



Clinical trial results:

A multicenter extension trial of subcutaneously administered AIN457 in patients with moderate to severe chronic plaque-type psoriasis

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use <https://www.novctrd.com/CtrdWeb/home.novfor> complete trial results.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2009-017234-51 |
| Trial protocol | DE FR IS NO |
| Global end of trial date | 18 October 2016 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 06 July 2018 |
| First version publication date | 06 July 2018 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | CAIN457A2211E1 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01132612 |
| 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 | 18 October 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 October 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of subcutaneously administered secukinumab in the treatment of moderate to severe chronic plaque-type psoriasis as assessed by vital signs, clinical laboratory variables, and adverse events (AEs) monitoring.

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 | 11 May 2010 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | France: 22 |
| Country: Number of subjects enrolled | Germany: 74 |
| Country: Number of subjects enrolled | Iceland: 16 |
| Country: Number of subjects enrolled | Israel: 8 |
| Country: Number of subjects enrolled | Japan: 37 |
| Country: Number of subjects enrolled | Norway: 7 |
| Country: Number of subjects enrolled | United States: 111 |
| Worldwide total number of subjects | 275 |
| EEA total number of subjects | 119 |

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 | 0 |

| | |
|---------------------------|-----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 262 |
| From 65 to 84 years | 13 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants continued their regimens as assigned in CAIN457A2211 (NCT00941031) and were enrolled into one of the following: fixed time interval regimen (FI), treatment at start of relapse regimen (SR) or open-label (OL). There were no more placebo treated patients at the end of the core. Therefore, there is no placebo arm in the extension.

Period 1

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

Arms

| | |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Fixed-time interval regimen |

Arm description:

Secukinumab 150 mg subcutaneous (sc) administered at Week 1 (baseline) of the extension study and every 12 weeks thereafter

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

Dosage and administration details:

Secukinumab 150 mg subcutaneous (sc) administered at Week 1 (baseline) of the extension study and every 12 weeks thereafter

| | |
|------------------|---------------------------------------|
| Arm title | Treatment at start of relapse regimen |
|------------------|---------------------------------------|

Arm description:

Placebo administered at Week 1 (baseline) of the extension study and every 12 weeks thereafter. If relapse, then switch to secukinumab 150 mg sc administered every 4 weeks

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

Dosage and administration details:

Placebo administered at Week 1 (baseline) of the extension study and every 12 weeks thereafter. If relapse, then switch to secukinumab 150 mg sc administered every 4 weeks

| | |
|--|------------------------|
| Investigational medicinal product name | Secukinumab |
| Investigational medicinal product code | AIN457A |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo administered at Week 1 (baseline) of the extension study and every 12 weeks thereafter. If

relapse, then switch to secukinumab 150 mg sc administered every 4 weeks

| | |
|--|------------------------|
| Arm title | Open-label |
| Arm description: Secukinumab 150 mg sc administered every 4 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Secukinumab |
| Investigational medicinal product code | Ain457 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: Secukinumab 150 mg sc administered every 4 weeks | |

| Number of subjects in period 1 | Fixed-time interval regimen | Treatment at start of relapse regimen | Open-label |
|---------------------------------------|-----------------------------|---------------------------------------|------------|
| Started | 46 | 42 | 187 |
| Completed | 6 | 7 | 17 |
| Not completed | 40 | 35 | 170 |
| Adverse event, serious fatal | - | - | 1 |
| Consent withdrawn by subject | 5 | 8 | 19 |
| Adverse event, non-fatal | 5 | 2 | 15 |
| Protocol deviation | - | - | 3 |
| Administrative problems | 5 | 1 | 52 |
| Lost to follow-up | 2 | 2 | 7 |
| Lack of efficacy | 23 | 22 | 73 |

Baseline characteristics

Reporting groups

| | |
|---|---------------------------------------|
| Reporting group title | Fixed-time interval regimen |
| Reporting group description: Secukinumab 150 mg subcutaneous (sc) administered at Week 1 (baseline) of the extension study and every 12 weeks thereafter | |
| Reporting group title | Treatment at start of relapse regimen |
| Reporting group description: Placebo administered at Week 1 (baseline) of the extension study and every 12 weeks thereafter. If relapse, then switch to secukinumab 150 mg sc administered every 4 weeks | |
| Reporting group title | Open-label |
| Reporting group description: Secukinumab 150 mg sc administered every 4 weeks. | |

| Reporting group values | Fixed-time interval regimen | Treatment at start of relapse regimen | Open-label |
|--|-----------------------------|---------------------------------------|------------|
| Number of subjects | 46 | 42 | 187 |
| 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) | 44 | 42 | 176 |
| From 65-84 years | 2 | 0 | 11 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 43.0 | 39.9 | 45.0 |
| standard deviation | ± 13.71 | ± 12.12 | ± 11.78 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 15 | 12 | 39 |
| Male | 31 | 30 | 148 |

| Reporting group values | Total | | |
|--|-------|--|--|
| Number of subjects | 275 | | |
| 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) | 262 | | |
| From 65-84 years | 13 | | |
| 85 years and over | 0 | | |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender, Male/Female | | | |
| Units: Subjects | | | |
| Female | 66 | | |
| Male | 209 | | |

End points

End points reporting groups

| | |
|---|---------------------------------------|
| Reporting group title | Fixed-time interval regimen |
| Reporting group description: Secukinumab 150 mg subcutaneous (sc) administered at Week 1 (baseline) of the extension study and every 12 weeks thereafter | |
| Reporting group title | Treatment at start of relapse regimen |
| Reporting group description: Placebo administered at Week 1 (baseline) of the extension study and every 12 weeks thereafter. If relapse, then switch to secukinumab 150 mg sc administered every 4 weeks | |
| Reporting group title | Open-label |
| Reporting group description: Secukinumab 150 mg sc administered every 4 weeks. | |

Primary: Number of participants with Adverse Events, Serious Adverse Events and Deaths

| | |
|--|--|
| End point title | Number of participants with Adverse Events, Serious Adverse Events and Deaths ^[1] |
| End point description: Safety was assessed by frequency of adverse events including serious adverse events. | |
| End point type | Primary |
| End point timeframe: up to week 351 | |

Notes:

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

Justification: Statistical analysis does not apply to this end point.

| End point values | Fixed-time interval regimen | Treatment at start of relapse regimen | Open-label | |
|-----------------------------|-----------------------------|---------------------------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 46 | 42 | 187 | |
| Units: Participants | | | | |
| Adverse events | 44 | 41 | 180 | |
| Serious adverse events | 9 | 4 | 43 | |
| Deaths | 0 | 0 | 1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least 50%, 75% or 90% improvement from baseline in Psoriasis Area and Severity Index (PASI) and IGA mod 2009 0 or 1 response

| | |
|-----------------|---|
| End point title | Number of participants with at least 50%, 75% or 90% improvement from baseline in Psoriasis Area and Severity Index (PASI) and IGA mod 2009 0 or 1 response |
|-----------------|---|

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). The IGA 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, 4 = severe and 5 = very severe.

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

End point timeframe:

Extension weeks: 1, 25, 73 and 301 (too few data points were available to perform analysis at week 301)

| End point values | Fixed-time interval regimen | Treatment at start of relapse regimen | Open-label | |
|---|-----------------------------|---------------------------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 46 | 42 | 187 | |
| Units: Number of participants | | | | |
| Extension week 1, PASI 50 (n=46,40,174) | 43 | 34 | 163 | |
| Extension week 1, PASI 75 (n=46,40,174) | 31 | 16 | 102 | |
| Extension week 1, PASI 90 (n=46,40,174) | 17 | 3 | 61 | |
| Ext. week 1, IGA mod 2009 0 or 1 (n=44,38,168) | 24 | 7 | 70 | |
| Extension week 25, PASI 50 (n=35,33,159) | 29 | 27 | 142 | |
| Extension week 25, PASI 75 (n=35,33,159) | 19 | 10 | 91 | |
| Extension week 25, PASI 90 (n=35,33,159) | 12 | 2 | 42 | |
| Ext. week 25, IGA mod 2009 0 or 1 (n=35,33,159) | 15 | 4 | 48 | |
| Extension week 73, PASI 50 (n=19,19,114) | 18 | 17 | 100 | |
| Extension week 73, PASI 75 (n=19,19,114) | 14 | 8 | 66 | |
| Extension week 73, PASI 90 (n=19,19,114) | 8 | 1 | 31 | |
| Ext. week 73, IGA mod 2009 0 or 1 (n=19,19,114) | 9 | 4 | 35 | |
| Extension week 301, PASI 50 (n=0,0,3) | 9999 | 9999 | 3 | |
| Extension week 301, PASI 75 (n=0,0,3) | 9999 | 9999 | 2 | |
| Extension week 301, PASI 90 (n=0,0,3) | 9999 | 9999 | 1 | |
| Extension week 301, IGA mod 2009 0 or 1 (n=0,0,3) | 9999 | 9999 | 1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Long-term immunogenicity assessed by the number of participants developing anti secukinumab antibodies during the trial

| | |
|-----------------|---|
| End point title | Long-term immunogenicity assessed by the number of participants developing anti secukinumab antibodies during the trial |
|-----------------|---|

End point description:

Describes the number of participants tested positive for anti-secukinumab antibodies. It refers to the number of participants who had no positive values at baseline but developed them only after start of secukinumab treatment.

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

End point timeframe:

up to week 351

| End point values | Fixed-time interval regimen | Treatment at start of relapse regimen | Open-label | |
|-----------------------------|-----------------------------|---------------------------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 46 | 41 | 184 | |
| Units: Participants | 0 | 0 | 1 | |

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 | AIN457A Fixed interval |
|-----------------------|------------------------|

Reporting group description:

AIN457A Fixed interval

| | |
|-----------------------|--------------------|
| Reporting group title | AIN457A open label |
|-----------------------|--------------------|

Reporting group description:

AIN457A open label

| | |
|-----------------------|--------------------------|
| Reporting group title | AIN457A Start of relapse |
|-----------------------|--------------------------|

Reporting group description:

AIN457A Start of relapse

| Serious adverse events | AIN457A Fixed interval | AIN457A open label | AIN457A Start of relapse |
|---|------------------------|--------------------|--------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 46 (19.57%) | 43 / 187 (22.99%) | 4 / 42 (9.52%) |
| number of deaths (all causes) | 0 | 1 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 2 / 187 (1.07%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon adenoma | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|----------------|-----------------|----------------|
| Colon cancer | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant melanoma | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 187 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleomorphic adenoma | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Superficial spreading melanoma stage unspecified | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 1 / 42 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 2 / 187 (1.07%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Fibrin D dimer increased | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Streptococcus test positive | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Laceration | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|----------------|
| Meniscus injury | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle injury | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendon injury | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 187 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 46 (0.00%) | 2 / 187 (1.07%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 0 / 187 (0.00%) | 1 / 42 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial paralysis | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 187 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 187 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic encephalopathy | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 187 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 1 / 42 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|----------------|
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intussusception | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 187 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 2 / 187 (1.07%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder stenosis | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| End stage renal disease | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 187 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 187 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 187 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tenosynovitis | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |

| | | | |
|---|----------------|-----------------|----------------|
| Abscess bacterial | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 187 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 4 / 187 (2.14%) | 1 / 42 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 4 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 0 / 187 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infected dermal cyst | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nail infection | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteomyelitis chronic | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paronychia | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal abscess | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Streptococcal infection | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 1 / 187 (0.53%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | AIN457A Fixed interval | AIN457A open label | AIN457A Start of relapse |
|---|------------------------|--------------------|--------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 42 / 46 (91.30%) | 164 / 187 (87.70%) | 35 / 42 (83.33%) |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 12 / 187 (6.42%) | 0 / 42 (0.00%) |
| occurrences (all) | 1 | 19 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 3 / 46 (6.52%) | 6 / 187 (3.21%) | 0 / 42 (0.00%) |
| occurrences (all) | 3 | 6 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | 10 / 187 (5.35%) | 2 / 42 (4.76%) |
| occurrences (all) | 2 | 16 | 3 |
| Ligament sprain | | | |

| | | | |
|--|------------------------|-------------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 1 / 46 (2.17%) 1 | 10 / 187 (5.35%) 12 | 2 / 42 (4.76%) 2 |
| Procedural pain subjects affected / exposed occurrences (all) | 4 / 46 (8.70%) 4 | 6 / 187 (3.21%) 6 | 0 / 42 (0.00%) 0 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 4 / 46 (8.70%) 5 | 26 / 187 (13.90%) 33 | 6 / 42 (14.29%) 10 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 3 / 46 (6.52%) 3 | 4 / 187 (2.14%) 4 | 0 / 42 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 11 / 46 (23.91%) 16 | 29 / 187 (15.51%) 66 | 6 / 42 (14.29%) 6 |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 2 / 46 (4.35%) 2 | 12 / 187 (6.42%) 16 | 3 / 42 (7.14%) 6 |
| Influenza like illness subjects affected / exposed occurrences (all) | 1 / 46 (2.17%) 2 | 12 / 187 (6.42%) 28 | 2 / 42 (4.76%) 5 |
| Pyrexia subjects affected / exposed occurrences (all) | 1 / 46 (2.17%) 3 | 9 / 187 (4.81%) 12 | 4 / 42 (9.52%) 4 |
| Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) | 2 / 46 (4.35%) 4 | 11 / 187 (5.88%) 15 | 0 / 42 (0.00%) 0 |
| Dental caries subjects affected / exposed occurrences (all) | 3 / 46 (6.52%) 3 | 6 / 187 (3.21%) 8 | 1 / 42 (2.38%) 1 |
| Diarrhoea subjects affected / exposed occurrences (all) | 2 / 46 (4.35%) 3 | 20 / 187 (10.70%) 26 | 2 / 42 (4.76%) 2 |

| | | | |
|---|------------------------|--------------------------|------------------------|
| Nausea subjects affected / exposed occurrences (all) | 3 / 46 (6.52%) 4 | 12 / 187 (6.42%) 12 | 3 / 42 (7.14%) 3 |
| Toothache subjects affected / exposed occurrences (all) | 4 / 46 (8.70%) 4 | 14 / 187 (7.49%) 19 | 1 / 42 (2.38%) 1 |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 46 (2.17%) 1 | 13 / 187 (6.95%) 17 | 3 / 42 (7.14%) 4 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 2 / 46 (4.35%) 2 | 20 / 187 (10.70%) 26 | 4 / 42 (9.52%) 6 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 5 / 46 (10.87%) 7 | 14 / 187 (7.49%) 26 | 3 / 42 (7.14%) 4 |
| Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all) | 4 / 46 (8.70%) 6 | 6 / 187 (3.21%) 9 | 0 / 42 (0.00%) 0 |
| Psoriasis subjects affected / exposed occurrences (all) | 13 / 46 (28.26%) 32 | 59 / 187 (31.55%) 145 | 16 / 42 (38.10%) 41 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 46 (0.00%) 0 | 11 / 187 (5.88%) 13 | 0 / 42 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 9 / 46 (19.57%) 14 | 43 / 187 (22.99%) 66 | 6 / 42 (14.29%) 8 |
| Arthritis subjects affected / exposed occurrences (all) | 3 / 46 (6.52%) 6 | 6 / 187 (3.21%) 6 | 1 / 42 (2.38%) 1 |
| Back pain | | | |

| | | | |
|-----------------------------|------------------|-------------------|------------------|
| subjects affected / exposed | 5 / 46 (10.87%) | 30 / 187 (16.04%) | 7 / 42 (16.67%) |
| occurrences (all) | 6 | 52 | 8 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 5 / 46 (10.87%) | 15 / 187 (8.02%) | 0 / 42 (0.00%) |
| occurrences (all) | 7 | 20 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | 8 / 187 (4.28%) | 3 / 42 (7.14%) |
| occurrences (all) | 4 | 8 | 4 |
| Neck pain | | | |
| subjects affected / exposed | 3 / 46 (6.52%) | 6 / 187 (3.21%) | 1 / 42 (2.38%) |
| occurrences (all) | 4 | 8 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 4 / 46 (8.70%) | 11 / 187 (5.88%) | 1 / 42 (2.38%) |
| occurrences (all) | 8 | 12 | 1 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | 21 / 187 (11.23%) | 1 / 42 (2.38%) |
| occurrences (all) | 3 | 30 | 1 |
| Conjunctivitis | | | |
| subjects affected / exposed | 4 / 46 (8.70%) | 4 / 187 (2.14%) | 0 / 42 (0.00%) |
| occurrences (all) | 5 | 10 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 9 / 187 (4.81%) | 4 / 42 (9.52%) |
| occurrences (all) | 1 | 9 | 4 |
| Influenza | | | |
| subjects affected / exposed | 4 / 46 (8.70%) | 14 / 187 (7.49%) | 2 / 42 (4.76%) |
| occurrences (all) | 5 | 17 | 2 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 20 / 46 (43.48%) | 91 / 187 (48.66%) | 16 / 42 (38.10%) |
| occurrences (all) | 58 | 260 | 30 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 10 / 187 (5.35%) | 1 / 42 (2.38%) |
| occurrences (all) | 2 | 13 | 1 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 3 / 46 (6.52%) | 4 / 187 (2.14%) | 2 / 42 (4.76%) |
| occurrences (all) | 4 | 4 | 2 |

| | | | |
|------------------------------------|-----------------|-------------------|----------------|
| Sinusitis | | | |
| subjects affected / exposed | 9 / 46 (19.57%) | 17 / 187 (9.09%) | 3 / 42 (7.14%) |
| occurrences (all) | 11 | 21 | 5 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 14 / 187 (7.49%) | 0 / 42 (0.00%) |
| occurrences (all) | 1 | 18 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 46 (6.52%) | 28 / 187 (14.97%) | 4 / 42 (9.52%) |
| occurrences (all) | 4 | 60 | 5 |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 46 (6.52%) | 6 / 187 (3.21%) | 4 / 42 (9.52%) |
| occurrences (all) | 3 | 9 | 6 |
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | 14 / 187 (7.49%) | 3 / 42 (7.14%) |
| occurrences (all) | 3 | 20 | 3 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 46 (0.00%) | 10 / 187 (5.35%) | 1 / 42 (2.38%) |
| occurrences (all) | 0 | 12 | 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 26 April 2010 | The purpose of the amendment was to correct an inconsistency in the study protocol title in the protocol synopsis section embedded in the study protocol. The PK collection number at Visit F12 was rectified for coherence. The global model patient information / informed consent was also revised to correct the inconsistency in the study protocol title. The changes described in this amended protocol, which occurred prior to study unblinding, were non-substantial and did not require IRB/IEC approval prior to implementation. |
| 09 May 2011 | The purpose of the amendment was to update the benefit-risk assessment for the treatment of plaque-type psoriasis with secukinumab after data from phase II study had become available. This assessment confirmed that this therapy was regarded as beneficial for the treated patients and therefore it was decided that the patients in study CAIN457A2211E1 should be offered the opportunity to continue receiving secukinumab for a longer period (prolongation of 3 years) than originally planned and in selected countries where the operational feasibility and practicality does exist. In addition, prolonging the treatment period allowed for gathering long-term efficacy and safety data. Additionally an interim analysis was introduced to support the submission of secukinumab for the treatment of moderate to severe chronic plaque-type psoriasis. |
| 27 June 2014 | The main purpose of this amendment was to provide continued treatment for patients in the trial for additional two years or until drug was commercially available in the market in the country of participation. This extension of the study allowed for safety, tolerability and efficacy data to be collected from the participating patients for a longer time period. Eligible patients were considered for participation in this extension of the study prolongation at given site, provided the amendment was approved at the time the patient completed the prolongation of CAIN457A22E1 (i.e. visit of Week 225). This amendment offered further extension of the study to all patients that have completed the Week 225 visit. The patients who continued, remained on the same treatment regimen they were taking in the extension prolongation part. The patients who did not continue beyond the Week 225 were moved to the non-treatment follow-up period. At the time of this amendment about 65 patients were on the trial. No patient was treated in the placebo arm. |

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.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use <https://www.novctrd.com/CtrdWeb/home.novfor> for complete trial results.

Notes:

