



Clinical trial results:

A randomized, double-blind, placebo controlled, multicenter study of subcutaneous secukinumab in prefilled syringes to demonstrate efficacy after twelve weeks of treatment, and to assess the safety, tolerability, usability and long-term efficacy in patients with chronic plaque-type psoriasis

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2011-006057-28 |
| Trial protocol | EE DE |
| Global end of trial date | 24 October 2016 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 08 November 2017 |
| First version publication date | 08 November 2017 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CAIN457A2308 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01555125 |
| 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, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |

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 | 24 October 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 October 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate the efficacy of secukinumab (150 mg and 300 mg) in patients with moderate to severe chronic plaque-type psoriasis with respect to both PASI 75 and IGA 0 or 1 response (co-primary endpoints) at Week 12 compared to placebo.

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 | 08 May 2012 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 2 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Canada: 19 |
| Country: Number of subjects enrolled | Estonia: 32 |
| Country: Number of subjects enrolled | France: 30 |
| Country: Number of subjects enrolled | Germany: 15 |
| Country: Number of subjects enrolled | United States: 81 |
| Worldwide total number of subjects | 177 |
| EEA total number of subjects | 77 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |

| | |
|--|-----|
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 162 |
| From 65 to 84 years | 15 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

"Study terminated by Sponsor" refers to the fact that - as per protocol – patients had to stop participating in the study in a given country where Secukinumab became available following approval.

Pre-assignment

Screening details:

This was a multicenter, randomized, double-blind, placebo-controlled, parallel-group study in patients with moderate to severe chronic, plaque-type psoriasis. There were 177 patients who were randomized and treated.

Period 1

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

Arms

| | |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes |
| Arm title | AIN457 150 mg |

Arm description:

Patients received one secukinumab 150 mg s.c. injection plus one placebo secukinumab s.c. injection at each dosing. In the open label phase only one 150 mg s.c. injection at each dosing

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab 150 mg |
| Investigational medicinal product code | AIN457 |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

150mg

| | |
|------------------|---------------|
| Arm title | AIN457 300 mg |
|------------------|---------------|

Arm description:

Patients received two secukinumab 150 mg s.c. injections at each dosing

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab 300 mg |
| Investigational medicinal product code | AIN457 |
| Other name | secukinumab |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

300mg

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Patients received placebo secukinumab (2 s.c. injections) at each dosing

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

Dosage and administration details:

Placebo

| Number of subjects in period 1 | AIN457 150 mg | AIN457 300 mg | Placebo |
|---------------------------------------|---------------|---------------|---------|
| Started | 59 | 59 | 59 |
| Completed | 58 | 56 | 56 |
| Not completed | 1 | 3 | 3 |
| Adverse event, serious fatal | 1 | - | - |
| Adverse event, non-fatal | - | 1 | 1 |
| Lost to follow-up | - | 2 | - |
| Subject/guardian decision | - | - | 2 |

Period 2

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

Arms

| | |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes |
| Arm title | AIN457 150 mg |

Arm description:

Patients received one secukinumab 150 mg s.c. injection plus one placebo secukinumab s.c. injection at each dosing. In the open label phase only one 150 mg s.c. injection at each dosing

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab 150 mg |
| Investigational medicinal product code | AIN457 |
| Other name | Secukinumab |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

secukinumab 150 mg

| | |
|------------------|---------------|
| Arm title | AIN457 300 mg |
|------------------|---------------|

Arm description:

Patients received two secukinumab 150 mg s.c. injections at each dosing

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab 300 mg |
| Investigational medicinal product code | AIN457 |
| Other name | Secukinumab |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| 300mg | |
| Arm title | Placebo - AIN457 150mg |

Arm description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re- randomized to AIN457 150 mg for the remainder of the study

| | |
|--|------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | AIN457 |
| Other name | Placebo |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| 150mg | |
| Arm title | Placebo - AIN457 300mg |

Arm description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re- randomized to AIN457 300 mg for the remainder of the study

| | |
|--|------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | AIN457 |
| Other name | Placebo |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| 300mg | |

| Number of subjects in period 2 | AIN457 150 mg | AIN457 300 mg | Placebo - AIN457 150mg |
|---------------------------------------|---------------|---------------|------------------------|
| Started | 58 | 56 | 29 |
| Completed | 48 | 52 | 25 |
| Not completed | 10 | 4 | 4 |
| Adverse event, serious fatal | - | - | - |
| Physician decision | - | - | 1 |
| Adverse event, non-fatal | 1 | 1 | - |
| Lost to follow-up | 2 | - | - |

| | | | |
|---------------------------|---|---|---|
| Subject/guardian decision | 1 | 2 | - |
| Lack of efficacy | 6 | 1 | 3 |

| Number of subjects in period 2 | Placebo - AIN457 300mg |
|--------------------------------|------------------------|
| Started | 27 |
| Completed | 25 |
| Not completed | 2 |
| Adverse event, serious fatal | 1 |
| Physician decision | - |
| Adverse event, non-fatal | - |
| Lost to follow-up | 1 |
| Subject/guardian decision | - |
| Lack of efficacy | - |

Period 3

| | |
|------------------------------|-------------------------|
| Period 3 title | Extension |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes |
| Arm title | AIN457 150 mg |

Arm description:

Secukinumab 150 mg regimen group administered secukinumab 150 mg s.c. injection plus a placebo secukinumab s.c. injection at each dosing

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab 150 mg |
| Investigational medicinal product code | AIN457 |
| Other name | secukinumab 150 mg |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

150mg

| | |
|------------------|---------------|
| Arm title | AIN457 300 mg |
|------------------|---------------|

Arm description:

Secukinumab 300 mg regimen group administered secukinumab 300 mg as 2 s.c. injections of the 150 mg dose at each dosing

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab 300 mg |
| Investigational medicinal product code | AIN457 |
| Other name | secukinumab 300 mg |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

300mg

| | |
|------------------|------------------------|
| Arm title | Placebo - AIN457 150mg |
|------------------|------------------------|

Arm description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re- randomized to AIN457 150 mg for the remainder of the study

| | |
|--|------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo - AIN457 150mg |
| Investigational medicinal product code | AIN457 |
| Other name | Placebo - AIN457 150mg |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

150

| | |
|------------------|------------------------|
| Arm title | Placebo - AIN457 300mg |
|------------------|------------------------|

Arm description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re randomized to AIN457 300 mg for the remainder of the study

| | |
|--|------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo - AIN457 300mg |
| Investigational medicinal product code | AIN457 |
| Other name | Placebo - AIN457 300mg |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

300

| Number of subjects in period 3^[1] | AIN457 150 mg | AIN457 300 mg | Placebo - AIN457 150mg |
|---|---------------|---------------|------------------------|
| Started | 46 | 51 | 23 |
| Completed | 1 | 0 | 0 |
| Not completed | 45 | 51 | 23 |
| Adverse event, non-fatal | 1 | 2 | 1 |
| Protocol deviation | 1 | - | - |
| Technical Problems | 1 | - | - |
| Study terminated by sponsor | 32 | 33 | 16 |
| Lost to follow-up | 2 | 1 | 2 |
| Subject/guardian decision | 1 | 9 | 1 |
| Lack of efficacy | 7 | 6 | 3 |

| Number of subjects in period 3^[1] | Placebo - AIN457 300mg |
|---|------------------------|
| Started | 23 |
| Completed | 1 |
| Not completed | 22 |
| Adverse event, non-fatal | 1 |
| Protocol deviation | - |
| Technical Problems | 1 |
| Study terminated by sponsor | 20 |
| Lost to follow-up | - |
| Subject/guardian decision | - |
| Lack of efficacy | - |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The number of subjects reported is correct

Period 4

| | |
|------------------------------|------------------|
| Period 4 title | Follow-Up Period |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------------|
| Are arms mutually exclusive? | No |
| Arm title | AIN457 150 mg |

Arm description:

Secukinumab 150 mg regimen group administered secukinumab 150 mg s.c. injection plus a placebo secukinumab s.c. injection at each dosing

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab 150 mg |
| Investigational medicinal product code | AIN457 |
| Other name | secukinumab 150 mg |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

150mg

| | |
|------------------|---------------|
| Arm title | AIN457 300 mg |
|------------------|---------------|

Arm description:

Secukinumab 300 mg regimen group administered secukinumab 300 mg as 2 s.c. injections of the 150 mg dose at each dosing

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab 300 mg |
| Investigational medicinal product code | AIN457 |
| Other name | secukinumab 300 mg |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

300mg

| | |
|------------------|------------------------|
| Arm title | Placebo - AIN457 150mg |
|------------------|------------------------|

Arm description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re- randomized to AIN457 150 mg for the remainder of the study

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

Dosage and administration details:

Placebo 150mg

| | |
|------------------|------------------------|
| Arm title | Placebo - AIN457 300mg |
|------------------|------------------------|

Arm description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re randomized to AIN457 300 mg for the remainder of the study

| | |
|--|------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo 300mg |
| Investigational medicinal product code | AIN457 |
| Other name | Placebo 300mg |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

300mg

| Number of subjects in period 4 | AIN457 150 mg | AIN457 300 mg | Placebo - AIN457 150mg |
|---------------------------------------|---------------|---------------|------------------------|
| Started | 36 | 31 | 19 |
| Completed | 32 | 30 | 18 |
| Not completed | 4 | 1 | 1 |
| Lost to follow-up | 1 | - | - |
| Subject/guardian decision | 3 | 1 | 1 |

| Number of subjects in period 4 | Placebo - AIN457 300mg |
|---------------------------------------|------------------------|
| Started | 18 |
| Completed | 17 |
| Not completed | 1 |
| Lost to follow-up | - |
| Subject/guardian decision | 1 |

Baseline characteristics

Reporting groups

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

Reporting group description:

Patients received one secukinumab 150 mg s.c. injection plus one placebo secukinumab s.c. injection at each dosing. In the open label phase only one 150 mg s.c. injection at each dosing

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

Reporting group description:

Patients received two secukinumab 150 mg s.c. injections at each dosing

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

Reporting group description:

Patients received placebo secukinumab (2 s.c. injections) at each dosing

| Reporting group values | AIN457 150 mg | AIN457 300 mg | Placebo |
|---|---------------|---------------|---------|
| Number of subjects | 59 | 59 | 59 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 51 | 58 | 53 |
| From 65-84 years | 8 | 1 | 6 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 46 | 45.1 | 46.5 |
| standard deviation | ± 15.09 | ± 12.57 | ± 14.14 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 19 | 21 | 20 |
| Male | 40 | 38 | 39 |

| Reporting group values | Total | | |
|---|-------|--|--|
| Number of subjects | 177 | | |
| Age categorical Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |

| | | | |
|---|-----|--|--|
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 162 | | |
| From 65-84 years | 15 | | |
| 85 years and over | 0 | | |
| Age Continuous Units: Years arithmetic mean standard deviation | - | | |
| Gender, Male/Female Units: Subjects | | | |
| Female | 60 | | |
| Male | 117 | | |

End points

End points reporting groups

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

Reporting group description:

Patients received one secukinumab 150 mg s.c. injection plus one placebo secukinumab s.c. injection at each dosing. In the open label phase only one 150 mg s.c. injection at each dosing

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

Reporting group description:

Patients received two secukinumab 150 mg s.c. injections at each dosing

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

Reporting group description:

Patients received placebo secukinumab (2 s.c. injections) at each dosing

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

Reporting group description:

Patients received one secukinumab 150 mg s.c. injection plus one placebo secukinumab s.c. injection at each dosing. In the open label phase only one 150 mg s.c. injection at each dosing

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

Reporting group description:

Patients received two secukinumab 150 mg s.c. injections at each dosing

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

Reporting group description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re- randomized to AIN457 150 mg for the remainder of the study

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

Reporting group description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re- randomized to AIN457 300 mg for the remainder of the study

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

Reporting group description:

Secukinumab 150 mg regimen group administered secukinumab 150 mg s.c. injection plus a placebo secukinumab s.c. injection at each dosing

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

Reporting group description:

Secukinumab 300 mg regimen group administered secukinumab 300 mg as 2 s.c. injections of the 150 mg dose at each dosing

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

Reporting group description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re- randomized to AIN457 150 mg for the remainder of the study

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

Reporting group description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re randomized to AIN457 300 mg for the remainder of the study

| | |
|--|-------------------------|
| Reporting group title | AIN457 150 mg |
| Reporting group description: Secukinumab 150 mg regimen group administered secukinumab 150 mg s.c. injection plus a placebo secukinumab s.c. injection at each dosing | |
| Reporting group title | AIN457 300 mg |
| Reporting group description: Secukinumab 300 mg regimen group administered secukinumab 300 mg as 2 s.c. injections of the 150 mg dose at each dosing | |
| Reporting group title | Placebo - AIN457 150mg |
| Reporting group description: Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re- randomized to AIN457 150 mg for the remainder of the study | |
| Reporting group title | Placebo - AIN457 300mg |
| Reporting group description: Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re randomized to AIN457 300 mg for the remainder of the study | |
| Subject analysis set title | placebo |
| Subject analysis set type | Full analysis |
| Subject analysis set description: placebo secukinumab (2 s.c. injections) at each dosing | |
| Subject analysis set title | placebo-AIN457 150mg |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re- randomized to AIN457 150 mg for the remainder of the study | |
| Subject analysis set title | Placebo-AIN457 300mg |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re randomized to AIN457 300 mg for the remainder of the study | |
| Subject analysis set title | Placebo - AIN457 300 mg |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re randomized to AIN457 300 mg for the remainder of the study | |
| Subject analysis set title | Placebo-AIN457 300mg |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re randomized to AIN457 300 mg for the remainder of the study | |
| Subject analysis set title | placebo |
| Subject analysis set type | Full analysis |
| Subject analysis set description: placebo secukinumab (2 s.c. injections) at each dosing | |
| Subject analysis set title | placebo |
| Subject analysis set type | Full analysis |

Subject analysis set description:

placebo secukinumab (2 s.c. injections) at each dosing

| | |
|----------------------------|----------------------|
| Subject analysis set title | Placebo-AIN457 300mg |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re randomized to AIN457 300 mg for the remainder of the study

| | |
|----------------------------|---------------|
| Subject analysis set title | placebo |
| Subject analysis set type | Full analysis |

Subject analysis set description:

placebo secukinumab (2 s.c. injections) at each dosing

| | |
|----------------------------|-------------------------|
| Subject analysis set title | Placebo - AIN457 300 mg |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re randomized to AIN457 300 mg for the remainder of the study

| | |
|----------------------------|----------------------|
| Subject analysis set title | Placebo-AIN457 300mg |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Patients were on Placebo in induction phase and if they were PASI 75 non responders at week 12, were re randomized to AIN457 300 mg for the remainder of the study

| | |
|----------------------------|-------------------|
| Subject analysis set title | Full analysis set |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Full analysis set (FAS) - All patients to whom study treatment was assigned

Primary: Efficacy of secukinumab compared to placebo in subjects with moderate to severe chronic plaque-type psoriasis at week 12 Measure: PASI 75 (psoriasis area and severity index) response"

| | |
|-----------------|--|
| End point title | Efficacy of secukinumab compared to placebo in subjects with moderate to severe chronic plaque-type psoriasis at week 12 Measure: PASI 75 (psoriasis area and severity index) response" ^[1] |
|-----------------|--|

End point description:

A 75% reduction in the Psoriasis Area and Severity Index (PASI) score (PASI 75) is the current benchmark of primary endpoints for most clinical trials of psoriasis

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

End point timeframe:

12 weeks

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo | |
|-----------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 59 | 58 | 59 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 69.5 | 75.9 | 0 | |

Statistical analyses

| | |
|---|-------------------------|
| Statistical analysis title | secukinumab 150 mg |
| Comparison groups | AIN457 150 mg v placebo |
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 |
| Method | Fisher exact |

| | |
|---|-----------------------------|
| Statistical analysis title | secukinumab 300 mg, placebo |
| Comparison groups | AIN457 300 mg v placebo |
| Number of subjects included in analysis | 117 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 |
| Method | Fisher exact |

Primary: Efficacy of secukinumab compared to placebo in subjects with moderate to severe chronic plaque-type psoriasis Measure:IGA (investigator's global assessment) with a 0 or 1 response at Week 12

| | |
|-----------------|---|
| End point title | Efficacy of secukinumab compared to placebo in subjects with moderate to severe chronic plaque-type psoriasis Measure:IGA (investigator's global assessment) with a 0 or 1 response at Week 12 ^[2] |
|-----------------|---|

End point description:

The IGA scale has been developed based on a previous version of the scale used in secukinumab phase II studies in collaboration with health authorities, in particular the FDA. The explanations/descriptions of the points on the scale have been improved to ensure appropriate differentiation between the points. The IGA used in this study is static, i.e. it refers exclusively to the subject's disease state at the time of the assessments, and does not attempt a comparison with any of the subject's previous disease states, whether at baseline or at a previous visit. IGA has a scale of 0-4 with the lower scores correlating to better performance. A score of 0= clear skin, 1= almost clear skin, 2=mild, 3=moderate,4=severe

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

End point timeframe:

12 weeks

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo | |
|-----------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 59 | 58 | 59 | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 52.5 | 69 | 0 | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Efficacy of secukinumab compared to placebo |
| Comparison groups | AIN457 150 mg v placebo |
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 |
| Method | Fisher exact |

| | |
|---|---|
| Statistical analysis title | Efficacy of secukinumab compared to placebo |
| Comparison groups | AIN457 300 mg v placebo |
| Number of subjects included in analysis | 117 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 |
| Method | Fisher exact |

Secondary: Absolute change from baseline in Self Injection Assessment Questionnaire (SIAQ) Domain Scores at Week 12

| | |
|-----------------|---|
| End point title | Absolute change from baseline in Self Injection Assessment Questionnaire (SIAQ) Domain Scores at Week 12 ^[3] |
|-----------------|---|

End point description:

The three domains of the POST SIAQ are feelings about injections, self-image, self-confidence, injection-site reactions, ease of use, and satisfaction with self-injection. The SIAQ items are scored on a semantic Likert-type scale where lower numbers indicate a worse experience. Domain scores range from 0 to 10. Subjects self-injecting at this visit completed this SIAQ questionnaire. The POST-SIAQ is taken after the injection at that visit.

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

End point timeframe:

Week 12

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo | |
|--------------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 59 | 59 | 59 | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Feelings about injections | 1.07 (± 1.912) | 0.85 (± 1.685) | 0.57 (± 1.509) | |
| Self confidence | 1.10 (± 2.331) | 1.08 (± 2.197) | 1.26 (± 2.009) | |
| Satisfaction with self-injection | 1.64 (± 2.163) | 1.62 (± 2.667) | 1.32 (± 2.629) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in Self-Injection Assessment Questionnaire (SIAQ) Domain Scores at week 48

| | |
|-----------------|---|
| End point title | Absolute change from baseline in Self-Injection Assessment Questionnaire (SIAQ) Domain Scores at week 48 ^[4] |
|-----------------|---|

End point description:

To measure subject satisfaction with the secukinumab PFS" Pre Filled Syringes. The SIAQ items are scored on a semantic Likert-type scale where lower numbers indicate a worse experience. Domain scores range from 0 to 10. Subjects self-injecting at this visit completed this SIAQ questionnaire. The POST-SIAQ is taken after the injection at that visit.

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

End point timeframe:

Baseline, Week 48

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo- AIN457 150mg | Placebo- AIN457 300mg |
|---|-----------------|-----------------|-----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 58 | 56 | 29 | 27 |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Feelings about injections (n=45, 52, 25, 24) | 0.93 (± 1.752) | 1.01 (± 2.103) | 0.63 (± 1.449) | 0.76 (± 1.321) |
| Self-confidence (n=45, 51, 25, 24) | 1.63 (± 3.173) | 1.24 (± 2.400) | 0.97 (± 1.811) | 0.94 (± 1.521) |
| Satisfaction, self-injection (n=43, 50, 25, 23) | 1.92 (± 2.239) | 2.15 (± 2.673) | 1.90 (± 3.250) | 0.54 (± 1.840) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with potential use related hazards at week 1

| | |
|-----------------|--|
| End point title | Percentage of subjects with potential use related hazards at week 1 ^[5] |
|-----------------|--|

End point description:

To assess potential use-related hazards with the secukinumab PFS for the subject

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

End point timeframe:

Week 1

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo | |
|--|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 59 | 59 | 59 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Needle stick in a critical area (n=0,0,0) | 0 | 0 | 0 | |
| Needle stick in non-critical area (n=0,0,1) | 0 | 0 | 1.7 | |
| Any part of the device swallowed (n=0,0,0) | 0 | 0 | 0 | |
| Allergic reaction to devise material (n=0,0,0) | 0 | 0 | 0 | |
| Pain due to bent needle (n=0,0,0) | 0 | 0 | 0 | |
| Any breakage of the devise (0,0,0) | 0 | 0 | 0 | |
| Swallowing of material debris observed (n=0,0,0) | 0 | 0 | 0 | |
| Any other problem (n=1,0,0) | 1.7 | 0 | 0 | |
| Less than full dose administered (n=1,0,0) | 1.7 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with successful self administration of study drug at week 1

| | |
|-----------------|---|
| End point title | Percentage of subjects with successful self administration of study drug at week 1 ^[6] |
|-----------------|---|

End point description:

To assess the subject's ability to follow instructions for use with the secukinumab PFS

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

End point timeframe:

Week 1

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo | |
|-----------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 58 | 57 | 59 | |
| Units: Percentage of participants | 100 | 100 | 100 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Responders with PASI equal to or greater than 50, PASI 75, PASI 90, PASI 100, (induction) with non-responder imputation

| | |
|-----------------|---|
| End point title | Percent of Responders with PASI equal to or greater than 50, PASI 75, PASI 90, PASI 100, (induction) with non-responder imputation ^[7] |
|-----------------|---|

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 50, 75, 90 and 100 were defined as participants achieving ≥ 50%, 75%, 90% or 100% improvement from baseline.

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

End point timeframe:

Week 12

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo | |
|-----------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 59 | 59 | 59 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 12 PASI 75 | 69.5 | 75.9 | 0.0 | |
| Week 12 PASI 50 | 86.4 | 87.9 | 5.1 | |
| Week 12 PASI 90 | 45.8 | 60.3 | 0 | |
| Week 12 PASI 100 | 8.5 | 43.1 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Responders with PASI equal to or greater than 50, PASI 75, PASI 90, PASI 100, (Maintenance, observed data)

| | |
|-----------------|--|
| End point title | Percent of Responders with PASI equal to or greater than 50, PASI 75, PASI 90, PASI 100, (Maintenance, observed data) ^[8] |
|-----------------|--|

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 50, 75, 90 and 100 were defined as participants achieving $\geq 50\%$, 75%, 90% or 100% improvement from baseline.

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

End point timeframe:

Week 52

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo- AIN457 150mg | Placebo - AIN457 300 mg |
|-----------------------------------|-----------------|-----------------|-----------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 59 | 58 | 29 | 27 |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 52 PASI 75 | 71.4 | 84.6 | 72.0 | 96.0 |
| Week 52 PASI 50 | 89.8 | 96.2 | 84.0 | 100.0 |
| Week 52 PASI 90 | 59.2 | 69.2 | 64.0 | 76.0 |
| Week 52 PASI 100 | 36.7 | 48.1 | 52.0 | 44.0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of responders with IGA mod 2011 score of 0 or 1, (Maintenance; observed data)

| | |
|-----------------|--|
| End point title | Percent of responders with IGA mod 2011 score of 0 or 1, (Maintenance; observed data) ^[9] |
|-----------------|--|

End point description:

The IGA mod 2011 scale is static, i.e. it referred exclusively to the participant's disease at the time of the assessment, and did not compare with any of the participant's previous disease states at previous visits. The scores are: 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate and 4 = severe.

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

End point timeframe:

Week 52

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo- AIN457 150mg | Placebo - AIN457 300 mg |
|-----------------------------------|-----------------|-----------------|-----------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 59 | 59 | 29 | 27 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 51 | 71.2 | 72 | 92 |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline for PASI score at Week 12, (induction)

| | |
|-----------------|--|
| End point title | Absolute change from baseline for PASI score at Week 12, (induction) ^[10] |
|-----------------|--|

End point description:

PASI: Combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72(maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section(head:01, arms:0.2 body:0.3 legs:0.4)

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

End point timeframe:

Week 12

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo | |
|--------------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 59 | 59 | 59 | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -16.33 (± 8.49) | -17.90 (± 8.74) | 0.50 (± 7.22) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline for PASI score over time up to week 52, (Maintenance; observed data)

| | |
|-----------------|--|
| End point title | Absolute change from baseline for PASI score over time up to week 52, (Maintenance; observed data) ^[11] |
|-----------------|--|

End point description:

PASI: Combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72(maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and

desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section(head:0.1, arms:0.2 body:0.3 legs:0.4)

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

End point timeframe:

Week 52

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo- AIN457 150mg | Placebo - AIN457 300 mg |
|--------------------------------------|-----------------|-----------------|-----------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 59 | 58 | 29 | 27 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -16.9 (± 8.27) | -18.7 (± 8.48) | -15.2 (± 5.38) | -20 (± 7.96) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants in each IGA mod 2011 category at Week 12, (induction)

| | |
|-----------------|--|
| End point title | Percentage of participants in each IGA mod 2011 category at Week 12, (induction) ^[12] |
|-----------------|--|

End point description:

The IGA mod 2011 scale is static, i.e. it referred exclusively to the participant's disease at the time of the assessment, and did not compare with any of the participant's previous disease states at previous visits. The scores are: 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate and 4 = severe

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

End point timeframe:

Week 12

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo | |
|-----------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 59 | 58 | 59 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| clear (n=6, 26, 0) | 10.2 | 44.8 | 0.0 | |
| almost clear (n=26, 17, 0) | 44.1 | 29.3 | 0.0 | |
| mild (n=12, 9, 1) | 20.3 | 15.5 | 1.7 | |
| moderate (n=14, 5, 34) | 23.7 | 8.6 | 57.6 | |
| severe (n=1, 1, 24) | 1.7 | 1.7 | 40.7 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants in each IGA mod 2011 category over time up to week 52, (Maintenance; observed data)

| | |
|-----------------|--|
| End point title | Percentage of participants in each IGA mod 2011 category over time up to week 52, (Maintenance; observed data) ^[13] |
|-----------------|--|

End point description:

The IGA mod 2011 scale is static, i.e. it referred exclusively to the participant's disease at the time of the assessment, and did not compare with any of the participant's previous disease states at previous visits. The scores are: 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate and 4 = severe.

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

End point timeframe:

Week 52

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo- AIN457 150mg | Placebo - AIN457 300 mg |
|-----------------------------------|-----------------|-----------------|-----------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 59 | 59 | 29 | 27 |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Clear | 36.7 | 48.1 | 52 | 44 |
| Almost clear | 14.3 | 23.1 | 20 | 48 |
| Mild | 18.4 | 19.2 | 4 | 4 |
| Moderate | 26.5 | 9.6 | 20 | 4 |
| Severe | 4.1 | 0 | 4 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in EQ-5D at week 12 (induction)

| | |
|-----------------|--|
| End point title | Change from baseline in EQ-5D at week 12 (induction) ^[14] |
|-----------------|--|

End point description:

EQ-5D: Participant rated questionnaire to assess health related quality of life in terms of a single utility score. Five domains are assessed mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) each with three possible score: 1 indicates no problems, better state of health; 3 indicates worst state of health (example "confined to bed") A visual analog scale (VAS) assesses the health status from 0 (worst possible health state) to 100 (best possible health state)

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |
| Notes: | |
| [14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. | |
| Justification: All arms do not apply to this end point | |

| End point values | AIN457 150 mg | AIN457 300 mg | placebo | |
|--------------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 59 | 59 | 59 | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | 12.1 (± 24.03) | 11.2 (± 18.02) | 0.8 (± 16.12) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in EQ-5D at week 12 and over time up to week 52, (Maintenance)

| | |
|-----------------|---|
| End point title | Change from baseline in EQ-5D at week 12 and over time up to week 52, (Maintenance) ^[15] |
|-----------------|---|

End point description:

ED-5Q: Participant rated questionnaire to assess health related quality of life in terms of a single utility score. Five domains are assessed mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) each with three possible score: 1 indicates no problems, better state of health; 3 indicates worst state of health (example "confined to bed") A visual analog scale (VAS) assesses the health status from 0 (worst possible health state) to 100 (best possible health state)

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

End point timeframe:

Week 52

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo- AIN457 150mg | Placebo- AIN457 300mg |
|--------------------------------------|-----------------|-----------------|-----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 57 | 57 | 29 | 26 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | 11.4 (± 24.79) | 13.5 (± 15.69) | 12.2 (± 15.05) | 19.7 (± 17.16) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Dermatology Life Quality Index (DLQI) total score, (Induction)

| | |
|-----------------|--|
| End point title | Change from Baseline in Dermatology Life Quality Index (DLQI) total score, (Induction) ^[16] |
|-----------------|--|

End point description:

The DLQI is a quality of life measure used in the psoriatic The 10-item questionnaire has a score range of 0 (best) to 30 (worst) with higher scores indicating poor quality of life. The instrument contains six functional scales (i.e., symptoms and feeling, daily activities, leisure, work and school, personal relationships, treatment). Each item has 4 response categories, ranging from 0 (not at all) to 3 (very much). "Not relevant" is also a valid response and is scored as 0. The DLQI total score is a sum of the 10 questions

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

End point timeframe:

Week 12

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo | |
|----------------------------------|------------------------|------------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 56 | 53 | 54 | |
| Units: Units on a scale | | | | |
| median (confidence interval 95%) | -78.6 (-85.9 to -67.5) | -85.0 (-90.9 to -77.7) | -16.7 (-25.3 to -3.0) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Dermatology Life Quality Index (DLQI) score over time up to week 52, (Maintenance)

| | |
|-----------------|--|
| End point title | Change from Baseline in Dermatology Life Quality Index (DLQI) score over time up to week 52, (Maintenance) ^[17] |
|-----------------|--|

End point description:

The DLQI is a quality of life measure used in the psoriatic The 10-item questionnaire has a score range of 0 (best) to 30 (worst) with higher scores indicating poor quality of life. The instrument contains six functional scales (i.e., symptoms and feeling, daily activities, leisure, work and school, personal relationships, treatment). Each item has 4 response categories, ranging from 0 (not at all) to 3 (very much). "Not relevant" is also a valid response and is scored as 0. The DLQI total score is a sum of the 10 questions

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

End point timeframe:

Week 52

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo- AIN457 150mg | Placebo- AIN457 300mg |
|----------------------------------|------------------------|------------------------|-----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 57 | 56 | 29 | 26 |
| Units: Units on a scale | | | | |
| median (confidence interval 95%) | -71.4 (-83.3 to -61.9) | -90.5 (-95.7 to -84.2) | -91.7 (-100 to -81.7) | -97.2 (-100 to -83.3) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a DLQI score of 0 or 1 at week 12, (Induction)

| | |
|-----------------|---|
| End point title | Percentage of participants achieving a DLQI score of 0 or 1 at week 12, (Induction) ^[18] |
|-----------------|---|

End point description:

The DLQI is a quality of life measure used in the psoriatic The 10-item questionnaire has a score range of 0 (best) to 30 (worst) with higher scores indicating poor quality of life. The instrument contains six functional scales (i.e., symptoms and feeling, daily activities, leisure, work and school, personal relationships, treatment). Each item has 4 response categories, ranging from 0 (not at all) to 3 (very much). "Not relevant" is also a valid response and is scored as 0. The DLQI total score is a sum of the 10 questions

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

End point timeframe:

Week 12

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo | |
|-----------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 57 | 53 | 54 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 54.4 | 54.7 | 7.4 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a DLQI score of 0 or 1 over time up to week 52, (Maintenance)

| | |
|-----------------|--|
| End point title | Percentage of participants achieving a DLQI score of 0 or 1 over time up to week 52, (Maintenance) ^[19] |
|-----------------|--|

End point description:

The DLQI is a quality of life measure used in the psoriatic The 10-item questionnaire has a score range of 0 (best) to 30 (worst) with higher scores indicating poor quality of life. The instrument contains six functional scales (i.e., symptoms and feeling, daily activities, leisure, work and school, personal

relationships, treatment). Each item has 4 response categories, ranging from 0 (not at all) to 3 (very much). "Not relevant" is also a valid response and is scored as 0. The DLQI total score is a sum of the 10 questions

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 52 | |

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo- AIN457 150mg | Placebo- AIN457 300mg |
|-----------------------------------|-----------------|-----------------|-----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 28 | 35 | 18 | 20 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 48.3 | 62.5 | 62.1 | 76.9 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Responders with PASI equal to or greater than 50, PASI 75, PASI 90, PASI 100 after week 52

| | |
|-----------------|---|
| End point title | Percent of Responders with PASI equal to or greater than 50, PASI 75, PASI 90, PASI 100 after week 52 ^[20] |
|-----------------|---|

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 50, 75, 90 and 100 were defined as participants achieving ≥ 50%, 75%, 90% or 100% improvement from baseline.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 172 | |

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo- AIN457 150mg | Placebo - AIN457 300 mg |
|-------------------------------------|-----------------|-----------------|-----------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 27 | 32 | 13 | 19 |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 172 PASI 75 (n=26, 25, 9, 17) | 96.3 | 78.1 | 69.2 | 89.5 |
| Week 172 PASI 50 (n=27, 32, 12, 18) | 100 | 100 | 92.3 | 94.7 |
| Week 172 PASI 90 (14, 21, 9, 11) | 51.9 | 65.6 | 69.2 | 57.9 |

| | | | | |
|-----------------------------------|------|------|------|------|
| Week 172 PASI 100 (n=6, 16, 6, 7) | 22.2 | 50.0 | 46.2 | 36.8 |
|-----------------------------------|------|------|------|------|

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline for PASI score after Week 52, (observed data)

| | |
|-----------------|---|
| End point title | Absolute change from baseline for PASI score after Week 52, (observed data) ^[21] |
|-----------------|---|

End point description:

PASI: Combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72(maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section(head:01, arms:0.2 body:0.3 legs:0.4)

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

End point timeframe:

Week 172

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo- AIN457 150mg | Placebo - AIN457 300 mg |
|--------------------------------------|-----------------|-----------------|-----------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 27 | 32 | 13 | 19 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -18 (± 6.97) | -18.7 (± 8.36) | -14.7 (± 5.97) | -19.4 (± 9.02) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of participants in each IGA mod 2011 category after Week 52 (observed data)

| | |
|-----------------|---|
| End point title | Percent of participants in each IGA mod 2011 category after Week 52 (observed data) ^[22] |
|-----------------|---|

End point description:

The IGA mod 2011 is a static scale, i.e., it refers exclusively to the participant's disease state at the time of the assessments and does not attempt a comparison to any of the participant's previous disease states at prior visits. The score ranges from 0 (clear) to 4 (severe). The score 0 is clear, 1 is almost clear, 2 is mild, 3 is moderate, and 4 is severe

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

End point timeframe:

Week 172

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All arms do not apply to this end point

| End point values | AIN457 150 mg | AIN457 300 mg | placebo- AIN457 150mg | Placebo - AIN457 300 mg |
|-----------------------------------|-----------------|-----------------|-----------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 27 | 32 | 13 | 19 |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Clear (7, 15, 7, 7) | 25.9 | 46.9 | 53.8 | 36.8 |
| Almost clear (n=3,4,1,2) | 11.1 | 12.5 | 7.7 | 10.5 |
| Mild (n=16,6,3,6) | 59.3 | 18.8 | 23.1 | 31.6 |
| Moderate (n=1,7,1,4) | 3.7 | 21.9 | 7.7 | 21.1 |
| Severe (n=0,0,1,0) | 0.0 | 0.0 | 7.7 | 0.0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants developing treatment emergent anti-secukinumab antibodies, immunogenicity

| | |
|-----------------|--|
| End point title | Number of participants developing treatment emergent anti-secukinumab antibodies, immunogenicity |
|-----------------|--|

End point description:

The development of anti-secunimubab anti-bodies will decrease a participant's ability to respond to secukinumab treatment. The number of participants developing anti-secukinumab anti-bodies was measured from Baseline to 8 weeks after last treatment

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

End point timeframe:

Baseline and at Week 12, 24, 52, 100, 148, and 196, 204

| End point values | AIN457 150 mg | AIN457 300 mg | Placebo | placebo- AIN457 150mg |
|-------------------------------|-----------------|-----------------|-----------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 59 | 59 | 3 | 29 |
| Units: Number of participants | 3 | 0 | 0 | 0 |

| End point values | Placebo- AIN457 300mg | | | |
|-----------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 27 | | | |

| | | | | |
|-------------------------------|---|--|--|--|
| Units: Number of participants | 0 | | | |
|-------------------------------|---|--|--|--|

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 19.1 |

Reporting groups

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

Reporting group description:

Patients received one secukinumab 150 mg s.c. injection plus one placebo secukinumab s.c. injection at each dosing

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

Reporting group description:

placebo secukinumab (2 s.c. injections) at each dosing

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

Reporting group description:

Patients received two secukinumab 150 mg s.c. injections at each dosing

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

Reporting group description:

Includes all patients in the AIN457 300 mg and in the placebo- AIN457 300 mg treatment groups

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

Reporting group description:

Includes all patients in the AIN457 150 mg and in the placebo- AIN457 150 mg treatment groups

| Serious adverse events | Induction AIN457 150 mg | Induction Placebo | Induction AIN457 300 mg |
|---|-------------------------|-------------------|-------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 1 / 59 (1.69%) | 3 / 59 (5.08%) |
| number of deaths (all causes) | 1 | 1 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| ADENOSQUAMOUS CELL LUNG CANCER | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |

| | | | | |
|--|---|----------------|----------------|----------------|
| BASAL CELL CARCINOMA | subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| BLADDER CANCER | subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| LYMPHOPROLIFERATIVE DISORDER | subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| Vascular disorders | | | | |
| THROMBOSIS | | | | |
| | subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| General disorders and administration site conditions | | | | |
| COMPLICATION ASSOCIATED WITH DEVICE | | | | |
| | subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| Reproductive system and breast disorders | | | | |
| POSTMENOPAUSAL HAEMORRHAGE | | | | |
| | subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| VAGINAL HAEMORRHAGE | | | | |
| | subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| Psychiatric disorders | | | | |
| DEPRESSION | | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| HIP FRACTURE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| PERIORBITAL HAEMATOMA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 | | | |
| ACUTE MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CARDIAC FAILURE CONGESTIVE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| CARDIO-RESPIRATORY ARREST | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| CORONARY ARTERY DISEASE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |

| | | | |
|---|----------------|----------------|----------------|
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 | | | |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| LOSS OF CONSCIOUSNESS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| SCIATICA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| VERTIGO | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 | | | |
| CROHN'S DISEASE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| RECTAL HAEMORRHAGE | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 | | | |
| DERMATITIS EXFOLIATIVE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 0 / 59 (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 | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| INTERVERTEBRAL DISC PROTRUSION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| LUMBAR SPINAL STENOSIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| OSTEOARTHRITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| CELLULITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| PNEUMONIA INFLUENZAL | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 0 / 59 (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 |
| SEPTIC VASCULITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (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 | | | |
| DIABETES MELLITUS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Entire Any AIN457 300 mg | Entire Any AIN457 150 mg | |
|--|-----------------------------|-----------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 10 / 86 (11.63%) | 10 / 88 (11.36%) | |
| number of deaths (all causes) | 1 | 1 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| ADENOSQUAMOUS CELL LUNG CANCER | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| BASAL CELL CARCINOMA | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BLADDER CANCER | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LYMPHOPROLIFERATIVE DISORDER | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| THROMBOSIS | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| COMPLICATION ASSOCIATED WITH DEVICE | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| POSTMENOPAUSAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VAGINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| DEPRESSION | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| ALCOHOL POISONING | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| HIP FRACTURE | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PERIORBITAL HAEMATOMA | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| ACUTE MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC FAILURE CONGESTIVE | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIO-RESPIRATORY ARREST | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| CORONARY ARTERY DISEASE | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DIZZINESS | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LOSS OF CONSCIOUSNESS | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SCIATICA | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| VERTIGO | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| CROHN'S DISEASE | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RECTAL HAEMORRHAGE | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| DERMATITIS EXFOLIATIVE | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INTERVERTEBRAL DISC PROTRUSION | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LUMBAR SPINAL STENOSIS | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 88 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OSTEOARTHRITIS | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| CELLULITIS | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 88 (2.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA INFLUENZAL | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SEPSIS | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SEPTIC VASCULITIS | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| DIABETES MELLITUS | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 88 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Induction AIN457 150 mg | Induction Placebo | Induction AIN457 300 mg |
|--|----------------------------|-------------------|----------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 29 / 59 (49.15%) | 22 / 59 (37.29%) | 24 / 59 (40.68%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| MELANOCYTIC NAEVUS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SKIN PAPILLOMA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SQUAMOUS CELL CARCINOMA | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| Vascular disorders HAEMATOMA subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 1 |
| HYPERTENSION subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 1 / 59 (1.69%) 1 | 1 / 59 (1.69%) 1 |
| General disorders and administration site conditions ASTHENIA subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| FATIGUE subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 1 | 0 / 59 (0.00%) 0 |
| INJECTION SITE OEDEMA subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| INJECTION SITE PAIN subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 4 | 1 / 59 (1.69%) 1 | 0 / 59 (0.00%) 0 |
| NON-CARDIAC CHEST PAIN subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| OEDEMA PERIPHERAL subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 1 |
| PYREXIA subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 2 / 59 (3.39%) 2 | 2 / 59 (3.39%) 2 |
| Immune system disorders SEASONAL ALLERGY subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 1 |
| Reproductive system and breast disorders | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| DYSMENORRHOEA subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 2 | 2 / 59 (3.39%) 3 |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 1 |
| DYSPNOEA subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| NASAL CONGESTION subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 1 | 0 / 59 (0.00%) 0 |
| OROPHARYNGEAL PAIN subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 1 |
| SINUS CONGESTION subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| WHEEZING subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| Psychiatric disorders | | | |
| ANXIETY subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| DEPRESSION subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 1 |
| INSOMNIA subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 1 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |

| | | | |
|--|----------------|----------------|----------------|
| BLOOD PRESSURE INCREASED | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD TRIGLYCERIDES INCREASED | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| C-REACTIVE PROTEIN INCREASED | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GAMMA-GLUTAMYLTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HEPATIC ENZYME INCREASED | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 0 | 0 | 1 |
| VITAMIN D DECREASED | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| WEIGHT INCREASED | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| ARTHROPOD BITE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONTUSION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FALL | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| LIGAMENT SPRAIN | | | |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LIMB INJURY | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE STRAIN | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| ROAD TRAFFIC ACCIDENT | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SKIN ABRASION | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac disorders | | | |
| ANGINA PECTORIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 4 / 59 (6.78%) | 4 / 59 (6.78%) | 0 / 59 (0.00%) |
| occurrences (all) | 11 | 4 | 0 |
| MIGRAINE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SCIATICA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 0 | 0 | 1 |
| SINUS HEADACHE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SYNCOPE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood and lymphatic system disorders | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| ANAEMIA subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| EOSINOPHILIA subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| Ear and labyrinth disorders VERTIGO subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 1 |
| Eye disorders BLEPHARITIS subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| Gastrointestinal disorders ABDOMINAL DISTENSION subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 1 |
| ABDOMINAL PAIN subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 1 / 59 (1.69%) 1 | 0 / 59 (0.00%) 0 |
| ABDOMINAL PAIN UPPER subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | 1 / 59 (1.69%) 1 | 1 / 59 (1.69%) 1 |
| COLITIS subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| CONSTIPATION subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| DENTAL CARIES subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 | 0 / 59 (0.00%) 0 |
| DIARRHOEA subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 1 / 59 (1.69%) 1 | 5 / 59 (8.47%) 6 |
| DYSPEPSIA | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| FLATULENCE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 3 / 59 (5.08%) |
| occurrences (all) | 0 | 1 | 3 |
| TOOTHACHE | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 1 / 59 (1.69%) | 0 / 59 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| VOMITING | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 2 / 59 (3.39%) |
| occurrences (all) | 0 | 0 | 2 |
| Skin and subcutaneous tissue disorders | | | |
| ACNE | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ACTINIC KERATOSIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| ALOPECIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| DERMAL CYST | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| DERMATITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DERMATITIS CONTACT | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 2 / 59 (3.39%) |
| occurrences (all) | 0 | 0 | 2 |
| ECZEMA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PRURITUS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 1 / 59 (1.69%) |
| occurrences (all) | 0 | 1 | 1 |
| PSORIASIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| URTICARIA PAPULAR | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| GLYCOSURIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMATURIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 0 | 0 | 1 |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 3 / 59 (5.08%) |
| occurrences (all) | 0 | 0 | 3 |
| BURSITIS | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 2 / 59 (3.39%) |
| occurrences (all) | 1 | 0 | 2 |
| INTERVERTEBRAL DISC PROTRUSION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE SPASMS | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| MYALGIA | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| NECK PAIN | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 1 | 0 | 1 |
| PSORIATIC ARTHROPATHY | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| SPINAL PAIN | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TENDONITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| ABSCCESS ORAL | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ACARODERMATITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BRONCHITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 1 / 59 (1.69%) |
| occurrences (all) | 0 | 1 | 1 |
| CELLULITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| CONJUNCTIVITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 0 | 0 | 1 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EAR INFECTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FOLLICULITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROENTERITIS VIRAL | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LABYRINTHITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | 5 / 59 (8.47%) | 3 / 59 (5.08%) |
| occurrences (all) | 4 | 5 | 3 |
| ORAL CANDIDIASIS | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 1 | 0 | 2 |
| ORAL HERPES | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 0 | 0 | 1 |
| OTITIS MEDIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| OTITIS MEDIA BACTERIAL | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PERIODONTITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PHARYNGITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 0 | 0 | 1 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RHINITIS | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 2 | 0 | 1 |
| SINUSITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SKIN BACTERIAL INFECTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| STAPHYLOCOCCAL INFECTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TINEA PEDIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TONGUE FUNGAL INFECTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TONSILLITIS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 59 (1.69%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| TOOTH ABSCESS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|----------------|----------------|----------------|
| TOOTH INFECTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 1 / 59 (1.69%) | 0 / 59 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VIRAL UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 1 | 0 | 1 |
| VULVOVAGINAL CANDIDIASIS | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 59 (0.00%) | 1 / 59 (1.69%) |
| occurrences (all) | 1 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| DIABETES MELLITUS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERCHOLESTEROLAEMIA | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 1 / 59 (1.69%) | 1 / 59 (1.69%) |
| occurrences (all) | 2 | 1 | 1 |
| HYPERTRIGLYCERIDAEMIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOSIDERAEMIA | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TYPE 2 DIABETES MELLITUS | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 59 (0.00%) | 0 / 59 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Entire Any AIN457 300 mg | Entire Any AIN457 150 mg | |
|---|-----------------------------|-----------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 74 / 86 (86.05%) | 70 / 88 (79.55%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| MELANOCYTIC NAEVUS | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| SKIN PAPILLOMA | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 88 (1.14%) | |
| occurrences (all) | 2 | 1 | |
| SQUAMOUS CELL CARCINOMA | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Vascular disorders | | | |
| HAEMATOMA | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 0 / 88 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| HYPERTENSION | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 3 / 88 (3.41%) | |
| occurrences (all) | 3 | 3 | |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 4 / 88 (4.55%) | |
| occurrences (all) | 1 | 4 | |
| FATIGUE | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| INJECTION SITE OEDEMA | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 88 (2.27%) | |
| occurrences (all) | 0 | 2 | |
| INJECTION SITE PAIN | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 1 | 6 | |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 2 / 88 (2.27%) | |
| occurrences (all) | 2 | 2 | |

| | | | |
|---|------------------------|---------------------|--|
| OEDEMA PERIPHERAL subjects affected / exposed occurrences (all) | 1 / 86 (1.16%) 1 | 2 / 88 (2.27%) 2 | |
| PYREXIA subjects affected / exposed occurrences (all) | 3 / 86 (3.49%) 3 | 6 / 88 (6.82%) 9 | |
| Immune system disorders SEASONAL ALLERGY subjects affected / exposed occurrences (all) | 5 / 86 (5.81%) 5 | 3 / 88 (3.41%) 3 | |
| Reproductive system and breast disorders DYSMENORRHOEA subjects affected / exposed occurrences (all) | 3 / 86 (3.49%) 12 | 0 / 88 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders COUGH subjects affected / exposed occurrences (all) | 9 / 86 (10.47%) 10 | 8 / 88 (9.09%) 9 | |
| DYSPNOEA subjects affected / exposed occurrences (all) | 2 / 86 (2.33%) 2 | 0 / 88 (0.00%) 0 | |
| NASAL CONGESTION subjects affected / exposed occurrences (all) | 4 / 86 (4.65%) 4 | 3 / 88 (3.41%) 3 | |
| OROPHARYNGEAL PAIN subjects affected / exposed occurrences (all) | 10 / 86 (11.63%) 13 | 5 / 88 (5.68%) 5 | |
| SINUS CONGESTION subjects affected / exposed occurrences (all) | 2 / 86 (2.33%) 2 | 2 / 88 (2.27%) 2 | |
| WHEEZING subjects affected / exposed occurrences (all) | 2 / 86 (2.33%) 2 | 2 / 88 (2.27%) 2 | |
| Psychiatric disorders ANXIETY | | | |

| | | | |
|-------------------------------------|----------------|----------------|--|
| subjects affected / exposed | 3 / 86 (3.49%) | 3 / 88 (3.41%) | |
| occurrences (all) | 3 | 4 | |
| DEPRESSION | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 6 / 88 (6.82%) | |
| occurrences (all) | 2 | 6 | |
| INSOMNIA | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 3 / 88 (3.41%) | |
| occurrences (all) | 1 | 3 | |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 88 (2.27%) | |
| occurrences (all) | 0 | 3 | |
| BLOOD PRESSURE INCREASED | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 88 (2.27%) | |
| occurrences (all) | 0 | 3 | |
| BLOOD TRIGLYCERIDES INCREASED | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 1 | 3 | |
| C-REACTIVE PROTEIN INCREASED | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| GAMMA-GLUTAMYLTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| HEPATIC ENZYME INCREASED | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| VITAMIN D DECREASED | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 88 (2.27%) | |
| occurrences (all) | 0 | 5 | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| WEIGHT INCREASED | | | |

| | | | |
|--|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 86 (2.33%) 2 | 0 / 88 (0.00%) 0 | |
| Injury, poisoning and procedural complications | | | |
| ARTHROPOD BITE | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 1 | 2 | |
| CONTUSION | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 4 / 88 (4.55%) | |
| occurrences (all) | 1 | 4 | |
| FALL | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 88 (1.14%) | |
| occurrences (all) | 2 | 1 | |
| LIGAMENT SPRAIN | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 1 | 2 | |
| LIMB INJURY | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 1 | 2 | |
| MUSCLE STRAIN | | | |
| subjects affected / exposed | 4 / 86 (4.65%) | 2 / 88 (2.27%) | |
| occurrences (all) | 4 | 2 | |
| ROAD TRAFFIC ACCIDENT | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 1 | 2 | |
| SKIN ABRASION | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 88 (2.27%) | |
| occurrences (all) | 0 | 2 | |
| Cardiac disorders | | | |
| ANGINA PECTORIS | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 88 (2.27%) | |
| occurrences (all) | 0 | 2 | |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 6 / 86 (6.98%) | 5 / 88 (5.68%) | |
| occurrences (all) | 20 | 34 | |
| MIGRAINE | | | |

| | | | |
|--|---|---|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>SCIATICA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>SINUS HEADACHE</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>SYNCOPE</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 86 (3.49%)</p> <p>3</p> <p>5 / 86 (5.81%)</p> <p>5</p> <p>2 / 86 (2.33%)</p> <p>2</p> <p>2 / 86 (2.33%)</p> <p>2</p> | <p>1 / 88 (1.14%)</p> <p>1</p> <p>0 / 88 (0.00%)</p> <p>0</p> <p>0 / 88 (0.00%)</p> <p>0</p> <p>0 / 88 (0.00%)</p> <p>0</p> | |
| <p>Blood and lymphatic system disorders</p> <p>ANAEMIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>EOSINOPHILIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 86 (0.00%)</p> <p>0</p> <p>1 / 86 (1.16%)</p> <p>1</p> | <p>5 / 88 (5.68%)</p> <p>5</p> <p>2 / 88 (2.27%)</p> <p>3</p> | |
| <p>Ear and labyrinth disorders</p> <p>VERTIGO</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 86 (3.49%)</p> <p>3</p> | <p>2 / 88 (2.27%)</p> <p>3</p> | |
| <p>Eye disorders</p> <p>BLEPHARITIS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 86 (0.00%)</p> <p>0</p> | <p>2 / 88 (2.27%)</p> <p>3</p> | |
| <p>Gastrointestinal disorders</p> <p>ABDOMINAL DISTENSION</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>ABDOMINAL PAIN</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>ABDOMINAL PAIN UPPER</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>COLITIS</p> | <p>2 / 86 (2.33%)</p> <p>2</p> <p>2 / 86 (2.33%)</p> <p>9</p> <p>4 / 86 (4.65%)</p> <p>7</p> | <p>0 / 88 (0.00%)</p> <p>0</p> <p>3 / 88 (3.41%)</p> <p>4</p> <p>1 / 88 (1.14%)</p> <p>3</p> | |

| | | | |
|--|----------------|------------------|--|
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 4 | 3 | |
| CONSTIPATION | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 5 / 88 (5.68%) | |
| occurrences (all) | 2 | 5 | |
| DENTAL CARIES | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 88 (1.14%) | |
| occurrences (all) | 2 | 1 | |
| DIARRHOEA | | | |
| subjects affected / exposed | 7 / 86 (8.14%) | 10 / 88 (11.36%) | |
| occurrences (all) | 16 | 11 | |
| DYSPEPSIA | | | |
| subjects affected / exposed | 5 / 86 (5.81%) | 2 / 88 (2.27%) | |
| occurrences (all) | 12 | 2 | |
| FLATULENCE | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 0 / 88 (0.00%) | |
| occurrences (all) | 7 | 0 | |
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 5 / 86 (5.81%) | 5 / 88 (5.68%) | |
| occurrences (all) | 5 | 7 | |
| NAUSEA | | | |
| subjects affected / exposed | 5 / 86 (5.81%) | 4 / 88 (4.55%) | |
| occurrences (all) | 5 | 5 | |
| TOOTHACHE | | | |
| subjects affected / exposed | 4 / 86 (4.65%) | 10 / 88 (11.36%) | |
| occurrences (all) | 4 | 12 | |
| VOMITING | | | |
| subjects affected / exposed | 6 / 86 (6.98%) | 4 / 88 (4.55%) | |
| occurrences (all) | 6 | 4 | |
| Skin and subcutaneous tissue disorders | | | |
| ACNE | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 3 / 88 (3.41%) | |
| occurrences (all) | 0 | 3 | |
| ACTINIC KERATOSIS | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 3 / 86 (3.49%) | 1 / 88 (1.14%) | |
| occurrences (all) | 5 | 1 | |
| ALOPECIA | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 0 / 88 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| DERMAL CYST | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 1 | 2 | |
| DERMATITIS | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 2 | 2 | |
| DERMATITIS CONTACT | | | |
| subjects affected / exposed | 5 / 86 (5.81%) | 2 / 88 (2.27%) | |
| occurrences (all) | 7 | 2 | |
| ECZEMA | | | |
| subjects affected / exposed | 5 / 86 (5.81%) | 3 / 88 (3.41%) | |
| occurrences (all) | 5 | 3 | |
| PRURITUS | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 2 / 88 (2.27%) | |
| occurrences (all) | 3 | 2 | |
| PSORIASIS | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 6 / 88 (6.82%) | |
| occurrences (all) | 3 | 8 | |
| URTICARIA PAPULAR | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Renal and urinary disorders | | | |
| GLYCOSURIA | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 88 (2.27%) | |
| occurrences (all) | 0 | 3 | |
| HAEMATURIA | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 3 / 88 (3.41%) | |
| occurrences (all) | 2 | 4 | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|--------------------------------|------------------|----------------|--|
| ARTHRALGIA | | | |
| subjects affected / exposed | 11 / 86 (12.79%) | 7 / 88 (7.95%) | |
| occurrences (all) | 15 | 10 | |
| BACK PAIN | | | |
| subjects affected / exposed | 6 / 86 (6.98%) | 4 / 88 (4.55%) | |
| occurrences (all) | 19 | 6 | |
| BURSITIS | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 1 / 88 (1.14%) | |
| occurrences (all) | 3 | 1 | |
| INTERVERTEBRAL DISC PROTRUSION | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 88 (2.27%) | |
| occurrences (all) | 0 | 2 | |
| MYALGIA | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 3 / 88 (3.41%) | |
| occurrences (all) | 2 | 3 | |
| NECK PAIN | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 3 / 88 (3.41%) | |
| occurrences (all) | 1 | 3 | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 6 / 86 (6.98%) | 5 / 88 (5.68%) | |
| occurrences (all) | 7 | 5 | |
| PSORIATIC ARTHROPATHY | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 2 / 88 (2.27%) | |
| occurrences (all) | 3 | 2 | |
| SPINAL PAIN | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 0 / 88 (0.00%) | |
| occurrences (all) | 11 | 0 | |
| TENDONITIS | | | |

| | | | |
|--|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 3 / 86 (3.49%) 3 | 2 / 88 (2.27%) 2 | |
| Infections and infestations | | | |
| ABSCCESS ORAL | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| ACARODERMATITIS | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| BRONCHITIS | | | |
| subjects affected / exposed | 4 / 86 (4.65%) | 5 / 88 (5.68%) | |
| occurrences (all) | 5 | 5 | |
| CELLULITIS | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| CONJUNCTIVITIS | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 2 | 3 | |
| CYSTITIS | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 1 | 2 | |
| EAR INFECTION | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 88 (1.14%) | |
| occurrences (all) | 2 | 1 | |
| FOLLICULITIS | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 2 / 88 (2.27%) | |
| occurrences (all) | 2 | 3 | |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 4 / 86 (4.65%) | 5 / 88 (5.68%) | |
| occurrences (all) | 4 | 5 | |
| GASTROENTERITIS VIRAL | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 88 (2.27%) | |
| occurrences (all) | 0 | 2 | |
| INFLUENZA | | | |
| subjects affected / exposed | 6 / 86 (6.98%) | 4 / 88 (4.55%) | |
| occurrences (all) | 6 | 5 | |

| | | | |
|-----------------------------|------------------|------------------|--|
| LABYRINTHITIS | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 3 / 88 (3.41%) | |
| occurrences (all) | 1 | 3 | |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 17 / 86 (19.77%) | 21 / 88 (23.86%) | |
| occurrences (all) | 32 | 37 | |
| ORAL CANDIDIASIS | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 88 (1.14%) | |
| occurrences (all) | 8 | 1 | |
| ORAL HERPES | | | |
| subjects affected / exposed | 5 / 86 (5.81%) | 0 / 88 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| OTITIS MEDIA | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 88 (1.14%) | |
| occurrences (all) | 2 | 2 | |
| OTITIS MEDIA BACTERIAL | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 88 (2.27%) | |
| occurrences (all) | 0 | 3 | |
| PERIODONTITIS | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 88 (1.14%) | |
| occurrences (all) | 2 | 2 | |
| PHARYNGITIS | | | |
| subjects affected / exposed | 4 / 86 (4.65%) | 3 / 88 (3.41%) | |
| occurrences (all) | 9 | 3 | |
| PNEUMONIA | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 0 / 88 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| RHINITIS | | | |
| subjects affected / exposed | 5 / 86 (5.81%) | 7 / 88 (7.95%) | |
| occurrences (all) | 5 | 9 | |
| SINUSITIS | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 7 / 88 (7.95%) | |
| occurrences (all) | 4 | 8 | |
| SKIN BACTERIAL INFECTION | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 1 | 2 | |

| | | | |
|---|------------------|------------------|--|
| STAPHYLOCOCCAL INFECTION | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| TINEA PEDIS | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 0 / 88 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| TONGUE FUNGAL INFECTION | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| TONSILLITIS | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 5 / 88 (5.68%) | |
| occurrences (all) | 2 | 5 | |
| TOOTH ABSCESS | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 2 / 88 (2.27%) | |
| occurrences (all) | 2 | 2 | |
| TOOTH INFECTION | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 3 / 88 (3.41%) | |
| occurrences (all) | 2 | 3 | |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 16 / 86 (18.60%) | 16 / 88 (18.18%) | |
| occurrences (all) | 30 | 22 | |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 4 / 86 (4.65%) | 5 / 88 (5.68%) | |
| occurrences (all) | 4 | 9 | |
| VIRAL UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 6 / 88 (6.82%) | |
| occurrences (all) | 4 | 8 | |
| VULVOVAGINAL CANDIDIASIS | | | |
| subjects affected / exposed | 5 / 86 (5.81%) | 2 / 88 (2.27%) | |
| occurrences (all) | 7 | 3 | |
| Metabolism and nutrition disorders | | | |
| DIABETES MELLITUS | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 3 / 88 (3.41%) | |
| occurrences (all) | 2 | 3 | |
| HYPERCHOLESTEROLAEMIA | | | |

| | | | |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 2 / 86 (2.33%) | 5 / 88 (5.68%) | |
| occurrences (all) | 2 | 5 | |
| HYPERTRIGLYCERIDAEMIA | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 88 (2.27%) | |
| occurrences (all) | 1 | 2 | |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 88 (2.27%) | |
| occurrences (all) | 0 | 2 | |
| HYPOSIDERAEMIA | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 88 (1.14%) | |
| occurrences (all) | 2 | 2 | |
| TYPE 2 DIABETES MELLITUS | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 88 (0.00%) | |
| occurrences (all) | 2 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 27 March 2012 | The opportunity for the patient to enter an extension study instead of a non-treatment follow-up period upon completion of the core study treatment period was described For permitted concomitant medications, the requirement of a stable dose for at least four weeks before Randomization was removed Urine pregnancy testing was clarified as not required for post-menopausal women Procedures at Screening for misrandomized patients were specified Corrections and clarifications were made to the study protocol, including inclusion of immunogenicity and PK sample analysis method and procedures, blinding |
| 20 March 2013 | Provided continued treatment for another 156 weeks or until the drug is available in the country of participation for eligible patients who were on active therapy during the Maintenance period Allowed for rescreening of patients, and specified rescreening procedures Specified that at Week 52 the sites will become aware which patients received placebo during the Maintenance period. After the Week 52 data base lock, the study will be open label Introduced home administration of study treatment for certain visits of the extension treatment period Clarified that abnormalities in vital signs or laboratory evaluations did not require protocol specified actions, but actions to be determined by the Investigator Provided instructions to report defects, malfunctions or product complaints of the prefilled syringe |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Efficacy results after Wk 172 can't be interpreted meaningfully due to low # of evaluable patients. As per protocol, availability of AIN457 in participating countries led to discontinuation of most patients before they reached the later visits.

Notes: