Clinical trial results:
A randomized, double-blind, placebo-controlled study of efficacy, safety and tolerability of secukinumab at 12 weeks administered with an i.v. or s.c. loading regimen compared to placebo in patients with active rheumatoid arthritis despite treatment with methotrexate

Summary

EudraCT number	2010-024516-34
Trial protocol	HU BG IT SK
Global end of trial date	30 December 2013

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	12 August 2015

Trial information

Trial identification

Sponsor protocol code	CAIN457F2206

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01359943
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Study Director, Novartis Pharma AG, 41 613241111,
Scientific contact	Study Director, 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	30 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 December 2013
Global end of trial reached?	Yes
Global end of trial date	30 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate at Week 12 the superior efficacy of secukinumab administered during induction with an i.v. loading regimen or a s.c. loading dose regimen compared to placebo in patients with active RA despite treatment with MTX using the ACR20 criteria.
For the primary analysis, the secukinumab regimens were pooled together

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	12 October 2011
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	Bulgaria: 50
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Hungary: 14
Country: Number of subjects enrolled	Italy: 27
Country: Number of subjects enrolled	Poland: 66
Country: Number of subjects enrolled	Slovakia: 42
Country: Number of subjects enrolled	United States: 21
Worldwide total number of subjects	221
EEA total number of subjects	199

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)	184
From 65 to 84 years	37
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were randomized to one of the following 3 treatment groups in a 2:2:1 ratio: secukinumab 10 mg/kg i.v., secukinumab 150 mg s.c. or placebo.

Period 1

Period 1 title	Double-blind (weeks 0 - 16)
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	secukinumab 10 mg/kg i.v. loading

Arm description:

secukinumab 10mg/kg i.v. loading at Weeks 0, 2 and 4, and placebo s.c. at weeks 0, 1, 2, 3 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457F
Other name	Secukinumab
Pharmaceutical forms	Injection
Routes of administration	Intracavernous use

Dosage and administration details:

Secukinumab i.v. (10 mg/kg)

Arm title	secukinumab 150 mg s.c.

Arm description:

secukinumab 150mg s.c. loading at Weeks 0, 1, 2, 3 and 4, and placebo i.v. at weeks 0, 2 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AINN457F
Other name	Secukinumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Secukinumab s.c. 150 mg

Arm title	placebo

Arm description:

placebo at Weeks 0, 1, 2, 3, 4, 8 & 12, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 16

Arm type	Placebo

Investigational medicinal product name	placebo
Investigational medicinal product code	AIN457F
Other name	placebo for i.v. infusion
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL 0.9% NaCl solution)

Number of subjects in period 1	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo
Started	88	89	44
Completed	86	85	44
Not completed	2	4	0
Consent withdrawn by subject	-	2	-
Adverse event, non-fatal	1	2	-
Abnormal laboratory values	1	-	-

Period 2

Period 2 title	Open label 150 mg s.c. (weeks 16 - 52)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	secukinumab 10 mg/kg i.v. loading

Arm description:

secukinumab 10mg/kg i.v. loading at Weeks 0, 2 and 4, and placebo s.c. at weeks 0, 1, 2, 3 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457F
Other name	Secukinumab
Pharmaceutical forms	Injection
Routes of administration	Intracavernous use

Dosage and administration details:

i.v. (10 mg/kg)

Arm title	secukinumab 150 mg s.c. loading

Arm description:

secukinumab 150mg s.c. loading at Weeks 0, 1, 2, 3 and 4, and placebo i.v. at weeks 0, 2 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8

Arm type	Experimental

Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457F
Other name	Secukinumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

s.c. 150 mg

Arm title	placebo

Arm description:

placebo at Weeks 0, 1, 2, 3, 4, 8 & 12, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 16

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	AIn457F
Other name	Secukinumab placebo
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL 0.9% NaCl solution

Number of subjects in period 2	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c. loading	placebo
Started	86	84	44
Completed	78	71	36
Not completed	8	13	8
Consent withdrawn by subject	1	3	4
Adverse event, non-fatal	3	5	1
Protocol deviation	-	1	-
Administrative problems	1	-	-
Abnormal laboratory values	-	1	-
Lack of efficacy	3	3	3

Period 3

Period 3 title	Follow-up (weeks 52 - 60) off treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No

Arm title	secukinumab 10 mg/kg i.v. loading

Arm description:

secukinumab 10mg/kg i.v. loading at Weeks 0, 2 and 4, and placebo s.c. at weeks 0, 1, 2, 3 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8

Arm type	Experimental
Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457F
Other name	
Pharmaceutical forms	Emulsion for injection/infusion
Routes of administration	Intracavernous use

Dosage and administration details:

10 mg/kg i.v.

Arm title	secukinumab 150 mg s.c. loading

Arm description:

secukinumab 150mg s.c. loading at Weeks 0, 1, 2, 3 and 4, and placebo i.v. at weeks 0, 2 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457F
Other name	Secukinumab
Pharmaceutical forms	Suspension and solvent for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

150 mg s.c

Arm title	placebo

Arm description:

placebo at Weeks 0, 1, 2, 3, 4, 8 & 12, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 16

Arm type	Placebo
Investigational medicinal product name	Secukinumab placebo
Investigational medicinal product code	AIN457F
Other name	Secukinumab placebo
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Intramuscular and intravenous use

Dosage and administration details:

100 mL 0.9% NaCl solution

Number of subjects in period 3	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c. loading	placebo
Started	78	71	36
Completed	78	69	36
Not completed	0	2	0
Consent withdrawn by subject	-	2	-

Baseline characteristics

Reporting groups	
Reporting group title	secukinumab 10 mg/kg i.v. loading
Reporting group description:	
secukinumab 10mg/kg i.v. loading at Weeks 0, 2 and 4, and placebo s.c. at weeks 0, 1, 2, 3 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8	
Reporting group title	secukinumab 150 mg s.c.
Reporting group description:	
secukinumab 150mg s.c. loading at Weeks 0, 1, 2, 3 and 4, and placebo i.v. at weeks 0, 2 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8	
Reporting group title	placebo
Reporting group description:	
placebo at Weeks 0, 1, 2, 3, 4, 8 & 12, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 16	

Reporting group values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo
Number of subjects	88	89	44
Age categorical Units: Subjects			
Adults (≥18-<65 years)	73	71	40
From ≥65-<75 years	13	17	4
≥75 years	2	1	0
Age Continuous | Units: Years			
arithmetic mean	53.8	54.5	53.5
standard deviation	± 11.81	± 12.26	± 9.33
Gender, Male/Female Units: Participants			
Female	67	72	37
Male	21	17	7

Reporting group values	Total		
Number of subjects	221		
Age categorical Units: Subjects			
Adults (≥18-<65 years)	184		
From ≥65-<75 years	34		
≥75 years	3		
Age Continuous | Units: Years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female Units: Participants			
Female	176		
Male	45		

End points

End points reporting groups

Reporting group title	secukinumab 10 mg/kg i.v. loading
Reporting group description:	
secukinumab 10mg/kg i.v. loading at Weeks 0, 2 and 4, and placebo s.c. at weeks 0, 1, 2, 3 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8	
Reporting group title	secukinumab 150 mg s.c.
Reporting group description:	
secukinumab 150mg s.c. loading at Weeks 0, 1, 2, 3 and 4, and placebo i.v. at weeks 0, 2 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8	
Reporting group title	placebo
Reporting group description:	
placebo at Weeks 0, 1, 2, 3, 4, 8 & 12, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 16	
Reporting group title	secukinumab 10 mg/kg i.v. loading
Reporting group description:	
secukinumab 10mg/kg i.v. loading at Weeks 0, 2 and 4, and placebo s.c. at weeks 0, 1, 2, 3 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8	
Reporting group title	secukinumab 150 mg s.c. loading
Reporting group description:	
secukinumab 150mg s.c. loading at Weeks 0, 1, 2, 3 and 4, and placebo i.v. at weeks 0, 2 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8	
Reporting group title	placebo
Reporting group description:	
placebo at Weeks 0, 1, 2, 3, 4, 8 & 12, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 16	
Reporting group title	secukinumab 10 mg/kg i.v. loading
Reporting group description:	
secukinumab 10mg/kg i.v. loading at Weeks 0, 2 and 4, and placebo s.c. at weeks 0, 1, 2, 3 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8	
Reporting group title	secukinumab 150 mg s.c. loading
Reporting group description:	
secukinumab 150mg s.c. loading at Weeks 0, 1, 2, 3 and 4, and placebo i.v. at weeks 0, 2 and 4, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 8	
Reporting group title	placebo
Reporting group description:	
placebo at Weeks 0, 1, 2, 3, 4, 8 & 12, followed by secukinumab 150mg s.c. every 4 weeks starting at Week 16	

Primary: Percentage of participants who achieve American College of Rheumatology Response of 20 (ACR20)

End point title	Percentage of participants who achieve American College of Rheumatology Response of 20 (ACR20)
End point description:	
A participant was considered to be a responder according to the ACR20 criteria if the participant had at least 20% improvement in both the tender joint count and swollen joint count measures, and in at least 3 of the following 5 measures: patient's assessment of pain, patient's global assessment of disease activity, physician's global assessment of disease activity, Health Assessment Questionnaire (HAQ©) score, and/or C-reactive protein (CRP)/Erythrocyte Sedimentation Rate (ESR).	
End point type	Primary
End point timeframe:	
12 weeks	

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	89	44	
Units: Percentage of participants				
number (not applicable)	53.4	44.9	40.9	

Statistical analyses

Statistical analysis title	To demonstrate secukinimab superiority at Week 12

Statistical analysis description:

primary objective was to demonstrate at Week 12 the superior efficacy ofsecukinumab administered during induction with an i.v. loading regimen or a s.c. loading dose regimencompared to placebo in patients with active RA despite treatment with MTX using the ACR20 criteria.For the primary analysis, the secukinumab regimens were pooled together.

Comparison groups	secukinumab 10 mg/kg i.v. loading v secukinumab 150 mg s.c. v placebo
Number of subjects included in analysis	221
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3559
Method	Regression, Logistic

Secondary: Percentage of participants who achieve ACR50 and ACR70

End point title	Percentage of participants who achieve ACR50 and ACR70

End point description:

A participant was considered to be a responder according to the ACR50 or ACR70 criteria if the participant had at least 50% or 70% improvement, respectively, in both the tender joint count and swollen joint count measures, and in at least 3 of the following 5 measures: patient's assessment of pain, patient's global assessment of disease activity, physician's global assessment of disease activity, Health Assessment Questionnaire (HAQ©) score, and/or C-reactive protein (CRP)/Erythrocyte Sedimentation Rate (ESR).

End point type	Secondary

End point timeframe:

12 weeks

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	89	44	
Units: Percentage of participants				
number (not applicable)				
ACR50	20.5	18	11.4	
ACR70	8	5.6	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Health Assessment Questionnaire-Disease Index (HAQ-DI) score.

End point title	Change from baseline in Health Assessment Questionnaire-Disease Index (HAQ-DI) score.

End point description:

The HAQ measures physical disability and functional status. It has 4 dimensions: disability, pain, drug side effects and dollar costs. In this trial, only the disability dimension was used. The disability dimension consists of 20 multiple choice items concerning difficulty in performing 8 common activities of daily living; dressing and grooming, arising, eating, walking, reaching, personal hygiene, gripping and activities. Participants choose from four response categories: 0 (without any difficulty), 1 (with some difficulty), 2 (with much difficulty) and 3 (unable to do). Within each of the 8 categories, only the item indicating the most severe impairment contributes to the category score. The HAQ score is calculated by summing the computed scores for each category and dividing by the number of categories answered. It ranges from 0 (without any difficulty) to 3 (unable to do). A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline, 12 Weeks

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	89	44	
Units: score on a scale				
least squares mean (standard error)	-0.35 (± 0.052)	-0.28 (± 0.053)	-0.17 (± 0.074)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in DAS28 using high sensitivity C-reactive protein (hsCRP) (DAS28-CRP)

End point title	Change from baseline in DAS28 using high sensitivity C-reactive protein (hsCRP) (DAS28-CRP)

End point description:

The Disease Activity Score (DAS) is a combined index to measure disease activity in RA participants. DAS28-CRP is determined using the following variables: 28-joint counts (tender28 and swollen28), CRP, and the participant's general health (GH) or global disease activity measured on a Visual Analogue Scale (VAS) of 100 mm (0 = and 100 =). Using the data from these variables, DAS28-CRP is calculated using the following formula: DAS28-4(crp) = 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.36*ln(CRP+1) + 0.014*GH + 0.96. The calculation results in a DAS28-CRP score from 0 to 10 indicating the current activity of the rheumatoid arthritis of your patient. A DAS28 above 5.1 means high disease activity whereas a DAS28 below 3.2 indicates low disease activity. Remission is achieved by a DAS28 lower than 2.6. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline, 12 weeks

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	82	43	
Units: score on a scale				
least squares mean (standard error)	-1.67 (± 0.119)	-1.65 (± 0.12)	-1.21 (± 0.166)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Disease Activity Score 28 response using ESR (DAS28-ESR)

End point title	Change from baseline in Disease Activity Score 28 response using ESR (DAS28-ESR)

End point description:

The Disease Activity Score (DAS) is a combined index to measure disease activity in RA participants. DAS28 is determined using the following variables: 28-joint counts (tender28 and swollen28), erythrocyte sedimentation rate (ESR), and the participant's general health (GH) or global disease activity measured on a Visual Analogue Scale (VAS) of 100 mm (0 = and 100 =). Using the data from these variables, DAS28-ESR is calculated using the following formula: DAS28 = 0.56 * sqrt(tender28) + 0.28 * sqrt(swollen28) + 0.70 * ln(ESR) + 0.014 * GH. The calculation results in a DAS28-ESR score from 0 to 10 indicating the current activity of the rheumatoid arthritis of your patient. A DAS28 above 5.1 means high disease activity whereas a DAS28 below 3.2 indicates low disease activity. Remission is achieved by a DAS28 lower than 2.6. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline, 12 weeks

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	82	43	
Units: score on a scale				
least squares mean (standard error)	-1.98 (± 0.126)	-1.8 (± 0.128)	-1.46 (± 0.179)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with European League Against Rheumatism (EULAR) response

End point title	Percentage of participants with European League Against Rheumatism (EULAR) response

End point description:

EULAR response criteria are based on DAS28 status in combination with DAS28 improvements. The EULAR response criteria are as follows: present DAS28 <3.2 with DAS28 improvement >1.2 corresponds to 'good response'; present DAS28 <3.2 with DAS28 improvement between 0.6 to 1.2, or present DAS28 between 3.2 to 5.1 with DAS28 improvement from 0.6 to >1.2, or present DAS28 >5.2 with DAS28 improvement >1.2 correspond to 'moderate response; present DAS28 <3.2 with DAS28 improvement <0.6, or present DAS28 between 3.2 to 5.1 with DAS28 improvement <0.6, or present DAS28 >5.1 with DAS28 improvement <0.6 to 1.2 correspond to 'no response'.

End point type	Secondary

End point timeframe:

baseline, 12 weeks

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	89	44	
Units: Percentage of participants				
number (not applicable)				
Good response	28.4	27	13.6	
Moderate response	46.6	44.9	52.3	
No response	25	28.1	34.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in swollen 66-joint count

End point title	Change from baseline in swollen 66-joint count

End point description:

The 66 joints assessed for swelling included the 8 distal interphalangeal, 10 proximal interphalangeal and 10 metacarpophalangeal joints of the hands, the 10 metatarsophalangeal and 10 proximal interphalangeal joints of the feet, the 2 wrists, 2 elbows , 2 shoulders , 2 acromioclavicular, 2 sternoclavicular, 2 temporomandibular, 2 knee, 2 talo-tibial, and 2 mid-tarsal joints. Swelling was graded present (1) or absent (0). A negative change in baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline, 12 weeks

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	89	44	
Units: Number of joints				
least squares mean (standard error)	-9.49 (± 0.607)	-9.81 (± 0.612)	-7.88 (± 0.863)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in tender 68-joint count

End point title	Change from baseline in tender 68-joint count

End point description:

The 68 joints assessed for tenderness included the 8 distal interphalangeal, 10 proximal interphalangeal and 10 metacarpophalangeal joints of the hands, the 10 metatarsophalangeal and 10 proximal interphalangeal joints of the feet, the 2 wrists, 2 elbows , 2 shoulders , 2 acromioclavicular, 2 sternoclavicular, 2 temporomandibular, 2 hip, 2 knee, 2 talo-tibial, and 2 mid-tarsal joints. Joint tenderness was graded present (1) or absent (0). A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline, 12 weeks

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	89	44	
Units: Number of joints				
least squares mean (standard error)	-10.31 (± 1.093)	-11.99 (± 1.099)	-9.5 (± 1.549)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in participant's assessment of rheumatoid arthritis (RA) pain

End point title	Change from baseline in participant's assessment of rheumatoid arthritis (RA) pain

End point description:

The patient’s assessment of pain was performed using 100 mm visual analog scale (VAS) ranging from 0 (no pain) to 100 (unbearable pain) after the question “Please indicate with a vertical mark through the horizontal line the most pain you had from your rheumatoid arthritis over the last 24 hours”. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline, 12 weeks

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	89	44	
Units: score on a scale				
least squares mean (standard error)	-14.41 (± 2.057)	-12.6 (± 2.071)	-6.66 (± 2.902)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in participant's global assessment of disease activity

End point title	Change from baseline in participant's global assessment of disease activity

End point description:

The patient’s global assessment of disease activity was performed using 100 mm VAS ranging from 0 (very good) to 100 (very poor), after the question "Considering all the ways rheumatoid arthritis affects you, please indicate with a vertical mark through the horizontal line how well you are doing today”. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline, 12 weeks

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	89	44	
Units: score on a scale				
least squares mean (standard error)	-18.58 (± 2.042)	-15.29 (± 2.063)	-9.93 (± 2.884)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in physician's global assessment of disease activity

End point title	Change from baseline in physician's global assessment of disease activity

End point description:

The physician’s global assessment of disease activity was performed using 100 mm VAS ranging from 0 (very good) to 100 (very poor), after the question “Considering all the ways rheumatoid arthritis affects your patient, how would you rate his or her current condition?”. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline, 12 weeks

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	89	44	
Units: score on a scale				
least squares mean (standard error)	-27.05 (± 1.925)	-29.01 (± 1.95)	18.88 (± 2.726)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in hsCRP

End point title	Change from baseline in hsCRP

End point description:

Blood for this assessment was obtained to identify the presence of inflammation, to determine its severity, and to monitor response to treatment. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline, 12 weeks

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	89	44	
Units: mg/L				
least squares mean (standard error)	-6 (± 0.938)	-5.72 (± 0.946)	-1.69 (± 1.336)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in ESR

End point title	Change from baseline in ESR

End point description:

Blood for this assessment was obtained to monitor disease activity and response to therapy. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline, 12 weeks

End point values	secukinumab 10 mg/kg i.v. loading	secukinumab 150 mg s.c.	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	89	44	
Units: mm/hr				
least squares mean (standard error)	-16.68 (± 1.409)	-12.43 (± 1.425)	-10.53 (± 1.993)	

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Up to Week 16 - AIN457 150 mg sc load

Reporting group description:

Up to Week 16 - AIN457 150 mg sc load

Reporting group title	Up to Week 16 - AIN457 10 mg/kg - 150mg

Reporting group description:

Up to Week 16 - AIN457 10 mg/kg - 150mg

Reporting group title	From Week 16 through Week 52 - AIN457 150 mg sc open label

Reporting group description:

From Week 16 through Week 52 - AIN457 150 mg sc open label

Reporting group title	Follow-up period - AIN457 150 mg sc open label

Reporting group description:

Follow-up period - AIN457 150 mg sc open label

Reporting group title	Up to Week 16 - Placebo

Reporting group description:

Up to Week 16 - Placebo

Serious adverse events	Up to Week 16 - AIN457 150 mg sc load	Up to Week 16 - AIN457 10 mg/kg - 150mg	From Week 16 through Week 52 - AIN457 150 mg sc open label
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 89 (3.37%)	2 / 88 (2.27%)	18 / 214 (8.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal adenoma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	0 / 214 (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
Brain neoplasm			

subjects affected / exposed	1 / 89 (1.12%)	0 / 88 (0.00%)	0 / 214 (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
Myelodysplastic syndrome			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	0 / 214 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Lymphoedema			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	0 / 214 (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			
Chest pain			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 88 (0.00%)	0 / 214 (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
Ovarian cyst			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			

subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid lung			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 89 (1.12%)	0 / 88 (0.00%)	0 / 214 (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
Investigations			
Arteriogram coronary			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	0 / 89 (0.00%)	1 / 88 (1.14%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Lumbar radiculopathy			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 89 (0.00%)	1 / 88 (1.14%)	0 / 214 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin and subcutaneous tissue disorders			
Photosensitivity reaction			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteochondrosis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporosis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Follow-up period - AIN457 150 mg sc open label	Up to Week 16 - Placebo	
Total subjects affected by serious			

adverse events			
subjects affected / exposed	3 / 214 (1.40%)	1 / 44 (2.27%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal adenoma			
subjects affected / exposed	1 / 214 (0.47%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 214 (0.47%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Lymphoedema			
subjects affected / exposed	1 / 214 (0.47%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Metrorrhagia			

subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid lung			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Arteriogram coronary			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			

subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Lumbar radiculopathy			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Photosensitivity reaction			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (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			
Osteoarthritis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondrosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			

subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Up to Week 16 - AIN457 150 mg sc load	Up to Week 16 - AIN457 10 mg/kg - 150mg	From Week 16 through Week 52 - AIN457 150 mg sc open label
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 89 (33.71%)	17 / 88 (19.32%)	78 / 214 (36.45%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 89 (2.25%)	1 / 88 (1.14%)	11 / 214 (5.14%)
occurrences (all)	2	1	11
Varicose vein			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	0 / 214 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Immunodeficiency			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	0 / 214 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 89 (0.00%)	1 / 88 (1.14%)	0 / 214 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	1 / 89 (1.12%)	0 / 88 (0.00%)	7 / 214 (3.27%)
occurrences (all)	1	0	8
Oropharyngeal pain			
subjects affected / exposed	0 / 89 (0.00%)	2 / 88 (2.27%)	3 / 214 (1.40%)
occurrences (all)	0	2	3

Pharyngeal erythema			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	0 / 214 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	0 / 214 (0.00%)
occurrences (all)	0	0	0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 89 (1.12%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences (all)	1	0	1
Hepatic enzyme increased			
subjects affected / exposed	2 / 89 (2.25%)	0 / 88 (0.00%)	0 / 214 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	0 / 214 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 89 (4.49%)	2 / 88 (2.27%)	5 / 214 (2.34%)
occurrences (all)	4	2	5
Sciatica			
subjects affected / exposed	0 / 89 (0.00%)	2 / 88 (2.27%)	2 / 214 (0.93%)
occurrences (all)	0	2	2
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	2 / 89 (2.25%)	0 / 88 (0.00%)	0 / 214 (0.00%)
occurrences (all)	2	0	0
Leukopenia			
subjects affected / exposed	2 / 89 (2.25%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences (all)	2	0	1
Thrombocytosis			

subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 89 (0.00%)	1 / 88 (1.14%)	0 / 214 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 89 (1.12%)	1 / 88 (1.14%)	5 / 214 (2.34%)
occurrences (all)	1	1	5
Dyspepsia			
subjects affected / exposed	2 / 89 (2.25%)	1 / 88 (1.14%)	0 / 214 (0.00%)
occurrences (all)	2	1	0
Nausea			
subjects affected / exposed	1 / 89 (1.12%)	2 / 88 (2.27%)	2 / 214 (0.93%)
occurrences (all)	1	3	2
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 89 (1.12%)	0 / 88 (0.00%)	0 / 214 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 89 (1.12%)	1 / 88 (1.14%)	0 / 214 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 89 (1.12%)	0 / 88 (0.00%)	3 / 214 (1.40%)
occurrences (all)	1	0	4
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 89 (1.12%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences (all)	1	0	1
Fibromyalgia			
subjects affected / exposed	2 / 89 (2.25%)	0 / 88 (0.00%)	0 / 214 (0.00%)
occurrences (all)	2	0	0
Rheumatoid arthritis			
subjects affected / exposed	5 / 89 (5.62%)	0 / 88 (0.00%)	12 / 214 (5.61%)
occurrences (all)	6	0	12

Spinal pain			
subjects affected / exposed	1 / 89 (1.12%)	1 / 88 (1.14%)	5 / 214 (2.34%)
occurrences (all)	1	1	5
Infections and infestations			
Cystitis			
subjects affected / exposed	2 / 89 (2.25%)	0 / 88 (0.00%)	2 / 214 (0.93%)
occurrences (all)	2	0	4
Erythema migrans			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	0 / 214 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 89 (1.12%)	2 / 88 (2.27%)	3 / 214 (1.40%)
occurrences (all)	1	2	3
Influenza			
subjects affected / exposed	1 / 89 (1.12%)	0 / 88 (0.00%)	4 / 214 (1.87%)
occurrences (all)	2	0	5
Laryngitis			
subjects affected / exposed	2 / 89 (2.25%)	1 / 88 (1.14%)	1 / 214 (0.47%)
occurrences (all)	2	1	1
Nasopharyngitis			
subjects affected / exposed	5 / 89 (5.62%)	5 / 88 (5.68%)	11 / 214 (5.14%)
occurrences (all)	5	5	14
Pharyngitis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 88 (0.00%)	6 / 214 (2.80%)
occurrences (all)	1	0	7
Oral herpes			
subjects affected / exposed	1 / 89 (1.12%)	0 / 88 (0.00%)	5 / 214 (2.34%)
occurrences (all)	1	0	5
Upper respiratory tract infection			
subjects affected / exposed	1 / 89 (1.12%)	1 / 88 (1.14%)	17 / 214 (7.94%)
occurrences (all)	1	1	19
Rhinitis			
subjects affected / exposed	0 / 89 (0.00%)	2 / 88 (2.27%)	3 / 214 (1.40%)
occurrences (all)	0	2	3
Urinary tract infection			

subjects affected / exposed	2 / 89 (2.25%)	0 / 88 (0.00%)	3 / 214 (1.40%)
occurrences (all)	2	0	3
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 88 (0.00%)	1 / 214 (0.47%)
occurrences (all)	1	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 88 (0.00%)	0 / 214 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Follow-up period - AIN457 150 mg sc open label	Up to Week 16 - Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 214 (4.67%)	18 / 44 (40.91%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Varicose vein			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Immune system disorders			
Immunodeficiency			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Pharyngeal erythema			

subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Mood altered			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Hepatic enzyme increased			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Leukopenia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Thrombocytosis			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	

Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	2	
Rash			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 214 (0.93%)	1 / 44 (2.27%)	
occurrences (all)	2	1	
Fibromyalgia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Rheumatoid arthritis			
subjects affected / exposed	5 / 214 (2.34%)	2 / 44 (4.55%)	
occurrences (all)	5	2	
Spinal pain			

subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Erythema migrans			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	2	
Gastroenteritis			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Laryngitis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	1 / 214 (0.47%)	4 / 44 (9.09%)	
occurrences (all)	1	5	
Pharyngitis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	0 / 214 (0.00%)	3 / 44 (6.82%)	
occurrences (all)	0	3	
Upper respiratory tract infection			
subjects affected / exposed	1 / 214 (0.47%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	0 / 214 (0.00%)	2 / 44 (4.55%)	
occurrences (all)	0	2	
Urinary tract infection			
subjects affected / exposed	0 / 214 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	

Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all) Hypocalcaemia subjects affected / exposed occurrences (all)	 0 / 214 (0.00%) 0 0 / 214 (0.00%) 0	 2 / 44 (4.55%) 2 1 / 44 (2.27%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported