Clinical trial results:
A randomized, double-blind, multicenter study to assess the efficacy and safety of 16 weeks secukinumab dosage interval shortening in comparison to continued standard treatment (4-weekly 300 mg s.c.) in patients with moderate-severe plaque type psoriasis who achieved less than almost clear skin after 16 weeks under the standard dose of secukinumab

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Summary

EudraCT number	2014-001974-32
Trial protocol	DE
Global end of trial date	15 September 2016
Results information	
Result version number	v1 (current)
This version publication date	07 July 2018
First version publication date	07 July 2018

Trial information

Trial identification	
Sponsor protocol code	AIN457ADE04
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02474069
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,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

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	15 September 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to demonstrate that 300 mg secukinumab administered every 2 weeks was superior in achieving PASI 90 at Week 32 compared to 300 mg secukinumab every 4 weeks in patients who, after treatment with the standard dose, had less than almost clear skin (PASI ≥ 75 to PASI < 90) at Week 16.

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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 772
Worldwide total number of subjects	772
EEA total number of subjects	772

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)	712
From 65 to 84 years	59
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

860 were screened (not shown here). In selection phase (SP), 772 received 300 mg s.c. open-label secukinumab at baseline, to week 12. Those who did not achieve at least PASI 75 at week 16 discontinued. Those who had less than clear or almost clear skin (at least PASI 75 but not PASI 90) rolled over into double blind comparative dosing phase (CDP)

Pre-assignment

Screening details:

and randomized 1:1 to: a.standard treatment: 300 mg s.c. secukinumab treatment every 4 weeks (weeks 16, 20, 24, & 28) and, to maintain the blind, placebo every 4 weeks
b. OR dosage interval shortening: 300 mg s.c. secukinumab treatment every 2 weeks.
Those who achieved at least clear or almost clear skin (≥ PASI 90) at week 16 discontinued study

Period 1

Period 1 title	Overall: Selection->CDP (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	SP - Secukinumab 300 mg s.c. (4-weekly)

Arm description:

In the SP, all patients were treated with open-label secukinumab 300 mg s.c. at baseline, Weeks 1, 2, 3, 4, 8, and 12.

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

In the SP, all patients were treated with open-label secukinumab 300 mg s.c. at baseline, Weeks 1, 2, 3, 4, 8, and 12.

Arm title	CDP - Secukinumab 300 mg s.c. (4-weekly)

Arm description:

In the CDP, patients received 300 mg s.c. secukinumab treatment every 4 weeks (Week 16, 20, 24, and 28) and placebo every 4 weeks (at Week 18, 22, 26 and 30).

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

In the CDP, patients received 300 mg s.c. secukinumab treatment every 4 weeks (Week 16, 20, 24, and 28) and placebo every 4 weeks (at Week 18, 22, 26 and 30).

Arm title	CDP - Secukinumab 300 mg s.c. (2-weekly)

Arm description:

In the CDP, patients received 300 mg s.c. secukinumab treatment every 2 weeks (at weeks 16, 18, 20,

22, 24, 26, 28 and 30)

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

In the CDP, patients received 300 mg s.c. secukinumab treatment every 2 weeks (at weeks 16, 18, 20, 22, 24, 26, 28 and 30)

Number of subjects in period 1	SP - Secukinumab 300 mg s.c. (4-weekly)	CDP - Secukinumab 300 mg s.c. (4-weekly)	CDP - Secukinumab 300 mg s.c. (2-weekly)
Started	772	162	163
Completed	749	153	157
Not completed	23	9	6
Physician decision	1	-	-
Consent withdrawn by subject	3	2	3
Withdrawal of informed Consent	3	-	-
Adverse event, non-fatal	8	3	2
Technical Problem	1	-	-
Lost to follow-up	4	4	1
No longer requires treatment	1	-	-
Lack of efficacy	1	-	-
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	Overall: Selection->CDP

Reporting group description: -

Reporting group values	Overall: Selection->CDP	Total	
Number of subjects	772	772	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	712	712	
From 65-84 years	59	59	
85 years and over	1	1	
Age Continuous Units: Years			
arithmetic mean	45.8		
standard deviation	± 13.72	-	
Gender Categorical			
Comparative dosing phase (CDP) only			
Units: Subjects			
Female	222	222	
Male	550	550	

Subject analysis sets

Subject analysis set title	SP - Secukinumab 300 mg s.c. (4-weekly
Subject analysis set type	Full analysis

Subject analysis set description:

In the SP, all patients were treated with open-label secukinumab 300 mg s.c. at baseline, Weeks 1, 2, 3, 4, 8, and 12. At Week 16

Reporting group values	SP - Secukinumab 300 mg s.c. (4-weekly		
Number of subjects	772		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		

Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	712		
From 65-84 years	59		
85 years and over	1		
Age Continuous			
Units: Years			
arithmetic mean	45.8		
standard deviation	± 13.72		
Gender Categorical			
Comparative dosing phase (CDP) only			
Units: Subjects			
Female	222		
Male	550		

End points

End points reporting groups

Reporting group title	SP - Secukinumab 300 mg s.c. (4-weekly)
Reporting group description:	
In the SP, all patients were treated with open-label secukinumab 300 mg s.c. at baseline, Weeks 1, 2, 3, 4, 8, and 12.	
Reporting group title	CDP - Secukinumab 300 mg s.c. (4-weekly)
Reporting group description:	
In the CDP, patients received 300 mg s.c. secukinumab treatment every 4 weeks (Week 16, 20, 24, and 28) and placebo every 4 weeks (at Week 18, 22, 26 and 30).	
Reporting group title	CDP - Secukinumab 300 mg s.c. (2-weekly)
Reporting group description:	
In the CDP, patients received 300 mg s.c. secukinumab treatment every 2 weeks (at weeks 16, 18, 20, 22, 24, 26, 28 and 30)	
Subject analysis set title	SP - Secukinumab 300 mg s.c. (4-weekly
Subject analysis set type	Full analysis
Subject analysis set description:	
In the SP, all patients were treated with open-label secukinumab 300 mg s.c. at baseline, Weeks 1, 2, 3, 4, 8, and 12. At Week 16	

Primary: Number of participants with PASI 90 response at Week 32

End point title	Number of participants with PASI 90 response at Week 32[1]
End point description:	
Number of participants with at least 90% 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).	
End point type	Primary
End point timeframe:	
at 32 weeks	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics do not apply to this end point.

End point values	CDP - Secukinumab 300 mg s.c. (4-weekly)	CDP - Secukinumab 300 mg s.c. (2-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	163		
Units: participants	93	105		

Statistical analyses

Statistical analysis title	Number of participants with PASI 90 resposne
Statistical analysis description:	
Logistic regression model: Logit (proportion) = treatment + PASI Score at baseline + PASI score at	

randomization + error

Comparison groups	CDP - Secukinumab 300 mg s.c. (4-weekly) v CDP - Secukinumab 300 mg s.c. (2-weekly)
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.087
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.07

Primary: Number of participants with PASI 90 response at Week 32 for PPS

End point title	Number of participants with PASI 90 response at Week 32 for PPS[2]

End point description:

Number of participants with at least 90% 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).

End point type	Primary

End point timeframe:

at week 32

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics do not apply to this end point.

End point values	CDP - Secukinumab 300 mg s.c. (4-weekly)	CDP - Secukinumab 300 mg s.c. (2-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	134		
Units: participants	81	85		

Statistical analyses

Statistical analysis title	Number of participants with PASI 90 response

Statistical analysis description:

Logistic regression model: Logit (proportion) = treatment + PASI Score at baseline + PASI score at randomization + error

Comparison groups	CDP - Secukinumab 300 mg s.c. (2-weekly) v CDP - Secukinumab 300 mg s.c. (4-weekly)

Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.281
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.28

Secondary: Selection Phase: Number of participants achieving (Psoriasis Area and Severity Index score)PASI 50, 75, 90, 100

End point title	Selection Phase: Number of participants achieving (Psoriasis Area and Severity Index score)PASI 50, 75, 90, 100[3]

End point description:

Number of participants with at least 50, 75, 90 or 100% 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).

End point type	Secondary

End point timeframe:

at weeks 1, 2, 3, 4, 8, 12 and 16

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics do not apply to this end point.

End point values	SP - Secukinumab 300 mg s.c. (4-weekly)			
Subject group type	Reporting group			
Number of subjects analysed	772			
Units: Number of participants				
Week 1, PASI 50 (n= 768)	43			
Week 1, PASI 75 (n= 768)	3			
Week 1, PASI 90 (n= 768)	0			
Week 1, PASI 100 (n= 768)	0			
Week 2, PASI 50 (n= 766)	232			
week 2, PASI 75 (n= 766)	25			
Week 2, PASI 90 (n= 766)	5			
Week 2, PASI 100 (n= 766)	1			
Week 3, PASI 50 (n= 766)	468			
Week 3, PASI 75 (n= 766)	128			
Week 3, PASI 90 (n= 766)	22			
Week 3, PASI 100 (n= 766)	3			

Week 4, PASI 50 (n= 768)	591			
Week 4, PASI 75 (n= 768)	281			
Week 4, PASI 90 (n= 768)	71			
Week 4, PASI 100 (n= 768)	12			
Week 8, PASI 50 (n= 762)	718			
Week 8, PASI 75 (n= 762)	538			
Week 8, PASI 90 (n= 762)	266			
Week 8, PASI 100 (n= 762)	70			
Week 12, PASI 50 (n= 761)	733			
Week 12, PASI 75 (n= 761)	611			
Week 12, PASI 90 (n= 761)	370			
Week 12, PASI 100 (n= 761)	110			
Week 16, PASI 50 (n= 753)	732			
Week 16, PASI 75 (n= 753)	698			
Week 16, PASI 90 (n= 753)	363			
Week 16, PASI 100 (n= 753)	124			

Statistical analyses

No statistical analyses for this end point

Secondary: Comparative Dose Phase: Number of participants achieving (Psoriasis Area and Severity Index score)PASI 50, 75, 90, 100

End point title	Comparative Dose Phase: Number of participants achieving (Psoriasis Area and Severity Index score)PASI 50, 75, 90, 100[4]

End point description:

Number of participants with at least 50, 75, 90 or 100% 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).

End point type	Secondary

End point timeframe:

at weeks 18, 22, 30, 32

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics do not apply to this end point.

End point values	CDP - Secukinumab 300 mg s.c. (4-weekly)	CDP - Secukinumab 300 mg s.c. (2-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	163		
Units: Number of participants				
Week 18, PASI 90 (n=162, 163)	42	36		
Week 18, PASI 100 (n=162, 163)	1	1		
Week 22, PASI 90 (n=162, 163)	70	67		
Week 22, PASI 100 (n=162, 163)	9	9		

Week 26, PASI 90 (n=162, 163)	85	94		
Week 26, PASI 100 (n=162, 163)	9	14		
Week 30, PASI 90 (n=162, 163)	93	104		
Week 30, PASI 100 (n=162, 163)	17	19		
Week 32, PASI 90 (n=162,163)	93	105		
Week 32, PASI 100 (n=162, 163)	22	26		

Statistical analyses

No statistical analyses for this end point

Secondary: Selection Phase:Summary of PASI total score

End point title	Selection Phase:Summary of PASI total score[5]

End point description:

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).

End point type	Secondary

End point timeframe:

at weeks 1,2,3,4,8, 12, 16

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics do not apply to this end point.

End point values	SP - Secukinumab 300 mg s.c. (4-weekly)			
Subject group type	Reporting group			
Number of subjects analysed	772			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
week 1 (n=768)	18.78 (± 9.629)			
week 2(n=766)	14.32 (± 8.435)			
week 3(n=766)	10.69 (± 7.372)			
week 4(n=768)	8.12 (± 6.494)			
week 8(n=762)	4.41 (± 4.544)			
Week 12 (n=761)	3.34 (± 3.833)			
Week 16 (n=753)	2.9 (± 3.816)			

Statistical analyses

No statistical analyses for this end point

Secondary: Comparative Dose Phase: Summary of PASI total score

End point title	Comparative Dose Phase: Summary of PASI total score[6]

End point description:

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).

End point type	Secondary

End point timeframe:

Weeks 18, 22, 26, 30 and 32

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics do not apply to this end point.

End point values	CDP - Secukinumab 300 mg s.c. (4-weekly)	CDP - Secukinumab 300 mg s.c. (2-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	163		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Week 18 (n=162, 163)	3.71 (± 2.532)	3.59 (± 2.595)		
Week 22 (n=161, 161)	3.24 (± 2.947)	3.07 (± 2.726)		
Week 26 (n=156, 160)	2.85 (± 2.852)	2.68 (± 3.393)		
Week 30 (n= 154, 158)	2.83 (± 3.339)	2.34 (± 2.812)		
Week 32 (n=153, 152)	2.84 (± 3.552)	2.11 (± 2.701)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients achieving Dermatology Life Quality Index (DLQI)

End point title	Number of patients achieving Dermatology Life Quality Index (DLQI)[7]

End point description:

The DLQI is a ten item general dermatology disability index designed to assess health-related quality of life in adult participants with skin diseases such as eczema, psoriasis, acne and viral worts. It is a self-administered questionnaire which includes domains of daily activity, leisure, personal relationships, symptoms and feelings, treatment and school/work activities. Each domain has 4 response categories ranging from 0 (not at all) to 3 (very much). "Not relevant" is a valid score also and is scored as 0. The DLQI total score is a sum of all 10 responses. Scores range from 0 to 30 with higher scores indicating greater health-related quality of life impairment.

End point type	Secondary

End point timeframe:

Weeks 4, 16

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics do not apply to this end point.

End point values	CDP - Secukinumab 300 mg s.c. (4-weekly)	CDP - Secukinumab 300 mg s.c. (2-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	163		
Units: participants				
Week 4 (n=160, NA)	13	9999		
Week 16	62	9999		
Week 18	65	58		
Week 22	70	73		
Week 26	69	83		
Week 30	75	89		
Week 32	82	96		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients achieving DLQI total score <= 5

End point title	Number of Patients achieving DLQI total score <= 5[8]

End point description:

The DLQI is a ten item general dermatology disability index designed to assess health-related quality of life in adult participants with skin diseases such as eczema, psoriasis, acne and viral worts. It is a self-administered questionnaire which includes domains of daily activity, leisure, personal relationships, symptoms and feelings, treatment and school/work activities. Each domain has 4 response categories ranging from 0 (not at all) to 3 (very much). "Not relevant" is a valid score also and is scored as 0. The DLQI total score is a sum of all 10 responses. Scores range from 0 to 30 with higher scores indicating greater health-related quality of life impairment.

End point type	Secondary

End point timeframe:

Weeks 4, 16, 18, 22, 26, 30, 32

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics do not apply to this end point.

End point values	CDP - Secukinumab 300 mg s.c. (4-weekly)	CDP - Secukinumab 300 mg s.c. (2-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	163		
Units: participants				
Week 4 (n=160, NA)	53	9999		
Week 16	113	9999		
Week 18	109	108		
Week 22	112	117		
Week 26	116	121		
Week 30	114	127		
Week 32	117	126		

Statistical analyses

No statistical analyses for this end point

Secondary: Selection Phase: Number of patients achieving Investigator global assessment (IGA) 0 or 1

End point title	Selection Phase: Number of patients achieving Investigator global assessment (IGA) 0 or 1[9]

End point description:

The IGA scale is static, i.e. it referred exclusively to the participant's disease at the time of the assessment, and did not compare with any of the participant's previous disease states at previous visits. The scores are: 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = severe and 5 = very severe.

End point type	Secondary

End point timeframe:

Weeks 4, 16

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Statistics do not apply to this end point.

End point values	SP - Secukinumab 300 mg s.c. (4-weekly)			
Subject group type	Reporting group			
Number of subjects analysed	772			
Units: Participants				
week 4 (n=768)	150			
week 16 (n=759)	446			

Statistical analyses

No statistical analyses for this end point

Secondary: Comparative Dose Phase: Number of patients achieving Investigator global assessment (IGA) 0 or 1

End point title	Comparative Dose Phase: Number of patients achieving Investigator global assessment (IGA) 0 or 1[10]

End point description:

The IGA scale is static, i.e. it referred exclusively to the participant's disease at the time of the assessment, and did not compare with any of the participant's previous disease states at previous visits. The scores are: 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = severe and 5 = very severe.

End point type	Secondary

End point timeframe:

Weeks 18, 22, 26, 30, 32

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics do not apply to this end point.

End point values	CDP - Secukinumab 300 mg s.c. (4-weekly)	CDP - Secukinumab 300 mg s.c. (2-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	163		
Units: Participants				
week 18 (n=162, 163)	67	68		
week 22 (n=161, 161)	88	90		
week 26 (n= 156, 160)	87	111		
week 30 (n=154, 158)	97	106		
week 32 (n=153, 152)	98	111		

Statistical analyses

No statistical analyses for this end point

Secondary: Selection Phase: Summary of IGA Score

End point title	Selection Phase: Summary of IGA Score[11]

End point description:

The IGA scale is static, i.e. it referred exclusively to the participant's disease at the time of the assessment, and did not compare with any of the participant's previous disease states at previous visits. The scores are: 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = severe and 5 = very severe.

End point type	Secondary

End point timeframe:

Weeks 4, 16

Notes:

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

End point values	SP - Secukinumab 300 mg s.c. (4-weekly)			
Subject group type	Reporting group			
Number of subjects analysed	772			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 4 (n=768)	2.1 (± 0.79)			
Week 16 (n=759)	1.26 (± 0.875)			

Statistical analyses

No statistical analyses for this end point

Secondary: Comparative Dose Phase:Summary of IGA Score

End point title	Comparative Dose Phase:Summary of IGA Score[12]

End point description:

The IGA scale is static, i.e. it referred exclusively to the participant's disease at the time of the assessment, and did not compare with any of the participant's previous disease states at previous visits. The scores are: 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = severe and 5 = very severe.

End point type	Secondary

End point timeframe:

Weeks 18, 22, 26, 30, 32

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics do not apply to this end point.

End point values	CDP - Secukinumab 300 mg s.c. (4-weekly)	CDP - Secukinumab 300 mg s.c. (2-weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	163		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 18 (n=162, 163)	1.63 (± 0.619)	1.64 (± 0.656)		
Week 22 (n= 161, 161)	1.46 (± 0.733)	1.42 (± 0.704)		
Week 26 (n=156, 160)	1.48 (± 0.758)	1.3 (± 0.759)		
Week 30 (n= 154, 158)	1.33 (± 0.848)	1.27 (± 0.803)		
Week 32 (n=153, 152)	1.3 (± 0.925)	1.13 (± 0.819)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Selection Phase: AIN457 300 mg s.c. (4-weekly)
Reporting group description:	
Selection Phase: AIN457 300 mg s.c. (4-weekly)	
Reporting group title	Comparative Dosing Phase: AIN457 300 mg s.c. (4-weekly)
Reporting group description:	
Comparative Dosing Phase: AIN457 300 mg s.c. (4-weekly)	
Reporting group title	Comparative Dosing Phase: AIN457 300 mg s.c. (2-weekly)
Reporting group description:	
Comparative Dosing Phase: AIN457 300 mg s.c. (2-weekly)	

Serious adverse events	Selection Phase: AIN457 300 mg s.c. (4-weekly)	Comparative Dosing Phase: AIN457 300 mg s.c. (4-weekly)	Comparative Dosing Phase: AIN457 300 mg s.c. (2-weekly)
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 772 (4.15%)	8 / 162 (4.94%)	4 / 163 (2.45%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-CELL LYMPHOMA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYCOSIS FUNGOIDES			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATIC CARCINOMA			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
HAEMORRHAGE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSIVE CRISIS			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHILLS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMPAIRED HEALING			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
ASTHMA EXERCISE INDUCED			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERVENTILATION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
MANIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANIC ATTACK			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC ENZYME INCREASED			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
CHEST INJURY			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONCUSSION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONTUSION			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMUR FRACTURE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HUMERUS FRACTURE			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIGAMENT RUPTURE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RADIAL HEAD DISLOCATION			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RADIUS FRACTURE			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STERNAL FRACTURE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TENDON RUPTURE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER LIMB FRACTURE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDITIS			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
CEREBRAL ISCHAEMIA			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERCOSTAL NEURALGIA			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
COLITIS ULCERATIVE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UMBILICAL HERNIA			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
BILIARY COLIC			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS CHRONIC			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
ACROKERATOSIS PARANEOPLASTICA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DERMATITIS EXFOLIATIVE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN ULCER			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
FIBRILLARY GLOMERULONEPHRITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL CYST HAEMORRHAGE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

URETEROLITHIASIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL OSTEOARTHRITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ERYSIPELAS			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MASTOIDITIS			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYODERMA			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUSITIS			

subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONSILLITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VARICELLA			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Selection Phase: AIN457 300 mg s.c. (4-weekly)	Comparative Dosing Phase: AIN457 300 mg s.c. (4-weekly)	Comparative Dosing Phase: AIN457 300 mg s.c. (2-weekly)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	510 / 772 (66.06%)	85 / 162 (52.47%)	87 / 163 (53.37%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
DYSPLASTIC NAEVUS			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
FIBROMA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
FIBROUS HISTIOCYTOMA			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MELANOCYTIC NAEVUS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MONOCLONAL GAMMOPATHY			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
SEBORRHOEIC KERATOSIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SKIN PAPILLOMA			
subjects affected / exposed	9 / 772 (1.17%)	3 / 162 (1.85%)	1 / 163 (0.61%)
occurrences (all)	9	3	1
Vascular disorders			
DIASTOLIC HYPERTENSION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
FLUSHING			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
HAEMATOMA			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	1	1	1
HAEMORRHAGE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
HYPERTENSION			
subjects affected / exposed	8 / 772 (1.04%)	3 / 162 (1.85%)	4 / 163 (2.45%)
occurrences (all)	8	3	4
LYMPHOEDEMA			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
PERIPHERAL VENOUS DISEASE			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0

VARICOSE VEIN			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
APPLICATION SITE HAEMATOMA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ASTHENIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
CHILLS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
DRUG THERAPEUTIC INCOMPATIBILITY			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
FATIGUE			
subjects affected / exposed	28 / 772 (3.63%)	4 / 162 (2.47%)	3 / 163 (1.84%)
occurrences (all)	46	4	6
FEELING HOT			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
IMPAIRED HEALING			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	10 / 772 (1.30%)	2 / 162 (1.23%)	1 / 163 (0.61%)
occurrences (all)	13	2	1
INJECTION SITE BRUISING			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
INJECTION SITE ERYTHEMA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
INJECTION SITE HAEMATOMA			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
INJECTION SITE HAEMORRHAGE			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
INJECTION SITE PAIN			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	4	0	1
INJECTION SITE PRURITUS			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
INJURY ASSOCIATED WITH DEVICE			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	4 / 772 (0.52%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	5	0	0
PERIPHERAL SWELLING			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	1	0	1
PUNCTURE SITE REACTION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PYREXIA			
subjects affected / exposed	9 / 772 (1.17%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	10	0	0
SENSATION OF FOREIGN BODY			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
THIRST			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			

SEASONAL ALLERGY			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
BALANOPOSTHITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
BREAST CYST			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
DYSMENORRHOEA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MENOPAUSAL SYMPTOMS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MENSTRUATION IRREGULAR			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
METRORRHAGIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PROSTATITIS			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
PRURITUS GENITAL			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	12 / 772 (1.55%)	0 / 162 (0.00%)	2 / 163 (1.23%)
occurrences (all)	13	0	2
DYSPHONIA			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
DYSPNOEA			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
EPISTAXIS			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	3	0
NASAL CONGESTION			
subjects affected / exposed	3 / 772 (0.39%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	3	1	0
NASAL INFLAMMATION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
NASAL MUCOSAL EROSION			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
OROPHARYNGEAL DISCOMFORT			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	12 / 772 (1.55%)	1 / 162 (0.62%)	2 / 163 (1.23%)
occurrences (all)	12	1	2
PHARYNGEAL INFLAMMATION			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
PRODUCTIVE COUGH			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
RHINORRHOEA			
subjects affected / exposed	10 / 772 (1.30%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	11	1	0
SLEEP APNOEA SYNDROME			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
THROAT IRRITATION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
ALCOHOL ABUSE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
DEPRESSION			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
INITIAL INSOMNIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
INSOMNIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MOOD SWINGS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
NERVOUSNESS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SLEEP DISORDER			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	3 / 772 (0.39%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	3	1	1
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
BILIRUBIN URINE PRESENT			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
BLOOD CHOLESTEROL INCREASED			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
BLOOD TRIGLYCERIDES INCREASED			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
BLOOD URINE PRESENT			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
BODY TEMPERATURE INCREASED			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ELECTROCARDIOGRAM ABNORMAL			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	1	0	1
ELECTROCARDIOGRAM Q WAVE ABNORMAL			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
HIGH DENSITY LIPOPROTEIN DECREASED			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
HUMAN CHORIONIC GONADOTROPIN INCREASED			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MONOCYTE COUNT INCREASED			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
PLATELET COUNT DECREASED			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
TRANSAMINASES INCREASED			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
WEIGHT INCREASED			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
Injury, poisoning and procedural complications			
ACCIDENT AT WORK			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ANIMAL BITE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	1	0	1
ANKLE FRACTURE			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
ARTHROPOD BITE			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
ARTHROPOD STING			

subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
BURN ORAL CAVITY			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
CERVICAL VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
CONTUSION			
subjects affected / exposed	5 / 772 (0.65%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	5	0	0
CRANIOCEREBRAL INJURY			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
FALL			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
FOREIGN BODY IN EYE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	3	0	1
HAND FRACTURE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
JOINT DISLOCATION			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
JOINT INJURY			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
LACERATION			
subjects affected / exposed	2 / 772 (0.26%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	2	1	0
LIGAMENT RUPTURE			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
LIGAMENT SPRAIN			

subjects affected / exposed	6 / 772 (0.78%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	6	0	0
LIMB INJURY			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
MENISCUS INJURY			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MUSCLE STRAIN			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
PLAQUE SHIFT			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
PROCEDURAL DIZZINESS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PROCEDURAL PAIN			
subjects affected / exposed	2 / 772 (0.26%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	3	1	1
RIB FRACTURE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SKIN ABRASION			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
SUBCUTANEOUS HAEMATOMA			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
SUNBURN			
subjects affected / exposed	2 / 772 (0.26%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	2	1	0
TENDON RUPTURE			

subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
THERMAL BURN			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
TOOTH FRACTURE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
UPPER LIMB FRACTURE			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
WOUND			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
Congenital, familial and genetic disorders			
CONGENITAL NAEVUS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	0	1	1
ATRIOVENTRICULAR BLOCK			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
BUNDLE BRANCH BLOCK LEFT			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SINUS ARRHYTHMIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
TACHYCARDIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

BURNING SENSATION			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
CERVICOGENIC VERTIGO			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
DIZZINESS			
subjects affected / exposed	3 / 772 (0.39%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	3	1	0
DYSAESTHESIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
DYSGEUSIA			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	2	0	1
HEADACHE			
subjects affected / exposed	60 / 772 (7.77%)	5 / 162 (3.09%)	5 / 163 (3.07%)
occurrences (all)	88	7	8
HYPERAESTHESIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MIGRAINE			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	2	0	1
NERVE COMPRESSION			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
NEURALGIA			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
NEURITIS			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1

NEUROPATHY PERIPHERAL			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ORTHOSTATIC INTOLERANCE			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
SCIATICA			
subjects affected / exposed	4 / 772 (0.52%)	1 / 162 (0.62%)	4 / 163 (2.45%)
occurrences (all)	4	1	4
SOMNOLENCE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
LEUKOCYTOSIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
LYMPHADENOPATHY			
subjects affected / exposed	2 / 772 (0.26%)	2 / 162 (1.23%)	0 / 163 (0.00%)
occurrences (all)	2	2	0
LYMPHOPENIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
NEUTROPENIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
THROMBOCYTOPENIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	1	0	1
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	1 / 772 (0.13%)	2 / 162 (1.23%)	0 / 163 (0.00%)
occurrences (all)	1	2	0
EAR PRURITUS			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
HYPOACUSIS			

subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
SUDDEN HEARING LOSS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
TINNITUS			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
TYMPANIC MEMBRANE PERFORATION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
VERTIGO			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
Eye disorders			
BLEPHARITIS			
subjects affected / exposed	3 / 772 (0.39%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	3	1	0
CATARACT			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
CHALAZION			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
CONJUNCTIVAL HYPERAEMIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
CONJUNCTIVITIS ALLERGIC			
subjects affected / exposed	4 / 772 (0.52%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	4	1	1
DRY EYE			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	3	0	1
ECZEMA EYELIDS			

subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	2	0	1
EYE IRRITATION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
EYE PAIN			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
EYE SWELLING			
subjects affected / exposed	2 / 772 (0.26%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	2	1	0
EYELID OEDEMA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	1	0	1
EYELIDS PRURITUS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
INTRAOCULAR HAEMATOMA			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
KERATITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
LACRIMATION INCREASED			
subjects affected / exposed	4 / 772 (0.52%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	4	0	0
VISUAL IMPAIRMENT			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ABDOMINAL PAIN			
subjects affected / exposed	2 / 772 (0.26%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	2	1	0

ABDOMINAL PAIN LOWER			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	17 / 772 (2.20%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	19	1	1
ANAL SKIN TAGS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ANORECTAL DISCOMFORT			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
APHTHOUS ULCER			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
COLITIS			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
COLITIS MICROSCOPIC			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
CONSTIPATION			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
DENTAL CARIES			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
DIARRHOEA			
subjects affected / exposed	34 / 772 (4.40%)	3 / 162 (1.85%)	1 / 163 (0.61%)
occurrences (all)	41	3	2
DRY MOUTH			
subjects affected / exposed	4 / 772 (0.52%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	4	0	0
DYSPEPSIA			
subjects affected / exposed	2 / 772 (0.26%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	2	1	0

DYSPHAGIA			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
EPULIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
FAECES SOFT			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
FLATULENCE			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
FREQUENT BOWEL MOVEMENTS			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
GASTRITIS			
subjects affected / exposed	5 / 772 (0.65%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	5	0	1
GASTRITIS EROSIVE			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
GASTROINTESTINAL PAIN			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	6 / 772 (0.78%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	6	0	1
GINGIVAL DISORDER			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
GINGIVAL EROSION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
HAEMORRHOIDS			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
HYPOAESTHESIA ORAL			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
INTRA-ABDOMINAL HAEMATOMA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
LARGE INTESTINE POLYP			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
LIP BLISTER			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
LIP DRY			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MALLORY-WEISS SYNDROME			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MOUTH SWELLING			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MOUTH ULCERATION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
NAUSEA			
subjects affected / exposed	9 / 772 (1.17%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	9	1	0
PARAESTHESIA ORAL			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
POUCHITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
TONGUE COATED			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	4	0	0
TONGUE DISCOLOURATION			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
TOOTHACHE			
subjects affected / exposed	9 / 772 (1.17%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	10	0	0
VASCULITIS GASTROINTESTINAL			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
VOMITING			
subjects affected / exposed	3 / 772 (0.39%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	3	1	1
Hepatobiliary disorders			
BILIARY COLIC			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
CHOLECYSTITIS			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
CHOLELITHIASIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
HEPATIC STEATOSIS			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
HYPERBILIRUBINAEMIA			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
ACTINIC KERATOSIS			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ALOPECIA			
subjects affected / exposed	5 / 772 (0.65%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	5	0	0
ALOPECIA AREATA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
BLISTER			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
BLOOD BLISTER			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
DERMAL CYST			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
DERMATITIS ALLERGIC			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
DERMATITIS CONTACT			
subjects affected / exposed	5 / 772 (0.65%)	2 / 162 (1.23%)	0 / 163 (0.00%)
occurrences (all)	5	2	0
DRUG ERUPTION			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
DRY SKIN			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
DYSHIDROTIC ECZEMA			
subjects affected / exposed	3 / 772 (0.39%)	2 / 162 (1.23%)	2 / 163 (1.23%)
occurrences (all)	4	2	2
ECZEMA			
subjects affected / exposed	10 / 772 (1.30%)	4 / 162 (2.47%)	1 / 163 (0.61%)
occurrences (all)	10	4	1
ECZEMA WEEPING			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ERYTHEMA			
subjects affected / exposed	2 / 772 (0.26%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	2	1	0
ERYTHEMA NODOSUM			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
HYPERHIDROSIS			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
INGROWING NAIL			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
INTERTRIGO			
subjects affected / exposed	8 / 772 (1.04%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	9	0	1
MILIARIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MYXOID CYST			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
PAIN OF SKIN			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PAPULE			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
PETECHIAE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PHOTODERMATOSIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PHOTOSENSITIVITY REACTION			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PRURIGO			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PRURITUS			
subjects affected / exposed	32 / 772 (4.15%)	2 / 162 (1.23%)	0 / 163 (0.00%)
occurrences (all)	34	2	0
PRURITUS ALLERGIC			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PRURITUS GENERALISED			
subjects affected / exposed	8 / 772 (1.04%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	9	1	1
PSORIASIS			
subjects affected / exposed	3 / 772 (0.39%)	2 / 162 (1.23%)	2 / 163 (1.23%)
occurrences (all)	3	2	2
PUSTULAR PSORIASIS			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
RASH			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	2	0	1
RASH MACULAR			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
RASH PAPULAR			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ROSACEA			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
SEBORRHOEA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SEBORRHOEIC DERMATITIS			

subjects affected / exposed	13 / 772 (1.68%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	14	0	1
SKIN ATROPHY			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
SKIN EXFOLIATION			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
SKIN FISSURES			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	1	0	1
SKIN IRRITATION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	1	0	1
SKIN PLAQUE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SKIN ULCER			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SKIN ULCER HAEMORRHAGE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SOLAR DERMATITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
URTICARIA			
subjects affected / exposed	7 / 772 (0.91%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	7	1	1
Renal and urinary disorders			
DYSURIA			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
HAEMATURIA			
subjects affected / exposed	5 / 772 (0.65%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	5	1	0

LEUKOCYTURIA			
subjects affected / exposed	4 / 772 (0.52%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	4	0	0
NEPHROLITHIASIS			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
POLLAKIURIA			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
PROTEINURIA			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
Endocrine disorders			
HYPERTHYROIDISM			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
HYPOTHYROIDISM			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
THYROID CYST			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	21 / 772 (2.72%)	4 / 162 (2.47%)	3 / 163 (1.84%)
occurrences (all)	23	5	3
ARTHRITIS			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
BACK PAIN			
subjects affected / exposed	9 / 772 (1.17%)	3 / 162 (1.85%)	3 / 163 (1.84%)
occurrences (all)	11	3	3
BURSITIS			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
FIBROMYALGIA			

subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
FLANK PAIN			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
JOINT CREPITATION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
JOINT EFFUSION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
JOINT SWELLING			
subjects affected / exposed	4 / 772 (0.52%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	4	0	0
METATARSALGIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MUSCLE SPASMS			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
MUSCLE TIGHTNESS			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	3	0	1
MUSCULOSKELETAL PAIN			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	1	0	1
MYALGIA			
subjects affected / exposed	4 / 772 (0.52%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	4	2	0

NECK PAIN			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
OSTEOARTHRITIS			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	2 / 163 (1.23%)
occurrences (all)	1	1	2
PAIN IN EXTREMITY			
subjects affected / exposed	12 / 772 (1.55%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	13	0	0
PATELLOFEMORAL PAIN SYNDROME			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PSORIATIC ARTHROPATHY			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
RHEUMATIC DISORDER			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SCOLIOSIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SPINAL OSTEOARTHRITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SPINAL PAIN			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SYNOVIAL CYST			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
TENDONITIS			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
TENOSYNOVITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0

Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ABSCESS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ANGULAR CHEILITIS			
subjects affected / exposed	5 / 772 (0.65%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	6	0	2
BACTERIAL INFECTION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
BACTERIAL RHINITIS			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
BACTERIAL VAGINOSIS			
subjects affected / exposed	0 / 772 (0.00%)	2 / 162 (1.23%)	0 / 163 (0.00%)
occurrences (all)	0	2	0
BALANITIS CANDIDA			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	2	0	1
BODY TINEA			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
BRONCHITIS			
subjects affected / exposed	10 / 772 (1.30%)	2 / 162 (1.23%)	2 / 163 (1.23%)
occurrences (all)	12	2	2
BRONCHITIS BACTERIAL			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
BRONCHITIS VIRAL			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
CANDIDA INFECTION			

subjects affected / exposed	5 / 772 (0.65%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	5	0	0
CONJUNCTIVITIS			
subjects affected / exposed	8 / 772 (1.04%)	1 / 162 (0.62%)	2 / 163 (1.23%)
occurrences (all)	8	1	2
CONJUNCTIVITIS BACTERIAL			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
CYSTITIS			
subjects affected / exposed	4 / 772 (0.52%)	2 / 162 (1.23%)	1 / 163 (0.61%)
occurrences (all)	4	2	1
CYSTITIS BACTERIAL			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	2
ECZEMA IMPETIGINOUS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
EPIDIDYMITIS			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
EPIGLOTTITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ERYSIPELAS			
subjects affected / exposed	2 / 772 (0.26%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	2	1	0
FOLLICULITIS			
subjects affected / exposed	13 / 772 (1.68%)	4 / 162 (2.47%)	2 / 163 (1.23%)
occurrences (all)	13	4	2
FUNGAL INFECTION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
FUNGAL SKIN INFECTION			
subjects affected / exposed	5 / 772 (0.65%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	5	0	0
FURUNCLE			

subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
GASTROENTERITIS			
subjects affected / exposed	7 / 772 (0.91%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	7	1	0
GASTROENTERITIS VIRAL			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
GASTROINTESTINAL INFECTION			
subjects affected / exposed	8 / 772 (1.04%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	8	1	1
GASTROINTESTINAL VIRAL INFECTION			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	2	0	1
GENITAL CANDIDIASIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
GENITAL INFECTION FUNGAL			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
GINGIVITIS			
subjects affected / exposed	4 / 772 (0.52%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	4	1	0
HELICOBACTER INFECTION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
HERPES SIMPLEX			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
HERPES VIRUS INFECTION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
HERPES ZOSTER			
subjects affected / exposed	2 / 772 (0.26%)	2 / 162 (1.23%)	0 / 163 (0.00%)
occurrences (all)	2	2	0

HERPES ZOSTER INFECTION NEUROLOGICAL			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
HORDEOLUM			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
IMPETIGO			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
INFLUENZA			
subjects affected / exposed	9 / 772 (1.17%)	2 / 162 (1.23%)	2 / 163 (1.23%)
occurrences (all)	9	2	3
LABYRINTHITIS			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
LARYNGITIS			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
LOCALISED INFECTION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0
LYME DISEASE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
MUCOSAL INFECTION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
NAIL BED INFECTION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
NASOPHARYNGITIS			

subjects affected / exposed	168 / 772 (21.76%)	23 / 162 (14.20%)	27 / 163 (16.56%)
occurrences (all)	204	26	30
OESOPHAGEAL CANDIDIASIS			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	14 / 772 (1.81%)	2 / 162 (1.23%)	3 / 163 (1.84%)
occurrences (all)	14	2	3
ORAL FUNGAL INFECTION			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	2	0
ORAL HERPES			
subjects affected / exposed	15 / 772 (1.94%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	19	1	1
ORCHITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
OTITIS EXTERNA			
subjects affected / exposed	4 / 772 (0.52%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	4	1	1
OTITIS MEDIA			
subjects affected / exposed	4 / 772 (0.52%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	4	0	1
OTITIS MEDIA ACUTE			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
PARONYCHIA			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	2	0	1
PERICHONDRITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PERIODONTITIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	1	0	1
PHARYNGITIS			

subjects affected / exposed	6 / 772 (0.78%)	2 / 162 (1.23%)	1 / 163 (0.61%)
occurrences (all)	6	3	1
PHARYNGITIS BACTERIAL			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
PULPITIS DENTAL			
subjects affected / exposed	5 / 772 (0.65%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	5	0	1
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
RHINITIS			
subjects affected / exposed	16 / 772 (2.07%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	16	1	0
SINUSITIS			
subjects affected / exposed	8 / 772 (1.04%)	2 / 162 (1.23%)	1 / 163 (0.61%)
occurrences (all)	8	2	1
SKIN CANDIDA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	1	0	1
SKIN INFECTION			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	2	0	1
STAPHYLOCOCCAL SKIN INFECTION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	2 / 772 (0.26%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	2	1	0
TINEA INFECTION			

subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	2	0	0
TINEA PEDIS			
subjects affected / exposed	8 / 772 (1.04%)	3 / 162 (1.85%)	1 / 163 (0.61%)
occurrences (all)	8	3	1
TONSILLITIS			
subjects affected / exposed	6 / 772 (0.78%)	1 / 162 (0.62%)	2 / 163 (1.23%)
occurrences (all)	6	1	2
TONSILLITIS BACTERIAL			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
TOOTH INFECTION			
subjects affected / exposed	2 / 772 (0.26%)	2 / 162 (1.23%)	0 / 163 (0.00%)
occurrences (all)	2	3	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	3 / 772 (0.39%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	3	1	0
URETHRITIS			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
URINARY TRACT INFECTION			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	3	0	1
VIRAL INFECTION			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	1	1	1
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	3	0	1
VULVOVAGINAL CANDIDIASIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
VULVOVAGINAL MYCOTIC INFECTION			

subjects affected / exposed	2 / 772 (0.26%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	3	1	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
DIABETES MELLITUS			
subjects affected / exposed	2 / 772 (0.26%)	1 / 162 (0.62%)	1 / 163 (0.61%)
occurrences (all)	2	1	1
FLUID RETENTION			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
GOUT			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
HAEMOSIDEROSIS			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	2 / 772 (0.26%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	2	1	0
HYPERKALAEMIA			
subjects affected / exposed	2 / 772 (0.26%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
HYPERLIPIDAEMIA			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	3 / 772 (0.39%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	3	0	0
HYPONATRAEMIA			
subjects affected / exposed	1 / 772 (0.13%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	1	1	0
IRON DEFICIENCY			
subjects affected / exposed	0 / 772 (0.00%)	1 / 162 (0.62%)	0 / 163 (0.00%)
occurrences (all)	0	1	0

TYPE 2 DIABETES MELLITUS			
subjects affected / exposed	0 / 772 (0.00%)	0 / 162 (0.00%)	1 / 163 (0.61%)
occurrences (all)	0	0	1
VITAMIN D DEFICIENCY			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0
ZINC DEFICIENCY			
subjects affected / exposed	1 / 772 (0.13%)	0 / 162 (0.00%)	0 / 163 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 July 2015	Treatment duration after randomization was corrected as study medication was only given until Week 30. At Week 32, no study medication was given; Inclusion criteria regarding previous therapy (number 5) were specified to at least one previous conventional systemic therapy; Inclusion criteria regarding chest infection (number 6) were specified, as the methodologies of sonography and ammography were not suitable to identify potential tuberculosis; In exclusion criteria 1 the list of other forms of psoriasis was changed from and to or; In exclusion criteria 13 the specification of uncontrolled hypertension was deleted; It was clarified that, for patients for whom the allocated treatment was missing and could not be replaced in time, a new medication number could be allocated via the unblinded Novartis personnel responsible for study drug packaging, and that in cases where allocation of a new medication number was not possible, unblinding and continuing treatment with open-label medication was allowed; Apremilast was added to the list of prohibited therapies; Discontinuation of study drug for female participants with a positive serum pregnancy test with hCG values > 5 mIU/ml was been added; The assessment schedule table was updated; The counting of affected nails was deleted as the assessment is part of the NAPSI; Time point of evaluation of BSA for eligibility was specified; Severity of PASI was adapted to match the inclusion criteria and the PASI value, which was used as a threshold for entering study phase 2 was corrected to > PASI 75; Assessment of neutrophil bands as part of the hematologic laboratory assessment was deleted; The hCG value which was regarded positive was reduced from > 10 mIU/ml to > 5 mIU/ml; Patients required a DLQI score of > 10 at baseline to be eligible for this study was added; Time when PNQ and PBQ were assessed was specified; Safety monitoring

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Notes: