Clinical trial results:
A 52-week, multicenter, randomized, double-blind study of secukinumab (300 mg) to demonstrate efficacy as assessed by Psoriasis Area and Severity Index and Investigator's Global Assessment after 12 weeks of treatment, compared to ustekinumab, and to assess long-term safety, tolerability, and efficacy in patients with moderate to severe plaque psoriasis (CLARITY).

Summary

EudraCT number	2015-002898-37
Trial protocol	HU SK IS PL CZ
Global end of trial date	09 July 2018

Results information

Result version number	v1
This version publication date	06 July 2019
First version publication date	06 July 2019

Trial information

Trial identification

Sponsor protocol code	CAIN457A2326

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02826603
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, 41 613 241 1111, novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharmaceuticals, 41 613 241 1111, 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	11 December 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The co-primary objectives were to demonstrate the superiority of secukinumab compared to ustekinumab in patients with moderate to severe plaque psoriasis with respect to both PASI 90 and IGA mod 2011 0 or 1 response at Week 12.

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	22 June 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	Canada: 27
Country: Number of subjects enrolled	Czech Republic: 12
Country: Number of subjects enrolled	Guatemala: 65
Country: Number of subjects enrolled	Hungary: 21
Country: Number of subjects enrolled	Iceland: 33
Country: Number of subjects enrolled	Korea, Republic of: 38
Country: Number of subjects enrolled	Malaysia: 30
Country: Number of subjects enrolled	Poland: 139
Country: Number of subjects enrolled	Slovakia: 10
Country: Number of subjects enrolled	United States: 707
Country: Number of subjects enrolled	Vietnam: 20
Worldwide total number of subjects	1102
EEA total number of subjects	215

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)	1
Adults (18-64 years)	981
From 65 to 84 years	120
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall, 1353 patients were screened of which 1102 patients completed the Screening phase; 251 patients were screen failures

Pre-assignment

Screening details:

The randomized set was defined as all patients who were randomized at the baseline visit. Unless otherwise specified, mis-randomized patients were excluded from the randomized set.

Mis-randomized patients were those who were screen failures, but had been randomized by the Investigator before eligibility was assessed, but had not been treated

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, Assessor

Blinding implementation details:

Designated Novartis personnel were unblinded following database lock for the interim analysis after all patients completed Week 16 visit. Field monitors/clinical research associates remained blinded until after final database lock. All blinded site personnel, including the assessor remained blinded to individual treatment allocation until after final database lock

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab 300mg (2 x 150 mg)

Arm description:

Secukinumab 300mg s.c. injection (2 150mg pre-fiilled syringes)

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	
Other name	AIN457
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Secukinumab 300mg s.c. injection (2 150mg pre-fiilled syringes)

Investigational medicinal product name	Ustekinumab
Investigational medicinal product code	
Other name	UST
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ustekinumab s.c. 45 mg or 90 mg (depending on body weight) using 45mg pre-filled syringes (1 or 2 syringes)

Arm title	Ustekinumab 45mg or 90mg

Arm description:

Ustekinumab s.c. 45 mg or 90 mg (depending on body weight) using 45mg pre-filled syringes (1 or 2 syringes)

Arm type	Active comparator

Investigational medicinal product name	ustekinumab
Investigational medicinal product code	
Other name	UST
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

45 mg or 90 mg pre-filled syringe(s)

Number of subjects in period 1	Secukinumab 300mg (2 x 150 mg)	Ustekinumab 45mg or 90mg
Started	550	552
Completed	489	488
Not completed	61	64
Adverse event, serious fatal	2	-
Physician decision	1	7
Consent withdrawn by subject	20	19
Adverse event, non-fatal	17	9
Pregnancy	1	2
Lost to follow-up	13	12
Noncompliance with treatment	-	2
New therapy for study indication	-	1
Lack of efficacy	4	9
Protocol deviation	3	3

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab 300mg (2 x 150 mg)
Reporting group description:	
Secukinumab 300mg s.c. injection (2 150mg pre-fiilled syringes)	
Reporting group title	Ustekinumab 45mg or 90mg
Reporting group description:	
Ustekinumab s.c. 45 mg or 90 mg (depending on body weight) using 45mg pre-filled syringes (1 or 2 syringes)	

Reporting group values	Secukinumab 300mg (2 x 150 mg)	Ustekinumab 45mg or 90mg	Total
Number of subjects	550	552	1102
Age, Customized Units: Subjects			
<65 years	488	494	982
>=65 years	60	48	108
>=75 years	2	10	12
Age Continuous			
average age of participants			
Units: years			
arithmetic mean	45.4	45.3	
standard deviation	± 14.09	± 14.16	-
Sex: Female, Male Units: Subjects			
Female	194	176	370
Male	356	376	732
Race/Ethnicity, Customized Units: Subjects			
Caucasian	416	410	826
Black	21	24	45
Asian	60	57	117
Native American	34	41	75
Pacific Islander	1	5	6
Unknown	4	2	6
Other	14	13	27

End points

End points reporting groups

Reporting group title	Secukinumab 300mg (2 x 150 mg)
Reporting group description:	
Secukinumab 300mg s.c. injection (2 150mg pre-fiilled syringes)	
Reporting group title	Ustekinumab 45mg or 90mg
Reporting group description:	
Ustekinumab s.c. 45 mg or 90 mg (depending on body weight) using 45mg pre-filled syringes (1 or 2 syringes)	

Primary: Participants who achieved Psoriasis Area and Severity Index (PASI) 90 response at Week 12

End point title	Participants who achieved Psoriasis Area and Severity Index (PASI) 90 response at Week 12
End point description:	
Number of participants who achieved ≥ 90% reduction in PASI compared to baseline. Logistic regression analysis of PASI 90 response at Week 12 PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, upper limbs, trunk, lower limbs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of body region (head: 0.1, upper limbs: 0.2, trunk: 0.3, lower limbs: 0.4).	
End point type	Primary
End point timeframe:	
Week 12	

End point values	Secukinumab 300mg (2 x 150 mg)	Ustekinumab 45mg or 90mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	552		
Units: participants	366	265		

Statistical analyses

Statistical analysis title	Statistical Analysis of Primary Outcome
Comparison groups	Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg
Number of subjects included in analysis	1102
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.21

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.72
upper limit	2.84

Primary: Participants with IGA mod 2011 0 or 1 at Week 12

End point title	Participants with IGA mod 2011 0 or 1 at Week 12
End point description:	
Investigator's Global Assessment uses a scale (IGA mod 2011) that rates disease from a score of 0 (clear skin) to 4 (severe disease)	
End point type	Primary
End point timeframe:	
Week 12	

End point values	Secukinumab 300mg (2 x 150 mg)	Ustekinumab 45mg or 90mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	552		
Units: participants	397	306		

Statistical analyses

Statistical analysis title	Statistical Analysis of Outcome Measure
Comparison groups	Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg
Number of subjects included in analysis	1102
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.63
upper limit	2.72

Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 75 response at Week 12

End point title	Participants who achieved Psoriasis Area and Severity Index

	(PASI) 75 response at Week 12
End point description:	
Number of participants who achieved ≥ 75% reduction in PASI at Week 12 compared to baseline.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Secukinumab 300mg (2 x 150 mg)	Ustekinumab 45mg or 90mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	552		
Units: participants	484	409		

Statistical analyses

Statistical analysis title	Statistical Analysis of Secondary Outcome
Comparison groups	Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg
Number of subjects included in analysis	1102
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.89
upper limit	3.62

Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 75 response at Week 4

End point title	Participants who achieved Psoriasis Area and Severity Index (PASI) 75 response at Week 4
End point description:	
Number of participants who achieved ≥ 75% reduction in PASI at Week 4 compared to baseline.	
End point type	Secondary
End point timeframe:	
Week 4	

End point values	Secukinumab 300mg (2 x 150 mg)	Ustekinumab 45mg or 90mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	552		
Units: participants	221	90		

Statistical analyses

Statistical analysis title	Statistical Analysis of Secondary Outcome
Comparison groups	Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg
Number of subjects included in analysis	1102
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.65
upper limit	4.71

Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 100 response at Week 16

End point title	Participants who achieved Psoriasis Area and Severity Index (PASI) 100 response at Week 16
End point description:	
Number of participants who achieved 100% reduction in PASI at Week 16 compared to baseline.	
End point type	Secondary
End point timeframe:	
Week 16	

End point values	Secukinumab 300mg (2 x 150 mg)	Ustekinumab 45mg or 90mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	552		
Units: participants	250	147		

Statistical analyses

Statistical analysis title	Statistical Analysis of Secondary Outcome
Comparison groups	Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg
Number of subjects included in analysis	1102
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	3.01

Secondary: Participants with IGA mod 2011 0 or 1 at 16 weeks

End point title	Participants with IGA mod 2011 0 or 1 at 16 weeks
End point description:	
Investigator's Global Assessment uses a scale (IGA mod 2011) that rates disease from a score of 0 (clear skin) to 4 (severe disease)	
End point type	Secondary
End point timeframe:	
Week 16	

End point values	Secukinumab 300mg (2 x 150 mg)	Ustekinumab 45mg or 90mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	552		
Units: participants	432	326		

Statistical analyses

Statistical analysis title	Statistical Analysis of Secondary Outcome
Comparison groups	Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg
Number of subjects included in analysis	1102
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.57

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.96
upper limit	3.37

Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 100 response at Week 12

End point title	Participants who achieved Psoriasis Area and Severity Index (PASI) 100 response at Week 12
End point description:	
Number of participants who achieved 100% reduction in PASI at Week 12 compared to baseline.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Secukinumab 300mg (2 x 150 mg)	Ustekinumab 45mg or 90mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	552		
Units: participants	210	111		

Statistical analyses

Statistical analysis title	Statistical Analysis of Secondary Outcome
Comparison groups	Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg
Number of subjects included in analysis	1102
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.89
upper limit	3.31

Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 75 response at Week 16

End point title	Participants who achieved Psoriasis Area and Severity Index (PASI) 75 response at Week 16

End point description:

Number of participants who achieved ≥ 75% reduction in PASI at Week 16 compared to baseline.

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab 300mg (2 x 150 mg)	Ustekinumab 45mg or 90mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	552		
Units: participants	506	441		

Statistical analyses

Statistical analysis title	Statistical Analysis of Secondary Outcome
Comparison groups	Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg
Number of subjects included in analysis	1102
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.96
upper limit	4.17

Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 90 response at Week 16

End point title	Participants who achieved Psoriasis Area and Severity Index (PASI) 90 response at Week 16

End point description:

Number of participants who achieved ≥ 90% reduction in PASI at Week 16 compared to baseline.

End point type	Secondary

End point timeframe:

Week 16

End point values	Secukinumab 300mg (2 x 150 mg)	Ustekinumab 45mg or 90mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	552		
Units: participants	423	299		

Statistical analyses

Statistical analysis title	Statistical Analysis of Secondary Outcome
Comparison groups	Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg
Number of subjects included in analysis	1102
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.19
upper limit	3.71

Secondary: Participants who achieved Psoriasis Area and Severity Index (PASI) 90 response at Week 52

End point title	Participants who achieved Psoriasis Area and Severity Index (PASI) 90 response at Week 52
End point description:	
Number of participants who achieved ≥ 90% reduction in PASI at Week 52 compared to baseline.	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	Secukinumab 300mg (2 x 150 mg)	Ustekinumab 45mg or 90mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	552		
Units: participants	402	330		

Statistical analyses

Statistical analysis title	Statististical Analysis of Secondary Outcome
Comparison groups	Secukinumab 300mg (2 x 150 mg) v Ustekinumab 45mg or 90mg
Number of subjects included in analysis	1102
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.41
upper limit	2.41

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AEs and SAEs were collected for maximum duration of treatment and follow up for a participant per protocol for 52 weeks. All cause mortality (deaths) was collected from First Patient First Visit (FPFV) to Last Patient Last Visit (LPLV) until 52 weeks	
Adverse event reporting additional description:	
All-cause mortality (deaths) was collected for as long as participants could be contacted from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV) up to a maximum of 52 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	AIN457 300 mg
Reporting group description:	
AIN457 300 mg	
Reporting group title	UST 45/90 mg
Reporting group description:	
UST 45/90 mg	
Reporting group title	All Patients
Reporting group description:	
All Patients	

Serious adverse events	AIN457 300 mg	UST 45/90 mg	All Patients
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 550 (5.27%)	21 / 552 (3.80%)	50 / 1102 (4.54%)
number of deaths (all causes)	2	0	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			

subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal squamous cell carcinoma			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
T-cell lymphoma			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 550 (0.36%)	1 / 552 (0.18%)	3 / 1102 (0.27%)
occurrences causally related to treatment / all	0 / 2	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Sudden cardiac death			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1

Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	2 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	3 / 550 (0.55%)	0 / 552 (0.00%)	3 / 1102 (0.27%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary thrombosis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			

subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device inappropriate shock delivery			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Comminuted fracture			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gun shot wound			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative ileus			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Toxicity to various agents			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Wrist fracture			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	3 / 550 (0.55%)	0 / 552 (0.00%)	3 / 1102 (0.27%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	2 / 550 (0.36%)	0 / 552 (0.00%)	2 / 1102 (0.18%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Loss of consciousness			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis erosive			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic skin eruption			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal infarct			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			

subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 550 (0.18%)	2 / 552 (0.36%)	3 / 1102 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	2 / 550 (0.36%)	0 / 552 (0.00%)	2 / 1102 (0.18%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			

subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin candida			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 552 (0.00%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 550 (0.00%)	1 / 552 (0.18%)	1 / 1102 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	AIN457 300 mg	UST 45/90 mg	All Patients
Total subjects affected by non-serious adverse events			
subjects affected / exposed	216 / 550 (39.27%)	229 / 552 (41.49%)	445 / 1102 (40.38%)
Vascular disorders			
Hypertension			
subjects affected / exposed	17 / 550 (3.09%)	22 / 552 (3.99%)	39 / 1102 (3.54%)
occurrences (all)	20	24	44
Nervous system disorders			
Headache			
subjects affected / exposed	26 / 550 (4.73%)	25 / 552 (4.53%)	51 / 1102 (4.63%)
occurrences (all)	31	30	61
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	26 / 550 (4.73%)	24 / 552 (4.35%)	50 / 1102 (4.54%)
occurrences (all)	40	26	66
Nausea			
subjects affected / exposed	6 / 550 (1.09%)	13 / 552 (2.36%)	19 / 1102 (1.72%)
occurrences (all)	6	15	21
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	17 / 550 (3.09%)	16 / 552 (2.90%)	33 / 1102 (2.99%)
occurrences (all)	19	19	38
Oropharyngeal pain			
subjects affected / exposed	14 / 550 (2.55%)	17 / 552 (3.08%)	31 / 1102 (2.81%)
occurrences (all)	15	17	32
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	12 / 550 (2.18%)	8 / 552 (1.45%)	20 / 1102 (1.81%)
occurrences (all)	13	8	21
Pruritus			
subjects affected / exposed	12 / 550 (2.18%)	18 / 552 (3.26%)	30 / 1102 (2.72%)
occurrences (all)	12	20	32
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	9 / 550 (1.64%)	14 / 552 (2.54%)	23 / 1102 (2.09%)
occurrences (all)	11	15	26
Back pain			
subjects affected / exposed	14 / 550 (2.55%)	20 / 552 (3.62%)	34 / 1102 (3.09%)
occurrences (all)	14	22	36
Infections and infestations			
Bronchitis			
subjects affected / exposed	8 / 550 (1.45%)	18 / 552 (3.26%)	26 / 1102 (2.36%)
occurrences (all)	8	19	27
Conjunctivitis			
subjects affected / exposed	12 / 550 (2.18%)	6 / 552 (1.09%)	18 / 1102 (1.63%)
occurrences (all)	14	6	20
Nasopharyngitis			
subjects affected / exposed	55 / 550 (10.00%)	54 / 552 (9.78%)	109 / 1102 (9.89%)
occurrences (all)	72	69	141
Sinusitis			
subjects affected / exposed	25 / 550 (4.55%)	18 / 552 (3.26%)	43 / 1102 (3.90%)
occurrences (all)	26	22	48
Upper respiratory tract infection			
subjects affected / exposed	49 / 550 (8.91%)	61 / 552 (11.05%)	110 / 1102 (9.98%)
occurrences (all)	56	69	125
Urinary tract infection			
subjects affected / exposed	13 / 550 (2.36%)	9 / 552 (1.63%)	22 / 1102 (2.00%)
occurrences (all)	14	9	23

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 April 2016	Per the new protocol, all drug administrations will be performed at the site in order to minimize potential influence of subjects' non-compliance at home administrations in this head to head study. Also, the Non-responder imputation method is updated. This change is in line with recommendations to impute subjects with all post-baseline missing values as non-responders according to the Intent-to-treat (ITT) principle.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported