Clinical trial results:
A Phase III randomized, double-blind, placebo-controlled multicenter study of subcutaneous secukinumab in prefilled syringes to demonstrate the efficacy at 24 weeks and to assess the long term efficacy, safety, tolerability and usability up to 5 years in patients with active rheumatoid arthritis who have an inadequate response to anti-TNF-agents

Summary

EudraCT number	2011-006058-94
Trial protocol	CZ DE IT PT GR
Global end of trial date	11 May 2015

Results information

Result version number	v1 (current)
This version publication date	20 May 2016
First version publication date	20 May 2016

Trial information

Trial identification

Sponsor protocol code	CAIN457F2311

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01770379
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	11 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 May 2015
Global end of trial reached?	Yes
Global end of trial date	11 May 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the efficacy of secukinumab 75 mg or 150 mg at Week 24 is superior to placebo in patients with active Rheumatoid Arthritis (RA) based on the proportion of patients achieving an American College of Rheumatology (ACR)20 response.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 October 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 9
Country: Number of subjects enrolled	Brazil: 11
Country: Number of subjects enrolled	Czech Republic: 16
Country: Number of subjects enrolled	Dominican Republic: 3
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Guatemala: 6
Country: Number of subjects enrolled	India: 20
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Japan: 28
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Panama: 7
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	South Africa: 5
Country: Number of subjects enrolled	United States: 82
Country: Number of subjects enrolled	Greece: 9
Worldwide total number of subjects	242
EEA total number of subjects	65

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)	201
From 65 to 84 years	41
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

RA classified by ACR 2010 revised criteria for at least 3 months before screening and at baseline, Disease activity criteria defined by ≥6 tender joints out of 68 and ≥ 6 swollen joints out of 66.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	AIN457 75 mg

Arm description:

Patients received AIN457 75 mg as subcutaneous (s.c.) loading dose once weekly at baseline (BSL), Weeks 1, 2, 3 and 4, followed by monthly maintenance starting at Week 4.
Patients on secukinumab 75 mg continued to receive secukinumab 75 mg via PFS every 4 weeks regardless of week 16 responder status.

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

Dosage and administration details:

75 mg in 0.5ml PFS for injection

Arm title	AIN457 150mg

Arm description:

Patients received AIN457 150 mg as subcutaneous (s.c.) loading dose once weekly at baseline (BSL), Weeks 1, 2, 3 and 4, followed by monthly maintenance starting at Week 4.
Patients on secukinumab 150 mg continued to receive secukinumab 150 mg via PFS every 4 weeks regardless of week 16 responder status.

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

Dosage and administration details:

150 mg in 1.0ml PFS for injection

Arm title	Placebo

Arm description:

Patients received placebo as subcutaneous (s.c.) loading dose once weekly at baseline (BSL), Weeks 1, 2, 3 and 4, followed by monthly maintenance starting at Week 4.
At Wk 16, patients were classified: responders or non-responders. Placebo patients who were non-responders were re-randomized at Wk 16 to AIN457 75 mg or AIN457 150 mg (1:1).

Patients on placebo who were responders continued to receive placebo until Wk 24; these patients were re-randomized to receive AIN457 75 mg or AIN457 150 mg (1:1).

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

Dosage and administration details:

placebo in 0.5 or 1.0ml PFS for injection (Double Dummy Design)

Number of subjects in period 1	AIN457 75 mg	AIN457 150mg	Placebo
Started	80	81	81
Completed	41	37	39
Not completed	39	44	42
Consent withdrawn by subject	7	10	7
Physician decision	-	1	2
Adverse event, non-fatal	1	3	2
study terminated by sponsor	22	23	22
Lost to follow-up	-	-	2
Technical issues	1	-	-
Lack of efficacy	8	6	6
Protocol deviation	-	1	1

Baseline characteristics

Reporting groups

Reporting group title	AIN457 75 mg

Reporting group description:

Patients received AIN457 75 mg as subcutaneous (s.c.) loading dose once weekly at baseline (BSL), Weeks 1, 2, 3 and 4, followed by monthly maintenance starting at Week 4.
Patients on secukinumab 75 mg continued to receive secukinumab 75 mg via PFS every 4 weeks regardless of week 16 responder status.

Reporting group title	AIN457 150mg

Reporting group description:

Patients received AIN457 150 mg as subcutaneous (s.c.) loading dose once weekly at baseline (BSL), Weeks 1, 2, 3 and 4, followed by monthly maintenance starting at Week 4.
Patients on secukinumab 150 mg continued to receive secukinumab 150 mg via PFS every 4 weeks regardless of week 16 responder status.

Reporting group title	Placebo

Reporting group description:

Patients received placebo as subcutaneous (s.c.) loading dose once weekly at baseline (BSL), Weeks 1, 2, 3 and 4, followed by monthly maintenance starting at Week 4.
At Wk 16, patients were classified: responders or non-responders. Placebo patients who were non-responders were re-randomized at Wk 16 to AIN457 75 mg or AIN457 150 mg (1:1).
Patients on placebo who were responders continued to receive placebo until Wk 24; these patients were re-randomized to receive AIN457 75 mg or AIN457 150 mg (1:1).

Reporting group values	AIN457 75 mg	AIN457 150mg	Placebo
Number of subjects	80	81	81
Age Categorical Units: participants			
<=18 years	0	0	0
Between 18 and 65 years	70	62	69
>=65 years	10	19	12
Age continuous Units: years			
geometric mean	53.2	55.1	54.2
standard deviation	± 10.2	± 12.7	± 11
Gender, Male/Female Units: participant			
Female	70	67	65
Male	10	14	16

Reporting group values	Total		
Number of subjects	242		
Age Categorical Units: participants			
<=18 years	0		
Between 18 and 65 years	201		
>=65 years	41		

Age continuous Units: years geometric mean standard deviation	- 		
Gender, Male/Female Units: participant			
Female	202		
Male	40		

End points

End points reporting groups

Reporting group title	AIN457 75 mg

Reporting group description:

Patients received AIN457 75 mg as subcutaneous (s.c.) loading dose once weekly at baseline (BSL), Weeks 1, 2, 3 and 4, followed by monthly maintenance starting at Week 4.
Patients on secukinumab 75 mg continued to receive secukinumab 75 mg via PFS every 4 weeks regardless of week 16 responder status.

Reporting group title	AIN457 150mg

Reporting group description:

Patients received AIN457 150 mg as subcutaneous (s.c.) loading dose once weekly at baseline (BSL), Weeks 1, 2, 3 and 4, followed by monthly maintenance starting at Week 4.
Patients on secukinumab 150 mg continued to receive secukinumab 150 mg via PFS every 4 weeks regardless of week 16 responder status.

Reporting group title	Placebo

Reporting group description:

Patients received placebo as subcutaneous (s.c.) loading dose once weekly at baseline (BSL), Weeks 1, 2, 3 and 4, followed by monthly maintenance starting at Week 4.
At Wk 16, patients were classified: responders or non-responders. Placebo patients who were non-responders were re-randomized at Wk 16 to AIN457 75 mg or AIN457 150 mg (1:1).
Patients on placebo who were responders continued to receive placebo until Wk 24; these patients were re-randomized to receive AIN457 75 mg or AIN457 150 mg (1:1).

Primary: Percentage of participants achieving an American College of Rheumatology Response 20 (ACR20).

End point title	Percentage of participants achieving an American College of Rheumatology Response 20 (ACR20).

End point description:

ACR20 response was defined as having a positive clinical response to treatment (individual improvement) in disease activity if the participant had at least 20% improvement in tender 68-joint count, swollen 66-joint count and at least 3 of the following 5 measures: patient's assessment of RA pain, patient's global assessment of disease activity, physician's global assessment of disease activity, subject self-assessed disability (Health Assessment Questionnaire [HAQ-DI] score), and/or acute phase reactant (high sensitivity c-reactive protein (hsCRP) or erythrocyte sedimentation rate (ESR). The ACR20 response results at week 24 used non-responder imputation.

End point type	Primary

End point timeframe:

Week 24

End point values	AIN457 75 mg	AIN457 150mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	80	81	81	
Units: percentage of participants				
number (not applicable)	37.5	38.3	27.2	

Statistical analyses

Statistical analysis title	AIN457A 75mg vs. Placebo
Comparison groups	AIN457 75 mg v Placebo
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	3.03

Statistical analysis title	AIN457A 150 mg vs. placebo
Comparison groups	AIN457 150mg v Placebo
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1574
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	3.15

Secondary: Change from baseline in Disease Activity Score utilizing CRP (DAS28-CRP)

End point title	Change from baseline in Disease Activity Score utilizing CRP (DAS28-CRP)

End point description:

The DAS28 is a measure of disease activity in RA based on Swollen and Tender Joint Counts (out of a total of 28), hsCRP and the Patient's Global Assessment of Disease Activity. A DAS28 score greater than 5.1 implies active disease, equal to or less than 3.2 low disease activity, and less than 2.6 remission. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Week 24

End point values	AIN457 75 mg	AIN457 150mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	80	81	81	
Units: Units on a scale				
least squares mean (standard error)	-1.56 (± 0.149)	-1.61 (± 0.148)	-1.01 (± 0.176)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Stanford Health Assessment Questionnaire Disability Index (HAQ-DI)

End point title	Change from baseline in Stanford Health Assessment Questionnaire Disability Index (HAQ-DI)

End point description:

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

End point type	Secondary

End point timeframe:

Week 24

End point values	AIN457 75 mg	AIN457 150mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	80	81	81	
Units: units on a scale				
least squares mean (standard error)	-0.42 (± 0.068)	-0.39 (± 0.068)	-0.13 (± 0.078)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving ACR50

End point title	Percentage of participants achieving ACR50

End point description:

ACR50 response was defined as having a positive clinical response to treatment (individual improvement) in disease activity if the participant had at least 50% improvement in tender 68-joint count, swollen 66-joint count and at least 3 of the following 5 measures: patient’s assessment of RA pain, patient’s global assessment of disease activity, physician’s global assessment of disease activity, subject self-assessed disability (Health Assessment Questionnaire [HAQ-DI] score), and/or acute phase reactant (high sensitivity c-reactive protein (hsCRP) or erythrocyte sedimentation rate (ESR). The

ACR50 response results at week 24 used non-responder imputation.

End point type	Secondary

End point timeframe:

Week 24

End point values	AIN457 75 mg	AIN457 150mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	80	81	81	
Units: Percentage of patients				
number (not applicable)	17.5	18.5	13.6	

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	18.0

Reporting groups	
Reporting group title	Any AIN457 75 mg
Reporting group description:	
Any AIN457 75 mg	
Reporting group title	Any AIN457 150 mg
Reporting group description:	
Any AIN457 150 mg	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Serious adverse events	Any AIN457 75 mg	Any AIN457 150 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 115 (10.43%)	9 / 115 (7.83%)	0 / 79 (0.00%)
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)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 79 (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
Injury, poisoning and procedural complications			
Synovial rupture			

subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 79 (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
Tendon rupture			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 79 (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			
Atrial fibrillation			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 79 (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
Nervous system disorders			
Dementia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 79 (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
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 79 (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			
Cholecystitis acute			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 79 (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
Cholecystitis chronic			

subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 79 (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
Hepatic function abnormal			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 79 (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
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 79 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 79 (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 / 115 (0.87%)	0 / 115 (0.00%)	0 / 79 (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
Osteonecrosis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 79 (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
Pain in extremity			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 79 (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

Rheumatoid arthritis			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Helicobacter infection			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 79 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 79 (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
Pneumonia			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 79 (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
Pulmonary tuberculosis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 79 (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

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

Non-serious adverse events	Any AIN457 75 mg	Any AIN457 150 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 115 (66.96%)	63 / 115 (54.78%)	35 / 79 (44.30%)
Investigations			
Weight increased			
subjects affected / exposed	2 / 115 (1.74%)	3 / 115 (2.61%)	0 / 79 (0.00%)
occurrences (all)	2	3	0

Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	1 / 115 (0.87%)	3 / 115 (2.61%)	0 / 79 (0.00%)
occurrences (all)	1	3	0
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 115 (4.35%)	6 / 115 (5.22%)	0 / 79 (0.00%)
occurrences (all)	5	7	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 115 (2.61%)	4 / 115 (3.48%)	1 / 79 (1.27%)
occurrences (all)	6	4	1
Headache			
subjects affected / exposed	6 / 115 (5.22%)	10 / 115 (8.70%)	2 / 79 (2.53%)
occurrences (all)	8	11	3
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	5 / 115 (4.35%)	1 / 115 (0.87%)	1 / 79 (1.27%)
occurrences (all)	9	4	6
Oedema peripheral			
subjects affected / exposed	1 / 115 (0.87%)	4 / 115 (3.48%)	2 / 79 (2.53%)
occurrences (all)	1	4	2
Pyrexia			
subjects affected / exposed	5 / 115 (4.35%)	0 / 115 (0.00%)	0 / 79 (0.00%)
occurrences (all)	5	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 115 (0.87%)	3 / 115 (2.61%)	1 / 79 (1.27%)
occurrences (all)	1	3	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 115 (1.74%)	3 / 115 (2.61%)	1 / 79 (1.27%)
occurrences (all)	2	4	1
Dental caries			
subjects affected / exposed	3 / 115 (2.61%)	0 / 115 (0.00%)	0 / 79 (0.00%)
occurrences (all)	3	0	0
Diarrhoea			

subjects affected / exposed	8 / 115 (6.96%)	9 / 115 (7.83%)	1 / 79 (1.27%)
occurrences (all)	12	9	1
Dyspepsia			
subjects affected / exposed	7 / 115 (6.09%)	3 / 115 (2.61%)	0 / 79 (0.00%)
occurrences (all)	7	3	0
Nausea			
subjects affected / exposed	4 / 115 (3.48%)	6 / 115 (5.22%)	1 / 79 (1.27%)
occurrences (all)	4	6	1
Stomatitis			
subjects affected / exposed	3 / 115 (2.61%)	0 / 115 (0.00%)	1 / 79 (1.27%)
occurrences (all)	4	0	1
Vomiting			
subjects affected / exposed	2 / 115 (1.74%)	6 / 115 (5.22%)	1 / 79 (1.27%)
occurrences (all)	2	6	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 115 (10.43%)	2 / 115 (1.74%)	0 / 79 (0.00%)
occurrences (all)	14	2	0
Oropharyngeal pain			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	2 / 79 (2.53%)
occurrences (all)	1	1	2
Rhinorrhoea			
subjects affected / exposed	1 / 115 (0.87%)	3 / 115 (2.61%)	0 / 79 (0.00%)
occurrences (all)	1	3	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
Rash			
subjects affected / exposed	5 / 115 (4.35%)	4 / 115 (3.48%)	1 / 79 (1.27%)
occurrences (all)	5	5	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 115 (2.61%)	1 / 115 (0.87%)	0 / 79 (0.00%)
occurrences (all)	3	1	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	5 / 115 (4.35%)	2 / 115 (1.74%)	3 / 79 (3.80%)
occurrences (all)	6	4	3
Back pain			
subjects affected / exposed	4 / 115 (3.48%)	4 / 115 (3.48%)	0 / 79 (0.00%)
occurrences (all)	4	4	0
Musculoskeletal pain			
subjects affected / exposed	5 / 115 (4.35%)	1 / 115 (0.87%)	0 / 79 (0.00%)
occurrences (all)	5	1	0
Muscle spasms			
subjects affected / exposed	0 / 115 (0.00%)	4 / 115 (3.48%)	0 / 79 (0.00%)
occurrences (all)	0	4	0
Pain in extremity			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	2 / 79 (2.53%)
occurrences (all)	0	2	2
Rheumatoid arthritis			
subjects affected / exposed	11 / 115 (9.57%)	10 / 115 (8.70%)	6 / 79 (7.59%)
occurrences (all)	13	14	7
Rheumatoid nodule			
subjects affected / exposed	0 / 115 (0.00%)	3 / 115 (2.61%)	0 / 79 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	14 / 115 (12.17%)	4 / 115 (3.48%)	4 / 79 (5.06%)
occurrences (all)	20	5	4
Cystitis			
subjects affected / exposed	4 / 115 (3.48%)	3 / 115 (2.61%)	1 / 79 (1.27%)
occurrences (all)	7	3	1
Gastroenteritis			
subjects affected / exposed	0 / 115 (0.00%)	3 / 115 (2.61%)	0 / 79 (0.00%)
occurrences (all)	0	3	0
Influenza			
subjects affected / exposed	5 / 115 (4.35%)	2 / 115 (1.74%)	0 / 79 (0.00%)
occurrences (all)	5	2	0
Lower respiratory tract infection			

subjects affected / exposed	3 / 115 (2.61%)	0 / 115 (0.00%)	0 / 79 (0.00%)
occurrences (all)	4	0	0
Labyrinthitis			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
Nasopharyngitis			
subjects affected / exposed	25 / 115 (21.74%)	23 / 115 (20.00%)	8 / 79 (10.13%)
occurrences (all)	41	41	8
Rhinitis			
subjects affected / exposed	5 / 115 (4.35%)	5 / 115 (4.35%)	1 / 79 (1.27%)
occurrences (all)	5	6	1
Sinusitis			
subjects affected / exposed	2 / 115 (1.74%)	2 / 115 (1.74%)	2 / 79 (2.53%)
occurrences (all)	2	2	2
Upper respiratory tract infection			
subjects affected / exposed	8 / 115 (6.96%)	9 / 115 (7.83%)	3 / 79 (3.80%)
occurrences (all)	9	10	4
Urinary tract infection			
subjects affected / exposed	9 / 115 (7.83%)	2 / 115 (1.74%)	2 / 79 (2.53%)
occurrences (all)	10	2	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 June 2012	• To align the sequence of the hierarchical testing strategy with latest FDA guidance released May 2013 for clinical trials in patients with RA. • To fulfill health authority requests with regards to local requirements for additional serological testing (hepatitis B, hepatitis C or Human Immunodeficiency Virus (HIV)) prior to initiation of therapy. • To fulfill a health authority request, to limit blinded study duration to reduce patient burden in administering a second syringe containing placebo to maintain blind At the time of this amendment, approximately half of the patients had been randomized. This amendment was not considered to have affected the interpretation of study results as the changes were minor and occurred prior to study unblinding.

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.

This study was terminated early (unrelated to safety) due to the analysis of AIN457F2309 study ,which the data showed that secukinumab is not comparable to current RA treatments thus closing the AIN457 RA program.

Notes: