



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 Ankylosing Spondylitis or nonradiographic axial SpondyloArthritis

Summary

EudraCT number	2019-001177-90
Trial protocol	BE GR SE CZ BG IT
Global end of trial date	20 December 2022

Results information

Result version number	v1 (current)
This version publication date	10 December 2023
First version publication date	10 December 2023

Trial information

Trial identification

Sponsor protocol code	CAIN457P12301
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04156620
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	20 December 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	20 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate that the efficacy of i.v. secukinumab at Week 16 is superior to placebo in subjects with active axSpA (AS and nr-axSpA) based on the proportion of subjects achieving an ASAS40 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	11 December 2019
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	Belgium: 4
Country: Number of subjects enrolled	Brazil: 23
Country: Number of subjects enrolled	Bulgaria: 24
Country: Number of subjects enrolled	Colombia: 28
Country: Number of subjects enrolled	Czechia: 76
Country: Number of subjects enrolled	Greece: 5
Country: Number of subjects enrolled	Guatemala: 18
Country: Number of subjects enrolled	India: 31
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Korea, Republic of: 23
Country: Number of subjects enrolled	Malaysia: 22
Country: Number of subjects enrolled	Philippines: 14
Country: Number of subjects enrolled	Poland: 76
Country: Number of subjects enrolled	Russian Federation: 86
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Thailand: 15
Country: Number of subjects enrolled	Turkey: 4
Country: Number of subjects enrolled	United States: 70

Worldwide total number of subjects	526
EEA total number of subjects	192

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)	510
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

769 participants were screened for the study and 527 participants were randomized. However, one patient was mis-randomized and never received any study drug and is therefore not included in the table below.

Period 1

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

Arms

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

Arm description:

Participants received AIN457 (secukinumab) 6 mg/kg i.v. at baseline, followed by AIN457 3 mg/kg i.v. every four 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	Intravenous use

Dosage and administration details:

3 mg/kg at Week 4 up to Week 52

Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

6 mg/kg loading dose at baseline

Arm title	Placebo - AIN457 3 mg/kg i.v.
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Arm description:

Participants received i.v. placebo at baseline visit, Weeks 4, 8, and 12, followed by AIN457 (secukinumab) 3 mg/kg i.v. at Week 16 and every four weeks through Week 48 (exposure through Week 52)

Arm type	placebo, experimental
Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg at Week 16 up to Week 52

Investigational medicinal product name	placebo matching secukinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0 mg/kg every 4 weeks for 16 weeks

Number of subjects in period 1	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.
Started	264	262
Completed Period 1	255	253
Started Period 2	255	251
Completed Period 2	233	235
Completed	227	233
Not completed	37	29
Adverse event - TP 1	5	2
Adverse event - TP 2	5	6
Pregnancy - TP 2	1	1
Death - TP 2	1	-
Physician decision - TP 2	4	2
Lost to follow-up TP 1	1	1
New therapy for study indication - TP 2	1	-
Subject decision - TP 1	3	5
Subject decision - TP 2	11	9
Progressive disease - TP 1	-	1
Lost to follow-up - TP 2	5	2

Baseline characteristics

Reporting groups

Reporting group title	AIN457 6 mg/kg - 3 mg/kg i.v.
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Reporting group description:

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

Reporting group title	Placebo - AIN457 3 mg/kg i.v.
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Reporting group description:

Participants received i.v. placebo at baseline visit, Weeks 4, 8, and 12, followed by AIN457 (secukinumab) 3 mg/kg i.v. at Week 16 and every four weeks through Week 48 (exposure through Week 52)

Reporting group values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.	Total
Number of subjects	264	262	526
Age Categorical Units: participants			
< 65 years	253	257	510
65 - 75 years	8	4	12
>= 75 years	3	1	4
Sex: Female, Male Units: participants			
Female	99	84	183
Male	165	178	343
Race/Ethnicity, Customized Units: Subjects			
White	180	179	359
Black or African American	7	6	13
Asian	59	47	106
American Indian or Alaska Native	17	25	42
Multiple	1	5	6
Disease condition Units: Subjects			
Ankylosing spondylitis	208	205	413
Non-radiographic axial spondylarthritis	56	57	113
Weight Units: kg			
arithmetic mean	77.61	78.08	
standard deviation	± 18.006	± 18.444	-

End points

End points reporting groups

Reporting group title	AIN457 6 mg/kg - 3 mg/kg i.v.
Reporting group description:	
Participants received AIN457 (secukinumab) 6 mg/kg i.v. at baseline, followed by AIN457 3 mg/kg i.v. every four weeks starting at Week 4 through Week 48 (exposure through Week 52)	
Reporting group title	Placebo - AIN457 3 mg/kg i.v.
Reporting group description:	
Participants received i.v. placebo at baseline visit, Weeks 4, 8, and 12, followed by AIN457 (secukinumab) 3 mg/kg i.v. at Week 16 and every four weeks through Week 48 (exposure through Week 52)	

Primary: Percentage of participants who achieved an ASAS40 (Assessment of SpondyloArthritis International Society criteria)

End point title	Percentage of participants who achieved an ASAS40 (Assessment of SpondyloArthritis International Society criteria)
End point description:	
ASAS40 is $\geq 40\%$ and an absolute improvement from baseline of ≥ 20 units (range 0–100) in ≥ 3 of the following 4 domains: back pain [10 cm visual analogue scale (VAS)], patient global assessment of disease activity (10 cm VAS), physical function (BASFI; range 0–100) and inflammation (mean score of items 5 and 6 of the BASDAI; both 10 cm VAS) without any worsening in the remaining domain. ASAS consists of 6 domains (4 main and 2 additional): 1. Patient's global assessment measured on a visual analog scale (VAS); 2. Patient's assessment of back pain, measured on a VAS; 3. Function represented by Bath Ankylosing Spondylitis Functional Index (BASFI) measured by VAS; 4. Inflammation represented by mean duration and severity of morning stiffness, on the BAS Disease Activity Index (BASDAI) as measured by VAS; 5. Spinal mobility represented by the BAS Metrology Index (BASMI) lateral spinal flexion assessment; 6. C-reactive protein (acute phase reactant).	
End point type	Primary
End point timeframe:	
Baseline to Week 16	

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264	262		
Units: percentage of participants				
number (confidence interval 95%)	40.85 (34.94 to 46.76)	22.94 (17.86 to 28.02)		

Statistical analyses

Statistical analysis title	ASAS40
Statistical analysis description:	
Week 16	
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo - AIN457 3 mg/kg i.v.

Number of subjects included in analysis	526
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	17.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.12
upper limit	25.71

Secondary: Percentage of participants who achieved Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-Reactive Protein (CRP) major improvement

End point title	Percentage of participants who achieved Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-Reactive Protein (CRP) major improvement
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End point description:

ASDAS-CRP was utilized to assess disease activity status. Parameters used for the ASDAS included: total back pain (BASDAI question 2), patient's global assessment of disease activity, peripheral pain/swelling (BASDAI question 3), duration of morning stiffness (BASDAI question 6) and CRP in mg/L. Disease activity states: inactive disease, moderate disease activity, high disease activity, and very high disease activity. The three values selected to separate these states are: < 1.3 between inactive disease and moderate disease activity; < 2.1 between moderate disease activity and high disease activity; and > 3.5 between high disease activity and very high disease activity. Selected cutoffs for improvement scores are a change of ≥ 1.1 unit for "minimal clinically important improvement" and a change of ≥ 2.0 units for "major improvement" .

End point type	Secondary
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End point timeframe:

Baseline to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264	262		
Units: percentage of participants				
number (confidence interval 95%)	27.99 (22.86 to 33.12)	7.54 (4.44 to 10.64)		

Statistical analyses

Statistical analysis title	ASDAS CRP major improvement
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo - AIN457 3 mg/kg i.v.

Number of subjects included in analysis	526
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	20.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.45
upper limit	26.44

Secondary: The change from baseline in total Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

End point title	The change from baseline in total Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)
End point description:	
BASDAI consists of a 0 through 10 scale (0 indicating no problem and 10 indicating the worst problem, captured as a continuous VAS), which was used to answer six questions pertaining to the five major symptoms of AS: fatigue, spinal pain, peripheral joint pain / swelling,, areas of localized tenderness (enthesitis, or inflammation of tendons and ligaments), morning stiffness duration, morning stiffness severity. To give each symptom equal weight, the mean of the two scores relating to morning stiffness is taken into account (questions 5 and 6). The resulting 0 to 10 score is added to the scores for questions 1 through 4. The resulting 0 to 50 score is divided by 5 to give a final 0 10 BASDAI score.	
End point type	Secondary
End point timeframe:	
Baseline to Week 16	

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	253	247		
Units: scores on a scale				
least squares mean (standard error)	-2.70 (± 0.144)	-1.69 (± 0.144)		

Statistical analyses

Statistical analysis title	BASDAI
Statistical analysis description:	
Week 16	
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo - AIN457 3 mg/kg i.v.

Number of subjects included in analysis	500
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS mean change
Point estimate	-1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.38
upper limit	-0.64
Variability estimate	Standard error of the mean
Dispersion value	0.189

Secondary: Percentage of participants who achieved an ASAS 5/6 (Assessment of SpondyloArthritis International Society criteria)

End point title	Percentage of participants who achieved an ASAS 5/6 (Assessment of SpondyloArthritis International Society criteria)
End point description:	The ASAS 5/6 improvement criteria is an improvement of $\geq 20\%$ in at least five of all six domains. A higher score on the VAS signifies higher severity. ASAS consists of 6 domains (4 main and 2 additional): 1. Patient's global assessment measured on a visual analog scale (VAS); 2. Patient's assessment of back pain, measured on a VAS; 3. Function represented by Bath Ankylosing Spondylitis Functional Index (BASFI) measured by VAS; 4. Inflammation represented by mean duration and severity of morning stiffness, on the BAS Disease Activity Index (BASDAI) as measured by VAS; 5. Spinal mobility represented by the BAS Metrology Index (BASMI) lateral spinal flexion assessment; 6. C-reactive protein (acute phase reactant).
End point type	Secondary
End point timeframe:	
Baseline to Week 16	

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264	262		
Units: percentage of participants				
number (confidence interval 95%)	43.92 (37.94 to 49.90)	21.77 (16.77 to 26.77)		

Statistical analyses

Statistical analysis title	ASAS 5/6
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo - AIN457 3 mg/kg i.v.

Number of subjects included in analysis	526
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	22.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.36
upper limit	29.95

Secondary: The change from baseline in total Bath Ankylosing Spondylitis Functional Index (BASFI)

End point title	The change from baseline in total Bath Ankylosing Spondylitis Functional Index (BASFI)
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End point description:

The BASFI is a set of 10 questions designed to determine the degree of functional limitation in subjects with AS. The questions were chosen on the basis of predominant input from subjects with AS. The first eight questions consider activities related to functional anatomy. The final two questions assess the subjects' ability to cope with everyday life. A 0-10 scale (captured as a continuous VAS) is used to answer the questions. The BASFI score is the mean of the ten scales – a value between 0 and 10.

End point type	Secondary
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End point timeframe:

Baseline to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	253	247		
Units: scores on a scale				
least squares mean (standard error)	-2.33 (± 0.147)	-1.39 (± 0.148)		

Statistical analyses

Statistical analysis title	BASFI
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Statistical analysis description:

Week 16

Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo - AIN457 3 mg/kg i.v.
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Number of subjects included in analysis	500
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS mean change
Point estimate	-0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	-0.56
Variability estimate	Standard error of the mean
Dispersion value	0.194

Secondary: The change from baseline in Short Form-36 Physical Component summary (SF-36 PCS)

End point title	The change from baseline in Short Form-36 Physical Component summary (SF-36 PCS)
End point description:	
The Short Form-36 Physical Component Summary (SF-36 PCS) is an instrument to measure health-related quality of life among healthy patients and patients with acute and chronic conditions. It consists of eight subscales (domains) that can be scored individually: Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, and Mental Health. Two overall summary scores, the Physical Component Summary (PCS) and the Mental Component Summary (MCS) also can be computed. The eight domains are based on a scale from 0-100 while PCS and MCS are norm-based scores with a mean of 50 and a standard deviation of 10. Higher scores indicate a higher level of functioning. A positive change from baseline score indicates an improvement.	
End point type	Secondary
End point timeframe:	
Baseline to Week 16	

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	254	247		
Units: scores on a scale				
least squares mean (standard error)	7.70 (± 0.473)	4.69 (± 0.473)		

Statistical analyses

Statistical analysis title	SF-36 PCS
Statistical analysis description:	
Week 16	
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo - AIN457 3 mg/kg i.

	v.
Number of subjects included in analysis	501
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS mean change
Point estimate	3.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	4.22
Variability estimate	Standard error of the mean
Dispersion value	0.615

Secondary: The change from baseline in Ankylosing Spondylitis Quality of Life (ASQoL)

End point title	The change from baseline in Ankylosing Spondylitis Quality of Life (ASQoL)
End point description:	
The ASQoL is a self-administered questionnaire designed to assess health-related quality of life in adult subjects with AS. The ASQoL contains 18 items with a dichotomous yes/no response option. A single point is assigned for each "yes" response and no points for each "no" response, resulting in overall scores that range from 0 (least severity) to 18 (highest severity). As such, lower scores indicate better quality of life. Items include an assessment of mobility/energy, self care and mood/emotion. The recall period is "at the moment".	
End point type	Secondary
End point timeframe:	
Baseline to Week 16	

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	254	247		
Units: scores on a scale				
least squares mean (standard error)	-4.65 (± 0.291)	-2.88 (± 0.290)		

Statistical analyses

Statistical analysis title	ASQoL
Statistical analysis description:	
Week 16	
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo - AIN457 3 mg/kg i.v.

Number of subjects included in analysis	501
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS mean change
Point estimate	-1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.51
upper limit	-1.04
Variability estimate	Standard error of the mean
Dispersion value	0.373

Secondary: The change from baseline in High sensitivity C-Reactive Protein (hsCRP)

End point title	The change from baseline in High sensitivity C-Reactive Protein (hsCRP)
End point description:	
This assessment (laboratory assessment) was performed in order to identify the presence of inflammation, to determine its severity and to monitor the response to treatment. Exponentially transformed LSM, the geometric mean ration of post-baseline/baseline. A value <1 indicates a reduced CRP	
End point type	Secondary
End point timeframe:	
Baseline to Week 16	

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	248		
Units: mg/L				
least squares mean (standard error)	0.39 (± 1.063)	0.89 (± 1.062)		

Statistical analyses

Statistical analysis title	hsCRP
Statistical analysis description:	
Week 16	
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo - AIN457 3 mg/kg i.v.

Number of subjects included in analysis	494
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Relative LS mean change
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.51

Secondary: Percentage of participants who achieved an ASAS20 (Assessment of SpondyloArthritis International Society criteria)

End point title	Percentage of participants who achieved an ASAS20 (Assessment of SpondyloArthritis International Society criteria)
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End point description:

The ASAS Response Criteria (ASAS20) is defined as an improvement of $\geq 20\%$ and ≥ 1 unit on a scale of 10 in at least three of the four main domains and no worsening of $\geq 20\%$ and ≥ 1 unit on a scale of 10 in the remaining domain. A higher score on the VAS signifies higher severity.

ASAS consists of 6 domains (4 main and 2 additional): 1. Patient's global assessment measured on a visual analog scale (VAS); 2. Patient's assessment of back pain, measured on a VAS; 3. Function represented by Bath Ankylosing Spondylitis Functional Index (BASFI) measured by VAS; 4. Inflammation represented by mean duration and severity of morning stiffness, on the BAS Disease Activity Index (BASDAI) as measured by VAS; 5. Spinal mobility represented by the BAS Metrology Index (BASMI) lateral spinal flexion assessment; 6. C-reactive protein (acute phase reactant).

End point type	Secondary
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End point timeframe:

Baseline to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264	262		
Units: percentage of participants				
number (confidence interval 95%)	63.94 (58.19 to 69.70)	40.53 (34.62 to 46.44)		

Statistical analyses

Statistical analysis title	ASAS20
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo - AIN457 3 mg/kg i.v.

Number of subjects included in analysis	526
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	23.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.61
upper limit	31.66

Secondary: The percentage of participants achieving Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-Reactive Protein (CRP) inactive disease.

End point title	The percentage of participants achieving Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-Reactive Protein (CRP) inactive disease.
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End point description:

ASDAS-CRP was utilized to assess disease activity status. Parameters used for the ASDAS included: total back pain (BASDAI question 2), patient's global assessment of disease activity, peripheral pain/swelling (BASDAI question 3), duration of morning stiffness (BASDAI question 6) and CRP in mg/L.

Disease activity states: inactive disease, moderate disease activity, high disease activity, and very high disease activity. The three values selected to separate these states are: < 1.3 between inactive disease and moderate disease activity; < 2.1 between moderate disease activity and high disease activity; and > 3.5 between high disease activity and very high disease activity. Selected cutoffs for improvement scores are a change of ≥ 1.1 unit for "minimal clinically important improvement" and a change of ≥ 2.0 units for "major improvement"

End point type	Secondary
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End point timeframe:

Baseline to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264	262		
Units: percentage of participants				
number (confidence interval 95%)	15.66 (11.53 to 19.78)	3.08 (1.00 to 5.15)		

Statistical analyses

Statistical analysis title	ASDAS CRP inactive disease
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Statistical analysis description:

Week 16

Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo - AIN457 3 mg/kg i.v.
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Number of subjects included in analysis	526
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	12.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.96
upper limit	17.19

Secondary: Percentage of participants who achieved ASAS20 (Assessment of SpondyloArthritis International Society criteria) partial remission.

End point title	Percentage of participants who achieved ASAS20 (Assessment of SpondyloArthritis International Society criteria) partial remission.
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End point description:

ASAS partial remission criteria are defined as a value not above 2 units in each of the four main ASAS domains on a scale of 0-10.

ASAS consists of 6 domains (4 main and 2 additional): 1. Patient's global assessment measured on a visual analog scale (VAS); 2. Patient's assessment of back pain, measured on a VAS; 3. Function represented by Bath Ankylosing Spondylitis Functional Index (BASFI) measured by VAS; 4.

Inflammation represented by mean duration and severity of morning stiffness, on the BAS Disease Activity Index (BASDAI) as measured by VAS; 5. Spinal mobility represented by the BAS Metrology Index (BASMI) lateral spinal flexion assessment; 6. C-reactive protein (acute phase reactant).

End point type	Secondary
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End point timeframe:

Baseline to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264	262		
Units: percentage of participants				
number (confidence interval 95%)	14.76 (10.49 to 19.03)	4.20 (1.77 to 6.63)		

Statistical analyses

Statistical analysis title	ASAS20 partial remission
Comparison groups	AIN457 6 mg/kg - 3 mg/kg i.v. v Placebo - AIN457 3 mg/kg i.v.

Number of subjects included in analysis	526
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	10.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.64
upper limit	15.47

Secondary: Change from baseline in Pittsburgh Sleep Quality Index (PSQI)

End point title	Change from baseline in Pittsburgh Sleep Quality Index (PSQI)
End point description:	The PSQI is a self-report questionnaire that assesses sleep quality over a 1-month time interval. Consisting of 19 items, the PSQI measures several different aspects of sleep, offering seven component scores and one composite score. The component scores consist of subjective sleep quality, sleep latency (i.e., how long it takes to fall asleep), sleep duration, habitual sleep efficiency (i.e., the percentage of time in bed that one is asleep), sleep disturbances, use of sleeping medication, and daytime dysfunction. Each item is weighted on a 0–3 interval scale. The global PSQI score is then calculated by totaling the seven component scores, providing an overall score ranging from 0 to 21, where lower scores denoted a healthier sleep quality.
End point type	Secondary
End point timeframe:	Baseline to Week 16

End point values	AIN457 6 mg/kg - 3 mg/kg i.v.	Placebo - AIN457 3 mg/kg i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	249	246		
Units: scores on a scale				
least squares mean (standard error)	-2.42 (± 0.222)	-1.76 (± 0.221)		

Statistical analyses

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

Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0234
Method	Regression, Logistic
Parameter estimate	LS mean change
Point estimate	-0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	-0.09
Variability estimate	Standard error of the mean
Dispersion value	0.292

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported for a maximum of 478 days for participants on AIN457 (including placebo switchers) and 182 days for participants on placebo which includes the 84 days in safety follow up.

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. The 6 mg/kg loading dose followed by the 3 mg/kg maintenance dose is the regimen which was specified in the protocol and SAP and approved by the FDA for this trial.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo

Reporting group title	Any AIN457
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Reporting group description:

Any AIN457

Serious adverse events	Placebo	Any AIN457	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 261 (1.15%)	32 / 517 (6.19%)	
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)			
Breast cancer			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seminoma			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			

subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst ruptured			
subjects affected / exposed	1 / 261 (0.38%)	0 / 517 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight decreased			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Hand fracture			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stab wound			
subjects affected / exposed	1 / 261 (0.38%)	0 / 517 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 261 (0.00%)	2 / 517 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Choroiditis			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 261 (0.00%)	2 / 517 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	0 / 261 (0.00%)	2 / 517 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	1 / 261 (0.38%)	0 / 517 (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			
Dermatitis atopic			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae virus infection			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dengue fever			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 261 (0.00%)	2 / 517 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 261 (0.00%)	1 / 517 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 517 (0.00%)	
occurrences causally related to treatment / all	1 / 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	Placebo	Any AIN457	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 261 (13.41%)	172 / 517 (33.27%)	
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 261 (3.45%)	17 / 517 (3.29%)	
occurrences (all)	10	27	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 261 (0.77%)	12 / 517 (2.32%)	
occurrences (all)	2	12	
Diarrhoea			

subjects affected / exposed occurrences (all)	5 / 261 (1.92%) 5	18 / 517 (3.48%) 19	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 261 (0.38%) 1	20 / 517 (3.87%) 32	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	10 / 261 (3.83%) 10	65 / 517 (12.57%) 71	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	6 / 261 (2.30%) 6	22 / 517 (4.26%) 23	
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 261 (0.38%) 1	11 / 517 (2.13%) 11	
Rhinitis subjects affected / exposed occurrences (all)	2 / 261 (0.77%) 2	11 / 517 (2.13%) 12	
Nasopharyngitis subjects affected / exposed occurrences (all)	7 / 261 (2.68%) 7	32 / 517 (6.19%) 32	
Pharyngitis subjects affected / exposed occurrences (all)	1 / 261 (0.38%) 1	13 / 517 (2.51%) 15	

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