Clinical trial results:
A multicenter, double-blind and open label, 4 year extension study of subcutaneous secukinumab in prefilled syringes, assessing long-term safety, tolerability and efficacy in patients with moderate to severe chronic plaque-type psoriasis treated with either a fixed dose regimen or on a retreatment at start of relapse regimen

Summary

EudraCT number	2012-000985-39
Trial protocol	CZ GB SK DE AT IT BG PL
Global end of trial date	04 May 2017

Results information

Result version number	v1 (current)
This version publication date	13 May 2018
First version publication date	13 May 2018

Trial information

Trial identification

Sponsor protocol code	CAIN457A2304E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01640951
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	04 May 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess long-term safety and tolerability of secukinumab in subjects with moderate to severe chronic plaque-type psoriasis who completed treatment in the core studies CAIN457A2304 and CAIN457A2307.

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	16 September 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	Austria: 1
Country: Number of subjects enrolled	Bulgaria: 46
Country: Number of subjects enrolled	Canada: 69
Country: Number of subjects enrolled	Czech Republic: 38
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Germany: 133
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Japan: 51
Country: Number of subjects enrolled	Poland: 31
Country: Number of subjects enrolled	Singapore: 5
Country: Number of subjects enrolled	Slovakia: 39
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	United States: 148
Country: Number of subjects enrolled	Vietnam: 54
Worldwide total number of subjects	675
EEA total number of subjects	343

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)	631
From 65 to 84 years	44
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

675 subjects from the core studies (CAIN457A2304 and CAIN457A2307) were enrolled at 112 sites. Subjects enrolled in the secukinumab 300 mg Open-Label (OL) arm came only from the CAIN457A2307 study, as such they were partial responders at Week 12, while all other subjects in the extension were PASI 75 responders at Week 12 in the core study.

Pre-assignment

Screening details:

At Week 156, subjects who rolled over from the CAIN457A2304 study were unblinded and provided an option to switch to one of the treatment options described below upon investigator judgment; subjects from the CAIN457A2307 study could administer study drug at home every 4 weeks, but were required to come for office visits every 12-16 weeks.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	AIN150FI

Arm description:

AIN457 150 mg - Fixed Interval (FI)

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

Dosage and administration details:

1 s.c. Secukinumab 150 mg Pre-filled seringue (PFS) injection + 1 s.c. Placebo (PBO) Secukinumab PFS injection every 4 weeks

Arm title	AIN150 FI_AIN300 FI

Arm description:

AIN457 150 mg FI switch to AIN457 300 mg FI (150 mg FI SW)

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

Dosage and administration details:

2 s.c. Secukinumab 150 mg PFS injections every 4 weeks

Arm title	AIN300 FI

Arm description:

AIN457 300 mg - Fixed Interval (FI)

Arm type	Experimental

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

Dosage and administration details:

2 s.c. Secukinumab 150 mg PFS injections every 4 weeks

Arm title	AIN150 SoR

Arm description:

AIN457 150 mg - Start of Relapse (SoR)

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

Dosage and administration details:

Start of relapse: 1 s.c. Secukinumab 150 mg PFS injection + 1 s.c. PBO Secukinumab PFS injection every 4 weeks.
Otherwise: 2 s.c. PBO Secukinumab PFS injections every 4 weeks

Arm title	AIN150 SOR_AIN300 FI

Arm description:

AIN457 150 mg SoR switch to AIN457 300 mg FI (150 mg SoR SW)

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

Dosage and administration details:

2 s.c. Secukinumab 150 mg PFS injections every 4 weeks

Arm title	AIN300 SoR

Arm description:

AIN457 300 mg - Start of Relapse (SoR)

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

Dosage and administration details:

Start of relapse: 2 s.c. Secukinumab 150 mg PFS injection every 4 weeks. Otherwise: 2 s.c. PBO Secukinumab PFS injections every 4 weeks.

Arm title	AIN300 SoR _ AIN300 FI

Arm description:

AIN457 300 mg SoR switch to AIN457 300 mg FI (300 mg SoR SW)

Arm type	Experimental

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

Dosage and administration details:

2 s.c. Secukinumab 150 mg PFS injections every 4 weeks

Arm title	AIN300 OL

Arm description:

AIN457 300 mg Open-label (OL)

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

Dosage and administration details:

Open Label - Secukinumab 300mg every 4 weeks

Number of subjects in period 1	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI
Started	77	75	168
Completed	31	60	126
Not completed	46	15	42
Adverse event, serious fatal	-	1	1
Physician decision	2	5	2
Adverse event, non-fatal	8	3	10
Protocol Deviation	-	1	2
Non-compliance with study treatment	-	-	1
Pregnancy	3	-	-
Subject/Guardian decision	12	4	13
Lost to follow-up	1	-	6
Lack of efficacy	20	1	7

Number of subjects in period 1	AIN150 SoR	AIN150 SOR_AIN300 FI	AIN300 SoR
Started	55	95	60
Completed	10	82	13
Not completed	45	13	47
Adverse event, serious fatal	-	-	-
Physician decision	2	2	3
Adverse event, non-fatal	6	1	11
Protocol Deviation	1	-	1
Non-compliance with study treatment	1	1	4

Pregnancy	4	-	-
Subject/Guardian decision	15	7	19
Lost to follow-up	2	2	3
Lack of efficacy	14	-	6

Number of subjects in period 1	AIN300 SoR _ AIN300 FI	AIN300 OL
Started	112	33
Completed	94	17
Not completed	18	16
Adverse event, serious fatal	-	2
Physician decision	3	-
Adverse event, non-fatal	1	3
Protocol Deviation	-	-
Non-compliance with study treatment	1	-
Pregnancy	2	-
Subject/Guardian decision	5	4
Lost to follow-up	1	1
Lack of efficacy	5	6

Baseline characteristics

Reporting groups	
Reporting group title	AIN150FI
Reporting group description:	
AIN457 150 mg - Fixed Interval (FI)	
Reporting group title	AIN150 FI_AIN300 FI
Reporting group description:	
AIN457 150 mg FI switch to AIN457 300 mg FI (150 mg FI SW)	
Reporting group title	AIN300 FI
Reporting group description:	
AIN457 300 mg - Fixed Interval (FI)	
Reporting group title	AIN150 SoR
Reporting group description:	
AIN457 150 mg - Start of Relapse (SoR)	
Reporting group title	AIN150 SOR_AIN300 FI
Reporting group description:	
AIN457 150 mg SoR switch to AIN457 300 mg FI (150 mg SoR SW)	
Reporting group title	AIN300 SoR
Reporting group description:	
AIN457 300 mg - Start of Relapse (SoR)	
Reporting group title	AIN300 SoR _ AIN300 FI
Reporting group description:	
AIN457 300 mg SoR switch to AIN457 300 mg FI (300 mg SoR SW)	
Reporting group title	AIN300 OL
Reporting group description:	
AIN457 300 mg Open-label (OL)	

Reporting group values	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI
Number of subjects	77	75	168
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	73	71	151
From 65-84 years	4	4	17
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	42.3	46.0	48.5
standard deviation	± 13.24	± 12.03	± 12.54

Sex: Female, Male Units: Subjects			
Female	38	25	50
Male	39	50	118
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	2
Asian	13	14	31
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	1	2
White	62	60	132
More than one race	0	0	0
Unknown or Not Reported	0	0	1

Reporting group values	AIN150 SoR	AIN150 SOR_AIN300 FI	AIN300 SoR
Number of subjects	55	95	60
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	54	88	60
From 65-84 years	1	7	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	42.7	48.0	45.2
standard deviation	± 12.23	± 12.13	± 12.08
Sex: Female, Male Units: Subjects			
Female	25	28	18
Male	30	67	42
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	5	21	9
Native Hawaiian or Other Pacific Islander	0	0	1
Black or African American	0	3	3
White	48	68	45
More than one race	0	0	0
Unknown or Not Reported	2	3	2

Reporting group values	AIN300 SoR _ AIN300 FI	AIN300 OL	Total
Number of subjects	112	33	675

Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	106	28	631
From 65-84 years	6	5	44
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	44.6	46.5	
standard deviation	± 13.09	± 13.99	-
Sex: Female, Male Units: Subjects			
Female	35	12	231
Male	77	21	444
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	2
Asian	26	4	123
Native Hawaiian or Other Pacific Islander	0	0	1
Black or African American	1	0	12
White	84	29	528
More than one race	0	0	0
Unknown or Not Reported	1	0	9

End points

End points reporting groups

Reporting group title	AIN150FI
Reporting group description: AIN457 150 mg - Fixed Interval (FI)	
Reporting group title	AIN150 FI_AIN300 FI
Reporting group description: AIN457 150 mg FI switch to AIN457 300 mg FI (150 mg FI SW)	
Reporting group title	AIN300 FI
Reporting group description: AIN457 300 mg - Fixed Interval (FI)	
Reporting group title	AIN150 SoR
Reporting group description: AIN457 150 mg - Start of Relapse (SoR)	
Reporting group title	AIN150 SOR_AIN300 FI
Reporting group description: AIN457 150 mg SoR switch to AIN457 300 mg FI (150 mg SoR SW)	
Reporting group title	AIN300 SoR
Reporting group description: AIN457 300 mg - Start of Relapse (SoR)	
Reporting group title	AIN300 SoR _ AIN300 FI
Reporting group description: AIN457 300 mg SoR switch to AIN457 300 mg FI (300 mg SoR SW)	
Reporting group title	AIN300 OL
Reporting group description: AIN457 300 mg Open-label (OL)	
Subject analysis set title	AIN150FI (NSW+SW)
Subject analysis set type	Full analysis
Subject analysis set description: AIN457 150 mg - Fixed Interval combined non-switch and switch	

Primary: Long-term safety and tolerability of Secukinumab

End point title	Long-term safety and tolerability of Secukinumab[1]
End point description: Analysis of absolute and relative frequencies for treatment emergent Adverse Event (AE), Serious Adverse Event (SAE) and Deaths by primary System Organ Class (SOC).	
End point type	Primary
End point timeframe: Week 268	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis performed

End point values	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI	AIN150 SoR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	75	168	55
Units: Percentage of participants				
number (not applicable)				
AEs by Primary System Organ Class (SOC)|	88.3	92.0	92.9	78.2
SAEs by Primary System Organ Class (SOC)|	20.8	24.0	23.8	16.4
Deaths by Primary System Organ Class (SOC)|	0.0	1.3	0.6	0.0

End point values	AIN150 SOR_AIN300 FI	AIN300 SoR	AIN300 SoR _ AIN300 FI	AIN300 OL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	60	112	33
Units: Percentage of participants				
number (not applicable)				
AEs by Primary System Organ Class (SOC)|	87.4	80.0	94.6	93.9
SAEs by Primary System Organ Class (SOC)|	20.0	18.3	17.0	36.4
Deaths by Primary System Organ Class (SOC)|	0.0	0.0	0.0	6.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants achieving Psoriasis Area and Severity Index (PASI) Score of 75 at weeks 52, 104, 156, 208 and 260

End point title	Percentage of Participants achieving Psoriasis Area and Severity Index (PASI) Score of 75 at weeks 52, 104, 156, 208 and 260

End point description:

PASI: Combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area * area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4).

End point type	Secondary

End point timeframe:

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

End point values	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI	AIN150 SoR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	75	168	55
Units: Percentage of Participants				
number (not applicable)				
Week 52|	69.7	65.3	88.9	38.2
Week 104|	63.3	54.8	80.9	40.0
Week 156|	85.0	49.3	78.4	62.5
Week 208|	80.0	78.3	87.9	63.6
Week 260|	89.7	71.4	88.5	50.0

End point values	AIN150 SOR_AIN300 FI	AIN300 SoR	AIN300 SoR _ AIN300 FI	AIN300 OL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	60	112	33
Units: Percentage of Participants				
number (not applicable)				
Week 52|	38.9	51.7	39.6	63.6
Week 104|	39.4	55.9	44.5	63.3
Week 156|	35.1	65.0	41.4	57.1
Week 208|	87.4	41.7	79.0	61.9
Week 260|	86.1	53.8	81.6	75.0

End point values	AIN150FI (NSW+SW)			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Percentage of Participants				
number (not applicable)				
Week 52|	67.5			
Week 104|	58.6			
Week 156|	61.7			
Week 208|	78.8			
Week 260|	77.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants achieving Psoriasis Area and Severity Index (PASI) Scores of 50, 90 and 100 Over time at weeks 52, 104, 156, 208 and 260

End point title	Percentage of Participants achieving Psoriasis Area and Severity Index (PASI) Scores of 50, 90 and 100 Over time at weeks 52, 104, 156, 208 and 260

End point description:

PASI: Combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area * area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4).

End point type	Secondary

End point timeframe:

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

End point values	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI	AIN150 SoR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	75	168	55
Units: Percentage of Participants				
number (not applicable)				
Week 52 / PASI 50|	89.5	98.7	98.8	80.0
Week 52 / PASI 90|	61.8	38.7	68.5	12.7
Week 52 / PASI 100|	31.6	16.0	43.8	3.6
Week 104 / PASI 50|	88.3	84.9	96.7	80.0
Week 104 / PASI 90|	46.7	23.3	64.5	16.7
Week 104 / PASI 100|	28.3	6.8	43.4	10.0
Week 156 / PASI 50|	100.0	86.7	97.1	93.8
Week 156 / PASI 90|	60.0	17.3	61.9	31.3
Week 156 / PASI 100|	45.0	8.0	41.7	6.3
Week 208 / PASI 50|	100.0	97.1	97.0	72.7
Week 208 / PASI 90|	51.4	49.3	65.9	27.3
Week 208 / PASI 100|	28.6	20.3	43.2	9.1
Week 260 / PASI 50|	100.0	96.4	97.5	100.0
Week 260 / PASI 90|	51.7	46.4	66.4	30.0
Week 260 / PASI 100|	31.0	17.9	41.0	10.0

End point values	AIN150 SOR_AIN300 FI	AIN300 SoR	AIN300 SoR _ AIN300 FI	AIN300 OL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	60	112	33
Units: Percentage of Participants				
number (not applicable)				
Week 52 / PASI 50|	86.3	91.4	88.3	93.9
Week 52 / PASI 90|	11.6	19.0	12.6	39.4
Week 52 / PASI 100|	2.1	8.6	3.6	9.1
Week 104 / PASI 50|	87.2	88.2	85.5	86.7
Week 104 / PASI 90|	9.6	14.7	18.2	26.7
Week 104 / PASI 100|	1.1	5.9	4.5	13.3
Week 156 / PASI 50|	88.3	85.0	90.1	90.5
Week 156 / PASI 90|	10.6	30.0	10.8	28.6
Week 156 / PASI 100|	4.3	0.0	3.6	19.0

Week 208 / PASI 50|	98.9	100.0	95.0	95.2
Week 208 / PASI 90|	64.4	16.7	53.0	23.8
Week 208 / PASI 100|	23.0	0.0	24.0	23.8
Week 260 / PASI 50|	97.5	100.0	54.0	87.5
Week 260 / PASI 90|	57.0	7.7	54.0	43.8
Week 260 / PASI 100|	29.1	7.7	18.4	25.0

End point values	AIN150FI (NSW+SW)			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Percentage of Participants				
number (not applicable)				
Week 52 / PASI 50|	94.0			
Week 52 / PASI 90|	50.3			
Week 52 / PASI 100|	23.8			
Week 104 / PASI 50|	86.5			
Week 104 / PASI 90|	33.8			
Week 104 / PASI 100|	16.5			
Week 156 / PASI 50|	91.3			
Week 156 / PASI 90|	32.2			
Week 156 / PASI 100|	20.9			
Week 208 / PASI 50|	98.1			
Week 208 / PASI 90|	50.0			
Week 208 / PASI 100|	23.1			
Week 260 / PASI 50|	97.6			
Week 260 / PASI 90|	48.2			
Week 260 / PASI 100|	22.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in Psoriasis Area and Severity Index (PASI) Score at weeks 52, 104, 156, 208 and 260

End point title	Percent change from Baseline in Psoriasis Area and Severity Index (PASI) Score at weeks 52, 104, 156, 208 and 260

End point description:

PASI: Combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area * area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4).

End point type	Secondary

End point timeframe:

Baseline, Week 52, Week 104, Week 156, Week 208, Week 260

End point values	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI	AIN150 SoR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	75	168	55
Units: Percent change				
arithmetic mean (standard deviation)				
Week 52|	-83.54 (± 21.744)	-81.47 (± 16.179)	-91.14 (± 13.377)	-65.13 (± 23.452)
Week 104|	-78.13 (± 26.278)	-72.47 (± 24.099)	-88.48 (± 16.273)	-63.17 (± 28.596)
Week 156|	-90.27 (± 11.543)	-71.48 (± 19.892)	-88.34 (± 15.555)	-78.97 (± 16.709)
Week 208|	-87.60 (± 12.296)	-85.06 (± 14.082)	-90.46 (± 14.116)	-72.64 (± 24.394)
Week 260|	-88.75 (± 10.928)	-84.10 (± 15.012)	-90.06 (± 14.639)	-76.20 (± 17.418)

End point values	AIN150 SOR_AIN300 FI	AIN300 SoR	AIN300 SoR _ AIN300 FI	AIN300 OL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	60	112	33
Units: Percent change				
arithmetic mean (standard deviation)				
Week 52|	-67.91 (± 21.521)	-75.63 (± 16.970)	-69.13 (± 18.976)	-79.75 (± 17.045)
Week 104|	-68.40 (± 18.057)	-67.62 (± 40.039)	-70.98 (± 19.720)	-76.10 (± 19.342)
Week 156|	-68.71 (± 18.094)	-77.40 (± 18.714)	-69.77 (± 18.586)	-76.12 (± 20.437)
Week 208|	-89.36 (± 12.978)	-74.38 (± 13.817)	-85.25 (± 17.018)	-79.12 (± 16.827)
Week 260|	-89.40 (± 12.763)	-78.13 (± 10.197)	-85.48 (± 17.116)	-81.47 (± 21.335)

End point values	AIN150FI (NSW+SW)			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Percent change				
arithmetic mean (standard deviation)				
Week 52|	-82.51 (± 19.147)			
Week 104|	-75.02 (± 25.168)			
Week 156|	-78.02 (± 19.576)			
Week 208|	-85.91 (± 13.501)			

Week 260|	-85.68 (± 13.867)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants achieving Investigator's Global Assessment modified 2011 (IGA) 2011 Score of 0 or 1 Over time at weeks 52, 104, 156, 208 and 260

End point title	Percentage of Participants achieving Investigator's Global Assessment modified 2011 (IGA) 2011 Score of 0 or 1 Over time at weeks 52, 104, 156, 208 and 260

End point description:

The IGA mod 2011 is a static scale, i.e., it refers exclusively to the participant's disease state at the time of the assessments and does not attempt a comparison to any of the participant's previous disease states at prior visits. The score ranges from 0 (clear) to 4 (severe). The score 0 is clear, 1 is almost clear, 2 is mild, 3 is moderate, and 4 is severe.

End point type	Secondary

End point timeframe:

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

End point values	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI	AIN150 SoR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	75	168	55
Units: Percentage of Participants				
number (not applicable)				
Week 52 / IGA 0/1|	59.2	50.7	69.1	20.0
Week 104 / IGA 0/1|	51.7	30.1	66.4	20.0
Week 156 / IGA 0/1|	62.5	21.3	56.8	37.5
Week 208 / IGA 0/1|	57.1	47.1	62.1	41.7
Week 260 / IGA 0/1|55.2	55.2	48.2	65.0	40.0

End point values	AIN150 SOR_AIN300 FI	AIN300 SoR	AIN300 SoR _ AIN300 FI	AIN300 OL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	60	112	33
Units: Percentage of Participants				
number (not applicable)				
Week 52 / IGA 0/1|	20.0	28.3	19.8	42.4
Week 104 / IGA 0/1|	16.0	17.6	17.3	23.3
Week 156 / IGA 0/1|	14.9	25.0	15.3	28.6
Week 208 / IGA 0/1|	63.2	8.3	52.0	23.8

Week 260 / IGA 0/1|55.2	58.2	30.8	54.0	37.5

End point values	AIN150FI (NSW+SW)			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Percentage of Participants				
number (not applicable)				
Week 52 / IGA 0/1|	55.0			
Week 104 / IGA 0/1|	39.8			
Week 156 / IGA 0/1|	35.7			
Week 208 / IGA 0/1|	50.5			
Week 260 / IGA 0/1|55.2	50.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from Baseline in Dermatology Life Quality Index (DLQI©) response at weeks 52, 104, 156, 208 and 260

End point title	Percentage change from Baseline in Dermatology Life Quality Index (DLQI©) response at weeks 52, 104, 156, 208 and 260

End point description:

The DLQI is a quality of life measure used in the psoriatic The 10-item questionnaire has a score range of 0 (best) to 30 (worst) with higher scores indicating poor quality of life. The instrument contains six functional scales (i.e., symptoms and feeling, daily activities, leisure, work and school, personal relationships, treatment). Each item has 4 response categories, ranging from 0 (not at all) to 3 (very much). "Not relevant" is also a valid response and is scored as 0. The DLQI total score is a sum of the 10 questions.

End point type	Secondary

End point timeframe:

Baseline, Week 52, Week 104, Week 156, Week 208, Week 260

End point values	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI	AIN150 SoR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	75	168	55
Units: Percent change				
median (confidence interval 95%)				
Week 52|	-77.3 (-87.5 to -68.3)	-85.7 (-90.0 to -77.8)	-93.3 (-95.5 to -90.3)	-65.0 (-74.7 to -55.6)
Week 104|	-70.8 (-83.3 to -63.3)	-73.8 (-80.4 to -65.9)	-87.5 (-93.3 to -83.3)	-71.9 (-80.2 to -58.6)
Week 156|	-89.3 (-97.4 to -81.0)	-67.9 (-75.0 to -60.0)	-91.7 (-93.8 to -86.4)	-79.6 (-91.7 to -58.3)
Week 208|	-87.5 (-97.4 to -82.1)	-81.3 (-88.9 to -72.4)	-92.1 (-96.0 to -88.3)	-75.0 (-86.1 to -56.5)

Week 260|	-90.9 (-95.5 to -76.2)	-84.8 (-91.7 to -76.2)	-92.3 (-95.0 to -83.3)	-75.0 (-100.0 to -44.9)

End point values	AIN150 SOR_AIN300 FI	AIN300 SoR	AIN300 SoR _ AIN300 FI	AIN300 OL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	60	112	33
Units: Percent change				
median (confidence interval 95%)				
Week 52|	-68.2 (-75.0 to -61.0)	-66.7 (-75.0 to -52.9)	-72.8 (-79.0 to -65.0)	-79.2 (-89.6 to -65.0)
Week 104|	-63.6 (-70.8 to -56.3)	-68.8 (-78.9 to -51.8)	-74.9 (-81.2 to -66.7)	-77.2 (-88.9 to -62.0)
Week 156|	-60.6 (-67.7 to -53.3)	-73.9 (-84.6 to -62.5)	-66.7 (-74.2 to -59.4)	-80.0 (-90.5 to -61.5)
Week 208|	-85.7 (-90.5 to -80.1)	-74.1 (-85.6 to -55.4)	-84.6 (-88.1 to -78.9)	-81.7 (-90.5 to -66.7)
Week 260|	-82.3 (-90.6 to -74.3)	-63.9 (-78.4 to -44.4)	-83.3 (-89.1 to -76.2)	-80.0 (-95.0 to -59.3)

End point values	AIN150FI (NSW+SW)			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Percent change				
median (confidence interval 95%)				
Week 52|	-81.8 (-87.5 to -75.0)			
Week 104|	-73.3 (-78.1 to -67.3)			
Week 156|	-75.0 (-80.0 to -69.3)			
Week 208|	-83.3 (-89.3 to -78.2)			
Week 260|	-86.1 (-91.7 to -78.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Dermatology Life Quality Index (DLQI©) response (DLQI 0 or 1) Over time at weeks 52, 104, 156, 208 and 260

End point title	Percentage of Participants with Dermatology Life Quality Index (DLQI©) response (DLQI 0 or 1) Over time at weeks 52, 104, 156, 208 and 260

End point description:

The DLQI is a quality of life measure used in the psoriatic The 10-item questionnaire has a score range of 0 (best) to 30 (worst) with higher scores indicating poor quality of life. The instrument contains six

functional scales (i.e., symptoms and feeling, daily activities, leisure, work and school, personal relationships, treatment). Each item has 4 response categories, ranging from 0 (not at all) to 3 (very much). "Not relevant" is also a valid response and is scored as 0. The DLQI total score is a sum of the 10 questions.

End point type	Secondary

End point timeframe:

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

End point values	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI	AIN150 SoR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	75	168	55
Units: Percentage of participants				
number (not applicable)				
Week 52|	59.7	57.3	72.7	32.7
Week 104|	54.5	47.2	64.7	41.2
Week 156|	66.7	37.3	67.4	43.8
Week 208|	62.2	52.9	70.5	30.8
Week 260|	55.2	54.4	65.5	60.0

End point values	AIN150 SOR_AIN300 FI	AIN300 SoR	AIN300 SoR – AIN300 FI	AIN300 OL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	60	112	33
Units: Percentage of participants				
number (not applicable)				
Week 52|	34.7	28.3	41.4	54.5
Week 104|	33.0	32.5	41.5	36.7
Week 156|	35.5	38.1	38.5	50.0
Week 208|	62.5	42.9	59.0	52.4
Week 260|	55.7	15.4	56.3	50.0

End point values	AIN150FI (NSW+SW)			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Percentage of participants				
number (not applicable)				
Week 52|	58.6			
Week 104|	50.7			
Week 156|	47.4			
Week 208|	56.1			
Week 260|	54.7			

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQOL 5-Dimension Health Status Questionnaire (EQ-5D©) Score and percent change from Baseline at weeks 52, 104 and 156

End point title	EuroQOL 5-Dimension Health Status Questionnaire (EQ-5D©) Score and percent change from Baseline at weeks 52, 104 and 156

End point description:

ED-5Q: Participant rated questionnaire to assess health related quality of life in terms of a single utility score. Five domains are assessed mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) each with three possible score: 1 indicates no problems, better state of health; 3 indicates worst state of health (example "confined to bed") A visual analog scale (VAS) assesses the health status from 0 (worst possible health state) to 100 (best possible health state).

End point type	Secondary

End point timeframe:

Baseline, Week 52, Week 104, Week 156

End point values	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI	AIN150 SoR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	75	168	55
Units: Percent change				
arithmetic mean (standard deviation)				
Week 52|	68.8 (± 137.47)	57.0 (± 137.79)	115.8 (± 666.41)	40.2 (± 94.91)
Week 104|	58.6 (± 122.96)	62.4 (± 156.21)	118.5 (± 689.52)	29.5 (± 70.63)
Week 156|	61.0 (± 114.81)	52.1 (± 115.04)	125.3 (± 677.23)	45.1 (± 102.64)

End point values	AIN150 SOR_AIN300 FI	AIN300 SoR	AIN300 SoR _ AIN300 FI	AIN300 OL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	60	112	33
Units: Percent change				
arithmetic mean (standard deviation)				
Week 52|	76.9 (± 222.97)	41.3 (± 140.42)	98.8 (± 359.93)	60.9 (± 74.18)
Week 104|	152.9 (± 902.21)	46.7 (± 142.85)	77.2 (± 150.86)	54.3 (± 84.82)

Week 156|	140.3 (± 778.86)	13.7 (± 25.16)	109.5 (± 373.51)	68.1 (± 96.22)

End point values	AIN150FI (NSW+SW)			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Percent change				
arithmetic mean (standard deviation)				
Week 52|	63.0 (± 137.30)			
Week 104|	60.6 (± 140.91)			
Week 156|	55.2 (± 114.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with treatment emergent anti-drug antibodies (ADA)

End point title	Number of Participants with treatment emergent anti-drug antibodies (ADA)

End point description:

The development of anti-secunimubab anti-bodies will decrease a participant's ability to respond to secukinumab treatment.

End point type	Secondary

End point timeframe:

Week 268

End point values	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI	AIN150 SoR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	75	168	55
Units: Participants	2	1	3	0

End point values	AIN150 SOR_AIN300 FI	AIN300 SoR	AIN300 SoR – AIN300 FI	AIN300 OL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	60	112	33
Units: Participants	4	0	4	2

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients with experiencing a Relapse

End point title	Percentage of patients with experiencing a Relapse

End point description:

Relapse is defined as greater than 50% loss of the maximal PASI improvement from baseline. PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). A negative mean percentage change indicates improvement.

End point type	Secondary

End point timeframe:

Week 260

End point values	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI	AIN150 SoR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	75	168	55
Units: Percentage of Participants				
number (not applicable)	31.2	40.0	19.6	61.8

End point values	AIN150 SOR_AIN300 FI	AIN300 SoR	AIN300 SoR _ AIN300 FI	AIN300 OL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	60	112	33
Units: Percentage of Participants				
number (not applicable)	52.6	43.3	56.3	36.4

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients with experiencing a Rebound

End point title	Percentage of patients with experiencing a Rebound

End point description:

Rebound of disease is defined as a worsening of PASI of > 125% of the value at baseline (core study), or new pustular, erythrodermic or more inflammatory psoriasis occurring within 8 weeks of stopping therapy (i.e., if this definition was fulfilled at more than 8 weeks after last study treatment administration, this was defined as rebound like event). PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs; each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). A negative mean percentage change indicates improvement.

End point type	Secondary

End point timeframe:

Up to Week 264 (8 weeks post last dose)

End point values	AIN150FI	AIN150 FI_AIN300 FI	AIN300 FI	AIN150 SoR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	75	168	55
Units: Percentage of participants				
number (confidence interval 95%)	11.5 (5.1 to 22.8)	5.8 (1.9 to 14.9)	5.0 (2.2 to 10.3)	9.4 (2.5 to 26.2)

End point values	AIN150 SOR_AIN300 FI	AIN300 SoR	AIN300 SoR _ AIN300 FI	AIN300 OL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	60	112	33
Units: Percentage of participants				
number (confidence interval 95%)	1.1 (0.1 to 7.0)	6.9 (1.2 to 24.2)	10.6 (5.7 to 18.5)	13.0 (3.4 to 34.7)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Any AIN457 150 mg

Reporting group description:

Any AIN457 150 mg

Reporting group title	Any AIN457 300 mg

Reporting group description:

Any AIN457 300 mg

Reporting group title	Any AIN457 dose

Reporting group description:

Any AIN457 dose

Serious adverse events	Any AIN457 150 mg	Any AIN457 300 mg	Any AIN457 dose
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 132 (18.94%)	119 / 543 (21.92%)	144 / 675 (21.33%)
number of deaths (all causes)	0	4	4
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	1 / 132 (0.76%)	3 / 543 (0.55%)	4 / 675 (0.59%)
occurrences causally related to treatment / all	0 / 1	1 / 3	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BENIGN LUNG NEOPLASM			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BENIGN NEOPLASM OF THYROID GLAND			

subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER ADENOCARCINOMA STAGE UNSPECIFIED			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CANCER			
subjects affected / exposed	1 / 132 (0.76%)	1 / 543 (0.18%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLANGIOCARCINOMA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON CANCER			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPLASTIC NAEVUS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOMETRIAL ADENOCARCINOMA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE DUCTAL BREAST CARCINOMA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALIGNANT MELANOMA			

subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATE CANCER			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE LEIOMYOMA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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			
AORTIC DILATATION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERY STENOSIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 132 (0.00%)	3 / 543 (0.55%)	3 / 675 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

PERIPHERAL SWELLING			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
ALCOHOL USE			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
ENDOMETRIOSIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENOMETRORRHAGIA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATOMEGALY			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE POLYP			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VULVA CYST			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
LUNG DISORDER			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 CAVITATION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 EMBOLISM			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
RESPIRATORY SYMPTOM			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THORACIC HAEMORRHAGE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
ADJUSTMENT DISORDER			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

DELIRIUM			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEPRESSION			
subjects affected / exposed	1 / 132 (0.76%)	1 / 543 (0.18%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUICIDE ATTEMPT			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
DEVICE MALFUNCTION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 132 (0.76%)	2 / 543 (0.37%)	3 / 675 (0.44%)
occurrences causally related to treatment / all	1 / 1	0 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 132 (0.00%)	3 / 543 (0.55%)	3 / 675 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			

subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	1 / 132 (0.76%)	3 / 543 (0.55%)	4 / 675 (0.59%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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			
ALCOHOL POISONING			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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	0 / 132 (0.00%)	3 / 543 (0.55%)	3 / 675 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRAIN CONTUSION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			

subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMUR FRACTURE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIP FRACTURE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JOINT DISLOCATION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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	1 / 132 (0.76%)	1 / 543 (0.18%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIMB CRUSHING INJURY			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENISCUS INJURY			
subjects affected / exposed	1 / 132 (0.76%)	1 / 543 (0.18%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RIB FRACTURE			

subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPLENIC INJURY			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TIBIA FRACTURE			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER LIMB FRACTURE			
subjects affected / exposed	0 / 132 (0.00%)	3 / 543 (0.55%)	3 / 675 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WRIST FRACTURE			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			

subjects affected / exposed	0 / 132 (0.00%)	3 / 543 (0.55%)	3 / 675 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA UNSTABLE			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AORTIC VALVE DISEASE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARRHYTHMIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
ARRHYTHMIA SUPRAVENTRICULAR			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 132 (0.76%)	4 / 543 (0.74%)	5 / 675 (0.74%)
occurrences causally related to treatment / all	0 / 1	1 / 4	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FLUTTER			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRADYCARDIA			

subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BUNDLE BRANCH BLOCK LEFT			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE ACUTE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
CARDIAC FAILURE CHRONIC			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONGESTIVE CARDIOMYOPATHY			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY OCCLUSION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 OSTIAL STENOSIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEFT VENTRICULAR DYSFUNCTION			

subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LONG QT SYNDROME			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CAROTID ARTERY STENOSIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARPAL TUNNEL SYNDROME			

subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CAUDA EQUINA SYNDROME			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVICOBRACHIAL SYNDROME			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CUBITAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEADACHE			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRACRANIAL ANEURYSM			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METABOLIC ENCEPHALOPATHY			

subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NERVE COMPRESSION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERONEAL NERVE PALSY			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCIATICA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
AUTOIMMUNE HAEMOLYTIC ANAEMIA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHOID TISSUE HYPERPLASIA			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			

VESTIBULAR DISORDER			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 INCONTINENCE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 HAEMORRHAGE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 OBSTRUCTION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE POLYP			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEUKOPLAKIA ORAL			

subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
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 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOOTHACHE			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
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			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS ACUTE			
subjects affected / exposed	3 / 132 (2.27%)	0 / 543 (0.00%)	3 / 675 (0.44%)
occurrences causally related to treatment / all	1 / 3	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLELITHIASIS			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC CIRRHOSIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 STEATOSIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 ALCOHOLIC			

subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMAL CYST			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 ALLERGIC			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PSORIASIS			
subjects affected / exposed	0 / 132 (0.00%)	3 / 543 (0.55%)	3 / 675 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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	1 / 132 (0.76%)	1 / 543 (0.18%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL INFARCT			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL INJURY			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL TUBULAR NECROSIS			

subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 INCONTINENCE			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 RETENTION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FLANK PAIN			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOOT DEFORMITY			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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	0 / 132 (0.00%)	3 / 543 (0.55%)	3 / 675 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOARTHRITIS			

subjects affected / exposed	2 / 132 (1.52%)	3 / 543 (0.55%)	5 / 675 (0.74%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PSORIATIC ARTHROPATHY			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROTATOR CUFF SYNDROME			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL PAIN			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TENOSYNOVITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ACUTE HEPATITIS B			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE SINUSITIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL ABSCESS			

subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICITIS			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BURSITIS INFECTIVE STAPHYLOCOCCAL			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC TONSILLITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CYSTITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPIDIDYMITIS			
subjects affected / exposed	1 / 132 (0.76%)	0 / 543 (0.00%)	1 / 675 (0.15%)
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 / 132 (0.00%)	3 / 543 (0.55%)	3 / 675 (0.44%)
occurrences causally related to treatment / all	0 / 0	2 / 3	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL INFECTION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORCHITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 BACTERIAL			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONSILLITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 132 (0.00%)	6 / 543 (1.10%)	6 / 675 (0.89%)
occurrences causally related to treatment / all	0 / 0	5 / 7	5 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			

subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUSITIS			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
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 STAPHYLOCOCCAL			
subjects affected / exposed	0 / 132 (0.00%)	1 / 543 (0.18%)	1 / 675 (0.15%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DIABETES MELLITUS			
subjects affected / exposed	0 / 132 (0.00%)	2 / 543 (0.37%)	2 / 675 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	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	93 / 132 (70.45%)	449 / 543 (82.69%)	542 / 675 (80.30%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	8 / 132 (6.06%)	63 / 543 (11.60%)	71 / 675 (10.52%)
occurrences (all)	8	71	79

General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	5 / 132 (3.79%)	16 / 543 (2.95%)	21 / 675 (3.11%)
occurrences (all)	5	17	22
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	4 / 132 (3.03%)	13 / 543 (2.39%)	17 / 675 (2.52%)
occurrences (all)	4	14	18
OEDEMA PERIPHERAL			
subjects affected / exposed	3 / 132 (2.27%)	17 / 543 (3.13%)	20 / 675 (2.96%)
occurrences (all)	3	23	26
PYREXIA			
subjects affected / exposed	3 / 132 (2.27%)	14 / 543 (2.58%)	17 / 675 (2.52%)
occurrences (all)	5	20	25
Immune system disorders			
SEASONAL ALLERGY			
subjects affected / exposed	0 / 132 (0.00%)	16 / 543 (2.95%)	16 / 675 (2.37%)
occurrences (all)	0	18	18
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	4 / 132 (3.03%)	51 / 543 (9.39%)	55 / 675 (8.15%)
occurrences (all)	4	61	65
DYSPNOEA			
subjects affected / exposed	3 / 132 (2.27%)	6 / 543 (1.10%)	9 / 675 (1.33%)
occurrences (all)	3	11	14
OROPHARYNGEAL PAIN			
subjects affected / exposed	4 / 132 (3.03%)	31 / 543 (5.71%)	35 / 675 (5.19%)
occurrences (all)	4	40	44
SINUS CONGESTION			
subjects affected / exposed	0 / 132 (0.00%)	11 / 543 (2.03%)	11 / 675 (1.63%)
occurrences (all)	0	14	14
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	4 / 132 (3.03%)	13 / 543 (2.39%)	17 / 675 (2.52%)
occurrences (all)	5	13	18
INSOMNIA			

subjects affected / exposed	3 / 132 (2.27%)	14 / 543 (2.58%)	17 / 675 (2.52%)
occurrences (all)	3	15	18
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	3 / 132 (2.27%)	7 / 543 (1.29%)	10 / 675 (1.48%)
occurrences (all)	4	14	18
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	2 / 132 (1.52%)	15 / 543 (2.76%)	17 / 675 (2.52%)
occurrences (all)	2	23	25
HEPATIC ENZYME INCREASED			
subjects affected / exposed	5 / 132 (3.79%)	10 / 543 (1.84%)	15 / 675 (2.22%)
occurrences (all)	5	10	15
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	1 / 132 (0.76%)	13 / 543 (2.39%)	14 / 675 (2.07%)
occurrences (all)	1	14	15
CONTUSION			
subjects affected / exposed	2 / 132 (1.52%)	22 / 543 (4.05%)	24 / 675 (3.56%)
occurrences (all)	2	25	27
FALL			
subjects affected / exposed	0 / 132 (0.00%)	11 / 543 (2.03%)	11 / 675 (1.63%)
occurrences (all)	0	11	11
LIGAMENT SPRAIN			
subjects affected / exposed	1 / 132 (0.76%)	12 / 543 (2.21%)	13 / 675 (1.93%)
occurrences (all)	2	12	14
MUSCLE STRAIN			
subjects affected / exposed	1 / 132 (0.76%)	19 / 543 (3.50%)	20 / 675 (2.96%)
occurrences (all)	1	22	23
Cardiac disorders			
TACHYCARDIA			
subjects affected / exposed	3 / 132 (2.27%)	1 / 543 (0.18%)	4 / 675 (0.59%)
occurrences (all)	6	1	7
Nervous system disorders			
DIZZINESS			

subjects affected / exposed	3 / 132 (2.27%)	12 / 543 (2.21%)	15 / 675 (2.22%)
occurrences (all)	3	13	16
HEADACHE			
subjects affected / exposed	11 / 132 (8.33%)	50 / 543 (9.21%)	61 / 675 (9.04%)
occurrences (all)	40	80	120
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	3 / 132 (2.27%)	11 / 543 (2.03%)	14 / 675 (2.07%)
occurrences (all)	3	13	16
DENTAL CARIES			
subjects affected / exposed	1 / 132 (0.76%)	11 / 543 (2.03%)	12 / 675 (1.78%)
occurrences (all)	1	11	12
DIARRHOEA			
subjects affected / exposed	8 / 132 (6.06%)	32 / 543 (5.89%)	40 / 675 (5.93%)
occurrences (all)	10	40	50
GASTRITIS			
subjects affected / exposed	4 / 132 (3.03%)	13 / 543 (2.39%)	17 / 675 (2.52%)
occurrences (all)	7	15	22
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	3 / 132 (2.27%)	12 / 543 (2.21%)	15 / 675 (2.22%)
occurrences (all)	3	12	15
NAUSEA			
subjects affected / exposed	8 / 132 (6.06%)	9 / 543 (1.66%)	17 / 675 (2.52%)
occurrences (all)	8	9	17
TOOTHACHE			
subjects affected / exposed	5 / 132 (3.79%)	21 / 543 (3.87%)	26 / 675 (3.85%)
occurrences (all)	5	22	27
VOMITING			
subjects affected / exposed	1 / 132 (0.76%)	16 / 543 (2.95%)	17 / 675 (2.52%)
occurrences (all)	1	16	17
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	3 / 132 (2.27%)	9 / 543 (1.66%)	12 / 675 (1.78%)
occurrences (all)	3	9	12
Skin and subcutaneous tissue disorders			

ACNE			
subjects affected / exposed	3 / 132 (2.27%)	3 / 543 (0.55%)	6 / 675 (0.89%)
occurrences (all)	3	3	6
ACTINIC KERATOSIS			
subjects affected / exposed	3 / 132 (2.27%)	6 / 543 (1.10%)	9 / 675 (1.33%)
occurrences (all)	3	17	20
DERMATITIS CONTACT			
subjects affected / exposed	1 / 132 (0.76%)	32 / 543 (5.89%)	33 / 675 (4.89%)
occurrences (all)	1	38	39
ECZEMA			
subjects affected / exposed	6 / 132 (4.55%)	25 / 543 (4.60%)	31 / 675 (4.59%)
occurrences (all)	9	31	40
PRURITUS			
subjects affected / exposed	9 / 132 (6.82%)	27 / 543 (4.97%)	36 / 675 (5.33%)
occurrences (all)	9	34	43
PSORIASIS			
subjects affected / exposed	7 / 132 (5.30%)	49 / 543 (9.02%)	56 / 675 (8.30%)
occurrences (all)	7	58	65
Renal and urinary disorders			
HAEMATURIA			
subjects affected / exposed	5 / 132 (3.79%)	11 / 543 (2.03%)	16 / 675 (2.37%)
occurrences (all)	5	13	18
Endocrine disorders			
HYPERTHYROIDISM			
subjects affected / exposed	3 / 132 (2.27%)	0 / 543 (0.00%)	3 / 675 (0.44%)
occurrences (all)	4	0	4
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	9 / 132 (6.82%)	63 / 543 (11.60%)	72 / 675 (10.67%)
occurrences (all)	12	90	102
BACK PAIN			
subjects affected / exposed	9 / 132 (6.82%)	53 / 543 (9.76%)	62 / 675 (9.19%)
occurrences (all)	17	65	82
BURSITIS			
subjects affected / exposed	2 / 132 (1.52%)	11 / 543 (2.03%)	13 / 675 (1.93%)
occurrences (all)	2	12	14

MUSCULOSKELETAL PAIN			
subjects affected / exposed	2 / 132 (1.52%)	16 / 543 (2.95%)	18 / 675 (2.67%)
occurrences (all)	3	20	23
MYALGIA			
subjects affected / exposed	0 / 132 (0.00%)	15 / 543 (2.76%)	15 / 675 (2.22%)
occurrences (all)	0	15	15
OSTEOARTHRITIS			
subjects affected / exposed	4 / 132 (3.03%)	17 / 543 (3.13%)	21 / 675 (3.11%)
occurrences (all)	6	20	26
PAIN IN EXTREMITY			
subjects affected / exposed	8 / 132 (6.06%)	22 / 543 (4.05%)	30 / 675 (4.44%)
occurrences (all)	8	24	32
PSORIATIC ARTHROPATHY			
subjects affected / exposed	3 / 132 (2.27%)	20 / 543 (3.68%)	23 / 675 (3.41%)
occurrences (all)	3	21	24
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	7 / 132 (5.30%)	51 / 543 (9.39%)	58 / 675 (8.59%)
occurrences (all)	8	74	82
CELLULITIS			
subjects affected / exposed	1 / 132 (0.76%)	15 / 543 (2.76%)	16 / 675 (2.37%)
occurrences (all)	1	17	18
CONJUNCTIVITIS			
subjects affected / exposed	3 / 132 (2.27%)	19 / 543 (3.50%)	22 / 675 (3.26%)
occurrences (all)	3	21	24
FOLLICULITIS			
subjects affected / exposed	3 / 132 (2.27%)	25 / 543 (4.60%)	28 / 675 (4.15%)
occurrences (all)	5	36	41
FURUNCLE			
subjects affected / exposed	2 / 132 (1.52%)	11 / 543 (2.03%)	13 / 675 (1.93%)
occurrences (all)	2	13	15
GASTROENTERITIS			
subjects affected / exposed	6 / 132 (4.55%)	23 / 543 (4.24%)	29 / 675 (4.30%)
occurrences (all)	6	28	34
HERPES ZOSTER			

subjects affected / exposed	6 / 132 (4.55%)	13 / 543 (2.39%)	19 / 675 (2.81%)
occurrences (all)	6	13	19
INFLUENZA			
subjects affected / exposed	12 / 132 (9.09%)	42 / 543 (7.73%)	54 / 675 (8.00%)
occurrences (all)	15	61	76
NASOPHARYNGITIS			
subjects affected / exposed	31 / 132 (23.48%)	185 / 543 (34.07%)	216 / 675 (32.00%)
occurrences (all)	84	449	533
ORAL HERPES			
subjects affected / exposed	1 / 132 (0.76%)	19 / 543 (3.50%)	20 / 675 (2.96%)
occurrences (all)	1	32	33
PHARYNGITIS			
subjects affected / exposed	5 / 132 (3.79%)	28 / 543 (5.16%)	33 / 675 (4.89%)
occurrences (all)	8	40	48
RHINITIS			
subjects affected / exposed	4 / 132 (3.03%)	22 / 543 (4.05%)	26 / 675 (3.85%)
occurrences (all)	4	25	29
SINUSITIS			
subjects affected / exposed	8 / 132 (6.06%)	30 / 543 (5.52%)	38 / 675 (5.63%)
occurrences (all)	14	35	49
TINEA PEDIS			
subjects affected / exposed	3 / 132 (2.27%)	12 / 543 (2.21%)	15 / 675 (2.22%)
occurrences (all)	3	13	16
TONSILLITIS			
subjects affected / exposed	5 / 132 (3.79%)	20 / 543 (3.68%)	25 / 675 (3.70%)
occurrences (all)	5	27	32
TOOTH ABSCESS			
subjects affected / exposed	2 / 132 (1.52%)	15 / 543 (2.76%)	17 / 675 (2.52%)
occurrences (all)	2	18	20
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	13 / 132 (9.85%)	62 / 543 (11.42%)	75 / 675 (11.11%)
occurrences (all)	23	105	128
URINARY TRACT INFECTION			
subjects affected / exposed	4 / 132 (3.03%)	23 / 543 (4.24%)	27 / 675 (4.00%)
occurrences (all)	4	32	36

VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 132 (0.00%)	26 / 543 (4.79%)	26 / 675 (3.85%)
occurrences (all)	0	31	31
Metabolism and nutrition disorders			
DIABETES MELLITUS			
subjects affected / exposed	1 / 132 (0.76%)	20 / 543 (3.68%)	21 / 675 (3.11%)
occurrences (all)	1	21	22
DYSLIPIDAEMIA			
subjects affected / exposed	3 / 132 (2.27%)	12 / 543 (2.21%)	15 / 675 (2.22%)
occurrences (all)	3	14	17
GOUT			
subjects affected / exposed	0 / 132 (0.00%)	11 / 543 (2.03%)	11 / 675 (1.63%)
occurrences (all)	0	12	12
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	1 / 132 (0.76%)	12 / 543 (2.21%)	13 / 675 (1.93%)
occurrences (all)	1	12	13
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 132 (0.00%)	12 / 543 (2.21%)	12 / 675 (1.78%)
occurrences (all)	0	14	14

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 April 2014	The results of protocol CAIN457A2304 showed that the re-treatment at start of relapse maintenance regimen (SoR) was not non-inferior to a fixed interval regimen (FI) with treatment every four weeks and that patients experienced better maintenance of effect with secukinumab 300 mg compared to secukinumab 150 mg; therefore, this amendment introduces an opportunity at week 156 for blinded subjects to 1) switch off of the SoR treatment regimen to treatment every four weeks and 2) to increase the secukinumab dose to 300 mg. All subjects will be unblinded at Week 156 and the investigator may switch to the subject one of these open label treatment option(s) depending on the current treatment assignment. Additionally, this amendment extends the treatment duration for an additional 104 weeks (for a total of 5 years, one year in the core study or studies and four years in the extension study) and the opportunity for home administration of the study drug. In case secukinumab becomes commercially available in a participating country, the study might be discontinued in the respective country. This extension of treatment will allow for safety, tolerability, and efficacy data to be collected from the participating subjects for up to a total of 5 years. At the time of this amendment, recruitment is complete with 675 subjects randomized into the trial across 15 countries and 112 sites and approximately 108 subjects have discontinued from the study. Since recruitment is complete and there is no change to protocol-mandated discontinuation, it is not expected that this amendment will have an impact on the study population or have a significant impact on the primary objective of the trial.
29 April 2015	FDA has requested the following post marketing commitment be applied to this study: "Complete the treatment and evaluation of subjects enrolled in the ongoing CAIN457A2304E1 trial for a duration of 4 years, unless a safety signal is identified that indicates the potential risks of such continued long-term treatment outweigh the benefits. Evaluation of subjects should continue through the end of the trial when achievable (even if treatment is not continued for the duration). Subjects will be followed for the occurrence of serious infection, tuberculosis, opportunistic infections, malignancy, hypersensitivity reactions, autoimmune disease, neurologic or demyelinating disease, cardiovascular, gastrointestinal or hematologic adverse events". Subjects who complete treatment period and follow-up period are evaluated for 4 years regarding respective adverse events. However, patient who prematurely discontinue treatment are evaluated for less than 4 years. Therefore, this amendment extends the evaluation of subjects who prematurely discontinue treatment regarding respective adverse events and concomitant medications in order to achieve a 4 year evaluation period. Evaluation of subjects should continue when achievable even if treatment is not continued for the duration. All subjects who prematurely discontinue treatment should complete all assessment of Week 260 (end of treatment visit) and of the follow-up period visits (Weeks 264 and 268). Subsequently, adverse events and use of concomitant medication will be evaluated by the investigator through telephone calls every 3 months for a duration of 4 years from the time when subject has been enrolled into CAIN457A2304E1 study. If deemed necessary by the investigator unplanned assessments at site might be scheduled during this time. In addition, the study will NOT be terminated in selected countries where the drug is commercially available.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported