Clinical trial results:
A multicenter, double-blind, randomized withdrawal extension study of subcutaneous secukinumab in prefilled syringes to demonstrate long-term efficacy, safety and tolerability up to 4 years in patients with moderate to severe chronic plaque-type psoriasis completing preceding psoriasis phase III studies with secukinumab

Summary

EudraCT number	2012-000533-39
Trial protocol	IS LV SE LT ES BE EE GB DE FI HU IT PL
Global end of trial date	26 June 2017

Results information

Result version number	v1 (current)
This version publication date	11 July 2018
First version publication date	11 July 2018

Trial information

Trial identification

Sponsor protocol code	CAIN457A2302E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01544595
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	26 June 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate the efficacy of secukinumab 150 mg or 300 mg in patients with moderate to severe chronic plaque-type psoriasis, who were PASI 75 responders at Week 52 of the core study, with respect to loss of PASI 75 up to Week 68 compared to placebo.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 June 2012
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	Argentina: 46
Country: Number of subjects enrolled	Australia: 32
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	Canada: 73
Country: Number of subjects enrolled	Colombia: 21
Country: Number of subjects enrolled	Estonia: 52
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	France: 44
Country: Number of subjects enrolled	Germany: 176
Country: Number of subjects enrolled	United Kingdom: 23
Country: Number of subjects enrolled	Guatemala: 55
Country: Number of subjects enrolled	Hungary: 27
Country: Number of subjects enrolled	Iceland: 55
Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Japan: 70
Country: Number of subjects enrolled	Korea, Republic of: 36
Country: Number of subjects enrolled	Latvia: 36
Country: Number of subjects enrolled	Lithuania: 23

Country: Number of subjects enrolled	Poland: 64
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Singapore: 3
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	Sweden: 6
Country: Number of subjects enrolled	Taiwan: 43
Country: Number of subjects enrolled	United States: 215
Worldwide total number of subjects	1146
EEA total number of subjects	538

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)	1055
From 65 to 84 years	91
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Among the 1146 patients who completed the screening phase, 995 “PASI 75 responder at week 52” patients were randomized in a double blind fashion to either active treatment or placebo & entered the randomized withdrawal period and 151 “partial responders at week 52" patients entered treatment period of the Extension.

Pre-assignment

Screening details:

1366 patients who completed the core studies (CAIN457A2302 or CAIN457A2303) and provided consent for participation in the extension study were screened, and 1146 (83.9%) completed the screening phase and entered the extension.

Period 1

Period 1 title	Status at Week 68
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Data analyst, Assessor, Subject

Blinding implementation details:

Randomised-Controlled

Arms

Are arms mutually exclusive?	No
Arm title	AIN457 150 mg –Randomized withdrawal period

Arm description:

PASI 75 responders at Week 52, treated with AIN 150 mg in core study and randomized to AIN150 mg

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

Dosage and administration details:

Secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration. The 150 mg/1 mL solution in PFS was used for s.c. 150 mg dose (1 syringe)

Arm title	AIN457 300 mg –Randomized withdrawal period

Arm description:

PASI 75 responders at Week 52, treated with AIN 300 mg in core study and randomized to AIN300 mg

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

Dosage and administration details:

Secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration. The 150 mg/1 mL solution in PFS was used for s.c. 300 mg dose (2 syringes)

Arm title	AIN457 150 mg Placebo - Randomized withdrawal period

Arm description:

PASI 75 responders at Week 52, treated with AIN 150 mg in core study and randomized to placebo

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

Dosage and administration details:

Secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration during the core study and randomized to placebo at week 52. Placebo secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration.

Arm title	AIN457 300 mg Placebo - Randomized withdrawal period

Arm description:

PASI 75 responders at Week 52, treated with AIN 300 mg in core study and randomized to placebo

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

Dosage and administration details:

Secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration (The 150 mg/1 mL solution in PFS was used for s.c. 300 mg dose (2 syringes)) during the core study and randomized to placebo at week 52. Placebo secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration.

Number of subjects in period 1	AIN457 150 mg –Randomized withdrawal period	AIN457 300 mg –Randomized withdrawal period	AIN457 150 mg Placebo - Randomized withdrawal period
Started	301	363	150
Completed	262	346	87
Not completed	39	17	63
Consent withdrawn by subject	-	1	1
Adverse event, non-fatal	3	2	1
Technical problems	1	-	-
Non-compliance with study treatment	1	-	-
Moved to treatment period ≤ wk 68	30	13	60
Lost to follow-up	1	1	-
Lack of efficacy	1	-	-
Protocol deviation	2	-	1

Number of subjects in period 1	AIN457 300 mg Placebo - Randomized withdrawal period
Started	181
Completed	130
Not completed	51

Consent withdrawn by subject	2
Adverse event, non-fatal	-
Technical problems	1
Non-compliance with study treatment	1
Moved to treatment period ≤ wk 68	46
Lost to follow-up	-
Lack of efficacy	-
Protocol deviation	1

Period 2

Period 2 title	Status at Week 156
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	AIN457 150 mg –Randomized withdrawal period

Arm description:

PASI 75 responders at Week 52, treated with AIN 150 mg in core study and randomized to AIN150 mg

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

Dosage and administration details:

Secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration. The 150 mg/1 mL solution in PFS was used for s.c. 150 mg dose (1 syringe)

Arm title	AIN457 300 mg –Randomized withdrawal period

Arm description:

PASI 75 responders at Week 52, treated with AIN 300 mg in core study and randomized to AIN300 mg

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

Dosage and administration details:

Secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration. The 150 mg/1 mL solution in PFS was used for s.c. 300 mg dose (2 syringes)

Arm title	AIN457 150 mg Placebo - Randomized withdrawal period

Arm description:

PASI 75 responders at Week 52, treated with AIN 150 mg in core study and randomized to placebo

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

Dosage and administration details:

Secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration during the core study and randomized to placebo at week 52. Placebo secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration.

Arm title	AIN457 300 mg Placebo - Randomized withdrawal period

Arm description:

PASI 75 responders at Week 52, treated with AIN 300 mg in core study and randomized to placebo

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

Dosage and administration details:

Secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration (The 150 mg/1 mL solution in PFS was used for s.c. 300 mg dose (2 syringes)) during the core study and randomized to placebo at week 52. Placebo secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration.

Arm title	AIN457 150 mg - Partial responders

Arm description:

PASI 50 responders / PASI 75 non responders at Week 52, treated with AIN 150 mg in core and extension study

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

Dosage and administration details:

Secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration. The 150 mg/1 mL solution in PFS was used for s.c. 150 mg dose (1 syringe)

Arm title	AIN457 300 mg - Partial responders

Arm description:

PASI 50 responders / PASI 75 non responders at Week 52, treated with AIN 300 mg in core and extension study

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

Dosage and administration details:

Secukinumab 150 mg/1 mL solution for injection was provided in PFS for s.c. administration. The 150 mg/1 mL solution in PFS was used for s.c. 300 mg dose (2 syringes)

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Partial responder patients were not in 2 arms in period 1 (Week 68). These patients were part of another arm at this time.

Number of subjects in period 2	AIN457 150 mg –Randomized withdrawal period	AIN457 300 mg –Randomized withdrawal period	AIN457 150 mg Placebo - Randomized withdrawal period
Started	301	363	150
Completed	184	285	10
Not completed	117	78	140
Consent withdrawn by subject	9	10	4
Physician decision	-	3	1
Adverse event, non-fatal	9	11	1
Technical problems	3	1	-
Moved to treatment period ≤ wk 156	86	44	131
Non-compliance with study treatement	-	1	-
Pregnancy	2	3	-
Lost to follow-up	4	4	-
Protocol deviation	3	1	2
Lack of efficacy	1	-	1

Number of subjects in period 2	AIN457 300 mg Placebo - Randomized withdrawal period	AIN457 150 mg - Partial responders	AIN457 300 mg - Partial responders
Started	181	98	53
Completed	15	60	38
Not completed	166	38	15
Consent withdrawn by subject	9	20	6
Physician decision	-	-	-
Adverse event, non-fatal	3	4	2
Technical problems	1	-	-
Moved to treatment period ≤ wk 156	145	-	-
Non-compliance with study treatement	1	-	1
Pregnancy	-	-	-
Lost to follow-up	1	4	1
Protocol deviation	2	-	-
Lack of efficacy	4	10	5

Baseline characteristics

Reporting groups	
Reporting group title	AIN457 150 mg –Randomized withdrawal period
Reporting group description:	
PASI 75 responders at Week 52, treated with AIN 150 mg in core study and randomized to AIN150 mg	
Reporting group title	AIN457 300 mg –Randomized withdrawal period
Reporting group description:	
PASI 75 responders at Week 52, treated with AIN 300 mg in core study and randomized to AIN300 mg	
Reporting group title	AIN457 150 mg Placebo - Randomized withdrawal period
Reporting group description:	
PASI 75 responders at Week 52, treated with AIN 150 mg in core study and randomized to placebo	
Reporting group title	AIN457 300 mg Placebo - Randomized withdrawal period
Reporting group description:	
PASI 75 responders at Week 52, treated with AIN 300 mg in core study and randomized to placebo	
Reporting group title	AIN457 150 mg - Partial responders
Reporting group description:	
PASI 50 responders / PASI 75 non responders at Week 52, treated with AIN 150 mg in core and extension study	
Reporting group title	AIN457 300 mg - Partial responders
Reporting group description:	
PASI 50 responders / PASI 75 non responders at Week 52, treated with AIN 300 mg in core and extension study	

Reporting group values	AIN457 150 mg –Randomized withdrawal period	AIN457 300 mg –Randomized withdrawal period	AIN457 150 mg Placebo - Randomized withdrawal period
Number of subjects	301	363	150
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	45.9	45.8	47.1
standard deviation	± 12.93	± 12.92	± 13.34
Sex: Female, Male			
Units: Subjects			
Female	83	102	45
Male	218	261	105
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian	213	276	115
Black	4	4	2
Asian	52	50	22
Native American	24	23	9
Pacific Islander	1	2	0
Unknown	0	1	1
Other	7	7	1

Reporting group values	AIN457 300 mg Placebo - Randomized withdrawal period	AIN457 150 mg - Partial responders	AIN457 300 mg - Partial responders
Number of subjects	181	98	53
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	45.4	46.8	48.5
standard deviation	± 13.09	± 12.78	± 11.98
Sex: Female, Male Units: Subjects			
Female	62	28	10
Male	119	70	43
Race/Ethnicity, Customized Units: Subjects			
Caucasian	136	73	42
Black	3	4	1
Asian	24	17	8
Native American	15	2	2
Pacific Islander	1	1	0
Unknown	1	0	0
Other	1	1	0

Reporting group values	Total		
Number of subjects	1146		
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	330		
Male	816		
Race/Ethnicity, Customized Units: Subjects			
Caucasian	855		
Black	18		
Asian	173		
Native American	75		
Pacific Islander	5		
Unknown	3		
Other	17		

End points

End points reporting groups

Reporting group title	AIN457 150 mg –Randomized withdrawal period
Reporting group description: PASI 75 responders at Week 52, treated with AIN 150 mg in core study and randomized to AIN150 mg	
Reporting group title	AIN457 300 mg –Randomized withdrawal period
Reporting group description: PASI 75 responders at Week 52, treated with AIN 300 mg in core study and randomized to AIN300 mg	
Reporting group title	AIN457 150 mg Placebo - Randomized withdrawal period
Reporting group description: PASI 75 responders at Week 52, treated with AIN 150 mg in core study and randomized to placebo	
Reporting group title	AIN457 300 mg Placebo - Randomized withdrawal period
Reporting group description: PASI 75 responders at Week 52, treated with AIN 300 mg in core study and randomized to placebo	
Reporting group title	AIN457 150 mg –Randomized withdrawal period
Reporting group description: PASI 75 responders at Week 52, treated with AIN 150 mg in core study and randomized to AIN150 mg	
Reporting group title	AIN457 300 mg –Randomized withdrawal period
Reporting group description: PASI 75 responders at Week 52, treated with AIN 300 mg in core study and randomized to AIN300 mg	
Reporting group title	AIN457 150 mg Placebo - Randomized withdrawal period
Reporting group description: PASI 75 responders at Week 52, treated with AIN 150 mg in core study and randomized to placebo	
Reporting group title	AIN457 300 mg Placebo - Randomized withdrawal period
Reporting group description: PASI 75 responders at Week 52, treated with AIN 300 mg in core study and randomized to placebo	
Reporting group title	AIN457 150 mg - Partial responders
Reporting group description: PASI 50 responders / PASI 75 non responders at Week 52, treated with AIN 150 mg in core and extension study	
Reporting group title	AIN457 300 mg - Partial responders
Reporting group description: PASI 50 responders / PASI 75 non responders at Week 52, treated with AIN 300 mg in core and extension study	
Subject analysis set title	AIN457 150 mg only
Subject analysis set type	Full analysis
Subject analysis set description: Patients staying strictly on AIN457 150mg from Week 52	
Subject analysis set title	AIN457 300 mg only
Subject analysis set type	Full analysis
Subject analysis set description: Patients staying strictly on AIN457 300mg from Week 52	
Subject analysis set title	Placebo - AIN457 150 mg
Subject analysis set type	Full analysis
Subject analysis set description: Patients randomized to placebo at Week 52, treated with AIN457 150mg after they relapsed	
Subject analysis set title	Placebo - AIN457 300 mg
Subject analysis set type	Full analysis
Subject analysis set description: Patients randomized to placebo at Week 52, treated with AIN457 300mg after they relapsed	

Subject analysis set title	Any AIN457 150 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety data from patients while on AIN457 150 mg	
Subject analysis set title	Any AIN457 300 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety data from patients while on AIN457 300 mg	
Subject analysis set title	Any AIN457
Subject analysis set type	Safety analysis
Subject analysis set description:	
safety data from patients while on any dose of AIN457	

Primary: Subjects with Loss of Psoriasis Area and Severity Index (PASI) 75 response up to Week 68

End point title	Subjects with Loss of Psoriasis Area and Severity Index (PASI) 75 response up to Week 68
End point description:	
The primary variable was the cumulative rate of patients who lost PASI 75 response up to Week 68 (time=0 being defined as Week 52). Loss of PASI 75 response was analyzed by means of a survival analysis defining "loss of PASI 75 response" as "failure". The term cumulative rate corresponded to 1 minus the survival function within this survival analysis, and the cumulative rate and the survival functions were dependent on time t. PASI 75 response: patients achieving ≥ 75% improvement (reduction) in PASI score compared to baseline of the core study were defined as PASI 75 responders.	
End point type	Primary
End point timeframe:	
At week 68 (16 weeks after week 52)	

End point values	AIN457 150 mg –Randomized withdrawal period	AIN457 300 mg –Randomized withdrawal period	AIN457 150 mg Placebo - Randomized withdrawal period	AIN457 300 mg Placebo - Randomized withdrawal period
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	297	363	150	180
Units: cumulative rate				
number (confidence interval 95%)	49.8 (25.8 to 79.7)	25.4 (9.8 to 56.5)	74.3 (56.9 to 88.8)	64.7 (52.0 to 77.2)

Statistical analyses

Statistical analysis title	Cumulative rate of PASI response
Statistical analysis description:	
The following hypotheses were tested for 52 weeks≤ t ≤68 weeks • H1: p1(t) – p0,1(t) = 0 versus HA1: p1(t)– p0,1(t) ≥ 0, • H2: p2(t) – p0,2(t) = 0 versus HA2: p2(t) – p0,2(t) ≥ 0,	
Comparison groups	AIN457 150 mg –Randomized withdrawal period v AIN457 150 mg Placebo - Randomized withdrawal period

Number of subjects included in analysis	447
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	0.42

Statistical analysis title	Cumulative rate of PASI response
Statistical analysis description:	
The following hypotheses were tested for 52 weeks≤ t ≤68 weeks • H1: p1(t) – p0,1(t) = 0 versus HA1: p1(t)– p0,1(t) ≥ 0, • H2: p2(t) – p0,2(t) = 0 versus HA2: p2(t) – p0,2(t) ≥ 0,	
Comparison groups	AIN457 300 mg –Randomized withdrawal period v AIN457 300 mg Placebo - Randomized withdrawal period
Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	0.29

Secondary: Number of participants with PASI 50, PASI 75, PASI 90, PASI 100 and IGA mod 2011 0 or 1 (observed data) - randomized withdrawal period

End point title	Number of participants with PASI 50, PASI 75, PASI 90, PASI 100 and IGA mod 2011 0 or 1 (observed data) - randomized withdrawal period
End point description:	
Psoriasis Area and Severity Index (PASI) 75 responder at week 52. Patients in the placebo groups were not evaluable after re-treatment with Secukinumab. PASI 75 Responders: patients with a PASI 75 response (patients achieving ≥75% improvement [reduction] in PASI score compared to baseline of the core study). PASI 50 response: patients achieving ≥ 50% improvement (reduction) in PASI score compared to baseline of the core study were defined as PASI 50 responders. PASI 90 response: patients achieving ≥ 90% improvement (reduction) in PASI score compared to baseline of the core study were defined as PASI 90 responders. PASI 100 response/remission: complete clearing of psoriasis (PASI=0)	
End point type	Secondary
End point timeframe:	
Week 52, 104, and 156	

End point values	AIN457 150 mg –Randomized withdrawal period	AIN457 300 mg –Randomized withdrawal period	AIN457 150 mg Placebo - Randomized withdrawal period	AIN457 300 mg Placebo - Randomized withdrawal period
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	297	363	150	180
Units: Number of participants				
Wk 52 - IGA 0/1|	208	309	112	157
Wk 52 - PASI 50|	297	363	149	180
Wk 52 - PASI 75|	296	361	149	179
Wk 52 - PASI 90|	190	303	105	156
Wk 52 - PASI 100|	93	191	54	96
Wk 104 - IGA 0/1 (n=260, 338, 20, 34)|	128	236	8	13
Wk 104 - PASI 50 (n=260, 338, 20,34)|	254	329	19	28
Wk 104 - PASI 75 (n=260, 338, 20,34)|	209	299	15	21
Wk 104 - PASI 90 (n=260, 338, 20,34)|	125	240	6	13
Wk 104 - PASI 100 (n=260, 338, 20,34)|	65	151	4	6
Wk 156 - IGA 0/1 (n=239, 324, 10,15)|	90	202	4	7
Wk 156 - PASI 50 (n=239, 324, 10,15)|	230	322	10	15
Wk 156 - PASI 75 (n=239, 324, 10,15)|	183	287	6	13
Wk 156 - PASI 90 (n=239, 324, 10,15)|	101	207	4	7
Wk 156 - PASI 100 (n=239, 324, 10,15)|	47	117	2	5

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participant with PASI 50, PASI 75, PASI 90, and PASI 100 (observed data) - entire study period

End point title	Number of participant with PASI 50, PASI 75, PASI 90, and PASI 100 (observed data) - entire study period

End point description:

Psoriasis Area and Severity Index (PASI) scoring system: The average degree of severity of each sign in each of the four body regions was assigned a score of 0-4. The area covered by lesions on each body region was estimated as a percentage of the total area of that particular body region.

End point type	Secondary

End point timeframe:

Week 52, Week 104, Week 156, week 208, week 260

End point values	AIN457 150 mg only	AIN457 300 mg only		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	164	416		
Units: Number of participants				
Wk 52 - PASI 50|	164	416		
Wk 52 - PASI 75|	121	361		
Wk 52 - PASI 90|	85	303		
Wk 52 - PASI 100|	54	191		
Wk 104 - PASI 50 (n=104, 377)|	99	359		
Wk 104 - PASI 75 (n=104, 377)|	76	314		
Wk 104 - PASI 90 (n=104, 377)|	62	243		
Wk 104 - PASI 100 (n=104, 377)|	46	153		
Wk 156 - PASI 50 (n=69, 361)|	67	351		
Wk 156 - PASI (n=69, 361)|	63	297		
Wk 156 - PASI 90 (n=69, 361)|	52	211		
Wk 156 - PASI 100 (n=69, 361)|	37	118		
Wk 208 - PASI 50 (n=58, 323)|	58	316		
Wk 208 - PASI 75 (n=58, 323)|	55	269		
Wk 208 - PASI 90 (n=58, 323)|	51	194		
Wk 208 - PASI 100 (n=58, 323)|	33	104		
Wk 260 - PASI 50 (n=51, 285)|	51	279		
Wk 260 - PASI 75 (n=51, 285)|	49	231		
Wk 260 - PASI 90 (n=51, 285)|	37	179		
Wk 260 - PASI 100 (n=51, 285)|	26	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline for PASI score over time (observed data) - Randomized withdrawal period

End point title	Percent change from baseline for PASI score over time (observed data) - Randomized withdrawal period

End point description:

The improvement (decrease from baseline) in PASI total scores observed at Week 52. Perc. change = 100 x Abs. change /Base. (Abs. change = Post - Base) For each post-baseline visit only patients with a value at both baseline and the respective post-baseline visit are included.

End point type	Secondary

End point timeframe:

Week 52, 104, and 156

End point values	AIN457 150 mg –Randomized withdrawal period	AIN457 300 mg –Randomized withdrawal period	AIN457 150 mg Placebo - Randomized withdrawal period	AIN457 300 mg Placebo - Randomized withdrawal period
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	297	363	150	180
Units: Percent change in PASI score				
arithmetic mean (standard deviation)				
Week 52 (baseline)|	-92.31 (± 7.878)	-95.98 (± 6.638)	-92.88 (± 8.435)	-96.16 (± 6.030)
Week 104 (n=260, 338, 20, 34)|	-85.88 (± 14.631)	-91.51 (± 13.221)	-82.67 (± 15.568)	-78.04 (± 20.986)
Week 156 (n=239, 324, 10, 15)|	-83.32 (± 17.341)	-90.50 (± 11.660)	-79.77 (± 15.172)	-86.35 (± 15.602)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline for PASI score over time (observed data) - entire study period

End point title	Percent change from baseline for PASI score over time (observed data) - entire study period

End point description:

Perc. change = 100 x Abs. change /Base. (Abs. change = Post - Base) For each post-baseline visit only patients with a value at both baseline and the respective post-baseline visit are included.

End point type	Secondary

End point timeframe:

Week 52, Week 104, Week 156, week 208, week 260

End point values	AIN457 150 mg only	AIN457 300 mg only		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	164	416		
Units: Percent change in PASI score				
arithmetic mean (standard deviation)				
Wk 52|	-85.93 (± 14.815)	-91.82 (± 11.889)		
Wk 104 (n=104, 377)|	-85.97 (± 18.811)	-88.86 (± 16.151)		
Wk 156 (n=69, 361)|	-93.03 (± 12.338)	-87.78 (± 15.114)		
Wk 208 (n=58, 323)|	-95.71 (± 7.868)	-88.25 (± 14.496)		
Wk 260 (n=51, 285)|	-93.65 (± 9.959)	-88.08 (± 14.983)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants in each IGA mod 2011 category (observed data)- randomized withdrawal period

End point title	Number of participants in each IGA mod 2011 category (observed data)- randomized withdrawal period

End point description:

Investigator Global Assessment (IGA) mod 2011; scale from 0 - 4. Score 0: Clear (No signs of psoriasis. Post-inflammatory hyperpigmentation could be Present). Score 1: Almost clear (Normal to pink coloration of lesions; no thickening; no to minimal focal scaling), Score 2: Mild (Pink to light red coloration; just detectable to mild thickening; predominantly fine scaling). Score 3: Moderate (Dull bright red, clearly distinguishable erythema; clearly distinguishable to moderate thickening; moderate scaling). Score 4: Severe (Bright to deep dark red coloration; severe thickening with hard edges; severe /coarse scaling covering almost all or all lesions). Patients in the placebo groups were not evaluable after re-treatment with Secukinumab

End point type	Secondary

End point timeframe:

Week 52 (baseline), 104, and 156

End point values	AIN457 150 mg –Randomized withdrawal period	AIN457 300 mg –Randomized withdrawal period	AIN457 150 mg Placebo - Randomized withdrawal period	AIN457 300 mg Placebo - Randomized withdrawal period
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	297	363	150	180
Units: Number of participants				
Wk 52 - clear|	95	188	56	94
Wk 52 - almost clear|	113	121	56	63
Wk 52 - mild|	75	44	33	22
Wk 52 - moderate|	14	9	4	1
Wk 52 - severe|	0	1	1	0
Wk 104 - clear (n=260, 338, 20, 34)|	66	152	3	4
Wk 104 - almost clear (n=260, 338, 20, 34)|	62	84	5	9
Wk 104 - mild v(n=260, 338, 20, 34)|	78	64	9	9
Wk 104 - moderate (n=260, 338, 20, 34)|	47	33	3	10
Wk 104 - severe (n=260, 338, 20, 34)|	7	5	0	2
Wk 156 - clear (n=239, 324, 10, 15)|	48	115	2	4
Wk 156 - almost clear (n=239, 324, 10, 15)|	42	87	2	3
Wk 156 - mild (n=239, 324, 10, 15)|	88	78	2	5
Wk 156 - moderate (n=239, 324, 10, 15)|	59	43	4	2
Wk 156 - severe (n=239, 324, 10, 15)|	2	1	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants in each IGA mod 2011 category (observed data) - entire study period

End point title	Number of participants in each IGA mod 2011 category (observed data) - entire study period

End point description:

Investigator's Global Assessment (IGA) mod 2011; scale from 0 - 4. Score 0= clear (no signs of psoriasis) Score 1 = almost clear no to minimal local scaling) Score 2 = mild (predominantly fine scaling) Score 3 = moderate (moderate scaling) Score 4 = severe (severe/coarse scaling covering almost all or all lesions)

End point type	Secondary

End point timeframe:

Week 52, Week 104, Week 156, week 208, week 260

End point values	AIN457 150 mg only	AIN457 300 mg only		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	164	416		
Units: Number of participants				
Wk 52 - clear|	56	188		
Wk 52 - almost clear|	38	123		
Wk 52 - mild|	44	71		
Wk 52 - moderate|	26	32		
Wk 52 - severe|	0	2		
Wk 104 - clear (n=104, 377)|	47	154		
Wk 104 - almost clear (n=104, 377)|	16	85		
Wk 104 - mild (n=104, 377)|	17	80		
Wk 104 - moderate (n=104, 377)|	19	51		
Wk 104 - severe (n=104, 377)|	5	7		
Wk 156 - clear (n=104, 377)|	37	116		
Wk 156 - almost clear (n=69, 361)|	13	90		
Wk 156 - mild (n=69, 361)|	11	91		
Wk 156 - moderate (n=69, 361)|	8	61		
Wk 156 - severe (n=69, 361)|	0	3		
Wk 208 - clear (n=58, 323)|	33	102		
Wk 208 - almost clear (n=58, 323)|	14	81		
Wk 208 - mild (n=58, 323)|	7	88		
Wk 208 - moderate (n=58, 323)|	3	47		
Wk 208 - severe (n=58, 323)|	1	5		
Wk 260 - clear (n=51, 285)|	27	97		
Wk 260 - almost clear (n=51, 285)|	12	65		
Wk 260 - mild (n=51, 285)|	8	66		
Wk 260 - moderate (n=51, 285)|	4	53		
Wk 260 - severe (n=51, 285)|	0	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with IGA mod 2011 0/1 response (observed data) - entire study period

End point title	Number of participants with IGA mod 2011 0/1 response (observed data) - entire study period

End point description:

Investigator's Global Assessment (IGA) mod 2011 0/1. Score 0= clear (no signs of psoriasis) Score 1 = almost clear no to minimal local scaling) Score 2 = mild (predominantly fine scaling) Score 3 = moderate (moderate scaling) Score 4 = severe (severe/coarse scaling covering almost all or all lesions) Based on this scale, a patient was considered as IGA mod 2011 0/1 responder if the patient achieved a score of 0 or 1 and improved by at least 2 points on the IGA scale compared to baseline.

End point type	Secondary

End point timeframe:

Week 52, Week 104, Week 156, week 208, week 260

End point values	AIN457 150 mg only	AIN457 300 mg only		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	164	416		
Units: Number of participants				
Wk 52|	94	311		
Wk 104 (n=104, 377)|	63	239		
Wk 156 (n=69, 361)|	50	206		
Wk 208 (n=58, 323)|	47	183		
Wk 260 (n=51, 285)|	39	162		

Statistical analyses

No statistical analyses for this end point

Secondary: Loss of IGA mod 2011 0 or 1 response over time for subjects with IGA mod 2011 0 or 1 response at Week 52 - randomized withdrawal period

End point title	Loss of IGA mod 2011 0 or 1 response over time for subjects with IGA mod 2011 0 or 1 response at Week 52 - randomized withdrawal period

End point description:

Summary for loss of IGA mod 2011 0 or 1 response over time for patients with response at Week 52. time = 0 refers to Week 52

End point type	Secondary

End point timeframe:

Week 68

End point values	AIN457 150 mg –Randomized withdrawal period	AIN457 300 mg –Randomized withdrawal period	AIN457 150 mg Placebo - Randomized withdrawal period	AIN457 300 mg Placebo - Randomized withdrawal period
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	297	363	150	180
Units: Loss of IGA mod 2011 0 or 1 response				
number (confidence interval 95%)	38.1 (29.8 to 47.7)	33.4 (25.7 to 42.6)	82.1 (71.2 to 90.8)	65.5 (53.8 to 77.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PASI 75 response - treatment period for re-treated after relapse

End point title	Time to PASI 75 response - treatment period for re-treated after relapse

End point description:

PASI 75 response since reinitiating treatment after relapse. time = 0 refers to Week 52

End point type	Secondary

End point timeframe:

up to week 260

End point values	Placebo - AIN457 150 mg	Placebo - AIN457 300 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	131	145		
Units: PASI 75 response				
number (confidence interval 95%)				
0 to <=4 wks|	38.5 (30.7 to 47.4)	51.0 (43.2 to 59.5)		
>12 to <=16 wks (n=21,13)|	91.2 (85.5 to 95.3)	95.1 (90.7 to 97.8)		
>80 to <=84 wks (n=2,1)|	96.8 (92.6 to 98.9)	98.8 (94.8 to 99.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to IGA mod 0 or 1 response - treatment period for re-treated after relapse

End point title	Time to IGA mod 0 or 1 response - treatment period for re-treated after relapse

End point description:
IGA mod 2011 0 or 1 response since reinitiating treatment after relapse for subjects with IGA 0 or 1 response at week 52 and not have IGA 0 or 1 response at relapse. time = 0 refers to Week 52

End point type	Secondary

End point timeframe:
up to week 260

End point values	Placebo - AIN457 150 mg	Placebo - AIN457 300 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	131	145		
Units: IGA 0 or 1 response				
number (confidence interval 95%)				
0 to <=4 wks (n=96,123)|	12.5 (7.3 to 21.0)	28.1 (21.0 to 37.0)		
>12 to <=16 wks (n=40,32)|	75.0 (66.0 to 83.1)	83.5 (76.3 to 89.4)		
>84 to <=88 wks (n=7,4)|	87.9 (80.0 to 93.8)	90.8 (84.5 to 95.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse over time - randomized withdrawal period

End point title	Relapse over time - randomized withdrawal period

End point description:
Time 0 = week 52

End point type	Secondary

End point timeframe:
up to week 156

End point values	AIN457 150 mg –Randomized withdrawal period	AIN457 300 mg –Randomized withdrawal period	AIN457 150 mg Placebo - Randomized withdrawal period	AIN457 300 mg Placebo - Randomized withdrawal period
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	297	363	150	180
Units: Relapse				
number (confidence interval 95%)				
0 to <=4 wks (n=286,353,150,180)|	0.3 (0.0 to 2.4)	0.3 (0.0 to 1.9)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)
>12 to <=16 wks (n=297,363,124,160)|	3.1 (1.6 to 5.9)	2.2 (1.1 to 4.4)	19.8 (13.9 to 27.7)	12.1 (8.0 to 18.1)
>92 to <=96 wks (n=188,292,11,15)|	21.5 (16.9 to 27.0)	9.4 (6.8 to 13.1)	88.1 (80.9 to 93.5)	86.1 (79.6 to 91.4)

>104 to <=108 wks (n=156,297,8,9)|	21.9 (17.3 to 27.5)	9.4 (6.8 to 13.1)	88.1 (80.9 to 93.5)	86.1 (79.6 to 91.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants experiencing relapse after last injection

End point title	Percentage of participants experiencing relapse after last injection

End point description:

Relapse: when the achieved maximal PASI improvement from baseline of core study was reduced by >50%. Time 0 = week 52

End point type	Secondary

End point timeframe:

up to week 16

End point values	AIN457 150 mg only	AIN457 300 mg only		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	164	416		
Units: relapses				
number (confidence interval 95%)				
0 to <=4 wks (n=158,415)|	7.2 (4.0 to 12.6)	2.0 (1.0 to 3.9)		
>12 to <=16 wks (n=66,208)|	34.0 (22.6 to 48.9)	28.4 (21.8 to 36.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants experiencing rebound after last injection

End point title	Percentage of participants experiencing rebound after last injection

End point description:

Rebound: PASI increases to > 125% of baseline (where baseline is the PASI at the randomization of the core study) or presence of new pustular psoriasis, new erythrodermic psoriasis or more inflammatory psoriasis occurring within 8 Weeks of stopping therapy (after the last dose of study treatment received). Rebound like event (RLE) was defined as increase of PASI of > 125% from baseline value or occurrence of new pustular, new erythrodermic or more inflammatory psoriasis any time after stopping therapy (last treatment administered) up to Week 68. Rebound was evaluated for the patients randomized to the placebo groups in the extension study; hence these patients received the last dose of secukinumab during the core studies.

End point type	Secondary

End point timeframe:

up to week 68

End point values	AIN457 150 mg only	AIN457 300 mg only		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	164	416		
Units: Percentage of participants				
number (confidence interval 95%)				
Rebound (<8 wks after last inj.; n=108,320)|	8.3 (4.1 to 15.6)	6.6 (4.2 to 10.0)		
RLE (< 12 wks after last inj., n=110,326)|	11.8 (6.7 to 19.7)	9.5 (6.7 to 13.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with Dermatology Life Quality Index response (DLQI 0 or 1) - randomized withdrawal period (observed data)

End point title	Number of patients with Dermatology Life Quality Index response (DLQI 0 or 1) - randomized withdrawal period (observed data)

End point description:

Dermatology Life Quality Index (DLQI) scores range from 0 to 30. Lower absolute scores on DLQI indicate better/improved health-related quality-of life impairment.

End point type	Secondary

End point timeframe:

Week 52 (baseline), 64, 76, 88, 104, 116, 128, 140, and 156

End point values	AIN457 150 mg –Randomized withdrawal period	AIN457 300 mg –Randomized withdrawal period	AIN457 150 mg Placebo - Randomized withdrawal period	AIN457 300 mg Placebo - Randomized withdrawal period
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	295	359	150	180
Units: Number of participants				
Week 52 (baseline)|	196	281	109	142
Week 64 (n=290,357,126,162)|	170	265	59	90
Week 76 (n=284,352,71,104)|	163	256	26	38
Week 88 (n=281,346,34,62)|	157	247	18	24
Week 104 (n=262,337,21,35)|	146	237	10	14
Week 116 (n=252,326,16,24)|	141	230	6	9
Week 128 (n=251,326,14,19)|	139	222	4	10
Week 140 (n=241,327,12,18)|	126	229	4	7
Week 156 (n=240,324,11,15)|	119	215	5	8

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Dermatology Life Quality Index response (DLQI 0 or 1) - entire treatment period

End point title	Number of subjects with Dermatology Life Quality Index response (DLQI 0 or 1) - entire treatment period

End point description:

Dermatology Life Quality Index (DLQI) scores range from 0 to 30. Lower absolute scores on DLQI indicate better/improved health-related quality-of life impairment.

End point type	Secondary

End point timeframe:

Week 52 (baseline), 64, 76, 88, 104, 116, 128, 140, and 156

End point values	AIN457 150 mg only	AIN457 300 mg only		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	164	416		
Units: Number of participants				
Week 52 (baseline, n=162,95)|	95	299		
Week 104 (n=113, 377)|	66	254		
week 156 (n=69,362)|	47	225		
Week 208 (n=53,328)|	41	207		
week 260 (n=52,286)|	42	174		

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D health state assessment (observed value)

End point title	EQ-5D health state assessment (observed value)

End point description:

EQ-5D: EuroQOL 5-Dimension Health Status Questionnaire. The EQ-5D© is a generic instrument to assess each patient’s health status. It provides a simple descriptive profile and a single index value for health status. The EQ visual analog scale records the respondent’s self-rated health on a vertical scale where the endpoints are labeled ‘Best imaginable health state’ and ‘Worst imaginable health state’. This information can be used as a quantitative measure of health outcome as judged by the individual respondents.

End point type	Secondary

End point timeframe:

week 64, 76, 88, 104, 116, 128, 140, and 156

End point values	AIN457 150 mg only	AIN457 300 mg only		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	164	416		
Units: Percent change				
arithmetic mean (standard deviation)				
Week 64 (n=155,404)|	-1.33 (± 22.506)	1.44 (± 26.815)		
Week 76 (n=144,398)|	-1.99 (± 22.339)	2.10 (± 28.493)		
Week 88 (n=130,387)|	-0.66 (± 24.558)	1.45 (± 28.269)		
Week 104 (n=112,376)|	-4.15 (± 27.823)	0.65 (± 23.454)		
Week 116 (n=93,364)|	-1.19 (± 21.022)	1.21 (± 23.681)		
Week 128 (n=84,365)|	-2.85 (± 23.584)	1.93 (± 27.840)		
Week 140 (n=75,367)|	0.09 (± 20.814)	-0.44 (± 18.504)		
Week 156 (n=67,365)|	2.13 (± 32.326)	1.19 (± 21.548)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical laboratory evaluation: the number of participants with clinically CTCAE - entire study period

End point title	Clinical laboratory evaluation: the number of participants with clinically CTCAE - entire study period

End point description:

CTCAE: common terminology criteria for adverse events. A subject with multiple variable measurements is counted only once under the worst condition. LLN = lowever limit of normal.

End point type	Secondary

End point timeframe:

approximately 4 years

End point values	Any AIN457 150 mg	Any AIN457 300 mg	Any AIN457	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	545	890	1113	
Units: 10E9/L				
Leukocytes (<LLN-3.0x10e9 /L, n=545,832,1037)|	55	59	114	
Leukocytes (<3.0-2.0 x 10e9 /L, n=545,866,1080)|	10	7	17	

Leukocytes (<2.0-1.0x10e9 /L, n=545,870,1085)|	1	0	1	
Leukocytes (<1.0x10e9 /L, n=545,870,1085)|	0	0	0	
Lymphocytes (<LLN-0.8x10e9 /L, n=545,840,1041)|	47	61	108	
Lymphocytes (<0.8-0.5x10e9 /L, n=545,861,1071)|	18	28	46	
Lymphocytes (<0.5-0.2 x 10e9 /L, n=545,864,1075)|	1	1	2	
Lymphocytes (<0.2x10e9 /L, n=545,864,1075)|	0	0	0	
Neutrophils (<LLN-1.5x10e9 /L, n=545,831,1037)|	54	69	123	
Neutrophils (<1.5-1.0x10e9 /L, n=545,861,1071)|	12	20	32	
Neutrophils (<1.0 - 0.5x10e9 /L, n=545,863,1074)|	7	4	11	
Neutrophils (<0.5x10e9 /L, n=545,864,1075)|	0	0	0	
Platelets (LLN-75x10e9 /L, n=545,836,1042)|	24	39	63	
Platelets (<75-50x10e9 /L, n=545,862,1074)|	2	2	4	
Platelets (<50-25 x 10e9 /L, n=545,862,1074)|	0	0	0	
Platelets (<25x10e9 /L, n=545,862,1074)|	0	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Electrocardiogram: Number of participants with ECG test results - entire treatment period

End point title	Electrocardiogram: Number of participants with ECG test results - entire treatment period

End point description:

QTcB: QT interval corrected using Bazett’s formula QTcF: QT interval corrected using Fridericia’s formula A patient with multiple variable measurements is counted only once under the worst condition.

End point type	Secondary

End point timeframe:

Approximately 4 years

End point values	Any AIN457 150 mg	Any AIN457 300 mg	Any AIN457	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	545	890	1113	
Units: Participants				
QTcB>500 msec (n=545,851,1060)|	1	2	3	
QTcB>480 msec (n=545,848,1056)|	8	23	30	
QTcB>450 msec (n=545,804,1004)|	86	159	218	

QTcB changes from baseline>30 ms (n=545,851,1060)|	124	223	316	
QTcB changes from baseline>60 ms (n=545,851,1060)|	7	19	25	
QTcF>500 msec (n=545,851,1060)|	0	1	1	
QTcF>480 msec (n=545,851,1059)|	3	6	8	
QTcF>450 msec (n=545,838,1043)|	35	67	93	
QTcF changes from baseline>30 ms (n=545,851,1060)|	69	127	184	
QTcF changes from baseline>60 ms (n=545,851,1060)|	1	3	4	
PR>250 msec (n=545,845,1051)|	4	5	8	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for AE	
Adverse event reporting additional description:	
AE additional description	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	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 dose
Reporting group description:	
Any AIN457 dose	
Reporting group title	AIN457 300 mg (Core)- Placebo
Reporting group description:	
AIN457 300 mg (Core)- Placebo	
Reporting group title	AIN457 150 mg (Core)- Placebo
Reporting group description:	
AIN457 150 mg (Core)- Placebo	

Serious adverse events	Any AIN457 150 mg	Any AIN457 300 mg	Any AIN457 dose
Total subjects affected by serious adverse events			
subjects affected / exposed	61 / 545 (11.19%)	143 / 890 (16.07%)	198 / 1113 (17.79%)
number of deaths (all causes)	0	2	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of colon			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal squamous cell carcinoma			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder cancer			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemangioma			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cancer metastatic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive breast carcinoma			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma in situ			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningioma benign			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lung			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	2 / 545 (0.37%)	1 / 890 (0.11%)	3 / 1113 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small cell lung cancer			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	1 / 545 (0.18%)	1 / 890 (0.11%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 545 (0.00%)	3 / 890 (0.34%)	3 / 1113 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion spontaneous complete			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chest discomfort			
subjects affected / exposed	0 / 545 (0.00%)	0 / 890 (0.00%)	0 / 1113 (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
Face oedema			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site granuloma			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoidosis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 890 (0.00%)	0 / 1113 (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
Reproductive system and breast			

disorders			
Menorrhagia			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal cyst			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal oedema			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal septum deviation			
subjects affected / exposed	1 / 545 (0.18%)	2 / 890 (0.22%)	3 / 1113 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal turbinate hypertrophy			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pleural effusion			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus polyp			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome			
subjects affected / exposed	2 / 545 (0.37%)	0 / 890 (0.00%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcoholism			
subjects affected / exposed	1 / 545 (0.18%)	1 / 890 (0.11%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aversion			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Depression			
subjects affected / exposed	3 / 545 (0.55%)	2 / 890 (0.22%)	5 / 1113 (0.45%)
occurrences causally related to treatment / all	1 / 4	0 / 2	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomania			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Substance abuse			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	1 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device loosening			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	2 / 545 (0.37%)	1 / 890 (0.11%)	3 / 1113 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac procedure complication			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	0 / 545 (0.00%)	0 / 890 (0.00%)	0 / 1113 (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
Fibula fracture			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 545 (0.00%)	3 / 890 (0.34%)	3 / 1113 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 545 (0.00%)	0 / 890 (0.00%)	0 / 1113 (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
Humerus fracture			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney rupture			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament injury			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament rupture			

subjects affected / exposed	1 / 545 (0.18%)	2 / 890 (0.22%)	3 / 1113 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 545 (0.00%)	3 / 890 (0.34%)	3 / 1113 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple fractures			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle rupture			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural hypertension			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue injury			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon injury			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 545 (0.00%)	3 / 890 (0.34%)	3 / 1113 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 545 (0.00%)	0 / 890 (0.00%)	0 / 1113 (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
Ulna fracture			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			

subjects affected / exposed	1 / 545 (0.18%)	2 / 890 (0.22%)	3 / 1113 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Malformation venous			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 545 (0.00%)	4 / 890 (0.45%)	4 / 1113 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Angina pectoris			
subjects affected / exposed	0 / 545 (0.00%)	4 / 890 (0.45%)	4 / 1113 (0.36%)
occurrences causally related to treatment / all	0 / 0	1 / 4	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 545 (0.18%)	9 / 890 (1.01%)	10 / 1113 (0.90%)
occurrences causally related to treatment / all	0 / 1	2 / 9	2 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Coronary artery disease			
subjects affected / exposed	1 / 545 (0.18%)	3 / 890 (0.34%)	4 / 1113 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 890 (0.00%)	0 / 1113 (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
Myocardial infarction			
subjects affected / exposed	1 / 545 (0.18%)	2 / 890 (0.22%)	3 / 1113 (0.27%)
occurrences causally related to treatment / all	0 / 1	1 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress cardiomyopathy			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia paroxysmal			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			

subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complex regional pain syndrome			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cranial nerve paralysis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic neuropathy			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	2 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drooling			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			

subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial aneurysm			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			
subjects affected / exposed	0 / 545 (0.00%)	0 / 890 (0.00%)	0 / 1113 (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
Seizure			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			

subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune thrombocytopenic purpura			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diverticulum intestinal			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspepsia			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	1 / 545 (0.18%)	1 / 890 (0.11%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus paralytic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated inguinal hernia			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal polyp			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal pseudo-obstruction			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritable bowel syndrome			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 545 (0.18%)	1 / 890 (0.11%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia, obstructive			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis acute			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	2 / 545 (0.37%)	1 / 890 (0.11%)	3 / 1113 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic steatosis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis acute			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis toxic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermal cyst			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis contact			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic foot			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriasis			
subjects affected / exposed	2 / 545 (0.37%)	3 / 890 (0.34%)	5 / 1113 (0.45%)
occurrences causally related to treatment / all	1 / 2	0 / 3	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Calculus urinary			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pollakiuria			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 890 (0.00%)	0 / 1113 (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
Endocrine disorders			
Hyperandrogenism			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid mass			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dupuytren's contracture			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemarthrosis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint instability			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			

subjects affected / exposed	1 / 545 (0.18%)	2 / 890 (0.22%)	3 / 1113 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteitis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 545 (0.18%)	4 / 890 (0.45%)	5 / 1113 (0.45%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriatic arthropathy			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal column stenosis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 890 (0.00%)	0 / 1113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess neck			

subjects affected / exposed	0 / 545 (0.00%)	0 / 890 (0.00%)	0 / 1113 (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
Acute sinusitis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	2 / 545 (0.37%)	2 / 890 (0.22%)	4 / 1113 (0.36%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	0 / 545 (0.00%)	0 / 890 (0.00%)	0 / 1113 (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
Bronchitis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 545 (0.00%)	2 / 890 (0.22%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis infective			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic tonsillitis			

subjects affected / exposed	0 / 545 (0.00%)	0 / 890 (0.00%)	0 / 1113 (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
Device related infection			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	3 / 545 (0.55%)	1 / 890 (0.11%)	4 / 1113 (0.36%)
occurrences causally related to treatment / all	1 / 3	0 / 2	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal bacteraemia			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epididymitis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia infection			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder empyema			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft infection			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site infection			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal candidiasis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oophoritis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			

subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal abscess			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 545 (0.18%)	4 / 890 (0.45%)	5 / 1113 (0.45%)
occurrences causally related to treatment / all	1 / 1	4 / 4	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinitis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 545 (0.00%)	4 / 890 (0.45%)	4 / 1113 (0.36%)
occurrences causally related to treatment / all	0 / 0	3 / 4	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	1 / 545 (0.18%)	1 / 890 (0.11%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	1 / 1	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal infection			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tick-borne viral encephalitis			

subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	2 / 545 (0.37%)	2 / 890 (0.22%)	4 / 1113 (0.36%)
occurrences causally related to treatment / all	3 / 3	1 / 2	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 545 (0.18%)	1 / 890 (0.11%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral pericarditis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 890 (0.00%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 545 (0.00%)	1 / 890 (0.11%)	1 / 1113 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 545 (0.18%)	1 / 890 (0.11%)	2 / 1113 (0.18%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	AIN457 300 mg (Core)- Placebo	AIN457 150 mg (Core)- Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 181 (7.18%)	4 / 150 (2.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal squamous cell carcinoma			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder cancer			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemangioma			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer metastatic			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive breast carcinoma			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma benign			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous complete			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face oedema			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site granuloma			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sarcoidosis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal cyst			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal septum deviation			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal turbinate hypertrophy			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus polyp			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcoholism			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aversion			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomania			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Substance abuse			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device loosening			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac procedure complication			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Contusion			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney rupture			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament injury			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle rupture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural hypertension			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue injury			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			

subjects affected / exposed	0 / 181 (0.00%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Malformation venous			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial fibrillation				
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)		
occurrences causally related to treatment / all	0 / 0	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Atrioventricular block complete				
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)		
occurrences causally related to treatment / all	0 / 0	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Coronary artery disease				
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)		
occurrences causally related to treatment / all	0 / 0	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Coronary artery stenosis				
subjects affected / exposed	0 / 181 (0.00%)	1 / 150 (0.67%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Myocardial infarction				
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)		
occurrences causally related to treatment / all	0 / 0	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Myocardial ischaemia				
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)		
occurrences causally related to treatment / all	0 / 0	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Stress cardiomyopathy				
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)		
occurrences causally related to treatment / all	0 / 0	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Tachycardia paroxysmal				
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)		
occurrences causally related to treatment / all	0 / 0	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Ventricular fibrillation				

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complex regional pain syndrome			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cranial nerve paralysis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drooling			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenic purpura			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal polyp			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal pseudo-obstruction			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal stenosis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia, obstructive			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic steatosis			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermal cyst			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis contact			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug eruption			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pollakiuria			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			

subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperandrogenism			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid mass			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dupuytren's contracture			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intervertebral disc protrusion			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint instability			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriatic arthropathy			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess neck			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	2 / 181 (1.10%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	0 / 181 (0.00%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 181 (0.55%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic tonsillitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal bacteraemia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder empyema			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft infection			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site infection			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal candidiasis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oophoritis			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal abscess			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal infection			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tick-borne viral encephalitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pericarditis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus			

subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Any AIN457 150 mg	Any AIN457 300 mg	Any AIN457 dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	386 / 545 (70.83%)	679 / 890 (76.29%)	889 / 1113 (79.87%)
Vascular disorders			
Hypertension			
subjects affected / exposed	42 / 545 (7.71%)	83 / 890 (9.33%)	119 / 1113 (10.69%)
occurrences (all)	48	98	146
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	24 / 545 (4.40%)	45 / 890 (5.06%)	65 / 1113 (5.84%)
occurrences (all)	35	72	107
Pyrexia			
subjects affected / exposed	7 / 545 (1.28%)	24 / 890 (2.70%)	31 / 1113 (2.79%)
occurrences (all)	9	30	39
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	8 / 545 (1.47%)	19 / 890 (2.13%)	27 / 1113 (2.43%)
occurrences (all)	9	20	29
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	27 / 545 (4.95%)	43 / 890 (4.83%)	66 / 1113 (5.93%)
occurrences (all)	36	47	83
Oropharyngeal pain			
subjects affected / exposed	23 / 545 (4.22%)	42 / 890 (4.72%)	65 / 1113 (5.84%)
occurrences (all)	25	47	72
Psychiatric disorders			
Anxiety			
subjects affected / exposed	8 / 545 (1.47%)	20 / 890 (2.25%)	28 / 1113 (2.52%)
occurrences (all)	9	25	34

Depression			
subjects affected / exposed	14 / 545 (2.57%)	10 / 890 (1.12%)	24 / 1113 (2.16%)
occurrences (all)	15	12	27
Insomnia			
subjects affected / exposed	11 / 545 (2.02%)	20 / 890 (2.25%)	30 / 1113 (2.70%)
occurrences (all)	13	26	39
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	13 / 545 (2.39%)	8 / 890 (0.90%)	21 / 1113 (1.89%)
occurrences (all)	14	11	25
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	9 / 545 (1.65%)	22 / 890 (2.47%)	31 / 1113 (2.79%)
occurrences (all)	11	25	36
Laceration			
subjects affected / exposed	9 / 545 (1.65%)	16 / 890 (1.80%)	25 / 1113 (2.25%)
occurrences (all)	9	18	27
Ligament sprain			
subjects affected / exposed	13 / 545 (2.39%)	21 / 890 (2.36%)	34 / 1113 (3.05%)
occurrences (all)	13	26	39
Muscle strain			
subjects affected / exposed	9 / 545 (1.65%)	17 / 890 (1.91%)	25 / 1113 (2.25%)
occurrences (all)	9	23	32
Procedural pain			
subjects affected / exposed	8 / 545 (1.47%)	21 / 890 (2.36%)	29 / 1113 (2.61%)
occurrences (all)	10	24	34
Nervous system disorders			
Headache			
subjects affected / exposed	36 / 545 (6.61%)	87 / 890 (9.78%)	116 / 1113 (10.42%)
occurrences (all)	64	158	222
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	11 / 545 (2.02%)	15 / 890 (1.69%)	25 / 1113 (2.25%)
occurrences (all)	12	18	30
Diarrhoea			

subjects affected / exposed	29 / 545 (5.32%)	53 / 890 (5.96%)	81 / 1113 (7.28%)
occurrences (all)	36	64	100
Gastritis			
subjects affected / exposed	11 / 545 (2.02%)	21 / 890 (2.36%)	31 / 1113 (2.79%)
occurrences (all)	12	22	34
Gastrooesophageal reflux disease			
subjects affected / exposed	12 / 545 (2.20%)	25 / 890 (2.81%)	37 / 1113 (3.32%)
occurrences (all)	12	27	39
Nausea			
subjects affected / exposed	9 / 545 (1.65%)	15 / 890 (1.69%)	24 / 1113 (2.16%)
occurrences (all)	10	16	26
Toothache			
subjects affected / exposed	10 / 545 (1.83%)	33 / 890 (3.71%)	43 / 1113 (3.86%)
occurrences (all)	12	38	50
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	5 / 545 (0.92%)	19 / 890 (2.13%)	23 / 1113 (2.07%)
occurrences (all)	5	31	36
Eczema			
subjects affected / exposed	8 / 545 (1.47%)	34 / 890 (3.82%)	41 / 1113 (3.68%)
occurrences (all)	13	42	55
Pruritus			
subjects affected / exposed	11 / 545 (2.02%)	24 / 890 (2.70%)	34 / 1113 (3.05%)
occurrences (all)	16	27	43
Psoriasis			
subjects affected / exposed	14 / 545 (2.57%)	39 / 890 (4.38%)	51 / 1113 (4.58%)
occurrences (all)	17	43	60
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	47 / 545 (8.62%)	80 / 890 (8.99%)	124 / 1113 (11.14%)
occurrences (all)	65	93	158
Back pain			
subjects affected / exposed	40 / 545 (7.34%)	76 / 890 (8.54%)	114 / 1113 (10.24%)
occurrences (all)	45	89	134
Musculoskeletal pain			

subjects affected / exposed	14 / 545 (2.57%)	19 / 890 (2.13%)	33 / 1113 (2.96%)
occurrences (all)	14	21	35
Myalgia			
subjects affected / exposed	10 / 545 (1.83%)	22 / 890 (2.47%)	32 / 1113 (2.88%)
occurrences (all)	11	27	38
Pain in extremity			
subjects affected / exposed	20 / 545 (3.67%)	29 / 890 (3.26%)	49 / 1113 (4.40%)
occurrences (all)	22	34	56
Psoriatic arthropathy			
subjects affected / exposed	11 / 545 (2.02%)	38 / 890 (4.27%)	47 / 1113 (4.22%)
occurrences (all)	11	42	53
Tendonitis			
subjects affected / exposed	5 / 545 (0.92%)	23 / 890 (2.58%)	28 / 1113 (2.52%)
occurrences (all)	6	23	29
Infections and infestations			
Bronchitis			
subjects affected / exposed	31 / 545 (5.69%)	63 / 890 (7.08%)	92 / 1113 (8.27%)
occurrences (all)	38	89	127
Conjunctivitis			
subjects affected / exposed	10 / 545 (1.83%)	30 / 890 (3.37%)	38 / 1113 (3.41%)
occurrences (all)	12	36	48
Cystitis			
subjects affected / exposed	10 / 545 (1.83%)	23 / 890 (2.58%)	31 / 1113 (2.79%)
occurrences (all)	10	27	37
Folliculitis			
subjects affected / exposed	13 / 545 (2.39%)	18 / 890 (2.02%)	31 / 1113 (2.79%)
occurrences (all)	16	19	35
Gastroenteritis			
subjects affected / exposed	24 / 545 (4.40%)	35 / 890 (3.93%)	59 / 1113 (5.30%)
occurrences (all)	28	43	71
Herpes zoster			
subjects affected / exposed	3 / 545 (0.55%)	25 / 890 (2.81%)	27 / 1113 (2.43%)
occurrences (all)	3	25	28
Influenza			
subjects affected / exposed	24 / 545 (4.40%)	54 / 890 (6.07%)	78 / 1113 (7.01%)
occurrences (all)	24	57	81

Nasopharyngitis			
subjects affected / exposed	145 / 545 (26.61%)	271 / 890 (30.45%)	375 / 1113 (33.69%)
occurrences (all)	280	548	828
Oral candidiasis			
subjects affected / exposed	7 / 545 (1.28%)	22 / 890 (2.47%)	29 / 1113 (2.61%)
occurrences (all)	10	40	50
Oral herpes			
subjects affected / exposed	12 / 545 (2.20%)	25 / 890 (2.81%)	36 / 1113 (3.23%)
occurrences (all)	19	39	58
Pharyngitis			
subjects affected / exposed	18 / 545 (3.30%)	38 / 890 (4.27%)	55 / 1113 (4.94%)
occurrences (all)	20	62	82
Rhinitis			
subjects affected / exposed	11 / 545 (2.02%)	30 / 890 (3.37%)	38 / 1113 (3.41%)
occurrences (all)	13	36	49
Sinusitis			
subjects affected / exposed	18 / 545 (3.30%)	51 / 890 (5.73%)	64 / 1113 (5.75%)
occurrences (all)	20	71	91
Tinea pedis			
subjects affected / exposed	9 / 545 (1.65%)	29 / 890 (3.26%)	38 / 1113 (3.41%)
occurrences (all)	10	34	44
Tonsillitis			
subjects affected / exposed	19 / 545 (3.49%)	31 / 890 (3.48%)	49 / 1113 (4.40%)
occurrences (all)	21	34	55
Tooth infection			
subjects affected / exposed	10 / 545 (1.83%)	18 / 890 (2.02%)	28 / 1113 (2.52%)
occurrences (all)	10	26	36
Upper respiratory tract infection			
subjects affected / exposed	52 / 545 (9.54%)	119 / 890 (13.37%)	153 / 1113 (13.75%)
occurrences (all)	77	228	305
Urinary tract infection			
subjects affected / exposed	15 / 545 (2.75%)	33 / 890 (3.71%)	46 / 1113 (4.13%)
occurrences (all)	18	50	68
Viral upper respiratory tract infection			

subjects affected / exposed	11 / 545 (2.02%)	21 / 890 (2.36%)	31 / 1113 (2.79%)
occurrences (all)	23	34	57
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	3 / 545 (0.55%)	18 / 890 (2.02%)	20 / 1113 (1.80%)
occurrences (all)	3	19	22
Hyperlipidaemia			
subjects affected / exposed	11 / 545 (2.02%)	9 / 890 (1.01%)	20 / 1113 (1.80%)
occurrences (all)	11	11	22
Hypertriglyceridaemia			
subjects affected / exposed	11 / 545 (2.02%)	18 / 890 (2.02%)	29 / 1113 (2.61%)
occurrences (all)	12	21	33

Non-serious adverse events	AIN457 300 mg (Core)- Placebo	AIN457 150 mg (Core)- Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	86 / 181 (47.51%)	75 / 150 (50.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 181 (3.31%)	5 / 150 (3.33%)	
occurrences (all)	6	5	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	2 / 181 (1.10%)	2 / 150 (1.33%)	
occurrences (all)	2	2	
Pyrexia			
subjects affected / exposed	2 / 181 (1.10%)	0 / 150 (0.00%)	
occurrences (all)	2	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 181 (0.55%)	2 / 150 (1.33%)	
occurrences (all)	1	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 181 (2.21%)	1 / 150 (0.67%)	
occurrences (all)	4	1	
Oropharyngeal pain			

subjects affected / exposed	3 / 181 (1.66%)	3 / 150 (2.00%)	
occurrences (all)	4	4	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 181 (0.55%)	1 / 150 (0.67%)	
occurrences (all)	1	1	
Depression			
subjects affected / exposed	2 / 181 (1.10%)	2 / 150 (1.33%)	
occurrences (all)	2	2	
Insomnia			
subjects affected / exposed	2 / 181 (1.10%)	2 / 150 (1.33%)	
occurrences (all)	2	2	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 181 (0.55%)	1 / 150 (0.67%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 181 (1.10%)	1 / 150 (0.67%)	
occurrences (all)	2	1	
Laceration			
subjects affected / exposed	0 / 181 (0.00%)	1 / 150 (0.67%)	
occurrences (all)	0	1	
Ligament sprain			
subjects affected / exposed	2 / 181 (1.10%)	1 / 150 (0.67%)	
occurrences (all)	2	1	
Muscle strain			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	0 / 181 (0.00%)	1 / 150 (0.67%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 181 (1.10%)	4 / 150 (2.67%)	
occurrences (all)	3	7	

Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 181 (0.55%)	2 / 150 (1.33%)	
occurrences (all)	1	2	
Diarrhoea			
subjects affected / exposed	5 / 181 (2.76%)	3 / 150 (2.00%)	
occurrences (all)	7	3	
Gastritis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 150 (0.67%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 181 (0.00%)	1 / 150 (0.67%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	2 / 181 (1.10%)	0 / 150 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences (all)	0	0	
Eczema			
subjects affected / exposed	2 / 181 (1.10%)	0 / 150 (0.00%)	
occurrences (all)	3	0	
Pruritus			
subjects affected / exposed	3 / 181 (1.66%)	2 / 150 (1.33%)	
occurrences (all)	3	2	
Psoriasis			
subjects affected / exposed	3 / 181 (1.66%)	1 / 150 (0.67%)	
occurrences (all)	3	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	13 / 181 (7.18%)	8 / 150 (5.33%)	
occurrences (all)	14	9	

Back pain			
subjects affected / exposed	5 / 181 (2.76%)	4 / 150 (2.67%)	
occurrences (all)	5	5	
Musculoskeletal pain			
subjects affected / exposed	0 / 181 (0.00%)	0 / 150 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	1 / 181 (0.55%)	3 / 150 (2.00%)	
occurrences (all)	1	3	
Pain in extremity			
subjects affected / exposed	2 / 181 (1.10%)	2 / 150 (1.33%)	
occurrences (all)	3	2	
Psoriatic arthropathy			
subjects affected / exposed	6 / 181 (3.31%)	8 / 150 (5.33%)	
occurrences (all)	6	9	
Tendonitis			
subjects affected / exposed	1 / 181 (0.55%)	1 / 150 (0.67%)	
occurrences (all)	1	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 181 (1.66%)	3 / 150 (2.00%)	
occurrences (all)	3	3	
Conjunctivitis			
subjects affected / exposed	1 / 181 (0.55%)	1 / 150 (0.67%)	
occurrences (all)	2	1	
Cystitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences (all)	1	0	
Folliculitis			
subjects affected / exposed	2 / 181 (1.10%)	1 / 150 (0.67%)	
occurrences (all)	2	1	
Gastroenteritis			
subjects affected / exposed	2 / 181 (1.10%)	3 / 150 (2.00%)	
occurrences (all)	2	3	
Herpes zoster			

subjects affected / exposed	0 / 181 (0.00%)	2 / 150 (1.33%)	
occurrences (all)	0	2	
Influenza			
subjects affected / exposed	6 / 181 (3.31%)	4 / 150 (2.67%)	
occurrences (all)	7	4	
Nasopharyngitis			
subjects affected / exposed	21 / 181 (11.60%)	17 / 150 (11.33%)	
occurrences (all)	29	23	
Oral candidiasis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 150 (0.67%)	
occurrences (all)	0	1	
Oral herpes			
subjects affected / exposed	2 / 181 (1.10%)	2 / 150 (1.33%)	
occurrences (all)	2	2	
Pharyngitis			
subjects affected / exposed	3 / 181 (1.66%)	1 / 150 (0.67%)	
occurrences (all)	5	1	
Rhinitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	3 / 181 (1.66%)	4 / 150 (2.67%)	
occurrences (all)	3	4	
Tinea pedis			
subjects affected / exposed	2 / 181 (1.10%)	0 / 150 (0.00%)	
occurrences (all)	2	0	
Tonsillitis			
subjects affected / exposed	3 / 181 (1.66%)	6 / 150 (4.00%)	
occurrences (all)	3	6	
Tooth infection			
subjects affected / exposed	1 / 181 (0.55%)	0 / 150 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	12 / 181 (6.63%)	8 / 150 (5.33%)	
occurrences (all)	14	10	
Urinary tract infection			

subjects affected / exposed	2 / 181 (1.10%)	3 / 150 (2.00%)	
occurrences (all)	2	4	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 181 (1.10%)	0 / 150 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 181 (0.00%)	1 / 150 (0.67%)	
occurrences (all)	0	1	
Hyperlipidaemia			
subjects affected / exposed	0 / 181 (0.00%)	2 / 150 (1.33%)	
occurrences (all)	0	2	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 181 (0.55%)	2 / 150 (1.33%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 April 2014	The purpose of this amendment was to provide continued treatment for patients in the trial for an additional 104 Weeks (or overall up to four years of treatment in the extension) or until the drug was commercially available in the market in the country of participation, whichever occurred first. This extension of treatment allowed for safety, tolerability, and efficacy data to be collected from the participating patients for a longer time period.
09 September 2014	The purpose of this amendment was to clarify the wording for countries not selected for early trial termination when the drug was commercially available, this study continued up to the end of additional 104 Weeks of treatment. It also clarified a discrepancy in the Assessment Schedule that PK samples at Week 140 were collected for all patients and at Week 144 in case of relapse.
29 April 2015	Patients who completed treatment period and follow-up period were evaluated for 4 years regarding respective adverse events. However, patient who prematurely discontinued treatment were evaluated for less than 4 years.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported