Clinical trial results:
A 52-week (plus extension until commercialization), single-arm study to evaluate psoriasis severity and its psychosocial impact using the Simplified Psoriasis Index (SPI) at 16 weeks, as well as long-term safety, tolerability and efficacy of secukinumab administered subcutaneously in participants suffering from moderate to severe psoriasis

Summary

EudraCT number	2014-003666-25
Trial protocol	FR
Global end of trial date	09 February 2017

Results information

Result version number	v1 (current)
This version publication date	24 February 2018
First version publication date	24 February 2018

Trial information

Trial identification

Sponsor protocol code	CAIN457AFR01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02595970
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	CH-4056, Basel, Switzerland,
Public contact	Study Director, Novartis Pharmaceuticals, 41 61 324 1111, Novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharmaceuticals, 41 61 324 1111, Novartis.email@novartis.com

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	07 November 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the benefit of secukinumab on the severity of psoriasis based on the SPI. This index comprises 3 components: severity (s), psychosocial (p) and intervention (i) evaluated by both the physician (proSPI) and the patient (self-administered: saSPI). Only the severity components were evaluated for the primary objective (both proSPI (s) and saSPI (s)). Changes at Week 16 compared to Baseline in patients suffering from moderate to severe plaque psoriasis were analyzed.

Protection of trial subjects:

This 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	20 May 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 120
Worldwide total number of subjects	120
EEA total number of subjects	120

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)	111
From 65 to 84 years	9

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study centers: This study involved 17 active centers who enrolled (or recruited) patients in France First patient enrolled: 20-May-2015 Last patient completed: 09-Feb-2017

Pre-assignment

Screening details:

No significant events in the study (for example, wash out, run-in) that occur after participant enrollment, but prior to assignment of participants to the treatment arm

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was an open label single-arm study; therefore treatment blinding was not necessary.

Arms

Arm title	Single Arm secukinumab

Arm description:

Weekly injections of 300mg of secukinumab during the first month (induction period), followed by monthly injections thereafter to week 48. During this extension period, patients continued to receive monthly injections until End of Extension visit.

Arm type	Experimental
Investigational medicinal product name	This was an open label single-arm study; therefore treatment blinding was not necessary.
Investigational medicinal product code	AIN457A
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Secukinumab is administered subcutaneously at a dosage of 300 mg per week during the induction phase (first month) and thereafter at a dosage of 300 mg per month.

Number of subjects in period 1	Single Arm secukinumab
Started	120
Completed	100
Not completed	20
Consent withdrawn by subject	2
Physician decision	2
Adverse event, non-fatal	5
Protocol deviation	4
Lack of efficacy	7

Baseline characteristics

Reporting groups	
Reporting group title	Single Arm secukinumab
Reporting group description:	
Weekly injections of 300mg of secukinumab during the first month (induction period), followed by monthly injections thereafter to week 48. During this extension period, patients continued to receive monthly injections until End of Extension visit.	

Reporting group values	Single Arm secukinumab	Total	
Number of subjects	120	120	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	111	111	
From 65-84 years	9	9	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	45.9		
standard deviation	± 17.17	-	
Gender, Male/Female Units: Subjects			
Female	37	37	
Male	83	83	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	1	1	
Native Hawaiian or Other Pacific Islander	1	1	
Black or African American	1	1	
White	116	116	
More than one race	0	0	
Unknown or Not Reported	0	0	
proSPI (s) Units: n/a			
arithmetic mean	24.9		
standard deviation	± 10.71	-	
saSPI (s) Units: n/a			
arithmetic mean	45.9		
standard deviation	± 17.7	-	

End points

End points reporting groups

Reporting group title	Single Arm secukinumab

Reporting group description:

Weekly injections of 300mg of secukinumab during the first month (induction period), followed by monthly injections thereafter to week 48. During this extension period, patients continued to receive monthly injections until End of Extension visit.

Primary: Severity component(s) of the Simplified Psoriasis Index (SPI)

End point title	Severity component(s) of the Simplified Psoriasis Index (SPI)[1]

End point description:

The primary efficacy outcome of this study evaluates the benefit of secukinumab on the severity of psoriasis based on the SPI. This index comprises 3 components: severity (SPIs), psychosocial (SPIp) and intervention (SPIi) and were evaluated by both health care professional (professional, proSPI) and the patient (self-administered: saSPI). Only the severity components were evaluated for the primary objective: proSPI (s) and saSPI (s). Changes at Week 16 compared to Baseline in patients suffering from moderate to severe plaque psoriasis were analyzed for the purpose of this study.

End point type	Primary

End point timeframe:

from baseline to 16 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this single arm study

End point values	Single Arm secukinumab			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: score SPI(s) (range: 0 to 50)				
arithmetic mean (standard deviation)				
W0|	24.89 (± 10.747)			
W16|	2.34 (± 6.144)			

Statistical analyses

No statistical analyses for this end point

Primary: Changes of saSPI (s) at Week 16 compared to Baseline

End point title	Changes of saSPI (s) at Week 16 compared to Baseline[2]

End point description:

The primary efficacy objective of the study was to evaluate the benefit of secukinumab on the severity of psoriasis based on the SPI. This index comprises 3 components: severity (SPIs), psychosocial (SPIp) and intervention (SPIi) and were evaluated by both health care professional (professional, proSPI) and the patient (self-administered: saSPI). Only the severity components were evaluated for the primary objective: proSPI (s) and saSPI (s). Changes at Week 16 compared to Baseline in patients suffering from moderate to severe plaque psoriasis were analyzed. proSPI (s) score range is 0 to 50. Higher score means worse condition

End point type	Primary

End point timeframe:

from baseline to 16 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this single arm study

End point values	Single Arm secukinumab			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: proSPI (s) score				
arithmetic mean (standard deviation)				
W0|	23.54 (± 10.412)			
W16|	1.99 (± 4.508)			

Statistical analyses

No statistical analyses for this end point

Secondary: PASI (Psoriasis Area Severity Index) score

End point title	PASI (Psoriasis Area Severity Index) score

End point description:

PASI score range: 0 (no disease) to 72 (maximal disease)

End point type	Secondary

End point timeframe:

week 0, 16, 52

End point values	Single Arm secukinumab			
Subject group type	Reporting group			
Number of subjects analysed	109			
Units: PASI score				
arithmetic mean (standard deviation)				
W0|	23.09 (± 10.541)			
W16|	2.23 (± 3.927)			
W52|	3.16 (± 5.427)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between PASI and proSPI (s)

End point title	Correlation between PASI and proSPI (s)
End point description:	
Psoriasis Area Severity Index vs Professional Version of Simplified Psoraisis Index (proSPI) score	
End point type	Secondary
End point timeframe:	
week 0, 16, 52	

End point values	Single Arm secukinumab			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: Correlation coefficient				
number (confidence interval 95%)				
WO|	0.691 (0.58 to 0.78)			
W16|	0.814 (0.74 to 0.87)			
W52|	0.927 (0.89 to 0.95)			

Statistical analyses

No statistical analyses for this end point

Secondary: proSPI (s, p and i) over time

End point title	proSPI (s, p and i) over time
End point description:	
Professional Version of Simplified Psoriasis Index (proSPI)	
End point type	Secondary
End point timeframe:	
weeks 0, 16, 52	

End point values	Single Arm secukinumab			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: proSPI score				
arithmetic mean (standard deviation)				
proSPI (s) - W0|	24.89 (± 10.747)			
proSPI (s) - W16|	1.83 (± 4.427)			
proSPI (s) - W52|	2.93 (± 6.557)			
proSPI (p) - W0|	7.80 (± 1.885)			
proSPI (p) - W16|	1.34 (± 2.201)			

proSPI (p) - W52|	1.59 (± 2.341)			
proSPI (i) - W0|	4.26 (± 1.924)			
proSPI (i) - W16|	4.78 (± 1.633)			
proSPI (i) - W52|	4.67 (± 1.613)			

Statistical analyses

No statistical analyses for this end point

Secondary: saSPI (s, p and i) over time

End point title	saSPI (s, p and i) over time

End point description:

Self-administered Simplified Psoriasis Index (saSPI)

End point type	Secondary

End point timeframe:

weeks 0, 16, 52

End point values	Single Arm secukinumab			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: saSPI score				
arithmetic mean (standard deviation)				
saSPI(s) - W0|	23.54 (± 10.412)			
saSPI(s) - W16|	1.80 (± 4.319)			
saSPI(s) - W52|	2.15 (± 4.229)			
saSPI(p) - W0|	8.18 (± 1.855)			
saSPI(p) - W16|	1.54 (± 2.299)			
saSPI(p) - W52|	1.47 (± 2.126)			
saSPI(i) - W0|	4.34 (± 1.940)			
saSPI(i) - W16|	4.39 (± 2.221)			
saSPI(i) - W52|	4.33 (± 2.276)			

Statistical analyses

No statistical analyses for this end point

Secondary: DLQI (Dermatology Life Quality Index) over time

End point title	DLQI (Dermatology Life Quality Index) over time

End point description:

DLQI score has a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired MEANING OF DLQI SCORES 0 – 1 no effect on patient's life 2 – 5 small effect on patient's life 6 – 10 moderate effect on patient's life 11 – 20 very large effect on patient's life 21 – 30 extremely large effect on patient's life

End point type	Secondary
End point timeframe: weeks 0, 16, 52	

End point values	Single Arm secukinumab			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: DLQI score (range : 0 - 30)				
arithmetic mean (standard deviation)				
WO| W16| W52|	13.6 (± 7.33) 2.1 (± 3.67) 1.9 (± 3.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: self-administered PASI (SA-PASI)

End point title	self-administered PASI (SA-PASI)
End point description: self-administered PASI (SA-PASI) score	
End point type	Secondary
End point timeframe: weeks 0, 16, 52	

End point values	Single Arm secukinumab			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: saPASI score (range: 0 to 72)				
arithmetic mean (standard deviation)				
WO| W16| W52|	25.8 (± 13.55) 2.6 (± 6.66) 3.3 (± 7.10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Psoriasis Symptom Diary (PSD) score

End point title	Psoriasis Symptom Diary (PSD) score

End point description:

assessment of pain, itching and scaling using the Psoriasis Symptom Diary questionnaire over time PSD scores range from 0 to 10, with higher scores indicating a worse condition

End point type	Secondary

End point timeframe:

weeks 0, 16, 52

End point values	Single Arm secukinumab			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: PSD scores				
arithmetic mean (standard deviation)				
Intensity of pain recorded in PSD- W0|	5.2 (± 3.18)			
Intensity of pain recorded in PSD - W16|	0.9 (± 2.00)			
Intensity of pain recorded in PSD - W52|	0.9 (± 1.78)			
Intensity of itching recorded in PSD - W0|	6.7 (± 2.85)			
Intensity of itching recorded in PSD - W16|	1.3 (± 2.21)			
Intensity of itching recorded in PSD - W52|	1.4 (± 2.11)			
Intensity of scaling recorded in PSD - W0|	6.5 (± 2.70)			
Intensity of scaling recorded in PSD - W16|	1.0 (± 1.96)			
Intensity of scaling recorded in PSD - W52|	1.3 (± 2.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between proSPI (for each component: s, p and i) and DLQI

End point title	Correlation between proSPI (for each component: s, p and i) and DLQI

End point description:

Correlation between proSPI (for each component: s, p and i) and DLQI is summarized in table below

End point type	Secondary

End point timeframe:

weeks 0, 16, 52

End point values	Single Arm secukinumab			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: correlation coefficient				
number (confidence interval 95%)				
proSPI (s) and DLQI - W0|	0.224 (0.05 to 0.39)			
proSPI (s) and DLQI - W16|	0.418 (0.25 to 0.56)			
proSPI (s) and DLQI - W52|	0.514 (0.34 to 0.65)			
proSPI (p) and DLQI - W0|	0.492 (0.34 to 0.62)			
proSPI (p) and DLQI - W16|	0.671 (0.55 to 0.76)			
proSPI (p) and DLQI - W52|	0.757 (0.65 to 0.83)			
proSPI (i) and DLQI - W0|	0.102 (-0.08 to 0.28)			
proSPI (i) and DLQI - W16|	0.016 (-0.17 to 0.20)			
proSPI (i) and DLQI - W52|	0.131 (-0.08 to 0.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between proSPI (for components p and i) and PASI

End point title	Correlation between proSPI (for components p and i) and PASI
End point description:	
Correlation between proSPI (p, i) and PASI score by visit (Full Analysis Set (observed)) is summarized in table below	
End point type	Secondary
End point timeframe:	
Over time (from Week 0 to Week 52)	

End point values	Single Arm secukinumab			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: correlation coefficient				
number (confidence interval 95%)				
proSPI (p) and PASI - W0|	0.173 (-0.01 to 0.34)			
proSPI (p) and PASI - W16|	0.678 (0.56 to 0.77)			
proSPI (p) and PASI - W52|	0.749 (0.64 to 0.83)			
proSPI (i) and PASI - W0|	0.014 (-0.17 to 0.19)			

proSPI (i) and PASI - W16|	0.105 (-0.08 to 0.29)			
proSPI (i) and PASI - W52|	0.172 (-0.04 to 0.36)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	AIN457 300mg

Reporting group description:

AIN457 300mg

Serious adverse events	AIN457 300mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 120 (10.83%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mycosis fungoides			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Meniscus injury			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tendon rupture			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery occlusion			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral ischaemia			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Punctate keratitis			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Stomatitis			

subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Strangulated umbilical hernia			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sleep apnoea syndrome			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Sjogren's syndrome			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			

subjects affected / exposed	1 / 120 (0.83%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	AIN457 300mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	86 / 120 (71.67%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 120 (7.50%)		
occurrences (all)	10		
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 120 (7.50%)		
occurrences (all)	13		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 120 (8.33%)		
occurrences (all)	10		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 120 (10.00%)		
occurrences (all)	21		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 120 (5.83%)		
occurrences (all)	8		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	11 / 120 (9.17%)		
occurrences (all)	12		
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	7 / 120 (5.83%)		
occurrences (all)	8		
Back pain			
subjects affected / exposed	13 / 120 (10.83%)		
occurrences (all)	15		
Infections and infestations			
Bronchitis			
subjects affected / exposed	11 / 120 (9.17%)		
occurrences (all)	12		
Influenza			
subjects affected / exposed	10 / 120 (8.33%)		
occurrences (all)	10		
Nasopharyngitis			
subjects affected / exposed	13 / 120 (10.83%)		
occurrences (all)	13		
Rhinitis			
subjects affected / exposed	11 / 120 (9.17%)		
occurrences (all)	13		
Viral upper respiratory tract infection			
subjects affected / exposed	8 / 120 (6.67%)		
occurrences (all)	8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported