Clinical trial results:
A randomized, double-blind, placebo-controlled multicenter study of Secukinumab (AIN457) to examine the clinical efficacy and the NSAID-sparing effect of Secukinumab over 16 weeks in patients with ankylosing spondylitis (ASTRUM)

Summary

EudraCT number	2015-004575-74
Trial protocol	DE
Global end of trial date	24 September 2019

Results information

Result version number	v1 (current)
This version publication date	02 October 2020
First version publication date	02 October 2020

Trial information

Trial identification

Sponsor protocol code	CAIN457FDE03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02763046
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 September 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to demonstrate that the efficacy of secukinumab 150 mg subcutaneous (s.c.) injection (with nonsteroidal anti-inflammatory drug (NSAID) tapering) is superior to placebo based on the proportion of patients achieving an Assessment of SpondyloArthritis international Society (ASAS) 20 response at Week 12. To show superiority, both secukinumab treatment arms were pooled and compared against placebo.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 May 2016
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: 211
Worldwide total number of subjects	211
EEA total number of subjects	211

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)	197
From 65 to 84 years	14

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in 40 investigative sites in Germany.

Pre-assignment

Screening details:

Participants were randomized 1:1:1 to one of the following treatment groups: secukinumab 150 mg s.c. with delayed NSAID tapering, secukinumab 150 mg s.c. with early NSAID tapering and placebo.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab - delayed NSAID tapering

Arm description:

Induction with secukinumab 150 mg s.c. once per week (Week 0, 1, 2, 3 and 4) followed by maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 8, 12, 16 and 20), with intermittent placebo injections at Week 5, 6, 7, 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (delayed tapering).

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

Dosage and administration details:

Induction with secukinumab 150 mg s.c. once per week (Week 0, 1, 2, 3 and 4) followed by maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 8, 12, 16 and 20), with intermittent placebo injections at Week 5, 6, 7, 17, 18 and 19 to maintain the blind.
NSAID tapering allowed from Week 4 (delayed tapering).

Arm title	Secukinumab - early NSAID tapering

Arm description:

Placebo at weeks 0, 1, 2, 3 to maintain the blind; followed by induction with secukinumab 150 mg s.c. once per week (Week 4, 5, 6, 7, 8) and maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 12, 16 and 20), with intermittent placebo injections at Week 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (early tapering).

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

Dosage and administration details:

Placebo at weeks 0, 1, 2, 3 to maintain the blind; followed by induction with secukinumab 150 mg s.c. once per week (Week 4, 5, 6, 7, 8) and maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 12, 16 and 20), with intermittent placebo injections at Week 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (early tapering).

Arm title	Placebo

Arm description:

Placebo s.c. at Week 0, 1, 2, 3, 4, 5, 6, 7, 8 and 12. After the Week 16 assessments of the secondary endpoint had been performed, these patients received weekly doses of secukinumab 150 mg s.c. (Week 16, 17, 18, 19 and 20). NSAID tapering allowed from Week 4.

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

Dosage and administration details:

Placebo s.c. at Week 0, 1, 2, 3, 4, 5, 6, 7, 8 and 12. After the Week 16 assessments of the secondary endpoint had been performed, these patients received weekly doses of secukinumab 150 mg s.c. (Week 16, 17, 18, 19 and 20).
NSAID tapering allowed from Week 4.

Number of subjects in period 1	Secukinumab - delayed NSAID tapering	Secukinumab - early NSAID tapering	Placebo
Started	71	70	70
Completed	62	65	62
Not completed	9	5	8
Physician decision	1	-	1
Adverse event, non-fatal	5	4	-
Subject/guardian decision	2	-	4
Lack of efficacy	1	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab - delayed NSAID tapering
Reporting group description:	
Induction with secukinumab 150 mg s.c. once per week (Week 0, 1, 2, 3 and 4) followed by maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 8, 12, 16 and 20), with intermittent placebo injections at Week 5, 6, 7, 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (delayed tapering).	
Reporting group title	Secukinumab - early NSAID tapering
Reporting group description:	
Placebo at weeks 0, 1, 2, 3 to maintain the blind; followed by induction with secukinumab 150 mg s.c. once per week (Week 4, 5, 6, 7, 8) and maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 12, 16 and 20), with intermittent placebo injections at Week 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (early tapering).	
Reporting group title	Placebo
Reporting group description:	
Placebo s.c. at Week 0, 1, 2, 3, 4, 5, 6, 7, 8 and 12. After the Week 16 assessments of the secondary endpoint had been performed, these patients received weekly doses of secukinumab 150 mg s.c. (Week 16, 17, 18, 19 and 20). NSAID tapering allowed from Week 4.	

Reporting group values	Secukinumab - delayed NSAID tapering	Secukinumab - early NSAID tapering	Placebo
Number of subjects	71	70	70
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	64	68	65
From 65-84 years	7	2	5
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	46.2	44.1	45.4
standard deviation	± 13.36	± 11.02	± 12.55
Sex: Female, Male Units: Participants			
Female	30	28	31
Male	41	42	39
Race/Ethnicity, Customized Units: Subjects			
Caucasian	69	67	68
Black	1	0	0
Asian	0	2	1
Other	1	1	1

Reporting group values	Total		
Number of subjects	211		
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)	197		
From 65-84 years	14		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	89		
Male	122		
Race/Ethnicity, Customized Units: Subjects			
Caucasian	204		
Black	1		
Asian	3		
Other	3		

End points

End points reporting groups

Reporting group title	Secukinumab - delayed NSAID tapering

Reporting group description:

Induction with secukinumab 150 mg s.c. once per week (Week 0, 1, 2, 3 and 4) followed by maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 8, 12, 16 and 20), with intermittent placebo injections at Week 5, 6, 7, 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (delayed tapering).

Reporting group title	Secukinumab - early NSAID tapering

Reporting group description:

Placebo at weeks 0, 1, 2, 3 to maintain the blind; followed by induction with secukinumab 150 mg s.c. once per week (Week 4, 5, 6, 7, 8) and maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 12, 16 and 20), with intermittent placebo injections at Week 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (early tapering).

Reporting group title	Placebo

Reporting group description:

Placebo s.c. at Week 0, 1, 2, 3, 4, 5, 6, 7, 8 and 12. After the Week 16 assessments of the secondary endpoint had been performed, these patients received weekly doses of secukinumab 150 mg s.c. (Week 16, 17, 18, 19 and 20). NSAID tapering allowed from Week 4.

Subject analysis set title	Secukinumab - pooled
Subject analysis set type	Full analysis

Subject analysis set description:

The 2 secukinumab arms (delayed NSAID tapering and early NSAID tapering) pooled.

Primary: Proportion of patients who achieved ASAS20 response in the pooled secukinumab group compared with the placebo group at Week 12

End point title	Proportion of patients who achieved ASAS20 response in the pooled secukinumab group compared with the placebo group at Week 12[1]

End point description:

ASAS (Assessment of SpondyloArthritis International Society criteria) 20 response is defined as an improvement from baseline of ≥20% and ≥1 unit on a scale of 0-10 in at least three of the four ASAS main domains and no worsening of ≥20% and ≥1 unit on a scale of 0-10 in the remaining domain. The four main ASAS domains are: Patient's global assessment of disease activity, back pain, function represented by ability to perform specific tasks (from Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]) and inflammation represented by mean duration and severity of morning stiffness. Non-responder imputation was applied for missing data.

End point type	Primary

End point timeframe:

Baseline, Week 12

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: For the analysis of the primary endpoint both secukinumab treatment arms were pooled and compared against placebo.

End point values	Placebo	Secukinumab - pooled		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	70	141		
Units: Percentage of participants				
number (not applicable)	44.3	51.1		

Statistical analyses

Statistical analysis title	ASAS20 response - Week 12
Comparison groups	Placebo v Secukinumab - pooled
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3512
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	2.36

Secondary: Proportion of patients who achieved ASAS20 response in each secukinumab group (delayed NSAID tapering and early NSAID tapering) compared with the placebo group

End point title	Proportion of patients who achieved ASAS20 response in each secukinumab group (delayed NSAID tapering and early NSAID tapering) compared with the placebo group

End point description:

ASAS (Assessment of SpondyloArthritis International Society criteria) 20 response is defined as an improvement from baseline of ≥20% and ≥1 unit on a scale of 0-10 in at least three of the four ASAS main domains and no worsening of ≥20% and ≥1 unit on a scale of 0-10 in the remaining domain. The four main ASAS domains are: Patient's global assessment of disease activity, back pain, function represented by ability to perform specific tasks (from Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]) and inflammation represented by mean duration and severity of morning stiffness. Non-responder imputation was applied for missing data.

End point type	Secondary

End point timeframe:

Baseline, Week 12, Week 16

End point values	Secukinumab - delayed NSAID tapering	Secukinumab - early NSAID tapering	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	70	70	
Units: Percentage of Participants				
number (not applicable)				
Week 12	52.1	50.0	44.3	
Week 16	56.3	50.0	41.4	

Statistical analyses

Statistical analysis title	ASAS20 response - Week 12
Comparison groups	Secukinumab - delayed NSAID tapering v Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.401
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	2.6

Statistical analysis title	ASAS20 response - Week 12
Comparison groups	Secukinumab - early NSAID tapering v Placebo
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4382
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	2.55

Statistical analysis title	ASAS20 response - Week 16
Comparison groups	Secukinumab - delayed NSAID tapering v Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0934
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	3.5

Statistical analysis title	ASAS20 response - Week 16
Comparison groups	Secukinumab - early NSAID tapering v Placebo
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2619
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	2.9

Secondary: Mean change from baseline in ASAS-NSAID score at Week 12

End point title	Mean change from baseline in ASAS-NSAID score at Week 12

End point description:

ASAS-NSAID score is used to present the NSAID (nonsteroidal anti-inflammatory drug) intake by considering the type of NSAID, the total dose and the number of days taking NSAID during a period of interest (PI). For the NSAID equivalence scoring system, "no NSAID intake" was set to a score value of 0, and the reference dose of 150 mg/day diclofenac was set to a score value of 100. The Daily diclofenac-equivalent dose score was derived by converting each daily dose of NSAID to a percentage dose equivalent of 150 mg diclofenac. ASAS-NSAID score = (equivalent NSAID score) x (days of intake during PI) x (days per week)/(PI in days).
A negative change from baseline indicates less NSAID consumption.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Secukinumab - delayed NSAID tapering	Secukinumab - early NSAID tapering	Placebo	Secukinumab - pooled
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	71	70	70	141
Units: Score on scale				
arithmetic mean (standard deviation)	-44.9 (± 47.32)	-40.3 (± 71.48)	-31.5 (± 36.54)	-42.6 (± 60.53)

Statistical analyses

Statistical analysis title	ASAS-NSAID score - Week 12
Comparison groups	Placebo v Secukinumab - pooled

Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0997
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS (least square) Mean
Point estimate	-10.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.55
upper limit	1.96
Variability estimate	Standard error of the mean
Dispersion value	6.25

Statistical analysis title	ASAS-NSAID score - Week 12
Comparison groups	Secukinumab - delayed NSAID tapering v Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0888
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean
Point estimate	-12.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.47
upper limit	1.87
Variability estimate	Standard error of the mean
Dispersion value	7.23

Statistical analysis title	ASAS-NSAID score - Week 12
Comparison groups	Secukinumab - early NSAID tapering v Placebo
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2484
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean
Point estimate	-8.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.36
upper limit	5.79

Variability estimate	Standard error of the mean
Dispersion value	7.18

Secondary: Mean change from baseline in ASAS-NSAID score in each secukinumab group after 12 weeks of exposure (at Week 12 in the secukinumab-delayed NSAID tapering group and at Week 16 in the secukinumab-early NSAID tapering group)

End point title	Mean change from baseline in ASAS-NSAID score in each secukinumab group after 12 weeks of exposure (at Week 12 in the secukinumab-delayed NSAID tapering group and at Week 16 in the secukinumab-early NSAID tapering group)[2]

End point description:

ASAS-NSAID score is used to present the NSAID (nonsteroidal anti-inflammatory drug) intake by considering the type of NSAID, the total dose and the number of days taking NSAID during a period of interest (PI). For the NSAID equivalence scoring system, "no NSAID intake" was set to a score value of 0, and the reference dose of 150 mg/day diclofenac was set to a score value of 100. The Daily diclofenac-equivalent dose score was derived by converting each daily dose of NSAID to a percentage dose equivalent of 150 mg diclofenac. ASAS-NSAID score = (equivalent NSAID score) x (days of intake during PI) x (days per week)/(PI in days).
A negative change from baseline indicates less NSAID consumption.
For this endpoint the analysis was performed after 12 weeks of exposure to secukinumab which was achieved at Week 12 in the secukinumab delayed NSAID tapering group but at Week 16 in the secukinumab early NSAID tapering group.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (delayed NSAID tapering), Week 16 (early NSAID tapering)

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: This endpoints refers to the secukinumab arms only. No statistics were planned for the placebo group.

End point values	Secukinumab - delayed NSAID tapering	Secukinumab - early NSAID tapering		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	70		
Units: Score on scale				
arithmetic mean (standard deviation)	-44.9 (± 47.32)	-42.5 (± 68.62)		

Statistical analyses

Statistical analysis title	delayed tapering (W12) vs early tapering (W16)
Comparison groups	Secukinumab - delayed NSAID tapering v Secukinumab - early NSAID tapering
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7735
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean
Point estimate	-2.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.11
upper limit	11.98

Secondary: Mean change from baseline in the BASDAI total score

End point title	Mean change from baseline in the BASDAI total score

End point description:

The BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) is a participant-reported assessment consisting of 6 questions that relate to 5 major symptoms relevant to ankylosing spondylitis: 1) Fatigue, 2) Spinal pain, 3) Peripheral arthritis, 4) Enthesitis, 5) Intensity, and 6) Duration of morning stiffness. Participants need to score each item with a score from 0 to 10 (captured as a continuous visual analog scale). Total score is obtained from the average of symptom scores ranging 0 (no problem) to 10 (worst problem), with a higher score indicating more severe symptoms.
A negative change from baseline in the total 0-10 BASDAI score indicates improvement.

End point type	Secondary

End point timeframe:

Baseline, Week 12, Week 16

End point values	Secukinumab - delayed NSAID tapering	Secukinumab - early NSAID tapering	Placebo	Secukinumab - pooled
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	71	70	70	141
Units: Score on scale				
arithmetic mean (standard deviation)				
Week 12	-2.1 (± 2.16)	-2.0 (± 2.10)	-1.8 (± 2.00)	-2.1 (± 2.12)
Week 16	-2.3 (± 1.90)	-2.0 (± 1.96)	-1.7 (± 1.96)	-2.2 (± 1.93)

Statistical analyses

Statistical analysis title	Week 12
Comparison groups	Placebo v Secukinumab - pooled
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1926
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	0.2

Variability estimate	Standard error of the mean
Dispersion value	0.3

Statistical analysis title	Week 12
Comparison groups	Secukinumab - delayed NSAID tapering v Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1914
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.14
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.35

Statistical analysis title	Week 12
Comparison groups	Secukinumab - early NSAID tapering v Placebo
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3397
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.01
upper limit	0.35
Variability estimate	Standard error of the mean
Dispersion value	0.34

Statistical analysis title	Week 16
Comparison groups	Secukinumab - delayed NSAID tapering v Placebo

Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0384
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.33

Statistical analysis title	Week 16
Comparison groups	Secukinumab - early NSAID tapering v Placebo
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2116
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.33

Secondary: Mean change from baseline in health-related Quality of Life as measured by the Short Form-36 Health Survey (SF-36) Physical Component Summary (PCS) Score

End point title	Mean change from baseline in health-related Quality of Life as measured by the Short Form-36 Health Survey (SF-36) Physical Component Summary (PCS) Score

End point description:

The Short Form-36 Health Survey (SF-36) measures the impact of disease on overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general mental health. Items 1-4 comprise the physical component of the SF-36 (SF-36 PCS) that is evaluated in this study. Scores on each item 1-4 were summed and averaged (range = 0-100 with higher scores indicating better levels of function and/or better health). A positive change from Baseline indicates improvement.

End point type	Secondary

End point timeframe:
Baseline, Week 12

End point values	Secukinumab - delayed NSAID tapering	Secukinumab - early NSAID tapering	Placebo	Secukinumab - pooled
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	71	70	70	141
Units: Score on scale				
arithmetic mean (standard deviation)	4.8 (± 7.03)	6.1 (± 6.92)	4.8 (± 7.43)	5.5 (± 6.98)

Statistical analyses

Statistical analysis title	Week 12
Comparison groups	Placebo v Secukinumab - pooled
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5384
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.38
upper limit	2.63
Variability estimate	Standard error of the mean
Dispersion value	1.02

Statistical analysis title	Week 12
Comparison groups	Secukinumab - delayed NSAID tapering v Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9251
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.43
upper limit	2.21

Variability estimate	Standard error of the mean
Dispersion value	1.18

Statistical analysis title	Week 12
Comparison groups	Secukinumab - early NSAID tapering v Placebo
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2432
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	3.66
Variability estimate	Standard error of the mean
Dispersion value	1.16

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from first dose of study treatment until end of study treatment plus 4 weeks post-treatment (median duration of 24 weeks).

Adverse event reporting additional description:

Any signs or symptoms that occurs from first study drug treatment until 30 days after last study drug treatment. AEs were analyzed by treatment period: Treatment Period 1 from first study drug administration through Week 16 (until the day before visit Week 16) and Treatment Period 2 (from the day of injection at visit Week 16 until study end).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Secukinumab - delayed NSAID tapering – Treatment Period 1

Reporting group description:

Induction with secukinumab 150 mg s.c. once per week (Week 0, 1, 2, 3 and 4) followed by maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 8, 12, 16 and 20), with intermittent placebo injections at Week 5, 6, 7, 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (delayed tapering).
Treatment Period 1: from first study drug administration at baseline through Week 16 (concretely: until the day before the injection of study drug scheduled at visit Week 16). This corresponds to the placebo-controlled period of the study.

Reporting group title	Secukinumab - early NSAID tapering - Treatment Period 1

Reporting group description:

Placebo at weeks 0, 1, 2, 3 to maintain the blind; followed by induction with secukinumab 150 mg s.c. once per week (Week 4, 5, 6, 7, 8) and maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 12, 16 and 20), with intermittent placebo injections at Week 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (early tapering).
Treatment Period 1: from first study drug administration at baseline through Week 16 (concretely: until the day before the injection of study drug scheduled at visit Week 16). This corresponds to the placebo-controlled period of the study.

Reporting group title	Placebo - Treatment Period 1

Reporting group description:

Placebo s.c. at Week 0, 1, 2, 3, 4, 5, 6, 7, 8 and 12. After the Week 16 assessments of the secondary endpoint had been performed, these patients received weekly doses of secukinumab 150 mg s.c. (Week 16, 17, 18, 19 and 20). NSAID tapering allowed from Week 4.
Treatment Period 1: from first study drug administration at baseline through Week 16 (concretely: until the day before the injection of study drug scheduled at visit Week 16). This corresponds to the placebo-controlled period of the study.

Reporting group title	Secukinumab - delayed NSAID tapering - Treatment Period 2

Reporting group description:

Induction with secukinumab 150 mg s.c. once per week (Week 0, 1, 2, 3 and 4) followed by maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 8, 12, 16 and 20), with intermittent placebo injections at Week 5, 6, 7, 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (delayed tapering).
Treatment Period 2: from the day of injection at visit Week 16 onwards until study end.

Reporting group title	Secukinumab - early NSAID tapering - Treatment Period 2

Reporting group description:

Placebo at weeks 0, 1, 2, 3 to maintain the blind; followed by induction with secukinumab 150 mg s.c. once per week (Week 4, 5, 6, 7, 8) and maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 12, 16 and 20), with intermittent placebo injections at Week 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (early tapering).
Treatment Period 2: from the day of injection at visit Week 16 onwards until study end.

Reporting group title	Placebo - Treatment Period 2

Reporting group description:

Placebo s.c. at Week 0, 1, 2, 3, 4, 5, 6, 7, 8 and 12. After the Week 16 assessments of the secondary endpoint had been performed, these patients received weekly doses of secukinumab 150 mg s.c. (Week 16, 17, 18, 19 and 20). NSAID tapering allowed from Week 4.
Treatment Period 2: from the day of injection at visit Week 16 onwards until study end.

Serious adverse events	Secukinumab - delayed NSAID tapering – Treatment Period 1	Secukinumab - early NSAID tapering - Treatment Period 1	Placebo - Treatment Period 1
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 71 (5.63%)	3 / 70 (4.29%)	1 / 70 (1.43%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Eye disorders			
Iridocyclitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (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
Abdominal pain			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (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
Colitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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
Crohn's disease			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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
Inguinal hernia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (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
Oesophageal ulcer			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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
Reproductive system and breast disorders			
Vaginal cyst			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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 and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Secukinumab - delayed NSAID tapering - Treatment Period 2	Secukinumab - early NSAID tapering - Treatment Period 2	Placebo - Treatment Period 2

Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	1 / 70 (1.43%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Eye disorders			
Iridocyclitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Vaginal cyst			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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			
Psoriasis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Secukinumab - delayed NSAID tapering – Treatment Period 1	Secukinumab - early NSAID tapering - Treatment Period 1	Placebo - Treatment Period 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 71 (74.65%)	56 / 70 (80.00%)	55 / 70 (78.57%)
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Haematoma			

subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	4 / 71 (5.63%)	3 / 70 (4.29%)	4 / 70 (5.71%)
occurrences (all)	4	3	4
Hypotension			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Discomfort			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	2 / 70 (2.86%)
occurrences (all)	0	1	5
Feeling hot			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Impaired healing			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Injection site pruritus			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Injection site urticaria			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Oedema peripheral			

subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Polyp			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	1	1	0
Thirst			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Seasonal allergy			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Menorrhagia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Uterine pain			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Vulvovaginal pain			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	2 / 70 (2.86%)
occurrences (all)	3	0	2
Dyspnoea exertional			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	1 / 70 (1.43%)
occurrences (all)	0	2	1
Rhinorrhoea			
subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	0 / 70 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Apathy			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Insomnia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Nervousness			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Restlessness			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Sleep disorder			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	2	0	0
Blood pressure decreased			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Blood pressure increased			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	1	1	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Laboratory test abnormal			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	2
Liver function test increased			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Red blood cell sedimentation rate increased			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Transaminases increased			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	2	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	1 / 70 (1.43%)
occurrences (all)	0	1	3
Bone contusion			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Hand fracture			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Ligament rupture			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Muscle injury			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Overdose			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Reactive gastropathy			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Road traffic accident			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Spinal column injury			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Wound			

subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Coronary artery disease			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	1	1	0
Tachycardia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Cervicobrachial syndrome			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	1 / 70 (1.43%)
occurrences (all)	1	1	1
Disturbance in attention			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	1 / 70 (1.43%)
occurrences (all)	0	2	1
Dysaesthesia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Dysgeusia			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	12 / 71 (16.90%)	10 / 70 (14.29%)	6 / 70 (8.57%)
occurrences (all)	25	18	23
Intercostal neuralgia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	1 / 70 (1.43%)
occurrences (all)	1	1	1
Nerve compression			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	2	0	1
Paresis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	1 / 70 (1.43%)
occurrences (all)	1	1	1
Tension headache			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	1	1	0

Iron deficiency anaemia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Lymph node pain			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Monoclonal B-cell lymphocytosis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Monocytosis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Neutrophilia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Tinnitus			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Vertigo			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	3 / 70 (4.29%)
occurrences (all)	1	0	13
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Dry eye			

subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Eye irritation			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Iritis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Macular degeneration			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Presbyopia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Uveitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Visual impairment			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 71 (4.23%)	3 / 70 (4.29%)	0 / 70 (0.00%)
occurrences (all)	4	4	0
Abdominal pain lower			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	3 / 71 (4.23%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	3	0	1
Aphthous ulcer			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	1	1	0

Colitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	3 / 71 (4.23%)	3 / 70 (4.29%)	3 / 70 (4.29%)
occurrences (all)	3	4	3
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	1 / 70 (1.43%)
occurrences (all)	0	2	1
Dyspepsia			
subjects affected / exposed	0 / 71 (0.00%)	3 / 70 (4.29%)	1 / 70 (1.43%)
occurrences (all)	0	3	1
Dysphagia			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	1	1	0
Enteritis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Frequent bowel movements			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Gingival discomfort			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0

Haematochezia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Hiatus hernia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Inguinal hernia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 71 (2.82%)	2 / 70 (2.86%)	5 / 70 (7.14%)
occurrences (all)	2	3	5
Stomatitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Hepatic steatosis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Dyshidrotic eczema			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	2	0	0
Eczema			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Eczema asteatotic			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	2 / 70 (2.86%)
occurrences (all)	1	0	2
Guttate psoriasis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	0 / 70 (0.00%)
occurrences (all)	0	2	0
Night sweats			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Palmoplantar pustulosis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Photosensitivity reaction			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	3 / 70 (4.29%)
occurrences (all)	1	1	3
Psoriasis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	2 / 71 (2.82%)	1 / 70 (1.43%)	3 / 70 (4.29%)
occurrences (all)	2	1	3
Rash maculo-papular			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Seborrhoea			

subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Skin exfoliation			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Skin fissures			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Skin irritation			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Solar dermatitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Xeroderma			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	1	1	0
Proteinuria			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Renal failure			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperprolactinaemia			

subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	3 / 71 (4.23%)	1 / 70 (1.43%)	6 / 70 (8.57%)
occurrences (all)	3	1	7
Arthralgia			
subjects affected / exposed	2 / 71 (2.82%)	2 / 70 (2.86%)	2 / 70 (2.86%)
occurrences (all)	2	2	2
Arthritis			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	1	1	0
Back pain			
subjects affected / exposed	4 / 71 (5.63%)	1 / 70 (1.43%)	1 / 70 (1.43%)
occurrences (all)	4	1	1
Bursitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Muscle tightness			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	3
Musculoskeletal pain			

subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Myalgia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Osteoarthritis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	4
Pain in extremity			
subjects affected / exposed	1 / 71 (1.41%)	2 / 70 (2.86%)	1 / 70 (1.43%)
occurrences (all)	1	5	4
Rheumatic fever			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Sacroiliitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Spinal osteoarthritis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Spinal pain			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	2 / 70 (2.86%)
occurrences (all)	0	1	3
Spondylitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	2 / 70 (2.86%)
occurrences (all)	0	1	2
Spondyloarthropathy			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	2 / 70 (2.86%)
occurrences (all)	1	0	2
Spondylolisthesis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Synovial cyst			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Tendon disorder			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Tendon pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	2
Tendonitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Tenosynovitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Infections and infestations			
Bacterial vaginosis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	5 / 71 (7.04%)	2 / 70 (2.86%)	3 / 70 (4.29%)
occurrences (all)	5	2	6
Candida infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Epstein-Barr virus infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Erysipelas			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	2	0

Fungal infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Fungal skin infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	2	0	0
Furuncle			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	2 / 71 (2.82%)	4 / 70 (5.71%)	3 / 70 (4.29%)
occurrences (all)	2	4	4
Gastroenteritis viral			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Gastrointestinal viral infection			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Herpes simplex			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Infected bite			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	2
Influenza			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	1 / 70 (1.43%)
occurrences (all)	1	1	1
Laryngitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1

Lyme disease			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	6 / 71 (8.45%)	13 / 70 (18.57%)	14 / 70 (20.00%)
occurrences (all)	6	17	16
Oesophageal candidiasis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Onychomycosis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	2 / 71 (2.82%)	2 / 70 (2.86%)	0 / 70 (0.00%)
occurrences (all)	2	2	0
Otitis externa			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Pulpitis dental			
subjects affected / exposed	1 / 71 (1.41%)	2 / 70 (2.86%)	0 / 70 (0.00%)
occurrences (all)	1	2	0
Respiratory tract infection			
subjects affected / exposed	2 / 71 (2.82%)	4 / 70 (5.71%)	3 / 70 (4.29%)
occurrences (all)	2	4	4

Respiratory tract infection viral			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	4 / 71 (5.63%)	0 / 70 (0.00%)	2 / 70 (2.86%)
occurrences (all)	5	0	2
Sinusitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Subcutaneous abscess			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Trichomoniasis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 71 (1.41%)	3 / 70 (4.29%)	1 / 70 (1.43%)
occurrences (all)	2	4	1
Urinary tract infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Uterine infection			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Pseudohyperkalaemia			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Pseudohypoglycaemia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Secukinumab - delayed NSAID tapering - Treatment Period 2	Secukinumab - early NSAID tapering - Treatment Period 2	Placebo - Treatment Period 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 71 (35.21%)	23 / 70 (32.86%)	22 / 70 (31.43%)
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Discomfort			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Impaired healing			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

Influenza like illness			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Injection site pruritus			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Injection site urticaria			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Polyp			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

Dysmenorrhoea			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Menorrhagia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Uterine pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pain			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 71 (0.00%)	3 / 70 (4.29%)	0 / 70 (0.00%)
occurrences (all)	0	3	0
Dyspnoea exertional			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 71 (0.00%)	3 / 70 (4.29%)	0 / 70 (0.00%)
occurrences (all)	0	3	0
Rhinorrhoea			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Apathy			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Nervousness			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Blood pressure decreased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Laboratory test abnormal			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Red blood cell sedimentation rate increased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Animal bite			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Bone contusion			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Hand fracture			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Joint dislocation			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Ligament rupture			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Muscle injury			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Overdose			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

Post-traumatic neck syndrome			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Reactive gastropathy			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	1	1	0
Spinal column injury			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Coronary artery disease			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Autonomic nervous system imbalance			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Cervicobrachial syndrome			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Dysaesthesia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	4 / 71 (5.63%)	3 / 70 (4.29%)	1 / 70 (1.43%)
occurrences (all)	4	4	1
Intercostal neuralgia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Nerve compression			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Paresis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Sciatica			

subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Tension headache			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Lymph node pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Monoclonal B-cell lymphocytosis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Monocytosis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Neutrophilia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Iritis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Macular degeneration			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Presbyopia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Uveitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Colitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	3 / 70 (4.29%)
occurrences (all)	1	1	3
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Enteritis			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Gingival discomfort			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

Hepatic steatosis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Dermatitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Dyshidrotic eczema			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Eczema asteatotic			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Guttate psoriasis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Palmoplantar pustulosis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Photosensitivity reaction			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Seborrhoea			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Solar dermatitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Xeroderma			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

Haematuria			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hyperprolactinaemia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	2	0	1
Arthralgia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Arthritis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Joint swelling			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Muscle tightness			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Rheumatic fever			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Sacroiliitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Spondylitis			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Spondyloarthropathy			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Spondylolisthesis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Synovial cyst			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Tendon disorder			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Tendon pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Tenosynovitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacterial vaginosis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	2 / 71 (2.82%)	1 / 70 (1.43%)	1 / 70 (1.43%)
occurrences (all)	2	1	1
Candida infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	2	0	0

Cystitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Epstein-Barr virus infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Erysipelas			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Fungal infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Furuncle			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Gastroenteritis viral			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Gastrointestinal infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal viral infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0

Infected bite			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Lyme disease			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	7 / 71 (9.86%)	5 / 70 (7.14%)	3 / 70 (4.29%)
occurrences (all)	7	6	3
Oesophageal candidiasis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	1	1	0
Otitis externa			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0

Pharyngitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Pulpitis dental			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	3 / 70 (4.29%)
occurrences (all)	1	1	3
Respiratory tract infection viral			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Subcutaneous abscess			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Trichomoniasis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Uterine infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Pseudohyperkalaemia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Pseudohypoglycaemia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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
10 December 2018	Based on the results from the MEASURE 3 (CAIN457F2314), MEASURE 4 (CAIN457F2320) and COAST V (Ixekizumab, NCT02696785) studies, the assumptions for the power calculation of the primary and a selection of secondary and exploratory objectives were re-evaluated, leading to changes in the statistical analysis plan. These 3 studies suggested that the placebo response might be somewhat higher, leading to a potentially smaller difference between active treatment and placebo than originally assumed during the planning of this trial. Therefore, in order to keep sufficient power, it was decided to pool the two secukinumab arms for the primary analysis. As a result of the secukinumab pooling introduced with the amendment, the number of randomized patients could be reduced to a smaller sample size (approximately 190 patients) than originally expected (about 204 patients), while maintaining adequate power for primary and secondary analyses.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported