Clinical trial results:
A 52-week, multicenter, randomized, double-blind study of subcutaneous secukinumab to demonstrate efficacy as assessed by Psoriasis Area and Severity Index at 16 weeks of treatment compared to ustekinumab and to assess long-term safety, tolerability and efficacy in subjects with moderate to severe plaque psoriasis (CLEAR)

Summary

EudraCT number	2013-003434-32
Trial protocol	NL ES AT GB DE PT IT SK BE HU GR EE BG DK
Global end of trial date	28 June 2016

Results information

Result version number	v1 (current)
This version publication date	12 July 2017
First version publication date	12 July 2017

Trial information

Trial identification

Sponsor protocol code	CAIN457A2317

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02074982
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	28 June 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate the superiority of secukinumab compared to ustekinumab in patients with moderate to severe plaque psoriasis based on the proportion of Psoriasis Area and Severity Index (PASI) 90 responders at Week 16.

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	25 February 2014
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	Australia: 28
Country: Number of subjects enrolled	Austria: 13
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Bulgaria: 28
Country: Number of subjects enrolled	Canada: 19
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	Estonia: 40
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 167
Country: Number of subjects enrolled	United Kingdom: 30
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Israel: 22
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Korea, Republic of: 18
Country: Number of subjects enrolled	Netherlands: 19
Country: Number of subjects enrolled	Norway: 4
Country: Number of subjects enrolled	Portugal: 28
Country: Number of subjects enrolled	Slovakia: 20

Country: Number of subjects enrolled	Spain: 70
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	Taiwan: 32
Country: Number of subjects enrolled	Turkey: 6
Country: Number of subjects enrolled	United States: 85
Worldwide total number of subjects	676
EEA total number of subjects	461

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)	623
From 65 to 84 years	51
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 676 patients who were randomized to the study, 571 patients completed the study (286 patients (84.9%) in the secukinumab group and 285 patients (84.1%) in the ustekinumab group. Efficacy Data up to 52 weeks and Safety Data included up to 104 weeks

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, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	AIN457 300 mg

Arm description:

patients received AIN457 (secukinumab) 300 mg (two secukinumab 150 mg injections) s.c. (subcutaneously) once every week at weeks 0, 1,2,3, followed by monthly dosing starting at week 4 to week 48 inclusive

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:

secukinumab 300 mg/day dose subcutaneous (sc) injections

Arm title	Ustekinumab

Arm description:

patients received ustekinumab 45/90 mg (weight depended, according to label) s.c. (subcutaneously) and/or placebo secukinumab injections once every week at weeks 0,1,2, and 3 followed by monthly dosing starting at week 4 to week 48 inclusive

Arm type	Active comparator
Investigational medicinal product name	Ustekinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Ustekinumab 45 mg or 90 mg/day

Number of subjects in period 1	AIN457 300 mg	Ustekinumab
Started	337	339
Full Analysis Set (FAS)	336	339
Safety Set (SF)	335	336
Completed	286	285
Not completed	51	54
Adverse event, serious fatal	-	2
Physician decision	1	1
Adverse event, non-fatal	15	7
Technical problems	-	2
Protocol deviation	4	3
Non-compliance with study treatment	-	2
Pregnancy	1	2
Lost to follow-up	9	10
Subject/guardian decision	15	24
Lack of efficacy	6	1

Baseline characteristics

Reporting groups	
Reporting group title	AIN457 300 mg
Reporting group description:	
patients received AIN457 (secukinumab) 300 mg (two secukinumab 150 mg injections) s.c. (subcutaneously) once every week at weeks 0, 1,2,3, followed by monthly dosing starting at week 4 to week 48 inclusive	
Reporting group title	Ustekinumab
Reporting group description:	
patients received ustekinumab 45/90 mg (weight depended, according to label) s.c. (subcutaneously) and/or placebo secukinumab injections once every week at weeks 0,1,2, and 3 followed by monthly dosing starting at week 4 to week 48 inclusive	

Reporting group values	AIN457 300 mg	Ustekinumab	Total
Number of subjects	337	339	676
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)	309	314	623
From 65-84 years	28	23	51
85 years and over	0	2	2
Age Continuous Units: years			
arithmetic mean	45.2	44.6	
standard deviation	± 13.95	± 13.67	-
Gender, Male/Female Units: Subjects			
Female	108	87	195
Male	229	252	481

End points

End points reporting groups

Reporting group title	AIN457 300 mg
Reporting group description:	
patients received AIN457 (secukinumab) 300 mg (two secukinumab 150 mg injections) s.c. (subcutaneously) once every week at weeks 0, 1,2,3, followed by monthly dosing starting at week 4 to week 48 inclusive	
Reporting group title	Ustekinumab
Reporting group description:	
patients received ustekinumab 45/90 mg (weight depended, according to label) s.c. (subcutaneously) and/or placebo secukinumab injections once every week at weeks 0,1,2, and 3 followed by monthly dosing starting at week 4 to week 48 inclusive	

Primary: Percentage of participants with moderate to severe plaque psoriasis who achieved Psoriasis Area and Severity Index (PASI) 90 at Week 16

End point title	Percentage of participants with moderate to severe plaque psoriasis who achieved Psoriasis Area and Severity Index (PASI) 90 at Week 16
End point description:	
Psoriasis Area and Severity Index (PASI) is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72(maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 90 responders were defined as participants achieving ≥ 90% improvement at Week 16	
End point type	Primary
End point timeframe:	
Week 16	

End point values	AIN457 300 mg	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	335		
Units: Percentage of Participants				
number (not applicable)	79	57.3		

Statistical analyses

Statistical analysis title	Superiority of AIN457 compared to ustekinumab
Comparison groups	AIN457 300 mg v Ustekinumab

Number of subjects included in analysis	669
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.01
upper limit	4.02

Secondary: Speed of onset based on the Percentage of participents achieving PASI 75 at Week 4

End point title	Speed of onset based on the Percentage of participents achieving PASI 75 at Week 4

End point description:

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

End point type	Secondary

End point timeframe:

Week 4

End point values	AIN457 300 mg	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	335		
Units: percentage of participants				
number (not applicable)	49.7	20.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with moderate to severe plaque psoriasis who achieved Psoriasis Area and Severity Index (PASI) 90 at Week 52

End point title	Percentage of participants with moderate to severe plaque psoriasis who achieved Psoriasis Area and Severity Index (PASI) 90 at Week 52

End point description:

Psoriasis Area and Severity Index (PASI) is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72(maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 90 responders were defined as participants achieving ≥ 90% improvement at Week 52

End point type	Secondary

End point timeframe:

Week 52

End point values	AIN457 300 mg	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	335		
Units: percentage of participants				
number (not applicable)	74.9	60.6		

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

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	AIN457

Reporting group description:

AIN457

Reporting group title	Ustekinumab

Reporting group description:

Ustekinumab

Serious adverse events	AIN457	Ustekinumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	41 / 335 (12.24%)	32 / 336 (9.52%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRAIN NEOPLASM BENIGN			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FIBROADENOMA OF BREAST			

subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMANGIOMA OF LIVER			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
KERATOACANTHOMA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG ADENOCARCINOMA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MALIGNANT MELANOMA IN SITU			
subjects affected / exposed	2 / 335 (0.60%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
AORTIC ANEURYSM RUPTURE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VARICOSE VEIN			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (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			

DEATH			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	1 / 335 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROSTATITIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UTERINE HAEMORRHAGE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ALVEOLITIS ALLERGIC			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERSTITIAL LUNG DISEASE			

subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
ALCOHOL ABUSE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INSOMNIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 335 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 335 (0.00%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC ENZYME INCREASED			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
ALCOHOL POISONING			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONCUSSION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FIBULA FRACTURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FOOT FRACTURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAND FRACTURE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HUMERUS FRACTURE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INJECTION RELATED REACTION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
JAW FRACTURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

LOWER LIMB FRACTURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
POST CONCUSSION SYNDROME			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RADIUS FRACTURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
HAMARTOMA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ANGINA UNSTABLE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FLUTTER			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

VENTRICULAR FAILURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
AMNESIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CAROTID ARTERY DISEASE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EMBOLIC STROKE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FACIAL PARESIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FACIAL SPASM			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEADACHE			

subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
POSTICTAL PARALYSIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
TYMPANIC MEMBRANE PERFORATION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
OCULAR HYPERTENSION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VITREOUS ADHESIONS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

INGUINAL HERNIA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS ACUTE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	1 / 335 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLELITHIASIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CIRRHOSIS ALCOHOLIC			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATITIS ACUTE			

subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NON-ALCOHOLIC FATTY LIVER			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
LICHENIFICATION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PEMPHIGOID			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEGMENTED HYALINISING VASCULITIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATURIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEPHROLITHIASIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

URINARY RETENTION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACK PAIN			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OSTEOARTHRITIS			
subjects affected / exposed	1 / 335 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL PAIN			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TENDONITIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
ABSCESS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

ABSCESS LIMB			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
APPENDICITIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIVERTICULITIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ERYSIPELAS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARYNGITIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NASAL ABSCESS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PILONIDAL CYST			

subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SCROTAL ABSCESS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TONSILLITIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
HYPONATRAEMIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	AIN457	Ustekinumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	270 / 335 (80.60%)	246 / 336 (73.21%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SKIN PAPILLOMA			
subjects affected / exposed	7 / 335 (2.09%)	4 / 336 (1.19%)	
occurrences (all)	8	4	
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	7 / 335 (2.09%)	0 / 336 (0.00%)	
occurrences (all)	7	0	
CONTUSION			
subjects affected / exposed	7 / 335 (2.09%)	8 / 336 (2.38%)	
occurrences (all)	7	9	
LIGAMENT SPRAIN			
subjects affected / exposed	6 / 335 (1.79%)	8 / 336 (2.38%)	
occurrences (all)	7	9	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	15 / 335 (4.48%)	18 / 336 (5.36%)	
occurrences (all)	15	18	
Nervous system disorders			
HEADACHE			
subjects affected / exposed	50 / 335 (14.93%)	46 / 336 (13.69%)	
occurrences (all)	100	103	
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	20 / 335 (5.97%)	12 / 336 (3.57%)	
occurrences (all)	26	13	
PYREXIA			
subjects affected / exposed	14 / 335 (4.18%)	8 / 336 (2.38%)	
occurrences (all)	16	9	
Gastrointestinal disorders			

ABDOMINAL PAIN			
subjects affected / exposed	7 / 335 (2.09%)	10 / 336 (2.98%)	
occurrences (all)	9	10	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	12 / 335 (3.58%)	6 / 336 (1.79%)	
occurrences (all)	12	11	
DIARRHOEA			
subjects affected / exposed	22 / 335 (6.57%)	24 / 336 (7.14%)	
occurrences (all)	37	31	
DYSPEPSIA			
subjects affected / exposed	10 / 335 (2.99%)	9 / 336 (2.68%)	
occurrences (all)	13	10	
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	7 / 335 (2.09%)	3 / 336 (0.89%)	
occurrences (all)	8	3	
NAUSEA			
subjects affected / exposed	12 / 335 (3.58%)	10 / 336 (2.98%)	
occurrences (all)	30	12	
TOOTHACHE			
subjects affected / exposed	12 / 335 (3.58%)	10 / 336 (2.98%)	
occurrences (all)	12	15	
VOMITING			
subjects affected / exposed	15 / 335 (4.48%)	7 / 336 (2.08%)	
occurrences (all)	23	8	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	21 / 335 (6.27%)	20 / 336 (5.95%)	
occurrences (all)	24	22	
OROPHARYNGEAL PAIN			
subjects affected / exposed	32 / 335 (9.55%)	18 / 336 (5.36%)	
occurrences (all)	40	24	
RHINORRHOEA			
subjects affected / exposed	7 / 335 (2.09%)	6 / 336 (1.79%)	
occurrences (all)	8	10	
Skin and subcutaneous tissue disorders			

DRY SKIN			
subjects affected / exposed	7 / 335 (2.09%)	4 / 336 (1.19%)	
occurrences (all)	7	4	
ECZEMA			
subjects affected / exposed	19 / 335 (5.67%)	12 / 336 (3.57%)	
occurrences (all)	25	17	
PRURITUS			
subjects affected / exposed	25 / 335 (7.46%)	28 / 336 (8.33%)	
occurrences (all)	35	35	
PRURITUS GENERALISED			
subjects affected / exposed	8 / 335 (2.39%)	8 / 336 (2.38%)	
occurrences (all)	9	10	
PSORIASIS			
subjects affected / exposed	22 / 335 (6.57%)	21 / 336 (6.25%)	
occurrences (all)	24	21	
SEBORRHOEIC DERMATITIS			
subjects affected / exposed	9 / 335 (2.69%)	5 / 336 (1.49%)	
occurrences (all)	10	5	
URTICARIA			
subjects affected / exposed	4 / 335 (1.19%)	7 / 336 (2.08%)	
occurrences (all)	4	9	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	9 / 335 (2.69%)	3 / 336 (0.89%)	
occurrences (all)	11	4	
DEPRESSION			
subjects affected / exposed	6 / 335 (1.79%)	9 / 336 (2.68%)	
occurrences (all)	6	9	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	36 / 335 (10.75%)	33 / 336 (9.82%)	
occurrences (all)	44	41	
BACK PAIN			
subjects affected / exposed	29 / 335 (8.66%)	26 / 336 (7.74%)	
occurrences (all)	36	32	
MUSCULOSKELETAL PAIN			

subjects affected / exposed	9 / 335 (2.69%)	7 / 336 (2.08%)	
occurrences (all)	10	10	
MYALGIA			
subjects affected / exposed	8 / 335 (2.39%)	6 / 336 (1.79%)	
occurrences (all)	9	6	
NECK PAIN			
subjects affected / exposed	7 / 335 (2.09%)	3 / 336 (0.89%)	
occurrences (all)	8	4	
PAIN IN EXTREMITY			
subjects affected / exposed	11 / 335 (3.28%)	11 / 336 (3.27%)	
occurrences (all)	12	13	
PSORIATIC ARTHROPATHY			
subjects affected / exposed	10 / 335 (2.99%)	11 / 336 (3.27%)	
occurrences (all)	11	12	
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	20 / 335 (5.97%)	14 / 336 (4.17%)	
occurrences (all)	23	15	
CONJUNCTIVITIS			
subjects affected / exposed	18 / 335 (5.37%)	8 / 336 (2.38%)	
occurrences (all)	26	10	
CYSTITIS			
subjects affected / exposed	9 / 335 (2.69%)	6 / 336 (1.79%)	
occurrences (all)	13	6	
EAR INFECTION			
subjects affected / exposed	9 / 335 (2.69%)	2 / 336 (0.60%)	
occurrences (all)	9	2	
FOLLICULITIS			
subjects affected / exposed	11 / 335 (3.28%)	4 / 336 (1.19%)	
occurrences (all)	13	4	
GASTROENTERITIS			
subjects affected / exposed	11 / 335 (3.28%)	12 / 336 (3.57%)	
occurrences (all)	13	13	
HERPES ZOSTER			
subjects affected / exposed	1 / 335 (0.30%)	10 / 336 (2.98%)	
occurrences (all)	1	10	

INFLUENZA			
subjects affected / exposed	33 / 335 (9.85%)	16 / 336 (4.76%)	
occurrences (all)	40	20	
NASOPHARYNGITIS			
subjects affected / exposed	96 / 335 (28.66%)	87 / 336 (25.89%)	
occurrences (all)	163	151	
ORAL CANDIDIASIS			
subjects affected / exposed	14 / 335 (4.18%)	2 / 336 (0.60%)	
occurrences (all)	22	2	
ORAL HERPES			
subjects affected / exposed	13 / 335 (3.88%)	6 / 336 (1.79%)	
occurrences (all)	19	6	
PHARYNGITIS			
subjects affected / exposed	10 / 335 (2.99%)	12 / 336 (3.57%)	
occurrences (all)	11	15	
RHINITIS			
subjects affected / exposed	13 / 335 (3.88%)	12 / 336 (3.57%)	
occurrences (all)	16	12	
SINUSITIS			
subjects affected / exposed	12 / 335 (3.58%)	9 / 336 (2.68%)	
occurrences (all)	13	9	
TINEA PEDIS			
subjects affected / exposed	10 / 335 (2.99%)	9 / 336 (2.68%)	
occurrences (all)	11	10	
TONSILLITIS			
subjects affected / exposed	11 / 335 (3.28%)	5 / 336 (1.49%)	
occurrences (all)	17	9	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	42 / 335 (12.54%)	36 / 336 (10.71%)	
occurrences (all)	74	45	
URINARY TRACT INFECTION			
subjects affected / exposed	15 / 335 (4.48%)	7 / 336 (2.08%)	
occurrences (all)	28	7	
VIRAL UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed occurrences (all)	11 / 335 (3.28%) 13	6 / 336 (1.79%) 6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 December 2014	Amendment 1: introduced an additional, week 24 analysis that was planned to deliver data to fulfill requirements of agencies data requests. At the time of this amendment, the enrolment into the study was completed.
19 February 2015	Amendment 2: provided continued treatment of patients on secukinumab for additional 52 weeks (overall up to 104 weeks). This extension of treatment allowed for safety, tolerability, and efficacy data to be collected from the participating patients over a longer period. The study could be terminated at any time for any reason by Novartis, including terminating the study only in selected countries where the drug was commercially available. This decision was made on a country-by-country basis as for some countries the study continued as planned even though secukinumab may have become commercially available. This protocol amendment also introduced new Week 52 analysis and specified that additional analyses might be conducted. This amendment also aligned the requirements for contraception methods to be used by patients during the study with the current safety profile of secukinumab and the Investigator`s Brochure. According to the Exclusion criteria (Section 4.2) of the study protocol women of childbearing potential must use 'highly effective' methods of contraception during dosing of study treatment and for 16 weeks after stopping treatment. Available data on secukinumab now only require 'effective' methods of contraception. (Section 3.6 Risks and Benefits and Investigator`s Brochure AIN457/secukinumab, Edition No.13 Section 5.2.14 Guidance for prevention of pregnancy). Therefore, the advice to female patients to prevent pregnancy was amended to be less restrictive and to allow use of effective methods of contraception.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported