Clinical trial results:
A randomized, double-blind, multicenter, 24-week study of subcutaneous secukinumab to assess anti-interleukin-17A treatment in plaque psoriasis patients with coexisting non-alcoholic fatty liver disease (pINPOINt).

Summary

EudraCT number	2019-003168-37
Trial protocol	DE
Global end of trial date	23 July 2021

Results information

Result version number	v1
This version publication date	26 June 2022
First version publication date	26 June 2022

Trial information

Trial identification

Sponsor protocol code	CAIN457ADE15

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04237116
WHO universal trial number (UTN)	-
Other trial identifiers	EudraCT: 2019-003168-37

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma GmbH
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma GmbH, 1 (862) 778-8300, novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharma GmbH, 1 (862) 778-8300, novartis.email@novartis.com
Sponsor organisation name	Novartis Pharma GmbH
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma GmbH, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma GmbH, 41 613241111, novartis.email@novartis.com
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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	12 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 July 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary study objective was to demonstrate superiority of secukinumab compared with placebo in patients with moderate to severe chronic plaque-type psoriasis and non-alcoholic fatty liver disease (NAFLD) with respect to PASI90 response at Week 12.

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	19 February 2020
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: 8
Country: Number of subjects enrolled	Spain: 2
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	10
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This trial had 10 participants at 7 sites in Germany and one site in Spain. 8 in Germany and 2 in Spain.

Patients who were still in the study when the sponsor terminated the study were counted as 'non-completers'

Pre-assignment

Screening details:

This study was prematurely discontinued after the enrollment of 10 patients, because the recruitment was too slow to achieve the planned number of patients within a reasonable time frame. No safety issues led to the decision to terminate the study prematurely.

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	Investigator, Monitor, Subject, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Investigational Arm - secukinumab

Arm description:

secukinumab 300mg s.c. weekly in first 4 weeks, followed by q4w up to Week 20; and placebo 300mg s.c. at weeks 13, 14 and 15 to maintain the blind

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:

300 mg s.c. (in 2 × 150 mg PFS)

Arm title	Control Arm - placebo

Arm description:

placebo 300 mg s.c. weekly in first 4 weeks, followed by q4w up to Week 8; and secukinumab 300 mg s.c. weekly for 4 weeks starting at Week 12, followed by q4w up to Week 20

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

Dosage and administration details:

300 mg s.c. (in 2 × 150 mg PFS)

Number of subjects in period 1	Investigational Arm - secukinumab	Control Arm - placebo
Started	7	3
Completed	3	1
Not completed	4	2
Study terminated by Sponsor	4	1
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups

Reporting group title	Investigational Arm - secukinumab
Reporting group description:	
secukinumab 300mg s.c. weekly in first 4 weeks, followed by q4w up to Week 20; and placebo 300mg s.c. at weeks 13, 14 and 15 to maintain the blind	
Reporting group title	Control Arm - placebo
Reporting group description:	
placebo 300 mg s.c. weekly in first 4 weeks, followed by q4w up to Week 8; and secukinumab 300 mg s.c. weekly for 4 weeks starting at Week 12, followed by q4w up to Week 20	

Reporting group values	Investigational Arm - secukinumab	Control Arm - placebo	Total
Number of subjects	7	3	10
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	7	3	10
>=65 years	0	0	0
Age Continuous Units: years			
arithmetic mean	41.6	32.0	
standard deviation	± 11.8	± 16.8	-
Sex: Female, Male Units: Participants			
Female	4	0	4
Male	3	3	6
Race/Ethnicity, Customized Units: Subjects			
White	7	3	10

Subject analysis sets

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set (FAS): Comprised all patients to whom study treatment/reference treatment had been assigned by randomization. According to the ITT principle, patients were analyzed according to the treatment they have been assigned to during the randomization procedure. As RAS and FAS populations were identical no separate analysis of the RAS population was performed.	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety Set (SAF): Included all patients who received at least one dose of study treatment/reference treatment. Patients were analyzed according to the study treatment received, where "treatment received" was defined as the randomized treatment, if the patient took at least one dose of that treatment, or the first treatment received, if the randomized treatment was never received.	

Reporting group values	Full Analysis Set	Safety Set	
Number of subjects	10	10	
Age Categorical Units: Participants			
<=18 years	0	0	
Between 18 and 65 years	10	10	
>=65 years	0	0	
Age Continuous Units: years			
arithmetic mean	38.7	38.7	
standard deviation	± 13.3	± 13.3	
Sex: Female, Male Units: Participants			
Female	4	4	
Male	6	6	
Race/Ethnicity, Customized Units: Subjects			
White	10	10	

End points

End points reporting groups

Reporting group title	Investigational Arm - secukinumab

Reporting group description:

secukinumab 300mg s.c. weekly in first 4 weeks, followed by q4w up to Week 20; and placebo 300mg s.c. at weeks 13, 14 and 15 to maintain the blind

Reporting group title	Control Arm - placebo

Reporting group description:

placebo 300 mg s.c. weekly in first 4 weeks, followed by q4w up to Week 8; and secukinumab 300 mg s.c. weekly for 4 weeks starting at Week 12, followed by q4w up to Week 20

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set (FAS): Comprised all patients to whom study treatment/reference treatment had been assigned by randomization. According to the ITT principle, patients were analyzed according to the treatment they have been assigned to during the randomization procedure. As RAS and FAS populations were identical no separate analysis of the RAS population was performed.

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety Set (SAF): Included all patients who received at least one dose of study treatment/reference treatment. Patients were analyzed according to the study treatment received, where "treatment received" was defined as the randomized treatment, if the patient took at least one dose of that treatment, or the first treatment received, if the randomized treatment was never received.

Primary: Mean and SD Change from baseline of PASI score up to week 12

End point title	Mean and SD Change from baseline of PASI score up to week 12[1]

End point description:

Psoriasis Area and Severity Index (PASI) 90 response is defined as ≥ 90% improvement (reduction) in PASI score compared to The primary analysis was planned to be performed comparing treatments with respect to the primary efficacy variable in a logistic regression model. It was planned to present the Odds Ratio and its 95%-confidence interval and p-value. The planned null hypothesis to be rejected was that the Odds Ratio of a PASI90 response for patients with secukinumab vs. patients with placebo is ≥1 after 12 weeks.

Due to the premature study termination and the limited number of treated patients with available data (7 patients in the secukinumab group and 3 patients in the placebo group), the extent of the originally planned statistical analyses of efficacy data was limited to descriptive summaries (absolute values per visit and changes from baseline; presented as mean and standard deviation) for the PASI score.

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

12 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 ANALYSIS WAS PLANNED.

End point values	Investigational Arm - secukinumab	Control Arm - placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	3		
Units: Mean				
arithmetic mean (standard deviation)				
Baseline	15.7 (± 4.22)	15.9 (± 3.39)		
Week 12	0.8 (± 1.14)	13.4 (± 0.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Alanine Aminotransferase (ALT) level up to week 12

End point title	Serum Alanine Aminotransferase (ALT) level up to week 12

End point description:

ALT is an enzyme that the liver releases when it becomes inflamed or damaged. ALT level measures liver function Parameter.

Normal range of values for ALT is about 7 to 56 units per liter (U/L). Higher levels of ALT in the blood indicate more liver problems.

Due to the premature study termination and the limited number of treated patients with available data (7 patients in the secukinumab group and 3 patients in the placebo group), the extent of the originally planned statistical analyses of efficacy data was limited to descriptive summaries (absolute values per visit and changes from baseline; presented as mean and standard deviation) for the ALT score.

No statistical analysis was planned for this secondary outcome.

End point type	Secondary

End point timeframe:

12 weeks

End point values	Investigational Arm - secukinumab	Control Arm - placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	3		
Units: U/L				
arithmetic mean (standard deviation)				
Baseline	60.5 (± 35.73)	89.0 (± 15.56)		
Week 12	43.3 (± 12.76)	85.5 (± 20.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean and SD of DLQI up to week 12

End point title	Mean and SD of DLQI up to week 12

End point description:

Dermatology Life Quality Index (DLQI) is calculated by summing the score of each domain resulting in a maximum of 30 and a minimum of 0. The higher the score, the more Quality of Life was impaired. Meaning of DLQI Scores: 0-1 = no effect at all 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.

Due to the premature study termination and the limited number of treated patients with available data (7 patients in the secukinumab group and 3 patients in the placebo group), the extent of the originally planned statistical analyses of efficacy data was limited to descriptive summaries (absolute values per visit and changes from baseline; presented as mean and standard deviation) for DLQI scores.

No statistical analysis was planned for this secondary outcome.

End point type	Secondary

End point timeframe:

12 weeks

End point values	Investigational Arm - secukinumab	Control Arm - placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	3		
Units: Mean				
arithmetic mean (standard deviation)				
Baseline	11.3 (± 5.56)	8.0 (± 8.49)		
Week 12	0.3 (± 0.50)	7.0 (± 8.49)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) and Serious Adverse Events were collected after signature of the informed consent form until 30 days after last dose of study treatment, and up to 12 weeks

Adverse event reporting additional description:

AEs and SAEs are any untoward sign or symptom that occurs during the study treatment and up to 12 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Secukinumab 300mg

Reporting group description:

Secukinumab 300mg

Reporting group title	Placebo

Reporting group description:

Placebo

Serious adverse events	Secukinumab 300mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (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: 5 %

Non-serious adverse events	Secukinumab 300mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)	2 / 3 (66.67%)	
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Low density lipoprotein increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Urinary sediment abnormal			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Urine analysis abnormal			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 7 (14.29%)	1 / 3 (33.33%)	
occurrences (all)	2	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Psoriasis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 7 (28.57%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Oral herpes			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 June 2020	The main purpose of this amendment is to allow for participation of study sites in Spain and to correct inconsistencies. Additionally, an exclusion criterion was modified to exclude latent tuberculosis patients without completed tuberculosis treatment prior to screening as this treatment may affect liver function parameters that are relevant to secondary endpoints

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to premature termination and limited number of treated patients the extent of originally planned statistical analyses of efficacy was limited to descriptive summaries for the PASI score, ALT values, and DLQI scores

Notes: