Clinical trial results:
A randomized, double-blind, multicenter 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 (SUNRISE)

Summary

EudraCT number	2018-002062-39
Trial protocol	GB FR DE SK CZ BE DK LT GR NL ES HU PL BG HR IT
Global end of trial date	19 July 2022

Results information

Result version number	v1 (current)
This version publication date	04 August 2023
First version publication date	04 August 2023

Trial information

Trial identification

Sponsor protocol code	CAIN457M2302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03713632
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	19 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate the efficacy of secukinumab compared to placebo with respect to Hidradenitis Suppurativa Clinical Response (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	25 February 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: 14
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Bulgaria: 10
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Colombia: 10
Country: Number of subjects enrolled	Croatia: 2
Country: Number of subjects enrolled	Czechia: 7
Country: Number of subjects enrolled	Denmark: 10
Country: Number of subjects enrolled	France: 71
Country: Number of subjects enrolled	Germany: 68
Country: Number of subjects enrolled	Greece: 13
Country: Number of subjects enrolled	Guatemala: 11
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	India: 6
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Israel: 9
Country: Number of subjects enrolled	Lebanon: 4
Country: Number of subjects enrolled	Lithuania: 10
Country: Number of subjects enrolled	Malaysia: 15

Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Philippines: 3
Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	Russian Federation: 15
Country: Number of subjects enrolled	Singapore: 9
Country: Number of subjects enrolled	Slovakia: 8
Country: Number of subjects enrolled	South Africa: 21
Country: Number of subjects enrolled	Spain: 27
Country: Number of subjects enrolled	Switzerland: 7
Country: Number of subjects enrolled	Turkey: 14
Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	United States: 81
Country: Number of subjects enrolled	Viet Nam: 5
Worldwide total number of subjects	543
EEA total number of subjects	285

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)	536
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants enrolled in 132 study sites worldwide.

Period 1

Period 1 title	Treatment Period 1 (until week 16)
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	AIN457 Q2W

Arm description:

Secukinumab 300mg every 2 weeks (Treatment Period 1 and 2)

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 300mgevery 2 weeks

Arm title	AIN457 Q4W

Arm description:

Secukinumab 300mg every 4 weeks (Treatment Period 1 and 2)

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 300mgevery 4 weeks

Arm title	Placebo

Arm description:

Placebo group to secukinumab 300mg (Treatment Period 1)

Arm type	Placebo
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	AIN457 Q2W	AIN457 Q4W	Placebo
Started	180	180	183
Full Analysis Set	180	180	183
Completed	170	169	167
Not completed	10	11	16
Consent withdrawn by subject	6	6	8
Adverse event, non-fatal	1	4	4
Technical problems	1	-	1
Pregnancy	-	-	1
Lost to follow-up	1	1	1
Lack of efficacy	1	-	1

Period 2	
Period 2 title	Treatment Period 2 (after week 16)
Is this the baseline period?	No
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	AIN457 Q2W
Arm description: Secukinumab 300mg every 2 weeks (Treatment Period 1 and 2)	
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	AIN457 Q4W
Arm description: Secukinumab 300mg every 4 weeks (Treatment Period 1 and 2)	
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 - Re-randomized to AIN457 Q2W

Arm description:
Placebo group, re-randomized to secukinumab 300mg Q2W at week 16 (Treatment Period 2)

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	Placebo - Re-randomized to AIN457 Q4W

Arm description:
Placebo group, re-randomized to secukinumab 300mg Q4W at week 16 (Treatment Period 2)

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

Number of subjects in period 2	AIN457 Q2W	AIN457 Q4W	Placebo - Re-randomized to AIN457 Q2W
Started	170	169	81
Completed	149	133	68
Not completed	21	36	13
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	9	18	9
Physician decision	1	2	-
Adverse event, non-fatal	6	3	2
Technical problems	1	-	-
Pregnancy	-	1	-
Lost to follow-up	1	8	1
Lack of efficacy	3	3	1

Number of subjects in period 2	Placebo - Re-randomized to AIN457 Q4W
Started	86
Completed	69
Not completed	17
Adverse event, serious fatal	-
Consent withdrawn by subject	12
Physician decision	2
Adverse event, non-fatal	1
Technical problems	-
Pregnancy	-
Lost to follow-up	-
Lack of efficacy	2

Baseline characteristics

Reporting groups	
Reporting group title	AIN457 Q2W
Reporting group description:	
Secukinumab 300mg every 2 weeks (Treatment Period 1 and 2)	
Reporting group title	AIN457 Q4W
Reporting group description:	
Secukinumab 300mg every 4 weeks (Treatment Period 1 and 2)	
Reporting group title	Placebo
Reporting group description:	
Placebo group to secukinumab 300mg (Treatment Period 1)	

Reporting group values	AIN457 Q2W	AIN457 Q4W	Placebo
Number of subjects	180	180	183
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	177	178	181
>=65 years	3	2	2
Age Continuous Units: Years			
arithmetic mean	37.3	35.5	36.2
standard deviation	± 11.48	± 11.41	± 11.25
Sex: Female, Male Units: Participants			
Female	98	103	105
Male	82	77	78
Race/Ethnicity, Customized Units: Subjects			
White	133	139	143
Black or African American	18	19	12
Asian	16	16	19
Native Hawaiian or Other Pacific Islander	1	0	0
American Indian or Alaska native	7	5	8
Multiple	4	1	1
Not Reported	1	0	0

Reporting group values	Total		
Number of subjects	543		
Age Categorical Units: Participants			
<=18 years	0		
Between 18 and 65 years	536		
>=65 years	7		
Age Continuous Units: Years			
arithmetic mean			

standard deviation	-		

Sex: Female, Male Units: Participants			
Female	306		
Male	237		
Race/Ethnicity, Customized Units: Subjects			
White	415		
Black or African American	49		
Asian	51		
Native Hawaiian or Other Pacific Islander	1		
American Indian or Alaska native	20		
Multiple	6		
Not Reported	1		

End points

End points reporting groups

Reporting group title	AIN457 Q2W
Reporting group description: Secukinumab 300mg every 2 weeks (Treatment Period 1 and 2)	
Reporting group title	AIN457 Q4W
Reporting group description: Secukinumab 300mg every 4 weeks (Treatment Period 1 and 2)	
Reporting group title	Placebo
Reporting group description: Placebo group to secukinumab 300mg (Treatment Period 1)	
Reporting group title	AIN457 Q2W
Reporting group description: Secukinumab 300mg every 2 weeks (Treatment Period 1 and 2)	
Reporting group title	AIN457 Q4W
Reporting group description: Secukinumab 300mg every 4 weeks (Treatment Period 1 and 2)	
Reporting group title	Placebo - Re-randomized to AIN457 Q2W
Reporting group description: Placebo group, re-randomized to secukinumab 300mg Q2W at week 16 (Treatment Period 2)	
Reporting group title	Placebo - Re-randomized to AIN457 Q4W
Reporting group description: Placebo group, re-randomized to secukinumab 300mg Q4W at week 16 (Treatment Period 2)	

Primary: Percentage of participants with Hidradenitis Suppurativa Clinical Response (HiSCR50)

End point title	Percentage of participants with Hidradenitis Suppurativa Clinical Response (HiSCR50)
End point description: HiSCR50 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. This endpoint was analyzed by logistic regression.	
End point type	Primary
End point timeframe: 16 weeks	

End point values	AIN457 Q2W	AIN457 Q4W	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	180	180	183	
Units: Percentage of Participants				
number (not applicable)	42.3	46.1	31.2	

Statistical analyses

Statistical analysis title	logistic regression
Comparison groups	AIN457 Q2W v Placebo
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0149 [1]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	2.55

Notes:

[1] - one-sided p-value

Statistical analysis title	logistic regression
Comparison groups	AIN457 Q4W v Placebo
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0022 [2]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.22
upper limit	2.96

Notes:

[2] - one-sided p-value

Secondary: Percentage change from baseline in AN count

End point title	Percentage change from baseline in AN count

End point description:

Percent change from baseline in abscesses and inflammatory nodules (AN) count. This endpoint was analyzed by analysis of covariance.

End point type	Secondary

End point timeframe:

Baseline, 16 weeks

End point values	AIN457 Q2W	AIN457 Q4W	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	180	180	183	
Units: Percentage change from baseline				
least squares mean (standard error)	-39.3 (± 4.43)	-45.5 (± 4.08)	-22.4 (± 4.84)	

Statistical analyses

Statistical analysis title	ANCOVA
Comparison groups	AIN457 Q4W v Placebo
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001 [3]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-22.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.24
upper limit	-10.63

Notes:

[3] - one-side p-value

Statistical analysis title	ANCOVA
Comparison groups	AIN457 Q2W v Placebo
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0051 [4]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-16.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.79
upper limit	-3.88

Notes:

[4] - one-side p-value

Secondary: Percentage of participants with Hidradenitis Suppurativa (HS) flares	
End point title	Percentage of participants with Hidradenitis Suppurativa (HS)

	flares

End point description:

Percentage of participants who experience at least one flare over 16 weeks. A flare is defined as at least a 25% increase in abscesses and inflammatory nodules (AN) count with a minimum increase of 2 AN relative to baseline. This endpoint was analyzed by logistic regression.

End point type	Secondary

End point timeframe:

16 weeks

End point values	AIN457 Q2W	AIN457 Q4W	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	180	180	183	
Units: Percentage of Participants				
number (not applicable)	20.1	15.6	27.0	

Statistical analyses

Statistical analysis title	logistic regression
Comparison groups	AIN457 Q4W v Placebo
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0049 [5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	0.84

Notes:

[5] - one-sided p-value

Statistical analysis title	logistic regression
Comparison groups	AIN457 Q2W v Placebo
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0732 [6]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	1.14

Notes:

[6] - one-sided p-value

Secondary: Percentage of participants achieving NRS30

End point title	Percentage of participants achieving NRS30

End point description:

Patients achieving Numerical Rating Scale score of 30 (NRS30) at week 16, defined as at least a 30% reduction and at least one unit reduction from baseline in the Patient's Global assessment of Skin Pain (where range 0 [no skin pain] to 10 [worst skin pain]). This endpoint was analyzed by logistic regression. The protocol defines this outcome measure to be tested using combined data with CAIN457M2301 (NCT03713619). As this record is supposed to contain only results from CAIN457M2302, descriptive data based only on CAIN457M2302 are presented.

End point type	Secondary

End point timeframe:

16 weeks

End point values	AIN457 Q2W	AIN457 Q4W	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	135	129	132	
Units: Percentage of participants				
number (not applicable)	38.6	34.7	22.4	

Statistical analyses

Statistical analysis title	logistic regression
Comparison groups	AIN457 Q4W v Placebo
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0206 [7]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	3.37

Notes:

[7] - one-sided p-value

Statistical analysis title	logistic regression
Comparison groups	AIN457 Q2W v Placebo
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0026 [8]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.28
upper limit	4.09

Notes:

[8] - one-sided p-value

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were reported from first dose of study treatment, up to approximately 52 weeks for AIN457 (up to 60 weeks for subjects who did not move to the extension study) and up to 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 60

Reporting group title	Any AIN457

Reporting group description:

Subjects who received at least 1 dose of secukinumab

Reporting group title	Any AIN457 Q2W

Reporting group description:

Subjects who received at least 1 dose of secukinumab 300 mg Q2W dose (including subjects who switched from placebo to secukinumab Q2W at Week 16). Adverse events were assessed up to Week 60

Reporting group title	Any AIN457 Q4W

Reporting group description:

Subjects who received at least 1 dose of secukinumab 300 mg Q4W dose (including subjects who switched from placebo to secukinumab Q4W at Week 16). Adverse events were assessed up to Week 60

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 60

Reporting group title	Placebo

Reporting group description:

Subjects who were randomized to matching placebo at the study entry. Adverse events were assessed up to Week 16

Serious adverse events	AIN457 Q2W	Any AIN457	Any AIN457 Q2W
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 180 (10.56%)	45 / 527 (8.54%)	22 / 261 (8.43%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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 cancer			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Unevaluable event			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 180 (1.11%)	2 / 527 (0.38%)	2 / 261 (0.77%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Amyloidosis			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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
Reproductive system and breast disorders			
Scrotal inflammation			

subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 180 (0.00%)	0 / 527 (0.00%)	0 / 261 (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			
Obsessive-compulsive disorder			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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
Ankle fracture			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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
Intentional overdose			

subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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
Joint dislocation			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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
Lower limb fracture			
subjects affected / exposed	1 / 180 (0.56%)	2 / 527 (0.38%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inflammatory bowel disease			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colitis ulcerative			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	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 / 180 (2.22%)	5 / 527 (0.95%)	5 / 261 (1.92%)
occurrences causally related to treatment / all	0 / 4	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 180 (1.11%)	2 / 527 (0.38%)	2 / 261 (0.77%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerular vascular disorder			

subjects affected / exposed	0 / 180 (0.00%)	0 / 527 (0.00%)	0 / 261 (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
Nephrolithiasis			
subjects affected / exposed	1 / 180 (0.56%)	2 / 527 (0.38%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvi-ureteric obstruction			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 180 (0.00%)	2 / 527 (0.38%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle spasms			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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 pneumonia			
subjects affected / exposed	0 / 180 (0.00%)	0 / 527 (0.00%)	0 / 261 (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
Cellulitis			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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
Colonic abscess			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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
Enterocolitis infectious			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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
Dermatitis infected			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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
Injection site abscess			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scrotal infection			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			

subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis externa			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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
Localised infection			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 180 (0.56%)	1 / 527 (0.19%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sweat gland infection			
subjects affected / exposed	1 / 180 (0.56%)	2 / 527 (0.38%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	1 / 1	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 180 (0.00%)	1 / 527 (0.19%)	0 / 261 (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 Q4W	AIN457 Q4W	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 266 (8.65%)	15 / 180 (8.33%)	5 / 183 (2.73%)
number of deaths (all causes)	2	1	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Breast cancer			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
General disorders and administration site conditions			
Unevaluable event			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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 / 266 (0.00%)	0 / 180 (0.00%)	1 / 183 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Amyloidosis			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Reproductive system and breast disorders			

Scrotal inflammation			
subjects affected / exposed	1 / 266 (0.38%)	0 / 180 (0.00%)	0 / 183 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	1 / 183 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Obsessive-compulsive disorder			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Depression			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Confusional state			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Ankle fracture			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Intentional overdose			

subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Joint dislocation			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Lower limb fracture			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Skull fracture			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Myocardial infarction			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Nervous system disorders			
Sciatica			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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			
Inflammatory bowel disease			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colitis ulcerative			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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 haemorrhage			
subjects affected / exposed	1 / 266 (0.38%)	0 / 180 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Cholecystitis			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Cholelithiasis			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Glomerular vascular disorder			

subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	1 / 183 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Pelvi-ureteric obstruction			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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			
Intervertebral disc protrusion			
subjects affected / exposed	2 / 266 (0.75%)	0 / 180 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Muscle spasms			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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			
Abscess			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Abscess limb			
subjects affected / exposed	1 / 266 (0.38%)	0 / 180 (0.00%)	0 / 183 (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

COVID-19 pneumonia			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	1 / 183 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 266 (0.38%)	0 / 180 (0.00%)	0 / 183 (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
Colonic abscess			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Enterocolitis infectious			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Dermatitis infected			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Injection site abscess			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Scrotal infection			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			

subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Otitis externa			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (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
Localised infection			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	0 / 183 (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
Soft tissue infection			
subjects affected / exposed	1 / 266 (0.38%)	0 / 180 (0.00%)	0 / 183 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 266 (0.00%)	0 / 180 (0.00%)	1 / 183 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sweat gland infection			
subjects affected / exposed	1 / 266 (0.38%)	0 / 180 (0.00%)	0 / 183 (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
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 266 (0.38%)	0 / 180 (0.00%)	0 / 183 (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

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

Non-serious adverse events	AIN457 Q2W	Any AIN457	Any AIN457 Q2W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	123 / 180 (68.33%)	348 / 527 (66.03%)	174 / 261 (66.67%)
Investigations			
Lipase increased			
subjects affected / exposed	3 / 180 (1.67%)	12 / 527 (2.28%)	5 / 261 (1.92%)
occurrences (all)	5	15	7
Gamma-glutamyltransferase increased			
subjects affected / exposed	5 / 180 (2.78%)	6 / 527 (1.14%)	5 / 261 (1.92%)
occurrences (all)	5	6	5
SARS-CoV-2 test positive			
subjects affected / exposed	3 / 180 (1.67%)	9 / 527 (1.71%)	5 / 261 (1.92%)
occurrences (all)	3	9	5
Weight decreased			
subjects affected / exposed	0 / 180 (0.00%)	4 / 527 (0.76%)	0 / 261 (0.00%)
occurrences (all)	0	4	0
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	1 / 180 (0.56%)	6 / 527 (1.14%)	1 / 261 (0.38%)
occurrences (all)	1	6	1
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 180 (6.11%)	21 / 527 (3.98%)	14 / 261 (5.36%)
occurrences (all)	11	23	16
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 180 (2.22%)	13 / 527 (2.47%)	6 / 261 (2.30%)
occurrences (all)	4	16	6
Headache			
subjects affected / exposed	31 / 180 (17.22%)	75 / 527 (14.23%)	39 / 261 (14.94%)
occurrences (all)	59	121	72
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	7 / 180 (3.89%)	21 / 527 (3.98%)	9 / 261 (3.45%)
occurrences (all)	12	28	15
Influenza like illness			

subjects affected / exposed	1 / 180 (0.56%)	6 / 527 (1.14%)	1 / 261 (0.38%)
occurrences (all)	1	9	1
Fatigue			
subjects affected / exposed	4 / 180 (2.22%)	14 / 527 (2.66%)	7 / 261 (2.68%)
occurrences (all)	4	20	8
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 180 (2.22%)	13 / 527 (2.47%)	7 / 261 (2.68%)
occurrences (all)	4	13	7
Abdominal pain			
subjects affected / exposed	4 / 180 (2.22%)	15 / 527 (2.85%)	5 / 261 (1.92%)
occurrences (all)	4	15	5
Abdominal pain upper			
subjects affected / exposed	3 / 180 (1.67%)	14 / 527 (2.66%)	4 / 261 (1.53%)
occurrences (all)	3	15	4
Constipation			
subjects affected / exposed	4 / 180 (2.22%)	5 / 527 (0.95%)	4 / 261 (1.53%)
occurrences (all)	4	5	4
Dental caries			
subjects affected / exposed	4 / 180 (2.22%)	5 / 527 (0.95%)	4 / 261 (1.53%)
occurrences (all)	4	5	4
Diarrhoea			
subjects affected / exposed	13 / 180 (7.22%)	38 / 527 (7.21%)	19 / 261 (7.28%)
occurrences (all)	16	48	22
Toothache			
subjects affected / exposed	6 / 180 (3.33%)	12 / 527 (2.28%)	7 / 261 (2.68%)
occurrences (all)	8	16	10
Nausea			
subjects affected / exposed	6 / 180 (3.33%)	19 / 527 (3.61%)	12 / 261 (4.60%)
occurrences (all)	7	21	13
Haemorrhoids			
subjects affected / exposed	1 / 180 (0.56%)	6 / 527 (1.14%)	1 / 261 (0.38%)
occurrences (all)	1	6	1
Vomiting			
subjects affected / exposed	2 / 180 (1.11%)	7 / 527 (1.33%)	6 / 261 (2.30%)
occurrences (all)	2	9	7

Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 180 (1.11%)	8 / 527 (1.52%)	3 / 261 (1.15%)
occurrences (all)	2	20	3
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	8 / 180 (4.44%)	17 / 527 (3.23%)	8 / 261 (3.07%)
occurrences (all)	8	18	8
Cough			
subjects affected / exposed	5 / 180 (2.78%)	15 / 527 (2.85%)	6 / 261 (2.30%)
occurrences (all)	5	15	6
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	3 / 180 (1.67%)	8 / 527 (1.52%)	4 / 261 (1.53%)
occurrences (all)	4	9	5
Eczema			
subjects affected / exposed	10 / 180 (5.56%)	18 / 527 (3.42%)	11 / 261 (4.21%)
occurrences (all)	11	19	12
Hidradenitis			
subjects affected / exposed	21 / 180 (11.67%)	57 / 527 (10.82%)	26 / 261 (9.96%)
occurrences (all)	40	91	47
Intertrigo			
subjects affected / exposed	4 / 180 (2.22%)	14 / 527 (2.66%)	6 / 261 (2.30%)
occurrences (all)	4	15	6
Pruritus			
subjects affected / exposed	8 / 180 (4.44%)	16 / 527 (3.04%)	11 / 261 (4.21%)
occurrences (all)	11	21	15
Psoriasis			
subjects affected / exposed	6 / 180 (3.33%)	12 / 527 (2.28%)	6 / 261 (2.30%)
occurrences (all)	6	12	6
Psychiatric disorders			
Depression			
subjects affected / exposed	6 / 180 (3.33%)	11 / 527 (2.09%)	6 / 261 (2.30%)
occurrences (all)	6	11	6
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	7 / 180 (3.89%)	20 / 527 (3.80%)	11 / 261 (4.21%)
occurrences (all)	7	23	12
Back pain			
subjects affected / exposed	4 / 180 (2.22%)	21 / 527 (3.98%)	7 / 261 (2.68%)
occurrences (all)	4	25	7
Myalgia			
subjects affected / exposed	3 / 180 (1.67%)	10 / 527 (1.90%)	4 / 261 (1.53%)
occurrences (all)	3	13	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 180 (2.78%)	12 / 527 (2.28%)	5 / 261 (1.92%)
occurrences (all)	5	12	5
COVID-19			
subjects affected / exposed	10 / 180 (5.56%)	27 / 527 (5.12%)	13 / 261 (4.98%)
occurrences (all)	10	27	13
Conjunctivitis			
subjects affected / exposed	4 / 180 (2.22%)	11 / 527 (2.09%)	4 / 261 (1.53%)
occurrences (all)	4	12	4
Ear infection			
subjects affected / exposed	4 / 180 (2.22%)	6 / 527 (1.14%)	5 / 261 (1.92%)
occurrences (all)	5	7	6
Folliculitis			
subjects affected / exposed	9 / 180 (5.00%)	13 / 527 (2.47%)	9 / 261 (3.45%)
occurrences (all)	10	14	10
Influenza			
subjects affected / exposed	5 / 180 (2.78%)	8 / 527 (1.52%)	7 / 261 (2.68%)
occurrences (all)	5	8	7
Sinusitis			
subjects affected / exposed	3 / 180 (1.67%)	10 / 527 (1.90%)	7 / 261 (2.68%)
occurrences (all)	3	11	7
Rhinitis			
subjects affected / exposed	4 / 180 (2.22%)	13 / 527 (2.47%)	6 / 261 (2.30%)
occurrences (all)	4	13	6
Pharyngitis			

subjects affected / exposed	3 / 180 (1.67%)	13 / 527 (2.47%)	4 / 261 (1.53%)
occurrences (all)	5	16	6
Oral candidiasis			
subjects affected / exposed	5 / 180 (2.78%)	8 / 527 (1.52%)	5 / 261 (1.92%)
occurrences (all)	6	12	6
Nasopharyngitis			
subjects affected / exposed	21 / 180 (11.67%)	53 / 527 (10.06%)	28 / 261 (10.73%)
occurrences (all)	28	65	35
Skin candida			
subjects affected / exposed	6 / 180 (3.33%)	12 / 527 (2.28%)	8 / 261 (3.07%)
occurrences (all)	7	16	10
Urinary tract infection			
subjects affected / exposed	7 / 180 (3.89%)	20 / 527 (3.80%)	8 / 261 (3.07%)
occurrences (all)	10	24	11
Upper respiratory tract infection			
subjects affected / exposed	13 / 180 (7.22%)	27 / 527 (5.12%)	16 / 261 (6.13%)
occurrences (all)	17	33	20
Tonsillitis			
subjects affected / exposed	2 / 180 (1.11%)	9 / 527 (1.71%)	4 / 261 (1.53%)
occurrences (all)	2	9	4
Sweat gland infection			
subjects affected / exposed	3 / 180 (1.67%)	11 / 527 (2.09%)	9 / 261 (3.45%)
occurrences (all)	4	15	12

Non-serious adverse events	Any AIN457 Q4W	AIN457 Q4W	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	174 / 266 (65.41%)	125 / 180 (69.44%)	84 / 183 (45.90%)
Investigations			
Lipase increased			
subjects affected / exposed	7 / 266 (2.63%)	7 / 180 (3.89%)	1 / 183 (0.55%)
occurrences (all)	8	8	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (0.00%)
occurrences (all)	1	1	0
SARS-CoV-2 test positive			

subjects affected / exposed	4 / 266 (1.50%)	4 / 180 (2.22%)	3 / 183 (1.64%)
occurrences (all)	4	4	3
Weight decreased			
subjects affected / exposed	4 / 266 (1.50%)	4 / 180 (2.22%)	0 / 183 (0.00%)
occurrences (all)	4	4	0
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	5 / 266 (1.88%)	4 / 180 (2.22%)	0 / 183 (0.00%)
occurrences (all)	5	4	0
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 266 (2.63%)	6 / 180 (3.33%)	2 / 183 (1.09%)
occurrences (all)	7	6	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 266 (2.63%)	7 / 180 (3.89%)	3 / 183 (1.64%)
occurrences (all)	10	10	3
Headache			
subjects affected / exposed	36 / 266 (13.53%)	27 / 180 (15.00%)	16 / 183 (8.74%)
occurrences (all)	49	39	23
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	12 / 266 (4.51%)	8 / 180 (4.44%)	3 / 183 (1.64%)
occurrences (all)	13	9	4
Influenza like illness			
subjects affected / exposed	5 / 266 (1.88%)	5 / 180 (2.78%)	0 / 183 (0.00%)
occurrences (all)	8	8	0
Fatigue			
subjects affected / exposed	7 / 266 (2.63%)	6 / 180 (3.33%)	2 / 183 (1.09%)
occurrences (all)	12	11	2
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 266 (2.26%)	4 / 180 (2.22%)	1 / 183 (0.55%)
occurrences (all)	6	4	1
Abdominal pain			

subjects affected / exposed	10 / 266 (3.76%)	7 / 180 (3.89%)	2 / 183 (1.09%)
occurrences (all)	10	7	2
Abdominal pain upper			
subjects affected / exposed	10 / 266 (3.76%)	9 / 180 (5.00%)	1 / 183 (0.55%)
occurrences (all)	11	9	1
Constipation			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	2 / 183 (1.09%)
occurrences (all)	1	1	2
Dental caries			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	19 / 266 (7.14%)	14 / 180 (7.78%)	13 / 183 (7.10%)
occurrences (all)	26	21	16
Toothache			
subjects affected / exposed	5 / 266 (1.88%)	5 / 180 (2.78%)	0 / 183 (0.00%)
occurrences (all)	6	6	0
Nausea			
subjects affected / exposed	7 / 266 (2.63%)	5 / 180 (2.78%)	4 / 183 (2.19%)
occurrences (all)	8	6	5
Haemorrhoids			
subjects affected / exposed	5 / 266 (1.88%)	5 / 180 (2.78%)	0 / 183 (0.00%)
occurrences (all)	5	5	0
Vomiting			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	1 / 183 (0.55%)
occurrences (all)	2	2	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	5 / 266 (1.88%)	5 / 180 (2.78%)	0 / 183 (0.00%)
occurrences (all)	17	17	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	9 / 266 (3.38%)	8 / 180 (4.44%)	1 / 183 (0.55%)
occurrences (all)	10	9	1
Cough			

subjects affected / exposed	9 / 266 (3.38%)	7 / 180 (3.89%)	3 / 183 (1.64%)
occurrences (all)	9	7	3
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	4 / 266 (1.50%)	4 / 180 (2.22%)	1 / 183 (0.55%)
occurrences (all)	4	4	1
Eczema			
subjects affected / exposed	7 / 266 (2.63%)	6 / 180 (3.33%)	1 / 183 (0.55%)
occurrences (all)	7	6	1
Hidradenitis			
subjects affected / exposed	31 / 266 (11.65%)	23 / 180 (12.78%)	14 / 183 (7.65%)
occurrences (all)	44	35	18
Intertrigo			
subjects affected / exposed	8 / 266 (3.01%)	5 / 180 (2.78%)	0 / 183 (0.00%)
occurrences (all)	9	5	0
Pruritus			
subjects affected / exposed	5 / 266 (1.88%)	3 / 180 (1.67%)	5 / 183 (2.73%)
occurrences (all)	6	4	5
Psoriasis			
subjects affected / exposed	6 / 266 (2.26%)	4 / 180 (2.22%)	0 / 183 (0.00%)
occurrences (all)	6	4	0
Psychiatric disorders			
Depression			
subjects affected / exposed	5 / 266 (1.88%)	5 / 180 (2.78%)	4 / 183 (2.19%)
occurrences (all)	5	5	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 266 (3.38%)	4 / 180 (2.22%)	5 / 183 (2.73%)
occurrences (all)	11	6	5
Back pain			
subjects affected / exposed	14 / 266 (5.26%)	12 / 180 (6.67%)	4 / 183 (2.19%)
occurrences (all)	18	16	4
Myalgia			
subjects affected / exposed	6 / 266 (2.26%)	4 / 180 (2.22%)	3 / 183 (1.64%)
occurrences (all)	9	7	3
Infections and infestations			

Bronchitis			
subjects affected / exposed	7 / 266 (2.63%)	5 / 180 (2.78%)	2 / 183 (1.09%)
occurrences (all)	7	5	2
COVID-19			
subjects affected / exposed	14 / 266 (5.26%)	7 / 180 (3.89%)	3 / 183 (1.64%)
occurrences (all)	14	7	9
Conjunctivitis			
subjects affected / exposed	7 / 266 (2.63%)	6 / 180 (3.33%)	0 / 183 (0.00%)
occurrences (all)	8	7	0
Ear infection			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (0.00%)
occurrences (all)	1	1	0
Folliculitis			
subjects affected / exposed	4 / 266 (1.50%)	2 / 180 (1.11%)	3 / 183 (1.64%)
occurrences (all)	4	2	3
Influenza			
subjects affected / exposed	1 / 266 (0.38%)	1 / 180 (0.56%)	0 / 183 (0.00%)
occurrences (all)	1	1	0
Sinusitis			
subjects affected / exposed	3 / 266 (1.13%)	3 / 180 (1.67%)	3 / 183 (1.64%)
occurrences (all)	4	4	3
Rhinitis			
subjects affected / exposed	7 / 266 (2.63%)	4 / 180 (2.22%)	1 / 183 (0.55%)
occurrences (all)	7	4	1
Pharyngitis			
subjects affected / exposed	9 / 266 (3.38%)	6 / 180 (3.33%)	3 / 183 (1.64%)
occurrences (all)	10	7	3
Oral candidiasis			
subjects affected / exposed	3 / 266 (1.13%)	1 / 180 (0.56%)	0 / 183 (0.00%)
occurrences (all)	6	1	0
Nasopharyngitis			
subjects affected / exposed	25 / 266 (9.40%)	18 / 180 (10.00%)	16 / 183 (8.74%)
occurrences (all)	30	22	19
Skin candida			
subjects affected / exposed	4 / 266 (1.50%)	4 / 180 (2.22%)	1 / 183 (0.55%)
occurrences (all)	6	6	1

Urinary tract infection			
subjects affected / exposed	12 / 266 (4.51%)	7 / 180 (3.89%)	5 / 183 (2.73%)
occurrences (all)	13	7	5
Upper respiratory tract infection			
subjects affected / exposed	11 / 266 (4.14%)	8 / 180 (4.44%)	7 / 183 (3.83%)
occurrences (all)	13	9	8
Tonsillitis			
subjects affected / exposed	5 / 266 (1.88%)	4 / 180 (2.22%)	0 / 183 (0.00%)
occurrences (all)	5	4	0
Sweat gland infection			
subjects affected / exposed	2 / 266 (0.75%)	2 / 180 (1.11%)	3 / 183 (1.64%)
occurrences (all)	3	3	3

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, Medical and Healthcare Products Regulatory Agency) 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, onsite 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 the secukinumab 300 mg Q2W when used in subjects with psoriasis over 90 kg. These data were not available at the time of the initial release of the protocol. In addition, following the FDA feedback this amendment introduced the value of the individual lesion count assessed at the randomization visit only to be used as 'baseline' in the statistical analyses, instead of the weighted average across the 2 screening visits and the baseline (randomization) visit. Moreover, a secondary endpoint evaluating only the 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 (CRP and ESR).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported