



## Clinical trial results:

**A Phase III randomized, double-blind, placebo-controlled multicenter study of subcutaneous secukinumab in prefilled syringes to demonstrate the efficacy at 24 weeks and to assess the long term efficacy, safety and tolerability up to 5 years in patients with Active Psoriatic Arthritis**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2012-004439-22  |
| Trial protocol           | GB BE CZ DE PL  |
| Global end of trial date | 09 January 2019 |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 01 January 2020 |
| First version publication date | 01 January 2020 |

### Trial information

#### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CAIN457F2312 |
|-----------------------|--------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01752634 |
| 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 613241111, Novartis.email@novartis.com |
| Scientific contact           | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, 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                       | 09 January 2019 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 09 January 2019 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective was to demonstrate that the efficacy of secukinumab 75 mg or 150 mg or 300 mg at Week 24 is superior to placebo in patients with active psoriatic arthritis (PsA) based on the proportion of patients achieving an American College of Rheumatology 20 (ACR20) response.

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                          | 14 April 2013 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Australia: 39          |
| Country: Number of subjects enrolled | Belgium: 7             |
| Country: Number of subjects enrolled | Canada: 26             |
| Country: Number of subjects enrolled | Czech Republic: 43     |
| Country: Number of subjects enrolled | Germany: 23            |
| Country: Number of subjects enrolled | United Kingdom: 44     |
| Country: Number of subjects enrolled | Poland: 40             |
| Country: Number of subjects enrolled | Russian Federation: 65 |
| Country: Number of subjects enrolled | Thailand: 5            |
| Country: Number of subjects enrolled | United States: 105     |
| Worldwide total number of subjects   | 397                    |
| EEA total number of subjects         | 157                    |

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)                     | 364 |
| From 65 to 84 years                      | 33  |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details:

The study population was comprised of subjects who had passed screening assessments, complied with eligibility criteria and had provided written consent.

### Pre-assignment

Screening details:

At baseline, all eligible subjects were randomized via Interactive Response Technology (IRT) to one of the 4 treatment arms.

At Week 16, Subjects on Placebo were rerandomized to receive secukinumab 150 mg s.c. or 300 mg s.c. from Week 16 (non-responder) or Week 24 (responder).

### Period 1

|                              |                                     |
|------------------------------|-------------------------------------|
| Period 1 title               | Up to Week 24 (Primary Analysis)    |
| Is this the baseline period? | Yes                                 |
| Allocation method            | Randomised - controlled             |
| Blinding used                | Double blind                        |
| Roles blinded                | Subject, Investigator, Data analyst |

### Arms

|                              |                                 |
|------------------------------|---------------------------------|
| Are arms mutually exclusive? | Yes                             |
| <b>Arm title</b>             | Secukinumab (AIN457) 75 mg s.c. |

Arm description:

Group 1- Secukinumab 75 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Secukinumab                                  |
| Investigational medicinal product code | AIN457                                       |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Secukinumab 75 mg s.c.

|                  |                                  |
|------------------|----------------------------------|
| <b>Arm title</b> | Secukinumab (AIN457) 150 mg s.c. |
|------------------|----------------------------------|

Arm description:

Group 2 - Secukinumab 150 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Secukinumab                                  |
| Investigational medicinal product code | AIN457                                       |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Secukinumab 150 mg s.c.

|                  |                                  |
|------------------|----------------------------------|
| <b>Arm title</b> | Secukinumab (AIN457) 300 mg s.c. |
|------------------|----------------------------------|

Arm description:

Group 3 - Secukinumab 300 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.

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

|   |  |
|---|--|
| Investigational medicinal product name                        | Secukinumab                                  |
| Investigational medicinal product code                        | AIN457                                       |
| Other name  |  |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration                                      | Subcutaneous use                             |
| Dosage and administration details:<br>Secukinumab 300 mg s.c. |  |
| <b>Arm title</b>  | Placebo                                      |

Arm description:

Placebo - rerandomized at Week 16 to receive secukinumab 150 mg s.c. or 300 mg s.c. from Week 16 (nonresponder) or Week 24 (responder).

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

Dosage and administration details:

Secukinumab 0 mg s.c.

| <b>Number of subjects in period 1</b> | Secukinumab<br>(AIN457) 75 mg s.c. | Secukinumab<br>(AIN457) 150 mg<br>s.c. | Secukinumab<br>(AIN457) 300 mg<br>s.c. |
|---------------------------------------|------------------------------------|--|--|
| Started                               | 99                                 | 100                                    | 100                                    |
| Completed                             | 93                                 | 95                                     | 97                                     |
| Not completed                         | 6                                  | 5                                      | 3                                      |
| Physician decision                    | -                                  | 1                                      | -                                      |
| Adverse event, non-fatal              | 3                                  | -                                      | 2                                      |
| Subject/guardian decision             | 1                                  | 1                                      | 1                                      |
| Lack of efficacy                      | 2                                  | 3                                      | -                                      |

| <b>Number of subjects in period 1</b> | Placebo |
|---------------------------------------|---------|
| Started                               | 98      |
| Completed                             | 88      |
| Not completed                         | 10      |
| Physician decision                    | -       |
| Adverse event, non-fatal              | 4       |
| Subject/guardian decision             | 3       |
| Lack of efficacy                      | 3       |

**Period 2**

|                              |                                     |
|------------------------------|-------------------------------------|
| Period 2 title               | Week 24 to Week 260                 |
| Is this the baseline period? | No                                  |
| Allocation method            | Randomised - controlled             |
| Blinding used                | Double blind                        |
| Roles blinded                | Subject, Investigator, Data analyst |

Blinding implementation details:

The study was open label label after Week 52 analysis was completed.

**Arms**

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                                 |
|------------------|---------------------------------|
| <b>Arm title</b> | Secukinumab (AIN457) 75 mg s.c. |
|------------------|---------------------------------|

Arm description:

Group 1- Secukinumab 75 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Secukinumab  |
| Investigational medicinal product code | AIN457   |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled pen, Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use   |

Dosage and administration details:

Secukinumab 75 mg s.c.

|                  |                                  |
|------------------|----------------------------------|
| <b>Arm title</b> | Secukinumab (AIN457) 150 mg s.c. |
|------------------|----------------------------------|

Arm description:

Group 2 - Secukinumab 150 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Secukinumab                                  |
| Investigational medicinal product code | AIN457                                       |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Secukinumab 150 mg s.c.

|                  |                                  |
|------------------|----------------------------------|
| <b>Arm title</b> | Secukinumab (AIN457) 300 mg s.c. |
|------------------|----------------------------------|

Arm description:

Group 3 - Secukinumab 300 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Secukinumab                                  |
| Investigational medicinal product code | AIN457                                       |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Secukinumab 300 mg s.c.

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | Placebo - AIN457 150 mg |
|------------------|-------------------------|

Arm description:

Placebo - rerandomized to AIN457 150 mg

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

|   |  |
|---|--|
| Investigational medicinal product name  | Secukinumab                                  |
| Investigational medicinal product code  | AIN457                                       |
| Other name                              |  |
| Pharmaceutical forms                    | Solution for injection in pre-filled syringe |
| Routes of administration                | Subcutaneous use                             |
| Dosage and administration details:      |  |
| Secukinumab 150 mg s.c.                 |  |
| Investigational medicinal product name  | Placebo                                      |
| Investigational medicinal product code  | Placebo                                      |
| Other name                              |  |
| Pharmaceutical forms                    | Solution for injection in pre-filled syringe |
| Routes of administration                | Subcutaneous use                             |
| Dosage and administration details:      |  |
| Secukinumab 0 mg s.c.                   |  |
| <b>Arm title</b>                        | Placebo - AIN457 300 mg                      |
| Arm description:                        |  |
| Placebo - rerandomized to AIN457 300 mg |  |
| Arm type                                | Experimental                                 |
| Investigational medicinal product name  | Secukinumab                                  |
| Investigational medicinal product code  | AIN457                                       |
| Other name                              |  |
| Pharmaceutical forms                    | Solution for injection in pre-filled syringe |
| Routes of administration                | Subcutaneous use                             |
| Dosage and administration details:      |  |
| Secukinumab 300 mg s.c.                 |  |
| Investigational medicinal product name  | Placebo                                      |
| Investigational medicinal product code  | Placebo                                      |
| Other name                              |  |
| Pharmaceutical forms                    | Solution for injection in pre-filled syringe |
| Routes of administration                | Subcutaneous use                             |
| Dosage and administration details:      |  |
| Secukinumab 0 mg s.c.                   |  |

| Number of subjects in period 2           | Secukinumab<br>(AIN457) 75 mg s.c. | Secukinumab<br>(AIN457) 150 mg<br>s.c. | Secukinumab<br>(AIN457) 300 mg<br>s.c. |
|--|------------------------------------|--|--|
|  |                                    |  |  |
| Started                                  | 93                                 | 95                                     | 97                                     |
| Completed                                | 59                                 | 65                                     | 64                                     |
| Not completed                            | 34                                 | 30                                     | 33                                     |
| Adverse event, serious fatal             | -                                  | 1                                      | -                                      |
| Physician decision                       | 1                                  | 2                                      | 4                                      |
| Noncompliance<br>with study<br>treatment | -                                  | -                                      | 1                                      |
| Adverse event, non-fatal                 | 4                                  | 8                                      | 8                                      |
| Pregnancy                                | -                                  | -                                      | 1                                      |
| Lost to follow-up                        | 2                                  | 2                                      | 3                                      |

|                           |    |    |   |
|---------------------------|----|----|---|
| Subject/guardian decision | 12 | 10 | 9 |
| Lack of efficacy          | 15 | 7  | 7 |

| <b>Number of subjects in period 2</b>    | Placebo - AIN457<br>150 mg | Placebo - AIN457<br>300 mg |
|--|----------------------------|----------------------------|
| Started                                  | 43                         | 45                         |
| Completed                                | 29                         | 31                         |
| Not completed                            | 14                         | 14                         |
| Adverse event, serious fatal             | -                          | -                          |
| Physician decision                       | 2                          | 1                          |
| Noncompliance<br>with study<br>treatment | -                          | -                          |
| Adverse event, non-fatal                 | 4                          | 2                          |
| Pregnancy                                | -                          | -                          |
| Lost to follow-up                        | -                          | 2                          |
| Subject/guardian decision                | 5                          | 5                          |
| Lack of efficacy                         | 3                          | 4                          |



## Baseline characteristics

### Reporting groups

|   |                                  |
|---|----------------------------------|
| Reporting group title   | Secukinumab (AIN457) 75 mg s.c.  |
| Reporting group description:<br>Group 1 - Secukinumab 75 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.   |                                  |
| Reporting group title   | Secukinumab (AIN457) 150 mg s.c. |
| Reporting group description:<br>Group 2 - Secukinumab 150 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.  |                                  |
| Reporting group title   | Secukinumab (AIN457) 300 mg s.c. |
| Reporting group description:<br>Group 3 - Secukinumab 300 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.  |                                  |
| Reporting group title   | Placebo                          |
| Reporting group description:<br>Placebo - rerandomized at Week 16 to receive secukinumab 150 mg s.c. or 300 mg s.c. from Week 16 (nonresponder) or Week 24 (responder). |                                  |

| Reporting group values                    | Secukinumab (AIN457) 75 mg s.c. | Secukinumab (AIN457) 150 mg s.c. | Secukinumab (AIN457) 300 mg s.c. |
|---|---------------------------------|----------------------------------|----------------------------------|
| Number of subjects                        | 99                              | 100                              | 100                              |
| Age Categorical<br>Units: Participants    |                                 |                                  |                                  |
| <=18 years                                | 0                               | 0                                | 0                                |
| Between 18 and 65 years                   | 93                              | 94                               | 90                               |
| >=65 years                                | 6                               | 6                                | 10                               |
| Age continuous<br>Units: years            |                                 |                                  |                                  |
| arithmetic mean                           | 48.6                            | 46.5                             | 46.9                             |
| standard deviation                        | ± 11.42                         | ± 11.72                          | ± 12.57                          |
| Sex: Female, Male<br>Units: Participants  |                                 |                                  |                                  |
| Female                                    | 52                              | 45                               | 49                               |
| Male                                      | 47                              | 55                               | 51                               |
| Race (NIH/OMB)<br>Units: Subjects         |                                 |                                  |                                  |
| American Indian or Alaska Native          | 0                               | 2                                | 0                                |
| Asian                                     | 5                               | 6                                | 2                                |
| Native Hawaiian or Other Pacific Islander | 1                               | 1                                | 0                                |
| Black or African American                 | 0                               | 0                                | 1                                |
| White                                     | 90                              | 90                               | 96                               |
| More than one race                        | 2                               | 1                                | 1                                |
| Unknown or Not Reported                   | 1                               | 0                                | 0                                |

| Reporting group values | Placebo | Total |  |
|------------------------|---------|-------|--|
| Number of subjects     | 98      | 397   |  |

|   |         |     |  |
|---|---------|-----|--|
| Age Categorical<br>Units: Participants    |         |     |  |
| <=18 years                                | 0       | 0   |  |
| Between 18 and 65 years                   | 87      | 364 |  |
| >=65 years                                | 11      | 33  |  |
| Age continuous<br>Units: years            |         |     |  |
| arithmetic mean                           | 49.9    |     |  |
| standard deviation                        | ± 12.53 | -   |  |
| Sex: Female, Male<br>Units: Participants  |         |     |  |
| Female                                    | 59      | 205 |  |
| Male                                      | 39      | 192 |  |
| Race (NIH/OMB)<br>Units: Subjects         |         |     |  |
| American Indian or Alaska Native          | 0       | 2   |  |
| Asian                                     | 1       | 14  |  |
| Native Hawaiian or Other Pacific Islander | 0       | 2   |  |
| Black or African American                 | 0       | 1   |  |
| White                                     | 94      | 370 |  |
| More than one race                        | 3       | 7   |  |
| Unknown or Not Reported                   | 0       | 1   |  |

## End points

### End points reporting groups

|   |                                  |
|---|----------------------------------|
| Reporting group title   | Secukinumab (AIN457) 75 mg s.c.  |
| Reporting group description:<br>Group 1- Secukinumab 75 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.    |                                  |
| Reporting group title   | Secukinumab (AIN457) 150 mg s.c. |
| Reporting group description:<br>Group 2 - Secukinumab 150 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.  |                                  |
| Reporting group title   | Secukinumab (AIN457) 300 mg s.c. |
| Reporting group description:<br>Group 3 - Secukinumab 300 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.  |                                  |
| Reporting group title   | Placebo                          |
| Reporting group description:<br>Placebo - rerandomized at Week 16 to receive secukinumab 150 mg s.c. or 300 mg s.c. from Week 16 (nonresponder) or Week 24 (responder). |                                  |
| Reporting group title   | Secukinumab (AIN457) 75 mg s.c.  |
| Reporting group description:<br>Group 1- Secukinumab 75 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.    |                                  |
| Reporting group title   | Secukinumab (AIN457) 150 mg s.c. |
| Reporting group description:<br>Group 2 - Secukinumab 150 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.  |                                  |
| Reporting group title   | Secukinumab (AIN457) 300 mg s.c. |
| Reporting group description:<br>Group 3 - Secukinumab 300 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.  |                                  |
| Reporting group title   | Placebo - AIN457 150 mg          |
| Reporting group description:<br>Placebo - rerandomized to AIN457 150 mg   |                                  |
| Reporting group title   | Placebo - AIN457 300 mg          |
| Reporting group description:<br>Placebo - rerandomized to AIN457 300 mg   |                                  |

### Primary: Number of participants achieving American College of Rheumatology 20 (ACR20) response criteria

|   |  |
|---|--|
| End point title   | Number of participants achieving American College of Rheumatology 20 (ACR20) response criteria |
| End point description:<br>ACR20 response was defined as having a positive clinical response to treatment (individual improvement) in disease activity if the participant had at least 20% improvement in tender 68-joint count, swollen 66-joint count and at least 3 of the following 5 measures: patient's assessment of RA pain, patient's global assessment of disease activity, physician's global assessment of disease activity, subject self-assessed disability (Health Assessment Questionnaire [HAQ-DI] score), and/or acute phase reactant (high sensitivity c-reactive protein (hsCRP) or erythrocyte sedimentation rate |  |

(ESR). The ACR20 response results at week 24 used non-responder imputation.

|                      |         |
|----------------------|---------|
| End point type       | Primary |
| End point timeframe: |         |
| Week 24              |         |

| End point values            | Secukinumab (AIN457) 75 mg s.c. | Secukinumab (AIN457) 150 mg s.c. | Secukinumab (AIN457) 300 mg s.c. | Placebo         |
|-----------------------------|---------------------------------|----------------------------------|----------------------------------|-----------------|
| Subject group type          | Reporting group                 | Reporting group                  | Reporting group                  | Reporting group |
| Number of subjects analysed | 99                              | 100                              | 100                              | 98              |
| Units: Participants         | 29                              | 51                               | 54                               | 15              |

### Statistical analyses

| Statistical analysis title              | Odds Ratio (OR)                           |
|---|---|
| Comparison groups                       | Secukinumab (AIN457) 75 mg s.c. v Placebo |
| Number of subjects included in analysis | 197                                       |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           |   |
| P-value                                 | = 0.02                                    |
| Method                                  | Regression, Logistic                      |
| Parameter estimate                      | Odds ratio (OR)                           |
| Point estimate                          | 2.32                                      |
| Confidence interval                     |   |
| level                                   | 95 %                                      |
| sides                                   | 2-sided                                   |
| lower limit                             | 1.14                                      |
| upper limit                             | 4.73                                      |

| Statistical analysis title              | Odds Ratio (OR)                            |
|---|--|
| Comparison groups                       | Secukinumab (AIN457) 150 mg s.c. v Placebo |
| Number of subjects included in analysis | 198  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | < 1  |
| Method                                  | Regression, Logistic                       |
| Parameter estimate                      | Odds ratio (OR)                            |
| Point estimate                          | 6.52                                       |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 3.25                                       |
| upper limit                             | 13.08                                      |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Odds Ratio (OR)                            |
| Comparison groups                       | Secukinumab (AIN457) 300 mg s.c. v Placebo |
| Number of subjects included in analysis | 198  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | < 0.0001                                   |
| Method                                  | Regression, Logistic                       |
| Parameter estimate                      | Odds ratio (OR)                            |
| Point estimate                          | 6.81                                       |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 3.42                                       |
| upper limit                             | 13.56                                      |

### Secondary: Number of participants achieving a PASI75 response in the subgroup of subjects who have $\geq 3\%$ skin involvement with psoriasis

|                 |  |
|-----------------|--|
| End point title | Number of participants achieving a PASI75 response in the subgroup of subjects who have $\geq 3\%$ skin involvement with psoriasis |
|-----------------|--|

End point description:

PASI is a combined assessment of a lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). The body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for a 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 section (head: 0.1, arms: 0.2, body: 0.3, legs: 0.4). PASI 75 response was defined as participants achieving  $\geq 75\%$  improvement from baseline. The PASI75 response results at week 24 used non-responder imputation.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 24              |           |

| End point values            | Secukinumab (AIN457) 75 mg s.c. | Secukinumab (AIN457) 150 mg s.c. | Secukinumab (AIN457) 300 mg s.c. | Placebo         |
|-----------------------------|---------------------------------|----------------------------------|----------------------------------|-----------------|
| Subject group type          | Reporting group                 | Reporting group                  | Reporting group                  | Reporting group |
| Number of subjects analysed | 50                              | 58                               | 41                               | 43              |
| Units: Participants         | 14                              | 28                               | 26                               | 7               |

### Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Odds Ratio (OR)                           |
| Comparison groups                       | Secukinumab (AIN457) 75 mg s.c. v Placebo |
| Number of subjects included in analysis | 93  |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           |   |
| P-value                                 | = 0.165                                   |
| Method                                  | Regression, Logistic                      |
| Parameter estimate                      | Odds ratio (OR)                           |
| Point estimate                          | 2.07                                      |
| Confidence interval                     |   |
| level                                   | 95 %                                      |
| sides                                   | 2-sided                                   |
| lower limit                             | 0.74                                      |
| upper limit                             | 5.81                                      |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Odds Ratio (OR)                            |
| Comparison groups                       | Secukinumab (AIN457) 150 mg s.c. v Placebo |
| Number of subjects included in analysis | 101  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | = 0.0006                                   |
| Method                                  | Regression, Logistic                       |
| Parameter estimate                      | Odds ratio (OR)                            |
| Point estimate                          | 5.7  |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 2.12                                       |
| upper limit                             | 15.34                                      |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Odds Ratio (OR)                            |
| Comparison groups                       | Secukinumab (AIN457) 300 mg s.c. v Placebo |
| Number of subjects included in analysis | 84   |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | < 0.0001                                   |
| Method                                  | Regression, Logistic                       |
| Parameter estimate                      | Odds ratio (OR)                            |
| Point estimate                          | 9.48                                       |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 3.33                                       |
| upper limit                             | 27   |

**Secondary: Number of participants achieving a PASI90 response in the subgroup of subjects who have  $\geq 3\%$  skin involvement with psoriasis**

|                 |  |
|-----------------|--|
| End point title | Number of participants achieving a PASI90 response in the subgroup of subjects who have $\geq 3\%$ skin involvement with psoriasis |
|-----------------|--|

## End point description:

PASI is a combined assessment of a lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). The body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for a 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 section (head: 0.1, arms: 0.2, body: 0.3, legs: 0.4). PASI 90 response was defined as participants achieving  $\geq 90\%$  improvement from baseline. The PASI90 response results at week 24 used non-responder imputation.

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

## End point timeframe:

Week 24

| End point values            | Secukinumab (AIN457) 75 mg s.c. | Secukinumab (AIN457) 150 mg s.c. | Secukinumab (AIN457) 300 mg s.c. | Placebo         |
|-----------------------------|---------------------------------|----------------------------------|----------------------------------|-----------------|
| Subject group type          | Reporting group                 | Reporting group                  | Reporting group                  | Reporting group |
| Number of subjects analysed | 50                              | 58                               | 41                               | 43              |
| Units: Participants         | 6                               | 19                               | 20                               | 4               |

**Statistical analyses**

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Odds Ratio (OR)                           |
| Comparison groups                       | Secukinumab (AIN457) 75 mg s.c. v Placebo |
| Number of subjects included in analysis | 93  |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           |   |
| P-value                                 | = 0.6421                                  |
| Method                                  | Regression, Logistic                      |
| Parameter estimate                      | Odds ratio (OR)                           |
| Point estimate                          | 1.38                                      |
| Confidence interval                     |   |
| level                                   | 95 %                                      |
| sides                                   | 2-sided                                   |
| lower limit                             | 0.36                                      |
| upper limit                             | 5.36                                      |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Odds Ratio (OR)                            |
| Comparison groups                       | Secukinumab (AIN457) 150 mg s.c. v Placebo |
| Number of subjects included in analysis | 101  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | = 0.0029                                   |
| Method                                  | Regression, Logistic                       |
| Parameter estimate                      | Odds ratio (OR)                            |
| Point estimate                          | 6.36                                       |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 1.89                                       |
| upper limit                             | 21.47                                      |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Odds Ratio (OR)                            |
| Comparison groups                       | Secukinumab (AIN457) 300 mg s.c. v Placebo |
| Number of subjects included in analysis | 84   |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | = 0.0002                                   |
| Method                                  | Regression, Logistic                       |
| Parameter estimate                      | Odds ratio (OR)                            |
| Point estimate                          | 10.74                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 3.13                                       |
| upper limit                             | 36.84                                      |

## Secondary: Change from baseline in DAS28-CRP

|  |                                   |
|--|-----------------------------------|
| End point title  | Change from baseline in DAS28-CRP |
| End point description:   |                                   |
| <p>The DAS28 is a measure of disease activity in RA. The score is calculated by a mathematical formula, which includes the tender joint count(TJC) and swollen joint count (SJC) out of a total of 28 joints, the high-sensitivity C-reactive protein (hsCRP), and the subject's 'global assessment' of disease activity/general health (GH). The subject's global assessment/GH was indicated by a visual analogue scale of 100 mm where the participant marked a point on a 100 mm line between 0 and 100 (0 indicated very good and 100 indicated very bad). The following formula was used to calculate DAS28: <math>DAS-CRP = 0.56 \cdot \sqrt{TJC28} + 0.28 \cdot \sqrt{SJC28} = 0.36 \cdot \ln(CRP+1) + 0.014 \cdot GH = 0.96</math>. A DAS28-CRP score &gt; 5.1 implies active disease, &lt;3.2 implies controlled disease and &lt;2.6 implies remission. A negative change from baseline indicates improvement.</p> |                                   |
| End point type   | Secondary                         |
| End point timeframe:   |                                   |
| Baseline, Week 24  |                                   |



| <b>End point values</b>             | Secukinumab (AIN457) 75 mg s.c. | Secukinumab (AIN457) 150 mg s.c. | Secukinumab (AIN457) 300 mg s.c. | Placebo              |
|-------------------------------------|---------------------------------|----------------------------------|----------------------------------|----------------------|
| Subject group type                  | Reporting group                 | Reporting group                  | Reporting group                  | Reporting group      |
| Number of subjects analysed         | 87                              | 91                               | 93                               | 32                   |
| Units: score on a scale             |                                 |                                  |                                  |                      |
| least squares mean (standard error) | -1.12 ( $\pm$ 0.111)            | -1.58 ( $\pm$ 0.109)             | -1.61 ( $\pm$ 0.110)             | -0.96 ( $\pm$ 0.149) |

## Statistical analyses

| <b>Statistical analysis title</b>       | Mean Difference                           |
|---|---|
| Comparison groups                       | Secukinumab (AIN457) 75 mg s.c. v Placebo |
| Number of subjects included in analysis | 119                                       |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           |   |
| P-value                                 | = 0.3763                                  |
| Method                                  | Mixed models analysis                     |
| Parameter estimate                      | Mean difference (net)                     |
| Point estimate                          | -0.16                                     |
| Confidence interval                     |   |
| level                                   | 95 %                                      |
| sides                                   | 2-sided                                   |
| lower limit                             | -0.53                                     |
| upper limit                             | 0.2                                       |

| <b>Statistical analysis title</b>       | Mean Difference                            |
|---|--|
| Comparison groups                       | Secukinumab (AIN457) 150 mg s.c. v Placebo |
| Number of subjects included in analysis | 123  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | = 0.0008                                   |
| Method                                  | Mixed models analysis                      |
| Parameter estimate                      | Mean difference (net)                      |
| Point estimate                          | -0.62                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | -0.98                                      |
| upper limit                             | -0.26                                      |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Mean Difference                            |
| Comparison groups                       | Secukinumab (AIN457) 300 mg s.c. v Placebo |
| Number of subjects included in analysis | 125  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | = 0.0004                                   |
| Method                                  | Mixed models analysis                      |
| Parameter estimate                      | Mean difference (net)                      |
| Point estimate                          | -0.65                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | -1.02                                      |
| upper limit                             | -0.29                                      |

## Secondary: Change from baseline in SF36-Physical Component Score

|                 |   |
|-----------------|---|
| End point title | Change from baseline in SF36-Physical Component Score |
|-----------------|---|

End point description:

The SF-36 is an instrument to measure health-related quality of life among healthy patients and patients with acute and chronic conditions

Score range is from 0 (no problems) to 100 (unable to perform the activity)

SF-36 is a 36 item questionnaire which measures Quality of Life across eight domains, which are both physically and emotionally based. Two overall summary scores, the Physical Component Summary (PCS) and Mental Component Summary (MCS) can be computed. In this study, SF-36 PCS is used.

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

End point timeframe:

Baseline, Week 24

| End point values                    | Secukinumab (AIN457) 75 mg s.c. | Secukinumab (AIN457) 150 mg s.c. | Secukinumab (AIN457) 300 mg s.c. | Placebo         |
|-------------------------------------|---------------------------------|----------------------------------|----------------------------------|-----------------|
| Subject group type                  | Reporting group                 | Reporting group                  | Reporting group                  | Reporting group |
| Number of subjects analysed         | 91                              | 96                               | 96                               | 33              |
| Units: Score on a scale             |                                 |                                  |                                  |                 |
| least squares mean (standard error) | 4.38 (± 0.750)                  | 6.39 (± 0.734)                   | 7.25 (± 0.740)                   | 1.95 (± 0.974)  |

## Statistical analyses

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Mean Difference                           |
| Comparison groups                 | Secukinumab (AIN457) 75 mg s.c. v Placebo |

|   |                       |
|---|-----------------------|
| Number of subjects included in analysis | 124                   |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| P-value                                 | = 0.0482              |
| Method                                  | Mixed models analysis |
| Parameter estimate                      | Mean difference (net) |
| Point estimate                          | 2.42                  |
| Confidence interval                     |                       |
| level                                   | 95 %                  |
| sides                                   | 2-sided               |
| lower limit                             | 0.02                  |
| upper limit                             | 4.83                  |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Mean Difference                            |
| Comparison groups                       | Secukinumab (AIN457) 150 mg s.c. v Placebo |
| Number of subjects included in analysis | 129  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | = 0.0003                                   |
| Method                                  | Mixed models analysis                      |
| Parameter estimate                      | Mean difference (net)                      |
| Point estimate                          | 4.44                                       |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 2.05                                       |
| upper limit                             | 6.83                                       |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Mean Difference                            |
| Comparison groups                       | Secukinumab (AIN457) 300 mg s.c. v Placebo |
| Number of subjects included in analysis | 129  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | < 0.0001                                   |
| Method                                  | Mixed models analysis                      |
| Parameter estimate                      | Mean difference (net)                      |
| Point estimate                          | 5.3  |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 2.91                                       |
| upper limit                             | 7.69                                       |

---

## Secondary: Change From Baseline in Stanford Health Assessment Questionnaire

---

## Disability Index (HAQ-DI)

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Stanford Health Assessment Questionnaire Disability Index (HAQ-DI) |
|-----------------|--|

### End point description:

The HAQ-DI assesses a subject's level of functional ability and includes questions of fine movements of the upper extremity, locomotor activities of the lower extremity, and activities that involve both upper and lower extremities. There are 20 questions in 8 categories of functioning including dressing, rising, eating, walking, hygiene, reach, grip and usual activities. The stem of each item asks 'Over the past week, "are you able to..." perform a particular task'. Each item is scored on a 4 point scale from 0 - 3, representing normal, no difficulty (0), some difficulty (1), much difficulty (2) and unable to do (3). The disability index score is calculated as the mean of the available category scores, ranging from 0 to 3. A negative change from baseline indicates improvement.

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

### End point timeframe:

Baseline, Week 24

| End point values                    | Secukinumab (AIN457) 75 mg s.c. | Secukinumab (AIN457) 150 mg s.c. | Secukinumab (AIN457) 300 mg s.c. | Placebo              |
|-------------------------------------|---------------------------------|----------------------------------|----------------------------------|----------------------|
| Subject group type                  | Reporting group                 | Reporting group                  | Reporting group                  | Reporting group      |
| Number of subjects analysed         | 89                              | 95                               | 95                               | 33                   |
| Units: Scores on a scale            |                                 |                                  |                                  |                      |
| least squares mean (standard error) | -0.32 ( $\pm$ 0.050)            | -0.48 ( $\pm$ 0.049)             | -0.56 ( $\pm$ 0.050)             | -0.31 ( $\pm$ 0.060) |

## Statistical analyses

| Statistical analysis title              | Mean Difference                           |
|---|---|
| Comparison groups                       | Secukinumab (AIN457) 75 mg s.c. v Placebo |
| Number of subjects included in analysis | 122                                       |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           |   |
| P-value                                 | = 0.9195                                  |
| Method                                  | Mixed models analysis                     |
| Parameter estimate                      | Mean difference (net)                     |
| Point estimate                          | -0.01                                     |
| Confidence interval                     |   |
| level                                   | 95 %                                      |
| sides                                   | 2-sided                                   |
| lower limit                             | -0.16                                     |
| upper limit                             | 0.15                                      |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Mean Difference                            |
| Comparison groups                       | Secukinumab (AIN457) 150 mg s.c. v Placebo |
| Number of subjects included in analysis | 128  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | = 0.0278                                   |
| Method                                  | Mixed models analysis                      |
| Parameter estimate                      | Mean difference (net)                      |
| Point estimate                          | -0.17                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | -0.32                                      |
| upper limit                             | -0.02                                      |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Mean Difference                            |
| Comparison groups                       | Secukinumab (AIN457) 300 mg s.c. v Placebo |
| Number of subjects included in analysis | 128  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | = 0.0013                                   |
| Method                                  | Mixed models analysis                      |
| Parameter estimate                      | Mean difference (net)                      |
| Point estimate                          | -0.25                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | -0.4                                       |
| upper limit                             | -0.1                                       |

## Secondary: Number of participants achieving American College of Rheumatology 50 (ACR50) response criteria

|   |  |
|---|--|
| End point title   | Number of participants achieving American College of Rheumatology 50 (ACR50) response criteria |
| End point description:<br>ACR20 response was defined as having a positive clinical response to treatment (individual improvement) in disease activity if the participant had at least 50% improvement in tender 68-joint count, swollen 66-joint count and at least 3 of the following 5 measures: patient's assessment of RA pain, patient's global assessment of disease activity, physician's global assessment of disease activity, subject self-assessed disability (Health Assessment Questionnaire [HAQ-DI] score), and/or acute phase reactant (high sensitivity c-reactive protein (hsCRP) or erythrocyte sedimentation rate (ESR). The ACR50 response results at week 24 used non-responder imputation. |  |
| End point type  | Secondary  |

End point timeframe:

Week 24

| End point values            | Secukinumab (AIN457) 75 mg s.c. | Secukinumab (AIN457) 150 mg s.c. | Secukinumab (AIN457) 300 mg s.c. | Placebo         |
|-----------------------------|---------------------------------|----------------------------------|----------------------------------|-----------------|
| Subject group type          | Reporting group                 | Reporting group                  | Reporting group                  | Reporting group |
| Number of subjects analysed | 99                              | 100                              | 100                              | 98              |
| Units: Participants         | 18                              | 35                               | 35                               | 7               |

### Statistical analyses

| Statistical analysis title              | Odds Ratio                                |
|---|---|
| Comparison groups                       | Secukinumab (AIN457) 75 mg s.c. v Placebo |
| Number of subjects included in analysis | 197                                       |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           |   |
| P-value                                 | = 0.0245                                  |
| Method                                  | Regression, Logistic                      |
| Parameter estimate                      | Odds ratio (OR)                           |
| Point estimate                          | 2.91                                      |
| Confidence interval                     |   |
| level                                   | 95 %                                      |
| sides                                   | 2-sided                                   |
| lower limit                             | 1.15                                      |
| upper limit                             | 7.36                                      |

| Statistical analysis title              | Odds Ratio                                 |
|---|--|
| Comparison groups                       | Secukinumab (AIN457) 300 mg s.c. v Placebo |
| Number of subjects included in analysis | 198  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | < 0.0001                                   |
| Method                                  | Regression, Logistic                       |
| Parameter estimate                      | Odds ratio (OR)                            |
| Point estimate                          | 7.15                                       |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 2.97                                       |
| upper limit                             | 17.22                                      |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Odds Ratio                                 |
| Comparison groups                       | Secukinumab (AIN457) 150 mg s.c. v Placebo |
| Number of subjects included in analysis | 198  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | < 0.0001                                   |
| Method                                  | Regression, Logistic                       |
| Parameter estimate                      | Odds ratio (OR)                            |
| Point estimate                          | 7.54                                       |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 3.11                                       |
| upper limit                             | 18.25                                      |

### Secondary: Number of participants with dactylitis in the subset of subjects who had dactylitis at baseline

|  |   |
|--|---|
| End point title  | Number of participants with dactylitis in the subset of subjects who had dactylitis at baseline |
| End point description:<br>Resolution of dactylitis was evaluated in the subset of patients who had disease activity at baseline. In this analysis, a lower percentage is desirable and resolution is defined as complete absence of the symptom. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Week 24  |   |

| End point values            | Secukinumab (AIN457) 75 mg s.c. | Secukinumab (AIN457) 150 mg s.c. | Secukinumab (AIN457) 300 mg s.c. | Placebo         |
|-----------------------------|---------------------------------|----------------------------------|----------------------------------|-----------------|
| Subject group type          | Reporting group                 | Reporting group                  | Reporting group                  | Reporting group |
| Number of subjects analysed | 33                              | 32                               | 46                               | 27              |
| Units: Participants         | 23                              | 16                               | 20                               | 23              |

### Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Odds Ratio                                |
| Comparison groups                       | Secukinumab (AIN457) 75 mg s.c. v Placebo |
| Number of subjects included in analysis | 60  |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           |   |
| P-value                                 | = 0.3149                                  |
| Method                                  | Regression, Logistic                      |
| Parameter estimate                      | Odds ratio (OR)                           |
| Point estimate                          | 0.51                                      |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.13    |
| upper limit         | 1.91    |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Odds Ratio                                 |
| Comparison groups                       | Secukinumab (AIN457) 150 mg s.c. v Placebo |
| Number of subjects included in analysis | 59   |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | = 0.0056                                   |
| Method                                  | Regression, Logistic                       |
| Parameter estimate                      | Odds ratio (OR)                            |
| Point estimate                          | 0.16                                       |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 0.04                                       |
| upper limit                             | 0.58                                       |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Odds Ratio                                 |
| Comparison groups                       | Secukinumab (AIN457) 300 mg s.c. v Placebo |
| Number of subjects included in analysis | 73   |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | = 0.0021                                   |
| Method                                  | Regression, Logistic                       |
| Parameter estimate                      | Odds ratio (OR)                            |
| Point estimate                          | 0.14                                       |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 0.04                                       |
| upper limit                             | 0.5  |

## Secondary: Number of participants with enthesitis in the subset of subjects who had enthesitis at baseline

|                 |   |
|-----------------|---|
| End point title | Number of participants with enthesitis in the subset of subjects who had enthesitis at baseline |
|-----------------|---|

End point description:

Resolution of enthesitis was evaluated in the subset of patients who had disease activity at baseline. In this analysis, a lower percentage is desirable and resolution is defined as complete absence of the symptom.

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



End point timeframe:

Week 24

| End point values            | Secukinumab (AIN457) 75 mg s.c. | Secukinumab (AIN457) 150 mg s.c. | Secukinumab (AIN457) 300 mg s.c. | Placebo         |
|-----------------------------|---------------------------------|----------------------------------|----------------------------------|-----------------|
| Subject group type          | Reporting group                 | Reporting group                  | Reporting group                  | Reporting group |
| Number of subjects analysed | 68                              | 64                               | 56                               | 65              |
| Units: Participants         | 46                              | 37                               | 29                               | 51              |

## Statistical analyses

| Statistical analysis title              | Odds Ratio                                |
|---|---|
| Comparison groups                       | Secukinumab (AIN457) 75 mg s.c. v Placebo |
| Number of subjects included in analysis | 133                                       |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           |   |
| P-value                                 | = 0.1678                                  |
| Method                                  | Regression, Logistic                      |
| Parameter estimate                      | Odds ratio (OR)                           |
| Point estimate                          | 0.58                                      |
| Confidence interval                     |   |
| level                                   | 95 %                                      |
| sides                                   | 2-sided                                   |
| lower limit                             | 0.26                                      |
| upper limit                             | 1.26                                      |

| Statistical analysis title              | Odds Ratio                                 |
|---|--|
| Comparison groups                       | Secukinumab (AIN457) 300 mg s.c. v Placebo |
| Number of subjects included in analysis | 121  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | = 0.0025                                   |
| Method                                  | Regression, Logistic                       |
| Parameter estimate                      | Odds ratio (OR)                            |
| Point estimate                          | 0.29                                       |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 0.13                                       |
| upper limit                             | 0.65                                       |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Odds Ratio                                 |
| Comparison groups                       | Secukinumab (AIN457) 150 mg s.c. v Placebo |
| Number of subjects included in analysis | 129  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           |  |
| P-value                                 | = 0.0108                                   |
| Method                                  | Regression, Logistic                       |
| Parameter estimate                      | Odds ratio (OR)                            |
| Point estimate                          | 0.36                                       |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | 0.17                                       |
| upper limit                             | 0.79                                       |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study Treatment until Last Patient Last Visit (LPLV), up to a maximum of 5 years.

Adverse event reporting additional description:

Patients randomized to Placebo are reported under Placebo for AEs starting before switching to Secukinumab and under the Secukinumab arm for AEs starting after switching to Secukinumab. Under “# of deaths resulting from AEs” all those deaths, resulting from SAEs that are deemed to be causally related to treatment by the investigator are reported.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 21.1   |

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Any AIN457 75 mg |
|-----------------------|------------------|

Reporting group description:

Any AIN457 75 mg

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

Reporting group description:

Any AIN457 300 mg

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

Reporting group description:

Placebo

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Any AIN457 150 mg |
|-----------------------|-------------------|

Reporting group description:

Any AIN457 150 mg

| Serious adverse events  | Any AIN457 75 mg | Any AIN457 300 mg | Placebo        |
|---|------------------|-------------------|----------------|
| Total subjects affected by serious adverse events                   |                  |                   |                |
| subjects affected / exposed   | 17 / 99 (17.17%) | 42 / 251 (16.73%) | 3 / 98 (3.06%) |
| 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) |                  |                   |                |
| B-cell lymphoma   |                  |                   |                |
| subjects affected / exposed   | 0 / 99 (0.00%)   | 0 / 251 (0.00%)   | 0 / 98 (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          |
| Penile squamous cell carcinoma                                      |                  |                   |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Prostate cancer                                 |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Squamous cell carcinoma                         |                |                 |                |
| subjects affected / exposed                     | 2 / 99 (2.02%) | 0 / 251 (0.00%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Squamous cell carcinoma of the tongue           |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Throat cancer                                   |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Thyroid cancer                                  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Uterine leiomyoma                               |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Vascular disorders                              |                |                 |                |
| Arteriosclerosis                                |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Deep vein thrombosis                            |                |                 |                |

|  |                |                 |                |
|--|----------------|-----------------|----------------|
| subjects affected / exposed                          | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Hypertension   |                |                 |                |
| subjects affected / exposed                          | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 2           | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0          |
| Peripheral arterial occlusive disease                |                |                 |                |
| subjects affected / exposed                          | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Vasculitis necrotising                               |                |                 |                |
| subjects affected / exposed                          | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0          |
| General disorders and administration site conditions |                |                 |                |
| Non-cardiac chest pain                               |                |                 |                |
| subjects affected / exposed                          | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Pyrexia  |                |                 |                |
| subjects affected / exposed                          | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Social circumstances                                 |                |                 |                |
| Pregnancy of partner                                 |                |                 |                |
| subjects affected / exposed                          | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Reproductive system and breast disorders             |                |                 |                |
| Cervical dysplasia                                   |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Dysmenorrhoea                                   |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                 |                |
| Chronic obstructive pulmonary disease           |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Dyspnoea  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Pneumothorax                                    |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Psychiatric disorders                           |                |                 |                |
| Alcohol abuse                                   |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Confusional state                               |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Dependence                                      |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| Suicidal ideation                               |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Product issues                                  |                |                 |                |
| Device dislocation                              |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Injury, poisoning and procedural complications  |                |                 |                |
| Alcohol poisoning                               |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Animal bite                                     |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Ankle fracture                                  |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Contusion                                       |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Femoral neck fracture                           |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Foot fracture                                   |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| Fractured ischium                               |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Fractured sacrum                                |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Head injury                                     |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Intervertebral disc injury                      |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Joint dislocation                               |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Limb traumatic amputation                       |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Pelvic fracture                                 |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Post-traumatic neck syndrome                    |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Procedural pain                                 |                |                 |                |



|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Pubis fracture                                  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Rib fracture                                    |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Scar  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Spinal compression fracture                     |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Cardiac disorders                               |                |                 |                |
| Atrial fibrillation                             |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Atrial flutter                                  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Cardiac failure congestive                      |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Coronary artery disease                         |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Myocardial infarction                           |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Ventricular fibrillation                        |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Nervous system disorders                        |                |                 |                |
| Carotid artery stenosis                         |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Cerebrovascular accident                        |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Cervical radiculopathy                          |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Facial paralysis                                |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Headache  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Hemiplegia                                      |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Migraine  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Seizure   |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Syncope   |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Transient ischaemic attack                      |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Ear and labyrinth disorders                     |                |                 |                |
| Deafness neurosensory                           |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Vertigo   |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Eye disorders                                   |                |                 |                |
| Vision blurred                                  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Visual acuity reduced transiently               |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Gastrointestinal disorders                      |                |                 |                |
| Anal fistula                                    |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Crohn's disease                                 |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Diarrhoea                                       |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Gastric ulcer                                   |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Gastrooesophageal reflux disease                |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Haemorrhoids                                    |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Incarcerated inguinal hernia                    |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Inflammatory bowel disease                      |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Inguinal hernia                                 |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Intestinal perforation                          |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Lumbar hernia                                   |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Nausea  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Umbilical hernia                                |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Hepatobiliary disorders                         |                |                 |                |
| Bile duct obstruction                           |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Cholecystitis                                   |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Hepatic lesion                                  |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Hypertransaminaemia                             |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Liver disorder                                  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                 |                |
| Photosensitivity reaction                       |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Psoriasis                                       |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Renal and urinary disorders                     |                |                 |                |
| Calculus urinary                                |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Musculoskeletal and connective tissue disorders |                |                 |                |
| Arthralgia                                      |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Arthritis reactive                              |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| Arthrofibrosis                                  |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Back pain                                       |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Cervical spinal stenosis                        |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Foot deformity                                  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Intervertebral disc protrusion                  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Muscular weakness                               |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Osteoarthritis                                  |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Osteonecrosis                                   |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Patellofemoral pain syndrome                    |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Pseudarthrosis                                  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Infections and infestations                     |                |                 |                |
| Abscess limb                                    |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Anal abscess                                    |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Cellulitis                                      |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Clostridium difficile infection                 |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Diverticulitis                                  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Erysipelas                                      |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Gastroenteritis norovirus                       |                |                 |                |



|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                                   | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Haematoma infection   |                |                 |                |
| subjects affected / exposed                                   | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0           | 0 / 0          |
| Hepatitis C   |                |                 |                |
| subjects affected / exposed                                   | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0           | 0 / 0          |
| Infectious colitis  |                |                 |                |
| subjects affected / exposed                                   | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Infective exacerbation of chronic obstructive airways disease |                |                 |                |
| subjects affected / exposed                                   | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Kidney infection  |                |                 |                |
| subjects affected / exposed                                   | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 2           | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0           | 0 / 0          |
| Osteomyelitis   |                |                 |                |
| subjects affected / exposed                                   | 0 / 99 (0.00%) | 2 / 251 (0.80%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0          | 0 / 3           | 0 / 0          |
| deaths causally related to treatment / all                    | 0 / 0          | 0 / 0           | 0 / 0          |
| Periorbital abscess   |                |                 |                |
| subjects affected / exposed                                   | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Peritonsillar abscess   |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Pharyngeal abscess                              |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Pneumocystis jirovecii pneumonia                |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Pneumonia                                       |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Post procedural infection                       |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Sepsis  |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Septic shock                                    |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Sinusitis                                       |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Subcutaneous abscess                            |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Viral infection                                 |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Metabolism and nutrition disorders              |                |                 |                |
| Dehydration                                     |                |                 |                |
| subjects affected / exposed                     | 0 / 99 (0.00%) | 1 / 251 (0.40%) | 0 / 98 (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          |
| Diabetes mellitus                               |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |
| Hyponatraemia                                   |                |                 |                |
| subjects affected / exposed                     | 1 / 99 (1.01%) | 0 / 251 (0.00%) | 0 / 98 (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          |

|   |                   |  |  |
|---|-------------------|--|--|
| <b>Serious adverse events</b>                                       | Any AIN457 150 mg |  |  |
| Total subjects affected by serious adverse events                   |                   |  |  |
| subjects affected / exposed   | 28 / 193 (14.51%) |  |  |
| number of deaths (all causes)                                       | 1                 |  |  |
| number of deaths resulting from adverse events                      | 0                 |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |  |  |
| B-cell lymphoma   |                   |  |  |
| subjects affected / exposed   | 1 / 193 (0.52%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 0             |  |  |
| Penile squamous cell carcinoma                                      |                   |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Prostate cancer                                 |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Squamous cell carcinoma                         |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Squamous cell carcinoma of the tongue           |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Throat cancer                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Thyroid cancer                                  |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Uterine leiomyoma                               |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Vascular disorders                              |                 |  |  |
| Arteriosclerosis                                |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Deep vein thrombosis                            |                 |  |  |

|  |                 |  |  |
|--|-----------------|--|--|
| subjects affected / exposed                          | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Hypertension   |                 |  |  |
| subjects affected / exposed                          | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Peripheral arterial occlusive disease                |                 |  |  |
| subjects affected / exposed                          | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Vasculitis necrotising                               |                 |  |  |
| subjects affected / exposed                          | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| General disorders and administration site conditions |                 |  |  |
| Non-cardiac chest pain                               |                 |  |  |
| subjects affected / exposed                          | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Pyrexia  |                 |  |  |
| subjects affected / exposed                          | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all      | 1 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Social circumstances                                 |                 |  |  |
| Pregnancy of partner                                 |                 |  |  |
| subjects affected / exposed                          | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Reproductive system and breast disorders             |                 |  |  |
| Cervical dysplasia                                   |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Dysmenorrhoea                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Chronic obstructive pulmonary disease           |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Dyspnoea  |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumothorax                                    |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychiatric disorders                           |                 |  |  |
| Alcohol abuse                                   |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Confusional state                               |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Dependence                                      |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Suicidal ideation                               |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Product issues                                  |                 |  |  |
| Device dislocation                              |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Injury, poisoning and procedural complications  |                 |  |  |
| Alcohol poisoning                               |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Animal bite                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Ankle fracture                                  |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Contusion                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Femoral neck fracture                           |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Foot fracture                                   |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| Fractured ischium                               |                 |  |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Fractured sacrum                                |                 |  |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Head injury                                     |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Intervertebral disc injury                      |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Joint dislocation                               |                 |  |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Limb traumatic amputation                       |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Pelvic fracture                                 |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Post-traumatic neck syndrome                    |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Procedural pain                                 |                 |  |  |  |



|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pubis fracture                                  |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Rib fracture                                    |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Scar  |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Spinal compression fracture                     |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac disorders                               |                 |  |  |
| Atrial fibrillation                             |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Atrial flutter                                  |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac failure congestive                      |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Coronary artery disease                         |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Myocardial infarction                           |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Ventricular fibrillation                        |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Nervous system disorders                        |                 |  |  |
| Carotid artery stenosis                         |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cerebrovascular accident                        |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cervical radiculopathy                          |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Facial paralysis                                |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Headache  |                 |  |  |
| subjects affected / exposed                     | 2 / 193 (1.04%) |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hemiplegia                                      |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Migraine  |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Seizure   |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Syncope   |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (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 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Ear and labyrinth disorders                     |                 |  |  |
| Deafness neurosensory                           |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Vertigo   |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Eye disorders                                   |                 |  |  |
| Vision blurred                                  |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Visual acuity reduced transiently               |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrointestinal disorders                      |                 |  |  |
| Anal fistula                                    |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Crohn's disease                                 |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Diarrhoea                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastric ulcer                                   |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrooesophageal reflux disease                |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Haemorrhoids                                    |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Incarcerated inguinal hernia                    |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Inflammatory bowel disease                      |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Inguinal hernia                                 |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Intestinal perforation                          |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Lumbar hernia                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Nausea  |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Umbilical hernia                                |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hepatobiliary disorders                         |                 |  |  |
| Bile duct obstruction                           |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cholecystitis                                   |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hepatic lesion                                  |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hypertransaminasaemia                           |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Liver disorder                                  |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Skin and subcutaneous tissue disorders          |                 |  |  |
| Photosensitivity reaction                       |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psoriasis                                       |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal and urinary disorders                     |                 |  |  |
| Calculus urinary                                |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Musculoskeletal and connective tissue disorders |                 |  |  |
| Arthralgia                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Arthritis reactive                              |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| Arthrofibrosis                                  |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Back pain                                       |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Cervical spinal stenosis                        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Foot deformity                                  |                 |  |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Intervertebral disc protrusion                  |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Muscular weakness                               |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Osteoarthritis                                  |                 |  |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Osteonecrosis                                   |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Patellofemoral pain syndrome                    |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pseudarthrosis                                  |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infections and infestations                     |                 |  |  |
| Abscess limb                                    |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Anal abscess                                    |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cellulitis                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Clostridium difficile infection                 |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Diverticulitis                                  |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Erysipelas                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastroenteritis norovirus                       |                 |  |  |



|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                                   | 1 / 193 (0.52%) |  |  |  |
| occurrences causally related to treatment / all               | 1 / 1           |  |  |  |
| deaths causally related to treatment / all                    | 0 / 0           |  |  |  |
| Haematoma infection   |                 |  |  |  |
| subjects affected / exposed                                   | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all               | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                    | 0 / 0           |  |  |  |
| Hepatitis C   |                 |  |  |  |
| subjects affected / exposed                                   | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all               | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                    | 0 / 0           |  |  |  |
| Infectious colitis  |                 |  |  |  |
| subjects affected / exposed                                   | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all               | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                    | 0 / 0           |  |  |  |
| Infective exacerbation of chronic obstructive airways disease |                 |  |  |  |
| subjects affected / exposed                                   | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all               | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                    | 0 / 0           |  |  |  |
| Kidney infection  |                 |  |  |  |
| subjects affected / exposed                                   | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all               | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                    | 0 / 0           |  |  |  |
| Osteomyelitis   |                 |  |  |  |
| subjects affected / exposed                                   | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all               | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                    | 0 / 0           |  |  |  |
| Periorbital abscess   |                 |  |  |  |
| subjects affected / exposed                                   | 1 / 193 (0.52%) |  |  |  |
| occurrences causally related to treatment / all               | 1 / 1           |  |  |  |
| deaths causally related to treatment / all                    | 0 / 0           |  |  |  |
| Peritonsillar abscess   |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Pharyngeal abscess                              |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Pneumocystis jirovecii pneumonia                |                 |  |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Pneumonia                                       |                 |  |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Post procedural infection                       |                 |  |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Sepsis  |                 |  |  |  |
| subjects affected / exposed                     | 1 / 193 (0.52%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |  |
| Septic shock                                    |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Sinusitis                                       |                 |  |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Subcutaneous abscess                            |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Viral infection                                 |                 |  |  |
| subjects affected / exposed                     | 2 / 193 (1.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Metabolism and nutrition disorders              |                 |  |  |
| Dehydration                                     |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Diabetes mellitus                               |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hyponatraemia                                   |                 |  |  |
| subjects affected / exposed                     | 0 / 193 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

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

| <b>Non-serious adverse events</b>                     | Any AIN457 75 mg | Any AIN457 300 mg  | Placebo          |
|---|------------------|--------------------|------------------|
| Total subjects affected by non-serious adverse events |                  |                    |                  |
| subjects affected / exposed                           | 63 / 99 (63.64%) | 171 / 251 (68.13%) | 39 / 98 (39.80%) |
| Vascular disorders                                    |                  |                    |                  |
| Hypertension  |                  |                    |                  |
| subjects affected / exposed                           | 6 / 99 (6.06%)   | 23 / 251 (9.16%)   | 3 / 98 (3.06%)   |
| occurrences (all)                                     | 7                | 25                 | 3                |
| Nervous system disorders                              |                  |                    |                  |
| Headache  |                  |                    |                  |
| subjects affected / exposed                           | 6 / 99 (6.06%)   | 18 / 251 (7.17%)   | 5 / 98 (5.10%)   |
| occurrences (all)                                     | 7                | 29                 | 6                |
| General disorders and administration site conditions  |                  |                    |                  |

|   |                        |                        |                     |
|---|------------------------|------------------------|---------------------|
| Fatigue<br>subjects affected / exposed<br>occurrences (all)           | 5 / 99 (5.05%)<br>5    | 11 / 251 (4.38%)<br>12 | 2 / 98 (2.04%)<br>2 |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all) | 5 / 99 (5.05%)<br>5    | 4 / 251 (1.59%)<br>5   | 0 / 98 (0.00%)<br>0 |
| Gastrointestinal disorders  |                        |                        |                     |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)         | 11 / 99 (11.11%)<br>14 | 23 / 251 (9.16%)<br>34 | 3 / 98 (3.06%)<br>6 |
| Nausea<br>subjects affected / exposed<br>occurrences (all)            | 7 / 99 (7.07%)<br>10   | 14 / 251 (5.58%)<br>25 | 4 / 98 (4.08%)<br>5 |
| Respiratory, thoracic and mediastinal disorders                       |                        |                        |                     |
| Cough<br>subjects affected / exposed<br>occurrences (all)             | 2 / 99 (2.02%)<br>2    | 12 / 251 (4.78%)<br>15 | 2 / 98 (2.04%)<br>2 |
| Skin and subcutaneous tissue disorders                                |                        |                        |                     |
| Psoriasis<br>subjects affected / exposed<br>occurrences (all)         | 7 / 99 (7.07%)<br>7    | 17 / 251 (6.77%)<br>22 | 4 / 98 (4.08%)<br>5 |
| Rash<br>subjects affected / exposed<br>occurrences (all)              | 1 / 99 (1.01%)<br>1    | 13 / 251 (5.18%)<br>15 | 3 / 98 (3.06%)<br>3 |
| Psychiatric disorders   |                        |                        |                     |
| Depression<br>subjects affected / exposed<br>occurrences (all)        | 5 / 99 (5.05%)<br>5    | 14 / 251 (5.58%)<br>15 | 2 / 98 (2.04%)<br>2 |
| Musculoskeletal and connective tissue disorders                       |                        |                        |                     |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)        | 7 / 99 (7.07%)<br>13   | 25 / 251 (9.96%)<br>49 | 4 / 98 (4.08%)<br>5 |
| Back pain<br>subjects affected / exposed<br>occurrences (all)         | 8 / 99 (8.08%)<br>8    | 21 / 251 (8.37%)<br>23 | 3 / 98 (3.06%)<br>3 |
| Bursitis  |                        |                        |                     |

|   |                        |                          |                      |
|---|------------------------|--------------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                | 5 / 99 (5.05%)<br>5    | 8 / 251 (3.19%)<br>9     | 0 / 98 (0.00%)<br>0  |
| Musculoskeletal pain<br>subjects affected / exposed<br>occurrences (all)        | 2 / 99 (2.02%)<br>3    | 12 / 251 (4.78%)<br>15   | 2 / 98 (2.04%)<br>2  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)           | 5 / 99 (5.05%)<br>7    | 11 / 251 (4.38%)<br>12   | 3 / 98 (3.06%)<br>4  |
| Psoriatic arthropathy<br>subjects affected / exposed<br>occurrences (all)       | 12 / 99 (12.12%)<br>12 | 23 / 251 (9.16%)<br>27   | 2 / 98 (2.04%)<br>2  |
| Infections and infestations   |                        |                          |                      |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                  | 7 / 99 (7.07%)<br>9    | 19 / 251 (7.57%)<br>25   | 2 / 98 (2.04%)<br>2  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                   | 3 / 99 (3.03%)<br>3    | 14 / 251 (5.58%)<br>16   | 0 / 98 (0.00%)<br>0  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)             | 23 / 99 (23.23%)<br>32 | 47 / 251 (18.73%)<br>104 | 8 / 98 (8.16%)<br>12 |
| Oral herpes<br>subjects affected / exposed<br>occurrences (all)                 | 5 / 99 (5.05%)<br>6    | 8 / 251 (3.19%)<br>15    | 2 / 98 (2.04%)<br>2  |
| Pharyngitis<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 99 (1.01%)<br>1    | 15 / 251 (5.98%)<br>26   | 0 / 98 (0.00%)<br>0  |
| Respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 5 / 99 (5.05%)<br>6    | 7 / 251 (2.79%)<br>8     | 0 / 98 (0.00%)<br>0  |
| Rhinitis<br>subjects affected / exposed<br>occurrences (all)                    | 5 / 99 (5.05%)<br>7    | 9 / 251 (3.59%)<br>10    | 0 / 98 (0.00%)<br>0  |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)                   | 6 / 99 (6.06%)<br>10   | 30 / 251 (11.95%)<br>47  | 1 / 98 (1.02%)<br>1  |

|   |                        |                         |                     |
|---|------------------------|-------------------------|---------------------|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 23 / 99 (23.23%)<br>37 | 58 / 251 (23.11%)<br>97 | 7 / 98 (7.14%)<br>7 |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)           | 8 / 99 (8.08%)<br>10   | 19 / 251 (7.57%)<br>31  | 4 / 98 (4.08%)<br>4 |

|  |  |  |  |
|--|--|--|--|
| <b>Non-serious adverse events</b>  | Any AIN457 150 mg                                    |  |  |
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed   | 132 / 193 (68.39%)                                   |  |  |
| Vascular disorders<br>Hypertension<br>subjects affected / exposed<br>occurrences (all)   | 14 / 193 (7.25%)<br>15                               |  |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)   | 16 / 193 (8.29%)<br>18                               |  |  |
| General disorders and administration site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)<br><br>Oedema peripheral<br>subjects affected / exposed<br>occurrences (all) | 6 / 193 (3.11%)<br>6<br><br>3 / 193 (1.55%)<br>3     |  |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)                                    | 19 / 193 (9.84%)<br>21<br><br>12 / 193 (6.22%)<br>13 |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)   | 13 / 193 (6.74%)<br>14                               |  |  |
| Skin and subcutaneous tissue disorders   |  |  |  |

|   |                         |  |  |
|---|-------------------------|--|--|
| Psoriasis<br>subjects affected / exposed<br>occurrences (all)   | 14 / 193 (7.25%)<br>16  |  |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)  | 8 / 193 (4.15%)<br>11   |  |  |
| Psychiatric disorders<br>Depression<br>subjects affected / exposed<br>occurrences (all)                           | 4 / 193 (2.07%)<br>4    |  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 24 / 193 (12.44%)<br>37 |  |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 11 / 193 (5.70%)<br>12  |  |  |
| Bursitis<br>subjects affected / exposed<br>occurrences (all)  | 7 / 193 (3.63%)<br>9    |  |  |
| Musculoskeletal pain<br>subjects affected / exposed<br>occurrences (all)  | 12 / 193 (6.22%)<br>19  |  |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)   | 5 / 193 (2.59%)<br>7    |  |  |
| Psoriatic arthropathy<br>subjects affected / exposed<br>occurrences (all)   | 24 / 193 (12.44%)<br>32 |  |  |
| Infections and infestations<br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)                     | 13 / 193 (6.74%)<br>18  |  |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)   | 10 / 193 (5.18%)<br>12  |  |  |

|                                   |                   |  |  |
|-----------------------------------|-------------------|--|--|
| Nasopharyngitis                   |                   |  |  |
| subjects affected / exposed       | 41 / 193 (21.24%) |  |  |
| occurrences (all)                 | 68                |  |  |
| Oral herpes                       |                   |  |  |
| subjects affected / exposed       | 2 / 193 (1.04%)   |  |  |
| occurrences (all)                 | 9                 |  |  |
| Pharyngitis                       |                   |  |  |
| subjects affected / exposed       | 6 / 193 (3.11%)   |  |  |
| occurrences (all)                 | 8                 |  |  |
| Respiratory tract infection       |                   |  |  |
| subjects affected / exposed       | 5 / 193 (2.59%)   |  |  |
| occurrences (all)                 | 11                |  |  |
| Rhinitis                          |                   |  |  |
| subjects affected / exposed       | 6 / 193 (3.11%)   |  |  |
| occurrences (all)                 | 7                 |  |  |
| Sinusitis                         |                   |  |  |
| subjects affected / exposed       | 16 / 193 (8.29%)  |  |  |
| occurrences (all)                 | 27                |  |  |
| Upper respiratory tract infection |                   |  |  |
| subjects affected / exposed       | 40 / 193 (20.73%) |  |  |
| occurrences (all)                 | 57                |  |  |
| Urinary tract infection           |                   |  |  |
| subjects affected / exposed       | 16 / 193 (8.29%)  |  |  |
| occurrences (all)                 | 23                |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 25 February 2014 | To expand the statistical hierarchy (primary plus ranked secondary variables) to include endpoints which are relevant to determining the overall therapeutic value of a therapy for PsA. These endpoints include but are not limited to PASI75, PASI90, DAS28-CRP, HAQDI, SF-36, dactylitis and enthesitis. |
| 21 October 2015  | To allow dose escalation of secukinumab administered s.c. every 4 weeks from 75 mg to 150 mg or 300 mg, and from 150 mg to 300 mg.  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported