Clinical trial results:
A randomized, double-blind, multi-center study assessing short (16 weeks) and long-term efficacy (up to 1 year), safety, and tolerability of 2 subcutaneous secukinumab dose regimens in adult patients with moderate to severe hidradenitis suppurativa (SUNSHINE).

Summary

EudraCT number	2018-002063-26
Trial protocol	GB FR DE PT HU SK CZ BE GR AT SE ES BG IT
Global end of trial date	26 July 2022

Results information

Result version number	v1 (current)
This version publication date	30 July 2023
First version publication date	30 July 2023

Trial information

Trial identification

Sponsor protocol code	CAIN457M2301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03713619
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novarts 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	Study Director, Novarts Pharma AG, 1 (862) 778-8300, 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	20 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of secukinumab compared to placebo with respect to HiSCR after 16 weeks of treatment.

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 January 2019
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	Argentina: 9
Country: Number of subjects enrolled	Australia: 18
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Bulgaria: 8
Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	Czechia: 18
Country: Number of subjects enrolled	France: 56
Country: Number of subjects enrolled	Germany: 64
Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Greece: 19
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	India: 10
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Japan: 22
Country: Number of subjects enrolled	Korea, Republic of: 9
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Philippines: 8

Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	Portugal: 26
Country: Number of subjects enrolled	Russian Federation: 17
Country: Number of subjects enrolled	Slovakia: 8
Country: Number of subjects enrolled	Spain: 26
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Switzerland: 11
Country: Number of subjects enrolled	Taiwan: 14
Country: Number of subjects enrolled	Turkey: 9
Country: Number of subjects enrolled	United States: 84
Worldwide total number of subjects	541
EEA total number of subjects	274

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)	534
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

544 enrolled but 1 patient was misrandomized and 2 had severe GCP violations.

Pre-assignment

Screening details:

There was a screening period of up to 4 weeks.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	secukinumab 1 - Q2W

Arm description:

Secukinumab 300mg every 2 weeks

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

Dosage and administration details:

Secukinumab 300mg every 2 weeks

Arm title	secukinumab 2 - Q4W

Arm description:

Secukinumab 300mg every 4 weeks

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

Dosage and administration details:

secukinumab 300mg every 4 weeks

Arm title	placebo

Arm description:

Placebo group to secukinumab 300mg

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

Dosage and administration details:
placebo

Number of subjects in period 1	secukinumab 1 - Q2W	secukinumab 2 - Q4W	placebo
Started	181	180	180
Completed	168	169	172
Not completed	13	11	8
Physician decision	1	1	1
Consent withdrawn by subject	4	9	5
Adverse event, non-fatal	4	-	1
Technical problems	1	-	-
Lost to follow-up	3	1	1

Baseline characteristics

Reporting groups	
Reporting group title	secukinumab 1 - Q2W
Reporting group description: Secukinumab 300mg every 2 weeks	
Reporting group title	secukinumab 2 - Q4W
Reporting group description: Secukinumab 300mg every 4 weeks	
Reporting group title	placebo
Reporting group description: Placebo group to secukinumab 300mg	

Reporting group values	secukinumab 1 - Q2W	secukinumab 2 - Q4W	placebo
Number of subjects	181	180	180
Age Categorical Units: participants			
<=18 years	0	0	0
Between 18 and 65 years	178	177	179
>=65 years	3	3	1
Age Continuous Units: years			
arithmetic mean	37.1	35.7	0
standard deviation	± 12.53	± 11.71	± 0
Sex: Female, Male Units: participants			
Female	102	100	102
Male	79	80	78
Race/Ethnicity, Customized Units: Subjects			
White	145	146	139
Black or African American	15	10	12
Asian	19	23	24
American Indian or Alaska Native	1	1	2
Multiple	1	0	3

Reporting group values	Total		
Number of subjects	541		
Age Categorical Units: participants			
<=18 years	0		
Between 18 and 65 years	534		
>=65 years	7		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		

Sex: Female, Male Units: participants			
Female	304		
Male	237		
Race/Ethnicity, Customized Units: Subjects			
White	430		
Black or African American	37		
Asian	66		
American Indian or Alaska Native	4		
Multiple	4		

Subject analysis sets

Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo group to secukinumab 300mg every 4 weeks	
Subject analysis set title	placebo 2
Subject analysis set type	Full analysis
Subject analysis set description: Placebo group to secukinumab 300mg	

Reporting group values	Placebo	placebo 2	
Number of subjects	180	180	
Age Categorical Units: participants			
<=18 years	0	0	
Between 18 and 65 years	179	0	
>=65 years	1	0	
Age Continuous Units: years			
arithmetic mean	35.5	52.2	
standard deviation	± 10.75	±	
Sex: Female, Male Units: participants			
Female	102	0	
Male	78	0	
Race/Ethnicity, Customized Units: Subjects			
White	139	0	
Black or African American	12	0	
Asian	24	0	
American Indian or Alaska Native	2	0	
Multiple	3	0	

End points

End points reporting groups

Reporting group title	secukinumab 1 - Q2W
Reporting group description: Secukinumab 300mg every 2 weeks	
Reporting group title	secukinumab 2 - Q4W
Reporting group description: Secukinumab 300mg every 4 weeks	
Reporting group title	placebo
Reporting group description: Placebo group to secukinumab 300mg	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo group to secukinumab 300mg every 4 weeks	
Subject analysis set title	placebo 2
Subject analysis set type	Full analysis
Subject analysis set description: Placebo group to secukinumab 300mg	

Primary: Proportion of participants with Hidradenitis Suppurativa clinical response (HiSCR)

End point title	Proportion of participants with Hidradenitis Suppurativa clinical response (HiSCR)

End point description:

HiSCR at Week 16 is defined as at least a 50% decrease in Abscess and inflammatory Nodule (AN) count compared to baseline with no increase in the number of abscesses and/or in the number of draining fistulas from baseline to Week 16. The baseline is defined as the last assessment (including unscheduled visits) obtained before/on the day of the first administration of the study treatment, or on the randomization date if there had been no drug administration.
The primary endpoint was analyzed by logistic regression. Missing data were multiply imputed based on the estimand strategy related to intercurrent events or missing at random assumption for all missing values not related to intercurrent events.
The number of participants reported in this record corresponds to the rounded average number of participants with response in 100 imputed data sets.

End point type	Primary

End point timeframe:

Baseline, 16 weeks

End point values	secukinumab 1 - Q2W	secukinumab 2 - Q4W	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	181	180	180	
Units: Rounded average number of subjects				
number (not applicable)	81.5	75.2	60.7	

Statistical analyses

Statistical analysis title	Proportion of participants with (HiSCR)
Statistical analysis description:	
Logistic regression analysis of HiSCR50 response at Week 16 (multiple imputation)	
Comparison groups	secukinumab 2 - Q4W v placebo
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0418
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	2.32

Statistical analysis title	Proportion of participants with (HiSCR)
Statistical analysis description:	
Logistic regression analysis of HiSCR50 response at Week 16 (multiple imputation)	
Comparison groups	secukinumab 1 - Q2W v placebo
Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	1.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	2.73

Secondary: Percentage change from baseline in AN count at Week 16

End point title	Percentage change from baseline in AN count at Week 16

End point description:

The HS affected areas, e.g. right and left axillary (armpit), right and left gluteal ("buttock"), right and left inguinal-femoral (groin), perineal, pubic, sternal, right and left sub-mammary (breast) and others were assessed by the physician for abscesses, inflammatory nodules, draining fistulas, total fistulas, and other lesions.
Inflammatory lesions, including abscesses, nodules, draining fistulae, total fistulae and other lesions were counted. The analysis method for percentage change from baseline in abscesses and inflammatory nodules (AN) count at Week 16 was an ANCOVA model.

End point type	Secondary

End point timeframe:
Baseline, 16 weeks

End point values	secukinumab 1 - Q2W	secukinumab 2 - Q4W	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	181	180	180	
Units: percentage change from baseline				
arithmetic mean (standard error)	-46.8 (± 3.33)	-42.4 (± 4.01)	-24.3 (± 4.33)	

Statistical analyses

Statistical analysis title	Percentage change from baseline in AN count
Statistical analysis description:	
Analysis of covariance of percentage change from baseline in AN count at Week 16 (multiple imputation)	
Comparison groups	secukinumab 2 - Q4W v placebo
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	ANCOVA
Parameter estimate	Least Square Mean difference
Point estimate	-18.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.32
upper limit	-7.6

Statistical analysis title	Percentage change from baseline in AN count
Statistical analysis description:	
Analysis of covariance of percentage change from baseline in AN count at Week 16 (multiple imputation)	
Comparison groups	secukinumab 1 - Q2W v placebo
Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Least square Mean Difference
Point estimate	-23.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.9
upper limit	-12.21

Secondary: Proportion of patients with Hidradenitis Suppurativa (HS) flares

End point title	Proportion of patients with Hidradenitis Suppurativa (HS)

End point description:

Flare was defined as at least a 25% increase in AN count with a minimum increase of 2 AN compared to baseline.
The proportion of patients with HS flares was analyzed by logistic regression.
The number of participants reported in this record corresponds to the rounded average number of participants with response in 100 imputed data sets

End point type	Secondary

End point timeframe:

Baseline, 16 weeks

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Stats analysis were not planned for all arms

End point values	secukinumab 1 - Q2W	secukinumab 2 - Q4W	placebo 2	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	181	180	180	
Units: rounded average number of participants				
number (not applicable)	27.8	41.7	52.2	

Statistical analyses

Statistical analysis title	Proportion of patients with HS flares

Statistical analysis description:

Logistic regression analysis of Flare over 16 weeks (multiple imputation)

Comparison groups	secukinumab 2 - Q4W v placebo 2
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0926
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.17

Statistical analysis title	Proportion of patients with HS flares
Statistical analysis description:	
Logistic regression analysis of Flare over 16 weeks (multiple imputation)	
Comparison groups	secukinumab 1 - Q2W v placebo 2
Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.73

Secondary: Participants achieving NRS30 (Skin pain)

End point title	Participants achieving NRS30 (Skin pain)

End point description:

The Patient's global assessment of skin pain - numerical rating scale (NRS) in the past 24 hours was used to assess pain "at its worst" and the average skin pain due to HS in the last 24 hours. The NRS is a segmented numeric version of the visual analog scale in which a respondent selects a whole number (0–10 integers) that best reflects the intensity of their pain ranging from 0 (no skin pain) to 10 (skin pain as bad as you can imagine).

NRS30 (skin pain) is defined as at least a 30% reduction and at least 2 units reduction from baseline in Patient's Global Assessment of Skin Pain - at worst.
This endpoint was analyzed by logistic regression. The number of participants reported in this record corresponds to the rounded average number of participants with response in 100 imputed data sets.

End point type	Secondary

End point timeframe:

Baseline, 16 weeks

End point values	secukinumab 1 - Q2W	secukinumab 2 - Q4W	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	181	180	180	
Units: rounded average number of participants				
number (not applicable)	97.2	84.4	57.8	

Statistical analyses

Statistical analysis title	Participants achieving NRS30
Statistical analysis description:	
Logistic regression analysis of skin pain/NRS30 response at Week 16 (pooled data, multiple imputation)	
Comparison groups	secukinumab 2 - Q4W v placebo
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0044
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	2.7

Statistical analysis title	Participants achieving NRS30
Statistical analysis description:	
Logistic regression analysis of skin pain/NRS30 response at Week 16 (pooled data, multiple imputation)	
Comparison groups	secukinumab 1 - Q2W v placebo
Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	2.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.37
upper limit	3.16

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were reported from first dose of study treatment, up to approximately 60 weeks for AIN457 (up to 52 weeks for subjects moving to extension study) and 16 weeks for placebo.

Adverse event reporting additional description:

AEs are any sign or symptom that occurs during the conduct of the trial and safety follow-up.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	AIN457 Q2W

Reporting group description:

Subjects who were randomized to AIN457 (secukinumab) 300mg Q2W dose regimen at the study entry. Adverse events were assessed up to Week 52

Reporting group title	AIN457 Q4W

Reporting group description:

Subjects who were randomized to AIN457 (secukinumab) 300mg Q4W dose regimen at the study entry. Adverse events were assessed up to Week 52

Reporting group title	Placebo

Reporting group description:

Subjects received matching placebo up to 16 weeks

Reporting group title	Any AIN457 Q2W

Reporting group description:

Subjects who received at least 1 dose of secukinumab 300 mg Q2W dose (e.g., subjects who switched from placebo to secukinumab Q2W at Week 16). Adverse events were assessed up to Week 52

Reporting group title	Any AIN457 Q4W

Reporting group description:

Subjects who received at least 1 dose of secukinumab 300 mg Q4W dose (e.g., subjects who switched from placebo to secukinumab Q4W at Week 16). Adverse events were assessed up to Week 52

Reporting group title	Any AIN457

Reporting group description:

Subjects who received at least 1 dose of secukinumab

Serious adverse events	AIN457 Q2W	AIN457 Q4W	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 181 (7.18%)	9 / 180 (5.00%)	6 / 180 (3.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung cancer metastatic			

subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer metastatic			
subjects affected / exposed	1 / 181 (0.55%)	0 / 180 (0.00%)	0 / 180 (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			
Hypertensive emergency			
subjects affected / exposed	0 / 181 (0.00%)	1 / 180 (0.56%)	0 / 180 (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
Thrombosis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 180 (0.00%)	0 / 180 (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
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Pyrexia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 181 (0.55%)	0 / 180 (0.00%)	0 / 180 (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
Sleep apnoea syndrome			

subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 181 (0.55%)	0 / 180 (0.00%)	0 / 180 (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
Suicide attempt			
subjects affected / exposed	1 / 181 (0.55%)	0 / 180 (0.00%)	0 / 180 (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
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	1 / 181 (0.55%)	0 / 180 (0.00%)	0 / 180 (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
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 180 (0.56%)	0 / 180 (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
Tachycardia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Nervous system disorders			
Dizziness			

subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Headache			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Sciatica			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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			
Abdominal pain			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Constipation			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 181 (0.55%)	0 / 180 (0.00%)	0 / 180 (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
Vomiting			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Skin and subcutaneous tissue disorders			

Hidradenitis			
subjects affected / exposed	3 / 181 (1.66%)	3 / 180 (1.67%)	2 / 180 (1.11%)
occurrences causally related to treatment / all	1 / 3	0 / 3	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
C3 glomerulopathy			
subjects affected / exposed	0 / 181 (0.00%)	1 / 180 (0.56%)	0 / 180 (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
Ureterolithiasis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 180 (0.56%)	0 / 180 (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
Breast cellulitis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 180 (0.56%)	0 / 180 (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
COVID-19			
subjects affected / exposed	1 / 181 (0.55%)	0 / 180 (0.00%)	0 / 180 (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
Cellulitis			

subjects affected / exposed	1 / 181 (0.55%)	1 / 180 (0.56%)	0 / 180 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Influenza			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Large intestine infection			
subjects affected / exposed	1 / 181 (0.55%)	0 / 180 (0.00%)	0 / 180 (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
Peritonsillar abscess			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Pneumonia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Post procedural infection			
subjects affected / exposed	0 / 181 (0.00%)	1 / 180 (0.56%)	0 / 180 (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
Sepsis			

subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Sweat gland infection			
subjects affected / exposed	1 / 181 (0.55%)	3 / 180 (1.67%)	0 / 180 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin candida			
subjects affected / exposed	0 / 181 (0.00%)	0 / 180 (0.00%)	0 / 180 (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
Urinary tract infection			
subjects affected / exposed	0 / 181 (0.00%)	1 / 180 (0.56%)	0 / 180 (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

Serious adverse events	Any AIN457 Q2W	Any AIN457 Q4W	Any AIN457
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 266 (6.77%)	19 / 267 (7.12%)	37 / 533 (6.94%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung cancer metastatic			
subjects affected / exposed	0 / 266 (0.00%)	0 / 267 (0.00%)	0 / 533 (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
Non-small cell lung cancer metastatic			
subjects affected / exposed	1 / 266 (0.38%)	0 / 267 (0.00%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive emergency			

subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	1 / 266 (0.38%)	0 / 267 (0.00%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 266 (0.38%)	0 / 267 (0.00%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome			
subjects affected / exposed	1 / 266 (0.38%)	0 / 267 (0.00%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 266 (0.38%)	0 / 267 (0.00%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			

subjects affected / exposed	1 / 266 (0.38%)	0 / 267 (0.00%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 266 (0.00%)	0 / 267 (0.00%)	0 / 533 (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
Meniscus injury			
subjects affected / exposed	1 / 266 (0.38%)	0 / 267 (0.00%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 266 (0.00%)	0 / 267 (0.00%)	0 / 533 (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
Inguinal hernia			
subjects affected / exposed	1 / 266 (0.38%)	0 / 267 (0.00%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	4 / 266 (1.50%)	4 / 267 (1.50%)	8 / 533 (1.50%)
occurrences causally related to treatment / all	1 / 4	1 / 4	2 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
C3 glomerulopathy			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			

subjects affected / exposed	0 / 266 (0.00%)	0 / 267 (0.00%)	0 / 533 (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
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	1 / 266 (0.38%)	0 / 267 (0.00%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 266 (0.38%)	1 / 267 (0.37%)	2 / 533 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cellulitis			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 266 (0.38%)	1 / 267 (0.37%)	2 / 533 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 266 (0.38%)	1 / 267 (0.37%)	2 / 533 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 266 (0.00%)	0 / 267 (0.00%)	0 / 533 (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
Infection			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Influenza			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine infection			
subjects affected / exposed	1 / 266 (0.38%)	0 / 267 (0.00%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 266 (0.00%)	2 / 267 (0.75%)	2 / 533 (0.38%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sweat gland infection			
subjects affected / exposed	1 / 266 (0.38%)	3 / 267 (1.12%)	4 / 533 (0.75%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin candida			
subjects affected / exposed	1 / 266 (0.38%)	0 / 267 (0.00%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 266 (0.00%)	1 / 267 (0.37%)	1 / 533 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	AIN457 Q2W	AIN457 Q4W	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	135 / 181 (74.59%)	132 / 180 (73.33%)	88 / 180 (48.89%)
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 181 (3.31%)	4 / 180 (2.22%)	2 / 180 (1.11%)
occurrences (all)	6	4	2
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 181 (1.66%)	4 / 180 (2.22%)	4 / 180 (2.22%)
occurrences (all)	5	4	4
Chest pain			
subjects affected / exposed	0 / 181 (0.00%)	5 / 180 (2.78%)	0 / 180 (0.00%)
occurrences (all)	0	5	0
Fatigue			
subjects affected / exposed	6 / 181 (3.31%)	11 / 180 (6.11%)	8 / 180 (4.44%)
occurrences (all)	7	12	8
Pyrexia			
subjects affected / exposed	13 / 181 (7.18%)	8 / 180 (4.44%)	2 / 180 (1.11%)
occurrences (all)	20	9	2
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 181 (0.55%)	1 / 180 (0.56%)	4 / 180 (2.22%)
occurrences (all)	1	2	13
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	9 / 181 (4.97%)	5 / 180 (2.78%)	3 / 180 (1.67%)
occurrences (all)	9	5	3
Cough			

subjects affected / exposed	4 / 181 (2.21%)	8 / 180 (4.44%)	1 / 180 (0.56%)
occurrences (all)	4	10	1
Rhinorrhoea			
subjects affected / exposed	8 / 181 (4.42%)	2 / 180 (1.11%)	2 / 180 (1.11%)
occurrences (all)	9	2	2
Psychiatric disorders			
Depression			
subjects affected / exposed	4 / 181 (2.21%)	2 / 180 (1.11%)	2 / 180 (1.11%)
occurrences (all)	4	2	2
Investigations			
Amylase increased			
subjects affected / exposed	3 / 181 (1.66%)	4 / 180 (2.22%)	0 / 180 (0.00%)
occurrences (all)	3	4	0
SARS-CoV-2 test negative			
subjects affected / exposed	6 / 181 (3.31%)	5 / 180 (2.78%)	2 / 180 (1.11%)
occurrences (all)	6	6	3
Lipase increased			
subjects affected / exposed	8 / 181 (4.42%)	7 / 180 (3.89%)	2 / 180 (1.11%)
occurrences (all)	8	7	2
SARS-CoV-2 test positive			
subjects affected / exposed	2 / 181 (1.10%)	4 / 180 (2.22%)	0 / 180 (0.00%)
occurrences (all)	2	4	0
Weight increased			
subjects affected / exposed	2 / 181 (1.10%)	5 / 180 (2.78%)	2 / 180 (1.11%)
occurrences (all)	2	5	2
White blood cell count increased			
subjects affected / exposed	1 / 181 (0.55%)	2 / 180 (1.11%)	4 / 180 (2.22%)
occurrences (all)	1	2	6
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	6 / 181 (3.31%)	4 / 180 (2.22%)	0 / 180 (0.00%)
occurrences (all)	6	4	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 181 (3.31%)	3 / 180 (1.67%)	3 / 180 (1.67%)
occurrences (all)	6	4	4

Headache			
subjects affected / exposed	33 / 181 (18.23%)	32 / 180 (17.78%)	14 / 180 (7.78%)
occurrences (all)	75	83	19
Migraine			
subjects affected / exposed	5 / 181 (2.76%)	1 / 180 (0.56%)	0 / 180 (0.00%)
occurrences (all)	6	1	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	4 / 181 (2.21%)	5 / 180 (2.78%)	1 / 180 (0.56%)
occurrences (all)	4	6	1
Abdominal pain			
subjects affected / exposed	7 / 181 (3.87%)	6 / 180 (3.33%)	1 / 180 (0.56%)
occurrences (all)	7	8	1
Nausea			
subjects affected / exposed	4 / 181 (2.21%)	8 / 180 (4.44%)	7 / 180 (3.89%)
occurrences (all)	10	10	7
Diarrhoea			
subjects affected / exposed	11 / 181 (6.08%)	16 / 180 (8.89%)	9 / 180 (5.00%)
occurrences (all)	14	24	9
Constipation			
subjects affected / exposed	1 / 181 (0.55%)	5 / 180 (2.78%)	0 / 180 (0.00%)
occurrences (all)	1	6	0
Toothache			
subjects affected / exposed	7 / 181 (3.87%)	6 / 180 (3.33%)	4 / 180 (2.22%)
occurrences (all)	7	13	4
Vomiting			
subjects affected / exposed	5 / 181 (2.76%)	7 / 180 (3.89%)	0 / 180 (0.00%)
occurrences (all)	5	10	0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	4 / 181 (2.21%)	2 / 180 (1.11%)	2 / 180 (1.11%)
occurrences (all)	4	2	2
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	4 / 181 (2.21%)	5 / 180 (2.78%)	2 / 180 (1.11%)
occurrences (all)	4	5	2
Dermatitis			

subjects affected / exposed	3 / 181 (1.66%)	4 / 180 (2.22%)	1 / 180 (0.56%)
occurrences (all)	6	4	1
Dermatitis contact			
subjects affected / exposed	3 / 181 (1.66%)	6 / 180 (3.33%)	0 / 180 (0.00%)
occurrences (all)	4	6	0
Eczema			
subjects affected / exposed	8 / 181 (4.42%)	6 / 180 (3.33%)	1 / 180 (0.56%)
occurrences (all)	11	10	1
Hidradenitis			
subjects affected / exposed	16 / 181 (8.84%)	17 / 180 (9.44%)	23 / 180 (12.78%)
occurrences (all)	18	29	26
Pruritus			
subjects affected / exposed	11 / 181 (6.08%)	6 / 180 (3.33%)	2 / 180 (1.11%)
occurrences (all)	12	6	2
Intertrigo			
subjects affected / exposed	10 / 181 (5.52%)	7 / 180 (3.89%)	2 / 180 (1.11%)
occurrences (all)	12	7	2
Psoriasis			
subjects affected / exposed	6 / 181 (3.31%)	5 / 180 (2.78%)	1 / 180 (0.56%)
occurrences (all)	10	5	2
Seborrhoeic dermatitis			
subjects affected / exposed	4 / 181 (2.21%)	5 / 180 (2.78%)	2 / 180 (1.11%)
occurrences (all)	4	5	2
Rash			
subjects affected / exposed	4 / 181 (2.21%)	4 / 180 (2.22%)	1 / 180 (0.56%)
occurrences (all)	4	4	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	7 / 181 (3.87%)	8 / 180 (4.44%)	8 / 180 (4.44%)
occurrences (all)	7	24	8
Arthralgia			
subjects affected / exposed	11 / 181 (6.08%)	6 / 180 (3.33%)	8 / 180 (4.44%)
occurrences (all)	12	10	8
Pain in extremity			

subjects affected / exposed	3 / 181 (1.66%)	4 / 180 (2.22%)	5 / 180 (2.78%)
occurrences (all)	3	5	5
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 181 (2.76%)	6 / 180 (3.33%)	3 / 180 (1.67%)
occurrences (all)	6	6	3
COVID-19			
subjects affected / exposed	5 / 181 (2.76%)	3 / 180 (1.67%)	0 / 180 (0.00%)
occurrences (all)	5	3	0
Cellulitis			
subjects affected / exposed	4 / 181 (2.21%)	3 / 180 (1.67%)	4 / 180 (2.22%)
occurrences (all)	4	3	4
Conjunctivitis			
subjects affected / exposed	5 / 181 (2.76%)	4 / 180 (2.22%)	1 / 180 (0.56%)
occurrences (all)	5	4	1
Ear infection			
subjects affected / exposed	3 / 181 (1.66%)	4 / 180 (2.22%)	0 / 180 (0.00%)
occurrences (all)	3	6	0
Folliculitis			
subjects affected / exposed	4 / 181 (2.21%)	4 / 180 (2.22%)	2 / 180 (1.11%)
occurrences (all)	4	4	2
Fungal skin infection			
subjects affected / exposed	4 / 181 (2.21%)	0 / 180 (0.00%)	0 / 180 (0.00%)
occurrences (all)	5	0	0
Gastroenteritis			
subjects affected / exposed	8 / 181 (4.42%)	4 / 180 (2.22%)	1 / 180 (0.56%)
occurrences (all)	9	4	1
Influenza			
subjects affected / exposed	1 / 181 (0.55%)	6 / 180 (3.33%)	4 / 180 (2.22%)
occurrences (all)	1	6	5
Nasopharyngitis			
subjects affected / exposed	32 / 181 (17.68%)	24 / 180 (13.33%)	13 / 180 (7.22%)
occurrences (all)	44	31	13
Sinusitis			
subjects affected / exposed	4 / 181 (2.21%)	2 / 180 (1.11%)	2 / 180 (1.11%)
occurrences (all)	4	3	2

Pharyngitis			
subjects affected / exposed	7 / 181 (3.87%)	5 / 180 (2.78%)	1 / 180 (0.56%)
occurrences (all)	8	5	1
Suspected COVID-19			
subjects affected / exposed	5 / 181 (2.76%)	3 / 180 (1.67%)	0 / 180 (0.00%)
occurrences (all)	5	3	0
Upper respiratory tract infection			
subjects affected / exposed	9 / 181 (4.97%)	13 / 180 (7.22%)	4 / 180 (2.22%)
occurrences (all)	12	14	4
Tonsillitis			
subjects affected / exposed	6 / 181 (3.31%)	2 / 180 (1.11%)	1 / 180 (0.56%)
occurrences (all)	9	2	1
Urinary tract infection			
subjects affected / exposed	9 / 181 (4.97%)	8 / 180 (4.44%)	3 / 180 (1.67%)
occurrences (all)	15	8	3
Vulvovaginal candidiasis			
subjects affected / exposed	4 / 181 (2.21%)	2 / 180 (1.11%)	0 / 180 (0.00%)
occurrences (all)	4	2	0
Vulvovaginal mycotic infection			
subjects affected / exposed	6 / 181 (3.31%)	2 / 180 (1.11%)	1 / 180 (0.56%)
occurrences (all)	8	3	1
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	4 / 181 (2.21%)	3 / 180 (1.67%)	0 / 180 (0.00%)
occurrences (all)	5	4	0

Non-serious adverse events	Any AIN457 Q2W	Any AIN457 Q4W	Any AIN457
Total subjects affected by non-serious adverse events			
subjects affected / exposed	184 / 266 (69.17%)	183 / 267 (68.54%)	367 / 533 (68.86%)
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 266 (3.01%)	5 / 267 (1.87%)	13 / 533 (2.44%)
occurrences (all)	8	5	13
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 266 (1.88%)	4 / 267 (1.50%)	9 / 533 (1.69%)
occurrences (all)	8	4	12

Chest pain			
subjects affected / exposed	0 / 266 (0.00%)	5 / 267 (1.87%)	5 / 533 (0.94%)
occurrences (all)	0	5	5
Fatigue			
subjects affected / exposed	8 / 266 (3.01%)	13 / 267 (4.87%)	21 / 533 (3.94%)
occurrences (all)	9	15	24
Pyrexia			
subjects affected / exposed	16 / 266 (6.02%)	12 / 267 (4.49%)	28 / 533 (5.25%)
occurrences (all)	24	14	38
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 266 (0.75%)	4 / 267 (1.50%)	6 / 533 (1.13%)
occurrences (all)	3	10	13
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	11 / 266 (4.14%)	7 / 267 (2.62%)	18 / 533 (3.38%)
occurrences (all)	11	7	18
Cough			
subjects affected / exposed	7 / 266 (2.63%)	10 / 267 (3.75%)	17 / 533 (3.19%)
occurrences (all)	7	13	20
Rhinorrhoea			
subjects affected / exposed	9 / 266 (3.38%)	4 / 267 (1.50%)	13 / 533 (2.44%)
occurrences (all)	10	4	14
Psychiatric disorders			
Depression			
subjects affected / exposed	6 / 266 (2.26%)	3 / 267 (1.12%)	9 / 533 (1.69%)
occurrences (all)	6	3	9
Investigations			
Amylase increased			
subjects affected / exposed	3 / 266 (1.13%)	5 / 267 (1.87%)	8 / 533 (1.50%)
occurrences (all)	3	5	8
SARS-CoV-2 test negative			
subjects affected / exposed	8 / 266 (3.01%)	7 / 267 (2.62%)	15 / 533 (2.81%)
occurrences (all)	8	10	18
Lipase increased			

subjects affected / exposed	8 / 266 (3.01%)	9 / 267 (3.37%)	17 / 533 (3.19%)
occurrences (all)	8	9	17
SARS-CoV-2 test positive			
subjects affected / exposed	4 / 266 (1.50%)	5 / 267 (1.87%)	9 / 533 (1.69%)
occurrences (all)	4	5	9
Weight increased			
subjects affected / exposed	3 / 266 (1.13%)	5 / 267 (1.87%)	8 / 533 (1.50%)
occurrences (all)	3	5	8
White blood cell count increased			
subjects affected / exposed	3 / 266 (1.13%)	2 / 267 (0.75%)	5 / 533 (0.94%)
occurrences (all)	3	2	5
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	8 / 266 (3.01%)	4 / 267 (1.50%)	12 / 533 (2.25%)
occurrences (all)	8	4	12
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 266 (2.63%)	5 / 267 (1.87%)	12 / 533 (2.25%)
occurrences (all)	7	6	13
Headache			
subjects affected / exposed	39 / 266 (14.66%)	46 / 267 (17.23%)	85 / 533 (15.95%)
occurrences (all)	85	122	207
Migraine			
subjects affected / exposed	5 / 266 (1.88%)	3 / 267 (1.12%)	8 / 533 (1.50%)
occurrences (all)	6	3	9
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	4 / 266 (1.50%)	9 / 267 (3.37%)	13 / 533 (2.44%)
occurrences (all)	4	10	14
Abdominal pain			
subjects affected / exposed	8 / 266 (3.01%)	10 / 267 (3.75%)	18 / 533 (3.38%)
occurrences (all)	8	12	20
Nausea			
subjects affected / exposed	6 / 266 (2.26%)	13 / 267 (4.87%)	19 / 533 (3.56%)
occurrences (all)	13	16	29
Diarrhoea			

subjects affected / exposed	12 / 266 (4.51%)	24 / 267 (8.99%)	36 / 533 (6.75%)
occurrences (all)	15	32	47
Constipation			
subjects affected / exposed	1 / 266 (0.38%)	5 / 267 (1.87%)	6 / 533 (1.13%)
occurrences (all)	1	6	7
Toothache			
subjects affected / exposed	9 / 266 (3.38%)	7 / 267 (2.62%)	16 / 533 (3.00%)
occurrences (all)	9	14	23
Vomiting			
subjects affected / exposed	6 / 266 (2.26%)	9 / 267 (3.37%)	15 / 533 (2.81%)
occurrences (all)	6	13	19
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	4 / 266 (1.50%)	3 / 267 (1.12%)	7 / 533 (1.31%)
occurrences (all)	4	3	7
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	5 / 266 (1.88%)	6 / 267 (2.25%)	11 / 533 (2.06%)
occurrences (all)	5	6	11
Dermatitis			
subjects affected / exposed	4 / 266 (1.50%)	5 / 267 (1.87%)	9 / 533 (1.69%)
occurrences (all)	7	5	12
Dermatitis contact			
subjects affected / exposed	3 / 266 (1.13%)	6 / 267 (2.25%)	9 / 533 (1.69%)
occurrences (all)	4	6	10
Eczema			
subjects affected / exposed	9 / 266 (3.38%)	9 / 267 (3.37%)	18 / 533 (3.38%)
occurrences (all)	12	13	25
Hidradenitis			
subjects affected / exposed	28 / 266 (10.53%)	26 / 267 (9.74%)	54 / 533 (10.13%)
occurrences (all)	31	43	74
Pruritus			
subjects affected / exposed	15 / 266 (5.64%)	8 / 267 (3.00%)	23 / 533 (4.32%)
occurrences (all)	16	8	24
Intertrigo			

subjects affected / exposed	11 / 266 (4.14%)	8 / 267 (3.00%)	19 / 533 (3.56%)
occurrences (all)	13	8	21
Psoriasis			
subjects affected / exposed	6 / 266 (2.26%)	5 / 267 (1.87%)	11 / 533 (2.06%)
occurrences (all)	10	5	15
Seborrhoeic dermatitis			
subjects affected / exposed	6 / 266 (2.26%)	6 / 267 (2.25%)	12 / 533 (2.25%)
occurrences (all)	6	6	12
Rash			
subjects affected / exposed	6 / 266 (2.26%)	5 / 267 (1.87%)	11 / 533 (2.06%)
occurrences (all)	6	5	11
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	7 / 266 (2.63%)	12 / 267 (4.49%)	19 / 533 (3.56%)
occurrences (all)	7	28	35
Arthralgia			
subjects affected / exposed	14 / 266 (5.26%)	9 / 267 (3.37%)	23 / 533 (4.32%)
occurrences (all)	17	13	30
Pain in extremity			
subjects affected / exposed	5 / 266 (1.88%)	5 / 267 (1.87%)	10 / 533 (1.88%)
occurrences (all)	5	7	12
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 266 (1.88%)	8 / 267 (3.00%)	13 / 533 (2.44%)
occurrences (all)	6	8	14
COVID-19			
subjects affected / exposed	6 / 266 (2.26%)	7 / 267 (2.62%)	13 / 533 (2.44%)
occurrences (all)	6	7	13
Cellulitis			
subjects affected / exposed	6 / 266 (2.26%)	6 / 267 (2.25%)	12 / 533 (2.25%)
occurrences (all)	7	6	13
Conjunctivitis			
subjects affected / exposed	5 / 266 (1.88%)	6 / 267 (2.25%)	11 / 533 (2.06%)
occurrences (all)	5	6	11
Ear infection			

subjects affected / exposed	3 / 266 (1.13%)	4 / 267 (1.50%)	7 / 533 (1.31%)
occurrences (all)	3	6	9
Folliculitis			
subjects affected / exposed	6 / 266 (2.26%)	4 / 267 (1.50%)	10 / 533 (1.88%)
occurrences (all)	7	4	11
Fungal skin infection			
subjects affected / exposed	4 / 266 (1.50%)	0 / 267 (0.00%)	4 / 533 (0.75%)
occurrences (all)	5	0	5
Gastroenteritis			
subjects affected / exposed	8 / 266 (3.01%)	4 / 267 (1.50%)	12 / 533 (2.25%)
occurrences (all)	9	4	13
Influenza			
subjects affected / exposed	1 / 266 (0.38%)	6 / 267 (2.25%)	7 / 533 (1.31%)
occurrences (all)	1	6	7
Nasopharyngitis			
subjects affected / exposed	40 / 266 (15.04%)	29 / 267 (10.86%)	69 / 533 (12.95%)
occurrences (all)	53	37	90
Sinusitis			
subjects affected / exposed	7 / 266 (2.63%)	2 / 267 (0.75%)	9 / 533 (1.69%)
occurrences (all)	8	3	11
Pharyngitis			
subjects affected / exposed	8 / 266 (3.01%)	7 / 267 (2.62%)	15 / 533 (2.81%)
occurrences (all)	9	7	16
Suspected COVID-19			
subjects affected / exposed	6 / 266 (2.26%)	7 / 267 (2.62%)	13 / 533 (2.44%)
occurrences (all)	6	9	15
Upper respiratory tract infection			
subjects affected / exposed	12 / 266 (4.51%)	17 / 267 (6.37%)	29 / 533 (5.44%)
occurrences (all)	18	18	36
Tonsillitis			
subjects affected / exposed	7 / 266 (2.63%)	4 / 267 (1.50%)	11 / 533 (2.06%)
occurrences (all)	10	5	15
Urinary tract infection			
subjects affected / exposed	10 / 266 (3.76%)	10 / 267 (3.75%)	20 / 533 (3.75%)
occurrences (all)	16	11	27
Vulvovaginal candidiasis			

subjects affected / exposed	4 / 266 (1.50%)	3 / 267 (1.12%)	7 / 533 (1.31%)
occurrences (all)	4	3	7
Vulvovaginal mycotic infection			
subjects affected / exposed	7 / 266 (2.63%)	4 / 267 (1.50%)	11 / 533 (2.06%)
occurrences (all)	11	5	16
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	4 / 266 (1.50%)	3 / 267 (1.12%)	7 / 533 (1.31%)
occurrences (all)	5	4	9

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 June 2020	The rationale for the amendment reflects the guidance released from several Health Authorities (FDA, EMA, MHRA) to introduce a level of flexibility in drug dispensation, protocol assessments and visit schedule if a major health care event requires it (i.e., COVID-19 pandemic). While adherence to protocol procedure and GCPs remains mandatory, Novartis has edited the wording in some sections of the protocol to allow the subjects in the trial to continue treatment while being monitored for safety in these situations. These changes were introduced to reduce the risk of exposure for subjects and study staff, and potentially the risk for transmission of infectious diseases (e.g., COVID-19). In addition, a 'special scenario' was added to the study design to ensure a careful, on site assessment of lesions at Week 52, by allowing for the possibility to perform up to 3 unscheduled visits in case lockdowns or mobility restriction would impede the subject or the site to perform the visit on site. In case of a global health crisis impeding the subjects (or the sites) to attend (or perform) Week 52 study visit on site, the subjects in the study were allowed to receive additional study treatment up to 12 weeks after Week 50, or until they could return to the study site to perform the Week 52 assessment (whichever occurs first). This additional, optional phase permitted the subjects to be assessed for eligibility to roll over to the 4-year long-term extension study. During this period, the subjects were continuously monitored for safety. Lastly, the Amendment 01 allowed for an increase in the number of randomized subjects up to 15% to account for the disruptive impact of the COVID-19 pandemic.
08 January 2021	The purpose of this amendment was to update the statistical analysis section including adjusting the split of the overall alpha level allocating 80 to testing the high dose secukinumab regimen (300 mg Q2W) versus placebo, based on the recent findings from Study CAIN457A2324 demonstrating an improved benefit of secukinumab 300 mg Q2W when used in subjects with psoriasis over 90 kg. These data were not available at the time of the initial production of the protocol. In addition, following the FDA feedback this amendment introduced the value of the individual lesion count assessed at the baseline visit only to be used as 'baseline' in the statistical analyses, instead of the weighted average across the two screening visits and the baseline (randomization) visit. Moreover, a secondary endpoint evaluating only the abscesses and inflammatory nodules (AN) count was added. Analyzing AN count on the original, continuous scale, enabled a more sensitive and granular approach to summarizing the clinical effect of treatment (Revuz 2009, Kimball et al 2018). Lastly, the exploratory objective section has been updated to include a specific analysis to evaluate the benefit of secukinumab in the bio-naive population and in the subjects with body weight above and below 90 kg, and to explore treatment effect with regard to inflammatory markers (C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported