Clinical trial results:
A Phase III randomized, double-blind, placebo-controlled multicenter study of subcutaneous secukinumab in prefilled syringes to demonstrate the efficacy at 24 weeks and to assess the long term efficacy, safety and tolerability up to 5 years in patients with Active Psoriatic Arthritis

Summary

EudraCT number	2012-004439-22
Trial protocol	GB BE CZ DE PL
Global end of trial date	09 January 2019

Results information

Result version number	v1 (current)
This version publication date	01 January 2020
First version publication date	01 January 2020

Trial information

Trial identification

Sponsor protocol code	CAIN457F2312

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01752634
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate that the efficacy of secukinumab 75 mg or 150 mg or 300 mg at Week 24 is superior to placebo in patients with active psoriatic arthritis (PsA) based on the proportion of patients achieving an American College of Rheumatology 20 (ACR20) response.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 April 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 39
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Canada: 26
Country: Number of subjects enrolled	Czech Republic: 43
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	United Kingdom: 44
Country: Number of subjects enrolled	Poland: 40
Country: Number of subjects enrolled	Russian Federation: 65
Country: Number of subjects enrolled	Thailand: 5
Country: Number of subjects enrolled	United States: 105
Worldwide total number of subjects	397
EEA total number of subjects	157

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	364
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study population was comprised of subjects who had passed screening assessments, complied with eligibility criteria and had provided written consent.

Pre-assignment

Screening details:

At baseline, all eligible subjects were randomized via Interactive Response Technology (IRT) to one of the 4 treatment arms.
At Week 16, Subjects on Placebo were rerandomized to receive secukinumab 150 mg s.c. or 300 mg s.c. from Week 16 (non-responder) or Week 24 (responder).

Period 1

Period 1 title	Up to Week 24 (Primary Analysis)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab (AIN457) 75 mg s.c.

Arm description:

Group 1- Secukinumab 75 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.

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

Dosage and administration details:

Secukinumab 75 mg s.c.

Arm title	Secukinumab (AIN457) 150 mg s.c.

Arm description:

Group 2 - Secukinumab 150 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.

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 s.c.

Arm title	Secukinumab (AIN457) 300 mg s.c.

Arm description:

Group 3 - Secukinumab 300 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.

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 300 mg s.c.

Arm title	Placebo

Arm description:

Placebo - rerandomized at Week 16 to receive secukinumab 150 mg s.c. or 300 mg s.c. from Week 16 (nonresponder) or Week 24 (responder).

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

Dosage and administration details:

Secukinumab 0 mg s.c.

Number of subjects in period 1	Secukinumab (AIN457) 75 mg s.c.	Secukinumab (AIN457) 150 mg s.c.	Secukinumab (AIN457) 300 mg s.c.
Started	99	100	100
Completed	93	95	97
Not completed	6	5	3
Physician decision	-	1	-
Adverse event, non-fatal	3	-	2
Subject/guardian decision	1	1	1
Lack of efficacy	2	3	-

Number of subjects in period 1	Placebo
Started	98
Completed	88
Not completed	10
Physician decision	-
Adverse event, non-fatal	4
Subject/guardian decision	3
Lack of efficacy	3

Period 2

Period 2 title	Week 24 to Week 260
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Blinding implementation details:

The study was open label label after Week 52 analysis was completed.

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab (AIN457) 75 mg s.c.

Arm description:

Group 1- Secukinumab 75 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.

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

Dosage and administration details:

Secukinumab 75 mg s.c.

Arm title	Secukinumab (AIN457) 150 mg s.c.

Arm description:

Group 2 - Secukinumab 150 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.

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 s.c.

Arm title	Secukinumab (AIN457) 300 mg s.c.

Arm description:

Group 3 - Secukinumab 300 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.

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 300 mg s.c.

Arm title	Placebo - AIN457 150 mg

Arm description:

Placebo - rerandomized to AIN457 150 mg

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 s.c.	
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details: Secukinumab 0 mg s.c.	
Arm title	Placebo - AIN457 300 mg
Arm description: Placebo - rerandomized to AIN457 300 mg	
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 300 mg s.c.	
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details: Secukinumab 0 mg s.c.	

Number of subjects in period 2	Secukinumab (AIN457) 75 mg s.c.	Secukinumab (AIN457) 150 mg s.c.	Secukinumab (AIN457) 300 mg s.c.
Started	93	95	97
Completed	59	65	64
Not completed	34	30	33
Adverse event, serious fatal	-	1	-
Physician decision	1	2	4
Noncompliance with study treatment	-	-	1
Adverse event, non-fatal	4	8	8
Pregnancy	-	-	1
Lost to follow-up	2	2	3

Subject/guardian decision	12	10	9
Lack of efficacy	15	7	7

Number of subjects in period 2	Placebo - AIN457 150 mg	Placebo - AIN457 300 mg
Started	43	45
Completed	29	31
Not completed	14	14
Adverse event, serious fatal	-	-
Physician decision	2	1
Noncompliance with study treatment	-	-
Adverse event, non-fatal	4	2
Pregnancy	-	-
Lost to follow-up	-	2
Subject/guardian decision	5	5
Lack of efficacy	3	4

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab (AIN457) 75 mg s.c.
Reporting group description:	
Group 1- Secukinumab 75 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.	
Reporting group title	Secukinumab (AIN457) 150 mg s.c.
Reporting group description:	
Group 2 - Secukinumab 150 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.	
Reporting group title	Secukinumab (AIN457) 300 mg s.c.
Reporting group description:	
Group 3 - Secukinumab 300 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.	
Reporting group title	Placebo
Reporting group description:	
Placebo - rerandomized at Week 16 to receive secukinumab 150 mg s.c. or 300 mg s.c. from Week 16 (nonresponder) or Week 24 (responder).	

Reporting group values	Secukinumab (AIN457) 75 mg s.c.	Secukinumab (AIN457) 150 mg s.c.	Secukinumab (AIN457) 300 mg s.c.
Number of subjects	99	100	100
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	93	94	90
>=65 years	6	6	10
Age continuous Units: years			
arithmetic mean	48.6	46.5	46.9
standard deviation	± 11.42	± 11.72	± 12.57
Sex: Female, Male Units: Participants			
Female	52	45	49
Male	47	55	51
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	2	0
Asian	5	6	2
Native Hawaiian or Other Pacific Islander	1	1	0
Black or African American	0	0	1
White	90	90	96
More than one race	2	1	1
Unknown or Not Reported	1	0	0

Reporting group values	Placebo	Total	
Number of subjects	98	397	

Age Categorical Units: Participants			
<=18 years	0	0	
Between 18 and 65 years	87	364	
>=65 years	11	33	
Age continuous Units: years			
arithmetic mean	49.9		
standard deviation	± 12.53	-	
Sex: Female, Male Units: Participants			
Female	59	205	
Male	39	192	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	2	
Asian	1	14	
Native Hawaiian or Other Pacific Islander	0	2	
Black or African American	0	1	
White	94	370	
More than one race	3	7	
Unknown or Not Reported	0	1	

End points

End points reporting groups

Reporting group title	Secukinumab (AIN457) 75 mg s.c.
Reporting group description:	
Group 1- Secukinumab 75 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.	
Reporting group title	Secukinumab (AIN457) 150 mg s.c.
Reporting group description:	
Group 2 - Secukinumab 150 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.	
Reporting group title	Secukinumab (AIN457) 300 mg s.c.
Reporting group description:	
Group 3 - Secukinumab 300 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.	
Reporting group title	Placebo
Reporting group description:	
Placebo - rerandomized at Week 16 to receive secukinumab 150 mg s.c. or 300 mg s.c. from Week 16 (nonresponder) or Week 24 (responder).	
Reporting group title	Secukinumab (AIN457) 75 mg s.c.
Reporting group description:	
Group 1- Secukinumab 75 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.	
Reporting group title	Secukinumab (AIN457) 150 mg s.c.
Reporting group description:	
Group 2 - Secukinumab 150 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.	
Reporting group title	Secukinumab (AIN457) 300 mg s.c.
Reporting group description:	
Group 3 - Secukinumab 300 mg at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until up to Week 260.	
Reporting group title	Placebo - AIN457 150 mg
Reporting group description:	
Placebo - rerandomized to AIN457 150 mg	
Reporting group title	Placebo - AIN457 300 mg
Reporting group description:	
Placebo - rerandomized to AIN457 300 mg	

Primary: Number of participants achieving American College of Rheumatology 20 (ACR20) response criteria

End point title	Number of participants achieving American College of Rheumatology 20 (ACR20) response criteria

End point description:

ACR20 response was defined as having a positive clinical response to treatment (individual improvement) in disease activity if the participant had at least 20% improvement in tender 68-joint count, swollen 66-joint count and at least 3 of the following 5 measures: patient's assessment of RA pain, patient's global assessment of disease activity, physician's global assessment of disease activity, subject self-assessed disability (Health Assessment Questionnaire [HAQ-DI] score), and/or acute phase reactant (high sensitivity c-reactive protein (hsCRP) or erythrocyte sedimentation rate

(ESR). The ACR20 response results at week 24 used non-responder imputation.

End point type	Primary
End point timeframe:	
Week 24	

End point values	Secukinumab (AIN457) 75 mg s.c.	Secukinumab (AIN457) 150 mg s.c.	Secukinumab (AIN457) 300 mg s.c.	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	99	100	100	98
Units: Participants	29	51	54	15

Statistical analyses

Statistical analysis title	Odds Ratio (OR)
Comparison groups	Secukinumab (AIN457) 75 mg s.c. v Placebo
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.02
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	4.73

Statistical analysis title	Odds Ratio (OR)
Comparison groups	Secukinumab (AIN457) 150 mg s.c. v Placebo
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
P-value	< 1
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.25
upper limit	13.08

Statistical analysis title	Odds Ratio (OR)
Comparison groups	Secukinumab (AIN457) 300 mg s.c. v Placebo
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.42
upper limit	13.56

Secondary: Number of participants achieving a PASI75 response in the subgroup of subjects who have ≥3% skin involvement with psoriasis

End point title	Number of participants achieving a PASI75 response in the subgroup of subjects who have ≥3% skin involvement with psoriasis

End point description:

PASI is a combined assessment of a lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). The body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for a 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). PASI 75 response was defined as participants achieving >= 75% improvement from baseline. The PASI75 response results at week 24 used non-responder imputation.

End point type	Secondary

End point timeframe:

Week 24

End point values	Secukinumab (AIN457) 75 mg s.c.	Secukinumab (AIN457) 150 mg s.c.	Secukinumab (AIN457) 300 mg s.c.	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	58	41	43
Units: Participants	14	28	26	7

Statistical analyses

Statistical analysis title	Odds Ratio (OR)
Comparison groups	Secukinumab (AIN457) 75 mg s.c. v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.165
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	5.81

Statistical analysis title	Odds Ratio (OR)
Comparison groups	Secukinumab (AIN457) 150 mg s.c. v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.12
upper limit	15.34

Statistical analysis title	Odds Ratio (OR)
Comparison groups	Secukinumab (AIN457) 300 mg s.c. v Placebo
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	9.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.33
upper limit	27

Secondary: Number of participants achieving a PASI90 response in the subgroup of subjects who have ≥3% skin involvement with psoriasis

End point title	Number of participants achieving a PASI90 response in the subgroup of subjects who have ≥3% skin involvement with psoriasis

End point description:

PASI is a combined assessment of a lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). The body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for a 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). PASI 90 response was defined as participants achieving >= 90% improvement from baseline. The PASI90 response results at week 24 used non-responder imputation.

End point type	Secondary

End point timeframe:

Week 24

End point values	Secukinumab (AIN457) 75 mg s.c.	Secukinumab (AIN457) 150 mg s.c.	Secukinumab (AIN457) 300 mg s.c.	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	58	41	43
Units: Participants	6	19	20	4

Statistical analyses

Statistical analysis title	Odds Ratio (OR)
Comparison groups	Secukinumab (AIN457) 75 mg s.c. v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6421
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	5.36

Statistical analysis title	Odds Ratio (OR)
Comparison groups	Secukinumab (AIN457) 150 mg s.c. v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0029
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.89
upper limit	21.47

Statistical analysis title	Odds Ratio (OR)
Comparison groups	Secukinumab (AIN457) 300 mg s.c. v Placebo
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	10.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.13
upper limit	36.84

Secondary: Change from baseline in DAS28-CRP

End point title	Change from baseline in DAS28-CRP

End point description:

The DAS28 is a measure of disease activity in RA. The score is calculated by a mathematical formula, which includes the tender joint count(TJC) and swollen joint count (SJC) out of a total of 28 joints, the high-sensitivity C-reactive protein (hsCRP), and the subject's 'global assessment' of disease activity/general health (GH). The subject's global assessment/GH was indicated by a visual analogue scale of 100 mm where the participant marked a point on a 100 mm line between 0 and 100 (0 indicated very good and 100 indicated very bad). The following formula was used to calculate DAS28: DAS-CRP = 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) = 0.36*ln(CRP+1) + 0.014*GH = 0.96. A DAS28-CRP score > 5.1 implies active disease, <3.2 implies controlled disease and <2.6 implies remission. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Secukinumab (AIN457) 75 mg s.c.	Secukinumab (AIN457) 150 mg s.c.	Secukinumab (AIN457) 300 mg s.c.	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	91	93	32
Units: score on a scale				
least squares mean (standard error)	-1.12 (± 0.111)	-1.58 (± 0.109)	-1.61 (± 0.110)	-0.96 (± 0.149)

Statistical analyses

Statistical analysis title	Mean Difference
Comparison groups	Secukinumab (AIN457) 75 mg s.c. v Placebo
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3763
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.2

Statistical analysis title	Mean Difference
Comparison groups	Secukinumab (AIN457) 150 mg s.c. v Placebo
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0008
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	-0.26

Statistical analysis title	Mean Difference
Comparison groups	Secukinumab (AIN457) 300 mg s.c. v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0004
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.02
upper limit	-0.29

Secondary: Change from baseline in SF36-Physical Component Score

End point title	Change from baseline in SF36-Physical Component Score

End point description:

The SF-36 is an instrument to measure health-related quality of life among healthy patients and patients with acute and chronic conditions

Score range is from 0 (no problems) to 100 (unable to perform the activity)
SF-36 is a 36 item questionnaire which measures Quality of Life across eight domains, which are both physically and emotionally based. Two overall summary scores, the Physical Component Summary (PCS) and Mental Component Summary (MCS) can be computed. In this study, SF-36 PCS is used.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Secukinumab (AIN457) 75 mg s.c.	Secukinumab (AIN457) 150 mg s.c.	Secukinumab (AIN457) 300 mg s.c.	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	91	96	96	33
Units: Score on a scale				
least squares mean (standard error)	4.38 (± 0.750)	6.39 (± 0.734)	7.25 (± 0.740)	1.95 (± 0.974)

Statistical analyses

Statistical analysis title	Mean Difference
Comparison groups	Secukinumab (AIN457) 75 mg s.c. v Placebo

Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0482
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	2.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	4.83

Statistical analysis title	Mean Difference
Comparison groups	Secukinumab (AIN457) 150 mg s.c. v Placebo
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0003
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	4.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.05
upper limit	6.83

Statistical analysis title	Mean Difference
Comparison groups	Secukinumab (AIN457) 300 mg s.c. v Placebo
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.91
upper limit	7.69

Secondary: Change From Baseline in Stanford Health Assessment Questionnaire

Disability Index (HAQ-DI)

End point title	Change From Baseline in Stanford Health Assessment Questionnaire Disability Index (HAQ-DI)

End point description:

The HAQ-DI assesses a subject's level of functional ability and includes questions of fine movements of the upper extremity, locomotor activities of the lower extremity, and activities that involve both upper and lower extremities. There are 20 questions in 8 categories of functioning including dressing, rising, eating, walking, hygiene, reach, grip and usual activities. The stem of each item asks 'Over the past week, "are you able to..." perform a particular task'. Each item is scored on a 4 point scale from 0 - 3, representing normal, no difficulty (0), some difficulty (1), much difficulty (2) and unable to do (3). The disability index score is calculated as the mean of the available category scores, ranging from 0 to 3. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Secukinumab (AIN457) 75 mg s.c.	Secukinumab (AIN457) 150 mg s.c.	Secukinumab (AIN457) 300 mg s.c.	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89	95	95	33
Units: Scores on a scale				
least squares mean (standard error)	-0.32 (± 0.050)	-0.48 (± 0.049)	-0.56 (± 0.050)	-0.31 (± 0.060)

Statistical analyses

Statistical analysis title	Mean Difference
Comparison groups	Secukinumab (AIN457) 75 mg s.c. v Placebo
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9195
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.15

Statistical analysis title	Mean Difference
Comparison groups	Secukinumab (AIN457) 150 mg s.c. v Placebo
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0278
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	-0.02

Statistical analysis title	Mean Difference
Comparison groups	Secukinumab (AIN457) 300 mg s.c. v Placebo
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0013
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.1

Secondary: Number of participants achieving American College of Rheumatology 50 (ACR50) response criteria

End point title	Number of participants achieving American College of Rheumatology 50 (ACR50) response criteria

End point description:

ACR20 response was defined as having a positive clinical response to treatment (individual improvement) in disease activity if the participant had at least 50% improvement in tender 68-joint count, swollen 66-joint count and at least 3 of the following 5 measures: patient’s assessment of RA pain, patient’s global assessment of disease activity, physician’s global assessment of disease activity, subject self-assessed disability (Health Assessment Questionnaire [HAQ-DI] score), and/or acute phase reactant (high sensitivity c-reactive protein (hsCRP) or erythrocyte sedimentation rate (ESR). The ACR50 response results at week 24 used non-responder imputation.

End point type	Secondary

End point timeframe:
Week 24

End point values	Secukinumab (AIN457) 75 mg s.c.	Secukinumab (AIN457) 150 mg s.c.	Secukinumab (AIN457) 300 mg s.c.	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	99	100	100	98
Units: Participants	18	35	35	7

Statistical analyses

Statistical analysis title	Odds Ratio
Comparison groups	Secukinumab (AIN457) 75 mg s.c. v Placebo
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0245
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	7.36

Statistical analysis title	Odds Ratio
Comparison groups	Secukinumab (AIN457) 300 mg s.c. v Placebo
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.97
upper limit	17.22

Statistical analysis title	Odds Ratio
Comparison groups	Secukinumab (AIN457) 150 mg s.c. v Placebo
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.11
upper limit	18.25

Secondary: Number of participants with dactylitis in the subset of subjects who had dactylitis at baseline

End point title	Number of participants with dactylitis in the subset of subjects who had dactylitis at baseline
End point description:	
Resolution of dactylitis was evaluated in the subset of patients who had disease activity at baseline. In this analysis, a lower percentage is desirable and resolution is defined as complete absence of the symptom.	
End point type	Secondary
End point timeframe:	
Week 24	

End point values	Secukinumab (AIN457) 75 mg s.c.	Secukinumab (AIN457) 150 mg s.c.	Secukinumab (AIN457) 300 mg s.c.	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	32	46	27
Units: Participants	23	16	20	23

Statistical analyses

Statistical analysis title	Odds Ratio
Comparison groups	Secukinumab (AIN457) 75 mg s.c. v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3149
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.51

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	1.91

Statistical analysis title	Odds Ratio
Comparison groups	Secukinumab (AIN457) 150 mg s.c. v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0056
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.58

Statistical analysis title	Odds Ratio
Comparison groups	Secukinumab (AIN457) 300 mg s.c. v Placebo
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0021
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.5

Secondary: Number of participants with enthesitis in the subset of subjects who had enthesitis at baseline

End point title	Number of participants with enthesitis in the subset of subjects who had enthesitis at baseline

End point description:

Resolution of enthesitis was evaluated in the subset of patients who had disease activity at baseline. In this analysis, a lower percentage is desirable and resolution is defined as complete absence of the symptom.

End point type	Secondary

End point timeframe:
Week 24

End point values	Secukinumab (AIN457) 75 mg s.c.	Secukinumab (AIN457) 150 mg s.c.	Secukinumab (AIN457) 300 mg s.c.	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	64	56	65
Units: Participants	46	37	29	51

Statistical analyses

Statistical analysis title	Odds Ratio
Comparison groups	Secukinumab (AIN457) 75 mg s.c. v Placebo
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1678
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	1.26

Statistical analysis title	Odds Ratio
Comparison groups	Secukinumab (AIN457) 300 mg s.c. v Placebo
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0025
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	0.65

Statistical analysis title	Odds Ratio
Comparison groups	Secukinumab (AIN457) 150 mg s.c. v Placebo
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0108
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	0.79

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study Treatment until Last Patient Last Visit (LPLV), up to a maximum of 5 years.

Adverse event reporting additional description:

Patients randomized to Placebo are reported under Placebo for AEs starting before switching to Secukinumab and under the Secukinumab arm for AEs starting after switching to Secukinumab. Under "# of deaths resulting from AEs" all those deaths, resulting from SAEs that are deemed to be causally related to treatment by the investigator are reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Any AIN457 75 mg

Reporting group description:

Any AIN457 75 mg

Reporting group title	Any AIN457 300 mg

Reporting group description:

Any AIN457 300 mg

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	Any AIN457 75 mg	Any AIN457 300 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 99 (17.17%)	42 / 251 (16.73%)	3 / 98 (3.06%)
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)			
B-cell lymphoma			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Penile squamous cell carcinoma			

subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Prostate cancer			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	2 / 99 (2.02%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Throat cancer			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Thyroid cancer			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Deep vein thrombosis			

subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Vasculitis necrotising			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Social circumstances			
Pregnancy of partner			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cervical dysplasia			

subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Dysmenorrhoea			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Dependence			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Suicidal ideation			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Animal bite			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Ankle fracture			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Femoral neck fracture			
subjects affected / exposed	1 / 99 (1.01%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fractured ischium			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Fractured sacrum			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Head injury			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc injury			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Limb traumatic amputation			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post-traumatic neck syndrome			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			

subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis fracture			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Rib fracture			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scar			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Spinal compression fracture			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 99 (1.01%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			

subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical radiculopathy			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiplegia			

subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Deafness neurosensory			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Vertigo			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Visual acuity reduced transiently			

subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Gastric ulcer			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Inflammatory bowel disease			

subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar hernia			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Nausea			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Umbilical hernia			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic lesion			

subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Hypertransaminasaemia			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Liver disorder			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Skin and subcutaneous tissue disorders			
Photosensitivity reaction			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriasis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Arthritis reactive			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Arthrofibrosis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical spinal stenosis			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Foot deformity			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 99 (1.01%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patellofemoral pain syndrome			

subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudarthrosis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 99 (1.01%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			

subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Haematoma infection			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis C			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious colitis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 99 (0.00%)	2 / 251 (0.80%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital abscess			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Peritonsillar abscess			

subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal abscess			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Pneumonia			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Sepsis			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			

subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 99 (0.00%)	0 / 251 (0.00%)	0 / 98 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 99 (0.00%)	1 / 251 (0.40%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 99 (1.01%)	0 / 251 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Any AIN457 150 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 193 (14.51%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	1 / 193 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Penile squamous cell carcinoma			

subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of the tongue				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Throat cancer				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thyroid cancer				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine leiomyoma				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Arteriosclerosis				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				

subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral arterial occlusive disease				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vasculitis necrotising				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Non-cardiac chest pain				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Social circumstances				
Pregnancy of partner				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Cervical dysplasia				

subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysmenorrhoea				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Alcohol abuse				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dependence				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Suicidal ideation				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device dislocation				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Alcohol poisoning				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Animal bite				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ankle fracture				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Contusion				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foot fracture				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Fractured ischium			
subjects affected / exposed	1 / 193 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fractured sacrum			
subjects affected / exposed	1 / 193 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc injury			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	1 / 193 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Limb traumatic amputation			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pelvic fracture			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Procedural pain			

subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pubis fracture				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Scar				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				

subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ventricular fibrillation				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Carotid artery stenosis				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cervical radiculopathy				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Facial paralysis				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	2 / 193 (1.04%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Hemiplegia				

subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Migraine				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Deafness neurosensory				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Vertigo				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Vision blurred				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Visual acuity reduced transiently				

subjects affected / exposed	1 / 193 (0.52%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Crohn's disease			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 193 (0.52%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Incarcerated inguinal hernia			
subjects affected / exposed	1 / 193 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inflammatory bowel disease			

subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar hernia				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Bile duct obstruction				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic lesion				

subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertransaminasaemia				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Liver disorder				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Photosensitivity reaction				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psoriasis				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Calculus urinary				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthritis reactive				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Arthrofibrosis			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cervical spinal stenosis			
subjects affected / exposed	1 / 193 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Foot deformity			
subjects affected / exposed	1 / 193 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 193 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Patellofemoral pain syndrome			

subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pseudarthrosis				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abscess limb				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis norovirus				

subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haematoma infection				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis C				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infectious colitis				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infective exacerbation of chronic obstructive airways disease				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Kidney infection				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periorbital abscess				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonsillar abscess				

subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngeal abscess				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural infection				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 193 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Septic shock				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	0 / 193 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subcutaneous abscess				

subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	2 / 193 (1.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 193 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Any AIN457 75 mg	Any AIN457 300 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 99 (63.64%)	171 / 251 (68.13%)	39 / 98 (39.80%)
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 99 (6.06%)	23 / 251 (9.16%)	3 / 98 (3.06%)
occurrences (all)	7	25	3
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 99 (6.06%)	18 / 251 (7.17%)	5 / 98 (5.10%)
occurrences (all)	7	29	6
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	5 / 99 (5.05%)	11 / 251 (4.38%)	2 / 98 (2.04%)
occurrences (all)	5	12	2
Oedema peripheral			
subjects affected / exposed	5 / 99 (5.05%)	4 / 251 (1.59%)	0 / 98 (0.00%)
occurrences (all)	5	5	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	11 / 99 (11.11%)	23 / 251 (9.16%)	3 / 98 (3.06%)
occurrences (all)	14	34	6
Nausea			
subjects affected / exposed	7 / 99 (7.07%)	14 / 251 (5.58%)	4 / 98 (4.08%)
occurrences (all)	10	25	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 99 (2.02%)	12 / 251 (4.78%)	2 / 98 (2.04%)
occurrences (all)	2	15	2
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	7 / 99 (7.07%)	17 / 251 (6.77%)	4 / 98 (4.08%)
occurrences (all)	7	22	5
Rash			
subjects affected / exposed	1 / 99 (1.01%)	13 / 251 (5.18%)	3 / 98 (3.06%)
occurrences (all)	1	15	3
Psychiatric disorders			
Depression			
subjects affected / exposed	5 / 99 (5.05%)	14 / 251 (5.58%)	2 / 98 (2.04%)
occurrences (all)	5	15	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 99 (7.07%)	25 / 251 (9.96%)	4 / 98 (4.08%)
occurrences (all)	13	49	5
Back pain			
subjects affected / exposed	8 / 99 (8.08%)	21 / 251 (8.37%)	3 / 98 (3.06%)
occurrences (all)	8	23	3
Bursitis			

subjects affected / exposed	5 / 99 (5.05%)	8 / 251 (3.19%)	0 / 98 (0.00%)
occurrences (all)	5	9	0
Musculoskeletal pain			
subjects affected / exposed	2 / 99 (2.02%)	12 / 251 (4.78%)	2 / 98 (2.04%)
occurrences (all)	3	15	2
Pain in extremity			
subjects affected / exposed	5 / 99 (5.05%)	11 / 251 (4.38%)	3 / 98 (3.06%)
occurrences (all)	7	12	4
Psoriatic arthropathy			
subjects affected / exposed	12 / 99 (12.12%)	23 / 251 (9.16%)	2 / 98 (2.04%)
occurrences (all)	12	27	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	7 / 99 (7.07%)	19 / 251 (7.57%)	2 / 98 (2.04%)
occurrences (all)	9	25	2
Influenza			
subjects affected / exposed	3 / 99 (3.03%)	14 / 251 (5.58%)	0 / 98 (0.00%)
occurrences (all)	3	16	0
Nasopharyngitis			
subjects affected / exposed	23 / 99 (23.23%)	47 / 251 (18.73%)	8 / 98 (8.16%)
occurrences (all)	32	104	12
Oral herpes			
subjects affected / exposed	5 / 99 (5.05%)	8 / 251 (3.19%)	2 / 98 (2.04%)
occurrences (all)	6	15	2
Pharyngitis			
subjects affected / exposed	1 / 99 (1.01%)	15 / 251 (5.98%)	0 / 98 (0.00%)
occurrences (all)	1	26	0
Respiratory tract infection			
subjects affected / exposed	5 / 99 (5.05%)	7 / 251 (2.79%)	0 / 98 (0.00%)
occurrences (all)	6	8	0
Rhinitis			
subjects affected / exposed	5 / 99 (5.05%)	9 / 251 (3.59%)	0 / 98 (0.00%)
occurrences (all)	7	10	0
Sinusitis			
subjects affected / exposed	6 / 99 (6.06%)	30 / 251 (11.95%)	1 / 98 (1.02%)
occurrences (all)	10	47	1

Upper respiratory tract infection			
subjects affected / exposed	23 / 99 (23.23%)	58 / 251 (23.11%)	7 / 98 (7.14%)
occurrences (all)	37	97	7
Urinary tract infection			
subjects affected / exposed	8 / 99 (8.08%)	19 / 251 (7.57%)	4 / 98 (4.08%)
occurrences (all)	10	31	4

Non-serious adverse events	Any AIN457 150 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	132 / 193 (68.39%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	14 / 193 (7.25%)		
occurrences (all)	15		
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 193 (8.29%)		
occurrences (all)	18		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 193 (3.11%)		
occurrences (all)	6		
Oedema peripheral			
subjects affected / exposed	3 / 193 (1.55%)		
occurrences (all)	3		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	19 / 193 (9.84%)		
occurrences (all)	21		
Nausea			
subjects affected / exposed	12 / 193 (6.22%)		
occurrences (all)	13		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	13 / 193 (6.74%)		
occurrences (all)	14		
Skin and subcutaneous tissue disorders			

Psoriasis			
subjects affected / exposed	14 / 193 (7.25%)		
occurrences (all)	16		
Rash			
subjects affected / exposed	8 / 193 (4.15%)		
occurrences (all)	11		
Psychiatric disorders			
Depression			
subjects affected / exposed	4 / 193 (2.07%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	24 / 193 (12.44%)		
occurrences (all)	37		
Back pain			
subjects affected / exposed	11 / 193 (5.70%)		
occurrences (all)	12		
Bursitis			
subjects affected / exposed	7 / 193 (3.63%)		
occurrences (all)	9		
Musculoskeletal pain			
subjects affected / exposed	12 / 193 (6.22%)		
occurrences (all)	19		
Pain in extremity			
subjects affected / exposed	5 / 193 (2.59%)		
occurrences (all)	7		
Psoriatic arthropathy			
subjects affected / exposed	24 / 193 (12.44%)		
occurrences (all)	32		
Infections and infestations			
Bronchitis			
subjects affected / exposed	13 / 193 (6.74%)		
occurrences (all)	18		
Influenza			
subjects affected / exposed	10 / 193 (5.18%)		
occurrences (all)	12		

Nasopharyngitis			
subjects affected / exposed	41 / 193 (21.24%)		
occurrences (all)	68		
Oral herpes			
subjects affected / exposed	2 / 193 (1.04%)		
occurrences (all)	9		
Pharyngitis			
subjects affected / exposed	6 / 193 (3.11%)		
occurrences (all)	8		
Respiratory tract infection			
subjects affected / exposed	5 / 193 (2.59%)		
occurrences (all)	11		
Rhinitis			
subjects affected / exposed	6 / 193 (3.11%)		
occurrences (all)	7		
Sinusitis			
subjects affected / exposed	16 / 193 (8.29%)		
occurrences (all)	27		
Upper respiratory tract infection			
subjects affected / exposed	40 / 193 (20.73%)		
occurrences (all)	57		
Urinary tract infection			
subjects affected / exposed	16 / 193 (8.29%)		
occurrences (all)	23		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 February 2014	To expand the statistical hierarchy (primary plus ranked secondary variables) to include endpoints which are relevant to determining the overall therapeutic value of a therapy for PsA. These endpoints include but are not limited to PASI75, PASI90, DAS28-CRP, HAQDI, SF-36, dactylitis and enthesitis.
21 October 2015	To allow dose escalation of secukinumab administered s.c. every 4 weeks from 75 mg to 150 mg or 300 mg, and from 150 mg to 300 mg.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported