Clinical trial results:
A multicenter, 12 week, randomized, double-blind, placebo-controlled biomarker study of secukinumab (AIN457) in rheumatoid arthritis patients followed by an open label extension.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2011-001220-38
Trial protocol	GB DE BE
Global end of trial date	13 February 2014

Results information

Result version number	v2 (current)
This version publication date	08 July 2016
First version publication date	31 July 2015
Version creation reason	• Correction of full data set A decimal point was missing from the least squares mean for the placebo arm of secondary outcome measure on DAS28 , under HLA-DRB1*SE carrier category.

Trial information

Trial identification

Sponsor protocol code	CAIN457F2208

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01426789
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	13 February 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether the treatment effect of secukinumab vs. placebo at Week 12 (measured by ACR20 response rate and change from baseline in DAS28) is associated with the presence/absence of the HLA-DRB1 *04 allelic group in rheumatoid arthritis (RA) patients

Protection of trial subjects:

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

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	08 August 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	Belgium: 5
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Russian Federation: 63
Country: Number of subjects enrolled	United States: 28
Worldwide total number of subjects	100
EEA total number of subjects	9

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)	92
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study included a 12 week, randomized, double blind phase (part 1), a 40 week, open label phase (part 2), and a 3 month safety follow-up. Participants from the secukinumab arm, who completed part 1 and had an ACR50 or greater response at week 12, and participants from the placebo arm, who completed part 1, were eligible for the open label phase.

Pre-assignment

Screening details:

101 Patients were enrolled in the study. One subject randomized to the placebo arm withdrew from the study before the first dose administration. One hundred participants received study treatment in part 1. Ten participants discontinued during part 1. At the end of part 1, 76 participants were eligible to take secukinumab treatment in part 2.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab

Arm description:

10 mg/kg intravenous (I.V.)

Arm type	Experimental
Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

In Part 1 (blinded period) participants randomized to AIN457 recived 10 mg/kg I.V.

Arm title	Placebo

Arm description:

Placebo i.v.

Arm type	Placebo
Investigational medicinal product name	Matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Matching Placebo to AIN457 I.V.

Number of subjects in period 1	Secukinumab	Placebo
Started	68	32
Completed	62	28
Not completed	6	4
Adverse event, non-fatal	3	-
Protocol deviation	-	1
Lost to follow-up	1	2
Lack of efficacy	2	1

Period 2	
Period 2 title	Part 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes
Arm title	Group 1
Arm description:	
Part 1: secukinumab 6 x 10 mg/kg i.v.; Part 2: secukinumab 300 mg sc monthly	
Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Part 1: secukinumab 6 x 10 mg/kg i.v.; Part 2: secukinumab 300 mg sc monthly	
Arm title	Group 2
Arm description:	
Part 1: secukinumab 6 x 10 mg/kg i.v.; part 2: no study treatment	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 3
Arm description:	
Part 1: placebo; Part 2: secukinumab 4 x 300 mg sc loading dose (at weeks 12, 13, 14 and 16), then 300 mg sc monthly	
Arm type	Experimental
Investigational medicinal product name	Secukiumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Part 1: placebo; Part 2: secukinumab 4 x 300 mg sc loading dose (at weeks 12, 13, 14 and 16), then 300 mg sc monthly

Arm title	Group 4
Arm description:	
Part 1: placebo; Part 2: no study treatment	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Group 1	Group 2	Group 3
Started	49	13	27
Completed	34	12	19
Not completed	15	1	8
Adverse event, serious fatal	1	-	1
Consent withdrawn by subject	-	1	2
Adverse event, non-fatal	2	-	1
Protocol deviation	1	-	-
Administrative problems	2	-	1
Lost to follow-up	4	-	1
Lack of efficacy	5	-	2

Number of subjects in period 2	Group 4
Started	1
Completed	1
Not completed	0
Adverse event, serious fatal	-
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Protocol deviation	-
Administrative problems	-
Lost to follow-up	-
Lack of efficacy	-

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab
Reporting group description:	
10 mg/kg intravenous (I.V.)	
Reporting group title	Placebo
Reporting group description:	
Placebo i.v.	

Reporting group values	Secukinumab	Placebo	Total
Number of subjects	68	32	100
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)	65	27	92
From 65-84 years	3	5	8
85 years and over	0	0	0
Age Continuous |			
Units: Years			
arithmetic mean	49.5	54.5	
standard deviation	± 11.45	± 10.3	-
Gender, Male/Female			
Units: Participants			
Female	48	25	73
Male	20	7	27

End points

End points reporting groups

Reporting group title	Secukinumab
Reporting group description:	
10 mg/kg intravenous (I.V.)	
Reporting group title	Placebo
Reporting group description:	
Placebo i.v.	
Reporting group title	Group 1
Reporting group description:	
Part 1: secukinumab 6 x 10 mg/kg i.v.; Part 2: secukinumab 300 mg sc monthly	
Reporting group title	Group 2
Reporting group description:	
Part 1: secukinumab 6 x 10 mg/kg i.v.; part 2: no study treatment	
Reporting group title	Group 3
Reporting group description:	
Part 1: placebo; Part 2: secukinumab 4 x 300 mg sc loading dose (at weeks 12, 13, 14 and 16), then 300 mg sc monthly	
Reporting group title	Group 4
Reporting group description:	
Part 1: placebo; Part 2: no study treatment	

Primary: Percentage of participants who achieve American College of Rheumatology Response of 20 (ACR20) in association with the presence or absence of the HLA-DRB1 *4 allelic group

End point title	Percentage of participants who achieve American College of Rheumatology Response of 20 (ACR20) in association with the presence or absence of the HLA-DRB1 *4 allelic group
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	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	28		
Units: Percentage of participants				
number (not applicable)				
HLADRB1 *04 carriers	45.2	10.7		
HLADRB1 *04 non-carriers	41.9	14.3		

Statistical analyses

Statistical analysis title	Change from Baseline ACR20 at 12 Weeks
Comparison groups	Placebo v Secukinumab
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.303
Method	ANCOVA

Primary: Change from baseline in Disease Activity Score 28 (DAS28) in association with the presence or absence of HLA-DRB1 04

End point title	Change from baseline in Disease Activity Score 28 (DAS28) in association with the presence or absence of HLA-DRB1 04

End point description:

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

End point type	Primary

End point timeframe:

baseline, 12 weeks

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	28		
Units: score on a scale				
least squares mean (standard error)				
HLA-DRB1 *04 carriers	-2.5 (± 0.5273)	-0.6 (± 0.575)		
HLA-DRB1 *04 non-carriers	-2.2 (± 0.5618)	-0.8 (± 0.6098)		

Statistical analyses

Statistical analysis title	Change from Baseline of DAS28-CRP
Comparison groups	Secukinumab v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.364
Method	ANCOVA

Secondary: Percentage of participants who achieve ACR50 and ACR70 with the presence/absence of the HLA-DRB1*04 allelic group

End point title	Percentage of participants who achieve ACR50 and ACR70 with the presence/absence of the HLA-DRB1*04 allelic group

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	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	28		
Units: Percentage of participants				
number (not applicable)				
ACR50: HLADRB1 *04 presence	38.7	7.1		
ACR50: HLADRB1 *04 absence	35.5	10.7		
ACR70: HLADRB1 *04 presence	8.1	0		
ACR70: HLADRB1 *04 absence	8.1	7.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in DAS28 in association with the presence or absence of HLA-DRB1 *SE (positive), HLA-DRB1 *401 (carrier) and HLA-DRB1 position 11 V/L and in association with other biomarkers

End point title	Change from baseline in DAS28 in association with the presence or absence of HLA-DRB1 *SE (positive), HLA-DRB1 *401 (carrier) and HLA-DRB1 position 11 V/L and in association with other biomarkers

End point description:

The DAS28 is a measure of disease activity in RA. The score is calculated by a complex mathematical

formula, which includes the tender joint count(TJC) and swollen joint count (SJC) out of a total of 28 joints, the high-sensitivity C-reactive protein (hsCRP), and the subject's 'global assessment' of disease activity/general health (GH). The subject's global assessment/GH was indicated by a visual analogue scale of 100 mm where the participant marked a point on a 100 mm line between 0 and 100 (0 indicated very good and 100 indicated very bad). The following formula was used to calculate DAS28: DAS-CRP = 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) = 0.36*ln(CRP+1) + 0.014*GH = 0.96. A DAS28-CRP score > 5.1 implies active disease, <3.2 implies controlled disease and <2.6 implied remission. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline, 12 weeks

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	28		
Units: score on a scale				
least squares mean (standard error)				
HLA-DRB1 *SE carrier	-2.6 (± 0.5049)	-0.5 (± 0.524)		
HLA-DRB1 *SE non-carrier	-2.3 (± 0.5376)	-2.2 (± 0.6977)		
HLA-DRB1 *0401 carrier	-2.4 (± 0.5922)	0.1 (± 0.7503)		
HLA-DRB1 *401 non-carrier	-2.3 (± 0.5133)	-0.9 (± 0.5456)		
HLA-DRB1 position 11 V/L carrier	-2.5 (± 0.4901)	-0.4 (± 0.5218)		
HLA-DRB1 position 11 V/L non-carrier	-2.2 (± 0.5706)	-2.2 (± 0.6954)		

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	16.1

Reporting groups

Reporting group title	Part 1: Secukinumab 10 mg/kg iv

Reporting group description:

Part 1: Secukinumab 10 mg/kg iv

Reporting group title	Part 1: Placebo

Reporting group description:

Part 1: Placebo

Reporting group title	Part 2: Group 1

Reporting group description:

Part 2: Group 1

Reporting group title	Part 2: Group 3

Reporting group description:

Part 2: Group 3

Serious adverse events	Part 1: Secukinumab 10 mg/kg iv	Part 1: Placebo	Part 2: Group 1
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 68 (5.88%)	2 / 32 (6.25%)	4 / 49 (8.16%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung carcinoma cell type unspecified stage IV			

subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (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
Metastases to lung			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (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
Ovarian adenoma			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis necrotising			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	0 / 49 (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			
Angina pectoris			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Multi-organ failure			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 32 (3.13%)	0 / 49 (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
Respiratory, thoracic and mediastinal disorders			
Idiopathic pulmonary fibrosis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	0 / 49 (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
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	0 / 68 (0.00%)	1 / 32 (3.13%)	0 / 49 (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			
Pain in extremity			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (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
Tendon disorder			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 68 (0.00%)	1 / 32 (3.13%)	0 / 49 (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
Lobar pneumonia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (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
Osteomyelitis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	0 / 49 (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
Peritonitis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2: Group 3		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 27 (14.81%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung carcinoma cell type unspecified stage IV				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Metastases to lung				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ovarian adenoma				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Arteriosclerosis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vasculitis necrotising				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina pectoris				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Multi-organ failure			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Idiopathic pulmonary fibrosis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Pain in extremity			

subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tendon disorder			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lobar pneumonia			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peritonitis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Part 1: Secukinumab 10 mg/kg iv	Part 1: Placebo	Part 2: Group 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 68 (19.12%)	9 / 32 (28.13%)	15 / 49 (30.61%)
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	4
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Injection site erythema			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 68 (0.00%)	1 / 32 (3.13%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Injection site induration			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			

subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 68 (1.47%)	1 / 32 (3.13%)	0 / 49 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
Aphthous stomatitis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	3 / 68 (4.41%)	1 / 32 (3.13%)	1 / 49 (2.04%)
occurrences (all)	3	1	1
Dysphagia			
subjects affected / exposed	0 / 68 (0.00%)	1 / 32 (3.13%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	0 / 68 (0.00%)	1 / 32 (3.13%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 68 (0.00%)	1 / 32 (3.13%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	1 / 49 (2.04%)
occurrences (all)	2	0	2
Oropharyngeal pain			
subjects affected / exposed	2 / 68 (2.94%)	1 / 32 (3.13%)	2 / 49 (4.08%)
occurrences (all)	2	1	2
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

Xeroderma			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	2
Rheumatoid arthritis			
subjects affected / exposed	1 / 68 (1.47%)	2 / 32 (6.25%)	7 / 49 (14.29%)
occurrences (all)	1	5	8
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	2 / 49 (4.08%)
occurrences (all)	1	0	2
Gastroenteritis viral			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	3 / 49 (6.12%)
occurrences (all)	0	0	3
Nasopharyngitis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	2 / 49 (4.08%)
occurrences (all)	1	0	2
Respiratory tract infection viral			
subjects affected / exposed	0 / 68 (0.00%)	2 / 32 (6.25%)	1 / 49 (2.04%)
occurrences (all)	0	2	1
Otitis media			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Rhinitis			

subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	2 / 49 (4.08%)
occurrences (all)	0	0	2
Tonsillitis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 32 (0.00%)	1 / 49 (2.04%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 68 (4.41%)	1 / 32 (3.13%)	1 / 49 (2.04%)
occurrences (all)	3	1	1
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 68 (0.00%)	0 / 32 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 2: Group 3		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 27 (44.44%)		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Alanine aminotransferase increased			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Blood pressure increased			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Injection site erythema			

subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Injection site haematoma subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Injection site induration subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Eye disorders Dry eye subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Gastrointestinal disorders Aphthous stomatitis subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Dysphagia subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Mouth ulceration subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Toothache subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Vomiting subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Xeroderma			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Bone pain			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Bursitis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Rheumatoid arthritis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Gastroenteritis viral			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		

Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Respiratory tract infection viral subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Otitis media subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 2		
Rhinitis subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Tonsillitis subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 2		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Metabolism and nutrition disorders Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 May 2011	In order to reduce the complexity of the study, blood sampling for Flow Cytometry studies was removed from the protocol.
09 May 2011	The duration of iv infusion in both treatment arms in Part 1 of the study was shortened to30 minutes from 120 minutes. Recent results from the clinical study (CAIN457A2228) that assessed the safety and tolerability of a shorter infusion time for secukinumab administration showed that secukinumab infusion over a 30-minute period is well tolerated and safe.
06 June 2011	Prior to FSFV, subjects were offered the opportunity to change for potential benefit (for subjects randomized to placebo) or continue potential benefit (for those subjects responding to treatment) of secukinumab.
06 June 2011	Subjects randomized to the placebo treatment who completed their Week 12 visit were offered open label treatment with secukinumab sc for 52 weeks.
06 June 2011	For subjects who achieved an ACR50 or greater response at Week 12, open label treatment was extended to total treatment duration of 52 weeks.
06 June 2011	Inclusion criterion no. 6 was re-worded for clarification
20 March 2012	The protocol was amended to clarify that subjects prematurely withdrawing from the study were intended to undergo a 12 weeks follow-up period, prior to the end of study visit.
20 March 2012	The screening window was extended to 28 days to facilitate recruitment.
20 March 2012	Further changes were made to clarify the treatment for subjects randomized to placebo, which were offered open-label treatment with secukinumab, to clarify unblinding procedures, testing procedure and interim analysis, and to facilitate study visit compliance.
21 March 2013	This amendment clarified the blinding and unblinding processes as well as the release of interim results to external parties after closing study Part 1

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported