



Clinical trial results:

Exploratory study on the kinetics of psoriasis symptoms, pruritus intensity and lesional biomarkers in patients with moderate to severe plaque-type psoriasis treated with subcutaneous secukinumab (300 mg) during a 16 week open-label run-in phase followed by a 16 week randomized, double-blind, placebo-controlled withdrawal phase.

Summary

EudraCT number	2014-002212-16
Trial protocol	DE
Global end of trial date	15 July 2016

Results information

Result version number	v1 (current)
This version publication date	30 July 2017
First version publication date	30 July 2017

Trial information

Trial identification

Sponsor protocol code	CAIN457ADE03
-----------------------	--------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02362789
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, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, 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	15 July 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of study CAIN457ADE03 was to demonstrate that secukinumab has superior efficacy compared to placebo on the pruritus intensity Visual Analogue Scale (VAS, the worst itching within a recall period of 24 hours as part of the Patient's Global Assessment of Chronic Pruritus, PGA-CP) measured at Week 32 in patients with moderate to severe psoriasis.

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	30 March 2015
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	Germany: 130
Worldwide total number of subjects	130
EEA total number of subjects	130

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)	121
From 65 to 84 years	9

85 years and over	0
-------------------	---

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 146 patients were screened into the study, 130 of whom entered the open-label run-in phase. 80 patients randomized to withdrawal phase.

Period 1

Period 1 title	Open-label run-in phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Open-label: secukinumab 300 mg s.c.
-----------	-------------------------------------

Arm description:

All patients received 300 mg secukinumab at weeks 0 (baseline) , 1, 2, 3, 4, 8, 12.

Arm type	Experimental
Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457A
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg secukinumab subcutaneous (two prefilled syringes each containing 150 mg secukinumab)

Number of subjects in period 1	Open-label: secukinumab 300 mg s.c.
Started	130
Completed	128
Not completed	2
Adverse event, serious fatal	1
Adverse event, non-fatal	1

Period 2

Period 2 title	Randomized Withdrawal Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	Randomized withdrawal: secukinumab 300mg s.c.
------------------	---

Arm description:

Patient who completed open-label run in phase by taking secukinumab 300 mg subcutaneous at week 0, 4, 8, 12 and achieved an extensive remission , was randomized to withdrawal phase at week 16 . Patients randomized to secukinumab 300 mg at week 16, received secukinumab 300 mg subcutaneous at weeks 16, 20, 24 and 28.

Arm type	Experimental
Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457A
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg secukinumab subcutaneous (two prefilled syringes each containing 150 mg secukinumab)

Arm title	Randomized withdrawal: placebo
------------------	--------------------------------

Arm description:

Patient who completed open-label run in phase by taking secukinumab 300 mg subcutaneous at week 0, 4, 8, 12 and achieved an extensive remission , was randomized to withdrawal phase at week 16 . Patients randomized to placebo at week 16, received matching placebo of Secukinumab 300 mg subcutaneous at weeks 16, 20, 24 and 28.

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

Dosage and administration details:

matching placebo of secukinumab 300 mg s.c. (administered as two injections of 150 mg)

Number of subjects in period 2^[1]	Randomized withdrawal: secukinumab 300mg s.c.	Randomized withdrawal: placebo
Started	42	38
Completed	38	26
Not completed	4	12
Consent withdrawn by subject	1	4
Subject/guardian decision	1	2
Lack of efficacy	2	6

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all patients who completed open-label run-in phase were eligible for randomized withdrawal phase.

Baseline characteristics

Reporting groups

Reporting group title	Open-label: secukinumab 300 mg s.c.
Reporting group description:	
All patients received 300 mg secukinumab at weeks 0 (baseline) , 1, 2, 3, 4, 8, 12.	

Reporting group values	Open-label: secukinumab 300 mg s.c.	Total	
Number of subjects	130	130	
Age Categorical			
Full Analysis Set			
Units: Subjects			
<65	121	121	
>=65	8	8	
>=75	1	1	
Age continuous			
Units: years			
arithmetic mean	46.8		
standard deviation	± 12.3	-	
Gender, Male/Female			
Units: Subjects			
Female	46	46	
Male	84	84	

Subject analysis sets

Subject analysis set title	Full Analysis Set - Randomized withdrawal phase
Subject analysis set type	Full analysis

Subject analysis set description:

Statistical Analysis for pruritus intensity VAS (the worst itching within a recall period of 24 hours as part of the PGA -CP) measured in the FAS-R at Week 32.

Reporting group values	Full Analysis Set - Randomized withdrawal phase		
Number of subjects	80		
Age Categorical			
Full Analysis Set			
Units: Subjects			
<65	73		
>=65	6		
>=75	1		
Age continuous			
Units: years			
arithmetic mean	46.7		
standard deviation	± 12.38		

Gender, Male/Female			
Units: Subjects			
Female	31		
Male	49		

End points

End points reporting groups

Reporting group title	Open-label: secukinumab 300 mg s.c.
Reporting group description: All patients received 300 mg secukinumab at weeks 0 (baseline) , 1, 2, 3, 4, 8, 12.	
Reporting group title	Randomized withdrawal: secukinumab 300mg s.c.
Reporting group description: Patient who completed open-label run in phase by taking secukinumab 300 mg subcutaneous at week 0, 4, 8, 12 and achieved an extensive remission , was randomized to withdrawal phase at week 16 . Patients randomized to secukinumab 300 mg at week 16, received secukinumab 300 mg subcutaneous at weeks 16, 20, 24 and 28.	
Reporting group title	Randomized withdrawal: placebo
Reporting group description: Patient who completed open-label run in phase by taking secukinumab 300 mg subcutaneous at week 0, 4, 8, 12 and achieved an extensive remission , was randomized to withdrawal phase at week 16 . Patients randomized to placebo at week 16, received matching placebo of Secukinumab 300 mg subcutaneous at weeks 16, 20, 24 and 28.	
Subject analysis set title	Full Analysis Set - Randomized withdrawal phase
Subject analysis set type	Full analysis
Subject analysis set description: Statistical Analysis for pruritus intensity VAS (the worst itching within a recall period of 24 hours as part of the PGA -CP) measured in the FAS-R at Week 32.	

Primary: Pruritus intensity VAS

End point title	Pruritus intensity VAS
End point description: The pruritus intensity visual analogue scales (VAS) (the worst itching within a recall period of 24 hours as part of the Patients Global Assessment of Chronic Pruritus (PGA -CP)) measured in the Full Analysis Set for the randomized withdrawal phase (FAS-R) at Week 32. Patient's Global Assessment of Chronic Pruritus (PGA-CP) is a self-administered questionnaire with a recall period of 24 hours including one component as visual analogue scales (VAS 0-100). The patients marked on the line the point that they feel represents their perception of their pruritus. 0 (no pruritus) - 100 (most severe pruritus).	
End point type	Primary
End point timeframe: 32 weeks	

End point values	Randomized withdrawal: secukinumab 300mg s.c.	Randomized withdrawal: placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42 ^[1]	38 ^[2]		
Units: units on a scale				
least squares mean (standard error)	8.8 (± 4.7)	27.1 (± 4.9)		

Notes:

[1] - all patients who received at least one dose of blinded study drug during randomized withdrawal phase

[2] - all patients who received at least one dose of blinded study drug during randomized withdrawal phase

Statistical analyses

Statistical analysis title	Statistical Analysis of Pruritis Intensity VAS
Statistical analysis description:	
The primary analysis method is covariance (ANCOVA) with factors center and treatment and with covariates PASI, body weight and VAS at baseline (=week 0). Adjusted means (LS-means) are given for the difference between treatments with a 95% confidence interval and a p-value.	
Comparison groups	Randomized withdrawal: secukinumab 300mg s.c. v Randomized withdrawal: placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0055
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-18.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.01
upper limit	-5.59

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	Open label: secukinumab 300 mg s.c.
-----------------------	-------------------------------------

Reporting group description:

All patients received 300 mg secukinumab subcutaneously at weeks 0 (baseline) , 1, 2, 3, 4, 8, 12.

Reporting group title	Randomized withdrawal: secukinumab 300 mg s.c.
-----------------------	--

Reporting group description:

Patient who completed open-label run in phase by taking secukinumab 300 mg subcutaneous at week 0, 4, 8, 12 and achieved an extensive remission , was randomized to withdrawal phase at week 16 . Patients randomized to secukinumab 300 mg at week 16, received secukinumab 300 mg subcutaneous at weeks 16, 20, 24 and 28.

Reporting group title	Randomized withdrawal: Placebo
-----------------------	--------------------------------

Reporting group description:

Patient who completed open-label run in phase by taking secukinumab 300 mg subcutaneous at week 0, 4, 8, 12 and achieved an extensive remission , was randomized to withdrawal phase at week 16 . Patients randomized to placebo at week 16, received matching placebo of Secukinumab 300 mg subcutaneous at weeks 16, 20, 24 and 28.

Serious adverse events	Open label: secukinumab 300 mg s.c.	Randomized withdrawal: secukinumab 300 mg s.c.	Randomized withdrawal: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 130 (4.62%)	2 / 42 (4.76%)	0 / 38 (0.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
HUMERUS FRACTURE			
subjects affected / exposed	1 / 130 (0.77%)	0 / 42 (0.00%)	0 / 38 (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
LIGAMENT RUPTURE			

subjects affected / exposed	1 / 130 (0.77%)	0 / 42 (0.00%)	0 / 38 (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			
ANEURYSM RUPTURED			
subjects affected / exposed	1 / 130 (0.77%)	0 / 42 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 130 (0.77%)	0 / 42 (0.00%)	0 / 38 (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
MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 130 (0.77%)	0 / 42 (0.00%)	0 / 38 (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
Gastrointestinal disorders			
CROHN'S DISEASE			
subjects affected / exposed	0 / 130 (0.00%)	1 / 42 (2.38%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			
subjects affected / exposed	1 / 130 (0.77%)	0 / 42 (0.00%)	0 / 38 (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
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	1 / 130 (0.77%)	0 / 42 (0.00%)	0 / 38 (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
Infections and infestations			
ERYSIPELAS			

subjects affected / exposed	1 / 130 (0.77%)	0 / 42 (0.00%)	0 / 38 (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
INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE			
subjects affected / exposed	0 / 130 (0.00%)	1 / 42 (2.38%)	0 / 38 (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
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 130 (0.77%)	0 / 42 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Open label: secukinumab 300 mg s.c.	Randomized withdrawal: secukinumab 300 mg s.c.	Randomized withdrawal: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 130 (33.08%)	16 / 42 (38.10%)	19 / 38 (50.00%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	1 / 130 (0.77%)	2 / 42 (4.76%)	2 / 38 (5.26%)
occurrences (all)	1	2	2
Nervous system disorders			
HEADACHE			
subjects affected / exposed	5 / 130 (3.85%)	3 / 42 (7.14%)	1 / 38 (2.63%)
occurrences (all)	6	3	1
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 130 (0.77%)	0 / 42 (0.00%)	3 / 38 (7.89%)
occurrences (all)	1	0	3
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	8 / 130 (6.15%)	0 / 42 (0.00%)	0 / 38 (0.00%)
occurrences (all)	8	0	0

Infections and infestations			
INFLUENZA			
subjects affected / exposed	2 / 130 (1.54%)	1 / 42 (2.38%)	2 / 38 (5.26%)
occurrences (all)	2	1	2
NASOPHARYNGITIS			
subjects affected / exposed	31 / 130 (23.85%)	12 / 42 (28.57%)	11 / 38 (28.95%)
occurrences (all)	40	14	12
RHINITIS			
subjects affected / exposed	0 / 130 (0.00%)	1 / 42 (2.38%)	2 / 38 (5.26%)
occurrences (all)	0	1	2
SINUSITIS			
subjects affected / exposed	0 / 130 (0.00%)	1 / 42 (2.38%)	2 / 38 (5.26%)
occurrences (all)	0	1	2

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