Clinical trial results:
A Randomized, Double-blind, Placebo-controlled Phase 3 Study to Evaluate the Efficacy and Safety of Brodalumab in Subjects With Psoriatic Arthritis: AMVISION-2

Summary

EudraCT number	2013-003553-16
Trial protocol	GR DE HU LV
Global end of trial date	01 October 2015

Results information

Result version number	v1 (current)
This version publication date	16 October 2016
First version publication date	16 October 2016

Trial information

Trial identification

Sponsor protocol code	20110144

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02024646
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen, Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	01 October 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 October 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of brodalumab compared to placebo, in patients with psoriatic arthritis, as measured by the proportion of subjects achieving an American College of Rheumatology 20% response (ACR20) response at week 16.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with the International Conference on Harmonisation's (ICH) guideline for Good Clinical Practice (GCP), applicable regulatory requirements, and the Sponsor's applicable policies.
The clinical study protocol (CSP) was reviewed and approved by an independent ethics committee (IEC) or institutional review board (IRB) at each clinical site prior to the enrollment of any study subjects.
All subjects provided written informed consent before undergoing any study-related procedures, including screening procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 March 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 122
Country: Number of subjects enrolled	Russian Federation: 56
Country: Number of subjects enrolled	Poland: 177
Country: Number of subjects enrolled	Canada: 32
Country: Number of subjects enrolled	Germany: 27
Country: Number of subjects enrolled	Hungary: 20
Country: Number of subjects enrolled	Latvia: 15
Country: Number of subjects enrolled	Mexico: 13
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Greece: 11
Worldwide total number of subjects	484
EEA total number of subjects	261

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)	446
From 65 to 84 years	38
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at 89 clinical centers in 10 countries worldwide. The first subject was randomized on 24 March 2014.

Pre-assignment

Screening details:

Eligible patients were randomized in a 1:1:1 ratio by interactive web response (IWR) system to receive either brodalumab (140 mg or 210 mg) or placebo. Randomization was stratified by baseline body weight (≤100 kg or >100 kg), prior use of a biologic, and geographic region.

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	Placebo

Arm description:

Participants received placebo subcutaneous injection at baseline, week 1, week 2 and then every 2 weeks (Q2W) thereafter up to week 22. From week 14 participants with an inadequate response began treatment with 210 mg brodalumab Q2W. From Week 24 all participants received brodalumab 210 mg Q2W.

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:

Administered by subcutaneous injection once every 2 weeks.

Investigational medicinal product name	Brodalumab
Investigational medicinal product code	AMG 827
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection once every 2 weeks.

Arm title	Brodalumab 140 mg

Arm description:

Participants received 140 mg brodalumab by subcutaneous injection at baseline, week 1, week 2 and then Q2W thereafter for up to 3 years.

Arm type	Experimental
Investigational medicinal product name	Brodalumab
Investigational medicinal product code	AMG 827
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection once every 2 weeks.

Arm title	Brodalumab 210 mg

Arm description:

Participants received 210 mg brodalumab by subcutaneous injection at baseline, week 1, week 2 and then Q2W thereafter for up to 3 years.

Arm type	Experimental
Investigational medicinal product name	Brodalumab
Investigational medicinal product code	AMG 827
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection once every 2 weeks.

Number of subjects in period 1	Placebo	Brodalumab 140 mg	Brodalumab 210 mg
Started	161	160	163
Ongoing study at week 16	146	152	149
Ongoing study at week 24	129	134	129
Ongoing study at week 52	41	45	40
Completed	0	0	0
Not completed	161	160	163
Consent withdrawn by subject	27	15	25
Sponsor’s decision	133	143	133
Lost to follow-up	1	2	5

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo subcutaneous injection at baseline, week 1, week 2 and then every 2 weeks (Q2W) thereafter up to week 22. From week 14 participants with an inadequate response began treatment with 210 mg brodalumab Q2W. From Week 24 all participants received brodalumab 210 mg Q2W.	
Reporting group title	Brodalumab 140 mg
Reporting group description:	
Participants received 140 mg brodalumab by subcutaneous injection at baseline, week 1, week 2 and then Q2W thereafter for up to 3 years.	
Reporting group title	Brodalumab 210 mg
Reporting group description:	
Participants received 210 mg brodalumab by subcutaneous injection at baseline, week 1, week 2 and then Q2W thereafter for up to 3 years.	

Reporting group values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg
Number of subjects	161	160	163
Age Categorical Units: Subjects			
Adults (18-64 years)	150	146	150
From 65-84 years	11	14	13
85 years and over	0	0	0
Age Continuous Units: years			
median	49	48	45
full range (min-max)	18 to 76	22 to 80	19 to 79
Gender Categorical Units: Subjects			
Female	85	80	84
Male	76	80	79
Race Units: Subjects			
White	154	150	159
Black or African American	0	1	0
Asian	1	0	0
American Indian or Alaska Native	3	5	2
Other	3	4	2
Tender joint count Units: joints			
arithmetic mean	20.9	20.5	17.2
standard deviation	± 14.33	± 15.66	± 12.5
Swollen joint count Units: joints			
arithmetic mean	11	11.4	11.1
standard deviation	± 8.55	± 9.19	± 8.49
Disease Activity Score 28-C-Reactive Protein (DAS28-CRP)			
The DAS28-CRP is a composite score to measure disease activity in patients with arthritis, derived from			

the following variables: • The number of swollen and tender joints assessed using the 28-joint count;• C-reactive protein (CRP) level • Patient's global assessment of disease activity assessed on a score from 0 to 100. The DAS28-CRP score ranges from approximately zero to ten. Higher DAS28-CRP scores indicate higher disease activity.Data available for 157, 160, 160 subjects in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	4.6	4.8	4.6
standard deviation	± 1.09	± 1.08	± 1.08
Health Assessment Questionnaire – Disability Index (HAQ-DI)			
The HAQ-DI asks subjects about the degree of difficulty they have in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and errands and chores). Responses in each functional area are scored from 0 indicating no difficulty to 3 indicating inability to perform a task in that area. The overall score is the average of the 8 category scores and ranges from 0 (no disability) to 3 (very severe, high dependency disability).			
Units: units on a scale			
arithmetic mean	1.1	1.1	1.1
standard deviation	± 0.61	± 0.7	± 0.61
Enthesitis score			
The enthesitis count is defined as the total number of 6 sites that have enthesitis. The sites assessed were: Lateral epicondyle (left/right), Medial femoral condyle (left/right), Achilles tendon insertion (left/right).			
Units: entheses			
arithmetic mean	1.7	1.7	1.6
standard deviation	± 1.78	± 1.95	± 1.81
Dactylitis score			
The dactylitis count is defined as the sum of 20 fingers/toes that exhibit dactylitis (absent 0, present 1).			
Units: digits			
arithmetic mean	2.4	1.7	1.9
standard deviation	± 3.99	± 3.37	± 3.45
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)			
BASDAI is a self-administered questionnaire composed of six items using an 11-point numerical rating scale from "0 = none" to "10 = very severe" for the first five items, and "0 = 0 hours" to "10 = 2 or more hours" for the sixth item that asks about the duration of morning stiffness. The BASDAI assesses the severity of fatigue, spinal and peripheral joint pain, localized tenderness, and morning stiffness. The final BASDAI score averages the individual assessments for a final score range of 0-10. Data available for 159, 160, and 162 subjects in each group respectively.			
Units: units on a scale			
arithmetic mean	5.2	5	5
standard deviation	± 2.09	± 2.3	± 2.16
Psoriasis Area and Severity Index (PASI) Score			
The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement. The total PASI score ranges from 0 to 72. The higher the total score, the more severe the disease. Data available for 160, 160, 163 subjects in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	8.9	9	7.9
standard deviation	± 9.86	± 11.23	± 9.36
Nail Psoriasis Severity Index (NAPSI)			
The NAPSI scale is an objective, numeric, and reproducible grading system for nail psoriasis that incorporates the many different features of nail psoriasis. Each quarter of the nail was scored for the presence (1) or absence (0) of 8 clinical features for a score of 0-4 for each feature. The total score for each nail ranges from 0 (absent) to 32 (worst). Data are reported for the worst nail for subjects with baseline nail involvement (58, 64 and 70 participants in each treatment group respectively).			
Units: units on a scale			
arithmetic mean	10.2	9.8	9.4

standard deviation	± 4.19	± 5.29	± 3.51
Dermatology Life Quality Index (DLQI)			
The DLQI is a skin disease-specific instrument to evaluate health-related quality of life. Participants evaluate the degree that psoriasis has affected their quality of life in the last week, including symptoms and feelings, daily and leisure activities, work or school activities, personal relationships and treatment related feelings. Participants answer 10 questions on a scale from 0 (not at all) to 3 (very much); the total score ranges from 0 (best possible score) to 30 (worst possible score). Data are available for 159, 160, 162 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	9.7	9.2	9.1
standard deviation	± 7.33	± 7.23	± 7.7
Psoriasis Severity Index (PSI) average Weekly Total Score			
The Psoriasis Symptom Inventory consists of eight psoriasis-specific items. Participants rated the severity of their symptoms in the last 24 hours on a scale from 'not at all' (0) to 'very severe' (4) in an electronic diary once a day. Total scores range from 0 to 32 with higher scores indicating worse symptoms. The daily assessment of the Psoriasis Symptom Inventory was analyzed as a weekly average. Data are available for 152, 144, and 148 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	15	13.9	13.8
standard deviation	± 7.6	± 7.68	± 8.58
Clinical Disease Activity Index (CDAI)			
The Clinical Disease Activity Index (CDAI) is a composite index that is calculated from: • 28 tender joint count, • 28 swollen joint count, • Patient's Global Assessment of Disease Activity measured on a 100 mm visual analog scale (VAS), where 0 mm = lowest disease activity and 100 mm = highest; • Physician's Global Assessment of Disease Activity - measured on a 100 mm VAS, where 0 mm = lowest disease activity and 100 mm = highest. The CDAI score ranges from 0-76 where lower scores indicate less disease activity. Data available for 157, 156, 162 subjects in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	27.3	29.4	26.6
standard deviation	± 12.59	± 13.13	± 12.76
Physician Global Assessment of Disease Activity			
Assessed on a 100 mm visual analog scale (VAS) from 0 (Very Well) on the left to 100 (Very Poorly) on the right end of the line. Data available for 157, 156, 162 subjects in each treatment group respectively			
Units: mm			
arithmetic mean	56.6	58.5	57.3
standard deviation	± 20.12	± 18.79	± 20.18
Patient Global Assessment of Disease			
Assessed on a 100 mm VAS from 0 (Very Well) on the left end of the line to 10 (Very Poorly) on the right. Data available for 159, 160, 162 subjects in each treatment group respectively.			
Units: mm			
arithmetic mean	56.7	57.5	53.6
standard deviation	± 21.84	± 22.01	± 23.65
Patient Global Assessment of Joint Pain			
Assessed on a 100 mm VAS from 0 (No Pain At All) to 100 (Worst Pain Imaginable). Data available for 159, 160, 162 subjects in each treatment group respectively.			
Units: mm			
arithmetic mean	50.4	49.3	48
standard deviation	± 23.29	± 24.61	± 23.84
Medical Outcomes Short Form-36 (SF-36) Physical Component Score			
The SF-36 assesses the general quality of life by evaluating the domains of physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The			

questionnaire consists of 36 questions that are completed by the participant. The individual domain scores are aggregated to derive a physical-component summary score and a mental-component summary score which range from 0 to 100, with higher scores indicating a better level of functioning. Data are available for 159, 160, 162 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	37.2	36	37.1
standard deviation	± 9.45	± 9.94	± 9.46
SF-36 Mental Component Score			
The SF-36 assesses the general quality of life by evaluating the domains of physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The questionnaire consists of 36 questions that are completed by the participant. The individual domain scores are aggregated to derive a physical-component summary score and a mental-component summary score which range from 0 to 100, with higher scores indicating a better level of functioning. Data are available for 159, 160, 162 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	50.5	52.6	51.1
standard deviation	± 11.01	± 9.6	± 9.45
C-Reactive Protein (CRP)			
Data available for 159, 160, 161 subjects in each treatment group respectively.			
Units: mg/L			
arithmetic mean	8.2	9.9	8.7
standard deviation	± 13.71	± 18.2	± 13.01
Erythrocyte Sedimentation Rate (ESR)			
Data available for 153, 157, 158 subjects in each treatment group respectively.			
Units: mm/hr			
arithmetic mean	23.3	29.1	27
standard deviation	± 21.04	± 23.49	± 19.7

Reporting group values	Total		
Number of subjects	484		
Age Categorical			
Units: Subjects			
Adults (18-64 years)	446		
From 65-84 years	38		
85 years and over	0		
Age Continuous			
Units: years			
median			
full range (min-max)	-		
Gender Categorical			
Units: Subjects			
Female	249		
Male	235		
Race			
Units: Subjects			
White	463		
Black or African American	1		
Asian	1		
American Indian or Alaska Native	10		
Other	9		
Tender joint count			
Units: joints			
arithmetic mean			
standard deviation	-		

Swollen joint count Units: joints arithmetic mean standard deviation	- 		
Disease Activity Score 28-C-Reactive Protein (DAS28-CRP)			
The DAS28-CRP is a composite score to measure disease activity in patients with arthritis, derived from the following variables: • The number of swollen and tender joints assessed using the 28-joint count;• C-reactive protein (CRP) level • Patient's global assessment of disease activity assessed on a score from 0 to 100. The DAS28-CRP score ranges from approximately zero to ten. Higher DAS28-CRP scores indicate higher disease activity.Data available for 157, 160, 160 subjects in each treatment group respectively.			
Units: units on a scale arithmetic mean standard deviation	- 		
Health Assessment Questionnaire – Disability Index (HAQ-DI)			
The HAQ-DI asks subjects about the degree of difficulty they have in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and errands and chores). Responses in each functional area are scored from 0 indicating no difficulty to 3 indicating inability to perform a task in that area. The overall score is the average of the 8 category scores and ranges from 0 (no disability) to 3 (very severe, high dependency disability).			
Units: units on a scale arithmetic mean standard deviation	- 		
Enthesitis score			
The enthesitis count is defined as the total number of 6 sites that have enthesitis. The sites assessed were: Lateral epicondyle (left/right), Medial femoral condyle (left/right), Achilles tendon insertion (left/right).			
Units: entheses arithmetic mean standard deviation	- 		
Dactylitis score			
The dactylitis count is defined as the sum of 20 fingers/toes that exhibit dactylitis (absent 0, present 1).			
Units: digits arithmetic mean standard deviation	- 		
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)			
BASDAI is a self-administered questionnaire composed of six items using an 11-point numerical rating scale from "0 = none" to "10 = very severe" for the first five items, and "0 = 0 hours" to "10 = 2 or more hours" for the sixth item that asks about the duration of morning stiffness. The BASDAI assesses the severity of fatigue, spinal and peripheral joint pain, localized tenderness, and morning stiffness. The final BASDAI score averages the individual assessments for a final score range of 0-10. Data available for 159, 160, and 162 subjects in each group respectively.			
Units: units on a scale arithmetic mean standard deviation	- 		
Psoriasis Area and Severity Index (PASI) Score			
The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement. The total PASI score ranges from 0 to 72. The higher the total score, the more severe the disease. Data available for 160, 160, 163 subjects in each treatment group respectively.			
Units: units on a scale arithmetic mean standard deviation	- 		
Nail Psoriasis Severity Index (NAPSI)			

The NAPSI scale is an objective, numeric, and reproducible grading system for nail psoriasis that incorporates the many different features of nail psoriasis. Each quarter of the nail was scored for the presence (1) or absence (0) of 8 clinical features for a score of 0-4 for each feature. The total score for each nail ranges from 0 (absent) to 32 (worst). Data are reported for the worst nail for subjects with baseline nail involvement (58, 64 and 70 participants in each treatment group respectively).			
Units: units on a scale arithmetic mean standard deviation	- 		
Dermatology Life Quality Index (DLQI)			
The DLQI is a skin disease-specific instrument to evaluate health-related quality of life. Participants evaluate the degree that psoriasis has affected their quality of life in the last week, including symptoms and feelings, daily and leisure activities, work or school activities, personal relationships and treatment related feelings. Participants answer 10 questions on a scale from 0 (not at all) to 3 (very much); the total score ranges from 0 (best possible score) to 30 (worst possible score). Data are available for 159, 160, 162 participants in each treatment group respectively.			
Units: units on a scale arithmetic mean standard deviation	- 		
Psoriasis Severity Index (PSI) average Weekly Total Score			
The Psoriasis Symptom Inventory consists of eight psoriasis-specific items. Participants rated the severity of their symptoms in the last 24 hours on a scale from 'not at all' (0) to 'very severe' (4) in an electronic diary once a day. Total scores range from 0 to 32 with higher scores indicating worse symptoms. The daily assessment of the Psoriasis Symptom Inventory was analyzed as a weekly average. Data are available for 152, 144, and 148 participants in each treatment group respectively.			
Units: units on a scale arithmetic mean standard deviation	- 		
Clinical Disease Activity Index (CDAI)			
The Clinical Disease Activity Index (CDAI) is a composite index that is calculated from: • 28 tender joint count, • 28 swollen joint count, • Patient's Global Assessment of Disease Activity measured on a 100 mm visual analog scale (VAS), where 0 mm = lowest disease activity and 100 mm = highest; • Physician's Global Assessment of Disease Activity - measured on a 100 mm VAS, where 0 mm = lowest disease activity and 100 mm = highest. The CDAI score ranges from 0-76 where lower scores indicate less disease activity. Data available for 157, 156, 162 subjects in each treatment group respectively.			
Units: units on a scale arithmetic mean standard deviation	- 		
Physician Global Assessment of Disease Activity			
Assessed on a 100 mm visual analog scale (VAS) from 0 (Very Well) on the left to 100 (Very Poorly) on the right end of the line. Data available for 157, 156, 162 subjects in each treatment group respectively			
Units: mm arithmetic mean standard deviation	- 		
Patient Global Assessment of Disease			
Assessed on a 100 mm VAS from 0 (Very Well) on the left end of the line to 10 (Very Poorly) on the right. Data available for 159, 160, 162 subjects in each treatment group respectively.			
Units: mm arithmetic mean standard deviation	- 		
Patient Global Assessment of Joint Pain			
Assessed on a 100 mm VAS from 0 (No Pain At All) to 100 (Worst Pain Imaginable). Data available for 159, 160, 162 subjects in each treatment group respectively.			
Units: mm			

arithmetic mean standard deviation	- -		
Medical Outcomes Short Form-36 (SF-36) Physical Component Score			
The SF-36 assesses the general quality of life by evaluating the domains of physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The questionnaire consists of 36 questions that are completed by the participant. The individual domain scores are aggregated to derive a physical-component summary score and a mental-component summary score which range from 0 to 100, with higher scores indicating a better level of functioning. Data are available for 159, 160, 162 participants in each treatment group respectively.			
Units: units on a scale arithmetic mean standard deviation	 -		
SF-36 Mental Component Score			
The SF-36 assesses the general quality of life by evaluating the domains of physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The questionnaire consists of 36 questions that are completed by the participant. The individual domain scores are aggregated to derive a physical-component summary score and a mental-component summary score which range from 0 to 100, with higher scores indicating a better level of functioning. Data are available for 159, 160, 162 participants in each treatment group respectively.			
Units: units on a scale arithmetic mean standard deviation	 -		
C-Reactive Protein (CRP)			
Data available for 159, 160, 161 subjects in each treatment group respectively.			
Units: mg/L arithmetic mean standard deviation	 -		
Erythrocyte Sedimentation Rate (ESR)			
Data available for 153, 157, 158 subjects in each treatment group respectively.			
Units: mm/hr arithmetic mean standard deviation	 -		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo subcutaneous injection at baseline, week 1, week 2 and then every 2 weeks (Q2W) thereafter up to week 22. From week 14 participants with an inadequate response began treatment with 210 mg brodalumab Q2W. From Week 24 all participants received brodalumab 210 mg Q2W.	
Reporting group title	Brodalumab 140 mg
Reporting group description:	
Participants received 140 mg brodalumab by subcutaneous injection at baseline, week 1, week 2 and then Q2W thereafter for up to 3 years.	
Reporting group title	Brodalumab 210 mg
Reporting group description:	
Participants received 210 mg brodalumab by subcutaneous injection at baseline, week 1, week 2 and then Q2W thereafter for up to 3 years.	

Primary: Percentage of Participants with an American College of Rheumatology (ACR) 20 Response at Week 16

End point title	Percentage of Participants with an American College of Rheumatology (ACR) 20 Response at Week 16
End point description:	
A participant was a responder if the following 3 criteria for improvement from Baseline were met: • ≥ 20% improvement in tender joint count; • ≥ 20% improvement in swollen joint count; and • ≥ 20% improvement in at least 3 of the 5 following parameters: ◦ Patient's assessment of joint pain (measured on a 100 mm VAS); ◦ Patient's Global Assessment (measured on a 100 mm VAS); ◦ Physician Global Assessment of disease activity (measured on a 100 mm VAS); ◦ Health Assessment Questionnaire - Disability Index (HAQ-DI) scale from 0 to 3, where zero represents no disability and three very severe, high-dependency disability; ◦ C-reactive protein level or erythrocyte sedimentation rate. This endpoint was analyzed in the Primary Analysis Set which consists of all randomized subjects who had the opportunity to complete the week 16 visit prior to termination of the study; Non-responder imputation was used for missing data in the primary analysis.	
End point type	Primary
End point timeframe:	
Baseline and Week 16	

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: percentage of participants				
number (not applicable)	24.7	48.9	41.8	

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Brodalumab 210 mg v Placebo
Number of subjects included in analysis	292
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0019 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference from placebo
Point estimate	17.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.5
upper limit	27.7

Notes:

[1] - To preserve the family-wise 2-sided type 1 error rate at 0.05 for the multiple comparisons of the 2 brodalumab doses with placebo, a sequential testing procedure was used to determine statistical significance for the primary and key secondary endpoints.
Nominal P-values are reported.
[2] - A stratified CMH test adjusting for baseline weight (≤ 100 kg, >100 kg), prior biologic use, and geographic region (North and Latin America, Central/Eastern Europe, Western Europe/Australia).

Statistical analysis title	Primary Analysis
Comparison groups	Placebo v Brodalumab 140 mg
Number of subjects included in analysis	287
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference from placebo
Point estimate	24.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.5
upper limit	35.1

Notes:

[3] - To preserve the family-wise 2-sided type 1 error rate at 0.05 for the multiple comparisons of the 2 brodalumab doses with placebo, a sequential testing procedure was used to determine statistical significance for the primary and key secondary endpoints.
Nominal P-values are reported.
[4] - A stratified CMH test adjusting for baseline weight (≤100 kg, >100 kg), prior biologic use, and geographic region (North and Latin America, Central/Eastern Europe, Western Europe/Australia).

Secondary: Percentage of Participants with a 75% or Greater Improvement from Baseline in Psoriasis Area and Severity Index Score (PASI 75) at Week 16

End point title	Percentage of Participants with a 75% or Greater Improvement from Baseline in Psoriasis Area and Severity Index Score (PASI 75) at Week 16

End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0 to 72, with higher scores indicating greater severity and/or more extensive psoriasis.
A PASI 75 response is defined as 75% or higher improvement from baseline in PASI score.

This analysis was performed on the psoriasis primary efficacy analysis set which consists of those subjects with baseline psoriasis body surface area (BSA) ≥ 3% who were randomized on or before 17 March 2015. Non-responder imputation was used for missing data.

End point type	Secondary

End point timeframe:

Baseline and week 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	108	92	106	
Units: percentage of participants				
number (not applicable)	10.2	50	65.1	

Statistical analyses

Statistical analysis title	Difference in Response Rate
Comparison groups	Placebo v Brodalumab 210 mg
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.0001 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference from placebo
Point estimate	54.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	44.2
upper limit	65.6

Notes:

[5] - To preserve the family-wise 2-sided type 1 error rate at 0.05 for the multiple comparisons of the 2 brodalumab doses with placebo, a sequential testing procedure was used to determine statistical significance for the primary and key secondary endpoints.
Nominal P-values are reported.

[6] - Stratified CMH test adjusting for baseline weight (≤ 100 kg, >100 kg), prior biologic use yes/no), and geographic region (North and Latin America, Central/Eastern Europe, Western Europe/Australia).

Statistical analysis title	Difference in Response rate
Comparison groups	Placebo v Brodalumab 140 mg
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.0001 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference from placebo
Point estimate	39.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	28.1
upper limit	51.5

Notes:

[7] - To preserve the family-wise 2-sided type 1 error rate at 0.05 for the multiple comparisons of the 2 brodalumab doses with placebo, a sequential testing procedure was used to determine statistical significance for the primary and key secondary endpoints.
Nominal P-values are reported.
[8] - Stratified CMH test adjusting for baseline weight (≤ 100 kg, >100 kg), prior biologic use yes/no), and geographic region (North and Latin America, Central/Eastern Europe, Western Europe/Australia).

Secondary: Change from Baseline in HAQ-DI at Week 16

End point title	Change from Baseline in HAQ-DI at Week 16

End point description:

The Disability Index of the Health Assessment Questionnaire (HAQ-DI) was utilized to assess the subject's physical function or disability according to the subject. The HAQ-DI asks about the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and errands and chores). Responses in each functional area are scored from 0 indicating no difficulty to 3 indicating inability to perform a task in that area. The overall score is the average of each of the 8 category scores and ranges from 0 (no disability) to 3 (very severe, high-dependency disability). The primary analysis set was used for this analysis, subjects with baseline and post-baseline results are included.

End point type	Secondary

End point timeframe:

Baseline and week 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	132	127	
Units: units on a scale				
least squares mean (standard error)	-0.167 (± 0.0426)	-0.308 (± 0.0433)	-0.336 (± 0.0431)	

Statistical analyses

Statistical analysis title	Comparison with Placebo
Comparison groups	Placebo v Brodalumab 210 mg
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.0023 [10]
Method	Mixed effects model repeated measures
Parameter estimate	LS mean difference
Point estimate	-0.169

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.278
upper limit	-0.061

Notes:

[9] - To preserve the family-wise 2-sided type 1 error rate at 0.05 for the multiple comparisons of the 2 brodalumab doses with placebo, a sequential testing procedure was used to determine statistical significance for the primary and key secondary endpoints.
Nominal P-values are reported.
[10] - The model includes visit, treatment, treatment by visit and baseline by visit interaction, baseline and baseline weight (≤ 100 kg, >100 kg), prior biologic use, and geographic region.

Statistical analysis title	Comparison with Placebo
Comparison groups	Placebo v Brodalumab 140 mg
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.0112 [12]
Method	Mixed effects model repeated measures
Parameter estimate	LS mean difference
Point estimate	-0.141
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.249
upper limit	-0.032

Notes:

[11] - To preserve the family-wise 2-sided type 1 error rate at 0.05 for the multiple comparisons of the 2 brodalumab doses with placebo, a sequential testing procedure was used to determine statistical significance for the primary and key secondary endpoints.
Nominal P-values are reported.
[12] - The model includes visit, treatment, treatment by visit and baseline by visit interaction, baseline and baseline weight (≤ 100 kg, >100 kg), prior biologic use, and geographic region.

Secondary: Percentage of Participants with a Psoriasis Symptom Inventory (PSI) response at Week 16

End point title	Percentage of Participants with a Psoriasis Symptom Inventory (PSI) response at Week 16

End point description:

The Psoriasis Symptom Inventory consists of eight psoriasis-specific items. Participants rated the severity of their symptoms in the last 24 hours on a scale from 'not at all' (0) to 'very severe' (4) in an electronic diary once a day. Total scores range from 0 to 32 with higher scores indicating worse symptoms. The daily assessment of the Psoriasis Symptom Inventory was analyzed as a weekly average. A PSI response is defined a total score ≤ 8 with no item scores > 1.
Analysis was performed in the psoriasis efficacy primary analysis set; non-responder imputation was used.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	104	82	99	
Units: percentage of participants				
number (not applicable)	10.6	36.6	53.5	

Statistical analyses

Statistical analysis title	Difference in Response Rate
Comparison groups	Placebo v Brodalumab 210 mg
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	< 0.0001 [14]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference from placebo
Point estimate	43
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.5
upper limit	54.4

Notes:

[13] - To preserve the family-wise 2-sided type 1 error rate at 0.05 for the multiple comparisons of the 2 brodalumab doses with placebo, a sequential testing procedure was used to determine statistical significance for the primary and key secondary endpoints.
Nominal P-values are reported.
[14] - Stratified CMH test adjusting for baseline weight (≤ 100 kg, >100 kg), prior biologic use yes/no), and geographic region (North and Latin America, Central/Eastern Europe, Western Europe/Australia).

Statistical analysis title	Difference in Response Rate
Comparison groups	Placebo v Brodalumab 140 mg
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.0003 [16]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference from placebo
Point estimate	26
Confidence interval	
level	95 %
sides	2-sided
lower limit	14
upper limit	38

Notes:

[15] - To preserve the family-wise 2-sided type 1 error rate at 0.05 for the multiple comparisons of the 2 brodalumab doses with placebo, a sequential testing procedure was used to determine statistical significance for the primary and key secondary endpoints.
Nominal P-values are reported.
[16] - Stratified CMH test adjusting for baseline weight (≤ 100 kg, >100 kg), prior biologic use yes/no), and geographic region (North and Latin America, Central/Eastern Europe, Western Europe/Australia).

Secondary: Percentage of Participants with an ACR 20 Response by Visit

End point title	Percentage of Participants with an ACR 20 Response by Visit

End point description:

A participant was a responder if the following 3 criteria for improvement from Baseline were met:
- ≥ 20% improvement in tender joint count;
- ≥ 20% improvement in swollen joint count; and
- ≥ 20% improvement in at least 3 of the 5 following parameters:
  - Patient's assessment of joint pain (measured on a 100 mm VAS);
  - Patient's Global Assessment (measured on a 100 mm VAS);
  - Physician Global Assessment of disease activity (measured on a 100 mm VAS);
  - Health Assessment Questionnaire - Disability Index (HAQ-DI) scale from 0 to 3, where zero represents no disability and three very severe, high-dependency disability;
  - C-reactive protein level or erythrocyte sedimentation rate.

This endpoint was analyzed in the Primary Analysis Set; Non-responder imputation was used for missing data.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8 and 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: percentage of participants				
number (not applicable)				
Week 2	11.6	17.7	21.9	
Week 4	19.2	27	38.4	
Week 8	28.1	36.2	45.9	
Week 12	27.4	41.8	47.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HAQ-DI by Visit

End point title	Change from Baseline in HAQ-DI by Visit

End point description:

The Disability Index of the Health Assessment Questionnaire (HAQ-DI) was utilized to assess the subject's physical function or disability according to the subject. The HAQ-DI asks about the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and errands and chores). Responses in each functional area are scored from 0 indicating no difficulty to 3 indicating inability to perform a task in that area. The overall score is the average of each of the 8 category scores and ranges from 0 (no disability) to 3 (very severe, high-dependency disability). The primary analysis set was used for this analysis; subjects with baseline and post-baseline results are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8 and 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: units on a scale				
least squares mean (standard error)				
Week 2 (N = 139, 135, 139)	-0.129 (± 0.0337)	-0.147 (± 0.0345)	-0.205 (± 0.0338)	
Week 4 (N = 137, 135, 139)	-0.178 (± 0.0377)	-0.244 (± 0.0385)	-0.291 (± 0.0378)	
Week 8 (N = 135, 132, 137)	-0.181 (± 0.0415)	-0.285 (± 0.0423)	-0.313 (± 0.0416)	
Week 12 (N = 131, 136, 136)	-0.208 (± 0.0435)	-0.285 (± 0.0439)	-0.346 (± 0.0435)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 75 at Each Visit

End point title	Percentage of Participants with a PASI 75 at Each Visit

End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0 to 72, with higher scores indicating greater severity and/or more extensive psoriasis.
A PASI 75 response is defined as 75% or higher improvement from baseline in PASI score.
This analysis was performed on the psoriasis primary efficacy analysis set which consists of those subjects with baseline psoriasis body surface area (BSA) ≥ 3% who were randomized on or before 17 March 2015. Non-responder imputation was used for missing data.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8 and 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	108	92	106	
Units: percentage of participants				
number (not applicable)				
Week 2	1.9	6.5	17.9	
Week 4	5.6	27.2	40.6	
Week 8	7.4	41.3	51.9	
Week 12	11.1	47.8	61.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PSI Response at Each Visit

End point title	Percentage of Participants with a PSI Response at Each Visit

End point description:

The Psoriasis Symptom Inventory consists of eight psoriasis-specific items. Participants rated the severity of their symptoms in the last 24 hours on a scale from 'not at all' (0) to 'very severe' (4) in an electronic diary once a day. Total scores range from 0 to 32 with higher scores indicating worse symptoms. The daily assessment of the Psoriasis Symptom Inventory was analyzed as a weekly average. A PSI response is defined a total score ≤ 8 with no item scores > 1.
Analysis was performed in the psoriasis efficacy primary analysis set; non-responder imputation was used.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 6, 8, 10, and 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	104	82	99	
Units: percentage of participants				
number (not applicable)				
Week 2	7.7	17.1	21.2	
Week 4	10.6	29.3	47.5	
Week 6	12.5	39	51.5	
Week 8	13.5	35.4	48.5	
Week 10	13.5	36.6	48.5	
Week 12	13.5	35.4	48.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an ACR 50 Response by Visit

End point title	Percentage of Participants with an ACR 50 Response by Visit

End point description:

A participant was a responder if the following 3 criteria for improvement from Baseline were met:
- ≥ 50% improvement in tender joint count;
- ≥ 50% improvement in swollen joint count; and
- ≥ 50% improvement in at least 3 of the 5 following parameters:
  - Patient's assessment of joint pain (measured on a 100 mm VAS);

◦ Patient's Global Assessment (measured on a 100 mm VAS);
◦ Physician Global Assessment of disease activity (measured on a 100 mm VAS);
◦ Health Assessment Questionnaire - Disability Index (HAQ-DI) scale from 0 to 3, where zero represents no disability and three very severe, high-dependency disability;
◦ C-reactive protein level or erythrocyte sedimentation rate.

This endpoint was analyzed in the Primary Analysis Set; Non-responder imputation was used for missing data.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12, and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: percentage of participants				
number (not applicable)				
Week 2	2.7	1.4	2.7	
Week 4	6.2	11.3	15.8	
Week 8	9.6	17	17.8	
Week 12	8.9	18.4	24	
Week 16	8.9	27.7	22.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an ACR 70 Response by Visit

End point title	Percentage of Participants with an ACR 70 Response by Visit

End point description:

A participant was a responder if the following 3 criteria for improvement from Baseline were met:
• ≥ 70% improvement in tender joint count;
• ≥ 70% improvement in swollen joint count; and
• ≥ 70% improvement in at least 3 of the 5 following parameters:
◦ Patient's assessment of joint pain (measured on a 100 mm VAS);
◦ Patient's Global Assessment (measured on a 100 mm VAS);
◦ Physician Global Assessment of disease activity (measured on a 100 mm VAS);
◦ Health Assessment Questionnaire - Disability Index (HAQ-DI) scale from 0 to 3, where zero represents no disability and three very severe, high-dependency disability;
◦ C-reactive protein level or erythrocyte sedimentation rate.

This endpoint was analyzed in the Primary Analysis Set; Non-responder imputation was used for missing data.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: percentage of participants				
number (not applicable)				
Week 2	0.7	0	1.4	
Week 4	2.1	2.8	4.8	
Week 8	4.8	5	8.9	
Week 12	2.1	9.2	10.3	
Week 16	3.4	12.8	10.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Tender Joint Count

End point title	Change from Baseline in Tender Joint Count

End point description:

A total of 68 joints were scored for the presence or absence of tenderness by an experienced, independent and blinded joint evaluator.
Analysis was performed in the primary analysis set; subjects with baseline and post-baseline results at each time point are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: joints				
least squares mean (standard error)				
Week 2 (N = 144, 137, 138)	-2.289 (± 0.7523)	-2.627 (± 0.7704)	-3.518 (± 0.7646)	
Week 4 (N = 140, 138, 139)	-4.45 (± 0.899)	-3.679 (± 0.9139)	-6.472 (± 0.908)	
Week 8 (N = 138, 136, 137)	-5.078 (± 0.9601)	-6.037 (± 0.9769)	-7.042 (± 0.9697)	
Week 12 (N = 133, 137, 135)	-4.803 (± 1.0081)	-6.071 (± 1.0182)	-8.443 (± 1.0147)	
Week 16 (N = 135, 131, 130)	-3.57 (± 1.0656)	-7.596 (± 1.0841)	-7.987 (± 1.0803)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Swollen Joint Count

End point title	Change from Baseline in Swollen Joint Count

End point description:

A total of 66 joints were scored for the presence or absence of swelling by an experienced, independent and blindedjoint evaluator. Analysis was performed in the primary analysis set; subjects with baseline and post-baseline results at each time point are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: joints				
least squares mean (standard error)				
Week 2 (N = 144, 137, 138)	-2.13 (± 0.5097)	-2.711 (± 0.5231)	-2.438 (± 0.5186)	
Week 4 (N = 140, 138, 139)	-2.931 (± 0.5381)	-3.49 (± 0.5483)	-4.495 (± 0.543)	
Week 8 (N = 138, 136, 137)	-3.643 (± 0.5874)	-5.316 (± 0.5985)	-5.301 (± 0.5926)	
Week 12 (N = 133, 137, 135)	-3.175 (± 0.618)	-5.754 (± 0.6256)	-5.946 (± 0.6216)	
Week 16 (N = 135, 130, 131)	-2.454 (± 0.6601)	-6.569 (± 0.6726)	-6.157 (± 0.6687)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient Global Assessment of Joint Pain

End point title	Change from Baseline in Patient Global Assessment of Joint Pain

End point description:

The severity of the subject's joint pain was assessed on a 100 mm visual analog scale. The subject drew a vertical line through a horizontal line to indicate how much pain they were experiencing "today" on a scale from 0 (No Pain At All) on the left and 100 (Worst Pain Imaginable) on the right end of the line. Analysis was performed in the primary analysis set; subjects with baseline and post-baseline results at each time point are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: mm				
least squares mean (standard error)				
Week 2 (N = 139, 135, 139)	-0.705 (± 1.8273)	-3.111 (± 1.8652)	-5.204 (± 1.8274)	
Week 4 (N = 137, 135, 139)	-1.28 (± 1.9124)	-3.654 (± 1.9506)	-9.303 (± 1.9182)	
Week 8 (N = 135, 132, 137)	-0.698 (± 2.0958)	-7.17 (± 2.1375)	-8.353 (± 2.1011)	
Week 12 (N = 131, 136, 136)	0.03 (± 2.1127)	-6.317 (± 2.1315)	-11.07 (± 2.1122)	
Week 16 (N = 134, 132, 127)	0.273 (± 2.1495)	-9.816 (± 2.1865)	-11.13 (± 2.1804)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient Global Assessment of Arthritis Activity

End point title	Change from Baseline in Patient Global Assessment of Arthritis Activity

End point description:

The subject's global assessment of his or her arthritis disease activity was assessed by completion of a 100 mm visual analog scale. The subject drew a vertical line through a horizontal line to indicate how they are doing based on all the ways their arthritis affects them at the time of completion, with a scale from 0 (Very Well) on the left to 100 (Very Poorly) on the right end of the line.
Analysis was performed in the primary analysis set; subjects with baseline and post-baseline results at each time point are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: mm				
least squares mean (standard error)				
Week 2 (N = 139, 135, 139)	-1.473 (± 1.779)	-6.673 (± 1.8189)	-6.752 (± 1.7792)	
Week 4 (N = 137, 135, 139)	-2.789 (± 1.9229)	-6.435 (± 1.9622)	-11.39 (± 1.9285)	
Week 8 (N = 135, 132, 137)	-2.731 (± 2.0658)	-11.22 (± 2.1093)	-10.96 (± 2.0729)	
Week 12 (N = 131, 136, 136)	-2.064 (± 2.0462)	-10.38 (± 2.0656)	-13.3 (± 2.0457)	
Week 16 (N = 134, 132, 127)	-1.472 (± 2.1119)	-12.33 (± 2.1507)	-14.05 (± 2.1458)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Physician Global Assessment of Arthritis Activity

End point title	Change from Baseline in Physician Global Assessment of Arthritis Activity

End point description:

The physician's global assessment of subjects' arthritis disease activity was assessed on a 100 mm visual analog scale from 0 (Very Well) to 100 (Very Poorly).
Analysis was performed in the primary analysis set; subjects with baseline and post-baseline results at each time point are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: mm				
least squares mean (standard error)				
Week 2 (N = 138, 131, 137)	-7.317 (± 1.7275)	-13.38 (± 1.7918)	-15.6 (± 1.7375)	
Week 4 (N = 134, 131, 140)	-10.4 (± 1.8609)	-14.35 (± 1.9169)	-21.69 (± 1.854)	
Week 8 (N = 133, 127, 137)	-11.41 (± 1.9231)	-21.22 (± 1.9934)	-24.08 (± 1.9276)	
Week 12 (N = 128, 133, 136)	-9.653 (± 2.0172)	-22.33 (± 2.0505)	-26.69 (± 2.0064)	
Week 16 (N = 131, 128, 127)	-11.45 (± 2.1523)	-23.88 (± 2.2099)	-26.88 (± 2.1775)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Erythrocyte Sedimentation Rate

End point title	Change from Baseline in Erythrocyte Sedimentation Rate

End point description:

Analysis was performed in the primary analysis set; subjects with baseline and post-baseline results at each time point are included.

End point type	Secondary
End point timeframe: Baseline and weeks 2, 4, 8, 12 and 16	

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: mm/hr				
arithmetic mean (standard deviation)				
Week 2 (N = 134, 132, 132)	-1.9 (± 15.07)	-3 (± 10.5)	-1.3 (± 13.51)	
Week 4 (N = 132, 134, 135)	-1.3 (± 17.73)	-1.6 (± 14.7)	-3.7 (± 15.18)	
Week 8 (N = 131, 131, 134)	0.8 (± 18.55)	-3.9 (± 16.9)	-4.9 (± 13.87)	
Week 12 (N = 127, 134, 131)	-1 (± 17.79)	-4 (± 15.64)	-5.7 (± 17.72)	
Week 16 (N = 128, 128, 124)	-0.6 (± 18.08)	-3.9 (± 15.7)	-6.8 (± 17.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in C-Reactive Protein (CRP)

End point title	Change from Baseline in C-Reactive Protein (CRP)
End point description: Analysis was performed in the primary analysis set; subjects with baseline and post-baseline results at each time point are included.	
End point type	Secondary
End point timeframe: Baseline and weeks 2, 4, 8, 12 and 16	

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: mg/L				
arithmetic mean (standard deviation)				
Week 2 (N = 140, 136, 138)	-0.38 (± 7.799)	-1.33 (± 20.432)	-2.37 (± 10.081)	
Week 4 (N = 139, 136, 138)	0.26 (± 11.678)	-0.84 (± 13.966)	-2.26 (± 11.96)	
Week 8 (N = 136, 135, 137)	0.77 (± 9.939)	-2.51 (± 11.142)	-2.25 (± 13.005)	
Week 12 (N = 132, 137, 134)	0.42 (± 10.148)	-2.21 (± 11.308)	-1.92 (± 11.96)	
Week 16 (N = 134, 131, 129)	0.14 (± 10.812)	-1.4 (± 12.554)	-2.83 (± 11.969)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Disease Activity Score 28-C-Reactive Protein (DAS28-CRP)

End point title	Change from Baseline in Disease Activity Score 28-C-Reactive Protein (DAS28-CRP)

End point description:

The DAS28-CRP is a composite score to measure disease activity in patients with arthritis, derived from the following variables:
• The number of swollen and tender joints assessed using the 28-joint count;
• C-reactive protein (CRP) level;
• Patient's global assessment of disease activity assessed on a VAS from 0 to 100.
The DAS28-CRP score ranges from approximately zero to ten. Higher DAS28-CRP scores indicate higher disease activity.
Analysis was performed in the primary analysis set; subjects with baseline and post-baseline results at each time point are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: units on a scale				
least squares mean (standard error)				
Week 2 (N = 136, 132, 132)	-0.213 (± 0.0739)	-0.511 (± 0.076)	-0.541 (± 0.0751)	
Week 4 (N = 134, 133, 132)	-0.408 (± 0.0858)	-0.651 (± 0.0876)	-0.94 (± 0.087)	
Week 8 (N = 133, 132, 134)	-0.497 (± 0.0964)	-1.013 (± 0.0983)	-1.018 (± 0.0973)	
Week 12 (N = 130, 136, 132)	-0.506 (± 0.1006)	-1.013 (± 0.1015)	-1.182 (± 0.1013)	
Week 16 (N = 133, 131, 126)	-0.332 (± 0.1061)	-1.179 (± 0.108)	-1.147 (± 0.1081)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

End point title	Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

End point description:

BASDAI is a self-administered questionnaire composed of six items using an 11-point numerical rating scale from "0 = none" to "10 = very severe" for the first five items, and "0 = 0 hours" to "10 = 2 or more hours" for the sixth item that asks about the duration of morning stiffness. The BASDAI assesses the severity of fatigue, spinal and peripheral joint pain, localized tenderness, and morning stiffness. The final BASDAI score averages the individual assessments for a final score range of 0-10.
Analyzed in the primary analysis set; subjects with baseline and post-baseline results at each time point are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: units on a scale				
least squares mean (standard error)				
Week 12 (N = 130, 135, 136)	-0.318 (± 0.1747)	-0.952 (± 0.1765)	-1.295 (± 0.1757)	
Week 16 (N = 134, 132, 127)	-0.34 (± 0.1694)	-1.113 (± 0.1738)	-1.337 (± 0.1739)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Dactylitis Score

End point title	Change from Baseline in Dactylitis Score

End point description:

Dactylitis was assessed for presence or absence on 20 digits (fingers and toes) by an independent assessor. The dactylitis count is defined as the sum of 20 fingers/toes that exhibit dactylitis (absent 0, present 1).
Analysis was performed in the primary analysis set; only subjects with baseline dactylitis count > 0 and post-baseline results are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: digits				
least squares mean (standard error)				

Week 4 (N = 70, 52, 69)	-1.019 (± 0.3962)	-1.327 (± 0.437)	-2.018 (± 0.3844)	
Week 12 (N = 65, 50, 66)	-1.057 (± 0.4232)	-2.278 (± 0.4654)	-2.31 (± 0.4105)	
Week 16 (N = 65, 48, 63)	-1.156 (± 0.4303)	-3.158 (± 0.4783)	-2.857 (± 0.4219)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Enthesitis Count

End point title	Change from Baseline in Enthesitis Count

End point description:

Enthesitis was assessed for presence or absence on 6 entheses by an independent assessor. The sites assessed were: Lateral epicondyle (left/right), Medial femoral condyle (left/right), Achilles tendon insertion (left/right). The enthesitis count is defined as the total number of 6 sites that have enthesitis. Analysis was performed in the primary analysis set; subjects with baseline enthesitis > 0 and post-baseline results are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 4, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: entheses				
least squares mean (standard error)				
Week 4 (N = 88, 77, 87)	-0.875 (± 0.1718)	-0.831 (± 0.1752)	-0.845 (± 0.1716)	
Week 12 (N = 82, 76, 84)	-0.713 (± 0.1911)	-1.245 (± 0.1944)	-1.087 (± 0.1888)	
Week 16 (N = 81, 72, 81)	-0.76 (± 0.1999)	-1.283 (± 0.2065)	-1.106 (± 0.1981)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 90 Response

End point title	Percentage of Participants with a PASI 90 Response

End point description:

A PASI 90 response is a 90% or greater improvement (reduction) from baseline in PASI score. The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0 to 72, with higher scores indicating greater severity and/or more extensive psoriasis. This analysis was performed on the psoriasis primary efficacy analysis set; Non-responder imputation was used for missing data.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12, and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	108	92	106	
Units: percentage of participants				
number (not applicable)				
Week 2	0	2.2	6.6	
Week 4	2.8	13	23.6	
Week 8	2.8	25	35.8	
Week 12	4.6	33.7	42.5	
Week 16	5.6	34.8	46.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 100 Response

End point title	Percentage of Participants with a PASI 100 Response

End point description:

A PASI 100 response is a 100% improvement (reduction) from baseline in PASI score. The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0 to 72, with higher scores indicating greater severity and/or more extensive psoriasis. This analysis was performed on the psoriasis primary efficacy analysis set; Non-responder imputation was used for missing data.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	108	92	106	
Units: percentage of participants				
number (not applicable)				
Week 2	0	0	2.8	
Week 4	0	4.3	14.2	
Week 8	2.8	13	27.4	
Week 12	4.6	16.3	32.1	
Week 16	3.7	19.6	34	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in PASI Score

End point title	Percent Change from Baseline in PASI Score

End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0 to 72, with higher scores indicating greater severity and/or more extensive psoriasis. This analysis was performed on the psoriasis primary efficacy analysis set; subjects with baseline and post-baseline results are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	108	92	106	
Units: percent change				
arithmetic mean (standard deviation)				
Week 2 (N = 107, 90, 101)	-6.36 (± 29.106)	-29.68 (± 50.269)	-38.67 (± 37.624)	
Week 4 (N = 104, 90, 104)	-12.33 (± 42.758)	-47.08 (± 44.93)	-60.33 (± 34.341)	
Week 8 (N = 104, 88, 101)	-8.21 (± 66.319)	-48.58 (± 68.894)	-64.64 (± 48.277)	
Week 12 (N = 98, 89, 101)	-11.8 (± 69.071)	-49.64 (± 87.796)	-68.32 (± 50.633)	
Week 16 (N=100, 84, 97)	-8.18 (± 60.382)	-46.08 (± 88.738)	-69.86 (± 55.772)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Body Surface Area (BSA) Involved With Psoriasis

End point title	Percentage of Body Surface Area (BSA) Involved With Psoriasis

End point description:

A measurement of psoriasis involvement, given as the assessor’s assessment of the proportion of the subject’s total body surface area involved with psoriasis.
This analysis was performed on the psoriasis primary efficacy analysis set; subjects with baseline and

post-baseline results are included.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	108	92	106	
Units: percent				
least squares mean (standard error)				
Week 2 (N = 107, 90, 101)	17.702 (± 0.817)	15.242 (± 0.884)	12.667 (± 0.8486)	
Week 4 (N = 104, 90, 104)	16.29 (± 1.0103)	10.834 (± 1.0915)	8.477 (± 1.0328)	
Week 8 (N = 104, 88, 101)	16.843 (± 1.053)	9.546 (± 1.1421)	6.643 (± 1.0773)	
Week 12 (N = 98, 88, 101)	15.862 (± 1.0848)	8.224 (± 1.172)	5.271 (± 1.105)	
Week 16 (N = 99, 84, 97)	16.405 (± 1.1032)	7.841 (± 1.1956)	4.196 (± 1.126)	

Statistical analyses

No statistical analyses for this end point

Secondary: Nail Psoriasis Severity Index (NAPSI) Score

End point title	Nail Psoriasis Severity Index (NAPSI) Score

End point description:

The NAPSI scale is an objective, numeric, and reproducible grading system for nail psoriasis that incorporates the many different features of nail psoriasis. Each quarter of the nail was scored for the presence (1) or absence (0) of 8 clinical features for a score of 0-4 for each feature. The total score for each nail ranges from 0 (absent) to 32 (worst). Results are reported for the primary analysis set for the worst nail for subjects with baseline NAPSI score ≥ 6 and post-baseline results.

End point type	Secondary

End point timeframe:

Weeks 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: units on a scale				
least squares mean (standard error)				
Week 12 (N = 46, 58, 60)	8.228 (± 0.6333)	5.879 (± 0.6016)	5.394 (± 0.6167)	

Week 16 (N = 47, 55, 58)	8.151 (± 0.6554)	5.098 (± 0.6312)	4.663 (± 0.6413)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Disease Activity Index (CDAI)

End point title	Change from Baseline in Clinical Disease Activity Index (CDAI)

End point description:

The Clinical Disease Activity Index (CDAI) is a composite index that is calculated as the sum of the:
- 28 tender joint count (TJC),
- 28 swollen joint count (SJC),
- Patient's Global Assessment of Disease Activity measured on a 100 mm visual analog scale (VAS), where 0 mm = lowest disease activity and 100 mm = highest;
- Physician's Global Assessment of Disease Activity - measured on a 100 mm VAS, where 0 mm = lowest disease activity and 100 mm = highest.

The CDAI score ranges from 0-76 where lower scores indicate less disease activity.
This analysis was performed in the primary analysis set; subjects with baseline and post-baseline results at each time point are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: units on a scale				
least squares mean (standard error)				
Week 2 (N = 136, 130, 134)	-2.93 (± 0.7645)	-5.555 (± 0.7928)	-6.085 (± 0.7728)	
Week 4 (N = 133, 131, 136)	-5.571 (± 0.8705)	-6.681 (± 0.8971)	-10.02 (± 0.8728)	
Week 8 (N = 133, 127, 135)	-6.135 (± 0.977)	-10.4 (± 1.0014)	-10.31 (± 0.9806)	
Week 12 (N = 128, 133, 135)	-5.694 (± 0.9849)	-10.6 (± 1.0046)	-12.27 (± 0.9826)	
Week 16 (N = 132, 128, 127)	-4.443 (± 1.0628)	-12.11 (± 1.0939)	-11.9 (± 1.0764)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Psoriatic Arthritis Response Criteria (PsARC) Response

End point title	Percentage of Participants with a Psoriatic Arthritis Response Criteria (PsARC) Response

End point description:

A PsARC response is defined as improvement in at least 2 of the following 4 measures, at least one of which must be tender joint count or swollen joint count, and no worsening in any of the 4 measures:
- Tender joint count,
- Swollen joint count,
- Patient global assessment of disease activity, measured on a 100 mm VAS, where 0=lowest disease activity and 100=highest;
- Physician global assessment of disease activity, measured on a 100 mm VAS, where 0=lowest disease activity and 100=highest.

Improvement or worsening is defined as decrease or increase, respectively, from baseline by ≥ 30%.
Analysis was performed in the psoriasis efficacy primary analysis set; non-responder imputation was used.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: percentage of participants				
number (not applicable)				
Week 2	23.3	36.2	36.3	
Week 4	32.2	44.7	58.9	
Week 8	39	56.7	55.5	
Week 12	41.1	57.4	63	
Week 16	34.9	59.6	59.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Psoriatic Arthritis Disease Activity Score (PASDAS)

End point title	Psoriatic Arthritis Disease Activity Score (PASDAS)

End point description:

The Psoriatic Arthritis Disease Activity Score consists of the following domains: tender joint count, swollen joint count, physician and patient global assessment of arthritis and skin, dactylitis, enthesitis, CRP and Medical Outcomes Survey Short form-36 (SF-36) physical component summary. The index score is calculated from each component using weighted coefficients; the total score ranges from approximately 0 to 10, where lower scores represent less disease activity.
This analysis was performed in the primary analysis set; subjects with baseline and post-baseline results at each time point are included.

End point type	Secondary

End point timeframe:

Weeks 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: units on a scale				
least squares mean (standard error)				
Week 12 (N = 124, 131, 131)	5.405 (± 0.1367)	4.54 (± 0.1395)	4.262 (± 0.1377)	
Week 16 (N = 128, 128, 126)	5.442 (± 0.144)	4.361 (± 0.148)	4.098 (± 0.1464)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Dermatology Life Quality Index (DLQI)

End point title	Change from Baseline in Dermatology Life Quality Index (DLQI)

End point description:

The dermatology life quality index (DLQI) is a skin disease-specific instrument to evaluate health-related quality of life. The DLQI questionnaire asks participants to evaluate the degree that psoriasis has affected their quality of life in the last week, and includes the following parameters: symptoms and feelings, daily activities, leisure activities, work or school activities, personal relationships and treatment related feelings. Participants answered 10 questions on a scale from 0 (not at all) to 3 (very much); the range of the total score is from 0 (best possible score) to 30 (worst possible score).
Analyzed in the primary analysis set; subjects with baseline and post-baseline results at each time point are included.

End point type	Secondary

End point timeframe:

Baseline and weeks 2, 4, 8, 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: units on a scale				
least squares mean (standard error)				
Week 2 (N = 139, 135, 139)	-1.442 (± 0.3739)	-3.716 (± 0.3825)	-4.461 (± 0.3748)	
Week 4 (N = 137, 135, 139)	-2.282 (± 0.3797)	-5.24 (± 0.3884)	-5.742 (± 0.3815)	
Week 8 (N = 135, 132, 137)	-1.814 (± 0.4356)	-5.836 (± 0.4445)	-6.04 (± 0.4367)	
Week 12 (N = 131, 136, 136)	-1.857 (± 0.4248)	-5.587 (± 0.4304)	-6.368 (± 0.4253)	
Week 16 (N = 134, 132, 127)	-1.698 (± 0.4392)	-5.537 (± 0.4475)	-6.541 (± 0.4445)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Medical Outcomes Short Form-36 (SF-36) Mental and Physical Component Scores

End point title	Change from Baseline in Medical Outcomes Short Form-36 (SF-36) Mental and Physical Component Scores

End point description:

The SF-36 assesses the general quality of life of participants by evaluating the domains of physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The questionnaire consists of 36 questions that are completed by the participant. The individual domain scores are aggregated to derive a physical-component summary score and a mental-component summary score which range from 0 to 100, with higher scores indicating a better level of functioning.
This analysis was performed in the primary analysis set; subjects with baseline and post-baseline results at each time point were included.

End point type	Secondary

End point timeframe:

Baseline and weeks 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: units on a scale				
least squares mean (standard error)				
Physical component: Week 12 (N = 130, 135, 136)	1.635 (± 0.7033)	4.134 (± 0.7149)	3.724 (± 0.7084)	
Physical component: Week 16 (N = 134, 132, 127)	1.313 (± 0.6958)	4.632 (± 0.7183)	4.887 (± 0.7156)	
Mental component: week 12 (N = 130, 135, 136)	3.571 (± 0.7081)	5.125 (± 0.7158)	5.524 (± 0.7107)	
Mental component: Week 16 (N = 134, 132, 127)	3.869 (± 0.7123)	5.05 (± 0.7319)	5.919 (± 0.7315)	

Statistical analyses

No statistical analyses for this end point

Secondary: Work Productivity and Activity Impairment (WPAI)

End point title	Work Productivity and Activity Impairment (WPAI)

End point description:

The WPAI is a 6-item generic questionnaire assessing the subject's work productivity and activity impairment due to a given condition. The generic version of the questionnaire can be customized to specific health conditions such as psoriatic arthritis (ie, WPAI-Psoratic Arthritis) by specifying the health condition of interest as psoriatic arthritis in the questions. The WPAI assesses the subject's work time missed (absenteeism), impairment at work or reduced on-the-job effectiveness (presenteeism), overall work impairment (abseentism and presenteeism, ie, work productivity loss), and activity impairment outside the work environment. The WPAI outcomes are expressed as impairment percentages whereby higher scores indicate greater impairment and less productivity (ie, worse outcomes).
Analyzed in the primary analysis set; the first 3 scores only include subjects who were employed at that time point.

End point type	Secondary

End point timeframe:

Weeks 12 and 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	141	146	
Units: percent impairment				
arithmetic mean (standard deviation)				
Absenteeism: Baseline (N = 88, 86, 97)	13.77 (± 27.804)	10.76 (± 22.532)	8.47 (± 19.438)	
Absenteeism: Week 12 (N = 79, 85, 94)	6.19 (± 16.496)	5.93 (± 19.419)	3.39 (± 12.726)	
Absenteeism: Week 16 (N = 76, 82, 89)	4.75 (± 14.995)	7.74 (± 21.162)	4.74 (± 16.456)	
Presenteeism:Baseline (N = 83, 82, 95)	39.64 (± 25.349)	38.05 (± 24.966)	40.63 (± 26.61)	
Presenteeism:Week 12 (N = 78, 82, 93)	29.23 (± 25.724)	25.73 (± 22.445)	22.26 (± 21.975)	
Presenteeism:Week 16 (N = 75, 79, 87)	28.53 (± 25.611)	23.8 (± 23)	22.76 (± 20.442)	
Work impairment: Baseline (N = 83, 82, 95)	43.29 (± 27.507)	41.03 (± 26.245)	43.3 (± 28.483)	
Work impairment: Week 12 (N = 78, 82, 93)	31.52 (± 28.267)	26.93 (± 23.676)	23.53 (± 23.32)	
Work impairment: Week 16 (N = 75, 79, 87)	30.17 (± 26.685)	26.58 (± 24.856)	24.34 (± 21.99)	
Activity Impairment: Baseline (N = 145, 141, 145)	45.17 (± 24.752)	44.11 (± 26.701)	46.21 (± 25.306)	
Activity Impairment: Week 12 (N = 131, 135, 137)	36.41 (± 24.809)	32.15 (± 25.227)	29.34 (± 25.987)	
Activity Impairment: Week 16 (N = 135, 132, 128)	38.89 (± 25.294)	29.32 (± 24.187)	29.84 (± 23.876)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Brodalumab at Week 16

End point title	Plasma Concentrations of Brodalumab at Week 16

End point description:

Plasma concentrations are calculated using log-transformed data from subjects with measurable levels > lower limit of quantitation (LLQ) of 50 ng/mL

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[17]	68	101	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()	2172 (± 395.4)	5746 (± 414.4)	

Notes:

[17] - Subjects did not receive brodalumab

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug until 30 days after last dose; up to 162 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo subcutaneous injection at baseline, week 1, week 2 and then every 2 weeks (Q2W) thereafter up to week 22. From week 14 participants with an inadequate response began treatment with 210 mg brodalumab Q2W. From Week 24 all participants received brodalumab 210 mg Q2W.	
Reporting group title	Brodalumab 210 mg Q2W
Reporting group description:	
Participants received 210 mg brodalumab by subcutaneous injection at baseline, week 1, week 2 and then Q2W thereafter for up to 3 years.	
Reporting group title	Brodalumab 140 mg Q2W
Reporting group description:	
Participants received 140 mg brodalumab by subcutaneous injection at baseline, week 1, week 2 and then Q2W thereafter for up to 3 years.	

Serious adverse events	Placebo	Brodalumab 210 mg Q2W	Brodalumab 140 mg Q2W
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 161 (7.45%)	7 / 163 (4.29%)	8 / 160 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 161 (0.62%)	2 / 163 (1.23%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	1 / 1	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (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
Hepatic enzyme increased			

subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (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
Fibula fracture			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (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
Humerus fracture			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (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
Road traffic accident			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (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
Dressler's syndrome			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (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

Myocardial infarction			
subjects affected / exposed	2 / 161 (1.24%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (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
Tremor			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal haemorrhage			

subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (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			
Leukoplakia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (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
Psoriasis			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (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
Osteonecrosis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (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
Psoriatic arthropathy			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (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
Infections and infestations			
Skin infection			

subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (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
Soft tissue infection			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (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
Tuberculosis			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (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

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

Non-serious adverse events	Placebo	Brodalumab 210 mg Q2W	Brodalumab 140 mg Q2W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	123 / 161 (76.40%)	114 / 163 (69.94%)	106 / 160 (66.25%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Blepharal papilloma			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Melanocytic naevus			

subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	0	0	2
Ocular neoplasm			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Thyroid neoplasm			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Aortic arteriosclerosis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Arteriosclerosis			
subjects affected / exposed	2 / 161 (1.24%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	2	0	0
Blood pressure fluctuation			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Blood pressure inadequately controlled			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	1 / 161 (0.62%)	2 / 163 (1.23%)	0 / 160 (0.00%)
occurrences (all)	1	2	0
Hot flush			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	5 / 161 (3.11%)	4 / 163 (2.45%)	8 / 160 (5.00%)
occurrences (all)	6	4	9
Lymphoedema			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Peripheral venous disease			

subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Varicose vein			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Bunion operation			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Mass excision			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Plastic surgery			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Tooth extraction			
subjects affected / exposed	2 / 161 (1.24%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	2	1	0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Application site bruise			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Application site pruritus			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	4 / 161 (2.48%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	5	0	1
Cyst			

subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Drug intolerance			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Enanthema			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	6 / 161 (3.73%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	6	1	1
Feeling hot			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Feeling jittery			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Inflammation			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	2 / 160 (1.25%)
occurrences (all)	0	1	2
Influenza like illness			
subjects affected / exposed	0 / 161 (0.00%)	2 / 163 (1.23%)	1 / 160 (0.63%)
occurrences (all)	0	2	1
Injection site bruising			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Injection site erythema			
subjects affected / exposed	2 / 161 (1.24%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	2	0	2
Injection site pain			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	2	0	2
Injection site pruritus			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	2	0	1
Injection site reaction			

subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1
Injection site swelling			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Mass			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Nodule			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	0 / 161 (0.00%)	2 / 163 (1.23%)	0 / 160 (0.00%)
occurrences (all)	0	2	0
Oedema peripheral			
subjects affected / exposed	4 / 161 (2.48%)	3 / 163 (1.84%)	2 / 160 (1.25%)
occurrences (all)	5	3	2
Pain			
subjects affected / exposed	2 / 161 (1.24%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	2	0	0
Peripheral swelling			
subjects affected / exposed	5 / 161 (3.11%)	0 / 163 (0.00%)	3 / 160 (1.88%)
occurrences (all)	6	0	3
Pyrexia			
subjects affected / exposed	0 / 161 (0.00%)	2 / 163 (1.23%)	1 / 160 (0.63%)
occurrences (all)	0	2	1
Temperature intolerance			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Immune system disorders			
Allergy to animal			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0

Drug hypersensitivity			
subjects affected / exposed	2 / 161 (1.24%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	2	1	1
Food allergy			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Hypersensitivity			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Seasonal allergy			
subjects affected / exposed	0 / 161 (0.00%)	2 / 163 (1.23%)	3 / 160 (1.88%)
occurrences (all)	0	2	3
Social circumstances			
Dental prosthesis user			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Dyspareunia			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Pruritus genital			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Allergic cough			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Asthma			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	2 / 160 (1.25%)
occurrences (all)	1	1	2

Catarrh			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	2 / 160 (1.25%)
occurrences (all)	0	1	2
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	7 / 161 (4.35%)	5 / 163 (3.07%)	2 / 160 (1.25%)
occurrences (all)	8	5	2
Dysphonia			
subjects affected / exposed	1 / 161 (0.62%)	2 / 163 (1.23%)	0 / 160 (0.00%)
occurrences (all)	1	2	0
Dyspnoea			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Dyspnoea exertional			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 161 (0.00%)	3 / 163 (1.84%)	0 / 160 (0.00%)
occurrences (all)	0	3	0
Nasal congestion			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Nasal oedema			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	9 / 161 (5.59%)	3 / 163 (1.84%)	5 / 160 (3.13%)
occurrences (all)	10	3	5
Paranasal sinus discomfort			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Paranasal sinus hypersecretion			

subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Pharyngeal inflammation			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Productive cough			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Pulmonary granuloma			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Rales			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Respiratory tract congestion			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	1 / 161 (0.62%)	2 / 163 (1.23%)	3 / 160 (1.88%)
occurrences (all)	1	2	7
Throat lesion			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Vocal cord atrophy			

subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Yawning			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Psychiatric disorders			
Adjustment disorder with depressed mood			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	1	1	1
Anxiety disorder			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Burnout syndrome			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1
Depression			
subjects affected / exposed	3 / 161 (1.86%)	2 / 163 (1.23%)	4 / 160 (2.50%)
occurrences (all)	3	2	4
Impatience			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Insomnia			

subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Mood altered			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Nervousness			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	1	2	2
Suicidal ideation			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	2	0	0
Liver injury			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Non-alcoholic steatohepatitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 161 (1.24%)	2 / 163 (1.23%)	2 / 160 (1.25%)
occurrences (all)	2	2	3
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 161 (1.86%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	4	0	2
Blood cholesterol increased			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Blood glucose decreased			

subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Blood glucose increased			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	1	1	1
Blood potassium increased			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	1 / 161 (0.62%)	2 / 163 (1.23%)	2 / 160 (1.25%)
occurrences (all)	1	2	2
Blood triglycerides increased			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Colonoscopy			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Heart rate increased			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Hepatic enzyme abnormal			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	2
Lipids abnormal			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Liver function test abnormal			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Low density lipoprotein increased			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			

subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	2	0	0
Lymphocyte count increased			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Mammogram abnormal			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Monocyte count increased			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	3
Neutrophil count increased			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	1	1	0
Platelet count decreased			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Thyroid gland scan abnormal			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Transaminases increased			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Vitamin D decreased			
subjects affected / exposed	0 / 161 (0.00%)	2 / 163 (1.23%)	0 / 160 (0.00%)
occurrences (all)	0	2	0
Weight decreased			
subjects affected / exposed	3 / 161 (1.86%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	4	0	1
Weight increased			
subjects affected / exposed	0 / 161 (0.00%)	2 / 163 (1.23%)	1 / 160 (0.63%)
occurrences (all)	0	3	1
White blood cell count decreased			

subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	0	0	3
White blood cell count increased			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	1	1	0
White blood cells urine positive			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Animal scratch			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	0	0	2
Ankle fracture			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Arthropod bite			
subjects affected / exposed	0 / 161 (0.00%)	2 / 163 (1.23%)	1 / 160 (0.63%)
occurrences (all)	0	2	1
Arthropod sting			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	1	1	0
Contusion			
subjects affected / exposed	3 / 161 (1.86%)	4 / 163 (2.45%)	4 / 160 (2.50%)
occurrences (all)	6	4	7
Eye contusion			
subjects affected / exposed	2 / 161 (1.24%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	2	0	1
Eye injury			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Face injury			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Fall			

subjects affected / exposed	3 / 161 (1.86%)	2 / 163 (1.23%)	2 / 160 (1.25%)
occurrences (all)	4	2	2
Foot fracture			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Joint capsule rupture			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	2	0	0
Joint injury			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1
Laceration			
subjects affected / exposed	1 / 161 (0.62%)	2 / 163 (1.23%)	0 / 160 (0.00%)
occurrences (all)	1	3	0
Ligament sprain			
subjects affected / exposed	2 / 161 (1.24%)	3 / 163 (1.84%)	0 / 160 (0.00%)
occurrences (all)	3	4	0
Limb injury			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	0	0	2
Lumbar vertebral fracture			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Meniscus injury			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	0	0	2
Muscle strain			
subjects affected / exposed	2 / 161 (1.24%)	2 / 163 (1.23%)	1 / 160 (0.63%)
occurrences (all)	3	2	1
Post-traumatic pain			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Road traffic accident			

subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	1	1	1
Splinter			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Sternal fracture			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Tendon rupture			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Tooth fracture			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	1	1	0
Wound			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	1	0	2
Wrist fracture			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Coronary artery disease			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Palpitations			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0

Tachycardia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Anosmia			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Burning sensation			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	0	0	2
Dizziness			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	3 / 160 (1.88%)
occurrences (all)	3	1	3
Dizziness postural			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	11 / 161 (6.83%)	4 / 163 (2.45%)	5 / 160 (3.13%)
occurrences (all)	11	5	6
Hypertensive encephalopathy			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	3 / 161 (1.86%)	2 / 163 (1.23%)	2 / 160 (1.25%)
occurrences (all)	3	3	2
Intercostal neuralgia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Loss of consciousness			

subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Lumbar radiculopathy			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	1 / 161 (0.62%)	3 / 163 (1.84%)	0 / 160 (0.00%)
occurrences (all)	3	4	0
Nerve compression			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Nerve root compression			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Neuralgia			
subjects affected / exposed	0 / 161 (0.00%)	2 / 163 (1.23%)	0 / 160 (0.00%)
occurrences (all)	0	2	0
Paraesthesia			
subjects affected / exposed	3 / 161 (1.86%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	3	0	0
Parkinson's disease			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Polyneuropathy			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1
Radiculopathy			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	2	0	0
Sciatica			
subjects affected / exposed	2 / 161 (1.24%)	2 / 163 (1.23%)	1 / 160 (0.63%)
occurrences (all)	2	2	1
Sinus headache			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Syncope			

subjects affected / exposed	2 / 161 (1.24%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	2	1	0
Tarsal tunnel syndrome			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Vocal cord paresis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1
Iron deficiency anaemia			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Leukocytosis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	2	1
Lymphadenopathy			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Lymphatic disorder			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Lymphopenia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1

Thrombocytopenia			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	2 / 160 (1.25%)
occurrences (all)	1	1	3
External ear inflammation			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	1	1	0
Paraesthesia ear			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Tinnitus			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	2 / 161 (1.24%)	3 / 163 (1.84%)	0 / 160 (0.00%)
occurrences (all)	2	3	0
Vertigo labyrinthine			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	2 / 160 (1.25%)
occurrences (all)	0	1	2
Blepharitis allergic			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Blepharospasm			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Cataract			

subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	0	0	2
Chalazion			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Conjunctival hyperaemia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Dry eye			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	1	0	2
Eye allergy			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Eye irritation			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Eye pain			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Eye pruritus			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	1	1	0
Fuchs' syndrome			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Glaucoma			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Uveitis			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	2
Vision blurred			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Visual acuity reduced			

subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Visual impairment			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	2	0
Vitreous degeneration			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Vitreous floaters			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Abdominal hernia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	4 / 161 (2.48%)	3 / 163 (1.84%)	0 / 160 (0.00%)
occurrences (all)	4	4	0
Abdominal pain upper			
subjects affected / exposed	4 / 161 (2.48%)	2 / 163 (1.23%)	1 / 160 (0.63%)
occurrences (all)	4	2	3
Abdominal rigidity			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Abdominal tenderness			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	2	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	2 / 160 (1.25%)
occurrences (all)	0	1	2
Colitis ulcerative			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	2	0

Constipation			
subjects affected / exposed	2 / 161 (1.24%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	2	1	1
Diarrhoea			
subjects affected / exposed	15 / 161 (9.32%)	12 / 163 (7.36%)	5 / 160 (3.13%)
occurrences (all)	22	13	6
Diverticulum intestinal			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	2	1
Dyspepsia			
subjects affected / exposed	4 / 161 (2.48%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	4	0	1
Dysphagia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Faeces discoloured			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	1	1	0
Gastritis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal telangiectasia			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	5 / 161 (3.11%)	4 / 163 (2.45%)	2 / 160 (1.25%)
occurrences (all)	5	4	2
Gingival atrophy			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	2	0	0

Haemorrhoids			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	10 / 161 (6.21%)	7 / 163 (4.29%)	5 / 160 (3.13%)
occurrences (all)	14	7	8
Oesophageal ulcer			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Oesophagitis			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Oral discomfort			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1
Salivary gland disorder			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1
Umbilical hernia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	7 / 161 (4.35%)	2 / 163 (1.23%)	2 / 160 (1.25%)
occurrences (all)	10	2	3
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Anhidrosis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Blister			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Decubitus ulcer			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Dermatitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1
Dermatitis acneiform			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Dermatitis allergic			
subjects affected / exposed	1 / 161 (0.62%)	2 / 163 (1.23%)	0 / 160 (0.00%)
occurrences (all)	1	4	0
Dermatitis contact			
subjects affected / exposed	2 / 161 (1.24%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	2	1	1
Diffuse alopecia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	1 / 161 (0.62%)	2 / 163 (1.23%)	2 / 160 (1.25%)
occurrences (all)	1	2	4
Dyshidrotic eczema			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	1	1	0
Erythema			

subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	2 / 160 (1.25%)
occurrences (all)	1	1	2
Guttate psoriasis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Hyperkeratosis			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	1	1	1
Intertrigo			
subjects affected / exposed	0 / 161 (0.00%)	2 / 163 (1.23%)	2 / 160 (1.25%)
occurrences (all)	0	2	2
Nail psoriasis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Pain of skin			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Papule			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Photosensitivity reaction			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	7 / 161 (4.35%)	2 / 163 (1.23%)	4 / 160 (2.50%)
occurrences (all)	9	2	4
Psoriasis			
subjects affected / exposed	6 / 161 (3.73%)	2 / 163 (1.23%)	4 / 160 (2.50%)
occurrences (all)	6	2	6
Rash			
subjects affected / exposed	4 / 161 (2.48%)	5 / 163 (3.07%)	3 / 160 (1.88%)
occurrences (all)	4	7	3
Rash macular			

subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Rosacea			
subjects affected / exposed	2 / 161 (1.24%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	2	1	0
Skin lesion			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	0	0	2
Skin mass			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Splinter haemorrhages			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Swelling face			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Urticaria			
subjects affected / exposed	2 / 161 (1.24%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	2	1	0
Xeroderma			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Diabetic nephropathy			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Dysuria			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Nephritis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Nephrolithiasis			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	1	1	1

Nephroptosis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Polyuria			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Renal cyst			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Renal failure			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1
Urinary incontinence			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	1	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	10 / 161 (6.21%)	5 / 163 (3.07%)	6 / 160 (3.75%)
occurrences (all)	11	5	6
Arthritis			
subjects affected / exposed	4 / 161 (2.48%)	2 / 163 (1.23%)	2 / 160 (1.25%)
occurrences (all)	5	2	2
Back pain			
subjects affected / exposed	9 / 161 (5.59%)	4 / 163 (2.45%)	4 / 160 (2.50%)
occurrences (all)	9	4	4
Bone pain			
subjects affected / exposed	0 / 161 (0.00%)	2 / 163 (1.23%)	0 / 160 (0.00%)
occurrences (all)	0	3	0
Fibromyalgia			

subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Foot deformity			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Groin pain			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Intervertebral disc disorder			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Intervertebral disc protrusion			
subjects affected / exposed	2 / 161 (1.24%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	2	1	0
Jaw cyst			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Joint range of motion decreased			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	0	0	2
Limb discomfort			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	5 / 161 (3.11%)	1 / 163 (0.61%)	4 / 160 (2.50%)
occurrences (all)	6	1	4
Muscular weakness			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal discomfort			

subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1
Musculoskeletal pain			
subjects affected / exposed	6 / 161 (3.73%)	3 / 163 (1.84%)	2 / 160 (1.25%)
occurrences (all)	8	4	2
Musculoskeletal stiffness			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	2	1	0
Myalgia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	2 / 160 (1.25%)
occurrences (all)	0	1	2
Myalgia intercostal			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	2 / 160 (1.25%)
occurrences (all)	0	1	2
Osteoarthritis			
subjects affected / exposed	2 / 161 (1.24%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	2	1	1
Osteonecrosis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	2	0
Osteoporotic fracture			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	5 / 161 (3.11%)	2 / 163 (1.23%)	2 / 160 (1.25%)
occurrences (all)	6	2	2
Pain in jaw			
subjects affected / exposed	2 / 161 (1.24%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	2	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Psoriatic arthropathy			

subjects affected / exposed	8 / 161 (4.97%)	7 / 163 (4.29%)	8 / 160 (5.00%)
occurrences (all)	8	10	9
Rotator cuff syndrome			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	0	0	2
Sjogren's syndrome			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Spinal osteoarthritis			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Spinal pain			
subjects affected / exposed	1 / 161 (0.62%)	5 / 163 (3.07%)	0 / 160 (0.00%)
occurrences (all)	1	8	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	2
Tenosynovitis			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Infections and infestations			
Abscess oral			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Acarodermatitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1
Bronchitis			
subjects affected / exposed	8 / 161 (4.97%)	4 / 163 (2.45%)	4 / 160 (2.50%)
occurrences (all)	9	5	4
Candida infection			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	1	1	0
Cellulitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	3

Chronic tonsillitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	3 / 161 (1.86%)	2 / 163 (1.23%)	3 / 160 (1.88%)
occurrences (all)	3	2	3
Conjunctivitis viral			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	2 / 161 (1.24%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	2	1	0
Ear infection			
subjects affected / exposed	1 / 161 (0.62%)	2 / 163 (1.23%)	0 / 160 (0.00%)
occurrences (all)	2	2	0
Eye infection bacterial			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	0	0	4
Fungal infection			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Gastritis viral			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	4 / 161 (2.48%)	3 / 163 (1.84%)	1 / 160 (0.63%)
occurrences (all)	5	3	1
Gastroenteritis viral			
subjects affected / exposed	2 / 161 (1.24%)	2 / 163 (1.23%)	0 / 160 (0.00%)
occurrences (all)	3	2	0
Gastrointestinal viral infection			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1

Gingivitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Helicobacter infection			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Herpes dermatitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Herpes simplex			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Herpes zoster			
subjects affected / exposed	2 / 161 (1.24%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	4	0	1
Incision site infection			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	5 / 161 (3.11%)	2 / 163 (1.23%)	2 / 160 (1.25%)
occurrences (all)	6	2	2
Labyrinthitis			
subjects affected / exposed	2 / 161 (1.24%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	2	0	0
Laryngitis			
subjects affected / exposed	5 / 161 (3.11%)	2 / 163 (1.23%)	4 / 160 (2.50%)
occurrences (all)	5	2	4
Latent tuberculosis			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Localised infection			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1

Lower respiratory tract infection			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	2 / 160 (1.25%)
occurrences (all)	0	2	2
Lung infection			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Mastitis fungal			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Nail bed infection			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	19 / 161 (11.80%)	26 / 163 (15.95%)	15 / 160 (9.38%)
occurrences (all)	25	28	17
Onychomycosis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Oral bacterial infection			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	1
Oral herpes			
subjects affected / exposed	1 / 161 (0.62%)	6 / 163 (3.68%)	3 / 160 (1.88%)
occurrences (all)	1	7	3
Otitis externa			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	0	1	2
Otitis media			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Paronychia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1

Parotitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Peritonsillar abscess			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	9 / 161 (5.59%)	5 / 163 (3.07%)	4 / 160 (2.50%)
occurrences (all)	10	5	5
Pharyngitis bacterial			
subjects affected / exposed	2 / 161 (1.24%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	2	0	1
Pharyngitis streptococcal			
subjects affected / exposed	2 / 161 (1.24%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	2	1	0
Pneumonia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Pulpitis dental			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	1	1	0
Pyuria			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Rash pustular			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	2	0	2
Rhinitis			
subjects affected / exposed	3 / 161 (1.86%)	3 / 163 (1.84%)	2 / 160 (1.25%)
occurrences (all)	3	3	2
Sinusitis			
subjects affected / exposed	5 / 161 (3.11%)	8 / 163 (4.91%)	2 / 160 (1.25%)
occurrences (all)	5	10	2

Staphylococcal infection			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Subcutaneous abscess			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Tinea pedis			
subjects affected / exposed	2 / 161 (1.24%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	2	0	0
Tinea versicolour			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	1	1	0
Tonsillitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	3	0	0
Tonsillitis bacterial			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Tooth abscess			
subjects affected / exposed	3 / 161 (1.86%)	2 / 163 (1.23%)	2 / 160 (1.25%)
occurrences (all)	3	2	2
Tooth infection			
subjects affected / exposed	0 / 161 (0.00%)	2 / 163 (1.23%)	0 / 160 (0.00%)
occurrences (all)	0	2	0
Tracheitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Tuberculosis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	21 / 161 (13.04%)	16 / 163 (9.82%)	16 / 160 (10.00%)
occurrences (all)	25	17	17
Urethritis			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1

Urinary tract infection			
subjects affected / exposed	4 / 161 (2.48%)	5 / 163 (3.07%)	8 / 160 (5.00%)
occurrences (all)	4	5	8
Vaginal infection			
subjects affected / exposed	3 / 161 (1.86%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	4	0	0
Viral infection			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Viral pharyngitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	1	0	1
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 161 (1.24%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	2	0	0
Dehydration			
subjects affected / exposed	0 / 161 (0.00%)	2 / 163 (1.23%)	0 / 160 (0.00%)
occurrences (all)	0	2	0
Diabetes mellitus			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	1	0	2
Glucose tolerance impaired			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Gout			

subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	5	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 161 (0.00%)	3 / 163 (1.84%)	0 / 160 (0.00%)
occurrences (all)	0	3	0
Hyperglycaemia			
subjects affected / exposed	2 / 161 (1.24%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	3	0	1
Hyperlipidaemia			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	2 / 160 (1.25%)
occurrences (all)	1	1	2
Hypertriglyceridaemia			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	1	1	1
Hyperuricaemia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	2 / 160 (1.25%)
occurrences (all)	1	0	2
Hypoglycaemia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 160 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Malnutrition			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Vitamin B12 deficiency			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 160 (0.63%)
occurrences (all)	0	0	1
Vitamin D deficiency			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	1 / 160 (0.63%)
occurrences (all)	1	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 March 2014	Based on the identification of suicidal behavior and suicidal ideation as potential risks and after discussion with regulatory agencies, the C-SSRS and the PHQ-8 depression scale were added as instruments to assess patient eligibility and monitor subject safety.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported