Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, Phase III Multicenter Study of Subcutaneous Secukinumab (150 mg) With and Without a Subcutaneous Loading Regimen to Assess Efficacy, Safety, and Tolerability up to 2 Years in Patients With Active Ankylosing Spondylitis

Summary

EudraCT number	2013-005575-41
Trial protocol	CZ DE AT NL FI NO DK GB ES SK BG PL GR IT
Global end of trial date	02 January 2018

Results information

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

Trial information

Trial identification

Sponsor protocol code	CAIN457F2320

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02159053
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Novartis Pharma AG, Clinical Disclosure Office, +41 613241111,
Scientific contact	Novartis Pharma AG, Clinical Disclosure Office, +41 613241111,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 January 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the efficacy of secukinumab 150 mg at Week 16 with or without a loading regimen is superior to placebo based on the proportion of subjects achieving an ASAS20 (Assessment of SpondyloArthritis International Society criteria) response.

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	18 May 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	Norway: 5
Country: Number of subjects enrolled	Poland: 49
Country: Number of subjects enrolled	Slovakia: 15
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Austria: 14
Country: Number of subjects enrolled	Bulgaria: 14
Country: Number of subjects enrolled	Czech Republic: 49
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	Finland: 10
Country: Number of subjects enrolled	Germany: 56
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Russian Federation: 35

Country: Number of subjects enrolled	Switzerland: 3
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	350
EEA total number of subjects	280

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)	334
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 85 centers in 19 countries.

Pre-assignment

Screening details:

A total of 424 subjects were screened, out of which 350 subjects completed the screening phase and were randomized to three treatment groups in 1:1:1 ratio.

Period 1

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

Blinding implementation details:

Randomized treatment assignments were double-blinded to subjects, investigators, and site personnel. Following the Week 16 database lock, the Sponsor was unblinded to treatment assignment. After the Week 52 database lock and analyses was completed, site personnel and patients were unblinded to the original randomized treatment assignment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab 150 mg with loading

Arm description:

Subjects were subcutaneously (s.c.) administered with 150 milligrams (mg) of secukinumab at baseline, Weeks 1, 2, and 3, followed by dosing every four weeks starting at Week 4.

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:

Subjects were administered with 150 mg secukinumab s.c. using pre-filled syringe.

Arm title	Secukinumab 150 mg without loading dose

Arm description:

Subjects were s.c. administered with 150 mg of secukinumab at baseline, followed by dosing every four weeks starting at Week 4, and with Placebo at Weeks 1, 2, and 3.

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:

Subjects were administered with 150 mg secukinumab s.c. using pre-filled syringe.

Arm title	Placebo

Arm description:

Subjects were s.c. administered with placebo matching to secukinumab at baseline, Weeks 1, 2, 3, 4, 8, and 12. Subjects were further administered with 150 mg of secukinumab every four weeks starting at Week 16.

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:

Subjects were administered with 150 mg secukinumab s.c. using pre-filled syringe.

Number of subjects in period 1	Secukinumab 150 mg with loading	Secukinumab 150 mg without loading dose	Placebo
Started	116	117	117
Subjects Week 16 onwards	116	117	113
Completed	96	96	97
Not completed	20	21	20
Physician decision	-	1	1
Adverse event, non-fatal	7	6	5
Death	2	-	1
Subject/guardian decision	8	10	6
Lack of efficacy	3	4	7

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab 150 mg with loading
Reporting group description:	
Subjects were subcutaneously (s.c.) administered with 150 milligrams (mg) of secukinumab at baseline, Weeks 1, 2, and 3, followed by dosing every four weeks starting at Week 4.	
Reporting group title	Secukinumab 150 mg without loading dose
Reporting group description:	
Subjects were s.c. administered with 150 mg of secukinumab at baseline, followed by dosing every four weeks starting at Week 4, and with Placebo at Weeks 1, 2, and 3.	
Reporting group title	Placebo
Reporting group description:	
Subjects were s.c. administered with placebo matching to secukinumab at baseline, Weeks 1, 2, 3, 4, 8, and 12. Subjects were further administered with 150 mg of secukinumab every four weeks starting at Week 16.	

Reporting group values	Secukinumab 150 mg with loading	Secukinumab 150 mg without loading dose	Placebo
Number of subjects	116	117	117
Age categorical Units: Subjects			
Adults (18-64 years)	110	114	110
From 65-84 years	6	3	7
Age continuous Units: years			
arithmetic mean	44.5	41.2	43.4
standard deviation	± 11.62	± 11.07	± 12.46
Gender categorical Units: Subjects			
Female	35	34	41
Male	81	83	76
Patient's global assessment of disease activity			
The patient’s global assessment of disease activity was performed using a 0-100 mm visual analog scale (VAS) ranging from not severe to very severe, after the question, "How active was your disease on average during the last week?”			
Units: Unit on Scale			
arithmetic mean	73.5	73.2	73.7
standard deviation	± 15.02	± 15.99	± 15.05
Total back pain (0-100 mm)			
Total back pain as measured by VAS ≥ 40 mm on a scale of 0-100 mm.			
Units: Unit on Scale			
arithmetic mean	74.9	74.2	75
standard deviation	± 13.07	± 14.18	± 13.80
Bath Ankylosing Spondylitis Disease Activity Index			
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) consisted of a 0 through 10 scale (0 being no problem and 10 being the worst problem, captured as a continuous VAS), which was used to answer 6 questions pertaining to the 5 major symptoms of Ankylosing Spondylitis: 1. Fatigue 2. Spinal pain 3. Joint pain / swelling			

4. Areas of localized tenderness (called enthesitis, or inflammation of tendons and ligaments) 5. Morning stiffness duration 6. Morning stiffness severity			
Units: Unit on Scale			
arithmetic mean	7	6.95	7.06
standard deviation	± 1.225	± 1.306	± 1.271
High sensitivity (hs) C-reactive protein			
High sensitivity C-reactive protein assessment was performed in order to identify the presence of inflammation, to determine its severity, and to monitor response to treatment.			
Units: Milligrams per Litre (mg/L)			
arithmetic mean	11.78	13.84	11.67
standard deviation	± 18.203	± 19.795	± 16.699

Reporting group values	Total		
Number of subjects	350		
Age categorical Units: Subjects			
Adults (18-64 years)	334		
From 65-84 years	16		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	110		
Male	240		
Patient's global assessment of disease activity			
The patient’s global assessment of disease activity was performed using a 0-100 mm visual analog scale (VAS) ranging from not severe to very severe, after the question, "How active was your disease on average during the last week?”			
Units: Unit on Scale			
arithmetic mean			
standard deviation	-		
Total back pain (0-100 mm)			
Total back pain as measured by VAS ≥ 40 mm on a scale of 0-100 mm.			
Units: Unit on Scale			
arithmetic mean			
standard deviation	-		
Bath Ankylosing Spondylitis Disease Activity Index			
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) consisted of a 0 through 10 scale (0 being no problem and 10 being the worst problem, captured as a continuous VAS), which was used to answer 6 questions pertaining to the 5 major symptoms of Ankylosing Spondylitis: 1. Fatigue 2. Spinal pain 3. Joint pain / swelling 4. Areas of localized tenderness (called enthesitis, or inflammation of tendons and ligaments) 5. Morning stiffness duration 6. Morning stiffness severity			
Units: Unit on Scale			
arithmetic mean			
standard deviation	-		
High sensitivity (hs) C-reactive protein			
High sensitivity C-reactive protein assessment was performed in order to identify the presence of			

inflammation, to determine its severity, and to monitor response to treatment.			
Units: Milligrams per Litre (mg/L) arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	Secukinumab 150 mg with loading

Reporting group description:

Subjects were subcutaneously (s.c.) administered with 150 milligrams (mg) of secukinumab at baseline, Weeks 1, 2, and 3, followed by dosing every four weeks starting at Week 4.

Reporting group title	Secukinumab 150 mg without loading dose

Reporting group description:

Subjects were s.c. administered with 150 mg of secukinumab at baseline, followed by dosing every four weeks starting at Week 4, and with Placebo at Weeks 1, 2, and 3.

Reporting group title	Placebo

Reporting group description:

Subjects were s.c. administered with placebo matching to secukinumab at baseline, Weeks 1, 2, 3, 4, 8, and 12. Subjects were further administered with 150 mg of secukinumab every four weeks starting at Week 16.

Subject analysis set title	All secukinumab 150 mg treated subjects
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects who were s.c. administered with secukinumab during the study.

Primary: Percentage of subjects responded for Assessment of Spondyloarthritis International Society 20 criteria (ASAS20) at 16 weeks

End point title	Percentage of subjects responded for Assessment of Spondyloarthritis International Society 20 criteria (ASAS20) at 16 weeks[1]

End point description:

ASAS 20 response is validated composite assessment, defined as improvement of ≥20% and ≥1 unit on scale of 10 in 3 main domains and no worsening of ≥20% and 1 unit on scale of 10 in 4th domain. Four main ASAS domains include:
1. Patient’s global assessment of disease activity, measured on 100mm VAS ranging from not severe to very severe
2. Patient’s assessment of back pain, measured on 100mm VAS ranging from no pain to unbearable pain
3. Function represented by Bath Ankylosing Spondylitis Functional Index (BASFI) average of 10 questions regarding ability to perform specific tasks as measured by 0-10 VAS scale
4. Inflammation represented by average of duration and severity of morning stiffness for last 2 questions on BASDAI scale (0- no problem, 10- worst problem)
The analysis was performed in Full analysis set (FAS) population, defined as all subjects who were randomized and received study treatment. Here, "Number of subjects analysed" signifies subjects evaluable for endpoint.

End point type	Primary

End point timeframe:

16 weeks

Notes:

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

End point values	Secukinumab 150 mg with loading	Secukinumab 150 mg without loading dose	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	110	112	
Units: Percentage of subjects				
number (confidence interval 95%)	60.5 (50.9 to 69.4)	65.5 (55.7 to 74.1)	49.1 (49.1 to 58.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects responded for ASAS 40 response at 16 weeks

End point title	Percentage of subjects responded for ASAS 40 response at 16 weeks

End point description:

ASAS 20 response is a validated composite assessment, defined as an improvement of ≥40% and 2 unit on a scale of 10 in three main domains and no worsening at all in the remaining domain within a defined time frame. Four main ASAS domains include:
1. Patient’s global assessment of disease activity measured on a 100 mm VAS ranging from not severe to very severe
2. Patient’s assessment of back pain, measured on a 100 mm VAS ranging from no pain to unbearable pain
3. Function represented by BASFI average of 10 questions regarding ability to perform specific tasks as measured by a 0-10 VAS scale
4. Inflammation represented by average of duration and severity of morning stiffness for last 2 questions on BASDAI scale (0 - no problem, 10 - worst problem)
The analysis was performed in FAS population. Here, "Number of subjects analysed" signifies subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Secukinumab 150 mg with loading	Secukinumab 150 mg without loading dose	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	110	112	
Units: Percentage of subjects				
number (confidence interval 95%)	39.5 (30.6 to 49.1)	38.2 (29.2 to 48.0)	29.5 (21.4 to 38.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in serum high sensitivity C-reactive protein (hsCRP) at 16 weeks

End point title	Change From Baseline in serum high sensitivity C-reactive protein (hsCRP) at 16 weeks

End point description:

Blood levels of C-reactive protein (CRP) is an acute phase reactant, which are indicative of inflammation and of its severity, and can be used to monitor treatment response. A hsCRP test is implemented to assess the efficacy of secukinumab (with or without load) versus placebo in reducing ankylosing spondylitis elicited systemic inflammation over the time. The analysis was performed in FAS population. Here, "Number of subjects analysed" signifies subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

Baseline, 16 weeks

End point values	Secukinumab 150 mg with loading	Secukinumab 150 mg without loading dose	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	113	109	112	
Units: Ratio				
arithmetic mean (standard deviation)	-4.23 (± 15.007)	-6.57 (± 12.778)	0.62 (± 11.699)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects responded for ASAS 5/6 response at 16 weeks

End point title	Percentage of subjects responded for ASAS 5/6 response at 16 weeks

End point description:

ASAS 5/6 response is validated composite assessment, defined as improvement of ≥20% in score in at least 5 of 6 clinical domains relevant to ankylosing spondylitis and no worsening in remaining domain. ASAS domains includes:
1. Patient’s global assessment of disease activity measured on 100 mm VAS ranging from not to very severe
2. Patient’s assessment of back pain, measured on 100 mm VAS ranging from no to unbearable pain
3. Function represented by BASFI average of 10 questions regarding ability to perform specific tasks as measured by 0-10 VAS scale
4. Inflammation represented by average of duration and severity of morning stiffness for last 2 questions on BASDAI scale (0- no problem, 10- worst problem)
5. Spinal mobility represented by the Bath Ankylosing Spondylitis Metrology Index (BASMI) lateral spinal flexion assessment
6. CRP
The analysis was performed in FAS population. Here, "Number of subjects analysed" signifies subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Secukinumab 150 mg with loading	Secukinumab 150 mg without loading dose	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	110	112	
Units: Percentage of subjects				
number (confidence interval 95%)	37.7 (29.0 to 47.3)	45.5 (36.0 to 55.2)	30.4 (22.2 to 39.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at 16 weeks

End point title	Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at 16 weeks

End point description:

BASDAI is a validated assessment tool using 0 through 10 scales (0- no problem, 10- worst problem) on continuous VAS, to answer 6 questions pertaining to 5 major symptoms of ankylosing spondylitis. Computed composite scores of 4 or greater indicate suboptimal disease control. Questions includes:
1. Fatigue
2. Spinal pain
3. Joint pain / swelling
4. Areas of localized tenderness (called enthesitis, or inflammation of tendons and ligaments)
5. Morning stiffness duration
6. Morning stiffness severity

Each symptom has equal weighting, the mean of two scores related to morning stiffness was taken (questions 5 and 6). The resulting 0 to 10 score was added to the scores from questions 1-4. The resulting 0 to 50 score was divided by 5 to give a final 0–10 BASDAI score.
BASDAI was a quick and simple index taking between 30 seconds and 2 minutes for completion. The analysis was performed in FAS population. Here, "Number of subjects analysed" signifies subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

Baseline, 16 weeks

End point values	Secukinumab 150 mg with loading	Secukinumab 150 mg without loading dose	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	110	112	
Units: Units on a scale				
arithmetic mean (standard deviation)	-2.405 (± 2.1206)	-2.533 (± 2.1463)	-1.917 (± 2.2221)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physical Function Component summary (PCS) of the Short-form Health Survey (SF-36)

End point title	Change From Baseline in Physical Function Component summary (PCS) of the Short-form Health Survey (SF-36)

End point description:

SF-36 is a 36 item questionnaire which measures Quality of Life across eight subscales that were scored individually: Physical Functioning, Role- Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, and Mental Health. The overall summary scores, SF-36 physical Component Summary (PCS) was used to assess improvement from baseline in the Health-Related Quality Of Life of subjects. The change in SF-36 scores were evaluated using MMRM. The analysis was performed in FAS population. Here, "Number of subjects analysed" signifies subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

Baseline, 16 weeks

End point values	Secukinumab 150 mg with loading	Secukinumab 150 mg without loading dose	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	112	113	
Units: Units on a scale				
arithmetic mean (standard deviation)	6.754 (± 6.9624)	7.242 (± 8.3627)	4.7 (± 7.5912)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) at 16 weeks

End point title	Change From Baseline in Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) at 16 weeks

End point description:

ASQoL is a self-administered 18 item questionnaire that assesses disease-specific quality of life (QoL), consisting of statements that are relevant to the physical and mental conditions for a subject with ankylosing spondylitis: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each statement is answered as a 'Yes' (scored as 1) or 'No' (scored as 0). All item scores are summed to give a total score. Total score ranges from 0 (good QoL) to 18 (poor QoL). The change in ASQoL scores was evaluated using a mixed effect repeated measures model (MMRM). The analysis was performed in FAS population. Here, "Number of subjects analysed" signifies subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

Baseline, 16 weeks

End point values	Secukinumab 150 mg with loading	Secukinumab 150 mg without loading dose	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	112	113	
Units: Units on a scale				
arithmetic mean (standard deviation)	-4.2 (± 4.63)	-4.7 (± 5.05)	-3 (± 4.74)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with adverse events (AEs), deaths, serious adverse events (SAEs) and related discontinuations at 104 weeks

End point title	Number of subjects with adverse events (AEs), deaths, serious adverse events (SAEs) and related discontinuations at 104 weeks

End point description:

AEs were defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during study, having been absent at baseline, or, if present at baseline, appears to worsen. SAEs were defined as any untoward medical occurrences that result in death, are life threatening, require (or prolong) hospitalization, cause persistent or significant disability/incapacity, result in congenital anomalies or birth defects, or are other conditions which in judgement of investigators represent significant hazards. The analysis was performed on the safety population, defined as all subjects who took at least one dose of study treatment during the treatment period.

End point type	Secondary

End point timeframe:

104 weeks

End point values	Secukinumab 150 mg with loading	Secukinumab 150 mg without loading dose	Placebo	All secukinumab 150 mg treated subjects
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	116	117	117	346
Units: Number of Subjects				
AEs	100	98	65	289
SAEs	16	11	4	39
Death	2	0	0	4
Discontinued study treatment due to any AEs	9	5	1	20

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects responded for ASAS 20 at week 4

End point title	Percentage of subjects responded for ASAS 20 at week 4

End point description:

ASAS 20 response is a validated composite assessment, defined as an improvement of ≥20% and 1 unit on a scale of 10 in three main domains and no worsening of ≥20% and 1 unit on a scale of 10 in the fourth domain within a defined time frame. Four main ASAS domains include:
1. Patient's global assessment of disease activity measured on a 100 mm VAS ranging from not severe to very severe
2. Patient's assessment of back pain, measured on a 100 mm VAS ranging from no pain to unbearable pain
3. Function represented by BASFI average of 10 questions regarding ability to perform specific tasks as measured by a 0-10 VAS scale
4. Inflammation represented by average of duration and severity of morning stiffness for last 2 questions on BASDAI scale (0 - no problem, 10 - worst problem)
The analysis was performed in FAS population. Here, "Number of subjects analysed" signifies subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

Week 4

End point values	Secukinumab 150 mg with loading	Secukinumab 150 mg without loading dose	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	116	114	115	
Units: Percentage of subjects				
number (confidence interval 95%)	49.1 (39.8 to 58.5)	55.3 (45.7 to 64.6)	40.0 (31.1 to 49.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects responded for ASAS 40 response at week 4

End point title	Percentage of subjects responded for ASAS 40 response at week 4

End point description:

ASAS 20 response is a validated composite assessment, defined as an improvement of at least 40% and 2 unit on a scale of 10 in three main domains and no worsening at all in the remaining domain within a defined time frame. Four main ASAS domains include:
1. Patient's global assessment of disease activity measured on a 100 mm VAS ranging from not severe to very severe
2. Patient's assessment of back pain, measured on a 100 mm VAS ranging from no pain to unbearable pain
3. Function represented by BASFI average of 10 questions regarding ability to perform specific tasks as measured by a 0-10 VAS scale
4. Inflammation represented by average of duration and severity of morning stiffness for last 2 questions on BASDAI scale (0 - no problem, 10 - worst problem)
The analysis was performed in FAS population. Here, "Number of subjects analysed" signifies subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:
Week 4

End point values	Secukinumab 150 mg with loading	Secukinumab 150 mg without loading dose	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	116	114	115	
Units: Percentage of subjects				
number (confidence interval 95%)	29.3 (21.4 to 38.6)	27.2 (19.5 to 36.5)	18.3 (11.9 to 26.8)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events are monitored from date of First Subject First Visit (FSFV) until Last Subject Last Visit (LSLV). All other adverse events are monitored from First Subject First Treatment until LSLV.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Secukinumab 150 mg without loading dose

Reporting group description:

Subjects were s.c. administered with 150 mg of secukinumab at baseline, followed by dosing every four weeks starting at Week 4, and with Placebo at Weeks 1, 2, and 3.

Reporting group title	Secukinumab 150 mg with loading

Reporting group description:

Subjects were s.c. administered with 150 mg of secukinumab at baseline, Weeks 1, 2, and 3, followed by dosing every four weeks starting at Week 4.

Reporting group title	Placebo

Reporting group description:

Subjects were s.c. administered with placebo matching to secukinumab at baseline, Weeks 1, 2, 3, 4, 8, and 12. Subjects were further administered with 150 mg of secukinumab every four weeks starting at Week 16.

Reporting group title	All secukinumab 150 mg treated subjects

Reporting group description:

All subjects who were s.c. administered with secukinumab during the study.

Serious adverse events	Secukinumab 150 mg without loading dose	Secukinumab 150 mg with loading	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 117 (9.40%)	18 / 116 (15.52%)	4 / 117 (3.42%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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
Malignant melanoma			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Prostate cancer			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Testis cancer			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 117 (0.00%)	2 / 116 (1.72%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral artery occlusion			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Reproductive system and breast disorders			
Rectocele			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			

subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Somatic symptom disorder			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Weight decreased			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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
Meniscus injury			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Tendon injury			

subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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
Tibia fracture			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Cardiac failure acute			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Pericarditis			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Nervous system disorders			
Basal ganglia haemorrhage			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Migraine			

subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
VIth nerve paralysis			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Iron deficiency anaemia			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Eye disorders			
Papilloedema			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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
Retinal detachment			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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
Colitis ulcerative			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Crohn's disease			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Diarrhoea			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Duodenitis			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Gastric ulcer			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Gastritis erosive			

subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Oesophagitis			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Bladder diverticulum			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Glomerulonephritis membranous			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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
Nephrolithiasis			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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
Proteinuria			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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 colic			

subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Bursitis			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Femoroacetabular impingement			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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
Myofascial pain syndrome			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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
Osteoarthritis			
subjects affected / exposed	0 / 117 (0.00%)	2 / 116 (1.72%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Appendicitis			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Atypical pneumonia			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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
Chronic tonsillitis			
subjects affected / exposed	1 / 117 (0.85%)	0 / 116 (0.00%)	0 / 117 (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
Erysipelas			
subjects affected / exposed	0 / 117 (0.00%)	2 / 116 (1.72%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (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
Tinea pedis			
subjects affected / exposed	0 / 117 (0.00%)	0 / 116 (0.00%)	0 / 117 (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

Serious adverse events	All secukinumab 150 mg treated subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 346 (12.43%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			

subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	0 / 346 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Testis cancer			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	2 / 346 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Peripheral artery occlusion			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Reproductive system and breast disorders			
Rectocele			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Somatic symptom disorder			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Weight decreased			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meniscus injury			

subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tendon injury			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure acute			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Myocardial infarction			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Myocardial ischaemia			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pericarditis			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Basal ganglia haemorrhage			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Migraine			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VIth nerve paralysis			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Iron deficiency anaemia			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Papilloedema			

subjects affected / exposed	1 / 346 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Retinal detachment				
subjects affected / exposed	1 / 346 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 346 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal fistula				
subjects affected / exposed	1 / 346 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis ulcerative				
subjects affected / exposed	2 / 346 (0.58%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Crohn's disease				
subjects affected / exposed	1 / 346 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 346 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				
subjects affected / exposed	1 / 346 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Duodenitis				

subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis erosive			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophagitis			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Bladder diverticulum			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Glomerulonephritis membranous			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			

subjects affected / exposed	1 / 346 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Proteinuria				
subjects affected / exposed	1 / 346 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal colic				
subjects affected / exposed	0 / 346 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	1 / 346 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	1 / 346 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bursitis				
subjects affected / exposed	1 / 346 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Femoroacetabular impingement				
subjects affected / exposed	0 / 346 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	1 / 346 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myofascial pain syndrome				

subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	2 / 346 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	2 / 346 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Atypical pneumonia			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic tonsillitis			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	3 / 346 (0.87%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Otitis media acute			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Tinea pedis			
subjects affected / exposed	1 / 346 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Secukinumab 150 mg without loading dose	Secukinumab 150 mg with loading	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	89 / 117 (76.07%)	90 / 116 (77.59%)	54 / 117 (46.15%)
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 117 (5.13%)	9 / 116 (7.76%)	2 / 117 (1.71%)
occurrences (all)	7	9	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 117 (2.56%)	4 / 116 (3.45%)	4 / 117 (3.42%)
occurrences (all)	3	5	5
Influenza like illness			
subjects affected / exposed	3 / 117 (2.56%)	2 / 116 (1.72%)	0 / 117 (0.00%)
occurrences (all)	3	2	0
Non-cardiac chest pain			
subjects affected / exposed	3 / 117 (2.56%)	0 / 116 (0.00%)	1 / 117 (0.85%)
occurrences (all)	3	0	3
Pyrexia			
subjects affected / exposed	1 / 117 (0.85%)	3 / 116 (2.59%)	1 / 117 (0.85%)
occurrences (all)	1	3	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 117 (3.42%)	6 / 116 (5.17%)	2 / 117 (1.71%)
occurrences (all)	4	9	2
Oropharyngeal pain			
subjects affected / exposed	5 / 117 (4.27%)	7 / 116 (6.03%)	1 / 117 (0.85%)
occurrences (all)	5	10	1
Rhinorrhoea			
subjects affected / exposed	3 / 117 (2.56%)	1 / 116 (0.86%)	0 / 117 (0.00%)
occurrences (all)	3	2	0
Psychiatric disorders			
Depression			

subjects affected / exposed	5 / 117 (4.27%)	0 / 116 (0.00%)	0 / 117 (0.00%)
occurrences (all)	5	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 117 (3.42%)	5 / 116 (4.31%)	1 / 117 (0.85%)
occurrences (all)	4	7	1
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 117 (3.42%)	3 / 116 (2.59%)	0 / 117 (0.00%)
occurrences (all)	4	4	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	4 / 117 (3.42%)	4 / 116 (3.45%)	0 / 117 (0.00%)
occurrences (all)	5	5	0
Fall			
subjects affected / exposed	0 / 117 (0.00%)	4 / 116 (3.45%)	1 / 117 (0.85%)
occurrences (all)	0	4	1
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	1 / 117 (0.85%)	4 / 116 (3.45%)	0 / 117 (0.00%)
occurrences (all)	1	4	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 117 (1.71%)	10 / 116 (8.62%)	5 / 117 (4.27%)
occurrences (all)	7	11	6
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 117 (2.56%)	1 / 116 (0.86%)	0 / 117 (0.00%)
occurrences (all)	3	1	0
Leukopenia			
subjects affected / exposed	1 / 117 (0.85%)	4 / 116 (3.45%)	1 / 117 (0.85%)
occurrences (all)	1	4	1
Neutropenia			
subjects affected / exposed	0 / 117 (0.00%)	1 / 116 (0.86%)	0 / 117 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	3 / 117 (2.56%)	3 / 116 (2.59%)	0 / 117 (0.00%)
occurrences (all)	3	3	0
Eye disorders			
Iridocyclitis			
subjects affected / exposed	1 / 117 (0.85%)	3 / 116 (2.59%)	0 / 117 (0.00%)
occurrences (all)	2	4	0
Iritis			
subjects affected / exposed	3 / 117 (2.56%)	1 / 116 (0.86%)	0 / 117 (0.00%)
occurrences (all)	4	2	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 117 (2.56%)	3 / 116 (2.59%)	0 / 117 (0.00%)
occurrences (all)	7	3	0
Abdominal pain upper			
subjects affected / exposed	1 / 117 (0.85%)	6 / 116 (5.17%)	0 / 117 (0.00%)
occurrences (all)	1	8	0
Diarrhoea			
subjects affected / exposed	11 / 117 (9.40%)	9 / 116 (7.76%)	6 / 117 (5.13%)
occurrences (all)	17	15	6
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 117 (2.56%)	1 / 116 (0.86%)	0 / 117 (0.00%)
occurrences (all)	3	1	0
Mouth ulceration			
subjects affected / exposed	2 / 117 (1.71%)	3 / 116 (2.59%)	1 / 117 (0.85%)
occurrences (all)	3	3	2
Nausea			
subjects affected / exposed	1 / 117 (0.85%)	8 / 116 (6.90%)	2 / 117 (1.71%)
occurrences (all)	1	9	6
Toothache			
subjects affected / exposed	3 / 117 (2.56%)	2 / 116 (1.72%)	0 / 117 (0.00%)
occurrences (all)	3	2	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	4 / 117 (3.42%)	2 / 116 (1.72%)	2 / 117 (1.71%)
occurrences (all)	4	2	2
Eczema			

subjects affected / exposed	3 / 117 (2.56%)	4 / 116 (3.45%)	3 / 117 (2.56%)
occurrences (all)	4	6	3
Pruritus			
subjects affected / exposed	3 / 117 (2.56%)	4 / 116 (3.45%)	2 / 117 (1.71%)
occurrences (all)	4	4	2
Rash			
subjects affected / exposed	3 / 117 (2.56%)	3 / 116 (2.59%)	0 / 117 (0.00%)
occurrences (all)	4	3	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	3 / 117 (2.56%)	0 / 116 (0.00%)	1 / 117 (0.85%)
occurrences (all)	3	0	1
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	11 / 117 (9.40%)	12 / 116 (10.34%)	5 / 117 (4.27%)
occurrences (all)	18	24	5
Arthralgia			
subjects affected / exposed	11 / 117 (9.40%)	2 / 116 (1.72%)	2 / 117 (1.71%)
occurrences (all)	14	2	3
Arthritis			
subjects affected / exposed	3 / 117 (2.56%)	0 / 116 (0.00%)	0 / 117 (0.00%)
occurrences (all)	4	0	0
Back pain			
subjects affected / exposed	7 / 117 (5.98%)	10 / 116 (8.62%)	5 / 117 (4.27%)
occurrences (all)	7	10	6
Musculoskeletal pain			
subjects affected / exposed	1 / 117 (0.85%)	3 / 116 (2.59%)	2 / 117 (1.71%)
occurrences (all)	1	3	4
Myalgia			
subjects affected / exposed	2 / 117 (1.71%)	4 / 116 (3.45%)	0 / 117 (0.00%)
occurrences (all)	2	4	0
Osteoarthritis			
subjects affected / exposed	0 / 117 (0.00%)	3 / 116 (2.59%)	0 / 117 (0.00%)
occurrences (all)	0	3	0
Pain in extremity			

subjects affected / exposed	5 / 117 (4.27%)	2 / 116 (1.72%)	0 / 117 (0.00%)
occurrences (all)	6	2	0
Spondylitis			
subjects affected / exposed	3 / 117 (2.56%)	1 / 116 (0.86%)	1 / 117 (0.85%)
occurrences (all)	3	1	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	8 / 117 (6.84%)	13 / 116 (11.21%)	1 / 117 (0.85%)
occurrences (all)	8	17	1
Ear infection			
subjects affected / exposed	0 / 117 (0.00%)	3 / 116 (2.59%)	0 / 117 (0.00%)
occurrences (all)	0	5	0
Fungal skin infection			
subjects affected / exposed	1 / 117 (0.85%)	5 / 116 (4.31%)	0 / 117 (0.00%)
occurrences (all)	1	7	0
Gastroenteritis			
subjects affected / exposed	3 / 117 (2.56%)	5 / 116 (4.31%)	2 / 117 (1.71%)
occurrences (all)	4	7	2
Herpes simplex			
subjects affected / exposed	1 / 117 (0.85%)	3 / 116 (2.59%)	0 / 117 (0.00%)
occurrences (all)	1	3	0
Influenza			
subjects affected / exposed	9 / 117 (7.69%)	7 / 116 (6.03%)	5 / 117 (4.27%)
occurrences (all)	13	11	5
Laryngitis			
subjects affected / exposed	2 / 117 (1.71%)	3 / 116 (2.59%)	0 / 117 (0.00%)
occurrences (all)	2	3	0
Nasopharyngitis			
subjects affected / exposed	29 / 117 (24.79%)	32 / 116 (27.59%)	10 / 117 (8.55%)
occurrences (all)	44	52	13
Oral herpes			
subjects affected / exposed	3 / 117 (2.56%)	4 / 116 (3.45%)	2 / 117 (1.71%)
occurrences (all)	4	6	2
Pharyngitis			
subjects affected / exposed	6 / 117 (5.13%)	2 / 116 (1.72%)	3 / 117 (2.56%)
occurrences (all)	6	2	3

Pulpitis dental			
subjects affected / exposed	0 / 117 (0.00%)	3 / 116 (2.59%)	0 / 117 (0.00%)
occurrences (all)	0	3	0
Respiratory tract infection			
subjects affected / exposed	10 / 117 (8.55%)	6 / 116 (5.17%)	3 / 117 (2.56%)
occurrences (all)	14	10	4
Rhinitis			
subjects affected / exposed	7 / 117 (5.98%)	3 / 116 (2.59%)	1 / 117 (0.85%)
occurrences (all)	9	3	1
Sinusitis			
subjects affected / exposed	4 / 117 (3.42%)	4 / 116 (3.45%)	0 / 117 (0.00%)
occurrences (all)	5	6	0
Tonsillitis			
subjects affected / exposed	3 / 117 (2.56%)	1 / 116 (0.86%)	0 / 117 (0.00%)
occurrences (all)	4	1	0
Tooth infection			
subjects affected / exposed	0 / 117 (0.00%)	3 / 116 (2.59%)	0 / 117 (0.00%)
occurrences (all)	0	3	0
Upper respiratory tract infection			
subjects affected / exposed	17 / 117 (14.53%)	11 / 116 (9.48%)	6 / 117 (5.13%)
occurrences (all)	24	16	6
Urinary tract infection			
subjects affected / exposed	2 / 117 (1.71%)	3 / 116 (2.59%)	0 / 117 (0.00%)
occurrences (all)	2	3	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 117 (0.85%)	1 / 116 (0.86%)	3 / 117 (2.56%)
occurrences (all)	1	1	3
Hyperlipidaemia			
subjects affected / exposed	1 / 117 (0.85%)	6 / 116 (5.17%)	1 / 117 (0.85%)
occurrences (all)	1	6	1

Non-serious adverse events	All secukinumab 150 mg treated subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	254 / 346 (73.41%)		
Vascular disorders			

Hypertension			
subjects affected / exposed	18 / 346 (5.20%)		
occurrences (all)	19		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 346 (2.31%)		
occurrences (all)	9		
Influenza like illness			
subjects affected / exposed	5 / 346 (1.45%)		
occurrences (all)	5		
Non-cardiac chest pain			
subjects affected / exposed	4 / 346 (1.16%)		
occurrences (all)	5		
Pyrexia			
subjects affected / exposed	8 / 346 (2.31%)		
occurrences (all)	8		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	18 / 346 (5.20%)		
occurrences (all)	22		
Oropharyngeal pain			
subjects affected / exposed	16 / 346 (4.62%)		
occurrences (all)	19		
Rhinorrhoea			
subjects affected / exposed	5 / 346 (1.45%)		
occurrences (all)	6		
Psychiatric disorders			
Depression			
subjects affected / exposed	6 / 346 (1.73%)		
occurrences (all)	9		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	10 / 346 (2.89%)		
occurrences (all)	12		
Aspartate aminotransferase increased			

subjects affected / exposed	8 / 346 (2.31%)		
occurrences (all)	9		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	10 / 346 (2.89%)		
occurrences (all)	13		
Fall			
subjects affected / exposed	5 / 346 (1.45%)		
occurrences (all)	5		
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	8 / 346 (2.31%)		
occurrences (all)	8		
Nervous system disorders			
Headache			
subjects affected / exposed	18 / 346 (5.20%)		
occurrences (all)	25		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 346 (1.45%)		
occurrences (all)	5		
Leukopenia			
subjects affected / exposed	8 / 346 (2.31%)		
occurrences (all)	9		
Neutropenia			
subjects affected / exposed	7 / 346 (2.02%)		
occurrences (all)	8		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	7 / 346 (2.02%)		
occurrences (all)	8		
Eye disorders			
Iridocyclitis			
subjects affected / exposed	7 / 346 (2.02%)		
occurrences (all)	9		
Iritis			

subjects affected / exposed	7 / 346 (2.02%)		
occurrences (all)	9		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 346 (2.31%)		
occurrences (all)	12		
Abdominal pain upper			
subjects affected / exposed	10 / 346 (2.89%)		
occurrences (all)	13		
Diarrhoea			
subjects affected / exposed	28 / 346 (8.09%)		
occurrences (all)	42		
Gastrooesophageal reflux disease			
subjects affected / exposed	5 / 346 (1.45%)		
occurrences (all)	5		
Mouth ulceration			
subjects affected / exposed	6 / 346 (1.73%)		
occurrences (all)	7		
Nausea			
subjects affected / exposed	13 / 346 (3.76%)		
occurrences (all)	16		
Toothache			
subjects affected / exposed	5 / 346 (1.45%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	6 / 346 (1.73%)		
occurrences (all)	6		
Eczema			
subjects affected / exposed	7 / 346 (2.02%)		
occurrences (all)	10		
Pruritus			
subjects affected / exposed	8 / 346 (2.31%)		
occurrences (all)	9		
Rash			

subjects affected / exposed occurrences (all)	9 / 346 (2.60%) 11		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	 3 / 346 (0.87%) 3		
Musculoskeletal and connective tissue disorders Ankylosing spondylitis subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Arthritis subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Osteoarthritis subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) Spondylitis subjects affected / exposed occurrences (all)	 29 / 346 (8.38%) 49 15 / 346 (4.34%) 23 4 / 346 (1.16%) 7 23 / 346 (6.65%) 25 6 / 346 (1.73%) 6 8 / 346 (2.31%) 8 5 / 346 (1.45%) 5 10 / 346 (2.89%) 11 4 / 346 (1.16%) 4		
Infections and infestations			

Bronchitis				
subjects affected / exposed	31 / 346 (8.96%)			
occurrences (all)	37			
Ear infection				
subjects affected / exposed	4 / 346 (1.16%)			
occurrences (all)	6			
Fungal skin infection				
subjects affected / exposed	7 / 346 (2.02%)			
occurrences (all)	9			
Gastroenteritis				
subjects affected / exposed	10 / 346 (2.89%)			
occurrences (all)	13			
Herpes simplex				
subjects affected / exposed	5 / 346 (1.45%)			
occurrences (all)	5			
Influenza				
subjects affected / exposed	19 / 346 (5.49%)			
occurrences (all)	31			
Laryngitis				
subjects affected / exposed	7 / 346 (2.02%)			
occurrences (all)	9			
Nasopharyngitis				
subjects affected / exposed	80 / 346 (23.12%)			
occurrences (all)	129			
Oral herpes				
subjects affected / exposed	9 / 346 (2.60%)			
occurrences (all)	15			
Pharyngitis				
subjects affected / exposed	10 / 346 (2.89%)			
occurrences (all)	12			
Pulpitis dental				
subjects affected / exposed	3 / 346 (0.87%)			
occurrences (all)	3			
Respiratory tract infection				
subjects affected / exposed	22 / 346 (6.36%)			
occurrences (all)	33			

Rhinitis subjects affected / exposed occurrences (all)	15 / 346 (4.34%) 17		
Sinusitis subjects affected / exposed occurrences (all)	9 / 346 (2.60%) 12		
Tonsillitis subjects affected / exposed occurrences (all)	10 / 346 (2.89%) 11		
Tooth infection subjects affected / exposed occurrences (all)	4 / 346 (1.16%) 4		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	37 / 346 (10.69%) 52		
Urinary tract infection subjects affected / exposed occurrences (all)	7 / 346 (2.02%) 8		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all)	3 / 346 (0.87%) 3		
Hyperlipidaemia subjects affected / exposed occurrences (all)	9 / 346 (2.60%) 9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported