Clinical trial results:
A randomized, double-blind, placebo-controlled, parallel group, Phase II, 24-week study investigating the efficacy, safety and tolerability of AIN457 in patients with active overuse tendinopathy refractory to oral NSAIDs/acetaminophen, physiotherapy or corticosteroid injections

Summary

EudraCT number	2017-003099-30
Trial protocol	DE NL GB
Global end of trial date	17 October 2019

Results information

Result version number	v1 (current)
This version publication date	01 November 2020
First version publication date	01 November 2020

Trial information

Trial identification

Sponsor protocol code	CAIN457X2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03344640
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Study Director, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharmaceuticals, 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	04 August 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of secukinumab 300 mg subcutaneous (s.c) vs. placebo in patients with overuse rotator cuff tendinopathy in relieving clinical symptoms at Week 14

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	15 December 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 15
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Netherlands: 16
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 33
Worldwide total number of subjects	96
EEA total number of subjects	63

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)	94
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Of all patients randomized (N= 98; 100%) in the study, a total of 96 patients (98%) were dosed (49 patients in the secukinumab 300 mg group and 47 patients in the placebo group)

Pre-assignment

Screening details:

2 patients were not dosed, one patient decided to discontinue on Day 1 due to a common cold and one patient was a run-in failure

Period 1

Period 1 title	Overall study
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	secukinumab

Arm description:

AIN457 300 mg subcutaneously (s.c.)

Arm type	Experimental
Investigational medicinal product name	secukinumab 150mg x 2
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Secukinumab pre-filled injections of 1 ml (150 mg) were supplied to the investigators at dose strength of 300 mg (2 injections of 150 mg) as single-blind packs.

Arm title	Placebo

Arm description:

Placebo s.c.

Arm type	Experimental
Investigational medicinal product name	placebo S.C. x 2
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo (2 injections) pre-filled injections were supplied as single-blind packs

Number of subjects in period 1	secukinumab	Placebo
Started	49	47
Completed	46	44
Not completed	3	3
Physician decision	1	1
Consent withdrawn by subject	1	2
Adverse event, non-fatal	1	-

Period 2	
Period 2 title	Follow-up epoch
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	secukinumab

Arm description:

AIN457 300 mg subcutaneously (s.c.)

Arm type	Experimental
Investigational medicinal product name	Secukinumab 300mg (2 x 150 mg/1ml)
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Secukinumab pre-filled injections of 1 ml (150 mg) were supplied to the investigators at dose strength of 300 mg (2 injections of 150 mg) as single-blind packs

Arm title	Placebo

Arm description:

Placebo s.c.

Arm type	Experimental
Investigational medicinal product name	Placebo s.c.
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

placebo (2 injections) pre-filledPinjections were supplied as single-blind packs.

Number of subjects in period 2	secukinumab	Placebo
Started	46	44
Completed	46	42
Not completed	0	2
Consent withdrawn by subject	-	2

Baseline characteristics

Reporting groups	
Reporting group title	secukinumab
Reporting group description:	
AIN457 300 mg subcutaneously (s.c.)	
Reporting group title	Placebo
Reporting group description:	
Placebo s.c.	

Reporting group values	secukinumab	Placebo	Total
Number of subjects	49	47	96
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	48	46	94
From 65-84 years	1	1	2
85 years and over	0	0	0
Age Continuous			
Demographic summary (Safety analysis set)			
Units: years			
arithmetic mean	44.8	49.1	
standard deviation	± 11.51	± 10.56	-
Sex: Female, Male			
41.7% of participants were female, and 58.3% were male			
Units: Participants			
Female	17	23	40
Male	32	24	56
Race/Ethnicity, Customized			
1% Asian, 4.2% Black or African American, 91.7% White, 1% Unknown, 2.1% Other			
Units: Subjects			
Asian	1	0	1
Black or African American	3	1	4
White	43	45	88
Unknown	1	0	1
Other	1	1	2

End points

End points reporting groups

Reporting group title	secukinumab
Reporting group description: AIN457 300 mg subcutaneously (s.c.)	
Reporting group title	Placebo
Reporting group description: Placebo s.c.	
Reporting group title	secukinumab
Reporting group description: AIN457 300 mg subcutaneously (s.c.)	
Reporting group title	Placebo
Reporting group description: Placebo s.c.	

Primary: The Western Ontario Rotator Cuff (WORC) patient reported outcome (PRO) score at week 14 in All Patients - Statistical Analysis results of total WORC scores at week 14

End point title	The Western Ontario Rotator Cuff (WORC) patient reported outcome (PRO) score at week 14 in All Patients - Statistical Analysis results of total WORC scores at week 14

End point description:

WORC PRO score at week 14. The WORC Index consists of 21 items divided into 5 Domains: Physical Symptoms (6 items), Sport/Recreation (4 items), Work Function (4 items), Lifestyle Function (4 items) and Emotional Function (3 items). The total scores and sub scores used were the percentages of the normal scores with 0 being worst and 100 being best.

All Patients - Statistical analysis results of WORC scores at Week 14

End point type	Primary
End point timeframe: Week 14 (Day 99)	

End point values	secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: Scores				
number (confidence interval 90%)	37.00 (30.10 to 43.90)	37.77 (30.40 to 45.15)		

Statistical analyses

Statistical analysis title	WORC score at week 14

Statistical analysis description:

All Patients at day 99

Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.875
Method	LS mean
Parameter estimate	Mean difference (final values)
Point estimate	-0.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.84
upper limit	7.3

Secondary: The Western Ontario Rotator Cuff (WORC) patient reported outcome (PRO) scores over time in All Patients

End point title	The Western Ontario Rotator Cuff (WORC) patient reported outcome (PRO) scores over time in All Patients

End point description:

WORC score at Days 15, 29, 57, 85, 127, and End of Study (day 169)

End point type	Secondary

End point timeframe:

Days 15, 29, 57, 85, 127, and End of Study

End point values	secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: Scores				
number (confidence interval 90%)				
Day 15	12.39 (6.99 to 17.79)	8.42 (2.66 to 14.18)		
Day 29	22.35 (16.38 to 28.32)	19.49 (13.11 to 25.86)		
Day 57	28.74 (22.19 to 35.29)	30.11 (23.08 to 37.13)		
Day 85	34.86 (28.18 to 41.53)	33.48 (26.35 to 40.61)		
Day 127	41.86 (34.96 to 48.77)	38.50 (31.12 to 45.88)		
End of Study	43.41 (36.21 to 50.61)	40.97 (33.27 to 48.66)		

Statistical analyses

Statistical analysis title	WORC score at day 15

Statistical analysis description: All patientts at day 15	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.19
Method	LS mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	3.97
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.03
upper limit	8.97

Statistical analysis title	WORC score at day 29
Statistical analysis description: All patients at day 29	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	3.97
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.39
upper limit	9.11

Statistical analysis title	WORC score at day 57
Statistical analysis description: All patients at day 57	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.761
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	0.761

Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.81
upper limit	6.08

Statistical analysis title	WORC score at day 85
Statistical analysis description: All patients at day 85	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.765
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	0.765
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.27
upper limit	9.03

Statistical analysis title	WORC score at day 129
Statistical analysis description: All patients at day 127	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.491
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	0.491
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.73
upper limit	11.45

Statistical analysis title	WORC score at EoS
Statistical analysis description: All patients at end of study	
Comparison groups	secukinumab v Placebo

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.639
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	2.44
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.19
upper limit	11.07

Secondary: Disability of Arm, Shoulder and Hand Questionnaire Score (QuickDASH) over time

End point title	Disability of Arm, Shoulder and Hand Questionnaire Score (QuickDASH) over time

End point description:

Patient Reported Outcome: Disability of Arm, Shoulder and Hand (QuickDASH) Questionnaire score. This questionnaire asks about symptoms as well participant's ability to do certain activities - range from 1 No difficulty to 5 Unable

End point type	Secondary

End point timeframe:

Days 15, 29, 57, 85, 99, 127, and End of Study

End point values	secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: Scores				
number (confidence interval 90%)				
Day 15	-11.64 (-16.14 to -7.14)	-8.23 (-13.02 to -3.44)		
Day 29	-18.31 (-23.20 to -13.41)	-16.95 (-22.18 to -11.73)		
Day 57	-22.43 (-27.55 to -17.30)	-24.01 (-29.49 to -18.52)		
Day 85	-28.14 (-33.55 to -22.73)	-27.22 (-32.98 to -21.45)		
Day 99	-29.45 (-34.72 to -24.19)	-30.69 (-36.30 to -25.07)		
Day 127	-32.86 (-38.26 to -27.46)	-31.99 (-37.75 to -26.23)		
End of Study	-33.89 (-39.27 to -28.50)	-35.40 (-41.13 to -29.67)		

Statistical analyses

Statistical analysis title	QuickDASH score over time
Statistical analysis description:	
Statistical analysis results of QuickDASH total score (PD Analysis Set) at day 99	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.735 [1]
Method	LS Mean
Parameter estimate	Difference and 90% CI versus Placebo
Point estimate	1.23
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.81
upper limit	7.28

Notes:

[1] - Difference and 90% CI versus placebo

Statistical analysis title	QuickDASH score at EoS
Statistical analysis description:	
Statistical analysis results of QuickDASH total score (PD analysis set) at End of Study	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.689
Method	LS Mean
Parameter estimate	Difference and 90% CI versus Placebo
Point estimate	1.51
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.76
upper limit	7.79

Secondary: American Shoulder and Elbow Surgeons (ASES) Score over time

End point title	American Shoulder and Elbow Surgeons (ASES) Score over time

End point description:

Patient Reported Outcome: American Shoulder and Elbow Surgeons Shoulder Evaluation Form (ASES) score is self-administered and has 17 questions in the areas of shoulder symptoms and functions. The ASES total score ranges from 0 to 100 (best).

End point type	Secondary

End point timeframe:

Days 15, 29, 57, 85, 99, 127, and End of Study

End point values	secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: Scores				
number (confidence interval 90%)				
Day 15	8.66 (3.98 to 13.33)	5.26 (0.26 to 10.25)		
Day 29	17.53 (12.35 to 22.71)	14.37 (8.82 to 19.92)		
Day 57	24.15 (18.34 to 29.96)	22.56 (16.31 to 28.81)		
Day 85	30.50 (24.51 to 36.50)	26.97 (20.51 to 33.43)		
Day 99	31.29 (25.28 to 37.31)	27.79 (21.33 to 34.26)		
Day 127	34.92 (28.80 to 41.05)	32.94 (26.33 to 39.56)		
End of Study	37.29 (30.97 to 43.62)	36.15 (29.33 to 42.97)		

Statistical analyses

Statistical analysis title	ASES total score at day 99
Statistical analysis description:	
Statistical analysis results of ASES total score (PD analysis) at day 99	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.411
Method	LS Mean
Parameter estimate	Difference and 90% CI vesus placebo
Point estimate	3.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.54
upper limit	10.54

Statistical analysis title	ASES score at EoS
Statistical analysis description:	
Statistical analysis results of ASES total score (PD analysis) at End of Study set)	
Comparison groups	secukinumab v Placebo

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.804
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	1.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.5
upper limit	8.78

Secondary: Your Health Today score over time

End point title	Your Health Today score over time

End point description:

Patient Reported Outcome: Statistical analysis results of EQ-5D-5L Index score for Your health Today questionnaire, which reflects how good or bad the subjets Health is on a scale from 0 (worst health) to 100 (best health).

Your health today reflects how good or bad the subjects health is on a scale from 0 (worst health) to 100 (best health)

End point type	Secondary

End point timeframe:

Days 15, 29, 57, 85, 99, 127, and End of Study

End point values	secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: Scores				
number (confidence interval 90%)				
Day 15	-0.22 (-4.02 to 3.58)	0.02 (-4.02 to 4.07)		
Day 29	3.27 (-0.71 to 7.25)	3.56 (-0.69 to 7.81)		
Day 57	3.19 (-1.07 to 7.45)	9.02 (4.45 to 13.59)		
Day 85	7.36 (2.84 to 11.89)	7.79 (2.96 to 12.62)		
Day 99	8.75 (4.13 to 13.38)	10.01 (5.09 to 14.94)		
Day 127	9.55 (5.29 to 13.80)	13.59 (9.05 to 18.13)		
End of Study	10.22 (4.84 to 15.60)	12.13 (6.36 to 17.89)		

Statistical analyses

Statistical analysis title	EQ-5D-5L Index score at day 99
Statistical analysis description:	
Statistical analysis results of Your Health Today EQ-5D-5L Index score at day 99 (PD Analysis Set)	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.706
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	-1.26
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.81
upper limit	4.29

Statistical analysis title	EQ-5D-5L Index score at End of Study
Statistical analysis description:	
Statistical analysis results of Your Health Today EQ-5D-5L Index score at End of Study	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.647
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	-1.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.79
upper limit	4.99

Secondary: EQ-5D-5L Index score over time

End point title	EQ-5D-5L Index score over time
End point description:	
Patient Reported Outcome: Statistical analysis results of EQ-5D-5L Index score, which contains 6 items to assess Health Status (mobility, self-care, usual activity, pain/discomfort, and anxiety/depression). Overall scores range from 0 to 1 with lower scores representing a higher Level of disfunction.	
End point type	Secondary
End point timeframe:	
Days 15, 29, 57, 85, 99, 127 and End of Study	

End point values	secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: Scores				
number (confidence interval 90%)				
Day 15	0.07 (0.05 to 0.10)	0.04 (0.01 to 0.07)		
Day 29	0.10 (0.07 to 0.13)	0.09 (0.05 to 0.12)		
Day 57	0.12 (0.09 to 0.15)	0.11 (0.08 to 0.15)		
Day 85	0.16 (0.13 to 0.19)	0.14 (0.10 to 0.18)		
Day 99	0.16 (0.13 to 0.20)	0.15 (0.11 to 0.19)		
Day 127	0.19 (0.15 to 0.23)	0.17 (0.13 to 0.21)		
End of Study	0.19 (0.16 to 0.23)	0.18 (0.14 to 0.22)		

Statistical analyses

Statistical analysis title	EQ-5D-5L Index score at day 99
Statistical analysis description:	
Statistical analysis results of of EQ-5D-5L Index score at day 99 (PD Analysis Set)	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.613
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	0.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.03
upper limit	0.06

Statistical analysis title	EQ-5D-5L Index score at EoS
Statistical analysis description:	
Statistical analysis results of of EQ-5D-5L Index score at End of Study (PD Analysis Set)	
Comparison groups	secukinumab v Placebo

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.74
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	0.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.04
upper limit	0.06

Secondary: Pain score over time using a VAS scale

End point title	Pain score over time using a VAS scale

End point description:

Pain intensity is assessed by a Visual Analog Scale (VAS) which is measured on a 10-cm line that represents a continuum between "no pain" and "worst pain"

End point type	Secondary

End point timeframe:

Days 15, 29, 57, 85, 99, 127 and then End of Study

End point values	secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: Scores				
number (confidence interval 90%)				
Day 15	-12.11 (-19.52 to -4.70)	-9.50 (-17.30 to -1.71)		
Day 29	-26.04 (-33.97 to -18.11)	-23.13 (-31.52 to -14.74)		
Day 57	-35.52 (-43.67 to -27.37)	-32.83 (-41.52 to -24.15)		
Day 85	-42.63 (-50.88 to -34.38)	-37.97 (-46.74 to -29.21)		
Day 99	-46.11 (-54.10 to -38.12)	-40.56 (-49.00 to -32.11)		
Day 127	-49.44 (-57.45 to -41.44)	-45.27 (-53.75 to -36.79)		
End of Study	-52.23 (-60.31 to -44.14)	-50.74 (-59.40 to -42.08)		

Statistical analyses

Statistical analysis title	VAS score at day 99

Statistical analysis description:	
Statistical analysis results of pain score using VAS scale (PD Analysis Set) at day 99	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.281
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	-5.55
Confidence interval	
level	90 %
sides	2-sided
lower limit	-14.07
upper limit	2.97

Statistical analysis title	VAS score at EoS
Statistical analysis description:	
Statistical analysis results of pain score using VAS scale (PD Analysis Set) at End of Study	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.78
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	-1.49
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.33
upper limit	7.35

Secondary: Patient global assessment (PGA) score using a VAS scale at End of Study

End point title	Patient global assessment (PGA) score using a VAS scale at End of Study
End point description:	
The patient's global assessment of disease activity is performed using a 100 mm Visual Analog Scale (VAS) ranging from "no activity" to "most active" in the last 24 hours.	
End point type	Secondary
End point timeframe:	
Days 15, 29, 57, 85, 99, 127 and End of Study	

End point values	secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: Scores				
number (confidence interval 95%)				
Day 15	-6.33 (-13.44 to 0.79)	-8.09 (-15.79 to -0.38)		
Day 29	-22.25 (-29.68 to -14.82)	-16.38 (-24.43 to -8.33)		
Day 57	-29.40 (-37.06 to -21.74)	-25.69 (-34.04 to -17.34)		
Day 85	-37.57 (-45.01 to -30.12)	-31.75 (-39.79 to -23.72)		
Day 99	-38.43 (-45.88 to -30.97)	-35.10 (-43.14 to -27.07)		
Day 127	-43.78 (-51.23 to -36.33)	-38.32 (-46.37 to -30.26)		
End of Study	-47.72 (-55.15 to -40.28)	-39.43 (-47.45 to -31.40)		

Statistical analyses

Statistical analysis title	Pain score at day 99
Statistical analysis description:	
Statistical analysis results of pain score using VAS scale (PD Analysis Set) at day 99	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.489
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	-3.32
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11.28
upper limit	4.64

Statistical analysis title	Pai score at EoS
Statistical analysis description:	
Statistical analysis results of pain score using VAS scale at End of Study	
Comparison groups	secukinumab v Placebo

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.087
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	-8.29
Confidence interval	
level	90 %
sides	2-sided
lower limit	-16.26
upper limit	-0.32

Secondary: Physician global assessment (PhGA) score using a VAS scale over time

End point title	Physician global assessment (PhGA) score using a VAS scale over time

End point description:

Physician global assessment (PhGA) score using a VAS scale (considering the last 24 hours)

End point type	Secondary

End point timeframe:

Days 15, 29, 57, 85, 99, 127 and End of Study

End point values	secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: Score				
number (confidence interval 90%)				
Day 15	-13.99 (-20.22 to -7.75)	-9.11 (-15.80 to -2.42)		
Day 29	-25.01 (-31.51 to -18.50)	-19.42 (-26.42 to -12.43)		
Day 57	-30.78 (-37.57 to -23.99)	-27.83 (-35.13 to -20.53)		
Day 85	-33.42 (-40.68 to -26.16)	-37.88 (-45.66 to -30.11)		
Day 99	-35.72 (-42.66 to -28.79)	-41.73 (-49.15 to -34.31)		
Day 127	-41.72 (-48.32 to -35.12)	-44.18 (-51.28 to -37.08)		
End of Study	-44.64 (-51.86 to -37.41)	-44.26 (-52.02 to -36.51)		

Statistical analyses

Statistical analysis title	PhGA score using VAS scale at day 99

Statistical analysis description:	
Statistical analysis results of PhGA score using VAS scale at day 99	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.21
Method	LS Mean
Parameter estimate	Difference and 99% CL versus placebo
Point estimate	6.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.9
upper limit	13.91

Statistical analysis title	PhGA score using VAS scale at End of Study
Statistical analysis description:	
Statistical analysis results of PhGA score using VAS scale at End of Study	
Comparison groups	secukinumab v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.942
Method	LS Mean
Parameter estimate	Difference and 90% CI versus placebo
Point estimate	-0.37
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.86
upper limit	8.11

Secondary: Pharmacokinetics - Cmin

End point title	Pharmacokinetics - Cmin[2]

End point description:

Mean trough concentrations

Cmin is a pharmacokinetics term for the minimum blood plasma concentration reached by a drug prior to administration of a second dose (mass/volume)

Serum trough concentrations of secukinumab 300 mg group was measured at Days 1, 29, 85 and EOS

No statistical analysis was planned for this primary outcome.

End point type	Secondary

End point timeframe:

Days 1, 29, 85 and EOS

Notes:

[2] - 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: The mean trough concentrations increased rapidly after the first four weekly doses (90.4 (30.7) µg/mL) and were lower at Week 12 (13.2 (6.67) µg/mL).

End point values	secukinumab			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: ug/mL				
arithmetic mean (standard deviation)				
Mean trough concentration after first 4 wkly doses	90.4 (± 30.7)			
Week 12	13.2 (± 6.67)			

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity assessment - Treatment emergent ADAs

End point title	Immunogenicity assessment - Treatment emergent ADAs

End point description:

Number of Participants with Treatment emergent Anti-secukinumab antibodies

No statistical analysis was planned for this primary outcome.

End point type	Secondary

End point timeframe:

Day 1 and EoS

End point values	secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: Participants				
Day 1	0	1		
End of Study	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with tendinosis grade score 1, 2 or 3 measured by magnetic resonance imaging (MRI) Sein scores

End point title	Number of participants with tendinosis grade score 1, 2 or 3 measured by magnetic resonance imaging (MRI) Sein scores

End point description:

Assessment of structural changes in the rotator cuff tendinopathy over time

The MRI Sein score was used to grade supraspinatus tendinosis using a modified 4-point scale from 0 to 3 and changes in grading over time were captured in the shift table. Grade 0 is normal, grade 1 is mild, Grade 2 is moderate and grade 3 is marked tendinosis.

In this Sein score assessment, only data from Day 99 and baseline could be compared, as only those two time points were double read and adjudicated in case the 2 readers had different results. At any other time-points (Day 57 and EOS), images were assessed only by one reader and thus could not be compared to baseline.

No statistical analysis was planned for this primary outcome.

End point type	Secondary

End point timeframe:

Baseline and Day 99

End point values	secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: participants				
Baseline grade 1	31	25		
Baseline grade 2	11	10		
Baseline grade 3	3	3		
Day 99 grade 1	31	26		
Day 99 grade 2	11	9		
Day 99 grade 3	3	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Approximately 40 weeks: 15 Dec 2017 through 17 Oct 2019	
Adverse event reporting additional description:	
Adverse Events (AEs) are any untoward sign or symptom that occurs during the study treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	AIN457 300 mg
Reporting group description:	
AIN457 300 mg	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Serious adverse events	AIN457 300 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 49 (0.00%)	0 / 47 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	AIN457 300 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 49 (73.47%)	34 / 47 (72.34%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign bone neoplasm			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Benign neoplasm of skin			
subjects affected / exposed	1 / 49 (2.04%)	1 / 47 (2.13%)	
occurrences (all)	2	1	
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	1 / 49 (2.04%)	2 / 47 (4.26%)	
occurrences (all)	1	2	
Feeling hot			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Injection site erythema			
subjects affected / exposed	1 / 49 (2.04%)	2 / 47 (4.26%)	
occurrences (all)	2	2	
Injection site haematoma			
subjects affected / exposed	2 / 49 (4.08%)	1 / 47 (2.13%)	
occurrences (all)	2	1	
Injection site pain			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Injection site paraesthesia			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Injection site pruritus			
subjects affected / exposed	1 / 49 (2.04%)	1 / 47 (2.13%)	
occurrences (all)	4	1	
Oedema peripheral			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			

subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Sinus congestion			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Throat irritation			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Phonophobia			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 49 (4.08%)	1 / 47 (2.13%)	
occurrences (all)	2	1	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 49 (2.04%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Red blood cell sedimentation rate increased			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	2	

Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	2 / 49 (4.08%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Hand fracture			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Infusion related reaction			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Injection related reaction			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	3	0	
Limb injury			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Meniscus injury			
subjects affected / exposed	1 / 49 (2.04%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Muscle strain			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Skin abrasion			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Tendon rupture			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Tooth fracture			

subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Wrist fracture			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	2 / 49 (4.08%)	1 / 47 (2.13%)	
occurrences (all)	2	1	
Dizziness postural			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	7 / 49 (14.29%)	7 / 47 (14.89%)	
occurrences (all)	15	10	
Paraesthesia			
subjects affected / exposed	1 / 49 (2.04%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Somnolence			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	3 / 49 (6.12%)	1 / 47 (2.13%)	
occurrences (all)	3	1	
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	2 / 49 (4.08%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Abdominal pain			
subjects affected / exposed	2 / 49 (4.08%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Abdominal pain upper			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	2 / 49 (4.08%)	1 / 47 (2.13%)	
occurrences (all)	2	1	
Faeces soft			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Irritable bowel syndrome			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	6 / 49 (12.24%)	5 / 47 (10.64%)	
occurrences (all)	9	5	
Vomiting			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Dermatitis			

subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Dermatitis allergic			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Keratolysis exfoliativa acquired			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Skin hyperpigmentation			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Skin ulcer			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 49 (4.08%)	2 / 47 (4.26%)	
occurrences (all)	4	2	
Back pain			
subjects affected / exposed	1 / 49 (2.04%)	4 / 47 (8.51%)	
occurrences (all)	1	4	
Muscle spasms			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			

subjects affected / exposed	3 / 49 (6.12%)	1 / 47 (2.13%)	
occurrences (all)	3	7	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	1 / 49 (2.04%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Neck pain			
subjects affected / exposed	3 / 49 (6.12%)	1 / 47 (2.13%)	
occurrences (all)	3	1	
Osteoarthritis			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Patellofemoral pain syndrome			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Spinal pain			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Tendon disorder			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Cellulitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	

Fungal skin infection			
subjects affected / exposed	3 / 49 (6.12%)	0 / 47 (0.00%)	
occurrences (all)	4	0	
Gastroenteritis			
subjects affected / exposed	2 / 49 (4.08%)	1 / 47 (2.13%)	
occurrences (all)	2	1	
Gastroenteritis viral			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Gastrointestinal infection			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Gastrointestinal viral infection			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Lymphangitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	8 / 49 (16.33%)	5 / 47 (10.64%)	
occurrences (all)	11	5	
Oral candidiasis			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Oral herpes			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Periodontitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Pulpitis dental			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	

Pustule			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	0 / 49 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	
Sinusitis			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	2 / 49 (4.08%)	4 / 47 (8.51%)	
occurrences (all)	3	6	
Urinary tract infection			
subjects affected / exposed	1 / 49 (2.04%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	0 / 49 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 March 2018	Updated to reflect current form standards and form prtection added

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

In general "End of Study" is Day 169 (week 24). But in the study it was handled in a way, that whenever a subject discontinued the last visit was the EoS visit.

Notes: