Clinical trial results:
An extension study to evaluate the sustainability of clinical benefits, safety and tolerability of secukinumab in patients with active Ankylosing Spondylitis

Summary

EudraCT number	2013-001089-40
Trial protocol	IT GB DE NL BG BE
Global end of trial date	16 March 2018

Results information

Result version number	v1 (current)
This version publication date	29 March 2019
First version publication date	29 March 2019

Trial information

Trial identification

Sponsor protocol code	CAIN457F2305E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01863732
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, 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	16 March 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the sustainability of subject benefits as quantified by the ASAS20 (Assessment of SpondyloArthritis International Society criteria) in the whole study population during long term (Week 260) treatment with secukinumab 75 and 150 mg provided as prefilled syringes

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	06 November 2013
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	Belgium: 16
Country: Number of subjects enrolled	Bulgaria: 21
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Mexico: 32
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Peru: 29
Country: Number of subjects enrolled	Russian Federation: 57
Country: Number of subjects enrolled	Taiwan: 48
Country: Number of subjects enrolled	Turkey: 3
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	274
EEA total number of subjects	96

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)	261
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

CAIN457F2305 core study consisted of a screening period of 4 Wks before randomization followed by a treatment period of 2 years (Wk 0 through Wk 104). At Wk 104, patients continued into the extension on the same dose of AIN457. If they were on Placebo in the core then randomized to either Group 1 or 2.

Pre-assignment

Screening details:

Group 1: AIN457 75mg plus placebo 150mg dosed every 4 weeks from Wk 104E1 to Wk 152. At Wk 156 (after unblinding), only AIN457 75mg was dosed or up titrated to AIN457 150mg. Group 2: AIN457 150mg plus placebo 75mg dosed every 4 weeks from Wk 104E1 through Wk 152. At Wk 156 (after unblinding), only secukinumab 150 mg was dosed.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab (AIN457) 75mg Grp1

Arm description:

Group 1: AIN457 75 mg plus placebo 150 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), only AIN457 75 mg was dosed. Secukinumab in PFS for s.c. self-administration Q4W

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

Dosage and administration details:

Secukinumab 75 mg in 0.5 mL in prefilled syringes subcutaneously every 4 weeks for until week 260

Investigational medicinal product name	Placebo
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:

Placebo to match Secukinumab 150 mg in 1 mL in prefilled syringes subcutaneously every 4 weeks for until week 156

Arm title	Secukinumab (AIN457) 75 to 150mg Grp1

Arm description:

Group 1: AIN457 75 mg plus placebo 150 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), was up titrated to AIN457 150 mg only. Secukinumab in PFS for s.c. self-administration Q4W

Arm type	Experimental

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

Dosage and administration details:

Secukinumab 75 mg in 0.5 mL in prefilled syringes subcutaneously every 4 weeks for until week 156 then up titrated to 150mg

Investigational medicinal product name	Placebo
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:

Placebo to match Secukinumab 150 mg in 1 mL in prefilled syringes subcutaneously every 4 weeks for until week 156

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

Dosage and administration details:

Secukinumab 150 mg in 1 mL in prefilled syringes subcutaneously every 4 weeks from week 156 until week 260

Arm title	Secukinumab (AIN457) 150mg Grp2

Arm description:

Group 2: AIN457 150 mg plus placebo 75 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), only AIN457 150 mg was dosed. Secukinumab in PFS for s.c. self-administration Q4W

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

Dosage and administration details:

Secukinumab 150 mg in 1 mL in prefilled syringes subcutaneously every 4 weeks for until week 260

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

Dosage and administration details:

Placebo to match Secukinumab 75 mg in 0.5 mL in prefilled syringes subcutaneously every 4 weeks for until week 156

Arm title	Pbo in Core then AIN457 75mg Grp1

Arm description:

Participants were on Placebo (Pbo) in Core and then in extension randomized to Group 1: secukinumab (AIN457) 75 mg plus placebo 150 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), only AIN457 75 mg was dosed.Secukinumab in PFS for s.c. self-administration Q4W

Arm type	Experimental

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

Dosage and administration details:

Secukinumab 75 mg in 0.5 mL in prefilled syringes subcutaneously every 4 weeks for until week 260

Investigational medicinal product name	Placebo
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:

Placebo to match Secukinumab 150 mg in 1 mL in prefilled syringes subcutaneously every 4 weeks for until week 156

Arm title	Pbo in Core then AIN457 75 to 150mg Grp1

Arm description:

Participants were on Placebo in Core and then in extension randomized to Group 1: secukinumab (AIN457) 75 mg plus placebo 150 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), was up titrated to AIN457 150 mg only. Secukinumab in PFS for s.c. self-administration Q4W

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

Dosage and administration details:

Secukinumab 75 mg in 0.5 mL in prefilled syringes subcutaneously every 4 weeks for until week 156 then up titrated to 150mg

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

Dosage and administration details:

Secukinumab 150 mg in 1 mL in prefilled syringes subcutaneously every 4 weeks from week 156 until week 260

Investigational medicinal product name	Placebo
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:

Placebo to match Secukinumab 150 mg in 1 mL in prefilled syringes subcutaneously every 4 weeks for until week 156

Arm title	Pbo in Core then AIN457 150mg Grp2

Arm description:

Participants were on Placebo (Pbo) in Core and then in extension randomized to Group 2: AIN457 150 mg plus placebo 75 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), only AIN457 150 mg was dosed. Secukinumab in PFS for s.c. self-administration Q4W

Arm type	Experimental

Investigational medicinal product name	Placebo
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:

Placebo to match Secukinumab 75 mg in 0.5 mL in prefilled syringes subcutaneously every 4 weeks for until week 156

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

Dosage and administration details:

Secukinumab 150 mg in 1 mL in prefilled syringes subcutaneously every 4 weeks for until week 260

Number of subjects in period 1	Secukinumab (AIN457) 75mg Grp1	Secukinumab (AIN457) 75 to 150mg Grp1	Secukinumab (AIN457) 150mg Grp2
Started	41	59	87
Completed	30	57	75
Not completed	11	2	12
Adverse event, serious fatal	1	-	-
Physician decision	1	-	-
Adverse event, non-fatal	1	1	-
Technical problems	-	-	1
Pregnancy	-	-	-
Lost to follow-up	1	1	2
Subject/guardian decision	6	-	9
Lack of efficacy	1	-	-

Number of subjects in period 1	Pbo in Core then AIN457 75mg Grp1	Pbo in Core then AIN457 75 to 150mg Grp1	Pbo in Core then AIN457 150mg Grp2
Started	23	23	41
Completed	15	20	33
Not completed	8	3	8
Adverse event, serious fatal	-	-	1
Physician decision	-	1	-
Adverse event, non-fatal	3	-	3
Technical problems	1	-	-
Pregnancy	-	-	1
Lost to follow-up	1	-	1
Subject/guardian decision	2	1	1
Lack of efficacy	1	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab (AIN457) 75mg Grp1
Reporting group description:	
Group 1: AIN457 75 mg plus placebo 150 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), only AIN457 75 mg was dosed. Secukinumab in PFS for s.c. self-administration Q4W	
Reporting group title	Secukinumab (AIN457) 75 to 150mg Grp1
Reporting group description:	
Group 1: AIN457 75 mg plus placebo 150 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), was up titrated to AIN457 150 mg only. Secukinumab in PFS for s.c. self-administration Q4W	
Reporting group title	Secukinumab (AIN457) 150mg Grp2
Reporting group description:	
Group 2: AIN457 150 mg plus placebo 75 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), only AIN457 150 mg was dosed. Secukinumab in PFS for s.c. self-administration Q4W	
Reporting group title	Pbo in Core then AIN457 75mg Grp1
Reporting group description:	
Participants were on Placebo (Pbo) in Core and then in extension randomized to Group 1: secukinumab (AIN457) 75 mg plus placebo 150 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), only AIN457 75 mg was dosed.Secukinumab in PFS for s.c. self-administration Q4W	
Reporting group title	Pbo in Core then AIN457 75 to 150mg Grp1
Reporting group description:	
Participants were on Placebo in Core and then in extension randomized to Group 1: secukinumab (AIN457) 75 mg plus placebo 150 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), was up titrated to AIN457 150 mg only. Secukinumab in PFS for s.c. self-administration Q4W	
Reporting group title	Pbo in Core then AIN457 150mg Grp2
Reporting group description:	
Participants were on Placebo (Pbo) in Core and then in extension randomized to Group 2: AIN457 150 mg plus placebo 75 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), only AIN457 150 mg was dosed. Secukinumab in PFS for s.c. self-administration Q4W	

Reporting group values	Secukinumab (AIN457) 75mg Grp1	Secukinumab (AIN457) 75 to 150mg Grp1	Secukinumab (AIN457) 150mg Grp2
Number of subjects	41	59	87
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	38	56	86
From 65-84 years	3	3	1
85 years and over	0	0	0

Age Continuous Units: years			
arithmetic mean	42.5	40.9	38.2
standard deviation	± 13.37	± 13.36	± 11.58
Sex: Female, Male Units: Subjects			
Female	12	13	29
Male	29	46	58
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	3	7
Asian	6	13	15
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	25	36	48
More than one race	0	0	0
Unknown or Not Reported	10	7	17

Reporting group values	Pbo in Core then AIN457 75mg Grp1	Pbo in Core then AIN457 75 to 150mg Grp1	Pbo in Core then AIN457 150mg Grp2
Number of subjects	23	23	41
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	21	21	39
From 65-84 years	2	2	2
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	43.0	40.0	42.5
standard deviation	± 13.00	± 12.43	± 12.13
Sex: Female, Male Units: Subjects			
Female	7	3	12
Male	16	20	29
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	3	5	8
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	13	17	28
More than one race	0	0	0
Unknown or Not Reported	6	1	4

Reporting group values	Total		
Number of subjects	274		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	261		
From 65-84 years	13		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	76		
Male	198		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	12		
Asian	50		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	167		
More than one race	0		
Unknown or Not Reported	45		

End points

End points reporting groups

Reporting group title	Secukinumab (AIN457) 75mg Grp1
Reporting group description:	
Group 1: AIN457 75 mg plus placebo 150 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), only AIN457 75 mg was dosed. Secukinumab in PFS for s.c. self-administration Q4W	
Reporting group title	Secukinumab (AIN457) 75 to 150mg Grp1
Reporting group description:	
Group 1: AIN457 75 mg plus placebo 150 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), was up titrated to AIN457 150 mg only. Secukinumab in PFS for s.c. self-administration Q4W	
Reporting group title	Secukinumab (AIN457) 150mg Grp2
Reporting group description:	
Group 2: AIN457 150 mg plus placebo 75 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), only AIN457 150 mg was dosed. Secukinumab in PFS for s.c. self-administration Q4W	
Reporting group title	Pbo in Core then AIN457 75mg Grp1
Reporting group description:	
Participants were on Placebo (Pbo) in Core and then in extension randomized to Group 1: secukinumab (AIN457) 75 mg plus placebo 150 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), only AIN457 75 mg was dosed.Secukinumab in PFS for s.c. self-administration Q4W	
Reporting group title	Pbo in Core then AIN457 75 to 150mg Grp1
Reporting group description:	
Participants were on Placebo in Core and then in extension randomized to Group 1: secukinumab (AIN457) 75 mg plus placebo 150 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), was up titrated to AIN457 150 mg only. Secukinumab in PFS for s.c. self-administration Q4W	
Reporting group title	Pbo in Core then AIN457 150mg Grp2
Reporting group description:	
Participants were on Placebo (Pbo) in Core and then in extension randomized to Group 2: AIN457 150 mg plus placebo 75 mg dosed every four weeks Week 104E1 through Week 152. Starting on Week 156 (after unblinding), only AIN457 150 mg was dosed. Secukinumab in PFS for s.c. self-administration Q4W	

Primary: Assessment of Spondyloarthritis International Society criteria (ASAS) 20 response from Week 104 to Week 260

End point title	Assessment of Spondyloarthritis International Society criteria (ASAS) 20 response from Week 104 to Week 260[1]
End point description:	
ASAS 20 response is a validated composite assessment, reflecting the proportion of treated patients who achieve within a defined time frame at least 20% improvement in score in at least 3 of a conventional set of 4 clinical domains relevant to AS and no worsening in the fourth domain. In this study, ASAS 20 is used to assess quantitatively the sustainability of clinical benefits of two dosage regimens of secukinumab over the treatment period from Week 104 to Week 260 No Statistical Analysis was performed	
End point type	Primary
End point timeframe:	
Week 104 to Week 260	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary outcome

End point values	Secukinumab (AIN457) 75mg Grp1	Secukinumab (AIN457) 75 to 150mg Grp1	Secukinumab (AIN457) 150mg Grp2	Pbo in Core then AIN457 75mg Grp1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	59	87	23
Units: % of responders				
number (not applicable)				
Week 104 (n=84,n=0, n=80,n=42,n=0, n=37)	71.4	0	80.0	78.6
Week 116 (n=96,n=0, n=84,n=46,n=0, n=41)	76.0	0	82.1	76.1
Week 128 (n=97,n=0, n=83,n=46,n=0, n=40)	70.1	0	77.1	84.8
Week 140 (n=96,n=0, n=84,n=45,n=0, n=40)	77.1	0	75.0	75.6
Week 156 (n=98,n=0, n=86,n=46,n=0, n=40)	75.5	0	80.2	76.1
Week 168 (n=95,n=0, n=83,n=42,n=0, n=37)	74.7	0	78.3	83.3
Week 180 (n=92,n=1, n=80,n=41,n=1, n=37)	81.5	100.0	80.0	82.9
Week 192 (n=82,n=12, n=79,n=36,n=6, n=37)	69.5	91.7	84.8	83.3
Week 208 (n=69,n=25, n=79,n=28,n=12, n=37)	71.0	80.0	79.7	78.6
Week 220 (n=51,n=39, n=77,n=23,n=14, n=36)	68.6	82.1	81.8	91.3
Week 232 (n=39,n=51, n=78,n=20,n=17, n=36)	82.1	72.5	82.1	80.0
Week 244 (n=30,n=57, n=78,n=15,n=20, n=34)	76.7	73.7	82.1	80.0
Week 260 (n=31,n=56, n=76,n=16,n=22, n=36)	67.7	73.2	77.6	81.3

End point values	Pbo in Core then AIN457 75 to 150mg Grp1	Pbo in Core then AIN457 150mg Grp2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	41		
Units: % of responders				
number (not applicable)				
Week 104 (n=84,n=0, n=80,n=42,n=0, n=37)	0	73.0		
Week 116 (n=96,n=0, n=84,n=46,n=0, n=41)	0	70.7		
Week 128 (n=97,n=0, n=83,n=46,n=0, n=40)	0	75.0		
Week 140 (n=96,n=0, n=84,n=45,n=0, n=40)	0	72.5		
Week 156 (n=98,n=0, n=86,n=46,n=0, n=40)	0	78.4		
Week 168 (n=95,n=0, n=83,n=42,n=0, n=37)	0	78.4		
Week 180 (n=92,n=1, n=80,n=41,n=1, n=37)	0	78.4		

Week 192 (n=82,n=12, n=79,n=36,n=6, n=37)	66.7	73.0		
Week 208 (n=69,n=25, n=79,n=28,n=12, n=37)	66.7	78.4		
Week 220 (n=51,n=39, n=77,n=23,n=14, n=36)	64.3	75.0		
Week 232 (n=39,n=51, n=78,n=20,n=17, n=36)	70.6	77.8		
Week 244 (n=30,n=57, n=78,n=15,n=20, n=34)	80.0	76.5		
Week 260 (n=31,n=56, n=76,n=16,n=22, n=36)	81.8	80.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Spondyloarthritis International Society criteria (ASAS) 40 response from Week 104 to Week 260

End point title	Assessment of Spondyloarthritis International Society criteria (ASAS) 40 response from Week 104 to Week 260

End point description:

ASAS 40 response is a validated composite assessment, reflecting the proportion of treated patients who achieve within a defined time frame at least 40% improvement in score in at least 3 of a conventional set of 4 clinical domains relevant to AS and no worsening in the fourth domain. In this study, ASAS 40 is used to assess quantitatively the sustainability of clinical benefits of two dosage regimens of secukinumab over the treatment period from Week 104 to Week 260 No Statistical Analysis was performed

End point type	Secondary

End point timeframe:

Week 104 to Week 260

End point values	Secukinumab (AIN457) 75mg Grp1	Secukinumab (AIN457) 75 to 150mg Grp1	Secukinumab (AIN457) 150mg Grp2	Pbo in Core then AIN457 75mg Grp1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	59	87	23
Units: % of responders				
number (not applicable)				
Week 104 (n=84,n=0, n=80,n=42,n=0, n=37)	53.6	0	65.0	57.1
Week 116 (n=96,n=0, n=84,n=46,n=0, n=41)	56.3	0	59.5	54.3
Week 128 (n=97,n=0, n=83,n=46,n=0, n=40)	54.6	0	68.7	58.7
Week 140 (n=96,n=0, n=84,n=45,n=0, n=40)	53.1	0	60.7	53.3
Week 156 (n=98,n=0, n=86,n=46,n=0, n=40)	50.0	0	62.8	54.3
Week 168 (n=95,n=0, n=83,n=42,n=0, n=37)	54.7	0	67.5	42.9
Week 180 (n=92,n=1, n=80,n=41,n=1, n=37)	53.3	0	68.8	53.7

Week 192 (n=82,n=12, n=79,n=36,n=6, n=37)	53.7	83.3	69.6	52.8
Week 208 (n=69,n=25, n=79,n=28,n=12, n=37)	43.5	76.0	60.8	64.3
Week 220 (n=51,n=39, n=77,n=23,n=14, n=36)	45.1	59.0	67.5	56.5
Week 232 (n=39,n=51, n=78,n=20,n=17, n=36)	59.0	64.7	66.7	60.0
Week 244 (n=30,n=57, n=78,n=15,n=20, n=34)	60.0	61.4	70.5	60.0
Week 260 (n=31,n=56, n=76,n=16,n=22, n=36)	54.8	48.2	64.5	56.3

End point values	Pbo in Core then AIN457 75 to 150mg Grp1	Pbo in Core then AIN457 150mg Grp2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	41		
Units: % of responders				
number (not applicable)				
Week 104 (n=84,n=0, n=80,n=42,n=0, n=37)	0	48.6		
Week 116 (n=96,n=0, n=84,n=46,n=0, n=41)	0	51.2		
Week 128 (n=97,n=0, n=83,n=46,n=0, n=40)	0	55.0		
Week 140 (n=96,n=0, n=84,n=45,n=0, n=40)	0	60.0		
Week 156 (n=98,n=0, n=86,n=46,n=0, n=40)	0	55.0		
Week 168 (n=95,n=0, n=83,n=42,n=0, n=37)	0	62.2		
Week 180 (n=92,n=1, n=80,n=41,n=1, n=37)	0.0	67.6		
Week 192 (n=82,n=12, n=79,n=36,n=6, n=37)	50.0	62.2		
Week 208 (n=69,n=25, n=79,n=28,n=12, n=37)	58.3	56.8		
Week 220 (n=51,n=39, n=77,n=23,n=14, n=36)	50.0	63.9		
Week 232 (n=39,n=51, n=78,n=20,n=17, n=36)	58.8	69.4		
Week 244 (n=30,n=57, n=78,n=15,n=20, n=34)	65.0	61.8		
Week 260 (n=31,n=56, n=76,n=16,n=22, n=36)	68.2	66.7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Any AIN457 75 mg
Reporting group description:	
Any AIN457 75 mg	
Reporting group title	Any AIN457 150 mg
Reporting group description:	
Any AIN457 150 mg	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Serious adverse events	Any AIN457 75 mg	Any AIN457 150 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 179 (20.11%)	33 / 263 (12.55%)	5 / 122 (4.10%)
number of deaths (all causes)	2	1	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Breast cancer			

subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Lymphoma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 263 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thymoma			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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			
Peripheral venous disease			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Varicose vein			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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 incomplete			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 179 (0.00%)	0 / 263 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Application site pain			

subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Chest discomfort			
subjects affected / exposed	1 / 179 (0.56%)	1 / 263 (0.38%)	0 / 122 (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
Pyrexia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Acute respiratory failure			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Asthma			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Dyspnoea			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Laryngeal oedema			

subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Nasal septum deviation			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Pulmonary fibrosis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Respiratory failure			
subjects affected / exposed	1 / 179 (0.56%)	1 / 263 (0.38%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 179 (0.00%)	0 / 263 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Depression			
subjects affected / exposed	0 / 179 (0.00%)	0 / 263 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Product issues			
Device failure			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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

Injury, poisoning and procedural complications			
Cartilage injury			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Cervical vertebral fracture			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Craniocerebral injury			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Dislocation of vertebra			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Injury			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Joint dislocation			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Laceration			
subjects affected / exposed	2 / 179 (1.12%)	0 / 263 (0.00%)	0 / 122 (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
Lower limb fracture			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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

Postoperative thrombosis			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Rib fracture			
subjects affected / exposed	0 / 179 (0.00%)	2 / 263 (0.76%)	0 / 122 (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
Spinal fracture			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Thoracic vertebral fracture			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Tibia fracture			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Upper limb fracture			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Atrial fibrillation			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Atrial tachycardia			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Cardiac failure			
subjects affected / exposed	1 / 179 (0.56%)	2 / 263 (0.76%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Cardiogenic shock			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Cardiomyopathy			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Cardiorenal syndrome			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Coronary artery stenosis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Mitral valve incompetence			

subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Myocardial infarction			
subjects affected / exposed	3 / 179 (1.68%)	3 / 263 (1.14%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Cerebrovascular accident			
subjects affected / exposed	1 / 179 (0.56%)	2 / 263 (0.76%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Embolic stroke			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Headache			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Hemiparesis			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Ischaemic stroke			

subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Migraine			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Stroke in evolution			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Trigeminal neuralgia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Vocal cord paresis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 263 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Abdominal lymphadenopathy			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Anaemia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 263 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			

subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Vertigo			
subjects affected / exposed	0 / 179 (0.00%)	0 / 263 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 179 (0.56%)	1 / 263 (0.38%)	0 / 122 (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
Iridocyclitis			
subjects affected / exposed	0 / 179 (0.00%)	2 / 263 (0.76%)	0 / 122 (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
Uveitis			
subjects affected / exposed	0 / 179 (0.00%)	2 / 263 (0.76%)	0 / 122 (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
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Crohn's disease			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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

Diarrhoea			
subjects affected / exposed	1 / 179 (0.56%)	1 / 263 (0.38%)	0 / 122 (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
Epigastric discomfort			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Gastritis			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Hiatus hernia			
subjects affected / exposed	2 / 179 (1.12%)	0 / 263 (0.00%)	0 / 122 (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
Intestinal obstruction			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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 hernia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Obstructive pancreatitis			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Pancreatitis acute			

subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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 acute			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Cholecystitis acute			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Cholelithiasis			
subjects affected / exposed	3 / 179 (1.68%)	0 / 263 (0.00%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis toxic			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Hepatosplenomegaly			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Renal and urinary disorders			

Renal colic			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Ureterolithiasis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	2 / 179 (1.12%)	3 / 263 (1.14%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Bursitis			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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

Osteoarthritis			
subjects affected / exposed	0 / 179 (0.00%)	2 / 263 (0.76%)	0 / 122 (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
Rotator cuff syndrome			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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 column stenosis			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Spondylolisthesis			
subjects affected / exposed	0 / 179 (0.00%)	1 / 263 (0.38%)	0 / 122 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	2 / 179 (1.12%)	0 / 263 (0.00%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Chronic sinusitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Helicobacter gastritis			

subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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	1 / 179 (0.56%)	1 / 263 (0.38%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary tuberculoma			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Pyelonephritis acute			
subjects affected / exposed	1 / 179 (0.56%)	1 / 263 (0.38%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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
Tonsillitis			
subjects affected / exposed	0 / 179 (0.00%)	2 / 263 (0.76%)	0 / 122 (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
Urinary tract infection			
subjects affected / exposed	1 / 179 (0.56%)	0 / 263 (0.00%)	0 / 122 (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	Any AIN457 150 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	126 / 179 (70.39%)	157 / 263 (59.70%)	45 / 122 (36.89%)
Vascular disorders			
Hypertension			
subjects affected / exposed	13 / 179 (7.26%)	11 / 263 (4.18%)	1 / 122 (0.82%)
occurrences (all)	15	12	1
Nervous system disorders			
Headache			
subjects affected / exposed	26 / 179 (14.53%)	28 / 263 (10.65%)	7 / 122 (5.74%)
occurrences (all)	35	55	12
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	14 / 179 (7.82%)	11 / 263 (4.18%)	1 / 122 (0.82%)
occurrences (all)	19	13	1
Eye disorders			
Uveitis			
subjects affected / exposed	10 / 179 (5.59%)	15 / 263 (5.70%)	2 / 122 (1.64%)
occurrences (all)	13	25	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	9 / 179 (5.03%)	9 / 263 (3.42%)	0 / 122 (0.00%)
occurrences (all)	11	10	0
Diarrhoea			
subjects affected / exposed	26 / 179 (14.53%)	29 / 263 (11.03%)	7 / 122 (5.74%)
occurrences (all)	37	47	7
Mouth ulceration			
subjects affected / exposed	10 / 179 (5.59%)	8 / 263 (3.04%)	3 / 122 (2.46%)
occurrences (all)	19	16	4
Nausea			
subjects affected / exposed	12 / 179 (6.70%)	12 / 263 (4.56%)	2 / 122 (1.64%)
occurrences (all)	15	15	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 179 (6.70%)	18 / 263 (6.84%)	2 / 122 (1.64%)
occurrences (all)	14	27	2
Oropharyngeal pain			

subjects affected / exposed	14 / 179 (7.82%)	18 / 263 (6.84%)	6 / 122 (4.92%)
occurrences (all)	27	27	6
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	11 / 179 (6.15%)	13 / 263 (4.94%)	4 / 122 (3.28%)
occurrences (all)	13	17	5
Arthralgia			
subjects affected / exposed	17 / 179 (9.50%)	24 / 263 (9.13%)	4 / 122 (3.28%)
occurrences (all)	30	33	5
Back pain			
subjects affected / exposed	13 / 179 (7.26%)	20 / 263 (7.60%)	0 / 122 (0.00%)
occurrences (all)	15	32	0
Neck pain			
subjects affected / exposed	9 / 179 (5.03%)	5 / 263 (1.90%)	0 / 122 (0.00%)
occurrences (all)	10	8	0
Pain in extremity			
subjects affected / exposed	9 / 179 (5.03%)	7 / 263 (2.66%)	2 / 122 (1.64%)
occurrences (all)	16	8	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	9 / 179 (5.03%)	17 / 263 (6.46%)	2 / 122 (1.64%)
occurrences (all)	11	17	2
Gastroenteritis			
subjects affected / exposed	10 / 179 (5.59%)	10 / 263 (3.80%)	1 / 122 (0.82%)
occurrences (all)	13	13	1
Influenza			
subjects affected / exposed	19 / 179 (10.61%)	26 / 263 (9.89%)	2 / 122 (1.64%)
occurrences (all)	29	39	2
Nasopharyngitis			
subjects affected / exposed	45 / 179 (25.14%)	63 / 263 (23.95%)	9 / 122 (7.38%)
occurrences (all)	87	135	9
Pharyngitis			
subjects affected / exposed	13 / 179 (7.26%)	24 / 263 (9.13%)	1 / 122 (0.82%)
occurrences (all)	20	32	1
Rhinitis			

subjects affected / exposed	6 / 179 (3.35%)	14 / 263 (5.32%)	0 / 122 (0.00%)
occurrences (all)	9	18	0
Upper respiratory tract infection			
subjects affected / exposed	29 / 179 (16.20%)	21 / 263 (7.98%)	2 / 122 (1.64%)
occurrences (all)	53	31	2
Urinary tract infection			
subjects affected / exposed	10 / 179 (5.59%)	12 / 263 (4.56%)	0 / 122 (0.00%)
occurrences (all)	12	21	0
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	18 / 179 (10.06%)	14 / 263 (5.32%)	5 / 122 (4.10%)
occurrences (all)	18	17	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 August 2015	Protocol Amendment 1: introduced the following changes: The study medication for patients on the 75 mg treatment arm was to be escalated from 75mg s.c. to 150 mg s.c. every 4 weeks for patients whose overall therapeutic response was not fully achieved with the current dose of 75 mg and could improve with a higher dose, as judged by the investigator. The escalation of the study medication could be determined at any site visit. For patients escalated to 150 mg, no dose reduction could be performed at a later time point. Following the Week 52 database lock (DBL) and interim analysis, based on the safety results of studies CAIN457F2305 and CAIN457F2310, the Data Monitoring Committee (DMC) review was no longer required. Protocol exclusion criterion #6 was changed to "Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using effective methods of contraception during the entire study or longer if required by locally approved prescribing information (e.g., 20 weeks in EU)." BASDAI 50 response had been recognized as a clinically relevant indicator of therapeutic response to biologic agents in the treatment of AS, and therefore was added as an exploratory endpoint. The Risks and Benefits section was updated to reflect the latest available information at that time

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported