Clinical trial results:
A randomized, multicenter STudy to evaluate the Effect of secukinumab 300 mg s.c. administered during 52 weeks to patients suffering from new-onset moderate to severe plaque Psoriasis as early Intervention compared to standard treatment with narrow-band UVB (STEPIn study)

Summary

EudraCT number	2015-002423-26
Trial protocol	ES FI GB EE SE NO DK CZ HU PL BG DE
Global end of trial date	16 June 2023

Results information

Result version number	v1 (current)
This version publication date	29 June 2024
First version publication date	29 June 2024

Trial information

Trial identification

Sponsor protocol code	CAIN457A2322

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03020199
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 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	16 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 June 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to determine whether early intervention with subcutaneous (s.c.) secukinumab 300 mg in patients with new-onset moderate to severe plaque psoriasis may lead to prolonged symptom-free periods by preventing reactivation of old lesions or ultimately totally hindering the occurrence of new lesions, i.e., changing the natural course of the disease (Main Study).

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	27 March 2017
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	Argentina: 5
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	Estonia: 14
Country: Number of subjects enrolled	Finland: 7
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Poland: 87
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Switzerland: 4
Worldwide total number of subjects	196
EEA total number of subjects	166

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)	196
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were enrolled in 2 study sites in Argentina, 4 in Bulgaria, 2 in Canada, 4 in Germany, 1 in Denmark, 3 in Estonia, 2 in Finland, 2 in Hungary, 6 in Poland, 8 in Spain, 2 in Sweden, 1 in Switzerland, and 4 in the United Kingdom.

Period 1

Period 1 title	Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab 300 mg

Arm description:

Eligible patients received 300 mg secukinumab by subcutaneous (s.c.) injection at baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 48 inclusive (treatment duration = 52 weeks) OR every 4 weeks until Week 100 inclusive (last dose administered at Week 100) (treatment duration = 104 weeks).

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

Dosage and administration details:

Eligible patients received 300 mg secukinumab by subcutaneous (s.c.) injection at baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 48 inclusive (treatment duration = 52 weeks) OR every 4 weeks until Week 100 inclusive (last dose administered at Week 100) (treatment duration = 104 weeks).

Arm title	Narrow-band ultraviolet B (nb-UVB)

Arm description:

Eligible patients received 1 or 2 cycles of narrow-band ultraviolet B (nb-UVB) of 12 weeks each with a maximum break of 28 weeks between cycles (patients with PASI 90 at Week 40 will not receive a second treatment cycle) (treatment duration = 52 weeks).

Arm type	Active comparator
Investigational medicinal product name	Narrow-band ultraviolet B (nb-UVB)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Radiopharmaceutical precursor
Routes of administration	Route of administration not applicable

Dosage and administration details:

Eligible patients received 1 or 2 cycles of narrow-band ultraviolet B (nb-UVB) of 12 weeks each with a maximum break of 28 weeks between cycles (patients with PASI 90 at Week 40 will not receive a second treatment cycle) (treatment duration = 52 weeks).

Number of subjects in period 1	Secukinumab 300 mg	Narrow-band ultraviolet B (nb-UVB)
Started	116	80
Modified Full Analysis Set (mFAS)	77 [1]	76
Subjects not treated	3 [2]	4 [3]
Main Study	80 [4]	80
Mechanistic Sub-study	36 [5]	0 [6]
Completed	103	46
Not completed	13	34
Subjects not treated	3	4
Physician decision	-	1
Adverse event, non-fatal	-	2
Lost to follow-up	1	6
Subject/guardian decision	8	15
Lack of efficacy	1	6

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Only randomized subjects in the Secukinumab 300 mg arm who did not get treated

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: In the Mechanistic Sub-study, 12 new-onset psoriasis patients (Arm A2) and 24 chronic plaque psoriasis patients (12 each in Arms C1 and C2) received similar secukinumab treatment. Arm A2 and C2 patients continued until Week 100 (104-week treatment), while Arm C1 ended at Week 48 (52-week treatment).

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Only subjects from the Mechanistic Study not accounted for as part of the Main study

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: In the Main Study, 80 new-onset psoriasis patients in Arm A1 (68 in Arm A1a, 12 in Arm A1b) received 300 mg secukinumab injections weekly for the first month, then every 4 weeks until Week 48 (52-week treatment).Arm A1b patients also joined the Mechanistic Sub-study.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: All randomized subjects who received at least one dose of study treatment during the Treatment Period

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Only randomized subjects in the Narrow-band ultraviolet B (nb-UVB) arm who did not get treated

Period 2

Period 2 title	Follow-up Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	No
Arm title	Secukinumab 300 mg

Arm description:

Eligible patients received 300 mg secukinumab by subcutaneous (s.c.) injection at baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 48 inclusive (treatment duration = 52 weeks) OR every 4 weeks until Week 100 inclusive (last dose administered at Week 100) (treatment duration = 104 weeks).

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

Dosage and administration details:

Eligible patients received 300 mg secukinumab by subcutaneous (s.c.) injection at baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 48 inclusive (treatment duration = 52 weeks) OR every 4 weeks until Week 100 inclusive (last dose administered at Week 100) (treatment duration = 104 weeks).

Arm title	Narrow-band ultraviolet B (nb-UVB)

Arm description:

Eligible patients received 1 or 2 cycles of narrow-band ultraviolet B (nb-UVB) of 12 weeks each with a maximum break of 28 weeks between cycles (patients with PASI 90 at Week 40 will not receive a second treatment cycle) (treatment duration = 52 weeks).

Arm type	Active comparator
Investigational medicinal product name	Narrow-band ultraviolet B (nb-UVB)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Radiopharmaceutical precursor
Routes of administration	Route of administration not applicable

Dosage and administration details:

Eligible patients received 1 or 2 cycles of narrow-band ultraviolet B (nb-UVB) of 12 weeks each with a maximum break of 28 weeks between cycles (patients with PASI 90 at Week 40 will not receive a second treatment cycle) (treatment duration = 52 weeks).

Number of subjects in period 2	Secukinumab 300 mg	Narrow-band ultraviolet B (nb-UVB)
Started	73	39
Main Study	67	39
Mechanistic Sub-study	6 [7]	0 [8]
Completed	13	8
Not completed	60	31
Physician decision	2	2
Study terminated by Sponsor	6	3
Disease relapse	32	7
Lost to follow-up	4	6
Subject/guardian decision	14	9
Lack of efficacy	1	2
Protocol deviation	1	2

Notes:

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only subjects from the Mechanistic Study not accounted for as part of the Main study

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: In the Main Study, 80 new-onset psoriasis patients in Arm B1 (68 in Arm B1a and 12 in Arm B1b) received 1 or 2 cycles of nb UVB of 12 weeks each with a maximum break of 28 weeks between cycles (patients with PASI 90 at Week 40 did not receive a second treatment cycle) (treatment duration = 52 weeks).Patients from Arm B1b participated also in the Mechanistic Sub-study, but is accounted as part of the Main Study.

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab 300 mg
Reporting group description:	
Eligible patients received 300 mg secukinumab by subcutaneous (s.c.) injection at baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 48 inclusive (treatment duration = 52 weeks) OR every 4 weeks until Week 100 inclusive (last dose administered at Week 100) (treatment duration = 104 weeks).	
Reporting group title	Narrow-band ultraviolet B (nb-UVB)
Reporting group description:	
Eligible patients received 1 or 2 cycles of narrow-band ultraviolet B (nb-UVB) of 12 weeks each with a maximum break of 28 weeks between cycles (patients with PASI 90 at Week 40 will not receive a second treatment cycle) (treatment duration = 52 weeks).	

Reporting group values	Secukinumab 300 mg	Narrow-band ultraviolet B (nb-UVB)	Total
Number of subjects	116	80	196
Age Categorical Units: Participants			
18 to 30 years	56	30	86
31 to 50 years	60	50	110
Sex: Female, Male Units: Participants			
Female	35	25	60
Male	81	55	136
Race/Ethnicity, Customized Units: Subjects			
Black or African American	1	1	2
Asian	2	3	5
American Indian or Alaska Native	0	1	1
White	113	72	185
Unknown	0	1	1
Other	0	2	2

End points

End points reporting groups

Reporting group title	Secukinumab 300 mg

Reporting group description:

Eligible patients received 300 mg secukinumab by subcutaneous (s.c.) injection at baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 48 inclusive (treatment duration = 52 weeks) OR every 4 weeks until Week 100 inclusive (last dose administered at Week 100) (treatment duration = 104 weeks).

Reporting group title	Narrow-band ultraviolet B (nb-UVB)

Reporting group description:

Eligible patients received 1 or 2 cycles of narrow-band ultraviolet B (nb-UVB) of 12 weeks each with a maximum break of 28 weeks between cycles (patients with PASI 90 at Week 40 will not receive a second treatment cycle) (treatment duration = 52 weeks).

Reporting group title	Secukinumab 300 mg

Reporting group description:

Eligible patients received 300 mg secukinumab by subcutaneous (s.c.) injection at baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 48 inclusive (treatment duration = 52 weeks) OR every 4 weeks until Week 100 inclusive (last dose administered at Week 100) (treatment duration = 104 weeks).

Reporting group title	Narrow-band ultraviolet B (nb-UVB)

Reporting group description:

Eligible patients received 1 or 2 cycles of narrow-band ultraviolet B (nb-UVB) of 12 weeks each with a maximum break of 28 weeks between cycles (patients with PASI 90 at Week 40 will not receive a second treatment cycle) (treatment duration = 52 weeks).

Subject analysis set title	Secukinumab 300 mg A1 (A1a+A1b)
Subject analysis set type	Full analysis

Subject analysis set description:

80 patients (68 in Arm A1a and 12 in Arm A1b) with new-onset psoriasis will receive 300 mg secukinumab by subcutaneous (s.c.) injection at baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 48 inclusive (treatment duration = 52 weeks).

Subject analysis set title	Narrow-band ultraviolet B (nb-UVB) B1 (B1a+B1b)
Subject analysis set type	Full analysis

Subject analysis set description:

80 patients (68 in Arm B1a and 12 in Arm B1b) with new-onset psoriasis received 1 or 2 cycles of narrow-band ultraviolet B (nb-UVB) of 12 weeks each with a maximum break of 28 weeks between cycles (patients with PASI 90 at Week 40 will not receive a second treatment cycle) (treatment duration = 52 weeks).

Primary: Number of participants who achieved Pain Assessment Severity Index (PASI) 90 at Week 52.

End point title	Number of participants who achieved Pain Assessment Severity Index (PASI) 90 at Week 52.

End point description:

The PASI quantifies the severity of a participant's psoriasis based on both "lesion severity" and the "percent of Body Surface Area (BSA)" affected. PASI is a composite scoring by the investigator of degree of erythema, induration, and scaling (each scored separately) for each of 4 body regions (head and neck, upper limbs, trunk [including axillae and groin], and lower limbs [including buttocks]), with adjustment for the percent of BSA involved for each body region and for the proportion of the body region to the whole body. The PASI composite score varies in increments of 0.1 and range from 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. PASI 90 response is a binary measure defined as at least a 90% improvement in PASI score at Week 52, relative to baseline PASI score.

End point type	Primary

End point timeframe:

Baseline, Week 52

End point values	Secukinumab 300 mg A1 (A1a+A1b)	Narrow-band ultraviolet B (nb-UVB) B1 (B1a+B1b)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	77	76		
Units: Participants	70	32		

Statistical analyses

Statistical analysis title	Week 52 PASI 90
Comparison groups	Secukinumab 300 mg A1 (A1a+A1b) v Narrow-band ultraviolet B (nb-UVB) B1 (B1a+B1b)
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	16.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.9
upper limit	48.3

Secondary: Number of participants who achieved PASI 90 at Week 104

End point title	Number of participants who achieved PASI 90 at Week 104

End point description:

The PASI quantifies the severity of a participant's psoriasis based on both "lesion severity" and the "percent of Body Surface Area (BSA)" affected. PASI is a composite scoring by the investigator of degree of erythema, induration, and scaling (each scored separately) for each of 4 body regions (head and neck, upper limbs, trunk [including axillae and groin], and lower limbs [including buttocks]), with adjustment for the percent of BSA involved for each body region and for the proportion of the body region to the whole body. The PASI composite score varies in increments of 0.1 and range from 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. PASI 90 response is a binary measure defined as at least a 90% improvement in PASI score at Week 104, relative to baseline PASI score.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Secukinumab 300 mg A1 (A1a+A1b)	Narrow-band ultraviolet B (nb-UVB) B1 (B1a+B1b)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	77	76		
Units: Participants	23	26		

Statistical analyses

Statistical analysis title	Week 104 PASI 90
Comparison groups	Secukinumab 300 mg A1 (A1a+A1b) v Narrow-band ultraviolet B (nb-UVB) B1 (B1a+B1b)
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.653
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	2.1

Secondary: Number of participants with IGA mod 2011 0/1 response at Week 52

End point title	Number of participants with IGA mod 2011 0/1 response at Week 52

End point description:

Investigators assessed the disease using the validated Investigator Global Assessment (IGA) mod 2011 and rated the disease from a score of 0 (clear skin) to 4 (severe disease). Response is defined as a score of 0 or 1 at Week 52.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Secukinumab 300 mg A1 (A1a+A1b)	Narrow-band ultraviolet B (nb-UVB) B1 (B1a+B1b)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	77	76		
Units: Percentage of participants				
number (confidence interval 95%)	85.7 (75.5 to 92.3)	36.8 (26.3 to 48.7)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent include AE from First dose to last dose plus 84 days. Follow-up phase include AE recorded after last dose plus 84 days.

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	26.0

Reporting groups

Reporting group title	Treatment emergent@Secukinumab 300 mg@(A1a+A1b+A2+C1+C2)

Reporting group description:

Treatment emergent@Secukinumab 300 mg@(A1a+A1b+A2+C1+C2)

Reporting group title	Follow-up@nb-UVB@(B1a+B1b)

Reporting group description:

Follow-up@nb-UVB@(B1a+B1b)

Reporting group title	Follow-up@Secukinumab 300 mg@(A1a+A1b+A2)

Reporting group description:

Follow-up@Secukinumab 300 mg@(A1a+A1b+A2)

Reporting group title	Treatment emergent@nb-UVB@(B1a+B1b)

Reporting group description:

Treatment emergent@nb-UVB@(B1a+B1b)

Serious adverse events	Treatment emergent@Secukinumab 300 mg@(A1a+A1b+A2+C1+C2)	Follow-up@nb-UVB@(B1a+B1b)	Follow-up@Secukinumab 300 mg@(A1a+A1b+A2)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 112 (5.36%)	1 / 76 (1.32%)	0 / 88 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 112 (0.89%)	0 / 76 (0.00%)	0 / 88 (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
Tibia fracture			

subjects affected / exposed	1 / 112 (0.89%)	0 / 76 (0.00%)	0 / 88 (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
Post procedural haemorrhage			
subjects affected / exposed	1 / 112 (0.89%)	0 / 76 (0.00%)	0 / 88 (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
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	0 / 112 (0.00%)	1 / 76 (1.32%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Umbilical hernia			
subjects affected / exposed	1 / 112 (0.89%)	0 / 76 (0.00%)	0 / 88 (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
Respiratory, thoracic and mediastinal disorders			
Vocal cord polyp			
subjects affected / exposed	0 / 112 (0.00%)	0 / 76 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	1 / 112 (0.89%)	0 / 76 (0.00%)	0 / 88 (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
Psychiatric disorders			
Acute stress disorder			
subjects affected / exposed	1 / 112 (0.89%)	0 / 76 (0.00%)	0 / 88 (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

Serious adverse events	Treatment emergent@nb-UVB@(B1a+B1b)		
Total subjects affected by serious			

adverse events			
subjects affected / exposed	1 / 76 (1.32%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Umbilical hernia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Vocal cord polyp			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Asthma			

subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Acute stress disorder			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Treatment emergent@Secukinumab 300 mg@(A1a+A1b+A2+C1+C2)	Follow-up@nb-UVB@(B1a+B1b)	Follow-up@Secukinumab 300 mg@(A1a+A1b+A2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 112 (25.89%)	2 / 76 (2.63%)	7 / 88 (7.95%)
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 112 (9.82%)	0 / 76 (0.00%)	1 / 88 (1.14%)
occurrences (all)	27	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 112 (6.25%)	1 / 76 (1.32%)	5 / 88 (5.68%)
occurrences (all)	8	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 112 (9.82%)	1 / 76 (1.32%)	3 / 88 (3.41%)
occurrences (all)	17	0	0
Upper respiratory tract infection			
subjects affected / exposed	8 / 112 (7.14%)	2 / 76 (2.63%)	0 / 88 (0.00%)
occurrences (all)	9	0	0

Non-serious adverse events	Treatment emergent@nb-UVB@(B1a+B1b)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 76 (10.53%)		

Nervous system disorders Headache subjects affected / exposed occurrences (all)	 1 / 76 (1.32%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 0 / 76 (0.00%) 0		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 5 / 76 (6.58%) 5 2 / 76 (2.63%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 April 2017	Amendment 1: • The IGA mod 2011 was included as additional secondary and exploratory objectives; • The assessment of epigenetic imprinting in skin biopsies was introduced as part of the exploratory objectives; • The upper limit of the age range for inclusion of subjects in the study was changed from 40 years to 50 years; • The risks-benefit section was updated with information on risks for secukinumab, biopsies and others; • The exclusion criterion involving barrier methods of contraception was modified to include applicable countries other than the UK; • The optional use of calcipotriol 50 µg/g and betamethasone 0.5 mg/g with nb UVB was further clarified; • The number of subjects per group in the Mechanistic Sub-study was reduced from 15 to 12; • The number of biopsies to be taken from lesional or resolved skin and from never-lesional skin was corrected
23 September 2019	Amendment 2: • Clarification was added that subjects who discontinued the study during the Follow-up Epoch would have all EOS assessments performed; • Inclusion criterion 3 was modified by allowing earlier episodes of mild psoriasis resolved spontaneously within 6 months; • Withdrawal of consent language was modified to align with the requirements of the General Data Protection Regulation; • Table 6-2 was updated to reflect that a biopsy had to be taken at Week 52 for Arm A2 and Arm C2 to ensure consistency with Table 6-1; • Table 6-3 was updated with the definition of EOS; • The hypothesis testing for the efficacy analyses was modified to 1-sided tests at 2.5% significance level instead of 2-sided at 5% significance level; • Age and BMI were included as covariates for the analyses; • The Wald's test was replaced by the Fisher's exact test, which is mainly used when the sample size is small or the proportions are extreme; • Clarification was added that missing data for the primary endpoint and the key secondary endpoint were to be imputed with modified multiple imputation method; • The power of the key secondary endpoint was re-assessed after considering dropout rates; • The assumptions for the sample size calculations were modified. The software for the calculation was modified from nQuery Advisor® 7.0 to PASS 11

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.

The study ended early due to few patients left in the long-term extension phase, hindering significant conclusions. This early termination did not impact the study's main or secondary goals, and the decision was not related to any safety concerns.

Notes: