



## Clinical trial results:

**A 52-week, multicenter, randomized, double-blind study of secukinumab (300 mg) to demonstrate efficacy as assessed by Psoriasis Area and Severity Index and Investigator's Global Assessment after 12 weeks of treatment, compared to ustekinumab, and to assess long-term safety, tolerability, and efficacy in patients with moderate to severe plaque psoriasis (CLARITY).**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-002898-37 |
| Trial protocol           | HU SK IS PL CZ |
| Global end of trial date | 09 July 2018   |

### Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v2 (current)  |
| This version publication date  | 30 July 2023  |
| First version publication date | 06 July 2019  |
| Version creation reason        | • Correction of full data set<br>AGE TABLE CORRECTED TO INCLUDE ONE 17 YEAR OLD PARTICIPANT |

### Trial information

#### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CAIN457A2326 |
|-----------------------|--------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02826603 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Novartis Pharma AG   |
| Sponsor organisation address | CH-4002, Basel, Switzerland,   |
| Public contact               | Clinical Disclosure Office, Novartis Pharma AG, 41 613 241 1111, novartis.email@novartis.com |
| Scientific contact           | Study Director, Novartis Pharmaceuticals, 41 613 241 1111, novartis.email@novartis.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                       | 11 December 2018 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 09 July 2018     |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The co-primary objectives were to demonstrate the superiority of secukinumab compared to ustekinumab in patients with moderate to severe plaque psoriasis with respect to both PASI 90 and IGA mod 2011 0 or 1 response at Week 12.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 22 June 2016 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Canada: 27             |
| Country: Number of subjects enrolled | Czech Republic: 12     |
| Country: Number of subjects enrolled | Guatemala: 65          |
| Country: Number of subjects enrolled | Hungary: 21            |
| Country: Number of subjects enrolled | Iceland: 33            |
| Country: Number of subjects enrolled | Korea, Republic of: 38 |
| Country: Number of subjects enrolled | Malaysia: 30           |
| Country: Number of subjects enrolled | Poland: 139            |
| Country: Number of subjects enrolled | Slovakia: 10           |
| Country: Number of subjects enrolled | United States: 707     |
| Country: Number of subjects enrolled | Vietnam: 20            |
| Worldwide total number of subjects   | 1102                   |
| EEA total number of subjects         | 215                    |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 1   |
| Adults (18-64 years)                      | 981 |
| From 65 to 84 years                       | 120 |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Overall, 1353 patients were screened of which 1102 patients completed the Screening phase; 251 patients were screen failures

### Pre-assignment

Screening details:

The randomized set was defined as all patients who were randomized at the baseline visit. Unless otherwise specified, mis-randomized patients were excluded from the randomized set.

Mis-randomized patients were those who were screen failures, but had been randomized by the Investigator before eligibility was assessed, but had not been treated

### Period 1

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

Blinding implementation details:

Designated Novartis personnel were unblinded following database lock for the interim analysis after all patients completed Week 16 visit. Field monitors/clinical research associates remained blinded until after final database lock. All blinded site personnel, including the assessor remained blinded to individual treatment allocation until after final database lock

### Arms

|                              |                                |
|------------------------------|--------------------------------|
| Are arms mutually exclusive? | Yes                            |
| <b>Arm title</b>             | Secukinumab 300mg (2 x 150 mg) |

Arm description:

Secukinumab 300mg s.c. injection (2 150mg pre-filled syringes)

|  |                  |
|--|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Secukinumab      |
| Investigational medicinal product code |                  |
| Other name                             | AIN457           |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Secukinumab 300mg s.c. injection (2 150mg pre-filled syringes)

|  |                  |
|--|------------------|
| Investigational medicinal product name | Ustekinumab      |
| Investigational medicinal product code |                  |
| Other name                             | UST              |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Ustekinumab s.c. 45 mg or 90 mg (depending on body weight) using 45mg pre-filled syringes (1 or 2 syringes)

|                  |                          |
|------------------|--------------------------|
| <b>Arm title</b> | Ustekinumab 45mg or 90mg |
|------------------|--------------------------|

Arm description:

Ustekinumab s.c. 45 mg or 90 mg (depending on body weight) using 45mg pre-filled syringes (1 or 2 syringes)

|          |                   |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

|  |                  |
|--|------------------|
| Investigational medicinal product name | ustekinumab      |
| Investigational medicinal product code |                  |
| Other name                             | UST              |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

45 mg or 90 mg pre-filled syringe(s)

| <b>Number of subjects in period 1</b> | Secukinumab<br>300mg (2 x 150 mg) | Ustekinumab 45mg<br>or 90mg |
|---------------------------------------|-----------------------------------|-----------------------------|
| Started                               | 550                               | 552                         |
| Completed                             | 489                               | 488                         |
| Not completed                         | 61                                | 64                          |
| Adverse event, serious fatal          | 2                                 | -                           |
| Physician decision                    | 1                                 | 7                           |
| Consent withdrawn by subject          | 20                                | 19                          |
| Adverse event, non-fatal              | 17                                | 9                           |
| Pregnancy                             | 1                                 | 2                           |
| Lost to follow-up                     | 13                                | 12                          |
| Noncompliance with treatment          | -                                 | 2                           |
| New therapy for study indication      | -                                 | 1                           |
| Lack of efficacy                      | 4                                 | 9                           |
| Protocol deviation                    | 3                                 | 3                           |

## Baseline characteristics

### Reporting groups

|   |                                |
|---|--------------------------------|
| Reporting group title   | Secukinumab 300mg (2 x 150 mg) |
| Reporting group description:<br>Secukinumab 300mg s.c. injection (2 150mg pre-filled syringes)  |                                |
| Reporting group title   | Ustekinumab 45mg or 90mg       |
| Reporting group description:<br>Ustekinumab s.c. 45 mg or 90 mg (depending on body weight) using 45mg pre-filled syringes (1 or 2 syringes) |                                |

| Reporting group values      | Secukinumab<br>300mg (2 x 150 mg) | Ustekinumab 45mg<br>or 90mg | Total |
|-----------------------------|-----------------------------------|-----------------------------|-------|
| Number of subjects          | 550                               | 552                         | 1102  |
| Age, Customized             |                                   |                             |       |
| Units: Subjects             |                                   |                             |       |
| <65 years                   | 488                               | 494                         | 982   |
| >=65 years                  | 60                                | 48                          | 108   |
| >=75 years                  | 2                                 | 10                          | 12    |
| Age Continuous              |                                   |                             |       |
| average age of participants |                                   |                             |       |
| Units: years                |                                   |                             |       |
| arithmetic mean             | 45.4                              | 45.3                        |       |
| standard deviation          | ± 14.09                           | ± 14.16                     | -     |
| Sex: Female, Male           |                                   |                             |       |
| Units: Subjects             |                                   |                             |       |
| Female                      | 194                               | 176                         | 370   |
| Male                        | 356                               | 376                         | 732   |
| Race/Ethnicity, Customized  |                                   |                             |       |
| Units: Subjects             |                                   |                             |       |
| Caucasian                   | 416                               | 410                         | 826   |
| Black                       | 21                                | 24                          | 45    |
| Asian                       | 60                                | 57                          | 117   |
| Native American             | 34                                | 41                          | 75    |
| Pacific Islander            | 1                                 | 5                           | 6     |
| Unknown                     | 4                                 | 2                           | 6     |
| Other                       | 14                                | 13                          | 27    |

## End points

### End points reporting groups

|                              |   |
|------------------------------|---|
| Reporting group title        | Secukinumab 300mg (2 x 150 mg)  |
| Reporting group description: | Secukinumab 300mg s.c. injection (2 150mg pre-filled syringes)  |
| Reporting group title        | Ustekinumab 45mg or 90mg  |
| Reporting group description: | Ustekinumab s.c. 45 mg or 90 mg (depending on body weight) using 45mg pre-filled syringes (1 or 2 syringes) |

### Primary: Participants who achieved Psoriasis Area and Severity Index (PASI) 90 response at Week 12

|                        |   |
|------------------------|---|
| End point title        | Participants who achieved Psoriasis Area and Severity Index (PASI) 90 response at Week 12   |
| End point description: | Number of participants who achieved $\geq 90\%$ reduction in PASI compared to baseline. Logistic regression analysis of PASI 90 response at Week 12 PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, upper limbs, trunk, lower limbs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of body region (head: 0.1, upper limbs: 0.2, trunk: 0.3, lower limbs: 0.4). |
| End point type         | Primary   |
| End point timeframe:   | Week 12   |

| End point values            | Secukinumab 300mg (2 x 150 mg) | Ustekinumab 45mg or 90mg |  |  |
|-----------------------------|--------------------------------|--------------------------|--|--|
| Subject group type          | Reporting group                | Reporting group          |  |  |
| Number of subjects analysed | 550                            | 552                      |  |  |
| Units: participants         | 366                            | 265                      |  |  |

### Statistical analyses

|   |   |
|---|---|
| Statistical analysis title              | Statistical Analysis of Primary Outcome                   |
| Comparison groups                       | Ustekinumab 45mg or 90mg v Secukinumab 300mg (2 x 150 mg) |
| Number of subjects included in analysis | 1102  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |   |
| P-value                                 | < 0.0001  |
| Method                                  | Regression, Logistic                                      |
| Parameter estimate                      | Odds ratio (OR)   |
| Point estimate                          | 2.21  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 1.72    |
| upper limit         | 2.84    |

### Primary: Participants with IGA mod 2011 0 or 1 at Week 12

|  |  |
|--|--|
| End point title  | Participants with IGA mod 2011 0 or 1 at Week 12 |
| End point description:<br>Investigator's Global Assessment uses a scale (IGA mod 2011) that rates disease from a score of 0 (clear skin) to 4 (severe disease) |  |
| End point type   | Primary  |
| End point timeframe:<br>Week 12  |  |

| End point values            | Secukinumab<br>300mg (2 x<br>150 mg) | Ustekinumab<br>45mg or 90mg |  |  |
|-----------------------------|--------------------------------------|-----------------------------|--|--|
| Subject group type          | Reporting group                      | Reporting group             |  |  |
| Number of subjects analysed | 550                                  | 552                         |  |  |
| Units: participants         | 397                                  | 306                         |  |  |

### Statistical analyses

|   |   |
|---|---|
| Statistical analysis title              | Statistical Analysis of Outcome Measure                   |
| Comparison groups                       | Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg |
| Number of subjects included in analysis | 1102  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |   |
| P-value                                 | < 0.0001  |
| Method                                  | Regression, Logistic                                      |
| Parameter estimate                      | Odds ratio (OR)   |
| Point estimate                          | 2.1   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 1.63  |
| upper limit                             | 2.72  |

### Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 75 response at Week 12

|                 |   |
|-----------------|---|
| End point title | Participants who achieved Psoriasis Area and Severity Index |
|-----------------|---|



End point description:

Number of participants who achieved  $\geq 75\%$  reduction in PASI at Week 12 compared to baseline.

End point type Secondary

End point timeframe:

Week 12

| End point values            | Secukinumab<br>300mg (2 x<br>150 mg) | Ustekinumab<br>45mg or 90mg |  |  |
|-----------------------------|--------------------------------------|-----------------------------|--|--|
| Subject group type          | Reporting group                      | Reporting group             |  |  |
| Number of subjects analysed | 550                                  | 552                         |  |  |
| Units: participants         | 484                                  | 409                         |  |  |

**Statistical analyses**

| Statistical analysis title              | Statistical Analysis of Secondary Outcome                 |
|---|---|
| Comparison groups                       | Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg |
| Number of subjects included in analysis | 1102  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |   |
| P-value                                 | < 0.0001  |
| Method                                  | Regression, Logistic                                      |
| Parameter estimate                      | Odds ratio (OR)   |
| Point estimate                          | 2.62  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 1.89  |
| upper limit                             | 3.62  |

**Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 75 response at Week 4**

End point title Participants who achieved Psoriasis Area and Severity Index (PASI) 75 response at Week 4

End point description:

Number of participants who achieved  $\geq 75\%$  reduction in PASI at Week 4 compared to baseline.

End point type Secondary

End point timeframe:

Week 4

|                             |                                      |                             |  |  |
|-----------------------------|--------------------------------------|-----------------------------|--|--|
| <b>End point values</b>     | Secukinumab<br>300mg (2 x<br>150 mg) | Ustekinumab<br>45mg or 90mg |  |  |
| Subject group type          | Reporting group                      | Reporting group             |  |  |
| Number of subjects analysed | 550                                  | 552                         |  |  |
| Units: participants         | 221                                  | 90                          |  |  |

### Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Statistical Analysis of Secondary Outcome                 |
| Comparison groups                       | Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg |
| Number of subjects included in analysis | 1102  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |   |
| P-value                                 | < 0.0001  |
| Method                                  | Regression, Logistic                                      |
| Parameter estimate                      | Odds ratio (OR)   |
| Point estimate                          | 3.53  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 2.65  |
| upper limit                             | 4.71  |

### Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 100 response at Week 16

|   |  |
|---|--|
| End point title   | Participants who achieved Psoriasis Area and Severity Index (PASI) 100 response at Week 16 |
| End point description:  |  |
| Number of participants who achieved 100% reduction in PASI at Week 16 compared to baseline. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Week 16   |  |

|                             |                                      |                             |  |  |
|-----------------------------|--------------------------------------|-----------------------------|--|--|
| <b>End point values</b>     | Secukinumab<br>300mg (2 x<br>150 mg) | Ustekinumab<br>45mg or 90mg |  |  |
| Subject group type          | Reporting group                      | Reporting group             |  |  |
| Number of subjects analysed | 550                                  | 552                         |  |  |
| Units: participants         | 250                                  | 147                         |  |  |

### Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Statistical Analysis of Secondary Outcome                 |
| Comparison groups                       | Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg |
| Number of subjects included in analysis | 1102  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |   |
| P-value                                 | < 0.0001  |
| Method                                  | Regression, Logistic                                      |
| Parameter estimate                      | Odds ratio (OR)   |
| Point estimate                          | 2.33  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 1.8   |
| upper limit                             | 3.01  |

### Secondary: Participants with IGA mod 2011 0 or 1 at 16 weeks

|                        |  |
|------------------------|--|
| End point title        | Participants with IGA mod 2011 0 or 1 at 16 weeks  |
| End point description: | Investigator's Global Assessment uses a scale (IGA mod 2011) that rates disease from a score of 0 (clear skin) to 4 (severe disease) |
| End point type         | Secondary  |
| End point timeframe:   |  |
| Week 16                |  |

| End point values            | Secukinumab<br>300mg (2 x<br>150 mg) | Ustekinumab<br>45mg or 90mg |  |  |
|-----------------------------|--------------------------------------|-----------------------------|--|--|
| Subject group type          | Reporting group                      | Reporting group             |  |  |
| Number of subjects analysed | 550                                  | 552                         |  |  |
| Units: participants         | 432                                  | 326                         |  |  |

### Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Statistical Analysis of Secondary Outcome                 |
| Comparison groups                       | Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg |
| Number of subjects included in analysis | 1102  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |   |
| P-value                                 | < 0.0001  |
| Method                                  | Regression, Logistic                                      |
| Parameter estimate                      | Odds ratio (OR)   |
| Point estimate                          | 2.57  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 1.96    |
| upper limit         | 3.37    |

### Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 100 response at Week 12

|   |  |
|---|--|
| End point title   | Participants who achieved Psoriasis Area and Severity Index (PASI) 100 response at Week 12 |
| End point description:<br>Number of participants who achieved 100% reduction in PASI at Week 12 compared to baseline. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Week 12   |  |

| End point values            | Secukinumab 300mg (2 x 150 mg) | Ustekinumab 45mg or 90mg |  |  |
|-----------------------------|--------------------------------|--------------------------|--|--|
| Subject group type          | Reporting group                | Reporting group          |  |  |
| Number of subjects analysed | 550                            | 552                      |  |  |
| Units: participants         | 210                            | 111                      |  |  |

### Statistical analyses

|   |   |
|---|---|
| Statistical analysis title              | Statistical Analysis of Secondary Outcome                 |
| Comparison groups                       | Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg |
| Number of subjects included in analysis | 1102  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |   |
| P-value                                 | < 0.0001  |
| Method                                  | Regression, Logistic                                      |
| Parameter estimate                      | Odds ratio (OR)   |
| Point estimate                          | 2.5   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 1.89  |
| upper limit                             | 3.31  |

### Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 75 response at Week 16

|  |   |
|--|---|
| End point title  | Participants who achieved Psoriasis Area and Severity Index (PASI) 75 response at Week 16 |
| End point description:<br>Number of participants who achieved $\geq 75\%$ reduction in PASI at Week 16 compared to baseline. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Week 16  |   |

| End point values            | Secukinumab<br>300mg (2 x<br>150 mg) | Ustekinumab<br>45mg or 90mg |  |  |
|-----------------------------|--------------------------------------|-----------------------------|--|--|
| Subject group type          | Reporting group                      | Reporting group             |  |  |
| Number of subjects analysed | 550                                  | 552                         |  |  |
| Units: participants         | 506                                  | 441                         |  |  |

### Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Statistical Analysis of Secondary Outcome                 |
| Comparison groups                       | Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg |
| Number of subjects included in analysis | 1102  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |   |
| P-value                                 | < 0.0001  |
| Method                                  | Regression, Logistic                                      |
| Parameter estimate                      | Odds ratio (OR)   |
| Point estimate                          | 2.86  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 1.96  |
| upper limit                             | 4.17  |

### Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 90 response at Week 16

|  |   |
|--|---|
| End point title  | Participants who achieved Psoriasis Area and Severity Index (PASI) 90 response at Week 16 |
| End point description:<br>Number of participants who achieved $\geq 90\%$ reduction in PASI at Week 16 compared to baseline. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Week 16  |   |

|                             |                                      |                             |  |  |
|-----------------------------|--------------------------------------|-----------------------------|--|--|
| <b>End point values</b>     | Secukinumab<br>300mg (2 x<br>150 mg) | Ustekinumab<br>45mg or 90mg |  |  |
| Subject group type          | Reporting group                      | Reporting group             |  |  |
| Number of subjects analysed | 550                                  | 552                         |  |  |
| Units: participants         | 423                                  | 299                         |  |  |

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Statistical Analysis of Secondary Outcome                 |
| Comparison groups                       | Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg |
| Number of subjects included in analysis | 1102  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |   |
| P-value                                 | < 0.0001  |
| Method                                  | Regression, Logistic                                      |
| Parameter estimate                      | Odds ratio (OR)   |
| Point estimate                          | 2.85  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 2.19  |
| upper limit                             | 3.71  |

## Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 90 response at Week 52

|  |   |
|--|---|
| End point title  | Participants who achieved Psoriasis Area and Severity Index (PASI) 90 response at Week 52 |
| End point description:   |   |
| Number of participants who achieved $\geq 90\%$ reduction in PASI at Week 52 compared to baseline. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Week 52  |   |

|                             |                                      |                             |  |  |
|-----------------------------|--------------------------------------|-----------------------------|--|--|
| <b>End point values</b>     | Secukinumab<br>300mg (2 x<br>150 mg) | Ustekinumab<br>45mg or 90mg |  |  |
| Subject group type          | Reporting group                      | Reporting group             |  |  |
| Number of subjects analysed | 550                                  | 552                         |  |  |
| Units: participants         | 402                                  | 330                         |  |  |

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Statistical Analysis of Secondary Outcome                 |
| Comparison groups                       | Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg |
| Number of subjects included in analysis | 1102  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |   |
| P-value                                 | < 0.0001  |
| Method                                  | Regression, Logistic                                      |
| Parameter estimate                      | Odds ratio (OR)   |
| Point estimate                          | 1.84  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 1.41  |
| upper limit                             | 2.41  |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected for maximum duration of treatment and follow up for a participant per protocol for 52 weeks. All cause mortality (deaths) was collected from First Patient First Visit (FPFV) to Last Patient Last Visit (LPLV) until 52 weeks

Adverse event reporting additional description:

All-cause mortality (deaths) was collected for as long as participants could be contacted from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV) up to a maximum of 52 weeks

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | AIN457 300 mg |
|-----------------------|---------------|

Reporting group description:

AIN457 300 mg

|                       |              |
|-----------------------|--------------|
| Reporting group title | UST 45/90 mg |
|-----------------------|--------------|

Reporting group description:

UST 45/90 mg

|                       |              |
|-----------------------|--------------|
| Reporting group title | All Patients |
|-----------------------|--------------|

Reporting group description:

All Patients

| Serious adverse events  | AIN457 300 mg    | UST 45/90 mg     | All Patients      |
|---|------------------|------------------|-------------------|
| Total subjects affected by serious adverse events                   |                  |                  |                   |
| subjects affected / exposed   | 29 / 550 (5.27%) | 21 / 552 (3.80%) | 50 / 1102 (4.54%) |
| number of deaths (all causes)                                       | 2                | 0                | 2                 |
| number of deaths resulting from adverse events                      | 0                | 0                | 0                 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                  |                   |
| Adenocarcinoma  |                  |                  |                   |
| subjects affected / exposed   | 0 / 550 (0.00%)  | 1 / 552 (0.18%)  | 1 / 1102 (0.09%)  |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 1            | 0 / 1             |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            | 0 / 0             |
| Basal cell carcinoma  |                  |                  |                   |
| subjects affected / exposed   | 0 / 550 (0.00%)  | 1 / 552 (0.18%)  | 1 / 1102 (0.09%)  |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 1            | 0 / 1             |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            | 0 / 0             |
| Invasive ductal breast carcinoma                                    |                  |                  |                   |



|  |                 |                 |                  |
|--|-----------------|-----------------|------------------|
| subjects affected / exposed                          | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all      | 0 / 0           | 1 / 1           | 1 / 1            |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0            |
| Laryngeal squamous cell carcinoma                    |                 |                 |                  |
| subjects affected / exposed                          | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0            |
| Squamous cell carcinoma of lung                      |                 |                 |                  |
| subjects affected / exposed                          | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0            |
| Squamous cell carcinoma of the oral cavity           |                 |                 |                  |
| subjects affected / exposed                          | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all      | 0 / 0           | 1 / 1           | 1 / 1            |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0            |
| T-cell lymphoma                                      |                 |                 |                  |
| subjects affected / exposed                          | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0            |
| Vascular disorders                                   |                 |                 |                  |
| Deep vein thrombosis                                 |                 |                 |                  |
| subjects affected / exposed                          | 2 / 550 (0.36%) | 1 / 552 (0.18%) | 3 / 1102 (0.27%) |
| occurrences causally related to treatment / all      | 0 / 2           | 1 / 1           | 1 / 3            |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0            |
| Orthostatic hypotension                              |                 |                 |                  |
| subjects affected / exposed                          | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0            |
| General disorders and administration site conditions |                 |                 |                  |
| Sudden cardiac death                                 |                 |                 |                  |
| subjects affected / exposed                          | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           | 0 / 1            |

|   |                 |                 |                  |
|---|-----------------|-----------------|------------------|
| Immune system disorders                         |                 |                 |                  |
| Anaphylactic reaction                           |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0           | 2 / 2            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Drug hypersensitivity                           |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                  |
| Acute respiratory failure                       |                 |                 |                  |
| subjects affected / exposed                     | 3 / 550 (0.55%) | 0 / 552 (0.00%) | 3 / 1102 (0.27%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0           | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Asthma  |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Pulmonary embolism                              |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Pulmonary thrombosis                            |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Psychiatric disorders                           |                 |                 |                  |
| Depression                                      |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Psychotic disorder                              |                 |                 |                  |

|   |                 |                 |                  |
|---|-----------------|-----------------|------------------|
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Product issues                                  |                 |                 |                  |
| Device inappropriate shock delivery             |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Investigations                                  |                 |                 |                  |
| Haemoglobin decreased                           |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Injury, poisoning and procedural complications  |                 |                 |                  |
| Comminuted fracture                             |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Fall  |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Gun shot wound                                  |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Incisional hernia                               |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Postoperative ileus                             |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |

|  |                                   |                                   |                                    |
|--|-----------------------------------|-----------------------------------|------------------------------------|
| Toxicity to various agents<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                           | 1 / 550 (0.18%)<br>0 / 1<br>0 / 1 | 0 / 552 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 1102 (0.09%)<br>0 / 1<br>0 / 1 |
| Wrist fracture<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                       | 0 / 550 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 552 (0.18%)<br>0 / 1<br>0 / 0 | 1 / 1102 (0.09%)<br>0 / 1<br>0 / 0 |
| Cardiac disorders<br>Angina pectoris<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                 | 1 / 550 (0.18%)<br>0 / 1<br>0 / 0 | 0 / 552 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 1102 (0.09%)<br>0 / 1<br>0 / 0 |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                  | 3 / 550 (0.55%)<br>0 / 3<br>0 / 0 | 0 / 552 (0.00%)<br>0 / 0<br>0 / 0 | 3 / 1102 (0.27%)<br>0 / 3<br>0 / 0 |
| Myocardial ischaemia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                 | 1 / 550 (0.18%)<br>0 / 1<br>0 / 0 | 0 / 552 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 1102 (0.09%)<br>0 / 1<br>0 / 0 |
| Ventricular tachycardia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                              | 2 / 550 (0.36%)<br>1 / 2<br>0 / 0 | 0 / 552 (0.00%)<br>0 / 0<br>0 / 0 | 2 / 1102 (0.18%)<br>1 / 2<br>0 / 0 |
| Nervous system disorders<br>Cerebrovascular accident<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | 0 / 550 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 552 (0.18%)<br>0 / 1<br>0 / 0 | 1 / 1102 (0.09%)<br>0 / 1<br>0 / 0 |
| Ischaemic stroke<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                     | 0 / 550 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 552 (0.18%)<br>0 / 1<br>0 / 0 | 1 / 1102 (0.09%)<br>0 / 1<br>0 / 0 |

|   |                 |                 |                  |
|---|-----------------|-----------------|------------------|
| Loss of consciousness                           |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Syncope   |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Blood and lymphatic system disorders            |                 |                 |                  |
| Lymphadenopathy                                 |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Gastrointestinal disorders                      |                 |                 |                  |
| Anal fissure                                    |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Colitis erosive                                 |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Colitis ulcerative                              |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Haemorrhoids                                    |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Pancreatitis acute                              |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |

|   |                 |                 |                  |
|---|-----------------|-----------------|------------------|
| Hepatobiliary disorders                         |                 |                 |                  |
| Cholecystitis                                   |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Skin and subcutaneous tissue disorders          |                 |                 |                  |
| Drug eruption                                   |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Toxic skin eruption                             |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Renal and urinary disorders                     |                 |                 |                  |
| Acute kidney injury                             |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Nephrolithiasis                                 |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Renal infarct                                   |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Musculoskeletal and connective tissue disorders |                 |                 |                  |
| Bursitis  |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Infections and infestations                     |                 |                 |                  |
| Bronchitis                                      |                 |                 |                  |

|   |                 |                 |                  |
|---|-----------------|-----------------|------------------|
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Cellulitis                                      |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 2 / 552 (0.36%) | 3 / 1102 (0.27%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Clostridium difficile colitis                   |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Dengue fever                                    |                 |                 |                  |
| subjects affected / exposed                     | 2 / 550 (0.36%) | 0 / 552 (0.00%) | 2 / 1102 (0.18%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Diverticulitis                                  |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Endocarditis                                    |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Peritonitis                                     |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Pharyngitis                                     |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Pneumonia streptococcal                         |                 |                 |                  |

|   |                 |                 |                  |
|---|-----------------|-----------------|------------------|
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Pyelonephritis acute                            |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Sepsis  |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Skin candida                                    |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Tonsillitis                                     |                 |                 |                  |
| subjects affected / exposed                     | 1 / 550 (0.18%) | 0 / 552 (0.00%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Urinary tract infection                         |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Metabolism and nutrition disorders              |                 |                 |                  |
| Dehydration                                     |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |
| Hyperglycaemia                                  |                 |                 |                  |
| subjects affected / exposed                     | 0 / 550 (0.00%) | 1 / 552 (0.18%) | 1 / 1102 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0            |



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

| <b>Non-serious adverse events</b>                     | AIN457 300 mg      | UST 45/90 mg       | All Patients        |
|---|--------------------|--------------------|---------------------|
| Total subjects affected by non-serious adverse events |                    |                    |                     |
| subjects affected / exposed                           | 216 / 550 (39.27%) | 229 / 552 (41.49%) | 445 / 1102 (40.38%) |
| Vascular disorders                                    |                    |                    |                     |
| Hypertension  |                    |                    |                     |
| subjects affected / exposed                           | 17 / 550 (3.09%)   | 22 / 552 (3.99%)   | 39 / 1102 (3.54%)   |
| occurrences (all)                                     | 20                 | 24                 | 44                  |
| Nervous system disorders                              |                    |                    |                     |
| Headache  |                    |                    |                     |
| subjects affected / exposed                           | 26 / 550 (4.73%)   | 25 / 552 (4.53%)   | 51 / 1102 (4.63%)   |
| occurrences (all)                                     | 31                 | 30                 | 61                  |
| Gastrointestinal disorders                            |                    |                    |                     |
| Diarrhoea   |                    |                    |                     |
| subjects affected / exposed                           | 26 / 550 (4.73%)   | 24 / 552 (4.35%)   | 50 / 1102 (4.54%)   |
| occurrences (all)                                     | 40                 | 26                 | 66                  |
| Nausea  |                    |                    |                     |
| subjects affected / exposed                           | 6 / 550 (1.09%)    | 13 / 552 (2.36%)   | 19 / 1102 (1.72%)   |
| occurrences (all)                                     | 6                  | 15                 | 21                  |
| Respiratory, thoracic and mediastinal disorders       |                    |                    |                     |
| Cough   |                    |                    |                     |
| subjects affected / exposed                           | 17 / 550 (3.09%)   | 16 / 552 (2.90%)   | 33 / 1102 (2.99%)   |
| occurrences (all)                                     | 19                 | 19                 | 38                  |
| Oropharyngeal pain                                    |                    |                    |                     |
| subjects affected / exposed                           | 14 / 550 (2.55%)   | 17 / 552 (3.08%)   | 31 / 1102 (2.81%)   |
| occurrences (all)                                     | 15                 | 17                 | 32                  |
| Skin and subcutaneous tissue disorders                |                    |                    |                     |
| Dermatitis contact                                    |                    |                    |                     |
| subjects affected / exposed                           | 12 / 550 (2.18%)   | 8 / 552 (1.45%)    | 20 / 1102 (1.81%)   |
| occurrences (all)                                     | 13                 | 8                  | 21                  |
| Pruritus  |                    |                    |                     |
| subjects affected / exposed                           | 12 / 550 (2.18%)   | 18 / 552 (3.26%)   | 30 / 1102 (2.72%)   |
| occurrences (all)                                     | 12                 | 20                 | 32                  |
| Musculoskeletal and connective tissue disorders       |                    |                    |                     |

|                                   |                   |                   |                    |
|-----------------------------------|-------------------|-------------------|--------------------|
| Arthralgia                        |                   |                   |                    |
| subjects affected / exposed       | 9 / 550 (1.64%)   | 14 / 552 (2.54%)  | 23 / 1102 (2.09%)  |
| occurrences (all)                 | 11                | 15                | 26                 |
| Back pain                         |                   |                   |                    |
| subjects affected / exposed       | 14 / 550 (2.55%)  | 20 / 552 (3.62%)  | 34 / 1102 (3.09%)  |
| occurrences (all)                 | 14                | 22                | 36                 |
| Infections and infestations       |                   |                   |                    |
| Bronchitis                        |                   |                   |                    |
| subjects affected / exposed       | 8 / 550 (1.45%)   | 18 / 552 (3.26%)  | 26 / 1102 (2.36%)  |
| occurrences (all)                 | 8                 | 19                | 27                 |
| Conjunctivitis                    |                   |                   |                    |
| subjects affected / exposed       | 12 / 550 (2.18%)  | 6 / 552 (1.09%)   | 18 / 1102 (1.63%)  |
| occurrences (all)                 | 14                | 6                 | 20                 |
| Nasopharyngitis                   |                   |                   |                    |
| subjects affected / exposed       | 55 / 550 (10.00%) | 54 / 552 (9.78%)  | 109 / 1102 (9.89%) |
| occurrences (all)                 | 72                | 69                | 141                |
| Sinusitis                         |                   |                   |                    |
| subjects affected / exposed       | 25 / 550 (4.55%)  | 18 / 552 (3.26%)  | 43 / 1102 (3.90%)  |
| occurrences (all)                 | 26                | 22                | 48                 |
| Upper respiratory tract infection |                   |                   |                    |
| subjects affected / exposed       | 49 / 550 (8.91%)  | 61 / 552 (11.05%) | 110 / 1102 (9.98%) |
| occurrences (all)                 | 56                | 69                | 125                |
| Urinary tract infection           |                   |                   |                    |
| subjects affected / exposed       | 13 / 550 (2.36%)  | 9 / 552 (1.63%)   | 22 / 1102 (2.00%)  |
| occurrences (all)                 | 14                | 9                 | 23                 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment  |
|---------------|--|
| 22 April 2016 | <p>Per the new protocol, all drug administrations will be performed at the site in order to minimize potential influence of subjects' non-compliance at home administrations in this head to head study.</p> <p>Also, the Non-responder imputation method is updated. This change is in line with recommendations to impute subjects with all post-baseline missing values as non-responders according to the Intent-to-treat (ITT) principle.</p> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported