Clinical trial results:
A phase III, randomized, double-blind, placebo-controlled multicenter study of subcutaneous secukinumab in autoinjectors, to demonstrate efficacy at 24 weeks and to assess the long term safety, tolerability and efficacy up to 3 years in subjects with active Psoriatic Arthritis

Summary

EudraCT number	2013-004002-25
Trial protocol	GB IT ES NL CZ BG
Global end of trial date	28 March 2018

Results information

Result version number	v1 (current)
This version publication date	14 March 2019
First version publication date	14 March 2019

Trial information

Trial identification

Sponsor protocol code	CAIN457F2318

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01989468
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	28 March 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

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

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	10 April 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 33
Country: Number of subjects enrolled	Bulgaria: 16
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	Czech Republic: 52
Country: Number of subjects enrolled	Germany: 68
Country: Number of subjects enrolled	United Kingdom: 51
Country: Number of subjects enrolled	Italy: 32
Country: Number of subjects enrolled	Netherlands: 18
Country: Number of subjects enrolled	Russian Federation: 61
Country: Number of subjects enrolled	Spain: 22
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	United States: 48
Worldwide total number of subjects	414
EEA total number of subjects	259

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	367
From 65 to 84 years	47
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were randomized to 1 of 3 treatment arms (1:1:1) and planned to be treated for 156 weeks. Placebo non-responders had the option to be re-randomized at Week 16 and placebo responders had the option to be re-randomized at Week 24. Thus, of the 137 original placebo patients 64 were re-randomized to AIN457 150 mg and 65 to AIN457 300 mg.

Pre-assignment

Screening details:

A screening period (SCR) running up to 10 weeks before randomization was used to assess eligibility.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	AIN457 150 mg

Arm description:

1 s.c. Secukinumab 150 mg autoinjector at Baseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	
Other name	Secukinumab 150 mg
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

1 s.c. Secukinumab 150 mg autoinjector at Baseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4

Arm title	AIN457 300 mg

Arm description:

2 s.c. Secukinumab 150 mg autoinjector at Baseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	
Other name	Secukinumab 300 mg
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

2 s.c. Secukinumab 150 mg autoinjector at Baseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4

Arm title	Placebo_AIN457 150 mg

Arm description:

Placebo switch to Secukinumab/AIN457 150 mg

Arm type	Placebo

Investigational medicinal product name	Secukinumab
Investigational medicinal product code	
Other name	Secukinumab 150 mg
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

1 s.c. Secukinumab 150 mg autoinjector at Baseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4

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

Dosage and administration details:

Matching Placebo at Baseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4

Arm title	Placebo_AIN457 300 mg

Arm description:

Placebo switch to Secukinumab/AIN457 300 mg

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

Dosage and administration details:

Matching Placebo at Baseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4

Investigational medicinal product name	Secukinumab
Investigational medicinal product code	
Other name	Secukinumab 300 mg
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

2 s.c. Secukinumab 150 mg autoinjector at Baseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4

Arm title	Placebo not rerandomized

Arm description:

Matching Placebo at Beseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.

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

Dosage and administration details:

Matching Placebo at Baseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4

Number of subjects in period 1	AIN457 150 mg	AIN457 300 mg	Placebo_AIN457 150 mg
Started	138	139	64
Completed	91	102	45
Not completed	47	37	19
Adverse event, serious fatal	3	-	1
Physician decision	4	1	-
Adverse event, non-fatal	10	15	4
Technical Problems	3	1	3
Pregnancy	-	1	-
Subject Guardian Decision	11	6	4
Lost to follow-up	5	2	-
Lack of efficacy	11	11	7

Number of subjects in period 1	Placebo_AIN457 300 mg	Placebo not rerandomized
Started	65	8
Completed	49	0
Not completed	16	8
Adverse event, serious fatal	-	-
Physician decision	1	-
Adverse event, non-fatal	5	4
Technical Problems	1	-
Pregnancy	-	-
Subject Guardian Decision	4	1
Lost to follow-up	1	1
Lack of efficacy	4	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	414	414	
Age Categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	367	367	
>=65 years	47	47	
Sex: Female, Male Units: Subjects			
Female	227	227	
Male	187	187	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	2	2	
Asian	9	9	
White	392	392	
Other	11	11	

Subject analysis sets	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Matching Placebo at Beseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Matching Placebo at Beseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Matching Placebo at Beseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Matching Placebo at Beseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.	
Subject analysis set title	Any AIN457 150 mg
Subject analysis set type	Full analysis
Subject analysis set description: Any patients exposed to AIN457 150 mg	
Subject analysis set title	Any AIN457 300 mg
Subject analysis set type	Full analysis

Subject analysis set description:
Any patients exposed to AIN457 300 mg

Subject analysis set title	Any AIN457
Subject analysis set type	Full analysis

Subject analysis set description:
Any patients exposed to AIN457

Reporting group values	Placebo	Placebo	Placebo
Number of subjects	137	59	36
Age Categorical Units: Subjects			
<=18 years	0		
Between 18 and 65 years	118		
>=65 years	19		
Sex: Female, Male Units: Subjects			
Female	78		
Male	59		
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	0		
Asian	4		
White	133		
Other	0		

Reporting group values	Placebo	Any AIN457 150 mg	Any AIN457 300 mg
Number of subjects	98	202	284
Age Categorical Units: Subjects			
<=18 years			
Between 18 and 65 years			
>=65 years			
Sex: Female, Male Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native			
Asian			
White			
Other			

Reporting group values	Any AIN457		
Number of subjects	406		
Age Categorical Units: Subjects			
<=18 years			
Between 18 and 65 years			
>=65 years			

Sex: Female, Male Units: Subjects			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native Asian White Other			

End points

End points reporting groups

Reporting group title	AIN457 150 mg
Reporting group description:	
1 s.c. Secukinumab 150 mg autoinjector at Baseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.	
Reporting group title	AIN457 300 mg
Reporting group description:	
2 s.c. Secukinumab 150 mg autoinjector at Baseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.	
Reporting group title	Placebo_AIN457 150 mg
Reporting group description:	
Placebo switch to Secukinumab/AIN457 150 mg	
Reporting group title	Placebo_AIN457 300 mg
Reporting group description:	
Placebo switch to Secukinumab/AIN457 300 mg	
Reporting group title	Placebo not rerandomized
Reporting group description:	
Matching Placebo at Beseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Matching Placebo at Beseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Matching Placebo at Beseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Matching Placebo at Beseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Matching Placebo at Beseline, Weeks 1, 2, 3, 4, followed by dosing every four weeks starting at Week 4.	
Subject analysis set title	Any AIN457 150 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Any patients exposed to AIN457 150 mg	
Subject analysis set title	Any AIN457 300 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Any patients exposed to AIN457 300 mg	
Subject analysis set title	Any AIN457
Subject analysis set type	Full analysis
Subject analysis set description:	
Any patients exposed to AIN457	

Primary: Proportion of patients achieving American College of Rheumatology 20 (ACR20) response criteria on secukinumab versus placebo at Week 24

End point title	Proportion of patients achieving American College of Rheumatology 20 (ACR20) response criteria on secukinumab versus placebo at Week 24[1][2]

End point description:

A patient will be considered as improved according the ACR20 criteria if she/he has at least 20% decrease in the swollen and tender joint count, and at least 20% improvements in 3 of the following 5 criteria: physical disability on the Health Assessment Questionnaire; pain score on a visual analog scale; patient global assessment; physician global assessment; and acute phase reactant [either erythrocyte sedimentation rate (ESR) or high sensitivity C-reactive protein (hsCRP)]

End point type	Primary

End point timeframe:

Week 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: AIN457 Baseline Period Arms (AIN457 150mg, AIN457 300mg) included under Arm Reporting Groups "Overall Study" and Placebo included under "Subject Analysis Set" => Summary descriptive analysis done.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: AIN457 Baseline Period Arms (AIN457 150mg, AIN457 300mg) included under Arm Reporting Groups "Overall Study" and Placebo included under "Subject Analysis Set" => Summary descriptive analysis done.

End point values	AIN457 150 mg	AIN457 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	138	139	137	
Units: Participants	58	67	22	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients achieving American College of Rheumatology 50 (ACR50) response criteria on secukinumab versus placebo at Week 24

End point title	Proportion of patients achieving American College of Rheumatology 50 (ACR50) response criteria on secukinumab versus placebo at Week 24[3]

End point description:

A patient will be considered as improved according the ACR50 criteria if she/he has at least 50% decreases in the swollen and tender joint count, and at least 50% improvements in 3 of the following 5 criteria: physical disability on the Health Assessment Questionnaire; pain score on a visual analog scale; patient global assessment; physician global assessment; and acute phase reactant [either erythrocyte sedimentation rate (ESR) or high sensitivity C-reactive protein (hsCRP)]

End point type	Secondary

End point timeframe:

Week 24

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: AIN457 Baseline Period Arms (AIN457 150mg, AIN457 300mg) included under Arm Reporting Groups "Overall Study" and Placebo included under "Subject Analysis Set" => Summary descriptive analysis done.

End point values	AIN457 150 mg	AIN457 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	138	139	137	
Units: Participants	26	48	12	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Disease Activity Score for 28 joints (DAS28-CRP) (utilizing hsCRP) in subjects treated with secukinumab versus placebo at Week 24

End point title	Change from baseline in Disease Activity Score for 28 joints (DAS28-CRP) (utilizing hsCRP) in subjects treated with secukinumab versus placebo at Week 24[4]

End point description:

DAS28-CRP is a measure of disease activity based on 28-Swollen and Tender Joint Count [proximal interphalangeal joints (10 joints) metacarpophalangeal joints (10) wrists (2) elbows (2) shoulders (2) knees (2)], CRP, and the Patient's Global Assessment of disease activity. Values range from 2.0 to 10.0 where higher values mean a higher disease activity. DAS28-CRP < 2.6 is interpreted as remission.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: AIN457 Baseline Period Arms (AIN457 150mg, AIN457 300mg) included under Arm Reporting Groups "Overall Study" and Placebo included under "Subject Analysis Set" => Summary descriptive analysis done.

End point values	AIN457 150 mg	AIN457 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	138	139	137	
Units: Unit on a scale				
least squares mean (standard error)	-1.24 (± 0.095)	-1.56 (± 0.093)	-0.64 (± 0.127)	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects achieving a Psoriatic Area and Severity Index 75 (PASI75) response in subjects on secukinumab versus placebo at Week 24

End point title	Proportion of subjects achieving a Psoriatic Area and Severity Index 75 (PASI75) response in subjects on secukinumab versus placebo at Week 24[5]

End point description:

PASI takes into account the extent of the disease, as well as the severity of erythema, scaling, and thickness in different body areas affected by psoriasis. A PASI75 represents an improvement in the PASI score of at least 75% as compared with baseline.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: AIN457 Baseline Period Arms (AIN457 150mg, AIN457 300mg) included under Arm Reporting Groups "Overall Study" and Placebo included under "Subject Analysis Set" => Summary descriptive analysis done.

End point values	AIN457 150 mg	AIN457 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	68	62	59	
Units: Participants	34	29	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Physical function component of the short-form health survey (SF-36-PCS) in subjects treated with secukinumab versus placebo at Week 24

End point title	Change from baseline in Physical function component of the short-form health survey (SF-36-PCS) in subjects treated with secukinumab versus placebo at Week 24[6]

End point description:

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.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: AIN457 Baseline Period Arms (AIN457 150mg, AIN457 300mg) included under Arm Reporting Groups "Overall Study" and Placebo included under "Subject Analysis Set" => Summary descriptive analysis done.

End point values	AIN457 150 mg	AIN457 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	138	139	137	
Units: Unit on a scale				
least squares mean (standard error)				
Mental Component Summary (MCS)	1.68 (± 0.837)	4.41 (± 0.822)	-0.10 (± 1.142)	
Physical Component Summary (PCS)	3.42 (± 0.600)	6.46 (± 0.590)	2.94 (± 0.830)	

Statistical analyses

No statistical analyses for this end point

Secondary: Psoriatic Area and Severity Index 90 (PASI90) response in subjects treated with secukinumab versus placebo at Week 24

End point title	Psoriatic Area and Severity Index 90 (PASI90) response in subjects treated with secukinumab versus placebo at Week 24[7]

End point description:

PASI takes into account the extent of the disease, as well as the severity of erythema, scaling, and thickness in different body areas affected by psoriasis. A PASI90 represents an improvement in the PASI score of at least 90% as compared with baseline.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: AIN457 Baseline Period Arms (AIN457 150mg, AIN457 300mg) included under Arm Reporting Groups "Overall Study" and Placebo included under "Subject Analysis Set" => Summary descriptive analysis done.

End point values	AIN457 150 mg	AIN457 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	68	62	59	
Units: Participants	25	21	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Health Assessment Questionnaire – Disability Index (HAQ-DI score) in subjects treated with secukinumab versus placebo at Week 24

End point title	Change from baseline in Health Assessment Questionnaire – Disability Index (HAQ-DI score) in subjects treated with secukinumab versus placebo at Week 24[8]

End point description:

The disability assessment component of the HAQ assesses a subjects 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 extremitites.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: AIN457 Baseline Period Arms (AIN457 150mg, AIN457 300mg) included under Arm Reporting Groups "Overall Study" and Placebo included under "Subject Analysis Set" => Summary descriptive analysis done.

End point values	AIN457 150 mg	AIN457 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	138	139	137	
Units: Unit on a scale				
least squares mean (standard error)	-0.27 (± 0.043)	-0.38 (± 0.042)	-0.17 (± 0.055)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall safety and tolerability

End point title	Overall safety and tolerability[9]

End point description:

Analysis of frequencies for treatment emergent Adverse Event (AE), Serious Adverse Event (SAE) and Deaths by primary System Organ Class (SOC).

End point type	Secondary

End point timeframe:

From first dose of study treatment to last study visit, up to 3 years

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: AIN457 Baseline Period Arms (AIN457 150mg, AIN457 300mg) included under Arm Reporting Groups "Overall Study" and Placebo included under "Subject Analysis Set" => Summary descriptive analysis done.

End point values	AIN457 150 mg	AIN457 300 mg	Placebo	Any AIN457 150 mg
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	138	139	137	202
Units: Participants				
number (not applicable)				
AEs by Primary System Organ Class (SOC)	176	230	81	176
SAEs by Primary System Organ Class (SOC)	42	4	9	42
Deaths by Primary System Organ Class (SOC)	4	0	0	4

End point values	Any AIN457 300 mg	Any AIN457		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	284	406		
Units: Participants				
number (not applicable)				
AEs by Primary System Organ Class (SOC)	230	363		
SAEs by Primary System Organ Class (SOC)	35	76		

Deaths by Primary System Organ Class (SOC)	0	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with Dactylitis at Week 24 in the subset of patients who had dactylitis at Baseline

End point title	Proportion of patients with Dactylitis at Week 24 in the subset of patients who had dactylitis at Baseline[10]

End point description:

The presence of dactylitis was assessed by dactylitis count (number of fingers and toes with dactylitis, with a range of 0-20). If dactylitis is present with any finger or toe, the patient is counted as a patient with dactylitis.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: AIN457 Baseline Period Arms (AIN457 150mg, AIN457 300mg) included under Arm Reporting Groups "Overall Study" and Placebo included under "Subject Analysis Set" => Summary descriptive analysis done.

End point values	AIN457 150 mg	AIN457 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	46	36	
Units: Participants	22	24	31	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with Enthesitis at Week 24 in the subset of patients who had enthesitis at Baseline

End point title	Proportion of patients with Enthesitis at Week 24 in the subset of patients who had enthesitis at Baseline[11]

End point description:

The presence of Enthesitis was assessed using a validated enthesitis index that uses 6 sites for evaluation of enthesitis: lateral epicondyle humerus L + R, proximal achilles L + R and medial condyle femur. If enthesitis is present at any of the 6 sites, the subject is counted as a subject with enthesitis.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: AIN457 Baseline Period Arms (AIN457 150mg, AIN457 300mg) included under Arm Reporting Groups "Overall Study" and Placebo included under "Subject Analysis Set" => Summary descriptive analysis done.

End point values	AIN457 150 mg	AIN457 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	95	88	98	
Units: Participants	60	53	83	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: All Adverse Events (AEs) are reported in this record from date of First Patient First Treatment (FPFT) until end of treatment exposure + 84 days safety follow-up.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

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

Serious adverse events	Any AIN457 150 mg	Any AIN457 300 mg	Any AIN457
Total subjects affected by serious adverse events			
subjects affected / exposed	42 / 202 (20.79%)	35 / 284 (12.32%)	76 / 406 (18.72%)
number of deaths (all causes)	4	0	4
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic lymphocytic leukaemia			

subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon adenoma			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Follicular thyroid cancer			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive papillary breast carcinoma			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lip squamous cell carcinoma			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melanocytic naevus			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Metastases to liver			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Metastases to spine			

subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Ovarian cancer stage IV			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Papillary thyroid cancer			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phyllodes tumour			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland neoplasm			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small cell lung cancer metastatic			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			

subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery thrombosis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cystocele			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menorrhagia			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ovarian cyst torsion			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectocele			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterovaginal prolapse			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal turbinate hypertrophy			
subjects affected / exposed	0 / 202 (0.00%)	0 / 284 (0.00%)	0 / 406 (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
Pleural effusion			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary mass			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sopor			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	1 / 202 (0.50%)	1 / 284 (0.35%)	2 / 406 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device loosening			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Weight decreased			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			

subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac valve rupture			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament rupture			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 202 (0.00%)	2 / 284 (0.70%)	2 / 406 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			

subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sternal fracture			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic arthrosis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic fracture			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			

subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 202 (0.00%)	0 / 284 (0.00%)	0 / 406 (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
Atrial fibrillation			
subjects affected / exposed	1 / 202 (0.50%)	1 / 284 (0.35%)	2 / 406 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 202 (0.00%)	0 / 284 (0.00%)	0 / 406 (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
Atrioventricular block complete			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block first degree			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Cardiac failure chronic			

subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diastolic dysfunction			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular hypertrophy			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	2 / 202 (0.99%)	0 / 284 (0.00%)	2 / 406 (0.49%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coma			

subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			
subjects affected / exposed	0 / 202 (0.00%)	0 / 284 (0.00%)	0 / 406 (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
Headache			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiplegia			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Quadriparesis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular disorder			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 202 (0.50%)	1 / 284 (0.35%)	2 / 406 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal prolapse			

subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammatory bowel disease			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary dyskinesia			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			

subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermal cyst			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eczema			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urethral stenosis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 202 (0.99%)	0 / 284 (0.00%)	2 / 406 (0.49%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	1 / 202 (0.50%)	1 / 284 (0.35%)	2 / 406 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fibromyalgia			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	2 / 202 (0.99%)	4 / 284 (1.41%)	6 / 406 (1.48%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriatic arthropathy			
subjects affected / exposed	0 / 202 (0.00%)	0 / 284 (0.00%)	0 / 406 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess jaw			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess of salivary gland			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			

subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 202 (0.50%)	1 / 284 (0.35%)	2 / 406 (0.49%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 202 (0.00%)	2 / 284 (0.70%)	2 / 406 (0.49%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eczema infected			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal sepsis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			

subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious mononucleosis			
subjects affected / exposed	0 / 202 (0.00%)	0 / 284 (0.00%)	0 / 406 (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
Joint abscess			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periodontitis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 202 (1.49%)	1 / 284 (0.35%)	4 / 406 (0.99%)
occurrences causally related to treatment / all	1 / 3	2 / 3	3 / 6
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Staphylococcal infection			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 202 (0.99%)	0 / 284 (0.00%)	2 / 406 (0.49%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			

subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 202 (0.50%)	0 / 284 (0.00%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obesity			
subjects affected / exposed	0 / 202 (0.00%)	1 / 284 (0.35%)	1 / 406 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 137 (6.57%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cancer pain			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic lymphocytic leukaemia			

subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colon adenoma				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Follicular thyroid cancer				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Invasive papillary breast carcinoma				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lip squamous cell carcinoma				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Melanocytic naevus				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to central nervous system				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to liver				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to spine				

subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian cancer stage IV				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatic carcinoma				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Papillary thyroid cancer				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Phyllodes tumour				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Salivary gland neoplasm				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small cell lung cancer metastatic				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Circulatory collapse				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				

subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral artery thrombosis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Varicose vein			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cystocele			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Menorrhagia			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Ovarian cyst torsion				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectocele				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterovaginal prolapse				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nasal turbinate hypertrophy				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pulmonary mass			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sopor			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	0 / 137 (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 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device loosening			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Weight decreased			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			

subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac valve rupture				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cervical vertebral fracture				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Joint dislocation				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ligament rupture				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar vertebral fracture				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radius fracture				

subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sternal fracture				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Traumatic arthrosis				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Traumatic fracture				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina pectoris				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic valve incompetence				

subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arrhythmia				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arteriosclerosis coronary artery				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block first degree				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure chronic				

subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiogenic shock				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diastolic dysfunction				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Left ventricular hypertrophy				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mitral valve incompetence				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Aphasia				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral ischaemia				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coma				

subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depressed level of consciousness				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Facial paresis				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemiplegia				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lacunar infarction				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Quadriparesis				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				

subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphadenopathy			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vestibular disorder			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Retinal detachment			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Anal prolapse			

subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis ulcerative				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inflammatory bowel disease				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Biliary dyskinesia				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				

subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis chronic			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermal cyst			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eczema			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urethral stenosis			
subjects affected / exposed	0 / 137 (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	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Fibromyalgia			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Foot deformity			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psoriatic arthropathy			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abscess jaw			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abscess of salivary gland			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis bacterial			

subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eczema infected			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterococcal sepsis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erysipelas			

subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infectious mononucleosis				
subjects affected / exposed	1 / 137 (0.73%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Joint abscess				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periodontitis				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal infection				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 137 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection				

subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Obesity			
subjects affected / exposed	0 / 137 (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: 2 %

Non-serious adverse events	Any AIN457 150 mg	Any AIN457 300 mg	Any AIN457
Total subjects affected by non-serious adverse events			
subjects affected / exposed	153 / 202 (75.74%)	201 / 284 (70.77%)	320 / 406 (78.82%)
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 202 (5.45%)	15 / 284 (5.28%)	26 / 406 (6.40%)
occurrences (all)	11	18	29
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	16 / 202 (7.92%)	10 / 284 (3.52%)	26 / 406 (6.40%)
occurrences (all)	17	17	34
Injection site erythema			
subjects affected / exposed	1 / 202 (0.50%)	2 / 284 (0.70%)	3 / 406 (0.74%)
occurrences (all)	1	2	3
Non-cardiac chest pain			

subjects affected / exposed	5 / 202 (2.48%)	2 / 284 (0.70%)	7 / 406 (1.72%)
occurrences (all)	5	2	7
Oedema peripheral			
subjects affected / exposed	1 / 202 (0.50%)	6 / 284 (2.11%)	7 / 406 (1.72%)
occurrences (all)	1	6	7
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	5 / 202 (2.48%)	2 / 284 (0.70%)	7 / 406 (1.72%)
occurrences (all)	5	2	7
Cough			
subjects affected / exposed	17 / 202 (8.42%)	12 / 284 (4.23%)	29 / 406 (7.14%)
occurrences (all)	22	15	37
Oropharyngeal pain			
subjects affected / exposed	10 / 202 (4.95%)	15 / 284 (5.28%)	25 / 406 (6.16%)
occurrences (all)	10	18	28
Psychiatric disorders			
Depression			
subjects affected / exposed	5 / 202 (2.48%)	3 / 284 (1.06%)	8 / 406 (1.97%)
occurrences (all)	5	3	8
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	11 / 202 (5.45%)	6 / 284 (2.11%)	17 / 406 (4.19%)
occurrences (all)	12	7	19
Aspartate aminotransferase increased			
subjects affected / exposed	8 / 202 (3.96%)	3 / 284 (1.06%)	11 / 406 (2.71%)
occurrences (all)	8	3	11
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 202 (2.48%)	11 / 284 (3.87%)	15 / 406 (3.69%)
occurrences (all)	5	12	17
Limb injury			
subjects affected / exposed	8 / 202 (3.96%)	2 / 284 (0.70%)	10 / 406 (2.46%)
occurrences (all)	9	2	11
Cardiac disorders			

Palpitations			
subjects affected / exposed	5 / 202 (2.48%)	4 / 284 (1.41%)	9 / 406 (2.22%)
occurrences (all)	5	4	9
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 202 (3.47%)	3 / 284 (1.06%)	10 / 406 (2.46%)
occurrences (all)	9	3	12
Headache			
subjects affected / exposed	18 / 202 (8.91%)	18 / 284 (6.34%)	36 / 406 (8.87%)
occurrences (all)	21	25	46
Sciatica			
subjects affected / exposed	4 / 202 (1.98%)	5 / 284 (1.76%)	9 / 406 (2.22%)
occurrences (all)	4	5	9
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 202 (2.97%)	3 / 284 (1.06%)	9 / 406 (2.22%)
occurrences (all)	6	3	9
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 202 (1.98%)	8 / 284 (2.82%)	12 / 406 (2.96%)
occurrences (all)	4	8	12
Abdominal pain upper			
subjects affected / exposed	10 / 202 (4.95%)	9 / 284 (3.17%)	17 / 406 (4.19%)
occurrences (all)	12	12	24
Constipation			
subjects affected / exposed	5 / 202 (2.48%)	6 / 284 (2.11%)	11 / 406 (2.71%)
occurrences (all)	5	6	11
Diarrhoea			
subjects affected / exposed	20 / 202 (9.90%)	19 / 284 (6.69%)	39 / 406 (9.61%)
occurrences (all)	22	24	46
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 202 (2.97%)	6 / 284 (2.11%)	12 / 406 (2.96%)
occurrences (all)	6	6	12
Mouth ulceration			
subjects affected / exposed	6 / 202 (2.97%)	2 / 284 (0.70%)	8 / 406 (1.97%)
occurrences (all)	7	2	9
Nausea			

subjects affected / exposed	12 / 202 (5.94%)	18 / 284 (6.34%)	30 / 406 (7.39%)
occurrences (all)	14	21	35
Vomiting			
subjects affected / exposed	4 / 202 (1.98%)	3 / 284 (1.06%)	7 / 406 (1.72%)
occurrences (all)	5	4	9
Skin and subcutaneous tissue disorders			
Ingrowing nail			
subjects affected / exposed	0 / 202 (0.00%)	0 / 284 (0.00%)	0 / 406 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	11 / 202 (5.45%)	15 / 284 (5.28%)	26 / 406 (6.40%)
occurrences (all)	14	15	29
Rash			
subjects affected / exposed	5 / 202 (2.48%)	2 / 284 (0.70%)	7 / 406 (1.72%)
occurrences (all)	7	2	9
Skin lesion			
subjects affected / exposed	1 / 202 (0.50%)	6 / 284 (2.11%)	7 / 406 (1.72%)
occurrences (all)	1	6	7
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 202 (0.00%)	4 / 284 (1.41%)	4 / 406 (0.99%)
occurrences (all)	0	4	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	17 / 202 (8.42%)	23 / 284 (8.10%)	40 / 406 (9.85%)
occurrences (all)	25	35	60
Arthritis			
subjects affected / exposed	1 / 202 (0.50%)	7 / 284 (2.46%)	8 / 406 (1.97%)
occurrences (all)	1	7	8
Back pain			
subjects affected / exposed	17 / 202 (8.42%)	24 / 284 (8.45%)	41 / 406 (10.10%)
occurrences (all)	24	28	52
Muscle spasms			
subjects affected / exposed	5 / 202 (2.48%)	4 / 284 (1.41%)	9 / 406 (2.22%)
occurrences (all)	5	4	9
Musculoskeletal pain			

subjects affected / exposed	0 / 202 (0.00%)	6 / 284 (2.11%)	6 / 406 (1.48%)
occurrences (all)	0	7	7
Myalgia			
subjects affected / exposed	2 / 202 (0.99%)	2 / 284 (0.70%)	4 / 406 (0.99%)
occurrences (all)	2	2	4
Osteoarthritis			
subjects affected / exposed	0 / 202 (0.00%)	14 / 284 (4.93%)	14 / 406 (3.45%)
occurrences (all)	0	19	19
Pain in extremity			
subjects affected / exposed	5 / 202 (2.48%)	5 / 284 (1.76%)	10 / 406 (2.46%)
occurrences (all)	5	5	10
Psoriatic arthropathy			
subjects affected / exposed	20 / 202 (9.90%)	21 / 284 (7.39%)	41 / 406 (10.10%)
occurrences (all)	23	25	48
Infections and infestations			
Bronchitis			
subjects affected / exposed	11 / 202 (5.45%)	23 / 284 (8.10%)	34 / 406 (8.37%)
occurrences (all)	15	26	41
Conjunctivitis			
subjects affected / exposed	4 / 202 (1.98%)	9 / 284 (3.17%)	13 / 406 (3.20%)
occurrences (all)	5	11	16
Cystitis			
subjects affected / exposed	6 / 202 (2.97%)	5 / 284 (1.76%)	11 / 406 (2.71%)
occurrences (all)	7	5	12
Ear infection			
subjects affected / exposed	1 / 202 (0.50%)	6 / 284 (2.11%)	7 / 406 (1.72%)
occurrences (all)	1	10	11
Gastroenteritis			
subjects affected / exposed	10 / 202 (4.95%)	10 / 284 (3.52%)	20 / 406 (4.93%)
occurrences (all)	12	10	22
Influenza			
subjects affected / exposed	12 / 202 (5.94%)	16 / 284 (5.63%)	26 / 406 (6.40%)
occurrences (all)	15	17	32
Lower respiratory tract infection			
subjects affected / exposed	6 / 202 (2.97%)	4 / 284 (1.41%)	10 / 406 (2.46%)
occurrences (all)	11	4	15

Nasopharyngitis			
subjects affected / exposed	44 / 202 (21.78%)	63 / 284 (22.18%)	105 / 406 (25.86%)
occurrences (all)	59	101	160
Oral candidiasis			
subjects affected / exposed	5 / 202 (2.48%)	6 / 284 (2.11%)	11 / 406 (2.71%)
occurrences (all)	17	12	29
Oral herpes			
subjects affected / exposed	4 / 202 (1.98%)	8 / 284 (2.82%)	12 / 406 (2.96%)
occurrences (all)	4	14	18
Otitis media			
subjects affected / exposed	0 / 202 (0.00%)	6 / 284 (2.11%)	6 / 406 (1.48%)
occurrences (all)	0	6	6
Pharyngitis			
subjects affected / exposed	4 / 202 (1.98%)	8 / 284 (2.82%)	12 / 406 (2.96%)
occurrences (all)	4	8	12
Respiratory tract infection			
subjects affected / exposed	6 / 202 (2.97%)	13 / 284 (4.58%)	18 / 406 (4.43%)
occurrences (all)	10	18	28
Respiratory tract infection viral			
subjects affected / exposed	0 / 202 (0.00%)	5 / 284 (1.76%)	5 / 406 (1.23%)
occurrences (all)	0	6	6
Rhinitis			
subjects affected / exposed	5 / 202 (2.48%)	7 / 284 (2.46%)	12 / 406 (2.96%)
occurrences (all)	5	8	13
Sinusitis			
subjects affected / exposed	10 / 202 (4.95%)	12 / 284 (4.23%)	22 / 406 (5.42%)
occurrences (all)	12	14	26
Tonsillitis			
subjects affected / exposed	4 / 202 (1.98%)	14 / 284 (4.93%)	18 / 406 (4.43%)
occurrences (all)	4	15	19
Upper respiratory tract infection			
subjects affected / exposed	27 / 202 (13.37%)	35 / 284 (12.32%)	61 / 406 (15.02%)
occurrences (all)	40	59	99
Urinary tract infection			
subjects affected / exposed	13 / 202 (6.44%)	20 / 284 (7.04%)	31 / 406 (7.64%)
occurrences (all)	16	28	44

Viral upper respiratory tract infection			
subjects affected / exposed	5 / 202 (2.48%)	4 / 284 (1.41%)	9 / 406 (2.22%)
occurrences (all)	8	5	13
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	6 / 202 (2.97%)	3 / 284 (1.06%)	9 / 406 (2.22%)
occurrences (all)	6	3	9
Vitamin D deficiency			
subjects affected / exposed	1 / 202 (0.50%)	6 / 284 (2.11%)	7 / 406 (1.72%)
occurrences (all)	1	6	7

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 137 (47.45%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences (all)	2		
Injection site erythema			
subjects affected / exposed	3 / 137 (2.19%)		
occurrences (all)	5		
Non-cardiac chest pain			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Cough			

subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	6 / 137 (4.38%) 6 1 / 137 (0.73%) 1		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	 0 / 137 (0.00%) 0		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	 1 / 137 (0.73%) 1 1 / 137 (0.73%) 1		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) Limb injury subjects affected / exposed occurrences (all)	 1 / 137 (0.73%) 1 1 / 137 (0.73%) 1		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	 0 / 137 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Sciatica	 2 / 137 (1.46%) 2 7 / 137 (5.11%) 8		

subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences (all)	3		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	7 / 137 (5.11%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	4 / 137 (2.92%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Ingrowing nail			
subjects affected / exposed	3 / 137 (2.19%)		
occurrences (all)	4		
Psoriasis			

subjects affected / exposed	3 / 137 (2.19%)		
occurrences (all)	3		
Rash			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	3 / 137 (2.19%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Arthritis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	3 / 137 (2.19%)		
occurrences (all)	3		
Osteoarthritis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Pain in extremity			

subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Psoriatic arthropathy			
subjects affected / exposed	5 / 137 (3.65%)		
occurrences (all)	5		
Infections and infestations			
Bronchitis			
subjects affected / exposed	6 / 137 (4.38%)		
occurrences (all)	7		
Conjunctivitis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Ear infection			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	3 / 137 (2.19%)		
occurrences (all)	4		
Lower respiratory tract infection			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	16 / 137 (11.68%)		
occurrences (all)	20		
Oral candidiasis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		

Otitis media			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Respiratory tract infection viral			
subjects affected / exposed	3 / 137 (2.19%)		
occurrences (all)	3		
Rhinitis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	4 / 137 (2.92%)		
occurrences (all)	4		
Tonsillitis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	7 / 137 (5.11%)		
occurrences (all)	7		
Urinary tract infection			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences (all)	2		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			

subjects affected / exposed occurrences (all)	0 / 137 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 December 2014	Amendment 1 was primarily issued for the following reasons: To expand the statistical hierarchy (primary plus ranked secondary variables) to include endpoints relevant to determining the overall therapeutic value of a therapy for PsA.
26 May 2016	Amendment 2 was primarily issued for the following reasons: a) Allowing dose escalation of secukinumab administered s.c. every 4 weeks from 150 mg to 300 mg b) Clarification on the duration of contraception
19 September 2016	Amendment 3 was primarily issued to include the correction of typographical and formatting errors and editorial changes for increased clarity of the text.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported