Clinical trial results:
A phase III, randomized, double-blind, placebo-controlled multicenter study of subcutaneous secukinumab (150 mg) in pre-filled syringe, with or without loading regimen, to demonstrate efficacy, safety and tolerability up to 2 years in patients with active psoriatic arthritis (FUTURE 4)

Summary

EudraCT number	2014-003849-10
Trial protocol	SE CZ BE BG DE GB PL FR IT
Global end of trial date	19 December 2017

Results information

Result version number	v1 (current)
This version publication date	24 November 2018
First version publication date	24 November 2018

Trial information

Trial identification

Sponsor protocol code	CAIN457F2336

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02294227
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
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 Pharmaceuticals, 41 613241111, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 December 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate that the efficacy of secukinumab 150 mg sc, with or without loading regimen, at Week 16 was superior to placebo based on proportion of patients achieving American College of Rheumatology 20 (ACR20) response in patients with active PsA. The primary objective was reported in the CAIN457F2336 PsA Interim analyses at Week 52 CSR dated 14-Jun-2017.

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	29 May 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 35
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Bulgaria: 5
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Czech Republic: 51
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 65
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Poland: 62
Country: Number of subjects enrolled	Russian Federation: 29
Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 44
Worldwide total number of subjects	334
EEA total number of subjects	219

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)	309
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

There were 341 patients originally randomized to one of 2 trearment groups. Seven placebo patients discontinued before week 16 an therefore not switched to treatment. Only 334 patients received treatment.

Pre-assignment

Screening details:

Participants were randomized 1:1:1.

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	Investigator, Monitor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab 150 mg

Arm description:

Secukinumab 150 mg s.c. with loading: Secukinumab 150 mg at Baseline, Weeks 1, 2 and 3, followed by dosing every four weeks starting at Week 4. After primary outcome evaluation, approval and implementation of Amendment 2 Secukinumab dose may have been escalated to 300 mg as judged appropriate by the investigator

Arm type	Experimental
Investigational medicinal product name	AIN457F
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

secukinumab 150 mg subcutaneous

Arm title	Secukinumab 150 mg No load

Arm description:

Secukinumab 150 mg s.c. without loading: Secukinumab 150 mg at baseline, followed by dosing every four weeks starting at Week 4, with Placebo at Weeks 1, 2 and 3. After primary outcome evaluation, approval and implementation of Amendment 2 Secukinumab dose may have been escalated to 300 mg as judged appropriate by the investigator

Arm type	Experimental
Investigational medicinal product name	AIN457F
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection, Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Secukinumab 150 mg subcutaneous

Arm title	Placebo

Arm description:

Placebo to Secukinumab at Baseline, Weeks 1, 2 and 3, followed by dosing every four weeks starting at Week 4 until Week 16/24, depending on patients responder status. From Week 16/24, patients were switched to Secukinumab 150 mg every four weeks. After primary outcome evaluation, approval and

implementation of Amendment 2 Secukinumab dose may have been escalated to 300 mg as judged appropriate by the investigator

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

Dosage and administration details:

150 mg subcutaneous injection

Number of subjects in period 1	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo
Started	114	113	107
Completed	89	88	95
Not completed	25	25	12
Adverse event, serious fatal	-	-	1
Physician decision	1	2	1
Adverse event, non-fatal	6	8	2
Subject/Guardian Decision	6	3	2
Lost to follow-up	1	-	-
Lack of efficacy	11	12	6

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab 150 mg
Reporting group description:	
Secukinumab 150 mg s.c. with loading: Secukinumab 150 mg at Baseline, Weeks 1, 2 and 3, followed by dosing every four weeks starting at Week 4. After primary outcome evaluation, approval and implementation of Amendment 2 Secukinumab dose may have been escalated to 300 mg as judged appropriate by the investigator	
Reporting group title	Secukinumab 150 mg No load
Reporting group description:	
Secukinumab 150 mg s.c. without loading: Secukinumab 150 mg at baseline, followed by dosing every four weeks starting at Week 4, with Placebo at Weeks 1, 2 and 3. After primary outcome evaluation, approval and implementation of Amendment 2 Secukinumab dose may have been escalated to 300 mg as judged appropriate by the investigator	
Reporting group title	Placebo
Reporting group description:	
Placebo to Secukinumab at Baseline, Weeks 1, 2 and 3, followed by dosing every four weeks starting at Week 4 until Week 16/24, depending on patients responder status. From Week 16/24, patients were switched to Secukinumab 150 mg every four weeks. After primary outcome evaluation, approval and implementation of Amendment 2 Secukinumab dose may have been escalated to 300 mg as judged appropriate by the investigator	

Reporting group values	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo
Number of subjects	114	113	107
Age categorical			
Actual number of subjects enrolled in the study by age category (Randomized analysis set)			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	106	102	101
From 65-84 years	8	11	6
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	48.3	50.4	48.5
standard deviation	± 12.17	± 11.78	± 12.12
Sex: Female, Male			
Units: Subjects			
Female	47	51	43
Male	67	62	64
Race/Ethnicity, Customized			
Units: Subjects			
Asian|	1	0	0
White|	113	113	107

Reporting group values	Total		
Number of subjects	334		
Age categorical			
Actual number of subjects enrolled in the study by age category (Randomized analysis set)			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	309		
From 65-84 years	25		
85 years and over	0		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Subjects			
Female	141		
Male	193		
Race/Ethnicity, Customized			
Units: Subjects			
Asian|	1		
White|	333		

End points

End points reporting groups

Reporting group title	Secukinumab 150 mg

Reporting group description:

Secukinumab 150 mg s.c. with loading: Secukinumab 150 mg at Baseline, Weeks 1, 2 and 3, followed by dosing every four weeks starting at Week 4. After primary outcome evaluation, approval and implementation of Amendment 2 Secukinumab dose may have been escalated to 300 mg as judged appropriate by the investigator

Reporting group title	Secukinumab 150 mg No load

Reporting group description:

Secukinumab 150 mg s.c. without loading: Secukinumab 150 mg at baseline, followed by dosing every four weeks starting at Week 4, with Placebo at Weeks 1, 2 and 3. After primary outcome evaluation, approval and implementation of Amendment 2 Secukinumab dose may have been escalated to 300 mg as judged appropriate by the investigator

Reporting group title	Placebo

Reporting group description:

Placebo to Secukinumab at Baseline, Weeks 1, 2 and 3, followed by dosing every four weeks starting at Week 4 until Week 16/24, depending on patients responder status. From Week 16/24, patients were switched to Secukinumab 150 mg every four weeks. After primary outcome evaluation, approval and implementation of Amendment 2 Secukinumab dose may have been escalated to 300 mg as judged appropriate by the investigator

Subject analysis set title	Placebo non-responder
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo to Secukinumab at Baseline, Weeks 1, 2 and 3, followed by dosing every four weeks starting at Week 4 until Week 16/24, depending on patients responder status. From Week 16/24, patients were switched to Secukinumab 150 mg every four weeks. After primary outcome evaluation, approval and implementation of Amendment 2 Secukinumab dose may have been escalated to 300 mg as judged appropriate by the investigator

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

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

End point description:

The ACR20 response is defined by at least 20% decrease in the swollen and tender joint count, and at least 20% improvement in 3 of the following 5 criteria: Health Assessment Questionnaire – Diability Index, pain score on a visual analog scale, patient global assessment of disease activity, physician global assessment of disease activity and acute phase reactant [either erythrocyte sedimentation rate (ESR) or high sensitivity C-reactive protein (hsCRP)]. ACR20 is used to assess the efficacy of secukinumab, with or without loading, versus placebo.

End point type	Primary

End point timeframe:

16 weeks

End point values	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	113	107	
Units: Participants	47	45	21	

Statistical analyses

Statistical analysis title	ACR20 comparison between groups at week 16
Comparison groups	Secukinumab 150 mg v Placebo
Number of subjects included in analysis	221
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	3.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.76
upper limit	5.97

Statistical analysis title	ACR20 comparison between groups at 16 weeks
Statistical analysis description: Secukinumab 150 mg No load	
Comparison groups	Secukinumab 150 mg No load v Placebo
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0003
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	3.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.66
upper limit	5.66

Secondary: Disease Activity Score (DAS-C28-CRP) score change from baseline using MMRM at week 16

End point title	Disease Activity Score (DAS-C28-CRP) score change from baseline using MMRM at week 16

End point description:

DAS28-CRP score change from baseline using MMRM up to Week 16. DAS-CRP values range between 2.0 and 10. The higher the score, the higher the disease severity. n: Number of subjects with measures

at both baseline and the corresponding post baseline visit.

End point type	Secondary

End point timeframe:

week 16

End point values	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	113	107	
Units: scores				
least squares mean (standard error)	-0.98 (± 0.106)	-0.84 (± 0.106)	-0.21 (± 0.107)	

Statistical analyses

No statistical analyses for this end point

Secondary: Psoriatic Area and Severity Index 75 (PASI75)

End point title	Psoriatic Area and Severity Index 75 (PASI75)

End point description:

PASI is a measure of disease activity based on extent of the disease, severity of erythema, scaling and thickness in different body areas affected by psoriasis. PASI75 is an improvement in the PASI score of at least 75% compared to baseline. PASI75 is used to assess the efficacy of secukinumab, with or without loading, versus placebo. PASI75 response using non-responder imputation and rescue penalty up to Week 16

End point type	Secondary

End point timeframe:

16 weeks

End point values	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	54	62	
Units: participants	29	27	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Short Form Health Survey Physical Component Score (SF-36-PCS)

End point title	Short Form Health Survey Physical Component Score (SF-36-PCS)[1]

End point description:

The SF-36-PCS is a 36 item questionnaire which measures Quality of Life across 8 domains (assessing both physical and mental health). Two overall summary scores, the Physical Component Summary (PCS) and Mental Component Summary (MCS) can be computed. SF-36-PCS is used to assess the efficacy of secukinumab, with or without loading, versus placebo.

End point type	Secondary

End point timeframe:

16 weeks

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo non-responder	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	114	113	77	
Units: scores				
least squares mean (standard error)	3.42 (± 0.5676)	3.44 (± 0.5678)	0.63 (± 0.586)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with American College of Rheumatology 50 (ACR50)

End point title	Number of participants with American College of Rheumatology 50 (ACR50)

End point description:

The ACR50 response is defined by at least 50% decrease in the swollen and tender joint count, and at least 50% improvement in 3 of the following 5 criteria: Health Assessment Questionnaire, pain score on a visual analog scale, patient global assessment of disease activity, physician global assessment of disease activity and acute phase reactant [either erythrocyte sedimentation rate (ESR) or high sensitivity C-reactive protein (hsCRP)]. ACR50 is used to assess the efficacy of secukinumab, with or without loading, versus placebo. This table is the ACR50 response using non-responder imputation and rescue penalty up to Week 16

End point type	Secondary

End point timeframe:

16 weeks

End point values	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	113	107	
Units: participants	26	19	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with American College of Rheumatology 20 (ACR20) response

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

End point description:

The ACR20 response is defined by at least 20% decrease in the swollen and tender joint count, and at least 20% improvement in 3 of the following 5 criteria: Health Assessment Questionnaire – Diability Index, pain score on a visual analog scale, patient global assessment of disease activity, physician global assessment of disease activity and acute phase reactant [either erythrocyte sedimentation rate (ESR) or high sensitivity C-reactive protein (hsCRP)]. ACR20 is used to assess the efficacy of secukinumab, with or without loading, versus placebo

End point type	Secondary

End point timeframe:

4 weeks

End point values	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	113	107	
Units: participants	33	26	22	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

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	47 / 334 (14.07%)	12 / 136 (8.82%)	59 / 334 (17.66%)
number of deaths (all causes)	1	1	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal adenoma			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
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	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibroma			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	1 / 334 (0.30%)	1 / 136 (0.74%)	2 / 334 (0.60%)
occurrences causally related to treatment / all	1 / 1	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroid tumour benign			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Undifferentiated sarcoma			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			

subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Raynaud's phenomenon			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
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 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
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			
Non-cardiac chest pain			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Immunosuppression			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Nasal turbinate hypertrophy			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Disorientation			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			

subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
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 fastener issue			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
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			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
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 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	1 / 334 (0.30%)	1 / 136 (0.74%)	2 / 334 (0.60%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rib fracture			
subjects affected / exposed	2 / 334 (0.60%)	0 / 136 (0.00%)	2 / 334 (0.60%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	1 / 334 (0.30%)	1 / 136 (0.74%)	2 / 334 (0.60%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	2 / 334 (0.60%)	0 / 136 (0.00%)	2 / 334 (0.60%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Myocardial ischaemia			

subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervicogenic headache			
subjects affected / exposed	0 / 334 (0.00%)	0 / 136 (0.00%)	0 / 334 (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
Facial paralysis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
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	2 / 334 (0.60%)	0 / 136 (0.00%)	2 / 334 (0.60%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			

subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 334 (0.00%)	0 / 136 (0.00%)	0 / 334 (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
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis alcoholic			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric compression			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 334 (0.00%)	0 / 136 (0.00%)	0 / 334 (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
Cervical spinal stenosis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
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 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
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 range of motion decreased			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Loose body in joint			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
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 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	3 / 334 (0.90%)	0 / 136 (0.00%)	3 / 334 (0.90%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyarthritis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriatic arthropathy			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Bacterial pyelonephritis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter gastroenteritis			

subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 334 (0.00%)	0 / 136 (0.00%)	0 / 334 (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
Gastroenteritis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal cyst			
subjects affected / exposed	0 / 334 (0.00%)	0 / 136 (0.00%)	0 / 334 (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
Pyelonephritis			
subjects affected / exposed	0 / 334 (0.00%)	1 / 136 (0.74%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 334 (0.30%)	0 / 136 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	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	5 / 114 (4.39%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal adenoma			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			

subjects affected / exposed	0 / 114 (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 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fibroma				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	0 / 114 (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 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Parathyroid tumour benign				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Undifferentiated sarcoma				

subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Raynaud's phenomenon			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombophlebitis			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Varicose vein			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Immune system disorders			
Immunosuppression			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 114 (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 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nasal turbinate hypertrophy			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Disorientation			

subjects affected / exposed	0 / 114 (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	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Device fastener issue			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laceration			

subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thermal burn				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute myocardial infarction				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				

subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial ischaemia			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cervicogenic headache			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Facial paralysis			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Abdominal hernia				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis ulcerative				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Crohn's disease				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	1 / 114 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Biliary colic				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis alcoholic				

subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ureteric compression			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 114 (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 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cervical spinal stenosis			

subjects affected / exposed	0 / 114 (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 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint range of motion decreased			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Loose body in joint			
subjects affected / exposed	0 / 114 (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 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Polyarthritis			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psoriatic arthropathy			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rotator cuff syndrome			

subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacterial pyelonephritis			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis A			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza			

subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pilonidal cyst				
subjects affected / exposed	1 / 114 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 114 (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 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral upper respiratory tract infection				
subjects affected / exposed	0 / 114 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Hyponatraemia				
subjects affected / exposed	0 / 114 (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	252 / 334 (75.45%)	89 / 136 (65.44%)	267 / 334 (79.94%)
Vascular disorders			
Hypertension			
subjects affected / exposed	28 / 334 (8.38%)	2 / 136 (1.47%)	30 / 334 (8.98%)
occurrences (all)	28	2	30
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 334 (3.89%)	3 / 136 (2.21%)	16 / 334 (4.79%)
occurrences (all)	15	3	18
Oedema peripheral			
subjects affected / exposed	5 / 334 (1.50%)	2 / 136 (1.47%)	7 / 334 (2.10%)
occurrences (all)	5	3	8
Pyrexia			
subjects affected / exposed	11 / 334 (3.29%)	1 / 136 (0.74%)	12 / 334 (3.59%)
occurrences (all)	12	1	13
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	16 / 334 (4.79%)	0 / 136 (0.00%)	16 / 334 (4.79%)
occurrences (all)	19	0	19
Oropharyngeal pain			
subjects affected / exposed	13 / 334 (3.89%)	3 / 136 (2.21%)	16 / 334 (4.79%)
occurrences (all)	18	3	21
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 334 (2.10%)	1 / 136 (0.74%)	8 / 334 (2.40%)
occurrences (all)	11	1	12
Hepatic enzyme increased			
subjects affected / exposed	6 / 334 (1.80%)	2 / 136 (1.47%)	8 / 334 (2.40%)
occurrences (all)	7	2	9
Weight increased			
subjects affected / exposed	6 / 334 (1.80%)	1 / 136 (0.74%)	7 / 334 (2.10%)
occurrences (all)	6	1	7

Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	10 / 334 (2.99%)	1 / 136 (0.74%)	11 / 334 (3.29%)
occurrences (all)	12	1	13
Fall			
subjects affected / exposed	11 / 334 (3.29%)	2 / 136 (1.47%)	13 / 334 (3.89%)
occurrences (all)	14	2	16
Limb injury			
subjects affected / exposed	10 / 334 (2.99%)	1 / 136 (0.74%)	11 / 334 (3.29%)
occurrences (all)	10	2	12
Cardiac disorders			
Ventricular extrasystoles			
subjects affected / exposed	3 / 334 (0.90%)	3 / 136 (2.21%)	6 / 334 (1.80%)
occurrences (all)	3	3	6
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 334 (1.50%)	0 / 136 (0.00%)	5 / 334 (1.50%)
occurrences (all)	6	0	6
Headache			
subjects affected / exposed	25 / 334 (7.49%)	5 / 136 (3.68%)	30 / 334 (8.98%)
occurrences (all)	36	5	41
Migraine			
subjects affected / exposed	6 / 334 (1.80%)	1 / 136 (0.74%)	7 / 334 (2.10%)
occurrences (all)	10	1	11
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	9 / 334 (2.69%)	3 / 136 (2.21%)	12 / 334 (3.59%)
occurrences (all)	16	3	19
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	8 / 334 (2.40%)	1 / 136 (0.74%)	9 / 334 (2.69%)
occurrences (all)	8	1	9
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	10 / 334 (2.99%)	1 / 136 (0.74%)	11 / 334 (3.29%)
occurrences (all)	12	1	13
Diarrhoea			

subjects affected / exposed	29 / 334 (8.68%)	4 / 136 (2.94%)	32 / 334 (9.58%)
occurrences (all)	39	4	43
Dyspepsia			
subjects affected / exposed	6 / 334 (1.80%)	3 / 136 (2.21%)	9 / 334 (2.69%)
occurrences (all)	6	3	9
Nausea			
subjects affected / exposed	19 / 334 (5.69%)	2 / 136 (1.47%)	21 / 334 (6.29%)
occurrences (all)	22	2	24
Toothache			
subjects affected / exposed	3 / 334 (0.90%)	3 / 136 (2.21%)	5 / 334 (1.50%)
occurrences (all)	3	3	6
Vomiting			
subjects affected / exposed	8 / 334 (2.40%)	2 / 136 (1.47%)	10 / 334 (2.99%)
occurrences (all)	8	2	10
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	6 / 334 (1.80%)	2 / 136 (1.47%)	8 / 334 (2.40%)
occurrences (all)	6	2	8
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	7 / 334 (2.10%)	0 / 136 (0.00%)	7 / 334 (2.10%)
occurrences (all)	7	0	7
Pruritus			
subjects affected / exposed	6 / 334 (1.80%)	2 / 136 (1.47%)	8 / 334 (2.40%)
occurrences (all)	6	2	8
Psoriasis			
subjects affected / exposed	7 / 334 (2.10%)	5 / 136 (3.68%)	12 / 334 (3.59%)
occurrences (all)	8	5	13
Rash			
subjects affected / exposed	6 / 334 (1.80%)	2 / 136 (1.47%)	8 / 334 (2.40%)
occurrences (all)	6	2	8
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 334 (3.29%)	4 / 136 (2.94%)	15 / 334 (4.49%)
occurrences (all)	11	4	15
Back pain			

subjects affected / exposed	14 / 334 (4.19%)	2 / 136 (1.47%)	15 / 334 (4.49%)
occurrences (all)	17	3	20
Osteoarthritis			
subjects affected / exposed	7 / 334 (2.10%)	2 / 136 (1.47%)	9 / 334 (2.69%)
occurrences (all)	7	2	9
Pain in extremity			
subjects affected / exposed	6 / 334 (1.80%)	1 / 136 (0.74%)	7 / 334 (2.10%)
occurrences (all)	6	1	7
Psoriatic arthropathy			
subjects affected / exposed	21 / 334 (6.29%)	12 / 136 (8.82%)	28 / 334 (8.38%)
occurrences (all)	28	18	46
Rotator cuff syndrome			
subjects affected / exposed	5 / 334 (1.50%)	2 / 136 (1.47%)	7 / 334 (2.10%)
occurrences (all)	6	2	8
Spinal pain			
subjects affected / exposed	6 / 334 (1.80%)	1 / 136 (0.74%)	7 / 334 (2.10%)
occurrences (all)	8	1	9
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 334 (0.00%)	0 / 136 (0.00%)	0 / 334 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	31 / 334 (9.28%)	8 / 136 (5.88%)	38 / 334 (11.38%)
occurrences (all)	37	10	47
Cystitis			
subjects affected / exposed	7 / 334 (2.10%)	3 / 136 (2.21%)	10 / 334 (2.99%)
occurrences (all)	10	4	14
Furuncle			
subjects affected / exposed	6 / 334 (1.80%)	1 / 136 (0.74%)	7 / 334 (2.10%)
occurrences (all)	6	1	7
Gastroenteritis			
subjects affected / exposed	15 / 334 (4.49%)	5 / 136 (3.68%)	19 / 334 (5.69%)
occurrences (all)	15	6	21
Gastroenteritis viral			
subjects affected / exposed	7 / 334 (2.10%)	1 / 136 (0.74%)	8 / 334 (2.40%)
occurrences (all)	7	1	8

Gingivitis			
subjects affected / exposed	6 / 334 (1.80%)	1 / 136 (0.74%)	7 / 334 (2.10%)
occurrences (all)	7	1	8
Influenza			
subjects affected / exposed	11 / 334 (3.29%)	4 / 136 (2.94%)	14 / 334 (4.19%)
occurrences (all)	16	6	22
Laryngitis			
subjects affected / exposed	5 / 334 (1.50%)	3 / 136 (2.21%)	8 / 334 (2.40%)
occurrences (all)	6	3	9
Nasopharyngitis			
subjects affected / exposed	86 / 334 (25.75%)	21 / 136 (15.44%)	96 / 334 (28.74%)
occurrences (all)	135	28	163
Oral herpes			
subjects affected / exposed	11 / 334 (3.29%)	4 / 136 (2.94%)	13 / 334 (3.89%)
occurrences (all)	15	5	20
Pharyngitis			
subjects affected / exposed	23 / 334 (6.89%)	4 / 136 (2.94%)	25 / 334 (7.49%)
occurrences (all)	32	5	37
Pulpitis dental			
subjects affected / exposed	8 / 334 (2.40%)	2 / 136 (1.47%)	10 / 334 (2.99%)
occurrences (all)	8	2	10
Respiratory tract infection			
subjects affected / exposed	10 / 334 (2.99%)	2 / 136 (1.47%)	11 / 334 (3.29%)
occurrences (all)	12	2	14
Rhinitis			
subjects affected / exposed	9 / 334 (2.69%)	5 / 136 (3.68%)	14 / 334 (4.19%)
occurrences (all)	10	5	15
Sinusitis			
subjects affected / exposed	29 / 334 (8.68%)	11 / 136 (8.09%)	34 / 334 (10.18%)
occurrences (all)	41	13	54
Tonsillitis			
subjects affected / exposed	10 / 334 (2.99%)	6 / 136 (4.41%)	14 / 334 (4.19%)
occurrences (all)	13	6	19
Upper respiratory tract infection			
subjects affected / exposed	48 / 334 (14.37%)	11 / 136 (8.09%)	55 / 334 (16.47%)
occurrences (all)	67	12	79

Urinary tract infection			
subjects affected / exposed	17 / 334 (5.09%)	1 / 136 (0.74%)	18 / 334 (5.39%)
occurrences (all)	20	1	21
Viral infection			
subjects affected / exposed	6 / 334 (1.80%)	2 / 136 (1.47%)	8 / 334 (2.40%)
occurrences (all)	6	2	8
Viral upper respiratory tract infection			
subjects affected / exposed	11 / 334 (3.29%)	2 / 136 (1.47%)	13 / 334 (3.89%)
occurrences (all)	13	2	15
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	9 / 334 (2.69%)	1 / 136 (0.74%)	9 / 334 (2.69%)
occurrences (all)	9	2	11
Hypercholesterolaemia			
subjects affected / exposed	13 / 334 (3.89%)	4 / 136 (2.94%)	17 / 334 (5.09%)
occurrences (all)	13	4	17
Hyperlipidaemia			
subjects affected / exposed	5 / 334 (1.50%)	2 / 136 (1.47%)	7 / 334 (2.10%)
occurrences (all)	5	2	7
Vitamin D deficiency			
subjects affected / exposed	6 / 334 (1.80%)	1 / 136 (0.74%)	7 / 334 (2.10%)
occurrences (all)	6	1	7

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	61 / 114 (53.51%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 114 (3.51%)		
occurrences (all)	4		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 114 (1.75%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		

Pyrexia			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 114 (1.75%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Hepatic enzyme increased			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Limb injury			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Ventricular extrasystoles			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all)	3 / 114 (2.63%) 4		
Headache subjects affected / exposed occurrences (all)	10 / 114 (8.77%) 12		
Migraine subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0		
Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 114 (2.63%) 3		
Dyspepsia subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	6 / 114 (5.26%) 6		
Toothache subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1		
Hepatobiliary disorders			

Hepatic steatosis			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	2 / 114 (1.75%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Psoriasis			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	2 / 114 (1.75%)		
occurrences (all)	2		
Osteoarthritis			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Psoriatic arthropathy			
subjects affected / exposed	5 / 114 (4.39%)		
occurrences (all)	5		
Rotator cuff syndrome			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		
Spinal pain			

subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		
Temporomandibular joint syndrome			
subjects affected / exposed	3 / 114 (2.63%)		
occurrences (all)	3		
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 114 (1.75%)		
occurrences (all)	2		
Cystitis			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Furuncle			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	3 / 114 (2.63%)		
occurrences (all)	3		
Gastroenteritis viral			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Gingivitis			
subjects affected / exposed	2 / 114 (1.75%)		
occurrences (all)	2		
Influenza			
subjects affected / exposed	2 / 114 (1.75%)		
occurrences (all)	2		
Laryngitis			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	16 / 114 (14.04%)		
occurrences (all)	18		
Oral herpes			
subjects affected / exposed	3 / 114 (2.63%)		
occurrences (all)	3		

Pharyngitis			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Pulpitis dental			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		
Respiratory tract infection			
subjects affected / exposed	2 / 114 (1.75%)		
occurrences (all)	2		
Rhinitis			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	6 / 114 (5.26%)		
occurrences (all)	7		
Urinary tract infection			
subjects affected / exposed	4 / 114 (3.51%)		
occurrences (all)	4		
Viral infection			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	4 / 114 (3.51%)		
occurrences (all)	4		
Hypercholesterolaemia			

subjects affected / exposed	1 / 114 (0.88%)		
occurrences (all)	1		
Hyperlipidaemia			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 June 2015	Update to inclusion and exclusion criteria
30 May 2016	Exploratory endpoint added: up-titration

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported