Clinical trial results:
A randomized, double-blind, placebo controlled, multicenter study of subcutaneous secukinumab, to demonstrate efficacy after twelve weeks of treatment and to assess safety, tolerability and long-term efficacy up to one year in subjects with moderate to severe chronic plaque-type psoriasis with or without psoriatic arthritis comorbidity

Summary

EudraCT number	2016-000524-25
Trial protocol	HU
Global end of trial date	20 November 2018

Results information

Result version number	v1 (current)
This version publication date	02 December 2019
First version publication date	02 December 2019

Trial information

Trial identification

Sponsor protocol code	CAIN457A2318

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03066609
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	CH4002, 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	20 November 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

the main objective for this trial was to demonstrate the superiority of secukinumab in subjects with moderate to severe chronic plaque-type psoriasis in terms of both PASI 75 and IGA mod 2011 0 or 1 response (co-primary endpoints) at Week 12 compared to placebo.

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	28 February 2017
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	China: 441
Country: Number of subjects enrolled	Hungary: 23
Country: Number of subjects enrolled	Malaysia: 12
Country: Number of subjects enrolled	Philippines: 18
Country: Number of subjects enrolled	Thailand: 35
Country: Number of subjects enrolled	Turkey: 14
Worldwide total number of subjects	543
EEA total number of subjects	23

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)	531
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 664 patients were screened and 543 patients were randomized to one of three treatment groups in the induction period: secukinumab 300 mg (n=272), secukinumab 150 mg (n=136), and placebo (n=135)

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	543
Number of subjects completed	543

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab 150mg

Arm description:

Secukinumab 150mg s.c.

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 for subcutaneous injection was supplied in a 150 mg 1 mL pre-filled syringe.

Arm title	Secukinumab 300mg

Arm description:

Secukinumab 300mg s.c.

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 for subcutaneous injection was supplied in a 150 mg 1 mL pre-filled syringe. two injections of the 150 mg dose

Arm title	placebo

Arm description:

Placebo to secukinumab s.c

Arm type	Placebo

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

Dosage and administration details:

Secukinumab placebo for sc injection was supplied as a 1 mL pre-filled syringe matching the appearance of 150 mg secukinumab syringe

Number of subjects in period 1	Secukinumab 150mg	Secukinumab 300mg	placebo
Started	136	272	135
Completed	134	270	133
Not completed	2	2	2
Adverse event, non-fatal	2	2	-
Pregnancy	-	-	1
Lack of efficacy	-	-	1

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab 150mg

Arm description:

Secukinumab 150mg s.c.

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 for subcutaneous injection was supplied in a 150 mg 1 mL pre-filled syringe.

Arm title	Secukinumab 300mg

Arm description:

Secukinumab 300mg s.c.

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 for subcutaneous injection was supplied in a 150 mg 1 mL pre-filled syringe. two injections of the 150 mg dose

Arm title	placebo - placebo

Arm description:

Placebo patients who remained on Placebo after week 12

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

Dosage and administration details:

Secukinumab placebo for sc injection was supplied as a 1 mL pre-filled syringe matching the appearance of 150 mg secukinumab syringe

Arm title	Placebo - secukinumab 300mg

Arm description:

patients switched to Secukinumab (AIN457) at week 12

Arm type	placebo switched to 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 for subcutaneous injection was supplied in a 150 mg 1 mL pre-filled syringe. 2 injections of 150 mg. Switch after placebo for 12 weeks.

Number of subjects in period 2	Secukinumab 150mg	Secukinumab 300mg	placebo - placebo
Started	134	270	4
Completed	127	266	2
Not completed	7	4	2
Adverse event, non-fatal	-	-	-
Pregnancy	1	-	-
Subject or guardian decision	4	2	1
Lost to follow-up	-	1	1
Lack of efficacy	2	1	-

Number of subjects in period 2	Placebo - secukinumab 300mg
Started	129

Completed	126
Not completed	3
Adverse event, non-fatal	1
Pregnancy	-
Subject or guardian decision	1
Lost to follow-up	-
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab 150mg
Reporting group description: Secukinumab 150mg s.c.	
Reporting group title	Secukinumab 300mg
Reporting group description: Secukinumab 300mg s.c.	
Reporting group title	placebo
Reporting group description: Placebo to secukinumab s.c	

Reporting group values	Secukinumab 150mg	Secukinumab 300mg	placebo
Number of subjects	136	272	135
Age categorical			
Based on Induction Period			
Units: Subjects			
Adults (< 65)	133	265	133
From 65-84 years	3	7	2
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	41	39.9	40.1
standard deviation	± 11.39	± 12.35	± 11.01
Sex: Female, Male			
Based on Induction Period			
Units: Subjects			
Female	37	67	27
Male	99	205	108
Race/Ethnicity, Customized			
Ethnicity Based on Induction Period			
Units: Subjects			
East Asian	109	220	109
Southeast Asian	19	32	16
South Asian	1	0	0
West Asian	0	3	0
other	6	17	10
not reported	1	0	0
Race/Ethnicity, Customized			
Race			
Units: Subjects			
Caucasian	7	20	10
Asian	129	252	125

Reporting group values	Total		
Number of subjects	543		

Age categorical			
Based on Induction Period			
Units: Subjects			
Adults (< 65)	531		
From 65-84 years	12		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Based on Induction Period			
Units: Subjects			
Female	131		
Male	412		
Race/Ethnicity, Customized			
Ethnicity Based on Induction Period			
Units: Subjects			
East Asian	438		
Southeast Asian	67		
South Asian	1		
West Asian	3		
other	33		
not reported	1		
Race/Ethnicity, Customized			
Race			
Units: Subjects			
Caucasian	37		
Asian	506		

End points

End points reporting groups	
Reporting group title	Secukinumab 150mg
Reporting group description: Secukinumab 150mg s.c.	
Reporting group title	Secukinumab 300mg
Reporting group description: Secukinumab 300mg s.c.	
Reporting group title	placebo
Reporting group description: Placebo to secukinumab s.c	
Reporting group title	Secukinumab 150mg
Reporting group description: Secukinumab 150mg s.c.	
Reporting group title	Secukinumab 300mg
Reporting group description: Secukinumab 300mg s.c.	
Reporting group title	placebo - placebo
Reporting group description: Placebo patients who remained on Placebo after week 12	
Reporting group title	Placebo - secukinumab 300mg
Reporting group description: patients switched to Secukinumab (AIN457) at week 12	

Primary: Psoriasis Area and Severity Index (PASI) 75 (multiple imputation)	
End point title	Psoriasis Area and Severity Index (PASI) 75 (multiple imputation)
End point description: Psoriasis Area and Severity Index (PASI) was assessed/calculated as per usual standard. result given in terms of count of participants with response in 100 imputations. 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, arms, trunk, legs; 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 section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4).	
End point type	Primary
End point timeframe: Week 12	

End point values	Secukinumab 150mg	Secukinumab 300mg	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	136	272	135	
Units: participants	112	254	6	

Statistical analyses

Statistical analysis title	PASI 75 Secukinumab 150 mg / Placebo
Statistical analysis description: PASI 75	
Comparison groups	Secukinumab 150mg v placebo
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	153.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	54.02
upper limit	438.67

Statistical analysis title	PASI 75 Secukinumab 300 mg / Placebo
Statistical analysis description: PASI 75	
Comparison groups	Secukinumab 300mg v placebo
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	557.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	187.2
upper limit	1663.4

Primary: Investigator`s Global Assessment (IGA) mod 2011 0/1 (multiple imputation)

End point title	Investigator`s Global Assessment (IGA) mod 2011 0/1 (multiple imputation)

End point description:

Investigator assessed disease using a validated scale (IGA mod 2011) and rate the disease from a score of 0 (clear skin) to 4 (severe disease). result given in terms of count of participants with response in 100 imputations. The Investigator’s Global Assessment (IGA) mod 2011 scale is static, i.e. it referred exclusively to the participant's disease at the time of the assessment, and did not compare with any of the participant's previous disease states at previous visits. The scores are: 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, and 4 = severe. Treatment success was defined as achievement of IGA mod 2001 score of 0 or 1.

End point type	Primary

End point timeframe:

Week 12

End point values	Secukinumab 150mg	Secukinumab 300mg	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	136	272	135	
Units: participants	92	214	4	

Statistical analyses

Statistical analysis title	IGA 150 mg / Placebo
Statistical analysis description:	
IGA	
Comparison groups	Secukinumab 150mg v placebo
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	75.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.81
upper limit	222.72

Statistical analysis title	IGA Secukinumab 300 mg / Placebo
Statistical analysis description:	
IGA	
Comparison groups	Secukinumab 300mg v placebo

Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	149.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	51.83
upper limit	432.42

Secondary: Psoriasis Area and Severity Index (PASI) 90 (multiple imputation)

End point title	Psoriasis Area and Severity Index (PASI) 90 (multiple imputation)

End point description:

Psoriasis Area and Severity Index (PASI) was assessed/calculated as per usual standard. result given in terms of count of participants with response in 100 imputations. 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, arms, trunk, legs; 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 section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4).

End point type	Secondary

End point timeframe:

Week 12

End point values	Secukinumab 150mg	Secukinumab 300mg	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	136	272	135	
Units: participants	85	210	2	

Statistical analyses

Statistical analysis title	PASI 90 Secukinumab 300 mg / Placebo

Statistical analysis description:

PASI 90

Comparison groups	Secukinumab 300mg v placebo

Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	246.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	58.41
upper limit	1037.1

Statistical analysis title	PASI 90 Secukinumab 150 mg / Placebo
Statistical analysis description:	
PASI 90	
Comparison groups	Secukinumab 150mg v placebo
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	114.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	26.94
upper limit	489.59

Secondary: efficacy of secukinumab in maintaining PASI 75 response at Week 52 in subjects who were PASI 75 responders at Week 12 (multiple imputation)

End point title	efficacy of secukinumab in maintaining PASI 75 response at Week 52 in subjects who were PASI 75 responders at Week 12 (multiple imputation)[1]

End point description:

Psoriasis Area and Severity Index (PASI) was assessed/calculated as per usual standard. result given in terms of count of participants with response in 100 imputations. 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, arms, trunk, legs; 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 section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4).

End point type	Secondary

End point timeframe:

Week 52

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There were only 4 patients in the placebo arm after week 12, therefore the analyses was not performed

End point values	Secukinumab 150mg	Secukinumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	242		
Units: participants	94	235		

Statistical analyses

No statistical analyses for this end point

Secondary: efficacy of secukinumab in maintaining IGA mod 2011 0 or 1 response at Week 52 in subjects who were IGA mod 2011 0 or 1 responders at Week 12 (multiple imputation)

End point title	efficacy of secukinumab in maintaining IGA mod 2011 0 or 1 response at Week 52 in subjects who were IGA mod 2011 0 or 1 responders at Week 12 (multiple imputation)[2]

End point description:

Investigator assessed disease using a validated scale (IGA mod 2011) and rate the disease from a score of 0 (clear skin) to 4 (severe disease). result given in terms of count of participants with response in 100 imputations. The Investigator’s Global Assessment (IGA) mod 2011 scale is static, i.e. it referred exclusively to the participant's disease at the time of the assessment, and did not compare with any of the participant's previous disease states at previous visits. The scores are: 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, and 4 = severe. Treatment success was defined as achievement of IGA mod 2001 score of 0 or 1.

End point type	Secondary

End point timeframe:

Week 52

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There were only 4 patients in the placebo arm after week 12, therefore the analyses was not performed

End point values	Secukinumab 150mg	Secukinumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	206		
Units: participants	65	162		

Statistical analyses

No statistical analyses for this end point

Secondary: PASI 50/75/90/100 and IGA mod 2011 0 or 1 response over time (multiple imputation)

End point title	PASI 50/75/90/100 and IGA mod 2011 0 or 1 response over

	time (multiple imputation)

End point description:

Number (%) of subjects with PASI 50, PASI 75, PASI 90, PASI 100 and IGA mod 2011 0 or 1 response

End point type	Secondary

End point timeframe:

week 1, week 12, week 24, week 52

End point values	Secukinumab 150mg	Secukinumab 300mg	placebo	Placebo - secukinumab 300mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	136	272	135	129
Units: participants				
Week 1 IGA 0/1	0	1	0	0
Week 1 PASI 50	5	25	1	0
Week 1 PASI 75	0	0	0	0
Week 1 PASI 90	0	0	0	0
Week 1 PASI 100	0	0	0	0
Week 12 IGA 0/1	92	214	4	0
Week 12 PASI 50	130	267	16	0
Week 12 PASI 75	112	254	6	0
Week 12 PASI 90	85	210	2	0
Week 12 PASI 100	28	81	1	0
Week 16 IGA 0/1	100	219	2	32
Week 16 PASI 50	134	270	4	108
Week 16 PASI 75	124	261	3	72
Week 16 PASI 90	98	233	2	22
Week 16 PASI 100	39	99	0	3
Week 24 IGA 0/1	91	217	1	88
Week 24 PASI 50	135	271	4	123
Week 24 PASI 75	123	257	2	113
Week 24 PASI 90	93	230	2	94
Week 24 PASI 100	47	107	0	31
Week 52 IGA 0/1	79	194	0	96
Week 52 PASI 50	128	269	4	126
Week 52 PASI 75	111	259	4	119
Week 52 PASI 90	86	218	1	101
Week 52 PASI 100	42	110	1	55

Statistical analyses

No statistical analyses for this end point

Secondary: American Collage of Rheumatology (ACR) Response 20/50/70

End point title	American Collage of Rheumatology (ACR) Response 20/50/70

End point description:

Percentage of patients who achieved ACR 20/50/70 at Week 12 and up to Week 52. The subset of

patients who had active PsA at baseline included 7 patients in the secukinumab 150 mg group, 17 patients in the secukinumab 300 mg group and 4 patients in the placebo group. ACR 20, 50 or 70 responses correspond, respectively, to at least 20%, 50% or 70% improvement in comparison with baseline in the number of tender and swollen joint counts, in addition to similar improvements in at least three of five other measure of disability or disease activity

End point type	Secondary

End point timeframe:

week 12, week 24, week 52

End point values	Secukinumab 150mg	Secukinumab 300mg	placebo	Placebo - secukinumab 300mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	17	4	4
Units: participants				
Week 12 ACR 20	4	13	0	0
Week 12 ACR 50	3	12	0	0
Week 12 ACR 70	2	6	0	0
Week 24 ACR 20	5	14	0	2
Week 24 ACR 50	4	10	0	1
Week 24 ACR 70	2	6	0	1
Week 52 ACR 20	4	13	0	3
Week 52 ACR 50	3	11	0	2
Week 52 ACR 70	2	8	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PASI 75 response up to Week 12

End point title	Time to PASI 75 response up to Week 12[3]

End point description:

Psoriasis Area and Severity Index (PASI) was assessed/calculated as per usual standard. result given in terms of count of participants with response in 100 imputations. 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, arms, trunk, legs; 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 section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4).

End point type	Secondary

End point timeframe:

week 12

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since only 3.7 % of the placebo patients achieved PASI 75 Response by week 12, this was not analysed

End point values	Secukinumab 150mg	Secukinumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	272		
Units: days				
median (confidence interval 95%)	57 (51 to 57)	55 (29 to 57)		

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	AIN457 300 mg
Reporting group description:	
AIN457 300 mg	
Reporting group title	AIN457 150 mg
Reporting group description:	
AIN457 150 mg	
Reporting group title	Any AIN457 dose
Reporting group description:	
Any AIN457 dose	
Reporting group title	Placebo
Reporting group description:	
Placebo	
Reporting group title	Any AIN457 300 mg
Reporting group description:	
Any AIN457 300 mg	

Serious adverse events	AIN457 300 mg	AIN457 150 mg	Any AIN457 dose
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 272 (3.31%)	5 / 136 (3.68%)	19 / 537 (3.54%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon adenoma			
subjects affected / exposed	0 / 272 (0.00%)	1 / 136 (0.74%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Comminuted fracture			

subjects affected / exposed	1 / 272 (0.37%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed	1 / 272 (0.37%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	1 / 272 (0.37%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 272 (0.00%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic vascular disorder			
subjects affected / exposed	0 / 272 (0.00%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 272 (0.00%)	1 / 136 (0.74%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 272 (0.00%)	1 / 136 (0.74%)	2 / 537 (0.37%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 272 (0.37%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Cerebral infarction			
subjects affected / exposed	1 / 272 (0.37%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic neuropathy			
subjects affected / exposed	0 / 272 (0.00%)	0 / 136 (0.00%)	1 / 537 (0.19%)
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			
Diabetic retinopathy			
subjects affected / exposed	0 / 272 (0.00%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	0 / 272 (0.00%)	1 / 136 (0.74%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	1 / 272 (0.37%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 272 (0.00%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth ulceration			
subjects affected / exposed	0 / 272 (0.00%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth impacted			
subjects affected / exposed	0 / 272 (0.00%)	1 / 136 (0.74%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 272 (0.00%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 272 (0.00%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic mass			
subjects affected / exposed	0 / 272 (0.00%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic steatosis			
subjects affected / exposed	0 / 272 (0.00%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythrodermic psoriasis			
subjects affected / exposed	0 / 272 (0.00%)	1 / 136 (0.74%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriasis			
subjects affected / exposed	0 / 272 (0.00%)	0 / 136 (0.00%)	0 / 537 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Glomerulonephritis chronic			
subjects affected / exposed	1 / 272 (0.37%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			

subjects affected / exposed	1 / 272 (0.37%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	1 / 272 (0.37%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 272 (0.00%)	0 / 136 (0.00%)	0 / 537 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	2 / 272 (0.74%)	0 / 136 (0.00%)	2 / 537 (0.37%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 272 (0.37%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 272 (0.37%)	0 / 136 (0.00%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 272 (0.37%)	0 / 136 (0.00%)	1 / 537 (0.19%)
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	0 / 272 (0.00%)	1 / 136 (0.74%)	1 / 537 (0.19%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo	Any AIN457 300 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 135 (1.48%)	14 / 401 (3.49%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon adenoma			
subjects affected / exposed	0 / 135 (0.00%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Comminuted fracture			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic vascular disorder			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina unstable			

subjects affected / exposed	0 / 135 (0.00%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	0 / 135 (0.00%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
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 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth ulceration			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth impacted			
subjects affected / exposed	0 / 135 (0.00%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic mass			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic steatosis			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythrodermic psoriasis			
subjects affected / exposed	0 / 135 (0.00%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Psoriasis			
subjects affected / exposed	1 / 135 (0.74%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Glomerulonephritis chronic			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
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 / 135 (0.00%)	1 / 401 (0.25%)	
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 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 135 (0.74%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 135 (0.00%)	2 / 401 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			

subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 135 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 135 (0.00%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	AIN457 300 mg	AIN457 150 mg	Any AIN457 dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	221 / 272 (81.25%)	115 / 136 (84.56%)	427 / 537 (79.52%)
Investigations			
Blood uric acid increased			
subjects affected / exposed	4 / 272 (1.47%)	4 / 136 (2.94%)	10 / 537 (1.86%)
occurrences (all)	7	4	14
C-reactive protein increased			
subjects affected / exposed	11 / 272 (4.04%)	7 / 136 (5.15%)	20 / 537 (3.72%)
occurrences (all)	14	9	25
Gamma-glutamyltransferase increased			
subjects affected / exposed	10 / 272 (3.68%)	2 / 136 (1.47%)	14 / 537 (2.61%)
occurrences (all)	14	2	18
Vascular disorders			
Hypertension			
subjects affected / exposed	19 / 272 (6.99%)	5 / 136 (3.68%)	27 / 537 (5.03%)
occurrences (all)	20	5	29
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 272 (3.68%)	4 / 136 (2.94%)	14 / 537 (2.61%)
occurrences (all)	18	5	23

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	14 / 272 (5.15%)	4 / 136 (2.94%)	22 / 537 (4.10%)
occurrences (all)	15	4	24
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	31 / 272 (11.40%)	13 / 136 (9.56%)	55 / 537 (10.24%)
occurrences (all)	40	23	81
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	18 / 272 (6.62%)	9 / 136 (6.62%)	31 / 537 (5.77%)
occurrences (all)	21	12	38
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	17 / 272 (6.25%)	13 / 136 (9.56%)	38 / 537 (7.08%)
occurrences (all)	18	15	41
Oropharyngeal pain			
subjects affected / exposed	25 / 272 (9.19%)	16 / 136 (11.76%)	48 / 537 (8.94%)
occurrences (all)	33	20	68
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	20 / 272 (7.35%)	10 / 136 (7.35%)	35 / 537 (6.52%)
occurrences (all)	30	11	46
Pruritus			
subjects affected / exposed	32 / 272 (11.76%)	12 / 136 (8.82%)	48 / 537 (8.94%)
occurrences (all)	36	15	56
Psoriasis			
subjects affected / exposed	3 / 272 (1.10%)	6 / 136 (4.41%)	9 / 537 (1.68%)
occurrences (all)	3	7	10
Urticaria			
subjects affected / exposed	24 / 272 (8.82%)	12 / 136 (8.82%)	42 / 537 (7.82%)
occurrences (all)	28	16	51
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 272 (4.04%)	4 / 136 (2.94%)	16 / 537 (2.98%)
occurrences (all)	13	5	19

Infections and infestations			
Folliculitis			
subjects affected / exposed	18 / 272 (6.62%)	6 / 136 (4.41%)	32 / 537 (5.96%)
occurrences (all)	23	6	38
Influenza			
subjects affected / exposed	28 / 272 (10.29%)	17 / 136 (12.50%)	55 / 537 (10.24%)
occurrences (all)	47	31	101
Nasopharyngitis			
subjects affected / exposed	44 / 272 (16.18%)	15 / 136 (11.03%)	72 / 537 (13.41%)
occurrences (all)	59	18	92
Pharyngitis			
subjects affected / exposed	24 / 272 (8.82%)	14 / 136 (10.29%)	49 / 537 (9.12%)
occurrences (all)	34	22	69
Rhinitis			
subjects affected / exposed	14 / 272 (5.15%)	2 / 136 (1.47%)	18 / 537 (3.35%)
occurrences (all)	14	4	20
Tinea pedis			
subjects affected / exposed	20 / 272 (7.35%)	5 / 136 (3.68%)	30 / 537 (5.59%)
occurrences (all)	23	6	34
Tonsillitis			
subjects affected / exposed	14 / 272 (5.15%)	5 / 136 (3.68%)	21 / 537 (3.91%)
occurrences (all)	16	5	23
Upper respiratory tract infection			
subjects affected / exposed	67 / 272 (24.63%)	41 / 136 (30.15%)	138 / 537 (25.70%)
occurrences (all)	98	67	208
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	2 / 272 (0.74%)	0 / 136 (0.00%)	2 / 537 (0.37%)
occurrences (all)	2	0	2
Hyperlipidaemia			
subjects affected / exposed	22 / 272 (8.09%)	11 / 136 (8.09%)	34 / 537 (6.33%)
occurrences (all)	22	11	34
Hyperuricaemia			
subjects affected / exposed	56 / 272 (20.59%)	25 / 136 (18.38%)	101 / 537 (18.81%)
occurrences (all)	85	35	148

Non-serious adverse events	Placebo	Any AIN457 300 mg	

Total subjects affected by non-serious adverse events subjects affected / exposed	71 / 135 (52.59%)	312 / 401 (77.81%)	
Investigations			
Blood uric acid increased			
subjects affected / exposed	5 / 135 (3.70%)	6 / 401 (1.50%)	
occurrences (all)	5	10	
C-reactive protein increased			
subjects affected / exposed	3 / 135 (2.22%)	13 / 401 (3.24%)	
occurrences (all)	3	16	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 135 (0.74%)	12 / 401 (2.99%)	
occurrences (all)	1	16	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 135 (2.96%)	22 / 401 (5.49%)	
occurrences (all)	4	24	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 135 (1.48%)	10 / 401 (2.49%)	
occurrences (all)	4	18	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 135 (0.74%)	18 / 401 (4.49%)	
occurrences (all)	1	20	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 135 (8.89%)	42 / 401 (10.47%)	
occurrences (all)	28	58	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	4 / 135 (2.96%)	22 / 401 (5.49%)	
occurrences (all)	4	26	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 135 (1.48%)	25 / 401 (6.23%)	
occurrences (all)	2	26	
Oropharyngeal pain			

subjects affected / exposed	3 / 135 (2.22%)	32 / 401 (7.98%)	
occurrences (all)	3	48	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 135 (0.00%)	25 / 401 (6.23%)	
occurrences (all)	0	35	
Pruritus			
subjects affected / exposed	11 / 135 (8.15%)	36 / 401 (8.98%)	
occurrences (all)	13	41	
Psoriasis			
subjects affected / exposed	0 / 135 (0.00%)	3 / 401 (0.75%)	
occurrences (all)	0	3	
Urticaria			
subjects affected / exposed	0 / 135 (0.00%)	30 / 401 (7.48%)	
occurrences (all)	0	35	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 135 (2.22%)	12 / 401 (2.99%)	
occurrences (all)	3	14	
Infections and infestations			
Folliculitis			
subjects affected / exposed	0 / 135 (0.00%)	26 / 401 (6.48%)	
occurrences (all)	0	32	
Influenza			
subjects affected / exposed	4 / 135 (2.96%)	38 / 401 (9.48%)	
occurrences (all)	5	70	
Nasopharyngitis			
subjects affected / exposed	5 / 135 (3.70%)	57 / 401 (14.21%)	
occurrences (all)	5	74	
Pharyngitis			
subjects affected / exposed	7 / 135 (5.19%)	35 / 401 (8.73%)	
occurrences (all)	13	47	
Rhinitis			
subjects affected / exposed	1 / 135 (0.74%)	16 / 401 (3.99%)	
occurrences (all)	1	16	
Tinea pedis			

subjects affected / exposed	1 / 135 (0.74%)	25 / 401 (6.23%)	
occurrences (all)	1	28	
Tonsillitis			
subjects affected / exposed	1 / 135 (0.74%)	16 / 401 (3.99%)	
occurrences (all)	1	18	
Upper respiratory tract infection			
subjects affected / exposed	13 / 135 (9.63%)	97 / 401 (24.19%)	
occurrences (all)	14	141	
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	5 / 135 (3.70%)	2 / 401 (0.50%)	
occurrences (all)	5	2	
Hyperlipidaemia			
subjects affected / exposed	11 / 135 (8.15%)	23 / 401 (5.74%)	
occurrences (all)	11	23	
Hyperuricaemia			
subjects affected / exposed	17 / 135 (12.59%)	76 / 401 (18.95%)	
occurrences (all)	18	113	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 June 2017	The aim of this amendment was to introduce a provision for a Week 16 analysis. This analysis included primary endpoint data at Week 12 and in addition data at Week 16 visit. This amendment also introduced the provision for additional subsequent interim analyses that may be conducted to fulfill any request from Health Authorities. In addition, this amendment was used to clarify minor inconsistencies between various protocol sections, and correct minor errors; these did not affect the study design or population.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported