



Clinical trial results:

A randomized, partially-blinded, active-controlled multicenter study of secukinumab to demonstrate reduction of radiographic progression versus GP2017 (adalimumab biosimilar) at 104 weeks and to assess the long term safety, tolerability and efficacy up to 2 years in patients with active ankylosing spondylitis

Summary

EudraCT number	2017-000679-10
Trial protocol	GB DE ES FR CZ SK FI DK NL PT PL GR RO
Global end of trial date	29 November 2021

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	CAIN457K2340
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03259074
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	29 November 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstrate the proportion of subjects on secukinumab (150 mg s.c. or 300 mg s.c.) with no radiographic progression as measured by mSASSS at Week 104 is superior to subjects on GP2017 (adalimumab biosimilar 40 mg s.c.).

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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 1
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	Chile: 40
Country: Number of subjects enrolled	Colombia: 7
Country: Number of subjects enrolled	Czechia: 71
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	Finland: 2
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Germany: 72
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Japan: 15
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 47
Country: Number of subjects enrolled	Mexico: 19
Country: Number of subjects enrolled	Monaco: 4
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Peru: 35

Country: Number of subjects enrolled	Philippines: 20
Country: Number of subjects enrolled	Poland: 80
Country: Number of subjects enrolled	Portugal: 18
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	Russian Federation: 126
Country: Number of subjects enrolled	Slovakia: 19
Country: Number of subjects enrolled	Spain: 62
Country: Number of subjects enrolled	Taiwan: 42
Country: Number of subjects enrolled	Turkey: 17
Country: Number of subjects enrolled	United Kingdom: 52
Country: Number of subjects enrolled	United States: 32
Worldwide total number of subjects	859
EEA total number of subjects	373

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)	814
From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 859 subjects were randomized to treatment at 171 sites in 30 countries in Europe, North America, South America, and Asia

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	AIN457 150 mg/placebo

Arm description:

AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104

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

Dosage and administration details:

150 mg and matching placebo

Arm title	AIN457 300 mg
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Arm description:

AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104

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

Dosage and administration details:

300 mg

Arm title	GP2017 40mg
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Arm description:

GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104

Arm type	Active comparator
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Investigational medicinal product name	adalimumab biosimilar
Investigational medicinal product code	GP2017
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

40 mg

Number of subjects in period 1	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg
Started	287	286	286
Completed	254	237	243
Not completed	33	49	43
Adverse event, serious fatal	1	1	3
Physician decision	4	12	10
Adverse event, non-fatal	9	12	8
Protocol Deviation	1	1	3
Progressive Disease	1	-	-
Pregnancy	1	1	-
Subject/Guardian Decision	13	16	14
Lost to follow-up	2	4	3
New Therapy For Study Indication	1	2	2

Baseline characteristics

Reporting groups

Reporting group title	AIN457 150 mg/placebo
Reporting group description: AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	
Reporting group title	AIN457 300 mg
Reporting group description: AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	
Reporting group title	GP2017 40mg
Reporting group description: GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104	

Reporting group values	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg
Number of subjects	287	286	286
Age categorical Units: Subjects			
Adults (18-64 years)	277	269	268
From 65-84 years	10	17	18
Age Continuous Units: years			
arithmetic mean	42.1	42.2	41.9
standard deviation	± 11.99	± 12.47	± 12.68
Sex: Female, Male Units:			
Female	57	63	65
Male	230	223	221
Race/Ethnicity, Customized Units: Subjects			
White	225	227	228
Black or African American	1	2	0
Asian	40	39	50
American Indian or Alaska Native	19	15	7
Other	1	0	0
Multiple	1	3	1
Modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) scores			
The modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) evaluates the outside corners of the vertebral spine for erosions, sclerosis, squaring, bony growths and spinal bridging. The mSASSS assesses the participant's spinal vertebrae for structural changes and scores each vertebrae from 0 (normal vertebrae) to 3 (bony growth that bridges one vertebrae to the neighboring vertebrae). A total of 24 vertebral corners are scored for a possible maximum grade of 72.			
Units: mSASSS scores			
arithmetic mean	17.602	16.527	15.695
standard deviation	± 21.3286	± 20.8153	± 19.4955

Reporting group values	Total		
Number of subjects	859		

Age categorical Units: Subjects			
Adults (18-64 years)	814		
From 65-84 years	45		
Age Continuous Units: years arithmetic mean standard deviation	-		
Sex: Female, Male Units:			
Female	185		
Male	674		
Race/Ethnicity, Customized Units: Subjects			
White	680		
Black or African American	3		
Asian	129		
American Indian or Alaska Native	41		
Other	1		
Multiple	5		
Modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) scores			
The modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) evaluates the outside corners of the vertebral spine for erosions, sclerosis, squaring, bony growths and spinal bridging. The mSASSS assesses the participant's spinal vertebrae for structural changes and scores each vertebrae from 0 (normal vertebrae) to 3 (bony growth that bridges one vertebrae to the neighboring vertebrae). A total of 24 vertebral corners are scored for a possible maximum grade of 72.			
Units: mSASSS scores arithmetic mean standard deviation	-		

End points

End points reporting groups

Reporting group title	AIN457 150 mg/placebo
Reporting group description: AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	
Reporting group title	AIN457 300 mg
Reporting group description: AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	
Reporting group title	GP2017 40mg
Reporting group description: GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104	

Primary: Percentage of participants with no radiographic progression (estimate + 95% CI) at Week 104 (Multiple imputation) (Full analysis set)

End point title	Percentage of participants with no radiographic progression (estimate + 95% CI) at Week 104 (Multiple imputation) (Full analysis set)
End point description: Radiographic progression was based on scores from the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). The mSASSS is the sum of scores assessing the vertebral corners of the lumbar and cervical spine as 0 (normal), 1 (erosion, sclerosis, or squaring), 2 (syndesmophyte), or 3 (bridging syndesmophyte) with a total range from 0-72. No radiographic progression was defined as the change from baseline in mSASSS score ≤ 0.5 .	
End point type	Primary
End point timeframe: Baseline and at Week 104	

End point values	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	287	286	286	
Units: Percentage of participants				
number (not applicable)	66.1	66.9	65.6	

Statistical analyses

Statistical analysis title	AIN157 150 vs GP2017 at Week 104
Comparison groups	AIN457 150 mg/placebo v GP2017 40mg

Number of subjects included in analysis	573
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7164 ^[1]
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.63
upper limit	9.64

Notes:

[1] - Logistic regression model with treatment as a factor and baseline mSASSS score as a covariate using marginal standardization method.

Statistical analysis title	AIN157 300 vs GP2017 at Week 104
Comparison groups	AIN457 300 mg v GP2017 40mg
Number of subjects included in analysis	572
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6925
Method	Regression, Logistic
Parameter estimate	Marginal difference
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.61
upper limit	9.95

Secondary: Change from Baseline in mSASSS (estimate + 95% CI) at Week 104 (Multiple imputation) (Full analysis set)

End point title	Change from Baseline in mSASSS (estimate + 95% CI) at Week 104 (Multiple imputation) (Full analysis set)
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End point description:

Radiographic changes in the spine were based on the change in score of the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) from baseline to Week 104.

The mSASSS is the sum of scores assessing the vertebral corners of the lumbar and cervical spine as 0 (normal), 1 (erosion, sclerosis, or squaring), 2 (syndesmophyte), or 3 (bridging syndesmophyte) with a total range from 0-72.

End point type	Secondary
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End point timeframe:

Baseline and at Week 104

End point values	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	287	286	286	
Units: mSASSS scores				
least squares mean (standard error)	0.54 (\pm 0.175)	0.55 (\pm 0.180)	0.72 (\pm 0.177)	

Statistical analyses

Statistical analysis title	AIN157 150 vs GP2017 at Week 104
Comparison groups	AIN457 150 mg/placebo v GP2017 40mg
Number of subjects included in analysis	573
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.646
upper limit	0.293

Statistical analysis title	AIN157 300 vs GP2017 at Week 104
Comparison groups	AIN457 300 mg v GP2017 40mg
Number of subjects included in analysis	572
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.639
upper limit	0.315

Secondary: Percentage of participants without new syndesmophytes by mSASSS (estimate + 95% CI) between baseline and Week 104 (Multiple imputation) (Syndesmophyte subset)

End point title	Percentage of participants without new syndesmophytes by mSASSS (estimate + 95% CI) between baseline and Week 104 (Multiple imputation) (Syndesmophyte subset)
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End point description:

Syndesmophytes are bony growths that develop on corner of the vertebrae of the spine which are indicators of AS. A participant was considered to have a syndesmophyte if at least one reader assessed vertebral corner as ≥ 2 at on the mSASSS scale at baseline. Only participants with a syndesmophyte at baseline were evaluated at Week 104 for new syndesmophytes. A new syndesmophyte was a

syndesmophyte present at Week 104 which was not present at baseline. Absence of new syndesmophyte was defined as having individual vertebral score < 2 on the mSASSS scale for all interpretable locations that had no syndesmophyte at baseline. Missing responses for subjects without new syndesmophyte at Week 104 were imputed by multiple imputation (MCMC).

End point type	Secondary
End point timeframe:	
Baseline and at Week 104	

End point values	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	211	204	212	
Units: Percentage of participants				
number (not applicable)	56.9	53.8	53.3	

Statistical analyses

Statistical analysis title	150 mg vs 300 mg AIN457 at Week 104
Comparison groups	AIN457 150 mg/placebo v AIN457 300 mg
Number of subjects included in analysis	415
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Marginal difference
Point estimate	4.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.62
upper limit	14.27

Statistical analysis title	AIN457 300 mg vs GP2017 40 mg at Week 104
Comparison groups	AIN457 300 mg v GP2017 40mg
Number of subjects included in analysis	416
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Marginal difference
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.13
upper limit	11.31

Secondary: Change from Baseline in MRI Berlin SI joint edema score (estimate + 95% CI) ANCOVA up to Week 104 (Observed data) (MRI subset)

End point title	Change from Baseline in MRI Berlin SI joint edema score (estimate + 95% CI) ANCOVA up to Week 104 (Observed data) (MRI subset)
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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. Higher scores indicate more inflammation.

End point type	Secondary
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End point timeframe:

Baseline and at Week 104

End point values	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	137	137	144	
Units: Berlin SI joint edema scores				
least squares mean (standard error)	-1.527 (\pm 0.1057)	-1.378 (\pm 0.1097)	-1.710 (\pm 0.1087)	

Statistical analyses

Statistical analysis title	AIN457 150 vs GP2017 at Week 104
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Statistical analysis description:

Week 104 - 150 mg

Comparison groups	AIN457 150 mg/placebo v GP2017 40mg
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS Means
Point estimate	0.183
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.48
Variability estimate	Standard error of the mean
Dispersion value	0.1517

Statistical analysis title	AIN457 300 mg vs GP2017 40 mg at Week 104
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Statistical analysis description:

Week 104 - 300 mg

Comparison groups	AIN457 300 mg v GP2017 40mg
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Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS Means
Point estimate	0.332
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.64
Variability estimate	Standard error of the mean
Dispersion value	0.1545

Secondary: Change from Baseline in Berlin modification of ASspiMRI-a edema score (estimate + 95% CI) up to Week 104 (MRI subset)

End point title	Change from Baseline in Berlin modification of ASspiMRI-a edema score (estimate + 95% CI) up to Week 104 (MRI subset)
End point description:	Magnetic Resonance Images (MRI) of the spine were assessed for the presence and severity of bone marrow edema in the spinal vertebrae according to the Berlin modification of the ASspiMRI-a edema score with a maximum score of 69. Higher scores indicate more inflammation.
End point type	Secondary
End point timeframe:	Baseline and at Week 104

End point values	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	137	137	144	
Units: Berlin mod. of ASspiMRI-a edema scores				
least squares mean (standard error)	-1.224 (\pm 0.2306)	-1.683 (\pm 0.2373)	-2.101 (\pm 0.2378)	

Statistical analyses

Statistical analysis title	AIN457 150 mg vs GP2017 at Week 104
Statistical analysis description:	Week 104 - 150 mg
Comparison groups	AIN457 150 mg/placebo v GP2017 40mg

Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS Means
Point estimate	0.877
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	1.53
Variability estimate	Standard error of the mean
Dispersion value	0.3316

Statistical analysis title	AIN457 300 mg vs GP2017 40 mg at Week 104
Statistical analysis description: Week 104 - 300 mg	
Comparison groups	AIN457 300 mg v GP2017 40mg
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS Means
Point estimate	0.419
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	1.08
Variability estimate	Standard error of the mean
Dispersion value	0.3357

Secondary: Percentage of responders for Assessment of SpondyloArthritis International Society 20 (ASAS20)

End point title	Percentage of responders for Assessment of SpondyloArthritis International Society 20 (ASAS20) ^[2]
End point description: Assessment of SpondyloArthritis International Society criteria (ASAS) consist of 4 domains measured on visual analog scales (VAS): 1. Patient's global assessment; 2. Patient's assessment of back pain; 3. Function represented by Bath Ankylosing Spondylitis Functional Index (BASFI) average of 10 questions; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). ASAS 20 response is defined as an improvement of $\geq 20\%$ and ≥ 1 unit on a scale of 10 in at least three of the four main domains and no worsening of $\geq 20\%$ and ≥ 1 unit on a scale of 10 in the remaining domain. A higher score on the VAS signifies higher severity.	
End point type	Secondary
End point timeframe: Week 104	

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The comparison was between 2 doses of AIN457 only.

End point values	AIN457 150 mg/placebo	AIN457 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	286		
Units: Percentage participants with ASAS20				
number (confidence interval 95%)	83.1 (77.8 to 87.4)	82.9 (77.3 to 87.4)		

Statistical analyses

Statistical analysis title	AIN457 150 mg vs AIN457 300 mg at Week 104
Comparison groups	AIN457 150 mg/placebo v AIN457 300 mg
Number of subjects included in analysis	573
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Marginal difference
Point estimate	1.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.1
upper limit	8.18

Secondary: Percentage of responders for Assessment of SpondyloArthritis International Society 40 (ASAS 40)

End point title	Percentage of responders for Assessment of SpondyloArthritis International Society 40 (ASAS 40) ^[3]
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End point description:

Assessment of SpondyloArthritis International Society criteria (ASAS) consist of 4 domains measured on visual analog scales (VAS): 1. Patient's global assessment; 2. Patient's assessment of back pain; 3. Function represented by Bath Ankylosing Spondylitis Functional Index (BASFI) average of 10 questions; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). ASAS40 response is defined as an improvement of $\geq 40\%$ 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
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End point timeframe:

Week 104

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The comparison was between 2 doses of AIN457 only.

End point values	AIN457 150 mg/placebo	AIN457 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	286		
Units: Percentage participants with ASAS40				
number (confidence interval 95%)	69.9 (63.7 to 75.4)	73.5 (67.3 to 78.9)		

Statistical analyses

Statistical analysis title	AIN457 150 mg vs AIN457 300 mg at Week 104
Comparison groups	AIN457 150 mg/placebo v AIN457 300 mg
Number of subjects included in analysis	573
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Marginal difference
Point estimate	-2.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.18
upper limit	5.51

Secondary: Percentage of responders for Assessment of SpondyloArthritis International Society with a partial remission response (Full analysis set)

End point title	Percentage of responders for Assessment of SpondyloArthritis International Society with a partial remission response (Full analysis set) ^[4]
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End point description:

The ASAS partial remission response criteria consisted of the following assessment domains measured on visual analogue scales (VAS): 1. Patient's global assessment; 2. Patient's assessment of back pain; 3. Function represented by BASFI average of 10 questions regarding ability to perform specific tasks; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). The ASAS partial remission criteria was defined as a value not above 2 units in each of the four domains on a scale of 10.

End point type	Secondary
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End point timeframe:

Week 104

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The comparison was between 2 doses of AIN457 only.

End point values	AIN457 150 mg/placebo	AIN457 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	286		
Units: Percentage participants				
number (confidence interval 95%)	31.5 (25.9 to 37.7)	30.2 (24.5 to 36.6)		

Statistical analyses

Statistical analysis title	AIN457 150 mg vs AIN457 300 mg at Week 104
Comparison groups	AIN457 150 mg/placebo v AIN457 300 mg
Number of subjects included in analysis	573
Analysis specification	Pre-specified
Analysis type	
Method	Marginal difference
Parameter estimate	Marginal difference
Point estimate	2.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.34
upper limit	9.69

Secondary: Percentage of participants with Assessment of SpondyloArthritis International Society for inactive disease response (Observed data) (Full analysis set)

End point title	Percentage of participants with Assessment of SpondyloArthritis International Society for inactive disease response (Observed data) (Full analysis set) ^[5]
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End point description:

The Ankylosing Spondylitis Disease Activity Score (ASDAS) is a composite index to assess disease activity in AS. Parameters used for the ASDAS include spinal pain (BASDAI question 2), the patient's global assessment of disease activity, peripheral pain/swelling (BASDAI question 3), duration of morning stiffness (BASDAI question 6) and C-reactive protein (CRP) in mg/L (Sieper 2009, Lukas 2009). Disease activity states are inactive disease, moderate disease activity, high disease activity, and very high disease activity. The 3 values selected to separate these states were < 1.3 between inactive disease and moderate disease activity, < 2.1 between moderate disease activity and high disease activity, and > 3.5 between high disease activity and very high disease activity. Selected cutoffs for improvement scores were a change ≥ 1.1 unit for "minimal clinically important improvement" and a change ≥ 2.0 units for "major improvement" (Machado 2011).

End point type	Secondary
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End point timeframe:

Week 104

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The comparison was between 2 doses of AIN457 only.

End point values	AIN457 150 mg/placebo	AIN457 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	286		
Units: Percentage of participants				
number (confidence interval 95%)	31.1 (25.5 to 37.4)	31.7 (25.7 to 38.3)		

Statistical analyses

Statistical analysis title	AIN457 150 mg vs AIN457 300 mg at Week 104
Comparison groups	AIN457 150 mg/placebo v AIN457 300 mg
Number of subjects included in analysis	573
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Marginal difference
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.08
upper limit	7.74

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus 84 days up to a maximum of 900 days for AIN457 and 939 days for GP2017.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	AIN457 150 mg/placebo
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Reporting group description:

AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104

Reporting group title	GP2017 40 mg
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Reporting group description:

GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104

Reporting group title	AIN457 300 mg
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Reporting group description:

AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104

Serious adverse events	AIN457 150 mg/placebo	GP2017 40 mg	AIN457 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	40 / 286 (13.99%)	32 / 285 (11.23%)	29 / 285 (10.18%)
number of deaths (all causes)	1	3	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chloroma			

subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ovarian cancer			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Iliac artery occlusion			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iliac artery stenosis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Drug intolerance			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device pain			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Immune system disorders			
Immunosuppression			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			

subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 286 (0.35%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 286 (0.35%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device issue			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Exposure during pregnancy			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Myocardial infarction			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Facial paresis			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain hypoxia			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar stroke			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Iridocyclitis			
subjects affected / exposed	2 / 286 (0.70%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Retinal detachment			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal vein occlusion			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Chronic gastrointestinal bleeding			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	3 / 286 (1.05%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	2 / 286 (0.70%)	0 / 285 (0.00%)	3 / 285 (1.05%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis eosinophilic			

subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorder			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileal ulcer			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 286 (0.35%)	2 / 285 (0.70%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			

subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Purpura			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 286 (0.35%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Micturition disorder			

subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	1 / 286 (0.35%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	3 / 286 (1.05%)	1 / 285 (0.35%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess intestinal			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Anal abscess			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 286 (0.35%)	1 / 285 (0.35%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 286 (0.35%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 286 (0.35%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epididymitis			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelitis			

subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral herpes			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 286 (0.00%)	2 / 285 (0.70%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	2 / 285 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Septic shock			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suspected COVID-19			
subjects affected / exposed	0 / 286 (0.00%)	1 / 285 (0.35%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 286 (0.00%)	2 / 285 (0.70%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 286 (0.35%)	0 / 285 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 286 (0.00%)	0 / 285 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	AIN457 150 mg/placebo	GP2017 40 mg	AIN457 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	106 / 286 (37.06%)	99 / 285 (34.74%)	107 / 285 (37.54%)
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 286 (3.85%)	15 / 285 (5.26%)	11 / 285 (3.86%)
occurrences (all)	12	16	12
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 286 (5.59%)	17 / 285 (5.96%)	17 / 285 (5.96%)
occurrences (all)	17	25	22
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	20 / 286 (6.99%)	11 / 285 (3.86%)	22 / 285 (7.72%)
occurrences (all)	25	12	27
Musculoskeletal and connective tissue disorders			

Ankylosing spondylitis subjects affected / exposed occurrences (all)	11 / 286 (3.85%) 12	12 / 285 (4.21%) 13	17 / 285 (5.96%) 23
Arthralgia subjects affected / exposed occurrences (all)	16 / 286 (5.59%) 21	12 / 285 (4.21%) 14	13 / 285 (4.56%) 16
Infections and infestations			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	17 / 286 (5.94%) 22	18 / 285 (6.32%) 22	25 / 285 (8.77%) 32
Nasopharyngitis subjects affected / exposed occurrences (all)	47 / 286 (16.43%) 61	44 / 285 (15.44%) 54	40 / 285 (14.04%) 55

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 August 2019	<p>1. Testing was revised from a pooled secukinumab dose group versus GP2017 in the primary objective to compare the individual secukinumab doses versus GP2017. Thus, the primary objective was changed as follows: "To demonstrate the proportion of subjects on secukinumab (combined 150 mg s.c. and or 300 mg s.c.) with no radiographic progression as measured by mSASSS at Week 104 is superior to subjects on GP2017 (adalimumab biosimilar 40 mg s.c.)." The statistical testing was altered to align with this change.</p> <p>2. The Withdrawal of Consent (WoC) language was revised according to the European Economic Area (EEA) General Data Protection Regulation (GDPR) required guidelines.</p>
04 February 2021	<p>The blinding strategy was aligned between subjects, investigators, site personnel and the Sponsor. The designated Sponsor personnel became unblinded to treatment group (GP2017 or secukinumab) but dose of secukinumab (150 mg or 300 mg) remained blinded.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported