



Clinical trial results:

A randomized, double-blind, placebo-controlled Phase III multicenter study of subcutaneous secukinumab in prefilled syringes to demonstrate the efficacy at 16 weeks and to assess the long-term efficacy, safety and tolerability up to 5 years in patients with active Ankylosing Spondylitis

Summary

EudraCT number	2012-000046-35
Trial protocol	GB CZ IT NL AT FI DE ES
Global end of trial date	18 September 2018

Results information

Result version number	v1 (current)
This version publication date	31 August 2019
First version publication date	31 August 2019

Trial information

Trial identification

Sponsor protocol code	CAIN457F2310
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01649375
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Study Director, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Study Director, Novartis 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	18 September 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	18 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate that the efficacy of secukinumab 75 mg sc or 150 mg sc at Week 16 was superior to placebo in patients with active AS based on the proportion of patients achieving an ASAS20 (Assessment of SpondyloArthritis International Society criteria) 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	18 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 9
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Czech Republic: 51
Country: Number of subjects enrolled	Finland: 17
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Russian Federation: 37
Country: Number of subjects enrolled	Singapore: 7
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Switzerland: 6
Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	United States: 21
Worldwide total number of subjects	219
EEA total number of subjects	136

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)	212
From 65 to 84 years	5
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Two hundred fifty-three subjects were screened and 219 were randomized

Period 1

Period 1 title	Up to Week 16
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
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Arm title	Secukinumab 75 mg
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Arm description:

Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Secukinumab 75 mg
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 75 mg once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4

Arm title	Secukinumab 150 mg
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Arm description:

Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks

Arm type	Experimental
Investigational medicinal product name	Secukinumab 150 mg
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Secukinumab 150 mg once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4

Arm title	Placebo
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Arm description:

Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16

Arm type	Placebo
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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 subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16

Number of subjects in period 1	Secukinumab 75 mg	Secukinumab 150 mg	Placebo
Started	73	72	74
Completed	68	66	66
Not completed	5	6	8
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	2	1	2
Physician decision	-	-	1
Adverse event, non-fatal	2	5	4
Lack of efficacy	-	-	1

Period 2

Period 2 title	Week 16 up to Week 260
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Trial continued to be blinded up to week 52 and then was unblinded for the remainder of the trial

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab 75 mg

Arm description:

Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Secukinumab 75 mg
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 75 mg once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4

Arm title	Secukinumab 150 mg
Arm description: Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	
Arm type	Experimental
Investigational medicinal product name	Secukinumab 150 mg
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 once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4	

Arm title	Placebo - secukinumab 75 mg
Arm description: Placebo patients re-randomized to secukinumab 75 mg subcutaneous injection every 4 weeks starting from week 16.	
Arm type	Experimental
Investigational medicinal product name	Secukinumab 75 mg
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: Patients re-randomized to secukinumab 75 mg subcutaneous injection every 4 weeks starting from week 16	

Arm title	Placebo - secukinumab 150 mg
Arm description: Placebo patients re-randomized to secukinumab 150 mg subcutaneous injection every 4 weeks starting from week 16.	
Arm type	Experimental
Investigational medicinal product name	Secukinumab 75 mg
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: Patients re-randomized to secukinumab 75 mg subcutaneous injection every 4 weeks starting from week 16	

Number of subjects in period 2	Secukinumab 75 mg	Secukinumab 150 mg	Placebo - secukinumab 75 mg
Started	68	66	32
Completed	48	53	20
Not completed	20	13	12
Adverse event, serious fatal	1	1	-
Consent withdrawn by subject	7	2	3
Physician decision	-	2	-
Adverse event, non-fatal	5	2	3

Non-compliance	-	1	1
Technical issues	-	1	1
Lack of efficacy	7	4	4

Number of subjects in period 2	Placebo - secukinumab 150 mg
Started	34
Completed	29
Not completed	5
Adverse event, serious fatal	-
Consent withdrawn by subject	1
Physician decision	-
Adverse event, non-fatal	2
Non-compliance	-
Technical issues	-
Lack of efficacy	2

Baseline characteristics

Reporting groups

Reporting group title	Secukinumab 75 mg
Reporting group description: Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	
Reporting group title	Secukinumab 150 mg
Reporting group description: Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	
Reporting group title	Placebo
Reporting group description: Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16	

Reporting group values	Secukinumab 75 mg	Secukinumab 150 mg	Placebo
Number of subjects	73	72	74
Age, Customized Units: Subjects			
< 65	70	70	72
>= 65 to 74	2	2	1
>= 75	1	0	1
Sex: Female, Male Units: Subjects			
Female	22	26	18
Male	51	46	56
Race/Ethnicity, Customized Units: Subjects			
White	70	69	70
Asian	3	2	4
American Indian or Alaska Native	0	1	0

Reporting group values	Total		
Number of subjects	219		
Age, Customized Units: Subjects			
< 65	212		
>= 65 to 74	5		
>= 75	2		
Sex: Female, Male Units: Subjects			
Female	66		
Male	153		
Race/Ethnicity, Customized Units: Subjects			
White	209		
Asian	9		
American Indian or Alaska Native	1		

End points

End points reporting groups

Reporting group title	Secukinumab 75 mg
Reporting group description: Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	
Reporting group title	Secukinumab 150 mg
Reporting group description: Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	
Reporting group title	Placebo
Reporting group description: Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16	
Reporting group title	Secukinumab 75 mg
Reporting group description: Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	
Reporting group title	Secukinumab 150 mg
Reporting group description: Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	
Reporting group title	Placebo - secukinumab 75 mg
Reporting group description: Placebo patients re-randomized to secukinumab 75 mg subcutaneous injection every 4 weeks starting from week 16.	
Reporting group title	Placebo - secukinumab 150 mg
Reporting group description: Placebo patients re-randomized to secukinumab 150 mg subcutaneous injection every 4 weeks starting from week 16.	

Primary: Percentage of participants achieving ASAS 20 (SpondyloArthritis International Society criteria) response at week 16

End point title	Percentage of participants achieving ASAS 20 (SpondyloArthritis International Society criteria) response at week 16
End point description: ASAS 20 response is a validated composite assessment, reflecting the proportion of treated patients who achieve within a defined timeframe an improvement of 20% and ≥ 1 unit on a scale of 10 in at least three of the four ASAS main domains and no worsening of $\geq 20\%$ and ≥ 1 unit in the remaining domain. ASAS 20 is used to assess the efficacy of at least one dose of secukinumab against placebo.	
End point type	Primary
End point timeframe: Baseline up to 16 weeks	

End point values	Secukinumab 75 mg	Secukinumab 150 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	72	74	
Units: percentage of participants				
number (not applicable)	41.1	61.1	28.4	

Statistical analyses

Statistical analysis title	75 mg vs placebo
Comparison groups	Secukinumab 75 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0967
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	3.67

Statistical analysis title	150 mg vs placebo
Comparison groups	Secukinumab 150 mg v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.14
upper limit	8.96

Secondary: Percentage of participants achieving ASAS 40 (SpondyloArthritis International Society criteria) response at week 16

End point title	Percentage of participants achieving ASAS 40 (SpondyloArthritis International Society criteria) response at week 16
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End point description:

ASAS 40 response is a validated composite assessment, reflecting the proportion of treated patients who achieve within a defined timeframe 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. ASAS 40 is used to assess the efficacy of at least one dose of secukinumab against placebo.

End point type	Secondary
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End point timeframe:

Baseline up to 16 weeks

End point values	Secukinumab 75 mg	Secukinumab 150 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	72	74	
Units: percentage of participants				
number (not applicable)	26.0	36.1	10.8	

Statistical analyses

Statistical analysis title	75 mg vs placebo
Comparison groups	Secukinumab 75 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0194
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	7.48

Statistical analysis title	150 mg vs placebo
Comparison groups	Secukinumab 150 mg v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.07

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.06
upper limit	12.44

Secondary: Change from baseline at week 16 in serum hsCRP

End point title	Change from baseline at week 16 in serum hsCRP
End point description:	
The change from baseline in hsCRP is expressed as a ratio of post-baseline to baseline values. With the ratio normalized to 1.0 at baseline, ratios less than 1.0 represent decreased post-baseline values, whereas ratios greater than 1.0 represent increased post-baseline values. Blood levels of C-reactive protein (CRP), an acute phase reactant, are indicative of inflammation and of its severity, and can be used to monitor treatment response. A high sensitivity CRP (hsCRP) test is implemented in this study to assess the efficacy of at least one dose of secukinumab versus placebo in reducing AS elicited systemic inflammation over time.	
End point type	Secondary
End point timeframe:	
16 weeks	

End point values	Secukinumab 75 mg	Secukinumab 150 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	72	74	
Units: mg/L				
least squares mean (standard error)	0.61 (± 1.103)	0.55 (± 1.104)	1.13 (± 1.105)	

Statistical analyses

Statistical analysis title	75 mg vs placebo
Comparison groups	Secukinumab 75 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	0.71

Statistical analysis title	150 mg vs placebo
Comparison groups	Secukinumab 150 mg v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.64

Secondary: Percentage of participants achieving ASAS 5/6 (SpondyloArthritis International Society criteria) response at week 16

End point title	Percentage of participants achieving ASAS 5/6 (SpondyloArthritis International Society criteria) response at week 16
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End point description:

ASAS 5/6 response is a validated composite assessment, reflecting the proportion of treated patients who achieve within a defined timeframe at least 20% improvement in score in at least 5 of a conventional set of 6 clinical domains relevant to AS. In this study, ASAS 5/6 is used to assess the efficacy of at least one dose of secukinumab against placebo.

End point type	Secondary
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End point timeframe:

Baseline up to 16 weeks

End point values	Secukinumab 75 mg	Secukinumab 150 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	72	74	
Units: percentage of participants				
number (not applicable)	34.2	43.1	8.1	

Statistical analyses

Statistical analysis title	75 mg vs placebo
Comparison groups	Secukinumab 75 mg v Placebo

Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0003
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.31
upper limit	16.26

Statistical analysis title	75 mg vs placebo
Comparison groups	Secukinumab 150 mg v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	9.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.47
upper limit	24.12

Secondary: Change from baseline at week 16 for total Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

End point title	Change from baseline at week 16 for total Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)
End point description: BASDAI is a validated assessment tool using 0 through 10 scales (0 indicating "no problem" and 10 indicating "worst problem"), to characterize six clinical domains pertaining to five major symptoms of AS perceived by the patients. Computed composite scores of 4 or greater indicate suboptimal disease control. In this study, the BASDAI is used to assess the efficacy of at least one dose of secukinumab versus placebo.	
End point type	Secondary
End point timeframe: Baseline up to 16 weeks	

End point values	Secukinumab 75 mg	Secukinumab 150 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	72	74	
Units: scores on a scale				
least squares mean (standard error)	-1.92 ($\pm$ 0.249)	-2.19 ($\pm$ 0.248)	-0.85 ($\pm$ 0.252)	

Statistical analyses

Statistical analysis title	75 mg vs placebo
Comparison groups	Secukinumab 75 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.77
upper limit	-0.37
Variability estimate	Standard error of the mean
Dispersion value	0.353

Statistical analysis title	150 mg vs placebo
Comparison groups	Secukinumab 150 mg v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.04
upper limit	-0.65
Variability estimate	Standard error of the mean
Dispersion value	0.353

Secondary: Change from baseline at week 16 in Physical Function Component

Summary (PCS) of the Medical Outcomes Study Questionnaire Short-form Health Survey (SF-36)

End point title	Change from baseline at week 16 in Physical Function Component Summary (PCS) of the Medical Outcomes Study Questionnaire Short-form Health Survey (SF-36)
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End point description:

SF-36 is a 36 item questionnaire which measures Quality of Life across eight domains, which are both physically and emotionally based. Two overall summary scores, the Physical Component Summary (PCS) and Mental Component Summary (MCS) can be computed. In this study, SF-36 PCS is used to assess improvement from baseline of at least one dose of secukinumab versus placebo.

End point type	Secondary
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End point timeframe:

Baseline up to 16 weeks

End point values	Secukinumab 75 mg	Secukinumab 150 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	72	74	
Units: scores on a scale				
least squares mean (standard error)	4.77 ($\pm$ 0.798)	6.06 ($\pm$ 0.784)	1.92 ($\pm$ 0.786)	

Statistical analyses

Statistical analysis title	75 mg vs placebo
Comparison groups	Secukinumab 75 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.011
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	2.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	5.03
Variability estimate	Standard error of the mean
Dispersion value	1.108

Statistical analysis title	150 mg vs placebo
Comparison groups	Secukinumab 150 mg v Placebo

Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	4.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.96
upper limit	6.32
Variability estimate	Standard error of the mean
Dispersion value	1.105

Secondary: Change from baseline at week 16 in ASQoL

End point title	Change from baseline at week 16 in ASQoL
End point description:	
ASQoL is an 18 item questionnaire that assesses disease-specific quality of life (QoL), consisting of statements that are relevant to the physical and mental conditions for a participant with AS: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each statement is answered by the participant as a 'Yes' (scored as 1) or 'No' (scored as 0). All item scores are summed to give a total score. Total score can range from 0 (good QoL) to 18 (poor QoL). In this study, ASQoL is used to assess improvement from baseline of at least one dose of secukinumab versus placebo.	
End point type	Secondary
End point timeframe:	
Baseline up to 16 weeks	

End point values	Secukinumab 75 mg	Secukinumab 150 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	72	74	
Units: scores on a scale				
least squares mean (standard error)	-3.33 (± 0.537)	-4.00 (± 0.528)	-1.37 (± 0.530)	

Statistical analyses

Statistical analysis title	75 mg vs placebo
Comparison groups	Secukinumab 75 mg v Placebo

Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0096
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.43
upper limit	-0.48
Variability estimate	Standard error of the mean
Dispersion value	0.748

Statistical analysis title	150 mg vs placebo
Comparison groups	Secukinumab 150 mg v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0005
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-2.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.09
upper limit	-1.16
Variability estimate	Standard error of the mean
Dispersion value	0.743

Secondary: Percentage of participants achieving ASAS partial remission at week 16

End point title	Percentage of participants achieving ASAS partial remission at week 16
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End point description:

ASAS partial remission is a composite assessment, reflecting the proportion of treated patients who achieve within a defined time frame a value not above 2 units in each of the 4 ASAS domains on a scale of 10. In this study ASAS partial remission is used to assess the efficacy of at least one dose of secukinumab versus placebo.

End point type	Secondary
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End point timeframe:

Baseline up to 16 weeks

End point values	Secukinumab 75 mg	Secukinumab 150 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	72	74	
Units: percentage of participants				
number (not applicable)	15.1	13.9	4.1	

Statistical analyses

Statistical analysis title	75 mg vs placebo
Comparison groups	Secukinumab 75 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0325
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	16.21

Statistical analysis title	150 mg vs placebo
Comparison groups	Secukinumab 150 mg v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0471
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	15.01

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

Adverse event reporting additional description:

AE additional description

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	Any AIN457 75 mg
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Reporting group description:

Any AIN457 75 mg

Reporting group title	Placebo
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Reporting group description:

Placebo

Reporting group title	Any AIN457 150 mg
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Reporting group description:

Any AIN457 150 mg

Serious adverse events	Any AIN457 75 mg	Placebo	Any AIN457 150 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 105 (23.81%)	4 / 74 (5.41%)	31 / 155 (20.00%)
number of deaths (all causes)	2	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Glioblastoma			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Malignant melanoma			

subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraganglion neoplasm			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superficial spreading melanoma stage unspecified			
subjects affected / exposed	0 / 105 (0.00%)	1 / 74 (1.35%)	0 / 155 (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
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Thrombophlebitis superficial			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
General disorders and administration site conditions			
Drug ineffective			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Immune system disorders			
Sarcoidosis			

subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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			
Nasal septum deviation			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Sleep apnoea syndrome			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
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			
subjects affected / exposed	0 / 105 (0.00%)	1 / 74 (1.35%)	0 / 155 (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
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion			

subjects affected / exposed	0 / 105 (0.00%)	1 / 74 (1.35%)	0 / 155 (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
Hip fracture			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Lumbar vertebral fracture			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Multiple injuries			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Spinal compression fracture			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Spinal cord injury cervical			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Splenic rupture			

subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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			
Acute coronary syndrome			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	2 / 105 (1.90%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Headache			

subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	2 / 155 (1.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	2 / 155 (1.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Quadripareisis			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Quadriplegia			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Iritis			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
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 disorders			

Abdominal hernia			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Abdominal pain upper			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
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 fissure			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
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 ischaemic			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Colitis microscopic			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Colitis ulcerative			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	2 / 105 (1.90%)	0 / 74 (0.00%)	2 / 155 (1.29%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated hiatus hernia			

subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Stress urinary incontinence			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Arthritis			
subjects affected / exposed	0 / 105 (0.00%)	1 / 74 (1.35%)	0 / 155 (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
Back pain			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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

Costochondritis			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 105 (0.00%)	1 / 74 (1.35%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Arthritis bacterial			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Febrile infection			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder abscess			

subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis salmonella			
subjects affected / exposed	0 / 105 (0.00%)	0 / 74 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Influenza			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Meningitis viral			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Pharyngitis			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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
Pneumonia			
subjects affected / exposed	2 / 105 (1.90%)	0 / 74 (0.00%)	2 / 155 (1.29%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Postoperative wound infection			
subjects affected / exposed	1 / 105 (0.95%)	0 / 74 (0.00%)	0 / 155 (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

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

Non-serious adverse events	Any AIN457 75 mg	Placebo	Any AIN457 150 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	76 / 105 (72.38%)	26 / 74 (35.14%)	99 / 155 (63.87%)
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 105 (8.57%)	0 / 74 (0.00%)	15 / 155 (9.68%)
occurrences (all)	10	0	15
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 105 (1.90%)	4 / 74 (5.41%)	3 / 155 (1.94%)
occurrences (all)	2	6	3
Headache			
subjects affected / exposed	9 / 105 (8.57%)	6 / 74 (8.11%)	15 / 155 (9.68%)
occurrences (all)	10	6	26
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 105 (3.81%)	5 / 74 (6.76%)	5 / 155 (3.23%)
occurrences (all)	4	5	9
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 105 (8.57%)	1 / 74 (1.35%)	17 / 155 (10.97%)
occurrences (all)	13	1	18
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 105 (4.76%)	1 / 74 (1.35%)	11 / 155 (7.10%)
occurrences (all)	6	1	12
Oropharyngeal pain			
subjects affected / exposed	4 / 105 (3.81%)	2 / 74 (2.70%)	8 / 155 (5.16%)
occurrences (all)	5	2	9
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	6 / 105 (5.71%)	1 / 74 (1.35%)	4 / 155 (2.58%)
occurrences (all)	6	1	4
Musculoskeletal and connective tissue disorders			

Ankylosing spondylitis subjects affected / exposed occurrences (all)	6 / 105 (5.71%) 6	1 / 74 (1.35%) 1	6 / 155 (3.87%) 9
Arthralgia subjects affected / exposed occurrences (all)	8 / 105 (7.62%) 14	2 / 74 (2.70%) 2	10 / 155 (6.45%) 12
Back pain subjects affected / exposed occurrences (all)	7 / 105 (6.67%) 8	2 / 74 (2.70%) 2	13 / 155 (8.39%) 13
Bursitis subjects affected / exposed occurrences (all)	6 / 105 (5.71%) 6	0 / 74 (0.00%) 0	4 / 155 (2.58%) 7
Musculoskeletal pain subjects affected / exposed occurrences (all)	7 / 105 (6.67%) 7	0 / 74 (0.00%) 0	8 / 155 (5.16%) 11
Osteoarthritis subjects affected / exposed occurrences (all)	6 / 105 (5.71%) 6	1 / 74 (1.35%) 1	4 / 155 (2.58%) 5
Pain in extremity subjects affected / exposed occurrences (all)	2 / 105 (1.90%) 2	1 / 74 (1.35%) 1	11 / 155 (7.10%) 13
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	15 / 105 (14.29%) 23	1 / 74 (1.35%) 1	14 / 155 (9.03%) 15
Gastroenteritis subjects affected / exposed occurrences (all)	6 / 105 (5.71%) 8	1 / 74 (1.35%) 1	13 / 155 (8.39%) 17
Influenza subjects affected / exposed occurrences (all)	13 / 105 (12.38%) 15	0 / 74 (0.00%) 0	14 / 155 (9.03%) 16
Nasopharyngitis subjects affected / exposed occurrences (all)	30 / 105 (28.57%) 71	3 / 74 (4.05%) 3	35 / 155 (22.58%) 73
Oral herpes			

subjects affected / exposed	6 / 105 (5.71%)	0 / 74 (0.00%)	8 / 155 (5.16%)
occurrences (all)	16	0	32
Pharyngitis			
subjects affected / exposed	6 / 105 (5.71%)	0 / 74 (0.00%)	3 / 155 (1.94%)
occurrences (all)	7	0	3
Rhinitis			
subjects affected / exposed	6 / 105 (5.71%)	1 / 74 (1.35%)	5 / 155 (3.23%)
occurrences (all)	7	1	5
Sinusitis			
subjects affected / exposed	5 / 105 (4.76%)	1 / 74 (1.35%)	8 / 155 (5.16%)
occurrences (all)	6	1	11
Upper respiratory tract infection			
subjects affected / exposed	13 / 105 (12.38%)	2 / 74 (2.70%)	16 / 155 (10.32%)
occurrences (all)	38	2	32
Urinary tract infection			
subjects affected / exposed	5 / 105 (4.76%)	2 / 74 (2.70%)	9 / 155 (5.81%)
occurrences (all)	6	2	13
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	5 / 105 (4.76%)	1 / 74 (1.35%)	8 / 155 (5.16%)
occurrences (all)	5	1	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 November 2013	-To expand the statistical hierarchy (primary plus ranked secondary variables) to include more endpoints which were relevant to determining the overall therapeutic value of a therapy for Ankylosing Spondylitis. These endpoints included but were not limited to ASQoL, BASDAI and SF-36. -Analysis was changed to include all patients in the FAS, rather than focusing only on the subset of patients who were TNFα-inhibitor naïve, as the FAS would be more representative of the general population of AS patients. - Align the primary and secondary assessments with the ASAS Handbook (Sieper et al 2009) -Limit blinded study duration to reduce patient burden in administering a second syringe containing placebo to maintain blind . As the primary endpoint analysis (PEA) was conducted after all patients completed Week 16, there was no longer a need for the sponsor to be blinded past this analysis. -The conduct of the interim analysis was revised. However, sites and patients remained blinded until all patients reached Week 52 to reduce bias when assessing the effect of the secukinumab doses over 52 weeks.
18 September 2015	-The study medication for patients on the 75 mg sc treatment arm could have been be escalated from 75 mg sc to 150 mg sc every 4 weeks for patients whose overall therapeutic response is not fully achieved with the current dose of 75 mg sc and may improve with a higher dose, as judged by the investigator. The escalation of the study medication may be determined at any site visit. - DMC discontinued after week 52. - To align with these specifications in local prescribing information, protocol exclusion criterion #12 was changed to: Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unwilling to use effective contraception during the entire study or longer if required by locally approved prescribing information. - Protocol exclusion criterion #16 was updated for greater clarity to "If the total bilirubin concentration is increased above 2 x ULN, total bilirubin should be differentiated into the direct and indirect reacting bilirubin."

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported