Clinical trial results:
A randomized, double-blind, placebo-controlled multicenter study of secukinumab 150 mg in patients with active nonradiographic axial spondyloarthritis to evaluate the safety, tolerability and efficacy up to 2 years, followed by an optional phase of either 150 mg or 300 mg randomized dose escalation for up to another 2 years

Summary

EudraCT number	2015-001106-33
Trial protocol	DE GB AT ES NL HU PT NO SE BE BG FR CZ IT
Global end of trial date	11 March 2021

Results information

Result version number	v2 (current)
This version publication date	09 June 2022
First version publication date	13 December 2021
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CAIN457H2315

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02696031
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	01 July 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate that secukinumab 150 mg s.c. (without load) at Week 52 was superior to placebo in TNF-alpha inhibitor naïve (TNFi-naïve) patients with active nr-axSpA based on the proportion of patients 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	29 April 2016
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	Australia: 27
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Bulgaria: 7
Country: Number of subjects enrolled	Czechia: 71
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 52
Country: Number of subjects enrolled	United Kingdom: 24
Country: Number of subjects enrolled	Hungary: 21
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Japan: 13
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Norway: 8
Country: Number of subjects enrolled	Poland: 65
Country: Number of subjects enrolled	Portugal: 14
Country: Number of subjects enrolled	Russian Federation: 54

Country: Number of subjects enrolled	Spain: 72
Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	Switzerland: 8
Country: Number of subjects enrolled	Turkey: 2
Country: Number of subjects enrolled	United States: 36
Worldwide total number of subjects	555
EEA total number of subjects	372

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)	546
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 1583 patients were screened for this study, of which 555 patients (35.1%) were randomized. Overall, 1028 patients (64.9%) discontinued prior to screening phase completion, most due to screen failure (1000 patients, 63.2%).

Pre-assignment

Screening details:

555 participants were planned and also analyzed.

Period 1

Period 1 title	Up to Week 104
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

This was a blinded placebo controlled study up to week 52. All patients received secukinumab 150 mg as open-label treatment from Week 52 up to Week 100, unless they had discontinued study treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab, Load, Core Phase

Arm description:

AIN457 150 mg s.c. load, Core Phase

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

Dosage and administration details:

secukinumab 150 mg Load

Arm title	Secukinumab, No Load, Core Phase

Arm description:

AIN457 150 mg s.c. no load, Core Phase

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

Dosage and administration details:

secukinumab 150 mg No Load

Arm title	Placebo, Core Phase

Arm description:

Placebo s.c., Core Phase

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

placebo (1 mL)

Number of subjects in period 1	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase
Started	185	184	186
Completed	146	143	149
Not completed	39	41	37
Physician decision	1	2	3
Consent withdrawn by subject	15	10	16
Pt completed wk 52 and then withdrew	-	1	-
Adverse event, non-fatal	7	11	5
Pregnancy	-	2	1
Lost to follow-up	2	3	1
Lack of efficacy	13	12	11
Protocol deviation	1	-	-

Period 2

Period 2 title	Extension phase from wk 104 to wk 208
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

At Week 104, all patients who finished the core phase according to the protocol were asked to continue in an optional, exploratory extension phase. Patients who achieved ASAS20 response at Week 104 (Core Phase Responders) were randomized to the treatment groups, which were blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	AIN457 150 mg Extension phase

Arm description:

AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 150 mg in the Extension phase (from Week 104 to week 208).

Arm type	Experimental

Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

secukinumab 150 mg

Arm title	AIN457 300 mg Extension phase

Arm description:

AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 300 mg in the Extension phase (from Week 104 to week 208).

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

Dosage and administration details:

secukinumab 300 mg

Arm title	AIN457 300 mg Open Label Extension phase

Arm description:

AIN457 150 mg Open Label Core Phase Non-Responders who were assigned at week 104 to the 300 mg Open Label in the Extension phase (from Week 104 to week 208).

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

Dosage and administration details:

secukinumab 300 mg

Number of subjects in period 2[1]	AIN457 150 mg Extension phase	AIN457 300 mg Extension phase	AIN457 300 mg Open Label Extension phase
Started	147	147	78
Completed	137	132	72
Not completed	10	15	6
Consent withdrawn by subject	6	8	2
Physician decision	1	1	-
Adverse event, non-fatal	1	4	1
Non-compliance with study treatment	1	-	-
Lost to follow-up	-	1	-
Lack of efficacy	1	1	3

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The counts are verified as correct; the treatment arms changed from the core phase to the extension phase.

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab, Load, Core Phase
Reporting group description: AIN457 150 mg s.c. load, Core Phase	
Reporting group title	Secukinumab, No Load, Core Phase
Reporting group description: AIN457 150 mg s.c. no load, Core Phase	
Reporting group title	Placebo, Core Phase
Reporting group description: Placebo s.c., Core Phase	

Reporting group values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase
Number of subjects	185	184	186
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)	183	180	183
From 65-84 years	2	4	3
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	39.1	39.8	39.3
standard deviation	± 11.45	± 11.68	± 11.47
Sex: Female, Male Units: Participants			
Female	105	100	95
Male	80	84	91
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	9	8	7
Not Hispanic or Latino	165	162	161
Unknown or Not Reported	11	14	18
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	0	2	0
Asian	4	8	11
Black or African American	0	2	1
White	176	165	167
Other	5	7	7

Reporting group values	Total		
Number of subjects	555		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	546		
From 65-84 years	9		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	300		
Male	255		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	24		
Not Hispanic or Latino	488		
Unknown or Not Reported	43		
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	2		
Asian	23		
Black or African American	3		
White	508		
Other	19		

End points

End points reporting groups

Reporting group title	Secukinumab, Load, Core Phase
Reporting group description: AIN457 150 mg s.c. load, Core Phase	
Reporting group title	Secukinumab, No Load, Core Phase
Reporting group description: AIN457 150 mg s.c. no load, Core Phase	
Reporting group title	Placebo, Core Phase
Reporting group description: Placebo s.c., Core Phase	
Reporting group title	AIN457 150 mg Extension phase
Reporting group description: AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 150 mg in the Extension phase (from Week 104 to week 208).	
Reporting group title	AIN457 300 mg Extension phase
Reporting group description: AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 300 mg in the Extension phase (from Week 104 to week 208).	
Reporting group title	AIN457 300 mg Open Label Extension phase
Reporting group description: AIN457 150 mg Open Label Core Phase Non-Responders who were assigned at week 104 to the 300 mg Open Label in the Extension phase (from Week 104 to week 208).	

Primary: The proportion of TNF naive participants who achieved an Assessment of Spondylo Arthritis International Society (ASAS) 40 response at week 16

End point title	The proportion of TNF naive participants who achieved an Assessment of Spondylo Arthritis International Society (ASAS) 40 response at week 16

End point description:

Assessment of SpondyloArthritis International Society criteria (ASAS) consist of 6 domains (4 main and 2 additional assessment domains): 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) average of 10 questions as measured by VAS; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) as measured by VAS; 5. Spinal mobility represented by the Bath Ankylosing Spondylitis Metrology Index (BASMI) lateral spinal flexion assessment; 6. C-reactive protein (acute phase reactant). ASAS40 response is defined as an improvement of ≥40% and ≥2 units on a scale of 10 in at least three of the four ASAS main domains and no worsening at all in the remaining domain. A higher score on the VAS signifies higher severity.

End point type	Primary

End point timeframe:

Week 16

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	164	166	171	
Units: Participants	68	70	50	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo
Statistical analysis description: week 16	
Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0197 [1]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	2.7

Notes:

[1] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo
Statistical analysis description: week 16	
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	337
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0146 [2]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	2.76

Notes:

[2] - unadjusted p-value

Primary: The proportion of TNF naive participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 40 response at week 52

End point title	The proportion of TNF naive participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 40 response at week 52

End point description:

Assessment of SpondyloArthritis International Society criteria (ASAS) consist of 6 domains (4 main and 2 additional assessment domains): 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) average of 10 questions as measured by VAS; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) as measured by VAS; 5. Spinal mobility represented by the Bath Ankylosing Spondylitis Metrology Index (BASMI) lateral spinal flexion assessment; 6. C-reactive protein (acute phase reactant). ASAS40 response is defined as an improvement of ≥40% and ≥2 units on a scale of 10 in at least three of the four ASAS main domains and no worsening at all in the remaining domain. A higher score on the VAS signifies higher severity.

End point type	Primary

End point timeframe:

Week 52

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	164	166	171	
Units: Participants	58	66	34	

Statistical analyses

Statistical analysis title	Secukinumab No Load v Placebo

Statistical analysis description:

week 52

Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	337
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [3]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.64
upper limit	4.36

Notes:

[3] - unadjusted p-value

Statistical analysis title	Secukinumab Load v Placebo

Statistical analysis description:

week 52

Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0017 [4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.35
upper limit	3.63

Notes:

[4] - unadjusted p-value

Secondary: The proportion of participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 40 response

End point title	The proportion of participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 40 response

End point description:

Assessment of SpondyloArthritis International Society criteria (ASAS) consist of 6 domains (4 main and 2 additional assessment domains): 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) average of 10 questions as measured by VAS; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) as measured by VAS; 5. Spinal mobility represented by the Bath Ankylosing Spondylitis Metrology Index (BASMI) lateral spinal flexion assessment; 6. C-reactive protein (acute phase reactant). ASAS40 response is defined as an improvement of ≥40% and ≥2 units on a scale of 10 in at least three of the four ASAS main domains and no worsening at all in the remaining domain. A higher score on the VAS signifies higher severity.

End point type	Secondary

End point timeframe:

Week 16 and week 52

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	185	184	186	
Units: Participants				
week 16	74	75	52	
week 52	62	70	36	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo

Statistical analysis description:

week 16

Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0108 [5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	2.74

Notes:
[5] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo
Statistical analysis description:	
week 16	
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	370
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0087 [6]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	2.78

Notes:
[6] - unadjusted p-value

Statistical analysis title	Secukinumab Load v Placebo
Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0016 [7]
Method	Regression, Linear
Parameter estimate	Odds ratio (OR)
Point estimate	2.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.34
upper limit	3.49

Notes:

[7] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	370
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [8]
Method	Regression, Linear
Parameter estimate	Median difference (net)
Point estimate	2.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.62
upper limit	4.19

Notes:

[8] - unadjusted p-value

Secondary: The proportion of participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 20 response

End point title	The proportion of participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 20 response

End point description:

Assessment of SpondyloArthritis International Society criteria (ASAS) consist of 6 domains (4 main and 2 additional assessment domains): 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) average of 10 questions as measured by VAS; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) as measured by VAS; 5. Spinal mobility represented by the Bath Ankylosing Spondylitis Metrology Index (BASMI) lateral spinal flexion assessment; 6. C-reactive protein (acute phase reactant). ASAS 20 response is defined as an improvement of ≥20% and ≥1 unit on a scale of 10 in at least three of the four main domains and no worsening of ≥20% and ≥1 unit on a scale of 10 in the remaining domain. A higher score on the VAS signifies higher severity.

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	185	184	186	
Units: Participants	105	107	85	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo
Statistical analysis description: week 16	
Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.026 [9]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	2.43

Notes:

[9] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo
Statistical analysis description: week 16	
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	370
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0149 [10]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	2.54

Notes:

[10] - unadjusted p-value

Secondary: The proportion of participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 5/6 response

End point title	The proportion of participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 5/6 response

End point description:

Assessment of SpondyloArthritis International Society criteria (ASAS) consist of 6 domains (4 main and 2 additional assessment domains): 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) average of 10 questions as measured by VAS; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) as measured by VAS; 5. Spinal mobility represented by the Bath Ankylosing Spondylitis Metrology Index (BASMI) lateral spinal flexion assessment; 6. C-reactive protein (acute phase reactant). The ASAS 5/6 improvement criteria is an improvement of ≥20% in at least five of all six domains. A higher score on the VAS signifies higher severity.

End point type	Secondary

End point timeframe:
Week 16

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	185	184	186	
Units: Participants	74	66	44	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo
Statistical analysis description: week 16	
Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0005 [11]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.43
upper limit	3.58

Notes:
[11] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo
Statistical analysis description: week 16	
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	370
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0094 [12]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.85

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	2.94

Notes:

[12] - unadjusted p-value

Secondary: The proportion of participants who achieved an Assessment of SpondyloArthritis International Society Partial Remission (ASAS PR)

End point title	The proportion of participants who achieved an Assessment of SpondyloArthritis International Society Partial Remission (ASAS PR)

End point description:

Assessment of SpondyloArthritis International Society criteria (ASAS) consist of 6 domains (4 main and 2 additional assessment domains): 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) average of 10 questions as measured by VAS; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) as measured by VAS; 5. Spinal mobility represented by the Bath Ankylosing Spondylitis Metrology Index (BASMI) lateral spinal flexion assessment; 6. C-reactive protein (acute phase reactant). The ASAS partial remission criteria are defined as a value not above 2 units in each of the four main domains on a scale of 10. A higher score on the VAS signifies higher severity.

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	185	184	186	
Units: Participants	40	39	13	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo

Statistical analysis description:

week 16

Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [13]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.95
upper limit	7.39

Notes:

[13] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo

Statistical analysis description:

week 16

Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	370
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001 [14]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.87
upper limit	7.1

Notes:

[14] - unadjusted p-value

Secondary: Change in Bath Ankylosing Spondylitis Functional Index (BASFI)

End point title	Change in Bath Ankylosing Spondylitis Functional Index (BASFI)

End point description:

The Bath Ankylosing Spondylitis Functional Index (BASFI) is a set of 10 questions designed to determine the degree of functional limitation in those subjects with AS. The ten questions were chosen with a major input from subjects with AS. The first 8 questions consider activities related to functional anatomy. The final 2 questions assess the subjects' ability to cope with everyday life. A 100 mm visual analog scale (VAS) is used to answer the questions. The mean of the ten questions gives the BASFI score – a value between 0 and 10. (0 being no problem and 10 being the worst problem, captured as a continuous visual analog scale (VAS)). A higher score on the VAS signifies higher severity.

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	181	177	177	
Units: Index				
least squares mean (standard error)	-1.75 (± 0.202)	-1.64 (± 0.204)	-1.01 (± 0.206)	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo
Statistical analysis description:	
week 16	
Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	358
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0041 [15]
Method	MMRM
Parameter estimate	LS Mean
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	-0.24
Variability estimate	Standard error of the mean
Dispersion value	0.259

Notes:

[15] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo
Statistical analysis description:	
week 16	
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	354
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0143 [16]
Method	MMRM
Parameter estimate	LS Mean
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.15
upper limit	-0.13
Variability estimate	Standard error of the mean
Dispersion value	0.259

Notes:

[16] - unadjusted p-value

Secondary: The proportion of patients to achieve a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50 response

End point title	The proportion of patients to achieve a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50 response

End point description:

The BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) consists of a 0 through 10 scale (0 being no problem and 10 being the worst problem, captured as a continuous VAS), which is used to answer 6 questions pertaining to the 5 major symptoms of AS. The BASDAI 50 is defined as an improvement of at least 50% in the BASDAI compared to baseline. A higher score on the VAS signifies higher severity.

End point type	Secondary

End point timeframe:

Week 16 and 52

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	185	184	186	
Units: Participants				
week 16	69	69	39	
week 52	57	65	37	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo

Statistical analysis description:

week 16

Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001 [17]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.58
upper limit	4.07

Notes:

[17] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo

Statistical analysis description:

week 16

Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase

Number of subjects included in analysis	370
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002 [18]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.51
upper limit	3.89

Notes:

[18] - unadjusted p-value

Statistical analysis title	Secukinumab Load v Placebo
Statistical analysis description:	
week 52	
Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0056 [19]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.22
upper limit	3.24

Notes:

[19] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo
Statistical analysis description:	
week 52	
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	370
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0005 [20]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.45
upper limit	3.78

Notes:

[20] - unadjusted p-value

Secondary: Change in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

End point title	Change in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

End point description:

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is a validated assessment tool using 1 through 10 scales (1 indicating "no problem" and 10 indicating " worst problem"), to characterize six clinical domains (fatigue, spinal pain, joint pain/selling, localized tenderness, morning stiffness duration, morning stiffness severity) pertaining to five major symptoms of Ankylosing Spondylitis (AS). The computed final BASDAI score is a value between 0 and 10 with a higher score indicating worse disease. A higher score on the VAS signifies higher severity.

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	181	177	177	
Units: scores on a scale				
least squares mean (standard error)	-2.35 (± 0.201)	-2.43 (± 0.203)	-1.46 (± 0.205)	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo

Statistical analysis description:

week 16

Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	358
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0006 [21]
Method	mixed model repeated measures (MMRM)
Parameter estimate	LS Mean of treatment difference
Point estimate	-0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	-0.38
Variability estimate	Standard error of the mean
Dispersion value	0.256

Notes:
[21] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo
Statistical analysis description:	
week 16	
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	354
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002 [22]
Method	mixed model repeated measures (MMRM)
Parameter estimate	LS Mean of Treatment Difference
Point estimate	-0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.47
upper limit	-0.47
Variability estimate	Standard error of the mean
Dispersion value	0.255

Notes:
[22] - unadjusted p-value

Secondary: Change in Ankylosing Spondylitis Quality of Life (ASQoL) scores at week 16

End point title	Change in Ankylosing Spondylitis Quality of Life (ASQoL) scores at week 16

End point description:

The Ankylosing Spondylitis Quality of Life scores (ASQoL) is a self-administered questionnaire designed to assess health-related quality of life in adult patients with Ankylosing Spondylitis. 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 score indicate better quality of life. Items include an assessment of mobility/energy, self-care and mood/emotion. The recall period is "at the moment," and the measure requires approximately 6 minutes to complete.

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	181	176	177	
Units: Scores on a scale				
least squares mean (standard error)	-3.45 (± 0.408)	-3.62 (± 0.414)	-1.84 (± 0.421)	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo
Statistical analysis description: week 16	
Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	358
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0008 [23]
Method	MMRM
Parameter estimate	LS Mean
Point estimate	-1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.54
upper limit	-0.67
Variability estimate	Standard error of the mean
Dispersion value	0.478

Notes:
[23] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo
Statistical analysis description: week 16	
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	353
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002 [24]
Method	MMRM
Parameter estimate	LS Mean
Point estimate	-1.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.72
upper limit	-0.84
Variability estimate	Standard error of the mean
Dispersion value	0.479

Notes:
[24] - unadjusted p-value

Secondary: Change in Ankylosing Spondylitis Quality of Life (ASQoL) scores at week 52

End point title	Change in Ankylosing Spondylitis Quality of Life (ASQoL) scores at week 52

End point description:

The Ankylosing Spondylitis Quality of Life scores (ASQoL) is a self-administered questionnaire designed to assess health-related quality of life in adult patients with Ankylosing Spondylitis. 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 score indicate better quality of life. Items include an assessment of mobility/energy, self-care and mood/emotion. The recall period is "at the moment," and the measure requires approximately 6 minutes to complete. Summary statistics are presented for participants (n) without intercurrent events.

End point type	Secondary

End point timeframe:

Week 52

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	88	54	
Units: Scores on a scale				
arithmetic mean (standard deviation)	-7.1 (± 4.77)	-7.6 (± 5.38)	-6.4 (± 4.64)	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo
Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0012 [25]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon (Mann-Whitney)

Notes:

[25] - Unadjusted p-value. The endpoint was analyzed by composite estimand strategy. Extreme unfavorable value is assigned for patients with treatment escape or missing data.

Statistical analysis title	Secukinumab No Load v Placebo
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [26]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon (Mann-Whitney)

Notes:

[26] - Unadjusted p-value. The endpoint was analyzed by composite estimand strategy. Extreme unfavorable value is assigned for patients with treatment escape or missing data.

Secondary: The proportion of patients who achieved an Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-Reactive Protein (CRP) inactive disease

End point title	The proportion of patients who achieved an Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-Reactive Protein (CRP) inactive disease

End point description:

Ankylosing Spondylitis Disease Activity Score (ASDAS) - C-reactive protein (CRP) inactive disease criteria are defined as a value below 1.3. Higher score indicates worse symptoms. The formula is: ASDAS-CRP = 0.121 x total back pain + 0.110 x patient global + 0.073 x peripheral pain/swelling + 0.058 x duration of morning stiffness + 0.579 x ln(hsCRP +1)

End point type	Secondary

End point timeframe:

Week 52

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	185	184	186	
Units: Participants	29	44	19	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo
Statistical analysis description: week 52	
Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0577 [27]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	3.45

Notes:

[27] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo

Statistical analysis description:	
week 52	
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	370
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0003 [28]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.65
upper limit	5.41

Notes:

[28] - unadjusted p-value

Secondary: Change in high sensitivity C-reactive protein

End point title	Change in high sensitivity C-reactive protein
End point description:	
High sensitivity C-reactive protein is measured as a marker of inflammation from blood samples during the study.	
End point type	Secondary
End point timeframe:	
Week 16	

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	180	176	175	
Units: ratio				
least squares mean (standard error)	0.64 (± 1.078)	0.64 (± 1.079)	0.91 (± 1.080)	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo
Statistical analysis description:	
week 16	
Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase

Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002 [29]
Method	MMRM
Parameter estimate	Relative Treatment Effect
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.84

Notes:

[29] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo

Statistical analysis description:

week 16

Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	351
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002 [30]
Method	MMRM
Parameter estimate	Relative Treatment Effect
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.84

Notes:

[30] - unadjusted p-value

Secondary: Change in Short Form-36 Physical Component Summary (SF-36 PCS)

End point title	Change 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:

Week 16

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	182	176	178	
Units: Scores on a Scale				
least squares mean (standard error)	5.71 (± 0.683)	5.57 (± 0.694)	2.93 (± 0.705)	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo
Statistical analysis description:	
week 16	
Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0006 [31]
Method	ANCOVA
Parameter estimate	LS Mean of Treatment Difference
Point estimate	2.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	4.34
Variability estimate	Standard error of the mean
Dispersion value	0.799
Notes:	
[31] - unadjusted p-value	

Statistical analysis title	Secukinumab No Load v Placebo
Statistical analysis description:	
week 16	
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	354
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0011 [32]
Method	ANCOVA
Parameter estimate	LS Mean of Treatment Difference
Point estimate	2.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	4.22
Variability estimate	Standard error of the mean
Dispersion value	0.803

Notes:
[32] - unadjusted p-value

Secondary: Change in Sacroiliac Joint Edema - week 16

End point title	Change in Sacroiliac Joint Edema - week 16

End point description:

Magnetic Resonance Images (MRI) of the Sacroiliac Joint (SIJ) were assessed for the presence and severity of SIJ bone marrow edema according to the Berlin Active Inflammatory Lesions Scoring with a maximum score of 24.

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	180	177	174	
Units: Scores on a Scale				
arithmetic mean (standard error)	-1.68 (± 0.24)	-1.03 (± 0.18)	-0.39 (± 0.15)	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo

Statistical analysis description:

week 16

Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	354
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [33]
Method	ANCOVA
Parameter estimate	ANCOVA

Notes:
[33] - unadjusted p-value

Statistical analysis title	Secukinumab No Load v Placebo

Statistical analysis description:

week 16

Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase

Number of subjects included in analysis	351
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [34]
Method	ANCOVA
Parameter estimate	ANCOVA

Notes:

[34] - unadjusted p-value

Secondary: Change in Sacroiliac Joint Edema - week 52

End point title	Change in Sacroiliac Joint Edema - week 52

End point description:

Magnetic Resonance Images (MRI) of the Sacroiliac Joint (SIJ) were assessed for the presence and severity of SIJ bone marrow edema according to the Berlin Active Inflammatory Lesions Scoring with a maximum score of 24.

End point type	Secondary

End point timeframe:

Week 52

End point values	Secukinumab, Load, Core Phase	Secukinumab, No Load, Core Phase	Placebo, Core Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	87	53	
Units: Scores on a scale				
arithmetic mean (standard deviation)	-2.9 (± 4.54)	-1.9 (± 3.40)	-0.1 (± 1.97)	

Statistical analyses

Statistical analysis title	Secukinumab Load v Placebo
Comparison groups	Secukinumab, Load, Core Phase v Placebo, Core Phase
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [35]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon (Mann-Whitney)

Notes:

[35] - Unadjusted p-value. The endpoint was analyzed by composite estimand strategy. Extreme unfavorable value is assigned for patients with treatment escape or missing data.

Statistical analysis title	Secukinumab No Load v Placebo
Comparison groups	Secukinumab, No Load, Core Phase v Placebo, Core Phase

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [36]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon (Mann-Whitney)

Notes:

[36] - Unadjusted p-value. The endpoint was analyzed by composite estimand strategy. Extreme unfavorable value is assigned for patients with treatment escape or missing data.

Adverse events information

Timeframe for reporting adverse events:

Adverse events are reported from first dose of study treatment until end of study treatment plus 12 wks post-treatment, up to a maximum timeframe of 1520 days (approx. 4.2 years).

Adverse event reporting additional description:

Safety results summarize long term data for all patients for the entire period of their study participation, which, for the majority of pts, combines the core phase and the extension phase (not all pts participated in the extension).

The table is presented by dose group, AIN457 150 mg and AIN457 300 mg and placebo.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Any AIN457 150 mg, in Core Phase and Extension Phase

Reporting group description:

Includes patients originally randomized to AIN457 150 mg (Load and No Load) at baseline and placebo patients switched to AIN457 150 mg before or at W52 (AEs occuring after the switch) who either were re-randomized (Core Phase Responders) to AIN457 150 mg at W104 or did not participate in the Extension Phase.

Reporting group title	Any AIN457 300 mg in Extension Phase

Reporting group description:

Includes patients re-randomized (Core Phase Responders) or re-assigned (Core Phase Non-Responders) to AIN457 300 mg at W104 (Extension Phase) and patients re-randomized (Core Phase Responders) to AIN457 150 mg at W104 who up-titrated to AIN457 300 mg (only AEs occurring after up-titration).

Reporting group title	Any AIN457, In Core Phase and Extension Phase

Reporting group description:

Includes patients randomized or switched (AEs occuring after the switch) to AIN457 150 mg (Load and No Load) who either were re-randomized (Core Phase Responders) to AIN457 150 mg or AIN457 300 mg at W104 or did not participate in the Extension Phase.

Reporting group title	Placebo, Core Phase

Reporting group description:

Includes patients originally randomized to Placebo (AEs until the time of a switch to AIN457 150 mg)

Serious adverse events	Any AIN457 150 mg, in Core Phase and Extension Phase	Any AIN457 300 mg in Extension Phase	Any AIN457, In Core Phase and Extension Phase
Total subjects affected by serious adverse events			
subjects affected / exposed	48 / 543 (8.84%)	11 / 254 (4.33%)	58 / 543 (10.68%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acrochordon			

subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibroadenoma of breast			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 543 (0.00%)	1 / 254 (0.39%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			
subjects affected / exposed	0 / 543 (0.00%)	1 / 254 (0.39%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 543 (0.00%)	0 / 254 (0.00%)	0 / 543 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic aneurysm			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 543 (0.00%)	0 / 254 (0.00%)	0 / 543 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Reproductive system and breast disorders			
Bartholin's cyst			
subjects affected / exposed	0 / 543 (0.00%)	0 / 254 (0.00%)	0 / 543 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix enlargement			
subjects affected / exposed	0 / 543 (0.00%)	0 / 254 (0.00%)	0 / 543 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial disorder			
subjects affected / exposed	0 / 543 (0.00%)	0 / 254 (0.00%)	0 / 543 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal prolapse			
subjects affected / exposed	0 / 543 (0.00%)	0 / 254 (0.00%)	0 / 543 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicocele			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumomediastinum			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal septum deviation			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Substance-induced mood disorder			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Arthroscopy			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Brain contusion			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 543 (0.00%)	0 / 254 (0.00%)	0 / 543 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tendon injury			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	1 / 543 (0.18%)	1 / 254 (0.39%)	2 / 543 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 543 (0.00%)	0 / 254 (0.00%)	0 / 543 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 543 (0.00%)	0 / 254 (0.00%)	0 / 543 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Myelopathy			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal claudication			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Iridocyclitis			
subjects affected / exposed	1 / 543 (0.18%)	1 / 254 (0.39%)	2 / 543 (0.37%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Appendiceal mucocoele			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			

subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	2 / 543 (0.37%)	1 / 254 (0.39%)	3 / 543 (0.55%)
occurrences causally related to treatment / all	1 / 2	1 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 543 (0.00%)	1 / 254 (0.39%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 543 (0.00%)	1 / 254 (0.39%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis acute			

subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary colic			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 543 (0.00%)	1 / 254 (0.39%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin disorder			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
IgA nephropathy			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			
subjects affected / exposed	0 / 543 (0.00%)	1 / 254 (0.39%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	0 / 543 (0.00%)	0 / 254 (0.00%)	0 / 543 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	3 / 543 (0.55%)	0 / 254 (0.00%)	3 / 543 (0.55%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back disorder			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	1 / 543 (0.18%)	1 / 254 (0.39%)	2 / 543 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Device related infection			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eczema infected			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiglottitis			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 543 (0.18%)	1 / 254 (0.39%)	2 / 543 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			

subjects affected / exposed	3 / 543 (0.55%)	0 / 254 (0.00%)	3 / 543 (0.55%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaccination site cellulitis			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral tracheitis			
subjects affected / exposed	0 / 543 (0.00%)	0 / 254 (0.00%)	0 / 543 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 543 (0.00%)	1 / 254 (0.39%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 543 (0.00%)	1 / 254 (0.39%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	0 / 543 (0.00%)	1 / 254 (0.39%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	1 / 543 (0.18%)	0 / 254 (0.00%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	0 / 543 (0.00%)	1 / 254 (0.39%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	0 / 543 (0.00%)	1 / 254 (0.39%)	1 / 543 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo, Core Phase		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 186 (4.30%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acrochordon			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fibroadenoma of breast			

subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal adenocarcinoma			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	1 / 186 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aortic aneurysm			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 186 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Bartholin's cyst			

subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cervix enlargement				
subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endometrial disorder				
subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ovarian cyst				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vaginal prolapse				
subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Varicocele				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pneumomediastinum				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nasal septum deviation				

subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Substance-induced mood disorder			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Arthroscopy			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Brain contusion			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clavicle fracture			
subjects affected / exposed	1 / 186 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin laceration			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tendon injury			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Wound dehiscence				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meniscus injury				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aortic valve incompetence				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Myelopathy				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Sciatica				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal claudication				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Iridocyclitis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Appendiceal mucocoele				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis ulcerative				

subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Crohn's disease				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal fistula				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatitis acute				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Biliary colic				

subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Skin disorder				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
IgA nephropathy				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Calculus urinary				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Arthritis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Back disorder				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc disorder				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Synovitis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Anal abscess				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				

subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eczema infected				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epiglottitis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postoperative wound infection				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subcutaneous abscess				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vaccination site cellulitis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral tracheitis				
subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonsillar abscess				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis streptococcal				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 186 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Diabetes mellitus				

subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic ketoacidosis			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Electrolyte imbalance			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 186 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Any AIN457 150 mg, in Core Phase and Extension Phase	Any AIN457 300 mg in Extension Phase	Any AIN457, In Core Phase and Extension Phase
Total subjects affected by non-serious adverse events			
subjects affected / exposed	320 / 543 (58.93%)	74 / 254 (29.13%)	335 / 543 (61.69%)
Vascular disorders			
Hypertension			
subjects affected / exposed	29 / 543 (5.34%)	5 / 254 (1.97%)	34 / 543 (6.26%)
occurrences (all)	31	5	36
Nervous system disorders			
Headache			
subjects affected / exposed	61 / 543 (11.23%)	7 / 254 (2.76%)	65 / 543 (11.97%)
occurrences (all)	76	11	87
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	55 / 543 (10.13%)	6 / 254 (2.36%)	61 / 543 (11.23%)
occurrences (all)	71	6	77
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	43 / 543 (7.92%)	6 / 254 (2.36%)	48 / 543 (8.84%)
occurrences (all)	57	6	63
Back pain			
subjects affected / exposed	36 / 543 (6.63%)	3 / 254 (1.18%)	38 / 543 (7.00%)
occurrences (all)	42	3	45
Infections and infestations			
Bronchitis			
subjects affected / exposed	23 / 543 (4.24%)	6 / 254 (2.36%)	28 / 543 (5.16%)
occurrences (all)	27	6	33
Nasopharyngitis			
subjects affected / exposed	137 / 543 (25.23%)	33 / 254 (12.99%)	146 / 543 (26.89%)
occurrences (all)	239	42	281
Sinusitis			
subjects affected / exposed	30 / 543 (5.52%)	5 / 254 (1.97%)	34 / 543 (6.26%)
occurrences (all)	39	5	44
Upper respiratory tract infection			
subjects affected / exposed	65 / 543 (11.97%)	16 / 254 (6.30%)	77 / 543 (14.18%)
occurrences (all)	109	18	127
Urinary tract infection			
subjects affected / exposed	38 / 543 (7.00%)	9 / 254 (3.54%)	42 / 543 (7.73%)
occurrences (all)	49	14	63
Pharyngitis			
subjects affected / exposed	27 / 543 (4.97%)	5 / 254 (1.97%)	31 / 543 (5.71%)
occurrences (all)	32	5	37

Non-serious adverse events	Placebo, Core Phase		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 186 (36.02%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 186 (1.61%)		
occurrences (all)	4		
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 186 (4.84%)		
occurrences (all)	11		

Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 10 / 186 (5.38%) 11		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 9 / 186 (4.84%) 10 3 / 186 (1.61%) 4		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all)	 2 / 186 (1.08%) 2 32 / 186 (17.20%) 48 3 / 186 (1.61%) 3 13 / 186 (6.99%) 13 4 / 186 (2.15%) 4 1 / 186 (0.54%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 November 2016	The powering of the study was re-evaluated, triggering a changed order in the testing hierarchy as well as adjustments of the population for the primary endpoint to TNFi-naïve patients only. After feedback from the FDA, changes were made to Analysis Plan B to focus on the no-load dosing regimen. The test for HLA-B27 was moved from the baseline visit to Screening Visit 2 to facilitate the screening process for the sites. The maximally allowed proportion of TNF-IR patients was changed from 30% to 20%. Historic MRIs were accepted, if taken within 3 months of baseline and in alignment of the imaging criteria to facilitate the re-screening process for patients and sites. The wording in the SAE reporting section was updated to be aligned with current and future SAE reporting processes. A decision was taken to replace the eSource system and collect the data for the study in OC/RDC in all countries.
11 July 2018	Addition of an extension phase to the current core protocol. The order of the secondary endpoints of the Analysis Plan B in the hierarchy was updated to elevate several Load regimen endpoints to reflect their clinical relevance. Addition of group-sequential testing for the Week 24 interim analysis of the Week 52 time points (Analysis Plan B). The wording for the Withdrawal of Consent section was updated to align with the European Economic Area (EEA) General Data Protection Regulation (GDPR) requirements.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported