# Clinical trial results:
# A 48 weeks study of three different dose regimens of BI 655066 administered subcutaneously in patients with moderate to severe chronic plaque psoriasis (randomised, dose-ranging, active-comparator-controlled (ustekinumab), double-blind within dose groups of BI 655066)

## Summary

| | |
|---|---|
| EudraCT number | 2012-004384-48 |
| Trial protocol | FI SE DE NO |
| Global end of trial date | 31 July 2015 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 14 August 2016 |
| First version publication date | 14 August 2016 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 1311.2 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02054481 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Boehringer Ingelheim |
| Sponsor organisation address | Binger Strasse 173, Ingelheim am Rhein, Germany, 55216 |
| Public contact | QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, +1 8002430127, clintriage.rdg@boehringer-ingelheim.com |
| Scientific contact | QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, +1 8002430127, clintriage.rdg@boehringer-ingelheim.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:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 15 September 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 25 November 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 July 2015 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The overall purpose of this trial is to assess clinical efficacy and safety of different subcutaneous doses of BI 655066 in adult patients with chronic plaque psoriasis in order to select doses for further clinical trials.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all patients as required.

Background therapy: -

Evidence for comparator:

Ustekinumab (Stelara®) administered by subcutaneous injection plus two saline injections at Week 0, Stelara® injection plus one saline injection at Weeks 4 and 16. Stelara® dose was 45 mg for patients with body weight ≤100 kg at randomisation or 90 mg for patients with body weight >100 kg at randomisation.

| | |
|---|---|
| Actual start date of recruitment | 26 February 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Canada: 37 |
| Country: Number of subjects enrolled | Finland: 4 |
| Country: Number of subjects enrolled | France: 30 |
| Country: Number of subjects enrolled | Germany: 27 |
| Country: Number of subjects enrolled | Norway: 7 |
| Country: Number of subjects enrolled | Sweden: 6 |
| Country: Number of subjects enrolled | United States: 120 |
| Worldwide total number of subjects | 231 |
| EEA total number of subjects | 74 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| 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) | 210 |
| From 65 to 84 years | 21 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

All subjects were screened for eligibility to participate in the trial. Subjects attended specialist sites which would then ensure that they (the subjects) met all strictly implemented inclusion/exclusion criteria. Subjects were not to be randomised to trial treatment if any one of the specific entry criteria were violated.

### Period 1

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

Blinding implementation details:

The different dose groups of BI 655066 were double-blind. Patients, investigators, and efficacy assessors were blinded to treatment. Stelara® was open-label to investigators and blinded to patients and efficacy assessors.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | BI 655066 18 mg |

Arm description:

18 mg BI 655066 administered by subcutaneous injection plus two placebo matching BI 655066 injections at Week 0, followed by two placebo matching BI 655066 injections each at Weeks 4 and 16.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BI 655066 18 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

18 mg BI 655066 administered by subcutaneous injection at Week 0.

| | |
|---|---|
| Investigational medicinal product name | Placebo matching BI 655066 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Two placebo matching BI 655066 injections administered each at Weeks 0, 4 and 16.

| | |
|---|---|
| **Arm title** | BI 655066 90 mg |

Arm description:

90 mg BI 655066 administered by subcutaneous injection plus two placebo matching BI 655066 injections at Week 0, followed by 90 mg BI 655066 plus one placebo matching BI 655066 injection at Weeks 4 and 16.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | BI 655066 90 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

90 mg BI 655066 administered by subcutaneous injection at Weeks 0, 4 and 16.

| | |
|---|---|
| Investigational medicinal product name | Placebo matching BI 655066 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

2 placebo matching BI 655066 injections administered at Weeks 0 and 1 placebo matching BI 655066 injection at Weeks 4 and 16.

| | |
|---|---|
| **Arm title** | BI 655066 180 mg |

Arm description:

180 mg BI 655066 administered by subcutaneous injection as two injections plus a placebo matching BI 655066 injection at Week 0, followed by 180 mg BI 655066 administered as two injections at Weeks 4 and 16.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BI 655066 180 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

180 mg BI 655066 administered by subcutaneous injection as two injections at Weeks 0, 4 and 16.

| | |
|---|---|
| Investigational medicinal product name | Placebo matching BI 655066 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo matching BI 655066 injection administered at Week 0.

| | |
|---|---|
| **Arm title** | Stelara® |

Arm description:

Stelara® administered by subcutaneous injection plus two saline injections at Week 0, Stelara® injection plus one saline injection at Weeks 4 and 16. Stelara® dose was 45 mg for patients with body weight ≤100 kg at randomisation or 90 mg for patients with body weight >100 kg at randomisation.

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

Dosage and administration details:

Stelara® 45 mg or 90 mg was administered by subcutaneous injection at Weeks 0, 4 and 16.

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

Dosage and administration details:

Saline injection was done at Weeks 0, 4 and 16. 2 injections at Week 0 and 1 injection at Weeks 4 and 16.

| **Number of subjects in period 1[1]** | BI 655066 18 mg | BI 655066 90 mg | BI 655066 180 mg |
|---|---|---|---|
| Started | 43 | 41 | 42 |
| Completed | 39 | 39 | 40 |
| Not completed | 4 | 2 | 2 |
| Adverse event, non-fatal | 1 | 1 | - |
| Lost to follow-up | 1 | - | - |
| Other reasoon | 2 | 1 | 2 |

| **Number of subjects in period 1[1]** | Stelara® |
|---|---|
| Started | 40 |
| Completed | 39 |
| Not completed | 1 |
| Adverse event, non-fatal | 1 |
| Lost to follow-up | - |
| Other reasoon | - |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline characteristics are based on patients who were randomised after successfully completing the screening period and received at least one dose of the trial medication.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | BI 655066 18 mg |
| Reporting group description: | |
| 18 mg BI 655066 administered by subcutaneous injection plus two placebo matching BI 655066 injections at Week 0, followed by two placebo matching BI 655066 injections each at Weeks 4 and 16. | |
| Reporting group title | BI 655066 90 mg |
| Reporting group description: | |
| 90 mg BI 655066 administered by subcutaneous injection plus two placebo matching BI 655066 injections at Week 0, followed by 90 mg BI 655066 plus one placebo matching BI 655066 injection at Weeks 4 and 16. | |
| Reporting group title | BI 655066 180 mg |
| Reporting group description: | |
| 180 mg BI 655066 administered by subcutaneous injection as two injections plus a placebo matching BI 655066 injection at Week 0, followed by 180 mg BI 655066 administered as two injections at Weeks 4 and 16. | |
| Reporting group title | Stelara® |
| Reporting group description: | |
| Stelara® administered by subcutaneous injection plus two saline injections at Week 0, Stelara® injection plus one saline injection at Weeks 4 and 16. Stelara® dose was 45 mg for patients with body weight ≤100 kg at randomisation or 90 mg for patients with body weight >100 kg at randomisation. | |

| Reporting group values | BI 655066 18 mg | BI 655066 90 mg | BI 655066 180 mg |
|---|---|---|---|
| Number of subjects | 43 | 41 | 42 |
| Age categorical<br>Units: Subjects | | | |

| Age Continuous | | | |
|---|---|---|---|
| Safety Set (SAF) which Included all randomised patients who received at least 1 dose of trial medication and was based on the first treatment received. | | | |
| Units: Years | | | |
| arithmetic mean | 44.1 | 49.3 | 44.9 |
| standard deviation | ± 14.2 | ± 13.3 | ± 14 |
| Gender, Male/Female<br>Units: Participants | | | |
| Female | 20 | 11 | 13 |
| Male | 23 | 30 | 29 |

| Reporting group values | Stelara® | Total | |
|---|---|---|---|
| Number of subjects | 40 | 166 | |
| Age categorical<br>Units: Subjects | | | |

| Age Continuous | | | |
|---|---|---|---|
| Safety Set (SAF) which Included all randomised patients who received at least 1 dose of trial medication and was based on the first treatment received. | | | |
| Units: Years | | | |
| arithmetic mean | 45.4 | | |
| standard deviation | ± 12.1 | - | |

| Gender, Male/Female<br>Units: Participants | | | |
|---|---|---|---|
| Female | 13 | 57 | |
| Male | 27 | 109 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | BI 655066 18 mg |
| Reporting group description: | |
| 18 mg BI 655066 administered by subcutaneous injection plus two placebo matching BI 655066 injections at Week 0, followed by two placebo matching BI 655066 injections each at Weeks 4 and 16. | |
| Reporting group title | BI 655066 90 mg |
| Reporting group description: | |
| 90 mg BI 655066 administered by subcutaneous injection plus two placebo matching BI 655066 injections at Week 0, followed by 90 mg BI 655066 plus one placebo matching BI 655066 injection at Weeks 4 and 16. | |
| Reporting group title | BI 655066 180 mg |
| Reporting group description: | |
| 180 mg BI 655066 administered by subcutaneous injection as two injections plus a placebo matching BI 655066 injection at Week 0, followed by 180 mg BI 655066 administered as two injections at Weeks 4 and 16. | |
| Reporting group title | Stelara® |
| Reporting group description: | |
| Stelara® administered by subcutaneous injection plus two saline injections at Week 0, Stelara® injection plus one saline injection at Weeks 4 and 16. Stelara® dose was 45 mg for patients with body weight ≤100 kg at randomisation or 90 mg for patients with body weight >100 kg at randomisation. | |
| Subject analysis set title | BI 655066 90+180 mg |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| 90 mg BI 655066 or 180 mg BI 655066 administered by subcutaneous injection at Weeks 0, 4 and 16, plus matching placebos. | |

### Primary: Achievement of ≥90% reduction from baseline PASI score (PASI90) at Week 12

| | |
|---|---|
| End point title | Achievement of ≥90% reduction from baseline PASI score (PASI90) at Week 12 |
| End point description: | |
| Percentage of participants who achieved ≥90% reduction from baseline in Psoriasis Area and Severity Index score (PASI90) at Week 12. PASI score ranges from 0 (best) to 72 (worst). Full Analysis Set (FAS): Which included all randomised patients who received at least 1 dose of trial medication and was based on the randomised treatment. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline and Week 12 | |

| End point values | BI 655066 18 mg | BI 655066 90 mg | BI 655066 180 mg | Stelara® |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43[1] | 41[2] | 42[3] | 40[4] |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 32.6 (19.1 to 48.5) | 73.2 (57.1 to 85.8) | 81 (65.9 to 91.4) | 40 (24.9 to 56.7) |

Notes:

[1] - FAS

[2] - FAS

[3] - FAS
[4] - FAS

| End point values | BI 655066 90+180 mg | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 83[5] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 77.1 (66.6 to 85.6) | | | |

Notes:
[5] - FAS

## Statistical analyses

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

Statistical analysis description:

The difference in proportion responding between BI 90+180 mg and Stelara® was estimated and tested using the Cochran-Mantel-Haenszel (CMH) risk difference estimate stratified by the randomisation factors of weight (≤100 kg vs. >100 kg) and prior exposure to 2 or more Tumour Necrosis Factor (TNF) antagonists with discontinuation due to lack of efficacy, with weights proposed by Greenland/Robins. Difference calculated as BI 90+180 mg minus Stelara®.

| | |
|---|---|
| Comparison groups | Stelara® v BI 655066 90+180 mg |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [6] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (net) |
| Point estimate | 36.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 19 |
| upper limit | 53.8 |

Notes:

[6] - Pairwise comparisons of all doses and treatments were conducted using the same CMH methods; 95% confidence intervals (CI) as well as nominal p-values of the comparison of doses were provided. There were no adjustments for multiplicity.

## Secondary: Achievement of ≥75% reduction from baseline in PASI score (PASI75) at Weeks 12 and 24

| End point title | Achievement of ≥75% reduction from baseline in PASI score (PASI75) at Weeks 12 and 24 |
|---|---|

End point description:

Percentage of participants who achieved ≥75% reduction from baseline in Psoriasis Area and Severity Index score (PASI75) at Weeks 12 and 24. PASI score ranges from 0 (best) to 72 (worst).

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

End point timeframe:

Baseline, Week 12 and Week 24

| End point values | BI 655066 18 mg | BI 655066 90 mg | BI 655066 180 mg | Stelara® |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43[7] | 41[8] | 42[9] | 40 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 12 | 67.4 (51.5 to 80.9) | 97.6 (87.1 to 99.9) | 90.5 (77.4 to 97.3) | 77.5 (61.5 to 89.2) |
| Week 24 | 55.8 (39.9 to 70.9) | 92.7 (80.1 to 98.5) | 92.9 (80.5 to 98.5) | 70 (53.5 to 83.4) |

Notes:

[7] - FAS

[8] - FAS

[9] - FAS

| End point values | BI 655066 90+180 mg | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 83[10] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 12 | 94 (86.5 to 98) | | | |
| Week 24 | 92.8 (84.9 to 97.3) | | | |

Notes:

[10] - FAS

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 (Week 12) |
|---|---|

Statistical analysis description:

The difference in proportion responding between BI 90+180 mg and Stelara® was estimated and tested using the Cochran-Mantel-Haenszel (CMH) risk difference estimate stratified by the randomisation factors of weight (≤100 kg vs. >100 kg) and prior exposure to 2 or more TNF antagonists with discontinuation due to lack of efficacy, with weights proposed by Greenland/Robins. Difference calculated as BI 90+180 mg minus Stelara®.

| | |
|---|---|
| Comparison groups | Stelara® v BI 655066 90+180 mg |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0355 [11] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (net) |
| Point estimate | 14.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1 |
| upper limit | 28.2 |

Notes:

[11] - Pairwise comparisons of all doses and treatments were conducted using the same CMH methods; 95% confidence intervals (CI) as well as nominal p-values of the comparison of doses were provided. There were no adjustments for multiplicity.

| Statistical analysis title | Statistical analysis 2 (Week 24) |
|---|---|

Statistical analysis description:

The difference in proportion responding between BI 90+180 mg and Stelara® was estimated and tested using the Cochran-Mantel-Haenszel (CMH) risk difference estimate stratified by the randomisation factors of weight (≤100 kg vs. >100 kg) and prior exposure to 2 or more TNF antagonists with discontinuation due to lack of efficacy, with weights proposed by Greenland/Robins. Difference calculated as BI 90+180 mg minus Stelara®.

| | |
|---|---|
| Comparison groups | Stelara® v BI 655066 90+180 mg |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0062 [12] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (net) |
| Point estimate | 21.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6 |
| upper limit | 36.2 |

Notes:

[12] - Pairwise comparisons of all doses and treatments were conducted using the same CMH methods; 95% confidence intervals (CI) as well as nominal p-values of the comparison of doses were provided. There were no adjustments for multiplicity.

## Secondary: Achievement of 100% reduction from baseline in PASI score (PASI100) at Week 12

| | |
|---|---|
| End point title | Achievement of 100% reduction from baseline in PASI score (PASI100) at Week 12 |

End point description:

Percentage of participants who achieved 100% reduction from baseline in Psoriasis Area and Severity Index score (PASI100) at Week 12.

PASI score ranges from 0 (best) to 72 (worst).

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

End point timeframe:

Baseline and Week 12

| End point values | BI 655066 18 mg | BI 655066 90 mg | BI 655066 180 mg | Stelara® |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43[13] | 41[14] | 42[15] | 40 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 14 (5.3 to 27.9) | 41.5 (26.3 to 57.9) | 50 (34.2 to 65.8) | 17.5 (7.3 to 32.8) |

Notes:

[13] - FAS

[14] - FAS

[15] - FAS

| End point values | BI 655066 90+180 mg | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 83[16] | | | |

| | | | | |
|---|---|---|---|---|
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 45.8 (34.8 to 57.1) | | | |

Notes:

[16] - FAS

### Statistical analyses

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

Statistical analysis description:

The difference in proportion responding between BI 90+180 mg and Stelara® was estimated and tested using the Cochran-Mantel-Haenszel (CMH) risk difference estimate stratified by the randomisation factors of weight (≤100 kg vs. >100 kg) and prior exposure to 2 or more TNF antagonists with discontinuation due to lack of efficacy, with weights proposed by Greenland/Robins. Difference calculated as BI 90+180 mg minus Stelara®.

| | |
|---|---|
| Comparison groups | Stelara® v BI 655066 90+180 mg |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0008 [17] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (net) |
| Point estimate | 27.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 11.3 |
| upper limit | 42.9 |

Notes:

[17] - Pairwise comparisons of all doses and treatments were conducted using the same CMH methods; 95% confidence intervals (CI) as well as nominal p-values of the comparison of doses were provided. There were no adjustments for multiplicity.

### Secondary: Achievement of ≥50% reduction from baseline in PASI score (PASI50) at Week 12

| End point title | Achievement of ≥50% reduction from baseline in PASI score (PASI50) at Week 12 |
|---|---|

End point description:

Percentage of participants who achieved ≥50% reduction from baseline in Psoriasis Area and Severity Index score (PASI50) at Week 12. PASI score ranges from 0 (best) to 72 (worst).

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

End point timeframe:

Baseline and Week 12

| **End point values** | BI 655066 18 mg | BI 655066 90 mg | BI 655066 180 mg | Stelara® |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43[18] | 41[19] | 42[20] | 40 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 93 (80.9 to 98.5) | 100 (91.4 to 100) | 95.2 (83.8 to 99.4) | 87.5 (73.2 to 95.8) |

Notes:

[18] - FAS

[19] - FAS

[20] - FAS

| End point values | BI 655066 90+180 mg | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 83[21] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 97.6 (91.6 to 99.7) | | | |

Notes:

[21] - FAS

## Statistical analyses

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

Statistical analysis description:

The difference in proportion responding between BI 90+180 mg and Stelara® was estimated and tested using the Cochran-Mantel-Haenszel (CMH) risk difference estimate stratified by the randomisation factors of weight (≤100 kg vs. >100 kg) and prior exposure to 2 or more TNF antagonists with discontinuation due to lack of efficacy, with weights proposed by Greenland/Robins. Difference calculated as BI 90+180 mg minus Stelara®.

| | |
|---|---|
| Comparison groups | Stelara® v BI 655066 90+180 mg |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0706 [22] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (net) |
| Point estimate | 10.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | 21.1 |

Notes:

[22] - Pairwise comparisons of all doses and treatments were conducted using the same CMH methods; 95% confidence intervals (CI) as well as nominal p-values of the comparison of doses were provided. There were no adjustments for multiplicity.

## Secondary: Achievement of PASI90 at Week 24

| End point title | Achievement of PASI90 at Week 24 |
|---|---|

End point description:

Percentage of participants who achieved PASI90 at Week 24. PASI score ranges from 0 (best) to 72 (worst).

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

End point timeframe:

Week 24

| End point values | BI 655066 18 mg | BI 655066 90 mg | BI 655066 180 mg | Stelara® |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43[23] | 41[24] | 42[25] | 40[26] |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 30.2 (17.2 to 46.1) | 65.9 (49.4 to 79.9) | 85.7 (71.5 to 94.6) | 55 (38.5 to 70.7) |

Notes:

[23] - FAS

[24] - FAS

[25] - FAS

[26] - FAS

| End point values | BI 655066 90+180 mg | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 83[27] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 75.9 (65.3 to 84.6) | | | |

Notes:

[27] - FAS

### Statistical analyses

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

Statistical analysis description:

The difference in proportion responding between BI 90+180 mg and Stelara® was estimated and tested using the Cochran-Mantel-Haenszel (CMH) risk difference estimate stratified by the randomisation factors of weight (≤100 kg vs. >100 kg) and prior exposure to 2 or more TNF antagonists with discontinuation due to lack of efficacy, with weights proposed by Greenland/Robins. Difference calculated as BI 90+180 mg minus Stelara®.

| | |
|---|---|
| Comparison groups | Stelara® v BI 655066 90+180 mg |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.03 [28] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (net) |
| Point estimate | 19.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.9 |
| upper limit | 37.7 |

Notes:

[28] - Pairwise comparisons of all doses and treatments were conducted using the same CMH methods; 95% confidence intervals (CI) as well as nominal p-values of the comparison of doses were provided. There were no adjustments for multiplicity.

### Secondary: Percentage change in PASI score from baseline at Week 12

| End point title | Percentage change in PASI score from baseline at Week 12 |
|---|---|

End point description:

Percentage change in Psoriasis Area and Severity Index (PASI) from baseline at Week 12.

PASI score ranges from 0 (best) to 72 (worst).

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

End point timeframe:

Baseline and Week 12

| End point values | BI 655066 18 mg | BI 655066 90 mg | BI 655066 180 mg | Stelara® |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 39[29] | 41[30] | 41[31] | 37[32] |
| Units: Percentage of PASI score | | | | |
| arithmetic mean (standard deviation) | -79.7 (± 19.5) | -93.4 (± 7.7) | -90.7 (± 23.1) | -82.1 (± 19.5) |

Notes:

[29] - FAS

[30] - FAS

[31] - FAS

[32] - FAS

| End point values | BI 655066 90+180 mg | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 82[33] | | | |
| Units: Percentage of PASI score | | | | |
| arithmetic mean (standard deviation) | -92.1 (± 17.1) | | | |

Notes:

[33] - FAS

### Statistical analyses

No statistical analyses for this end point

## Secondary: Achievement of sPGA clear or almost clear at Week 12

| End point title | Achievement of sPGA clear or almost clear at Week 12 |
|---|---|

End point description:

Percentage of participants who achieved static Physician Global Assessment (sPGA) clear or almost clear at Week 12. sPGA is assessed on a six-point scale from 0 (clear) to 5 (severe).

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

End point timeframe:

Week 12

| End point values | BI 655066 18 mg | BI 655066 90 mg | BI 655066 180 mg | Stelara® |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43[34] | 41[35] | 42[36] | 40 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 62.8 (46.7 to 77) | 90.2 (76.9 to 97.3) | 90.5 (77.4 to 97.3) | 67.5 (50.9 to 81.4) |

Notes:

[34] - FAS

[35] - FAS

[36] - FAS

| End point values | BI 655066 90+180 mg | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 83[37] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 90.4 (81.9 to 95.7) | | | |

Notes:

[37] - FAS

## Statistical analyses

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

Statistical analysis description:

The difference in proportion responding between BI 90+180 mg and Stelara® was estimated and tested using the Cochran-Mantel-Haenszel (CMH) risk difference estimate stratified by the randomisation factors of weight (≤100 kg vs. >100 kg) and prior exposure to 2 or more TNF antagonists with discontinuation due to lack of efficacy, with weights proposed by Greenland/Robins. Difference calculated as BI 90+180 mg minus Stelara®.

| | |
|---|---|
| Comparison groups | Stelara® v BI 655066 90+180 mg |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0072 [38] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (net) |
| Point estimate | 21.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.7 |
| upper limit | 36.6 |

Notes:

[38] - Pairwise comparisons of all doses and treatments were conducted using the same CMH methods; 95% confidence intervals (CI) as well as nominal p-values of the comparison of doses were provided. There were no adjustments for multiplicity.

## Secondary: Time to loss of PASI50 response

| End point title | Time to loss of PASI50 response |
|---|---|

End point description:

Time to loss of PASI50 response. 99999: Summary statistics were not calculable due to low number of patients with events.

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

End point timeframe:

From first drug administration until end of follow-up period, up to 48 weeks.

| End point values | BI 655066 18 mg | BI 655066 90 mg | BI 655066 180 mg | Stelara® |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43[39] | 41[40] | 42[41] | 40[42] |
| Units: Days | | | | |
| median (confidence interval 95%) | 253 (212 to 285) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 338 (253 to 99999) |

Notes:

[39] - FAS

[40] - FAS

[41] - FAS

[42] - FAS

| End point values | BI 655066 90+180 mg | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 83[43] | | | |
| Units: Days | | | | |
| median (confidence interval 95%) | 99999 (99999 to 99999) | | | |

Notes:

[43] - FAS

## Statistical analyses

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

Statistical analysis description:

BI 655066 treatment groups BI 90 mg + 180 mg were tested vs. Stelara® using a stratified Kaplan-Meier estimate and the log-rank test.

| | |
|---|---|
| Comparison groups | Stelara® v BI 655066 90+180 mg |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [44] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.1844 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.1 |
| upper limit | 0.4 |

Notes:

[44] - Pairwise comparisons of all doses and treatments were conducted using the same CMH methods; 95% confidence intervals (CI) as well as nominal p-values of the comparison of doses were provided. There were no adjustments for multiplicity.

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| From first drug administration until 15 weeks after the last drug administration, up to 231 days. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 18.1 |

| Reporting groups | |
|---|---|
| Reporting group title | BI 655066 18 mg |
| Reporting group description: | |
| 18 mg BI 655066 administered by subcutaneous injection plus two placebo matching BI 655066 injections at Week 0, followed by two placebo matching BI 655066 injections each at Weeks 4 and 16. | |
| Reporting group title | BI 655066 90 mg |
| Reporting group description: | |
| 90 mg BI 655066 administered by subcutaneous injection plus two placebo matching BI 655066 injections at Week 0, followed 90 mg BI 655066 plus one placebo matching BI 655066 injection at Weeks 4 and 16. | |
| Reporting group title | BI 655066 180 mg |
| Reporting group description: | |
| 180 mg BI 655066 administered by subcutaneous injection as two injections plus a placebo matching BI 655066 injection at Week 0, followed 180 mg BI 655066 administered as two injections at Weeks 4 and 16. | |
| Reporting group title | Stelara® |
| Reporting group description: | |
| Stelara® administered by subcutaneous injection plus two saline injections at Week 0, Stelara® injection plus one saline injection at Weeks 4 and 16. Stelara® dose was 45 mg for patients with body weight ≤100 kg at randomisation or 90 mg for patients with body weight >100 kg at randomisation. | |

| Serious adverse events | BI 655066 18 mg | BI 655066 90 mg | BI 655066 180 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | 6 / 41 (14.63%) | 0 / 42 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 1 / 41 (2.44%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salivary gland neoplasm | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 43 (0.00%) | 1 / 41 (2.44%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Pelvic fracture | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 1 / 41 (2.44%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery occlusion | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 1 / 41 (2.44%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 1 / 41 (2.44%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 1 / 41 (2.44%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Allergy to arthropod bite | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 1 / 41 (2.44%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema multiforme | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 41 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 41 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Perineal abscess | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 41 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Stelara® | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 40 (7.50%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Salivary gland neoplasm | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rib fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coronary artery occlusion | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Headache | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Iron deficiency anaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Allergy to arthropod bite | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema multiforme | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Perineal abscess | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 40 (2.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| **Non-serious adverse events** | BI 655066 18 mg | BI 655066 90 mg | BI 655066 180 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 33 / 43 (76.74%) | 32 / 41 (78.05%) | 29 / 42 (69.05%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | 2 / 41 (4.88%) | 3 / 42 (7.14%) |
| occurrences (all) | 6 | 2 | 3 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 1 / 41 (2.44%) | 3 / 42 (7.14%) |
| occurrences (all) | 1 | 1 | 3 |
| Psoriasis | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | 1 / 41 (2.44%) | 0 / 42 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 2 / 41 (4.88%) | 3 / 42 (7.14%) |
| occurrences (all) | 2 | 2 | 3 |
| Back pain | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | 4 / 41 (9.76%) | 1 / 42 (2.38%) |
| occurrences (all) | 2 | 4 | 1 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 1 / 41 (2.44%) | 3 / 42 (7.14%) |
| occurrences (all) | 0 | 1 | 3 |
| Infections and infestations | | | |
| Folliculitis | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | 1 / 41 (2.44%) | 1 / 42 (2.38%) |
| occurrences (all) | 3 | 1 | 1 |
| Gastroenteritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 43 (2.33%) | 4 / 41 (9.76%) | 0 / 42 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 15 / 43 (34.88%) | 14 / 41 (34.15%) | 11 / 42 (26.19%) |
| occurrences (all) | 19 | 20 | 17 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 3 / 41 (7.32%) | 1 / 42 (2.38%) |
| occurrences (all) | 0 | 4 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 1 / 42 (2.38%) |
| occurrences (all) | 1 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 3 / 41 (7.32%) | 1 / 42 (2.38%) |
| occurrences (all) | 0 | 3 | 1 |

| **Non-serious adverse events** | Stelara® | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 29 / 40 (72.50%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 40 (10.00%) | | |
| occurrences (all) | 5 | | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | | |
| occurrences (all) | 1 | | |
| Psoriasis | | | |
| subjects affected / exposed | 3 / 40 (7.50%) | | |
| occurrences (all) | 3 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | | |
| occurrences (all) | 2 | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | | |
| occurrences (all) | 1 | | |
| Myalgia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 40 (7.50%) | | |
| occurrences (all) | 3 | | |
| Infections and infestations | | | |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 5 / 40 (12.50%) | | |
| occurrences (all) | 6 | | |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | | |
| occurrences (all) | 1 | | |
| Sinusitis | | | |
| subjects affected / exposed | 4 / 40 (10.00%) | | |
| occurrences (all) | 4 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | | |
| occurrences (all) | 1 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 31 March 2014 | Global protocol amendment 1 introduced the following key changes:<br>1. The inclusion criterion 8 was modified to add having vasectomized sexual partner(s) as an acceptable option of contraception for female patients.<br>2. Rules for blinding/unblinding of the trial team, investigators, efficacy assessors, and patients were specified. Unblinding of the trial bioanalyst and bioanalytical laboratory to support PK/ADA sample bioanalysis was introduced and blinded data reviews of PK/ADA results by the trial team were specified.<br>3. A restriction on the use of moisturizers/emollients containing retinoids and the use of tanning beds was introduced. Their use was not allowed as it could ameliorate psoriasis disease activity.<br>4. It was specified that body temperature could be measured orally or tympanically. The same BP recording instrument was to be used if possible.<br>5. Procedures for re-screening of patients in exceptional cases were introduced.<br>6. Further details on the procedure of obtaining skin biopsies were added. |
| 25 June 2014 | Global protocol amendment 2 allowed for a pre-randomisation call to the IRT for logistical reasons. |
| 03 July 2014 | Global protocol amendment 3 introduced the following key changes:<br>1. Rules for roll-over to the open-label extension study 1311.13 were specified<br>2. Exclusion criterion 4 was specified with regards to latent and active tuberculosis. Patients with latent or active TB were to continue to be excluded from the trial, but in case of a positive QuantiFERON test and documentation of adequately treated infection with no signs and symptoms of currently ongoing active or latent TB infection, the patients could have been included.<br>3. Exclusion criterion 11, concerning prior participation in another trial, was modified to be consistent with the restricted medication rules. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported