Clinical trial results:
A randomized, double-blind, placebo-controlled, parallel group, phase III multicenter study of intravenous secukinumab to compare efficacy at 16 weeks with placebo and to assess safety and tolerability up to 52 weeks in subjects with active Psoriatic Arthritis

Summary

EudraCT number	2019-001176-11
Trial protocol	BG GR
Global end of trial date	17 May 2022

Results information

Result version number	v1 (current)
This version publication date	25 May 2023
First version publication date	25 May 2023

Trial information

Trial identification

Sponsor protocol code	CAIN457P12302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04209205
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 Pharmac AG , 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharmac 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	17 May 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstrate that the efficacy of i.v. secukinumab at Week 16 was superior to placebo in subjects with active PsA based on the proportion of patients achieving an ACR50 response.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 January 2020
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	Brazil: 9
Country: Number of subjects enrolled	Bulgaria: 20
Country: Number of subjects enrolled	Colombia: 14
Country: Number of subjects enrolled	Czechia: 49
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Guatemala: 12
Country: Number of subjects enrolled	India: 12
Country: Number of subjects enrolled	Malaysia: 6
Country: Number of subjects enrolled	Philippines: 15
Country: Number of subjects enrolled	Poland: 47
Country: Number of subjects enrolled	Russian Federation: 11
Country: Number of subjects enrolled	South Africa: 63
Country: Number of subjects enrolled	Thailand: 18
Country: Number of subjects enrolled	Turkey: 1
Country: Number of subjects enrolled	United States: 100
Worldwide total number of subjects	381
EEA total number of subjects	120

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)	335
From 65 to 84 years	46
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

479 participants were screened and and 381 were randomized.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	AIN457 6 mg/kg - 3 mg/kg i.v.

Arm description:

AIN457 6 mg/kg i.v. infusion at baseline, followed by AIN457 3 mg/kg i.v. infusion every 4 weeks starting at Week 4 through Week 48 (exposure through Week 52).

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

Dosage and administration details:

AIN457 6 mg/kg - 3 mg/kg i.v.

Arm title	Placebo to AIN457 3 mg/kg i.v.

Arm description:

Matching placebo from baseline to Week 16 and switch to AIN457 3 mg/kg i.v. infusion every 4 weeks through Week 48 (exposure through Week 52).

Arm type	both placebo and experimental
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

matching placebo 6 mg/kg - 3 mg/kg i.v.

Number of subjects in period 1	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.
Started	191	190
Completed	173	167
Not completed	18	23
Physician decision	1	1
Subject decision	10	10
Adverse event, non-fatal	2	3
Protocol deviation	-	1
Death - placebo not switched	-	1
Adverse event - placebo not switched	-	1
Lost to follow-up	3	1
Progressive disease	1	-
Subject decision - placebo not switched	-	5
New therapy for study indication	1	-

Baseline characteristics

Reporting groups	
Reporting group title	AIN457 6 mg/kg - 3 mg/kg i.v.
Reporting group description:	
AIN457 6 mg/kg i.v. infusion at baseline, followed by AIN457 3 mg/kg i.v. infusion every 4 weeks starting at Week 4 through Week 48 (exposure through Week 52).	
Reporting group title	Placebo to AIN457 3 mg/kg i.v.
Reporting group description:	
Matching placebo from baseline to Week 16 and switch to AIN457 3 mg/kg i.v. infusion every 4 weeks through Week 48 (exposure through Week 52).	

Reporting group values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.	Total
Number of subjects	191	190	381
Age Categorical Units: Participants			
<65 years	170	165	335
65-74 years	17	24	41
>= 75 years	4	1	5
Sex: Female, Male Units: Participants			
Female	104	105	209
Male	87	85	172
Race/Ethnicity, Customized Units: Subjects			
White	148	153	301
Black or African American	5	1	6
Asian	25	26	51
American Indian or Alaska Native	10	9	19
More than one race	3	1	4

End points

End points reporting groups

Reporting group title	AIN457 6 mg/kg - 3 mg/kg i.v.
Reporting group description:	
AIN457 6 mg/kg i.v. infusion at baseline, followed by AIN457 3 mg/kg i.v. infusion every 4 weeks starting at Week 4 through Week 48 (exposure through Week 52).	
Reporting group title	Placebo to AIN457 3 mg/kg i.v.
Reporting group description:	
Matching placebo from baseline to Week 16 and switch to AIN457 3 mg/kg i.v. infusion every 4 weeks through Week 48 (exposure through Week 52).	

Primary: American College of Rheumatology 50 (ACR50) response comparison between treatment groups using non-responder imputation at Week 16 (Full analysis set)

End point title	American College of Rheumatology 50 (ACR50) response comparison between treatment groups using non-responder imputation at Week 16 (Full analysis set)
End point description:	
Percentage of participants with active psoriatic arthritis (PsA) who achieved an American College of Rheumatology 50 (ACR50) response The ACR50 is a composite measure defined as both improvement of 50% in the number of tender and number of swollen joints, and a 50% improvement in three of the following five criteria: patient global assessment, physician global assessment, functional ability measure [most often Health Assessment Questionnaire (HAQ)], visual analog pain scale, and erythrocyte sedimentation rate or C-reactive protein (CRP)	
End point type	Primary
End point timeframe:	
Baseline up to Week 16	

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	12		
Units: Percentage of responders				
arithmetic mean (confidence interval 95%)	31.35 (24.80 to 37.90)	6.33 (2.87 to 9.79)		

Statistical analyses

Statistical analysis title	ACR50
Comparison groups	Placebo to AIN457 3 mg/kg i.v. v AIN457 6 mg/kg - 3 mg/kg i.v.

Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	25.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.61
upper limit	32.43

Secondary: American College of Rheumatology 20 (ACR20) response comparison between treatment groups using on-responder imputation at Week 16 (Full analysis set)

End point title	American College of Rheumatology 20 (ACR20) response comparison between treatment groups using on-responder imputation at Week 16 (Full analysis set)

End point description:

Percentage of participants with an American College of Rheumatology 20% (ACR20) response. A participant was a responder if the following 3 criteria for improvement from Baseline were met: • ≥ 20% improvement in 78 tender joint count; • ≥ 20% improvement in 76 swollen joint count; and • ≥ 20% improvement in at least 3 of the 5 following parameters: ◦ Patient's assessment of pain (measured on a 100 mm visual analog scale [VAS]); ◦ Patient's global assessment of disease activity (measured on a 100 mm VAS); ◦ Physician's global assessment of disease activity (measured on a 100 mm VAS); ◦ Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index (HAQ-DI)); ◦ C-Reactive Protein.

End point type	Secondary

End point timeframe:

Baseline up to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	55		
Units: Percentage of responders				
arithmetic mean (confidence interval 95%)	59.60 (52.67 to 66.52)	29.01 (22.57 to 35.44)		

Statistical analyses

Statistical analysis title	ACR20
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo to AIN457 3 mg/kg i.v.

Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	30.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.14
upper limit	40.05

Secondary: Minimal disease activity (MDA 5/7) comparison between treatment groups using on-responder imputation at Week 16 (Full analysis set)

End point title	Minimal disease activity (MDA 5/7) comparison between treatment groups using on-responder imputation at Week 16 (Full analysis set)
End point description:	
MDA is assessed as 5 of the 7 following: ≤ 1 tender and swollen joint; entheseal count, PASI ≤ 1 or BSA ≤3%, PsA ≤ 15 and disease activity ≤ 20 (VAS) and HAQ-DI© ≤ 0.5	
End point type	Secondary
End point timeframe:	
Baseline up to Week 16	

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	10		
Units: Percentage of responders				
arithmetic mean (confidence interval 95%)	22.45 (16.57 to 28.33)	5.28 (2.10 to 8.46)		

Statistical analyses

Statistical analysis title	MDA 5/7
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo to AIN457 3 mg/kg i.v.
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	17.17

Confidence interval	
level	95 %
sides	2-sided
lower limit	10.48
upper limit	23.85

Secondary: Psoriasis Area and Severity Index 90(PASi90) comparison between treatment groups using on-responder imputation at Week 16 (Full analysis set)

End point title	Psoriasis Area and Severity Index 90(PASi90) comparison between treatment groups using on-responder imputation at Week 16 (Full analysis set)

End point description:

Change from baseline of a 90% reduction in the PASI score for patients with a >= 3% body surface area psoriasis at baseline. Four body surface areas are evaluated (head, trunk and upper and lower limbs) for plaque, erythema, scaling and thickness. The degree of severity of each sign in each of the 4 body areas was assigned a score of 0 to 4. Scores ranged from 0 to 72 and higher scores represent worsening severity.

End point type	Secondary

End point timeframe:

Baseline up to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	7		
Units: Percentage of responders				
arithmetic mean (confidence interval 95%)	47.85 (38.15 to 57.54)	6.46 (1.83 to 11.09)		

Statistical analyses

Statistical analysis title	PASi90
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo to AIN457 3 mg/kg i.v.
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	41.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	30.64
upper limit	52.13

Secondary: Health Assessment Questionnaire - Disability Index (HAQ-DI) score change from baseline using mixed model repeated measures (MMRM) at Week 16 (Full analysis set)

End point title	Health Assessment Questionnaire - Disability Index (HAQ-DI) score change from baseline using mixed model repeated measures (MMRM) at Week 16 (Full analysis set)

End point description:

The Health Assessment Questionnaire - Disability Index is a patient-reported questionnaire consisting of 20 questions referring to eight domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and usual activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task are summed and averaged to provide an overall score ranging from 0 to 3, where zero represents no disability and three very severe, high-dependency disability. Negative mean changes from Baseline in the overall score indicate improvement in functional ability.

End point type	Secondary

End point timeframe:

Baseline up to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	183		
Units: scores on a scale				
least squares mean (standard error)	-0.39 (± 0.035)	0.15 (± 0.035)		

Statistical analyses

Statistical analysis title	HAQ-DI
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo to AIN457 3 mg/kg i.v.
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least squares mean
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.043

Secondary: Psoriatic Arthritis Disease Activity Score (PASDAS) change from baseline using mixed model repeated measures (MMRM) at Week 16 (Full analysis set)

End point title	Psoriatic Arthritis Disease Activity Score (PASDAS) change from baseline using mixed model repeated measures (MMRM) at Week 16 (Full analysis set)

End point description:

PASDAS is a composite measure developed to assess disease activity in Psoriatic arthritis. It is calculated by utilizing seven measures: Patient reported measures (excluding mental component) (SF-36-PCS), skin, peripheral joint counts (tender and swollen joint counts), dactylitis (LDI), enthesitis (LEI), acute phase response (CRP), and patient and physician global VAS scores. Lower score indicates better outcome.

End point type	Secondary

End point timeframe:

Baseline up to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	170		
Units: composite scores				
least squares mean (standard error)	-2.24 (± 0.103)	-1.11 (± 0.103)		

Statistical analyses

Statistical analysis title	PASDAS
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo to AIN457 3 mg/kg i.v.
Number of subjects included in analysis	345
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least squares mean
Point estimate	-1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.38
upper limit	0.87
Variability estimate	Standard error of the mean
Dispersion value	0.129

Secondary: Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) score change from baseline using mixed model repeated measures (MMRM) at Week 16 (Full analysis set)

End point title	Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) score change from baseline using mixed model repeated measures (MMRM) at Week 16 (Full analysis set)

End point description:

The FACIT-Fatigue is a 13 item questionnaire that assesses self-reported fatigue and its impact upon daily activities and function. Response scale ranges from 0-4 and the total score range is 0 - 52. Higher scores indicate better quality of life

End point type	Secondary

End point timeframe:

Baseline up to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	183		
Units: scores on a scale				
least squares mean (standard error)	6.15 (± 0.759)	3.30 (± 0.750)		

Statistical analyses

Statistical analysis title	FACIT-F
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo to AIN457 3 mg/kg i.v.
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0024
Method	Mixed models analysis
Parameter estimate	Least squares mean
Point estimate	2.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	4.68
Variability estimate	Standard error of the mean
Dispersion value	0.933

Secondary: Short Form 36-Physical Component Summary (SF36-PCS) score change

from baseline using mixed model repeated measures (MMRM) at Week 16 (Full analysis set)

End point title	Short Form 36-Physical Component Summary (SF36-PCS) score change from baseline using mixed model repeated measures (MMRM) at Week 16 (Full analysis set)

End point description:

The SF-36 is used to measure health-related quality of life with acute and chronic conditions. It consists of eight subscales that can be scored individually: Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, and Mental Health. Range of scoring is 0 - 100, with higher scores indicating better health status.

End point type	Secondary

End point timeframe:

Baseline up to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	182		
Units: scores on a scale				
least squares mean (standard error)	6.47 (± 0.558)	2.34 (± 0.550)		

Statistical analyses

Statistical analysis title	SF36-PCS
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo to AIN457 3 mg/kg i.v.
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least squares mean
Point estimate	4.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	5.46
Variability estimate	Standard error of the mean
Dispersion value	0.676

Secondary: Modified Nail Psoriasis Severity Index (mNAPSI) score change from baseline using mixed model repeated measures (MMRM) at Week 16 (Full analysis set)

End point title	Modified Nail Psoriasis Severity Index (mNAPSI) score change from baseline using mixed model repeated measures (MMRM)

	at Week 16 (Full analysis set)

End point description:

The mNAPSI is an instrument to assess psoriatic nail involvement. Three groups of features (onycholysis and oil-drop dyshromia, pitting and crumbling) graded on a scale from 0 to 3. The next 4 abnormalities were graded as absent or present (leukonychia, splinter hemorrhages, hyperkeratosis and red spots in the lunula). The total score is 13 and the lower score indicates a better outcome.

End point type	Secondary

End point timeframe:

Baseline up to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	118		
Units: scores				
least squares mean (standard error)	-9.25 (± 1.069)	-3.14 (± 1.084)		

Statistical analyses

Statistical analysis title	mNAPSI
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo to AIN457 3 mg/kg i.v.
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least squares mean
Point estimate	-6.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.96
upper limit	-3.26
Variability estimate	Standard error of the mean
Dispersion value	1.447

Secondary: Percentage of participants with complete resolution of dactylitis at Week 16 using non-responder imputation (Dactylitis subset)

End point title	Percentage of participants with complete resolution of dactylitis at Week 16 using non-responder imputation (Dactylitis subset)

End point description:

The Leeds Dactylitis Index (LDI) measures the ratio of the circumference of the affected (swollen) digit to the circumference of the digit on the opposite hand or foot, using a minimum difference of 10% to define a dactylitic digit. The ratio of circumference is multiplied by a tenderness score, using a

modification of LDI that is a binary score (1 for tender, 0 for non-tender). The LDI requires a finger circumference gauge or a dactylometer to measure digital circumference. Scores range from 0 - 20 and lower score indicating better outcome.

End point type	Secondary

End point timeframe:

Baseline up to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	23		
Units: Percentage of responders				
arithmetic mean (confidence interval 95%)	59.53 (48.96 to 70.11)	32.05 (21.33 to 42.76)		

Statistical analyses

Statistical analysis title	Dactylitis
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo to AIN457 3 mg/kg i.v.
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0003
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	27.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.43
upper limit	42.55

Secondary: Percentage of participants with complete resolution of enthesitis at Week 16 using non-responder imputation (Enthesitis subset (LEI))

End point title	Percentage of participants with complete resolution of enthesitis at Week 16 using non-responder imputation (Enthesitis subset (LEI))

End point description:

Enthesitis is inflammation of the enthesis which is where a a tendon or ligament attaches to the bone. The Leeds enthesitis index (LEI) is a validated index that uses 6 sites for evaluation of enthesitis: lateral epicondyle humerus L + R, proximal achilles L + R and medial condyle femur L+R. If enthesitis is present at any of the 6 sites, the subject is counted as a subject with enthesitis.

End point type	Secondary

End point timeframe:

Baseline up to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo to AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	43		
Units: Percentage of responders				
arithmetic mean (confidence interval 95%)	55.52 (46.92 to 64.12)	39.16 (30.14 to 48.19)		

Statistical analyses

Statistical analysis title	enthesitis
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo to AIN457 3 mg/kg i.v.
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0102
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	16.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.88
upper limit	28.82

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment up to a maximum of 481 days which included an approximate follow up period of 8 weeks for AIN457 treatment group.

Adverse event reporting additional description:

Any subjects randomized to Placebo were counted under 'Placebo' before being switched to AIN457 and under 'Any AIN457' after being switched to AIN457. A subject with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Any AIN457

Reporting group description:

Any AIN457

Reporting group title	Placebo

Reporting group description:

Placebo

Serious adverse events	Any AIN457	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 374 (5.88%)	4 / 190 (2.11%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Procedural complication			

subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention postoperative			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 374 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cerebrovascular accident			
subjects affected / exposed	0 / 374 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin lesion			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	2 / 374 (0.53%)	2 / 190 (1.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			

subjects affected / exposed	6 / 374 (1.60%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 374 (0.53%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pharyngitis			

subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 374 (0.27%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Any AIN457	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	136 / 374 (36.36%)	35 / 190 (18.42%)	
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	8 / 374 (2.14%)	1 / 190 (0.53%)	
occurrences (all)	8	1	
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 374 (2.94%)	2 / 190 (1.05%)	
occurrences (all)	11	2	
Alanine aminotransferase increased			
subjects affected / exposed	12 / 374 (3.21%)	4 / 190 (2.11%)	
occurrences (all)	13	4	
Weight increased			
subjects affected / exposed	10 / 374 (2.67%)	1 / 190 (0.53%)	
occurrences (all)	10	1	
SARS-CoV-2 test positive			
subjects affected / exposed	12 / 374 (3.21%)	2 / 190 (1.05%)	
occurrences (all)	13	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	12 / 374 (3.21%)	1 / 190 (0.53%)	
occurrences (all)	13	1	
Nervous system disorders			

Headache			
subjects affected / exposed	12 / 374 (3.21%)	5 / 190 (2.63%)	
occurrences (all)	15	6	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 374 (2.41%)	2 / 190 (1.05%)	
occurrences (all)	11	2	
Nausea			
subjects affected / exposed	11 / 374 (2.94%)	2 / 190 (1.05%)	
occurrences (all)	12	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	14 / 374 (3.74%)	3 / 190 (1.58%)	
occurrences (all)	15	3	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	17 / 374 (4.55%)	1 / 190 (0.53%)	
occurrences (all)	19	1	
Bronchitis			
subjects affected / exposed	8 / 374 (2.14%)	0 / 190 (0.00%)	
occurrences (all)	8	0	
COVID-19			
subjects affected / exposed	37 / 374 (9.89%)	7 / 190 (3.68%)	
occurrences (all)	37	7	
Nasopharyngitis			
subjects affected / exposed	13 / 374 (3.48%)	3 / 190 (1.58%)	
occurrences (all)	14	3	
Pharyngitis			
subjects affected / exposed	9 / 374 (2.41%)	1 / 190 (0.53%)	
occurrences (all)	10	1	
Upper respiratory tract infection			
subjects affected / exposed	10 / 374 (2.67%)	6 / 190 (3.16%)	
occurrences (all)	14	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported