63 <sup>[26]</sup>   |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| Week 2                            | 47.6                 |  |  |  |
| Week 4                            | 46                   |  |  |  |
| Week 8                            | 44.4                 |  |  |  |
| Week 12                           | 42.9                 |  |  |  |
| Week 16                           | 46                   |  |  |  |
| Week 20                           | 50.8                 |  |  |  |
| Week 24                           | 54                   |  |  |  |
| Week 36                           | 58.7                 |  |  |  |
| Week 48                           | 54                   |  |  |  |
| Week 60                           | 52.4                 |  |  |  |
| Week 72                           | 54                   |  |  |  |
| Week 84                           | 52.4                 |  |  |  |
| Week 96                           | 49.2                 |  |  |  |
| Week 108                          | 54                   |  |  |  |
| Week 120                          | 50.8                 |  |  |  |
| Week 132                          | 46                   |  |  |  |
| Week 144                          | 54                   |  |  |  |
| Week 156                          | 52.4                 |  |  |  |
| Week 168                          | 52.4                 |  |  |  |
| Week 180                          | 52.4                 |  |  |  |
| Week 192                          | 52.4                 |  |  |  |

Notes:

[26] - All participants with baseline skin pain NRS-at worst  $\geq 3$  and with evaluable data at given time point

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants in the EW/EOW/EW, EW/PBO/EW, and PBO/PBO/EW Analysis Populations Achieving Skin Pain NRS30 - At Worst at Each Visit Among Participants With Baseline Skin Pain NRS At Worst $\geq 3$

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants in the EW/EOW/EW, EW/PBO/EW, and PBO/PBO/EW Analysis Populations Achieving Skin Pain NRS30 - At Worst at Each Visit Among Participants With Baseline Skin Pain NRS At Worst $\geq 3$ <sup>[27]</sup> |
|-----------------|---|

End point description:

The 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 participants before they went to bed and responded to the items based on a recall period of the "last 24 hours." The percentage of participants who achieved at least 30% reduction and at least 1 unit reduction from Baseline in the NRS (NRS30) - at worst at each visit among participants with baseline skin pain NRS - at worst  $\geq 3$  are presented. Weekly averages of daily assessments were analyzed. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits. n=number of participants at given time point.

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

End point timeframe:

Entry of M12-555, and Weeks 4, 8, 12, 18, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, and 192

Notes:

[27] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                  | EW/EOW/EW            | EW/PBO/EW            | PBO/PBO/EW           |  |
|-----------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed       | 65 <sup>[28]</sup>   | 64 <sup>[29]</sup>   | 84 <sup>[30]</sup>   |  |
| Units: percentage of participants |                      |                      |                      |  |
| number (not applicable)           |                      |                      |                      |  |
| Entry of M12-555 (n=65,64,84)     | 40                   | 21.9                 | 22.6                 |  |
| Week 4 (n=61,58,83)               | 47.5                 | 43.1                 | 44.6                 |  |
| Week 8 (n=62,63,83)               | 45.2                 | 47.6                 | 51.8                 |  |
| Week 12 (n=63,63,83)              | 41.3                 | 54                   | 51.8                 |  |
| Week 18 (n=63,63,83)              | 47.6                 | 50.8                 | 55.4                 |  |
| Week 24 (n=63,63,83)              | 42.9                 | 47.6                 | 54.2                 |  |
| Week 36 (n=63,63,83)              | 49.2                 | 47.6                 | 55.4                 |  |
| Week 48 (n=63,63,83)              | 47.6                 | 50.8                 | 56.6                 |  |
| Week 60 (n=63,63,83)              | 47.6                 | 50.8                 | 50.6                 |  |
| Week 72 (n=63,63,83)              | 47.6                 | 42.9                 | 50.6                 |  |
| Week 84 (n=63,63,83)              | 50.8                 | 46                   | 48.2                 |  |
| Week 96 (n=63,63,83)              | 50.8                 | 55.6                 | 48.2                 |  |
| Week 108 (n=63,63,83)             | 50.8                 | 42.9                 | 50.6                 |  |
| Week 120 (n=63,63,83)             | 42.9                 | 47.6                 | 45.8                 |  |
| Week 132 (n=63,63,83)             | 41.3                 | 47.6                 | 48.2                 |  |
| Week 144 (n=63,63,83)             | 41.3                 | 50.8                 | 47                   |  |
| Week 156 (n=63,63,83)             | 39.7                 | 46                   | 49.4                 |  |
| Week 168 (n=63,63,83)             | 41.3                 | 49.2                 | 48.2                 |  |
| Week 180 (n=63,63,83)             | 41.3                 | 49.2                 | 48.2                 |  |
| Week 192 (n=63,63,83)             | 41.3                 | 49.2                 | 48.2                 |  |

Notes:

[28] - All participants with baseline skin pain NRS-at worst  $\geq 3$  and with evaluable data at given time point

[29] - All participants with baseline skin pain NRS-at worst  $\geq 3$  and with evaluable data at given time point

[30] - All participants with baseline skin pain NRS-at worst  $\geq 3$  and with evaluable data at given time point

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants in the PBO/EW/EW Analysis Population Achieving Skin Pain NRS30 - At Worst at Each Visit Among Participants With Baseline Skin Pain NRS At Worst $\geq 3$

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants in the PBO/EW/EW Analysis Population Achieving Skin Pain NRS30 - At Worst at Each Visit Among Participants With Baseline Skin Pain NRS At Worst $\geq 3$ <sup>[31]</sup> |
|-----------------|---|

End point description:

The 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 participants before they went to bed and responded to the items based on a recall period of the "last 24 hours." The percentage of participants who achieved at least 30% reduction and at least 1 unit reduction from Baseline in the NRS (NRS30) - at worst at each visit among participants with baseline skin pain NRS - at worst  $\geq 3$  are presented. Weekly averages of daily

assessments were analyzed. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits. n=number of participants at given time point.

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

End point timeframe:

Entry of Period B in prior phase 3 study, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, and 204

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                  | PBO/EW/EW            |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 79 <sup>[32]</sup>   |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| Entry of Period B (n=79)          | 31.6                 |  |  |  |
| Week 12 (n=64)                    | 51.6                 |  |  |  |
| Week 24 (n=76)                    | 55.3                 |  |  |  |
| Week 36 (n=77)                    | 55.8                 |  |  |  |
| Week 48 (n=77)                    | 53.2                 |  |  |  |
| Week 60 (n=77)                    | 58.4                 |  |  |  |
| Week 72 (n=77)                    | 64.9                 |  |  |  |
| Week 84 (n=77)                    | 63.6                 |  |  |  |
| Week 96 (n=77)                    | 62.3                 |  |  |  |
| Week 108 (n=78)                   | 55.1                 |  |  |  |
| Week 120 (n=78)                   | 56.4                 |  |  |  |
| Week 132 (n=78)                   | 53.8                 |  |  |  |
| Week 144 (n=78)                   | 55.1                 |  |  |  |
| Week 156 (n=78)                   | 51.3                 |  |  |  |
| Week 168 (n=78)                   | 57.7                 |  |  |  |
| Week 180 (n=78)                   | 57.7                 |  |  |  |
| Week 192 (n=78)                   | 56.4                 |  |  |  |
| Week 204 (n=78)                   | 57.7                 |  |  |  |

Notes:

[32] - All participants with baseline skin pain NRS-at worst  $\geq 3$  and with evaluable data at given time point

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Participants in the EW/EW/EW Analysis Population Achieving Skin Pain NRS30 - On Average at Each Visit Among Participants With Baseline Skin Pain NRS On Average $\geq 3$

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants in the EW/EW/EW Analysis Population Achieving Skin Pain NRS30 - On Average at Each Visit Among Participants With Baseline Skin Pain NRS On Average $\geq 3$ <sup>[33]</sup> |
|-----------------|--|

End point description:

The 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 participants before they went to bed and responded to the items based on a recall period of the "last 24 hours." The percentage of participants who achieved at least 30% reduction and at least 1 unit reduction from Baseline in the NRS (NRS30) - on average at each visit

among participants with baseline skin pain NRS - on average  $\geq 3$  are presented. Weekly averages of daily assessments were analyzed. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits.

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

End point timeframe:

Weeks 2 (first dose of adalimumab in prior phase 3 study), 4, 8, 12, 16, 20, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, and 192

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                  | EW/EW/EW             |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 50 <sup>[34]</sup>   |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| Week 2                            | 56                   |  |  |  |
| Week 4                            | 52                   |  |  |  |
| Week 8                            | 48                   |  |  |  |
| Week 12                           | 46                   |  |  |  |
| Week 16                           | 40                   |  |  |  |
| Week 20                           | 50                   |  |  |  |
| Week 24                           | 46                   |  |  |  |
| Week 36                           | 58                   |  |  |  |
| Week 48                           | 56                   |  |  |  |
| Week 60                           | 56                   |  |  |  |
| Week 72                           | 56                   |  |  |  |
| Week 84                           | 56                   |  |  |  |
| Week 96                           | 54                   |  |  |  |
| Week 108                          | 50                   |  |  |  |
| Week 120                          | 48                   |  |  |  |
| Week 132                          | 56                   |  |  |  |
| Week 144                          | 56                   |  |  |  |
| Week 156                          | 58                   |  |  |  |
| Week 168                          | 56                   |  |  |  |
| Week 180                          | 56                   |  |  |  |
| Week 192                          | 56                   |  |  |  |

Notes:

[34] - All participants with baseline skin pain NRS-on average  $\geq 3$  with evaluable data at given time point

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants in the EW/EOW/EW, EW/PBO/EW, and PBO/PBO/EW Analysis Populations Achieving Skin Pain NRS30 - On Average at Each Visit Among Participants With Baseline Skin Pain NRS On Average $\geq 3$

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants in the EW/EOW/EW, EW/PBO/EW, and PBO/PBO/EW Analysis Populations Achieving Skin Pain NRS30 - On Average at Each Visit Among Participants With Baseline Skin Pain NRS On Average $\geq 3$ <sup>[35]</sup> |
|-----------------|---|

**End point description:**

The 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 participants before they went to bed and responded to the items based on a recall period of the "last 24 hours." The percentage of participants who achieved at least 30% reduction and at least 1 unit reduction from Baseline in the NRS (NRS30) - on average at each visit among participants with baseline skin pain NRS - on average  $\geq 3$  are presented. Weekly averages of daily assessments were analyzed. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits. n=number of participants at given time point.

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

**End point timeframe:**

Entry of M12-555, and Weeks 4, 8, 12, 18, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, and 192

**Notes:**

[35] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                  | EW/EOW/EW            | EW/PBO/EW            | PBO/PBO/EW           |  |
|-----------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed       | 55 <sup>[36]</sup>   | 53 <sup>[37]</sup>   | 69 <sup>[38]</sup>   |  |
| Units: percentage of participants |                      |                      |                      |  |
| number (not applicable)           |                      |                      |                      |  |
| Entry of M12-555 (n=55,53,69)     | 43.6                 | 37.7                 | 31.9                 |  |
| Week 4 (n=51,47,68)               | 49                   | 46.8                 | 61.8                 |  |
| Week 8 (n=52,52,68)               | 46.2                 | 55.8                 | 61.8                 |  |
| Week 12 (n=53,52,68)              | 39.6                 | 59.6                 | 58.8                 |  |
| Week 18 (n=53,52,68)              | 45.3                 | 59.6                 | 63.2                 |  |
| Week 24 (n=53,52,68)              | 39.6                 | 53.8                 | 54.4                 |  |
| Week 36 (n=53,52,68)              | 45.3                 | 48.1                 | 58.8                 |  |
| Week 48 (n=53,52,68)              | 47.2                 | 51.9                 | 58.8                 |  |
| Week 60 (n=53,52,68)              | 43.4                 | 53.8                 | 55.9                 |  |
| Week 72 (n=53,52,68)              | 47.2                 | 59.6                 | 55.9                 |  |
| Week 84 (n=53,52,68)              | 49.1                 | 48.1                 | 52.9                 |  |
| Week 96 (n=53,52,68)              | 47.2                 | 57.7                 | 57.4                 |  |
| Week 108 (n=53,52,68)             | 49.1                 | 44.2                 | 54.4                 |  |
| Week 120 (n=53,52,68)             | 39.6                 | 48.1                 | 54.4                 |  |
| Week 132 (n=53,52,68)             | 43.4                 | 50                   | 54.4                 |  |
| Week 144 (n=53,52,68)             | 43.4                 | 50                   | 54.4                 |  |
| Week 156 (n=53,52,68)             | 43.4                 | 46.2                 | 55.9                 |  |
| Week 168 (n=53,52,68)             | 43.4                 | 48.1                 | 54.4                 |  |
| Week 180 (n=53,52,68)             | 43.4                 | 48.1                 | 54.4                 |  |
| Week 192 (n=53,52,68)             | 43.4                 | 48.1                 | 54.4                 |  |

**Notes:**

[36] - All participants with baseline skin pain NRS-on average  $\geq 3$  with evaluable data at given time point

[37] - All participants with baseline skin pain NRS-on average  $\geq 3$  with evaluable data at given time point

[38] - All participants with baseline skin pain NRS-on average  $\geq 3$  with evaluable data at given time point

**Statistical analyses**

No statistical analyses for this end point

**Primary: Percentage of Participants in the PBO/EW/EW Analysis Population Achieving Skin Pain NRS30 - On Average at Each Visit Among Participants With Baseline Skin Pain NRS On Average  $\geq 3$**

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants in the PBO/EW/EW Analysis Population Achieving Skin Pain NRS30 - On Average at Each Visit Among Participants With Baseline Skin Pain NRS On Average $\geq 3$ <sup>[39]</sup> |
|-----------------|---|

End point description:

The 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 participants before they went to bed and responded to the items based on a recall period of the "last 24 hours." The percentage of participants who achieved at least 30% reduction and at least 1 unit reduction from Baseline in the NRS (NRS30) - on average at each visit among participants with baseline skin pain NRS - on average  $\geq 3$  are presented. Weekly averages of daily assessments were analyzed. LOCF: The last completed evaluation from the previous visit was carried forward to impute missing data at later visits. n=number of participants at given time point.

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

End point timeframe:

Entry of Period B in prior phase 3 study, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, and 204

Notes:

[39] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data were summarized for this endpoint per protocol.

| End point values                  | PBO/EW/EW            |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 62 <sup>[40]</sup>   |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| Entry of Period B (n=62)          | 30.6                 |  |  |  |
| Week 12 (n=49)                    | 59.2                 |  |  |  |
| Week 24 (n=59)                    | 61                   |  |  |  |
| Week 36 (n=60)                    | 61.7                 |  |  |  |
| Week 48 (n=60)                    | 53.3                 |  |  |  |
| Week 60 (n=60)                    | 60                   |  |  |  |
| Week 72 (n=60)                    | 58.3                 |  |  |  |
| Week 84 (n=60)                    | 60                   |  |  |  |
| Week 96 (n=60)                    | 61.7                 |  |  |  |
| Week 108 (n=61)                   | 62.3                 |  |  |  |
| Week 120 (n=61)                   | 62.3                 |  |  |  |
| Week 132 (n=61)                   | 59                   |  |  |  |
| Week 144 (n=61)                   | 60.7                 |  |  |  |
| Week 156 (n=61)                   | 55.7                 |  |  |  |
| Week 168 (n=61)                   | 62.3                 |  |  |  |
| Week 180 (n=61)                   | 62.3                 |  |  |  |
| Week 192 (n=61)                   | 60.7                 |  |  |  |
| Week 204 (n=61)                   | 62.3                 |  |  |  |

Notes:

[40] - All participants with baseline skin pain NRS-on average  $\geq 3$  with evaluable data at given time point

**Statistical analyses**

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) were collected from first dose of study drug until 70 days after the last dose of study drug (up to 225 weeks).

Adverse event reporting additional description:

TEAEs and TESAEs were defined as AEs and SAEs with an onset date on or after the first dose of adalimumab in either M12-555 or in prior studies M11-313 or M11-810, excluding AEs and SAEs with onset date during a protocol-defined treatment gap.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

### Reporting groups

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

Reporting group description:

Participants who received at least 1 dose of adalimumab (40 mg every week) in M12-555.

| Serious adverse events  | All Adalimumab    |  |  |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events                   |                   |  |  |
| subjects affected / exposed   | 99 / 508 (19.49%) |  |  |
| number of deaths (all causes)                                       | 3                 |  |  |
| number of deaths resulting from adverse events                      |                   |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |  |  |
| Breast cancer stage III   |                   |  |  |
| subjects affected / exposed   | 1 / 508 (0.20%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 0             |  |  |
| Cardiac myxoma  |                   |  |  |
| subjects affected / exposed   | 1 / 508 (0.20%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 0             |  |  |
| Hodgkin's disease   |                   |  |  |
| subjects affected / exposed   | 1 / 508 (0.20%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 0             |  |  |
| Invasive breast carcinoma   |                   |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Metastases to liver                             |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Pancreatic carcinoma                            |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 1 / 1           |  |  |
| Papillary cystadenoma lymphomatosum             |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Seminoma  |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Squamous cell carcinoma of skin                 |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Vascular disorders                              |                 |  |  |
| Deep vein thrombosis                            |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hypertension                                    |                 |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hypertensive crisis                             |                 |  |  |

|  |                 |  |  |
|--|-----------------|--|--|
| subjects affected / exposed                          | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Pregnancy, puerperium and perinatal conditions       |                 |  |  |
| Abortion spontaneous                                 |                 |  |  |
| subjects affected / exposed                          | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| General disorders and administration site conditions |                 |  |  |
| Non-cardiac chest pain                               |                 |  |  |
| subjects affected / exposed                          | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Pyrexia  |                 |  |  |
| subjects affected / exposed                          | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Social circumstances                                 |                 |  |  |
| Sexual abuse   |                 |  |  |
| subjects affected / exposed                          | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Reproductive system and breast disorders             |                 |  |  |
| Ovarian cyst   |                 |  |  |
| subjects affected / exposed                          | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Pelvic prolapse                                      |                 |  |  |
| subjects affected / exposed                          | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Uterine cyst   |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Dysfunctional uterine bleeding                  |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Acute pulmonary oedema                          |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Acute respiratory failure                       |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pleurisy  |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumonitis                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory distress                            |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory failure                             |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychiatric disorders                           |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Suicidal ideation                               |                 |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Investigations                                  |                 |  |  |
| Autoantibody positive                           |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Body temperature increased                      |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Injury, poisoning and procedural complications  |                 |  |  |
| Accidental overdose                             |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Ankle fracture                                  |                 |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Burns second degree                             |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Contusion                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Foot fracture                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| Joint injury                                    |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Lower limb fracture                             |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Meniscus injury                                 |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Procedural dizziness                            |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Procedural nausea                               |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Procedural pain                                 |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Radial head dislocation                         |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Scar  |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Tendon rupture                                  |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Upper limb fracture                             |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Congenital, familial and genetic disorders      |                 |  |  |
| Odontogenic cyst                                |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac disorders                               |                 |  |  |
| Angina pectoris                                 |                 |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac arrest                                  |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac failure                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Palpitations                                    |                 |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Nervous system disorders                        |                 |  |  |
| Cerebrovascular accident                        |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Coma hepatic                                    |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Hemiplegia                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Transient ischaemic attack                      |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Blood and lymphatic system disorders            |                 |  |  |
| Lymphadenitis                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrointestinal disorders                      |                 |  |  |
| Autoimmune pancreatitis                         |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Crohn's disease                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Incarcerated umbilical hernia                   |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Peritoneal cyst                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |



|   |                  |  |  |
|---|------------------|--|--|
| Hepatobiliary disorders                         |                  |  |  |
| Cholangitis                                     |                  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Cholelithiasis                                  |                  |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%)  |  |  |
| occurrences causally related to treatment / all | 0 / 2            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Skin and subcutaneous tissue disorders          |                  |  |  |
| Cutis laxa                                      |                  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Hidradenitis                                    |                  |  |  |
| subjects affected / exposed                     | 29 / 508 (5.71%) |  |  |
| occurrences causally related to treatment / all | 1 / 39           |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Pustular psoriasis                              |                  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%)  |  |  |
| occurrences causally related to treatment / all | 1 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Pyoderma gangrenosum                            |                  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%)  |  |  |
| occurrences causally related to treatment / all | 1 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Dermatitis contact                              |                  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Renal and urinary disorders                     |                  |  |  |
| Acute kidney injury                             |                  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Ureteric obstruction                            |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Musculoskeletal and connective tissue disorders |                 |  |  |
| Back pain                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Intervertebral disc protrusion                  |                 |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Joint instability                               |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Muscle spasms                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infections and infestations                     |                 |  |  |
| Appendicitis                                    |                 |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cellulitis                                      |                 |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| Erysipelas                                      |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Groin abscess                                   |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Infection                                       |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Peritonitis                                     |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Peritonsillar abscess                           |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Periumbilical abscess                           |                 |  |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Pilonidal cyst                                  |                 |  |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Pneumonia                                       |                 |  |  |  |
| subjects affected / exposed                     | 3 / 508 (0.59%) |  |  |  |
| occurrences causally related to treatment / all | 2 / 3           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Pneumonia chlamydial                            |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumonia viral                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Postoperative wound infection                   |                 |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pyelonephritis                                  |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Sepsis  |                 |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Septic shock                                    |                 |  |  |
| subjects affected / exposed                     | 2 / 508 (0.39%) |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Vulval abscess                                  |                 |  |  |
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Metabolism and nutrition disorders              |                 |  |  |
| Obesity   |                 |  |  |
| subjects affected / exposed                     | 3 / 508 (0.59%) |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Type 2 diabetes mellitus                        |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 508 (0.20%) |  |  |
| 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 %

|   |                    |  |  |
|---|--------------------|--|--|
| <b>Non-serious adverse events</b>                     | All Adalimumab     |  |  |
| Total subjects affected by non-serious adverse events |                    |  |  |
| subjects affected / exposed                           | 349 / 508 (68.70%) |  |  |
| Vascular disorders                                    |                    |  |  |
| Hypertension  |                    |  |  |
| subjects affected / exposed                           | 28 / 508 (5.51%)   |  |  |
| occurrences (all)                                     | 31                 |  |  |
| Nervous system disorders                              |                    |  |  |
| Headache  |                    |  |  |
| subjects affected / exposed                           | 80 / 508 (15.75%)  |  |  |
| occurrences (all)                                     | 149                |  |  |
| General disorders and administration site conditions  |                    |  |  |
| Pyrexia   |                    |  |  |
| subjects affected / exposed                           | 29 / 508 (5.71%)   |  |  |
| occurrences (all)                                     | 42                 |  |  |
| Gastrointestinal disorders                            |                    |  |  |
| Diarrhoea   |                    |  |  |
| subjects affected / exposed                           | 33 / 508 (6.50%)   |  |  |
| occurrences (all)                                     | 36                 |  |  |
| Nausea  |                    |  |  |
| subjects affected / exposed                           | 32 / 508 (6.30%)   |  |  |
| occurrences (all)                                     | 37                 |  |  |
| Respiratory, thoracic and mediastinal disorders       |                    |  |  |
| Cough   |                    |  |  |
| subjects affected / exposed                           | 27 / 508 (5.31%)   |  |  |
| occurrences (all)                                     | 31                 |  |  |
| Skin and subcutaneous tissue disorders                |                    |  |  |
| Hidradenitis  |                    |  |  |
| subjects affected / exposed                           | 125 / 508 (24.61%) |  |  |
| occurrences (all)                                     | 237                |  |  |

|   |                   |  |  |
|---|-------------------|--|--|
| Musculoskeletal and connective tissue disorders |                   |  |  |
| Arthralgia                                      |                   |  |  |
| subjects affected / exposed                     | 38 / 508 (7.48%)  |  |  |
| occurrences (all)                               | 44                |  |  |
| Back pain                                       |                   |  |  |
| subjects affected / exposed                     | 33 / 508 (6.50%)  |  |  |
| occurrences (all)                               | 41                |  |  |
| Infections and infestations                     |                   |  |  |
| Bronchitis                                      |                   |  |  |
| subjects affected / exposed                     | 37 / 508 (7.28%)  |  |  |
| occurrences (all)                               | 48                |  |  |
| Gastroenteritis                                 |                   |  |  |
| subjects affected / exposed                     | 26 / 508 (5.12%)  |  |  |
| occurrences (all)                               | 33                |  |  |
| Influenza                                       |                   |  |  |
| subjects affected / exposed                     | 40 / 508 (7.87%)  |  |  |
| occurrences (all)                               | 58                |  |  |
| Nasopharyngitis                                 |                   |  |  |
| subjects affected / exposed                     | 92 / 508 (18.11%) |  |  |
| occurrences (all)                               | 172               |  |  |
| Sinusitis                                       |                   |  |  |
| subjects affected / exposed                     | 29 / 508 (5.71%)  |  |  |
| occurrences (all)                               | 43                |  |  |
| Upper respiratory tract infection               |                   |  |  |
| subjects affected / exposed                     | 84 / 508 (16.54%) |  |  |
| occurrences (all)                               | 140               |  |  |
| Urinary tract infection                         |                   |  |  |
| subjects affected / exposed                     | 40 / 508 (7.87%)  |  |  |
| occurrences (all)                               | 49                |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 11 October 2012 | The main purpose of this amendment was to add pharmacokinetic adalimumab concentration and anti-adalimumab antibody (AAA) assays to some study visits, and update phase 2 safety and efficacy information in the background section.  |
| 07 August 2013  | The main purpose of this amendment was to add new safety monitoring language, incorporate new CDC guidelines on TB screening, add additional prohibited therapy (recently approved biologic therapies), add biomarker time points at weeks 12 and 48 visits, and add collection of information regarding surgery performed for chronic hidradenitis suppurativa (HS). |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported