Clinical trial results:
A randomized, open-label, multicenter trial to assess the efficacy of subcutaneous secukinumab after twelve weeks of treatment, and to assess the long-term safety, tolerability and efficacy in subjects from 6 to less than 18 years of age with moderate to severe chronic plaque psoriasis

Summary

EudraCT number	2017-004515-39
Trial protocol	BE ES DE CZ EE PL
Global end of trial date	12 September 2023

Results information

Result version number	v1 (current)
This version publication date	16 March 2024
First version publication date	16 March 2024

Trial information

Trial identification

Sponsor protocol code	CAIN457A2311

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03668613
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharmaceuticals, 41 613241111, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000380-PIP01-08
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 September 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of secukinumab in pediatric subjects aged 6 years to less than 18 years old with moderate to severe chronic plaque psoriasis with respect to PASI 75 and IGA mod 2011 0 or 1 response (co-primary endpoints) at Week 12, compared to placebo (historical control).

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	29 August 2018
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	Czechia: 5
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Estonia: 7
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Peru: 5
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	84
EEA total number of subjects	54

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)	33
Adolescents (12-17 years)	51
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 92 subjects were screened of which 84 subjects completed the screening phase and were randomized to the Secukinumab Low dose and High dose groups in a 1:1 ratio.

Pre-assignment

Screening details:

A total of 92 subjects were screened of which 84 subjects completed the screening phase and were randomized to the Secukinumab Low dose and High dose groups in a 1:1 ratio.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	AIN457 Low dose

Arm description:

Subcutaneous (s.c.) secukinumab injections at randomization and weekly until Week 4, thereafter every 4 weeks until Wk 204. Patients received secukinumab 75 mg (if weighing < 50kg) or 150 mg (if weighing >= 50kg)

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457
Other name	Cosentyx
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous (s.c.) secukinumab injections at randomization and weekly until Week 4, thereafter every 4 weeks until Wk 204. Patients received secukinumab 75 mg (if weighing < 50kg) or 150 mg (if weighing >= 50kg)

Arm title	AIN457 High dose

Arm description:

Subcutaneous (s.c.) secukinumab injections at randomization and weekly until Week 4, thereafter every 4 weeks until Wk 204. Patients received secukinumab 75 mg (if weighing < 25kg) or 150mg (if weighing 25 to < 50kg) or 300 mg (if weighing >=50 kg)

Arm type	Experimental
Investigational medicinal product name	Secukinumab
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Other name	Cosentyx
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous (s.c.) secukinumab injections at randomization and weekly until Week 4, thereafter every 4 weeks until Wk 204. Patients received secukinumab 75 mg (if weighing < 25kg) or 150mg (if weighing 25 to < 50kg) or 300 mg (if weighing >=50 kg)

Number of subjects in period 1	AIN457 Low dose	AIN457 High dose
Started	42	42
Completed	31	36
Not completed	11	6
Physician decision	1	-
Consent withdrawn by subject	2	1
Adverse event, non-fatal	1	2
Pregnancy	-	2
Lack of efficacy	5	1
Protocol deviation	1	-
Guardian decision	1	-

Baseline characteristics

Reporting groups	
Reporting group title	AIN457 Low dose
Reporting group description:	
Subcutaneous (s.c.) secukinumab injections at randomization and weekly until Week 4, thereafter every 4 weeks until Wk 204. Patients received secukinumab 75 mg (if weighing < 50kg) or 150 mg (if weighing >= 50kg)	
Reporting group title	AIN457 High dose
Reporting group description:	
Subcutaneous (s.c.) secukinumab injections at randomization and weekly until Week 4, thereafter every 4 weeks until Wk 204. Patients received secukinumab 75 mg (if weighing < 25kg) or 150mg (if weighing 25 to < 50kg) or 300 mg (if weighing >=50 kg)	

Reporting group values	AIN457 Low dose	AIN457 High dose	Total
Number of subjects	42	42	84
Age Categorical Units: Participants			
6 to <12 years	17	16	33
12 to <18 years	25	26	51
Sex: Female, Male Units: Participants			
Female	20	25	45
Male	22	17	39
Race/Ethnicity, Customized Units: Subjects			
White	39	38	77
Black or African American	1	0	1
Asian	1	0	1
American Indian or Alaska Native	1	4	5

End points

End points reporting groups

Reporting group title	AIN457 Low dose
Reporting group description:	
Subcutaneous (s.c.) secukinumab injections at randomization and weekly until Week 4, thereafter every 4 weeks until Wk 204. Patients received secukinumab 75 mg (if weighing < 50kg) or 150 mg (if weighing >= 50kg)	
Reporting group title	AIN457 High dose
Reporting group description:	
Subcutaneous (s.c.) secukinumab injections at randomization and weekly until Week 4, thereafter every 4 weeks until Wk 204. Patients received secukinumab 75 mg (if weighing < 25kg) or 150mg (if weighing 25 to < 50kg) or 300 mg (if weighing >=50 kg)	

Primary: Number and Percentage of Participants with PASI 75 response

End point title	Number and Percentage of Participants with PASI 75 response
End point description:	
Psoriasis Area and Severity Index (PASI):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, trunk, upper limbs and lower limbs); 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,Thickening (plaque elevation, induration) & Scaling(desquamation). Scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section(head: 0.1, upper limbs: 0.2 body: 0.3 lower limbs: 0.4). Psoriasis Area and Severity Index (PASI) will be assessed/calculated as per standard procedure. PASI 75 represents the percentage (or number)of patients who have achieved a 75% or more reduction in their PASI score from baseline. PASI 100 indicates patients who have achieved a complete resolution of all disease.	
End point type	Primary
End point timeframe:	
Week 12	

End point values	AIN457 Low dose	AIN457 High dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	42		
Units: Participants	39	39		

Statistical analyses

Statistical analysis title	AIN457 Low dose v historical placebo
Statistical analysis description:	
Compared to historical placebo	
Comparison groups	AIN457 Low dose v AIN457 High dose

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
Method	Bayesian method using (MAP)
Parameter estimate	Predicted Log-OR
Point estimate	4.862
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.422
upper limit	6.782

Statistical analysis title	AIN457 High dose v historical placebo
Statistical analysis description:	
Compared to historical placebo	
Comparison groups	AIN457 High dose v AIN457 Low dose
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
Method	Bayesian method using (MAP)
Parameter estimate	Predicted log-OR
Point estimate	4.836
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.422
upper limit	6.772

Primary: Number and percentage of participants with IGA mod 2011 0 or 1 response

End point title	Number and percentage of participants with IGA mod 2011 0 or 1 response
End point description:	
Investigator will assess the disease using the validated Investigator Global Assessment (IGA) mod 2011 and rate the disease from a score of 0 (clear skin) to 4 (severe disease)	
End point type	Primary
End point timeframe:	
Week 12	

End point values	AIN457 Low dose	AIN457 High dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	42		
Units: Participants	33	35		

Statistical analyses

Statistical analysis title	AIN457 High dose v historical placebo
Statistical analysis description: Compared to historical placebo	
Comparison groups	AIN457 High dose v AIN457 Low dose
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
Method	Bayesian method using (MAP)
Parameter estimate	Predicted log-OR
Point estimate	4.606
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.919
upper limit	6.78

Statistical analysis title	AIN457 Low dose v historical placebo
Statistical analysis description: Compared to historical placebo	
Comparison groups	AIN457 Low dose v AIN457 High dose
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
Method	Bayesian method using (MAP)
Parameter estimate	Predicted log -OR
Point estimate	4.292
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.638
upper limit	6.513

Secondary: Number and percentage of participants with PASI 90 response

End point title	Number and percentage of participants with PASI 90 response

End point description:

Psoriasis Area and Severity Index (PASI) was assessed/calculated as per the standard procedure.

PASI 90 represents the percentage (or number) of patients who have achieved a 90% or more reduction in their PASI score from baseline. PASI 100 indicates patients who have achieved a complete resolution of all disease.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	AIN457 Low dose	AIN457 High dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	42		
Units: Participants	29	32		

Statistical analyses

Statistical analysis title	AIN457 Low dose v AIN457 High dose
Comparison groups	AIN457 High dose v AIN457 Low dose
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
Method	Bayesian method using (MAP)
Parameter estimate	Predicted log-OR
Point estimate	4.709
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.201
upper limit	6.58

Statistical analysis title	AIN457 Low dose v AIN457 High dose
Comparison groups	AIN457 Low dose v AIN457 High dose
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
Method	Bayesian method using (MAP)
Parameter estimate	Predicted log-OR
Point estimate	4.367
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.916
upper limit	6.202

Secondary: Secukinumab concentration in serum

End point title	Secukinumab concentration in serum

End point description:

Mean (Standard Deviation) Secukinumab concentration levels in serum over time.

End point type	Secondary

End point timeframe:

Baleine, Weeks 4, 12, 13, 14, 15, 16, 24, 52, 104, 156, 208

End point values	AIN457 Low dose	AIN457 High dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	42		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Baseline	0.00 (± 0.00)	0.00 (± 0.00)		
Week 4 (n=40,40)	74.2 (± 33.0)	135 (± 45.3)		
Week 12 (n=40, 39)	34.8 (± 10.9)	69.6 (± 29.2)		
Week 13 (n=38,33)	47.1 (± 17.4)	91.2 (± 34.1)		
Week 14 (n=40, 39)	40.9 (± 15.5)	78.4 (± 29.8)		
Week 15 (n=38,35)	34.6 (± 12.4)	65.7 (± 28.9)		
Week 16 (n=40,37)	30.9 (± 11.2)	55.2 (± 24.9)		
Week 24 (n=42, 38)	26.0 (± 10.8)	48.0 (± 21.4)		
Week 52 (n=37,38)	25.0 (± 9.01)	42.7 (± 17.0)		
Week 104 (n=39,33)	21.9 (± 10.8)	39.3 (± 12.1)		
Week 156 (n=34,32)	19.3 (± 8.68)	35.0 (± 14.1)		
Week 208 (n=25,28)	16.7 (± 6.25)	38.8 (± 17.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary table of Adverse Events

End point title	Summary table of Adverse Events

End point description:

An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a clinical investigation participant after providing written informed consent for participation in the study.

Treatment emergent adverse events in this study are events that started after the first dose of study treatment and until 84 days after the last study treatment, or events present prior to the first dose of treatment which increased in severity based on preferred term within 84 days after the last study treatment.

End point type	Secondary

End point timeframe:

Adverse events are reported from the first dose of study-drug until the end of the treatment period (at

Week 208) plus 16 weeks additional follow up reporting, for a maximum timeframe of approximately 224 weeks.

End point values	AIN457 Low dose	AIN457 High dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	42		
Units: Participants				
Subjects with any AE(s)	33	35		
-Deaths	0	0		
- Non-fatal SAE(s)	4	2		
- Discontinued study treatment due to any AE(s)	1	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are reported from the first dose of study-drug until the end of the treatment period (at Week 208) plus 16 weeks additional follow up reporting, for a maximum timeframe of approximately 224 weeks.

Adverse event reporting additional description:

Treatment emergent adverse events in this study are events that started after the first dose of study treatment and until 84 days after the last study treatment, or events present prior to the first dose of treatment which increased in severity based on preferred term within 84 days after the last study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	AIN457 Low dose

Reporting group description:

AIN457 Low dose

Reporting group title	AIN457 High dose

Reporting group description:

AIN457 High dose

Serious adverse events	AIN457 Low dose	AIN457 High dose	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 42 (9.52%)	2 / 42 (4.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Tibia fracture			
subjects affected / exposed	1 / 42 (2.38%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	1 / 42 (2.38%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Intentional self-injury			

subjects affected / exposed	1 / 42 (2.38%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 42 (2.38%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious mononucleosis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 42 (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	AIN457 Low dose	AIN457 High dose	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 42 (71.43%)	27 / 42 (64.29%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 42 (7.14%)	2 / 42 (4.76%)	
occurrences (all)	5	2	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	3 / 42 (7.14%)	1 / 42 (2.38%)	
occurrences (all)	3	1	
Neutropenia			

subjects affected / exposed	3 / 42 (7.14%)	1 / 42 (2.38%)	
occurrences (all)	4	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 42 (14.29%)	1 / 42 (2.38%)	
occurrences (all)	8	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 42 (9.52%)	2 / 42 (4.76%)	
occurrences (all)	4	2	
Diarrhoea			
subjects affected / exposed	2 / 42 (4.76%)	3 / 42 (7.14%)	
occurrences (all)	3	3	
Vomiting			
subjects affected / exposed	3 / 42 (7.14%)	2 / 42 (4.76%)	
occurrences (all)	3	2	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	7 / 42 (16.67%)	2 / 42 (4.76%)	
occurrences (all)	7	3	
Eczema			
subjects affected / exposed	4 / 42 (9.52%)	0 / 42 (0.00%)	
occurrences (all)	5	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 42 (7.14%)	1 / 42 (2.38%)	
occurrences (all)	5	1	
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 42 (2.38%)	7 / 42 (16.67%)	
occurrences (all)	3	13	
COVID-19			
subjects affected / exposed	11 / 42 (26.19%)	9 / 42 (21.43%)	
occurrences (all)	12	9	
Influenza			

subjects affected / exposed	3 / 42 (7.14%)	1 / 42 (2.38%)	
occurrences (all)	3	1	
Nasopharyngitis			
subjects affected / exposed	13 / 42 (30.95%)	7 / 42 (16.67%)	
occurrences (all)	23	12	
Rhinitis			
subjects affected / exposed	1 / 42 (2.38%)	3 / 42 (7.14%)	
occurrences (all)	1	4	
Tonsillitis			
subjects affected / exposed	2 / 42 (4.76%)	4 / 42 (9.52%)	
occurrences (all)	2	6	
Upper respiratory tract infection			
subjects affected / exposed	0 / 42 (0.00%)	6 / 42 (14.29%)	
occurrences (all)	0	7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 September 2020	The key features of the amendment dated 25-Sep-2020 were changes required due to the COVID-19 pandemic, the addition of inflammatory bowel disease (IBD) as an example for discontinuation of treatment, removal of a sensitivity analysis, and the addition of growth/weight and maturation measurements to the Safety assessments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported