Clinical trial results:
A randomized, double-blind, placebo-controlled, phase III multicenter study of subcutaneous secukinumab in prefilled syringes, to compare efficacy at 16 weeks with placebo and to assess safety and tolerability up to 52 weeks in subjects with active Ankylosing Spondylitis

Summary

EudraCT number	2015-005021-39
Trial protocol	GB CZ
Global end of trial date	19 March 2019

Results information

Result version number	v1 (current)
This version publication date	03 April 2020
First version publication date	03 April 2020

Trial information

Trial identification

Sponsor protocol code	CAIN457F2308

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02896127
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	Study Lead, 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	19 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the efficacy of secukinumab 150 mg s.c. at Week 16 is superior to placebo in subjects with active AS based on the proportion of subjects achieving an ASAS20 (Assessment of SpondyloArthritis International Society criteria) response. The results were reported in the 16-week CAIN457F2308 CSR dated 09-Jan-2019 and are not repeated in detail in this 52-week report.

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 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 327
Country: Number of subjects enrolled	Czech Republic: 55
Country: Number of subjects enrolled	United Kingdom: 35
Country: Number of subjects enrolled	Korea, Republic of: 41
Worldwide total number of subjects	458
EEA total number of subjects	90

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)	455
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Majority of subjects completed 52 weeks of treatment

Pre-assignment

Screening details:

Four out of the 153 assigned to the placebo group discontinued before Week 16

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab

Arm description:

Secukinumab 150 mg s.c.

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

Dosage and administration details:

secukinumab 150 mg (1 mL, 150 mg/mL) s.c. PFS

Arm title	Placebo

Arm description:

Placebo s.c.

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

Dosage and administration details:

Placebo s.c.

Number of subjects in period 1	Secukinumab	Placebo
Started	305	153
Completed	278	142
Not completed	27	11
Physician decision	1	1

Consent withdrawn by subject	12	4
Adverse event, non-fatal	9	2
Technical problems	1	-
Pregnancy	2	-
Lost to follow-up	-	1
Lack of efficacy	2	3

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab
Reporting group description: Secukinumab 150 mg s.c.	
Reporting group title	Placebo
Reporting group description: Placebo s.c.	

Reporting group values	Secukinumab	Placebo	Total
Number of subjects	305	153	458
Age Categorical			
The mean age of participants was 34.4 years			
Units:			
<=18 years	0	0	0
Between 18 and 65 years	303	152	455
>=65 years	2	1	3
Sex: Female, Male			
FAS			
Units:			
Female	53	21	74
Male	252	132	384
Race/Ethnicity, Customized			
FAS			
Units: Subjects			
Asian	239	130	369
White	64	23	87
Other	2	0	2

Subject analysis sets	
Subject analysis set title	Placebo - AIN457 150 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo - AIN457 150mg	
Subject analysis set title	Placebo - AIN457 150mg
Subject analysis set type	Full analysis
Subject analysis set description: placebo plus AIN457 150mg	
Subject analysis set title	Placebo - AIN457 150mg s.c.
Subject analysis set type	Full analysis
Subject analysis set description: Placebo - AIN457 150mg s.c.	
Subject analysis set title	Placebo - AIN457 150mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo - AIN457 150mg	
Subject analysis set title	Placebo - AIN457 150mg s.c.

Subject analysis set type	Full analysis
Subject analysis set description: Placebo plus AIN457 150mg s.c.	
Subject analysis set title	Placebo - AIN5457 150mg
Subject analysis set type	Full analysis
Subject analysis set description: placebo plus AIN457	

Reporting group values	Placebo - AIN457 150 mg	Placebo - AIN457 150mg	Placebo - AIN457 150mg s.c.
Number of subjects	146	146	146
Age Categorical			
The mean age of participants was 34.4 years			
Units:			
<=18 years Between 18 and 65 years >=65 years	0	0	0
Sex: Female, Male			
FAS			
Units:			
Female Male			
Race/Ethnicity, Customized			
FAS			
Units: Subjects			
Asian White Other			

Reporting group values	Placebo - AIN457 150mg	Placebo - AIN457 150mg s.c.	Placebo - AIN5457 150mg
Number of subjects	149	149	146
Age Categorical			
The mean age of participants was 34.4 years			
Units:			
<=18 years Between 18 and 65 years >=65 years	0	0	0
Sex: Female, Male			
FAS			
Units:			
Female Male			
Race/Ethnicity, Customized			
FAS			
Units: Subjects			
Asian White Other			

End points

End points reporting groups

Reporting group title	Secukinumab
Reporting group description: Secukinumab 150 mg s.c.	
Reporting group title	Placebo
Reporting group description: Placebo s.c.	
Subject analysis set title	Placebo - AIN457 150 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo - AIN457 150mg	
Subject analysis set title	Placebo - AIN457 150mg
Subject analysis set type	Full analysis
Subject analysis set description: placebo plus AIN457 150mg	
Subject analysis set title	Placebo - AIN457 150mg s.c.
Subject analysis set type	Full analysis
Subject analysis set description: Placebo - AIN457 150mg s.c.	
Subject analysis set title	Placebo - AIN457 150mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo - AIN457 150mg	
Subject analysis set title	Placebo - AIN457 150mg s.c.
Subject analysis set type	Full analysis
Subject analysis set description: Placebo plus AIN457 150mg s.c.	
Subject analysis set title	Placebo - AIN5457 150mg
Subject analysis set type	Full analysis
Subject analysis set description: placebo plus AIN457	

Primary: The proportion of participants who achieve an ASAS 20 response (Assessment of SpondyloArthritis International Society criteria)

End point title	The proportion of participants who achieve an ASAS 20 response (Assessment of SpondyloArthritis International Society criteria)
End point description: ASAS20 response is defined as an improvement of ≥20% and ≥1 units on a scale of 10 in at least three of the four ASAS main domains and no worsening of ≥20% and ≥1 unit on a scale of 10 in the remaining domain	
End point type	Primary
End point timeframe: Week 16	

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	305	153		
Units: participants	178	56		

Statistical analyses

Statistical analysis title	Proportion of participants with ASAS20 response
Comparison groups	Placebo v Secukinumab
Number of subjects included in analysis	458
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.65
upper limit	3.69

Secondary: The proportion of participants who achieve an ASAS40 response

End point title	The proportion of participants who achieve an ASAS40 response

End point description:

ASAS40 response is defined as an improvement of ≥40% and ≥2 units on a scale of 10 in at least three of the four ASAS main domains and no worsening at all in the remaining domain

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab	Placebo	Placebo - AIN457 150 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	294	146	146	
Units: participants	138	27	27	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in hsCRP over time

End point title	Change in hsCRP over time

End point description:

hsCRP is measured as a marker of inflammation from blood samples during the study

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab	Placebo	Placebo - AIN457 150mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	295	146	146	
Units: scores				
arithmetic mean (standard deviation)	-11.78 (± 22.919)	-0.79 (± 20.023)	-0.79 (± 20.023)	

Statistical analyses

No statistical analyses for this end point

Secondary: The proportion of participants who achieve an ASAS 5/6

End point title	The proportion of participants who achieve an ASAS 5/6

End point description:

The ASAS 5/6 improvement criteria is an improvement of ≥20% in at least five of all six domains

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab	Placebo	Placebo - AIN457 150mg s.c.	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	295	146	146	
Units: percent of participants				
number (confidence interval 95%)	50.5 (44.7 to 56.3)	19.2 (13.3 to 26.7)	19.2 (13.3 to 26.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with BASDAI response at 16 weeks

End point title	Participants with BASDAI response at 16 weeks

End point description:

The BASDAI or Bath Ankylosing Spondylitis Disease Activity Index consists of a 0 through 10 scale (0 being no problem and 10 being the worst problem, captured as a continuous VAS), which is used to answer 6 questions pertaining to the 5 major symptoms of AS

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab	Placebo	Placebo - AIN457 150mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	295	149	149	
Units: percent of participants				
number (confidence interval 95%)	41.7 (36.0 to 47.6)	22.6 (16.3 to 30.4)	22.6 (16.3 to 30.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Short Form (36) - PCS Responders (Improvement of >= 2.5 Points)

End point title	Change in Short Form (36) - PCS Responders (Improvement of >= 2.5 Points)

End point description:

The Physical Component Summary (PCS) SF-36 is an instrument to measure health-related quality of life among healthy patients and patients with acute and chronic conditions

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab	Placebo	Placebo - AIN457 150mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	301	149	149	
Units: percent of participants				
number (confidence interval 95%)	71.8 (66.3 to 76.7)	61.1 (52.7 to 68.8)	61.1 (52.7 to 68.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Short Form (36) - MCS Responders (Improvement of >= 2.5 Points)

End point title	Change in Short Form (36) - MCS Responders (Improvement of >= 2.5 Points)

End point description:

The Mental Component Summary (MCS) SF-36 is an instrument to measure health-related quality of life among healthy patients and patients with acute and chronic conditions

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab	Placebo	Placebo - AIN457 150mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	301	149	149	
Units: percent of participants				
number (confidence interval 95%)	60.5 (54.7 to 66.0)	55.0 (46.7 to 63.1)	55.0 (46.7 to 63.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in ASQoL score over time

End point title	Change in ASQoL score over time

End point description:

The Ankylosing Spondylitis Quality of Life (ASQoL) is an instrument to assess health-related quality of life among adult patients with Ankylosing Spondylitis

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab	Placebo	Placebo - AIN457 150mg s.c.	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	305	153	149	
Units: scores				
arithmetic mean (standard deviation)	-4.6 (± 4.98)	-2.6 (± 4.28)	-2.6 (± 4.28)	

Statistical analyses

No statistical analyses for this end point

Secondary: The proportion of patients who achieve an ASAS partial remission

End point title	The proportion of patients who achieve an ASAS partial remission

End point description:

The The Assessment in SpondyloArthritis International Society (ASAS) partial remission criteria are defined as a value not above 2 units in each of the four main domains on a scale of 10

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab	Placebo	Placebo - AIN5457 150mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	294	146	146	
Units: percent of participants				
number (confidence interval 95%)	17.7 (13.6 to 22.6)	7.5 (4.0 to 13.4)	7.5 (4.0 to 13.4)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for AE	
Adverse event reporting additional description:	
AE additional description	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

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

Serious adverse events	Placebo	Any AIN457 150 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 153 (1.96%)	33 / 453 (7.28%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Cyst			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Mediastinal cyst			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 453 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Electric injury			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve injury			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin injury			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vascular injury			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Bronchogenic cyst			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Lacunar infarction			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuritis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness neurosensory			

subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden hearing loss			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Iridocyclitis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uveitis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Appendix disorder			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal fistula			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Hydronephrosis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 153 (0.00%)	2 / 453 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	1 / 153 (0.65%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint swelling			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb mass			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 153 (0.00%)	3 / 453 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Appendicitis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 153 (0.00%)	2 / 453 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 453 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 153 (0.00%)	1 / 453 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo	Any AIN457 150 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 153 (39.22%)	282 / 453 (62.25%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 153 (1.96%)	24 / 453 (5.30%)	
occurrences (all)	4	33	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 153 (1.31%)	10 / 453 (2.21%)	
occurrences (all)	2	11	
Protein urine present			
subjects affected / exposed	0 / 153 (0.00%)	11 / 453 (2.43%)	
occurrences (all)	0	13	
White blood cell count decreased			
subjects affected / exposed	0 / 153 (0.00%)	17 / 453 (3.75%)	
occurrences (all)	0	33	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 153 (1.96%)	11 / 453 (2.43%)	
occurrences (all)	3	11	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 153 (2.61%)	5 / 453 (1.10%)	
occurrences (all)	4	6	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 153 (0.00%)	12 / 453 (2.65%)	
occurrences (all)	0	12	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 153 (0.65%)	15 / 453 (3.31%)	
occurrences (all)	1	19	
Diarrhoea			
subjects affected / exposed	6 / 153 (3.92%)	35 / 453 (7.73%)	
occurrences (all)	8	49	
Mouth ulceration			

subjects affected / exposed	2 / 153 (1.31%)	18 / 453 (3.97%)	
occurrences (all)	3	22	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	3 / 153 (1.96%)	24 / 453 (5.30%)	
occurrences (all)	3	25	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 153 (1.96%)	10 / 453 (2.21%)	
occurrences (all)	3	11	
Oropharyngeal pain			
subjects affected / exposed	2 / 153 (1.31%)	18 / 453 (3.97%)	
occurrences (all)	2	21	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 153 (0.00%)	10 / 453 (2.21%)	
occurrences (all)	0	11	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 153 (3.27%)	13 / 453 (2.87%)	
occurrences (all)	6	16	
Back pain			
subjects affected / exposed	4 / 153 (2.61%)	7 / 453 (1.55%)	
occurrences (all)	5	8	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 153 (6.54%)	46 / 453 (10.15%)	
occurrences (all)	10	57	
Pharyngitis			
subjects affected / exposed	1 / 153 (0.65%)	14 / 453 (3.09%)	
occurrences (all)	1	15	
Upper respiratory tract infection			
subjects affected / exposed	29 / 153 (18.95%)	145 / 453 (32.01%)	
occurrences (all)	38	215	
Urinary tract infection			

subjects affected / exposed	5 / 153 (3.27%)	16 / 453 (3.53%)	
occurrences (all)	6	20	
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	1 / 153 (0.65%)	12 / 453 (2.65%)	
occurrences (all)	1	13	
Hyperlipidaemia			
subjects affected / exposed	1 / 153 (0.65%)	26 / 453 (5.74%)	
occurrences (all)	1	27	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 March 2018	Amendment 1 Due to changes in the regulatory environment in China, a primary endpoint analysis can be implemented and used for submission purpose. This will allow a much earlier (approximately 9 months) submission than originally planned. To enable this, an additional analysis will be performed after all patients have completed the Week 16 for the primary endpoint assessments. Although unblinding will occur after the Week 16 database lock, the original randomization to active treatment vs placebo will continue to remain blinded to all investigators, site personnel and patients until all patients have completed the study (Week 60 Follow up) and the final database lock has occurred.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported