Clinical trial results:
A Randomized, Double-blind, Placebo-controlled Phase 3 Study to Evaluate the Efficacy, Safety, and Effect on Radiographic Progression of Brodalumab in Subjects With Psoriatic Arthritis: AMVISION-1

Summary

EudraCT number	2013-003554-25
Trial protocol	GR CZ BE HU IT GB ES SK EE BG FR
Global end of trial date	22 October 2015

Results information

Result version number	v1 (current)
This version publication date	06 November 2016
First version publication date	06 November 2016

Trial information

Trial identification

Sponsor protocol code	20090406

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02029495
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	22 October 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 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 (140 mg every 2 weeks (Q2W) and 210 mg Q2W) compared to placebo in subjects with active psoriatic arthritis (PsA), as measured by the proportion of subjects achieving an 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 that are consistent with International Conference on Harmonisation (ICH)/Good Clinical Practice (GCP) and applicable regulatory requirements.
The final Clinical Study Protocol (CSP), including the final version of the Subject Information and Consent Form(s), was approved in writing by the Independent Ethics Committee (IEC) and Institutional Review Board (IRB) before enrollment of any subject into the study.
The Principal Investigator at each center ensured that the subject was given full and adequate oral and written information about the aims, methods, anticipated benefits, and potential hazards of the study. The informed consent form was signed and personally dated by the subject and by the person who conducted the informed consent discussion.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 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	Poland: 139
Country: Number of subjects enrolled	United States: 107
Country: Number of subjects enrolled	Russian Federation: 71
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Czech Republic: 19
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Slovakia: 15
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	Mexico: 12
Country: Number of subjects enrolled	Switzerland: 12
Country: Number of subjects enrolled	Bulgaria: 9
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	Estonia: 9
Country: Number of subjects enrolled	Italy: 9

Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	Belgium: 2
Worldwide total number of subjects	478
EEA total number of subjects	267

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)	427
From 65 to 84 years	51
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited at 121 clinical sites in 17 countries worldwide. The first subject enrolled on 06 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 biologic use, and geographic region (North America, Central and Eastern Europe, Western Europe, and Latin America).

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	Investigator, Subject

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.

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	158	159
Received Treatment	159	158	158
Ongoing Study at Week 16	95	101	108
Ongoing Study at Week 24	68	76	84
Ongoing Study at Week 52	10	12	14
Completed	0	0	0
Not completed	161	158	159
Consent withdrawn by subject	31	29	15
Lost to follow-up	1	1	-
Decision by sponsor	129	128	144

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	158	159
Age Categorical Units: Subjects			
Adults (18-64 years)	145	138	144
From 65-84 years	16	20	15
Age Continuous Units: years			
arithmetic mean	48.1	49.9	49.1
standard deviation	± 11.79	± 12.8	± 12.24
Gender Categorical Units: Subjects			
Female	80	80	70
Male	81	78	89
Race Units: Subjects			
White	152	152	155
Asian	4	0	0
American Indian or Alaska Native	0	0	2
Other	5	6	2
Ethnicity Units: Subjects			
Hispanic or Latino	11	9	19
Not Hispanic or Latino	150	149	140
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, 158, 159 subjects in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	6.4	8.2	7.7
standard deviation	± 7.96	± 8.63	± 9.2

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, 151, and 149 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	11.9	13.5	13.7
standard deviation	± 7.27	± 8.2	± 7.43
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, 157, 156 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	8	9.5	8.1
standard deviation	± 7.03	± 7.85	± 6.89
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, 157, and 156 subjects in each group respectively.			
Units: units on a scale			
arithmetic mean	5.6	5.5	5.4
standard deviation	± 1.88	± 2.04	± 2.05
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). Data are available for 160, 158, 159 participants in each treatment group respectively.			
Units: entheses			
arithmetic mean	1.9	1.8	1.6
standard deviation	± 1.94	± 2	± 1.87
Dactylitis Score			
The dactylitis count is defined as the sum of 20 fingers/toes that exhibit dactylitis (absent 0, present 1). Data are available for 160, 158, 159 participants in each treatment group respectively.			
Units: digits			
arithmetic mean	2.3	2.6	2.2
standard deviation	± 3.55	± 4.23	± 3.86
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). Data are available for 159, 157, 156 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	1.2	1.3	1.2
standard deviation	± 0.59	± 0.65	± 0.57
Swollen Joint Count			
Data available for 160, 158, and 159 subjects in each treatment group respectively.			
Units: joints			

arithmetic mean	12.3	13.3	12.4
standard deviation	± 8.33	± 10.1	± 10.2
Tender Joint Count			
Data available for 160, 158, and 159 subjects in each treatment group respectively.			
Units: joints			
arithmetic mean	21.4	23.4	20.7
standard deviation	± 14.8	± 15.5	± 14.4
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 158, 157, and 155 subjects in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	5	5.2	4.9
standard deviation	± 1.1	± 1.2	± 1.1
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, 157, 155 subjects in each treatment group respectively			
Units: mm			
arithmetic mean	58.5	60.3	58.5
standard deviation	± 18	± 21.2	± 19.3
Patient Global Assessment of Disease Activity			
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, 157, 156 subjects in each treatment group respectively.			
Units: mm			
arithmetic mean	58.9	59.9	58.6
standard deviation	± 23.3	± 23.1	± 22.9
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, 157, 156 subjects in each treatment group respectively.			
Units: mm			
arithmetic mean	53.7	54.8	52.5
standard deviation	± 23.5	± 23.5	± 24.9
C-Reactive Protein (CRP)			
Data available for 161, 158, 158 subjects in each treatment group respectively.			
Units: mg/L			
arithmetic mean	15.3	19.4	17.1
standard deviation	± 21.83	± 29.92	± 26.59
Erythrocyte Sedimentation Rate (ESR)			
Data available for 157, 155, 157 subjects in each treatment group respectively.			
Units: mm/hr			
arithmetic mean	35.2	35.8	38.8
standard deviation	± 25.55	± 22.9	± 31.85
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 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 156, 157, and 155 subjects in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	29.1	31.6	28.7
standard deviation	± 13.57	± 14.17	± 13.46
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, rolephysical, 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, 157, and 156 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	33.3	32.6	34.6
standard deviation	± 8.59	± 9.45	± 9.06
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, 157, 156 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	53.2	52.7	53.2
standard deviation	± 10.23	± 10.35	± 10.53

Reporting group values	Total		
Number of subjects	478		
Age Categorical Units: Subjects			
Adults (18-64 years)	427		
From 65-84 years	51		
Age Continuous Units: years arithmetic mean standard deviation	- -		
Gender Categorical Units: Subjects			
Female	230		
Male	248		
Race Units: Subjects			
White	459		
Asian	4		
American Indian or Alaska Native	2		
Other	13		
Ethnicity Units: Subjects			
Hispanic or Latino	39		
Not Hispanic or Latino	439		
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, 158, 159 subjects 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, 151, and 149 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, 157, 156 participants in each treatment group respectively.			
Units: units on a scale 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, 157, and 156 subjects in each group respectively.			
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). Data are available for 160, 158, 159 participants in each treatment group respectively.			
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). Data are available for 160, 158, 159 participants in each treatment group respectively.			
Units: digits 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). Data are available for 159, 157, 156 participants in each treatment group respectively.			
Units: units on a scale arithmetic mean			

standard deviation	-		
Swollen Joint Count			
Data available for 160, 158, and 159 subjects in each treatment group respectively.			
Units: joints arithmetic mean standard deviation	- 		
Tender Joint Count			
Data available for 160, 158, and 159 subjects in each treatment group respectively.			
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 158, 157, and 155 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, 157, 155 subjects in each treatment group respectively			
Units: mm arithmetic mean standard deviation	- 		
Patient Global Assessment of Disease Activity			
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, 157, 156 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, 157, 156 subjects in each treatment group respectively.			
Units: mm arithmetic mean standard deviation	- 		
C-Reactive Protein (CRP)			
Data available for 161, 158, 158 subjects in each treatment group respectively.			
Units: mg/L arithmetic mean standard deviation	- 		
Erythrocyte Sedimentation Rate (ESR)			
Data available for 157, 155, 157 subjects in each treatment group respectively.			
Units: mm/hr 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 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 156, 157, and 155 subjects in each treatment group respectively.			
Units: units on a scale 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, rolephysical, 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, 157, and 156 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, 157, 156 participants in each treatment group respectively.			
Units: units on a scale 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	122	118	121	
Units: percentage of participants				
number (not applicable)	13.9	39.8	51.2	

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Placebo v Brodalumab 140 mg
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference from placebo
Point estimate	25.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.1
upper limit	36.7

Notes:

[1] - Cochran-Mantel-Haenszel approach stratified by baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes/no) and geographic region (North and Latin American, Central/Eastern Europe, Western Europe).

Statistical analysis title	Primary Analysis
Comparison groups	Placebo v Brodalumab 210 mg
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference from placebo
Point estimate	37.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	26.5
upper limit	48.1

Notes:

[2] - Cochran-Mantel-Haenszel approach stratified by baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes/no) and geographic region (North and Latin American, Central/Eastern Europe, Western Europe).

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	78	90	77	
Units: percentage of participants				
number (not applicable)	10.3	48.9	75.3	

Statistical analyses

Statistical analysis title	Difference in Response Rate
Comparison groups	Placebo v Brodalumab 210 mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference from placebo
Point estimate	65.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	53.3
upper limit	76.8

Notes:

[3] - Cochran-Mantel-Haenszel test stratified by baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes/no), baseline PASI score (≤ median, > median) and region (North and Latin America, Central and Eastern Europe, Western Europe/Australia).

Statistical analysis title	Difference in Response Rates
Comparison groups	Placebo v Brodalumab 140 mg
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference from placebo
Point estimate	38.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	26.3
upper limit	51

Notes:

[4] - Cochran-Mantel-Haenszel test stratified by baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes/no), baseline PASI score (≤ median, > median) and region (North and Latin America, Central and 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	93	98	106	
Units: units on a scale				
least squares mean (standard error)	-0.101 (± 0.0484)	-0.339 (± 0.0478)	-0.469 (± 0.0468)	

Statistical analyses

Statistical analysis title	Comparison with Placebo
Comparison groups	Placebo v Brodalumab 140 mg
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002 [5]
Method	Mixed effects model repeated measures
Parameter estimate	LS mean difference
Point estimate	-0.237
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.362
upper limit	-0.112

Notes:

[5] - The model contains visit, treatment, treatment-by-visit and baseline-by-visit interaction, baseline, and three randomization strata (baseline weight, prior biologic use, and geographic region).

Statistical analysis title	Comparison with Placebo
Comparison groups	Placebo v Brodalumab 210 mg

Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [6]
Method	Mixed effects model repeated measures
Parameter estimate	Least squares (LS) mean difference
Point estimate	-0.368
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.491
upper limit	-0.244

Notes:

[6] - The model contains visit, treatment, treatment-by-visit and baseline-by-visit interaction, baseline, and three randomization strata (baseline weight, 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	72	88	73	
Units: percentage of participants				
number (not applicable)	8.3	45.5	49.3	

Statistical analyses

Statistical analysis title	Difference in Response Rate
Comparison groups	Placebo v Brodalumab 210 mg

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference from placebo
Point estimate	41
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.9
upper limit	54.1

Notes:

[7] - Cochran-Mantel-Haenszel approach stratified by baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes/no), and geographic region (North and Latin American, Central/Eastern Europe, Western Europe)

Statistical analysis title	Difference in Response Rate
Comparison groups	Placebo v Brodalumab 140 mg
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference from placebo
Point estimate	37.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.9
upper limit	49.3

Notes:

[8] - Cochran-Mantel-Haenszel approach stratified by baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes/no), and geographic region (North and Latin American, Central/Eastern Europe, Western Europe).

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 in the primary analysis.

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	122	118	121	
Units: percentage of participants				
number (not applicable)				
Week 2	9	18.6	23.1	
Week 4	11.5	23.7	39.7	
Week 8	16.4	41.5	52.9	
Week 12	18.9	40.7	52.9	

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	112	115	113	
Units: units on a scale				
least squares mean (standard error)				
Week 2 (N = 112, 115, 113)	-0.043 (± 0.0362)	-0.123 (± 0.0364)	-0.227 (± 0.0364)	
Week 4 (N = 109, 114, 112)	-0.081 (± 0.0409)	-0.197 (± 0.0407)	-0.354 (± 0.0407)	
Week 8 (N = 102, 111, 114)	-0.101 (± 0.0451)	-0.279 (± 0.0442)	-0.387 (± 0.0439)	
Week 12 (N = 100, 108, 112)	-0.125 (± 0.0496)	-0.31 (± 0.0486)	-0.412 (± 0.0481)	

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; 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	78	90	77	
Units: percentage of participants				
number (not applicable)				
Week 2	2.6	14.4	20.8	
Week 4	6.4	35.6	54.5	
Week 8	9	47.8	71.4	
Week 12	9	51.1	83.1	

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 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, and 15

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72	88	73	
Units: percentage of participants				
number (not applicable)				
Week 1	9.7	9.1	11	
Week 2	9.7	21.6	20.5	
Week 3	6.9	28.4	38.4	
Week 4	6.9	38.6	47.9	
Week 5	5.6	37.5	47.9	
Week 6	4.2	45.5	46.6	
Week 7	8.3	43.2	57.5	
Week 8	9.7	43.2	54.8	
Week 9	6.9	43.2	53.4	
Week 10	5.6	43.2	49.3	
Week 11	9.7	46.6	53.4	
Week 12	8.3	43.2	50.7	
Week 13	5.6	43.2	54.8	
Week 14	9.7	43.2	50.7	
Week 15	6.9	48.9	49.3	

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	122	118	121	
Units: percentage of participants				
number (not applicable)				
Week 2	0.8	4.2	4.1	
Week 4	2.5	11	11.6	
Week 8	4.9	16.9	25.6	
Week 12	4.9	17.8	29.8	
Week 16	4.1	20.3	29.8	

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	122	118	121	
Units: percentage of participants				
number (not applicable)				
Week 2	0	0	1.7	
Week 4	0	2.5	4.1	
Week 8	1.6	6.8	10.7	
Week 12	2.5	9.3	12.4	
Week 16	2.5	10.2	14.9	

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, 14, 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	122	118	121	
Units: joints				
least squares mean (standard error)				
Week 2 (N = 115, 115, 117)	-2.471 (± 0.8609)	-4.209 (± 0.8738)	-5.857 (± 0.8566)	
Week 4 (N = 111, 114, 117)	-2.752 (± 0.932)	-5.594 (± 0.935)	-6.99 (± 0.9129)	
Week 8 (N = 103, 109, 117)	-3.417 (± 1.0241)	-8.46 (± 1.0162)	-9.183 (± 0.9814)	
Week 12 (N = 100, 107, 116)	-2.205 (± 1.1855)	-8.512 (± 1.1732)	-9.493 (± 1.1315)	
Week 14 (N = 99, 105, 113)	-1.515 (± 1.2202)	-9.879 (± 1.2059)	-9.999 (± 1.1626)	
Week 16 (N = 93, 98, 110)	0.591 (± 1.2844)	-10.82 (± 1.264)	-8.765 (± 1.2115)	

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 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, 14, 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	122	118	121	
Units: joints				
least squares mean (standard error)				
Week 2 (N = 115, 115, 117)	-2.7 (± 0.6737)	-3.238 (± 0.6737)	-2.893 (± 0.6691)	
Week 4 (N = 111, 114, 117)	-2.316 (± 0.6391)	-3.737 (± 0.6368)	-4.325 (± 0.6252)	
Week 8 (N = 103, 109, 117)	-2.451 (± 0.731)	-5.548 (± 0.7205)	-5.95 (± 0.6989)	
Week 12 (N = 100, 107, 116)	-2.44 (± 0.7858)	-5.949 (± 0.7724)	-6.467 (± 0.7469)	
Week 14 (N = 99, 105, 113)	-1.662 (± 0.793)	-6.574 (± 0.779)	-6.661 (± 0.7531)	
Week 16 (N = 93, 98, 110)	-0.216 (± 0.8879)	-6.912 (± 0.8698)	-5.829 (± 0.8343)	

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	122	118	121	
Units: mm				
least squares mean (standard error)				
Week 2 (N = 112, 115, 113)	3.984 (± 1.9556)	0.254 (± 1.9584)	-4.852 (± 1.9619)	
Week 4 (N = 109, 114, 112)	4.672 (± 2.1652)	-3.359 (± 2.1429)	-9.03 (± 2.1462)	
Week 8 (N = 102, 111, 114)	2.685 (± 2.3086)	-7.256 (± 2.2534)	-12.98 (± 2.236)	
Week 12 (N = 100, 108, 112)	3.123 (± 2.4577)	-6.31 (± 2.402)	-14.36 (± 2.3714)	
Week 16 (N = 93, 98, 106)	3.919 (± 2.4394)	-7.635 (± 2.3942)	-16.5 (± 2.3507)	

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	122	118	121	
Units: mm				
least squares mean (standard error)				
Week 2 (N = 112, 115, 113)	0.375 (± 1.877)	-3.247 (± 1.8953)	-7.492 (± 1.8882)	
Week 4 (N = 109, 114, 112)	2.375 (± 2.0807)	-5.291 (± 2.0747)	-13.41 (± 2.0677)	
Week 8 (N = 102, 111, 114)	0.524 (± 2.1619)	-8.264 (± 2.1278)	-16.89 (± 2.1036)	
Week 12 (N = 100, 108, 112)	0.015 (± 2.3726)	-7.668 (± 2.3296)	-18.22 (± 2.2912)	
Week 16 (N = 93, 98, 106)	2.16 (± 2.4211)	-10.62 (± 2.3911)	-19.95 (± 1.3332)	

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	122	118	121	
Units: mm				
least squares mean (standard error)				
Week 2 (N = 110, 115, 112)	-5.576 (± 1.8452)	-11.4 (± 1.8303)	-16.73 (± 1.8436)	
Week 4 (N = 104, 113, 110)	-10.35 (± 2.0579)	-16.56 (± 2.0072)	-22.22 (± 2.0203)	
Week 8 (N = 98, 111, 112)	-9.832 (± 2.199)	-21.14 (± 2.1124)	-27.4 (± 2.103)	
Week 12 (N = 96, 107, 112)	-9.305 (± 2.2447)	-24.24 (± 2.1652)	-28.44 (± 2.1354)	
Week 16 (N = 92, 98, 105)	-8.125 (± 2.3987)	-27.39 (± 2.3369)	-29.22 (± 2.2903)	

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	122	118	121	
Units: mg/L				
arithmetic mean (standard deviation)				
Week 2 (N = 114, 117, 115)	1.75 (± 13.315)	-4.81 (± 25.738)	-5.9 (± 20.412)	
Week 4 (N = 112, 116, 116)	-1.05 (± 12.231)	-6.05 (± 24.632)	-7.21 (± 18.933)	
Week 8 (N = 103, 111, 117)	-0.5 (± 14.042)	-6.27 (± 27.959)	-6.11 (± 17.657)	
Week 12 (N = 102, 109, 115)	-1.31 (± 14.526)	-5.56 (± 29.137)	-5.95 (± 15.335)	
Week 16 (N = 94, 98, 108)	-1.37 (± 17.314)	-6.94 (± 29.973)	-6.41 (± 12.685)	

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	122	118	121	
Units: mm/hr				
arithmetic mean (standard deviation)				
Week 2 (N = 109, 113, 115)	1.8 (± 14.62)	-3.9 (± 16.95)	-7.6 (± 19.25)	
Week 4 (N = 109, 112, 115)	-0.3 (± 16.63)	-6 (± 20.81)	-7.8 (± 21.9)	
Week 8 (N = 102, 107, 115)	-0.9 (± 15.44)	-6.6 (± 19.83)	-11.1 (± 21.69)	
Week 12 (N = 96, 107, 115)	0.4 (± 20.35)	-8.9 (± 20.38)	-10.8 (± 23.74)	
Week 16 (N = 92, 94, 107)	-2.4 (± 18.43)	-7.5 (± 21.91)	-11.4 (± 21.54)	

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	122	118	121	
Units: units on a scale				
least squares mean (standard error)				
Week 2 (N = 109, 111, 111)	-0.212 (± 0.085)	-0.442 (± 0.0866)	-0.794 (± 0.0853)	
Week 4 (N = 108, 112, 111)	-0.279 (± 0.0937)	-0.694 (± 0.0942)	-1.075 (± 0.093)	
Week 8 (N = 100, 107, 114)	-0.418 (± 0.1108)	-0.99 (± 0.1099)	-1.246 (± 0.1071)	
Week 12 (N = 96, 107, 111)	-0.296 (± 0.1184)	-1.021 (± 0.1161)	-1.323 (± 0.1133)	
Week 16 (N = 93, 98, 104)	-0.152 (± 0.1282)	-1.201 (± 0.1264)	-1.405 (± 0.1229)	

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	122	118	121	
Units: digits				
least squares mean (standard error)				
Week 4 (N = 55, 59, 61)	-0.713 (± 0.3861)	-1.164 (± 0.3862)	-1.526 (± 0.368)	
Week 12 (N = 52, 55, 62)	-1.012 (± 0.4639)	-2.688 (± 0.463)	-3.058 (± 0.4307)	
Week 16 (N = 45, 50, 57)	-0.47 (± 0.5358)	-2.981 (± 0.522)	-2.851 (± 0.4883)	

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 postbaseline 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	122	118	121	
Units: entheses				
least squares mean (standard error)				
Week 4 (N = 78, 72, 60)	-0.496 (± 0.1863)	-0.805 (± 0.193)	-0.92 (± 0.2042)	

Week 12 (N = 70, 68, 61)	-0.485 (± 0.2084)	-1.209 (± 0.2123)	-1.399 (± 0.2194)	
Week 16 (N = 63, 60, 56)	-0.403 (± 0.2192)	-1.099 (± 0.2243)	-1.318 (± 0.2316)	

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	122	118	121	
Units: units on a scale				
least squares mean (standard error)				
Week 12 (N = 100, 108, 112)	-0.219 (± 0.2051)	-0.86 (± 0.2019)	-1.468 (± 0.1968)	
Week 16 (N = 92, 98, 106)	-0.117 (± 0.2066)	-1.049 (± 0.2038)	-1.777 (± 0.1979)	

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	122	118	121	
Units: units on a scale				
least squares mean (standard error)				
Week 2 (N = 108, 112, 112)	-3.312 (± 0.9322)	-4.767 (± 0.9328)	-7.698 (± 0.9266)	
Week 4 (N = 103, 111, 109)	-3.54 (± 0.9621)	-7.03 (± 0.9464)	-10.23 (± 0.9423)	
Week 8 (N = 97, 108, 112)	-4.56 (± 1.1225)	-10.64 (± 1.094)	-11.94 (± 1.0747)	
Week 12 (N = 93, 106, 111)	-4.127 (± 1.2229)	-10.74 (± 1.1828)	-13.21 (± 1.1578)	
Week 16 (N = 92, 98, 105)	-1.319 (± 1.2992)	-13.1 (± 1.265)	-13.26 (± 1.232)	

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	122	118	121	
Units: percentage of participants				
number (not applicable)				
Week 2	18	33.1	38.8	
Week 4	23.8	39.8	50.4	
Week 8	23	51.7	58.7	
Week 12	24.6	53.4	65.3	
Week 16	19.7	51.7	62.8	

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	122	118	121	
Units: units on a scale				
least squares mean (standard error)				
Week 12 (N = 92, 105, 110)	5.963 (± 0.1567)	4.864 (± 0.1501)	4.276 (± 0.1467)	
Week 16 (N = 91, 98, 102)	6.133 (± 0.1676)	4.675 (± 0.1622)	4.104 (± 0.1594)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Van der Heijde modified Total Sharp Score (mTSS) at Week 24

End point title	Change from Baseline in Van der Heijde modified Total Sharp Score (mTSS) at Week 24

End point description:

The modified Total Sharp Score (mTSS) is a measure of change in joint health using radiography of the hands and feet. Bony erosions of the joints and the narrowing of the space between the joints are quantified by the erosion (ES) and joint space narrowing (JSN) scores. Erosions of the hands were scored on a scale from 0 to 5, and erosions of the feet were scored from 0 to 10. JSN was scored on a scale from 0 to 4. The total mTSS score is a sum of the erosion and joint scores and ranges from 0 (normal) to 528 (worst).
The full analysis set (all randomized participants) was used for this analysis; subjects with baseline and post-baseline results are included.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	97	104	
Units: units on a scale				
arithmetic mean (standard deviation)	0.823 (± 2.9911)	0.342 (± 1.2843)	0.356 (± 2.4669)	

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	78	90	77	
Units: percentage of participants				
number (not applicable)				
Week 2	1.3	5.6	6.5	

Week 4	2.6	18.9	28.6	
Week 8	2.6	24.4	53.2	
Week 12	5.1	37.8	61	
Week 16	7.7	40	64.9	

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	78	90	77	
Units: percentage of participants				
number (not applicable)				
Week 2	1.3	2.2	3.9	
Week 4	2.6	11.1	13	
Week 8	2.6	15.6	32.5	
Week 12	2.6	18.9	42.9	
Week 16	3.8	20	48.1	

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	78	90	77	
Units: percent change				
arithmetic mean (standard deviation)				
Week 2 (N = 74, 90, 73)	-9.37 (± 29.614)	-37.57 (± 31.835)	-48.21 (± 29.79)	
Week 4 (N = 70, 88, 73)	-10.59 (± 65.285)	-52.06 (± 39.626)	-63.47 (± 60.345)	
Week 8 (N = 68, 86, 76)	-11.95 (± 53.453)	-57.06 (± 53.538)	-74.14 (± 77.71)	
Week 12 (N = 68, 85, 75)	-2.93 (± 64.279)	-60.8 (± 44.703)	-86.69 (± 23.551)	
Week 16 (N = 63, 77, 69)	-0.26 (± 79.793)	-65.03 (± 43.748)	-87.44 (± 23.857)	

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	78	90	77	
Units: percent involvement				
least squares mean (standard error)				
Week 2 (N = 74, 90, 73)	15.642 (± 0.9755)	12.967 (± 0.9081)	13.076 (± 0.9803)	
Week 4 (N = 70, 88, 73)	15.432 (± 1.1574)	10.658 (± 1.0596)	7.819 (± 1.1391)	

Week 8 (N = 68, 86, 76)	14.928 (± 1.251)	9.693 (± 1.1375)	5.712 (± 1.2159)	
Week 12 (N = 68, 85, 75)	14.938 (± 1.2732)	8.766 (± 1.159)	3.153 (± 1.2356)	
Week 16 (N = 63, 77, 69)	15.923 (± 1.4281)	7.285 (± 1.2991)	2.308 (± 1.3841)	

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	122	118	121	
Units: units on a scale				
least squares mean (standard error)				
Week 2 (N = 112, 115, 113)	-1.335 (± 0.4176)	-2.655 (± 0.4191)	-3.661 (± 0.4194)	
Week 4 (N = 109, 114, 112)	-1.71 (± 0.4275)	-4.211 (± 0.425)	-4.967 (± 0.4245)	
Week 8 (N = 102, 111, 114)	-1.834 (± 0.456)	-4.54 (± 0.4486)	-5.499 (± 0.4453)	
Week 12 (N = 100, 108, 112)	-1.7 (± 0.4788)	-4.677 (± 0.4716)	-6.17 (± 0.4668)	
Week 16 (N = 93, 98, 106)	-1.543 (± 0.5011)	-4.498 (± 0.4945)	-6.131 (± 0.4862)	

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	122	118	121	
Units: units on a scale				
least squares mean (standard error)				
Physical Component: Week 12 (N = 100, 108, 112)	1.612 (± 0.8791)	3.806 (± 0.8706)	6.143 (± 0.8412)	
Physical Component: Week 16 (N = 92, 98, 106)	0.481 (± 0.9084)	4.715 (± 0.9019)	7.503 (± 0.8679)	
Mental Component: Week 12 (N = 100, 108, 112)	2.09 (± 0.8115)	4.812 (± 0.7977)	3.424 (± 0.7782)	
Mental Component: Week 16 (N = 92, 98, 106)	2.542 (± 0.8214)	4.4 (± 0.8098)	3.821 (± 0.7863)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Brodalumab

End point title	Plasma Concentration of Brodalumab

End point description:

Plasma concentrations are calculated using log-transformed data from subjects with measurable levels > lower limit of quantitation (LLOQ) of 50 ng/mL. The Pharmacokinetic (PK) analysis set included all subjects in the safety subset who had at least 1 evaluable PK concentration measurement.

End point type	Secondary

End point timeframe:

Weeks 1, 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	0[9]	155	154	
Units: ng/mL				
geometric mean (standard deviation)				
Week 1 (N = 129, 141)	()	2017 (± 3712.5)	5528 (± 5546.4)	
Week 2 (N = 138, 140)	()	4807 (± 6051.7)	11870 (± 9902.7)	
Week 4 (N = 106, 136)	()	2341 (± 5151.7)	8912 (± 10920)	
Week 8 (N = 51, 112)	()	2100 (± 4124)	7029 (± 11579)	
Week 12 (N = 50, 107)	()	1233 (± 3089.5)	4830 (± 12370)	
Week 16 (N = 33, 84)	()	1929 (± 2511.6)	5276 (± 10970)	

Notes:

[9] - 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 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.	
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.	

Serious adverse events	Placebo	Brodalumab 140 mg Q2W	Brodalumab 210 mg Q2W
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 159 (7.55%)	7 / 158 (4.43%)	11 / 158 (6.96%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (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
Squamous cell carcinoma of the vulva			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
Uterine leiomyoma			

subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
Vulval cancer stage 0			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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			
Vasculitis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (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
Surgical and medical procedures			
Arthrodesis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (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
Reproductive system and breast disorders			
Hydrometra			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (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
Nasal septum deviation			

subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major depression			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (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			
Arthropod bite			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (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
Eye injury			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
Injury			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
Iris injury			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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

Keratorhexis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
Spinal fracture			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (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
Tendon rupture			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (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			
Acute myocardial infarction			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
Atrial fibrillation			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Lens dislocation			

subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (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
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (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
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (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
Skin necrosis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chondropathy			

subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (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
Muscular weakness			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (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	1 / 159 (0.63%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
Synovial disorder			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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
Infected fistula			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (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
Infectious mononucleosis			

subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (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
Urosepsis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (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

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

Non-serious adverse events	Placebo	Brodalumab 140 mg Q2W	Brodalumab 210 mg Q2W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	95 / 159 (59.75%)	102 / 158 (64.56%)	98 / 158 (62.03%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	3	0
Angiomyolipoma			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Enchondroma			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Melanocytic naevus			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	1
Seborrhoeic keratosis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Diastolic hypertension			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Haematoma			

subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Hot flush			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	6 / 159 (3.77%)	2 / 158 (1.27%)	7 / 158 (4.43%)
occurrences (all)	6	2	10
Hypotension			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Peripheral venous disease			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Venous thrombosis limb			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Acrochordon excision			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Bunion operation			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Bone lesion excision			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Tooth extraction			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Wound closure			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			

Application site pruritus			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Asthenia			
subjects affected / exposed	0 / 159 (0.00%)	3 / 158 (1.90%)	0 / 158 (0.00%)
occurrences (all)	0	3	0
Chest discomfort			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Chills			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Drug intolerance			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Face oedema			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	2 / 159 (1.26%)	2 / 158 (1.27%)	1 / 158 (0.63%)
occurrences (all)	2	2	1
Foreign body reaction			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Inflammation			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Injection site erythema			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	7	1	2
Injection site haematoma			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	1	2	0
Injection site pain			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1

Injection site pruritus			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Injection site reaction			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	2 / 158 (1.27%)
occurrences (all)	0	0	2
Local swelling			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Nodule			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Medical device complication			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Oedema			
subjects affected / exposed	2 / 159 (1.26%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	2	0	0
Oedema peripheral			
subjects affected / exposed	2 / 159 (1.26%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	2	0	1
Peripheral swelling			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Pyrexia			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Drug hypersensitivity			

subjects affected / exposed	2 / 159 (1.26%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	2	0	0
Hypersensitivity			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Multiple allergies			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	2
Seasonal allergy			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Breast pain			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Endometrial hyperplasia			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Hydrometra			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Ovarian cyst			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	1
Prostatitis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Allergic sinusitis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Asthma			
subjects affected / exposed	3 / 159 (1.89%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	3	1	0
Catarrh			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	4 / 159 (2.52%)	2 / 158 (1.27%)	2 / 158 (1.27%)
occurrences (all)	5	2	2
Dyspnoea			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	3 / 159 (1.89%)	1 / 158 (0.63%)	2 / 158 (1.27%)
occurrences (all)	3	1	2
Nasal congestion			
subjects affected / exposed	3 / 159 (1.89%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	3	0	0
Respiratory disorder			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Respiratory tract congestion			
subjects affected / exposed	0 / 159 (0.00%)	2 / 158 (1.27%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Rhinitis allergic			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Rhinorrhoea			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0

Upper respiratory tract inflammation			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Agitation			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Anger			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	2 / 159 (1.26%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	2	1	0
Bruxism			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	0 / 159 (0.00%)	3 / 158 (1.90%)	0 / 158 (0.00%)
occurrences (all)	0	3	0
Depression			
subjects affected / exposed	1 / 159 (0.63%)	2 / 158 (1.27%)	0 / 158 (0.00%)
occurrences (all)	1	2	0
Emotional disorder			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 159 (0.63%)	3 / 158 (1.90%)	1 / 158 (0.63%)
occurrences (all)	1	3	1
Nightmare			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Sleep disorder			

subjects affected / exposed	0 / 159 (0.00%)	2 / 158 (1.27%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Investigations			
Alanine aminotransferase abnormal			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	3 / 159 (1.89%)	2 / 158 (1.27%)	2 / 158 (1.27%)
occurrences (all)	3	2	3
Aspartate aminotransferase abnormal			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 159 (1.26%)	0 / 158 (0.00%)	3 / 158 (1.90%)
occurrences (all)	2	0	3
Blood cholesterol increased			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Haematology test abnormal			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	3 / 159 (1.89%)	0 / 158 (0.00%)	2 / 158 (1.27%)
occurrences (all)	3	0	2
Haemoglobin decreased			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Hepatic enzyme increased			

subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
High density lipoprotein decreased			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Liver function test abnormal			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Low density lipoprotein increased			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Neutrophil count increased			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Platelet count increased			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Streptococcus test positive			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Transaminases increased			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Vitamin D decreased			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	1	1	0
Weight decreased			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Weight increased			

subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	5 / 158 (3.16%)
occurrences (all)	0	1	5
White blood cell count increased			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Arthropod bite			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	2	1	0
Burns second degree			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	4 / 159 (2.52%)	2 / 158 (1.27%)	1 / 158 (0.63%)
occurrences (all)	4	2	1
Hand fracture			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Humerus fracture			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Laceration			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	1
Ligament rupture			

subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Limb crushing injury			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Ligament sprain			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	2 / 158 (1.27%)
occurrences (all)	1	1	2
Limb injury			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	1 / 159 (0.63%)	2 / 158 (1.27%)	0 / 158 (0.00%)
occurrences (all)	1	2	0
Meniscus injury			
subjects affected / exposed	0 / 159 (0.00%)	2 / 158 (1.27%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Radius fracture			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Skin abrasion			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Synovial rupture			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Tendon rupture			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Upper limb fracture			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Wound			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Coronary artery disease			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	2 / 159 (1.26%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	2	0	0
Tachycardia			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Ageusia			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Carpal tunnel syndrome			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Cluster headache			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 159 (0.63%)	3 / 158 (1.90%)	1 / 158 (0.63%)
occurrences (all)	1	3	1
Headache			
subjects affected / exposed	4 / 159 (2.52%)	4 / 158 (2.53%)	5 / 158 (3.16%)
occurrences (all)	5	4	5
Hemianopia			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Hypoaesthesia			

subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Lethargy			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Migraine			
subjects affected / exposed	2 / 159 (1.26%)	2 / 158 (1.27%)	0 / 158 (0.00%)
occurrences (all)	2	2	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Restless legs syndrome			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	1	2	0
Resting tremor			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	3 / 159 (1.89%)	2 / 158 (1.27%)	2 / 158 (1.27%)
occurrences (all)	3	3	3
Sinus headache			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 159 (0.63%)	3 / 158 (1.90%)	2 / 158 (1.27%)
occurrences (all)	1	4	2
Iron deficiency anaemia			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	2 / 158 (1.27%)
occurrences (all)	0	0	2
Leukopenia			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	1

Lymphadenitis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Lymphadenopathy			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Microcytic anaemia			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Tinnitus			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Vertigo			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Diplopia			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Eye pain			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Iridocyclitis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			

subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Photophobia			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Uveitis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 159 (0.00%)	3 / 158 (1.90%)	0 / 158 (0.00%)
occurrences (all)	0	3	0
Abdominal pain lower			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	3 / 158 (1.90%)
occurrences (all)	0	1	3
Abdominal tenderness			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Aphthous ulcer			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Apical granuloma			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Dental caries			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0

Dental necrosis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Dental cyst			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	6 / 159 (3.77%)	5 / 158 (3.16%)	2 / 158 (1.27%)
occurrences (all)	6	5	2
Dyspepsia			
subjects affected / exposed	0 / 159 (0.00%)	3 / 158 (1.90%)	0 / 158 (0.00%)
occurrences (all)	0	3	0
Gastritis			
subjects affected / exposed	2 / 159 (1.26%)	2 / 158 (1.27%)	1 / 158 (0.63%)
occurrences (all)	2	2	1
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 159 (1.26%)	2 / 158 (1.27%)	1 / 158 (0.63%)
occurrences (all)	2	2	1
Gastrointestinal inflammation			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Gingival pain			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Glossitis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Glossodynia			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Haematemesis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1

Haematochezia			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	1	1	0
Inguinal hernia			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 159 (0.63%)	3 / 158 (1.90%)	1 / 158 (0.63%)
occurrences (all)	1	3	1
Oral mucosa erosion			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Oral mucosal erythema			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Salivary gland enlargement			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Actinic cheilitis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Asteatosis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	0 / 159 (0.00%)	2 / 158 (1.27%)	1 / 158 (0.63%)
occurrences (all)	0	2	1
Dermatitis			

subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	2 / 158 (1.27%)
occurrences (all)	0	0	2
Dermatitis contact			
subjects affected / exposed	0 / 159 (0.00%)	2 / 158 (1.27%)	0 / 158 (0.00%)
occurrences (all)	0	3	0
Drug eruption			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	2
Eczema nummular			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	1 / 159 (0.63%)	3 / 158 (1.90%)	2 / 158 (1.27%)
occurrences (all)	1	3	2
Ingrowing nail			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Nail bed inflammation			
subjects affected / exposed	0 / 159 (0.00%)	2 / 158 (1.27%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Photosensitivity reaction			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 159 (0.00%)	2 / 158 (1.27%)	2 / 158 (1.27%)
occurrences (all)	0	2	2
Pruritus generalised			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Psoriasis			
subjects affected / exposed	5 / 159 (3.14%)	1 / 158 (0.63%)	2 / 158 (1.27%)
occurrences (all)	7	1	2
Pustular psoriasis			

subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	1 / 159 (0.63%)	3 / 158 (1.90%)	1 / 158 (0.63%)
occurrences (all)	1	3	1
Rash macular			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Scar pain			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Skin erosion			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Skin ulcer			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Skin fissures			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Xeroderma			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1

Haematuria			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	1
Nephrolithiasis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Renal cyst			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Renal impairment			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Hyperthyroidism			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	2
Arthralgia			
subjects affected / exposed	1 / 159 (0.63%)	8 / 158 (5.06%)	4 / 158 (2.53%)
occurrences (all)	1	10	4
Back pain			
subjects affected / exposed	4 / 159 (2.52%)	3 / 158 (1.90%)	0 / 158 (0.00%)
occurrences (all)	4	3	0
Bone pain			

subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Bursitis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Dactylitis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Muscle contracture			
subjects affected / exposed	2 / 159 (1.26%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	2	0	0
Muscle spasms			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	2 / 158 (1.27%)
occurrences (all)	1	1	2
Musculoskeletal pain			
subjects affected / exposed	1 / 159 (0.63%)	2 / 158 (1.27%)	0 / 158 (0.00%)
occurrences (all)	1	2	0
Neck pain			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Osteopenia			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	1 / 159 (0.63%)	3 / 158 (1.90%)	1 / 158 (0.63%)
occurrences (all)	1	4	1
Psoriatic arthropathy			

subjects affected / exposed	5 / 159 (3.14%)	4 / 158 (2.53%)	1 / 158 (0.63%)
occurrences (all)	5	4	1
Spinal pain			
subjects affected / exposed	2 / 159 (1.26%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	2	0	0
Synovial cyst			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	1
Tendonitis			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	1	1	1
Tendon pain			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	2
Angular cheilitis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	2 / 158 (1.27%)
occurrences (all)	0	0	2
Candida infection			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	4 / 159 (2.52%)	5 / 158 (3.16%)	5 / 158 (3.16%)
occurrences (all)	5	5	6
Cellulitis			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	1	1	1
Chronic tonsillitis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Chronic sinusitis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0

Conjunctivitis			
subjects affected / exposed	0 / 159 (0.00%)	2 / 158 (1.27%)	1 / 158 (0.63%)
occurrences (all)	0	2	1
Conjunctivitis bacterial			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Cutaneous tuberculosis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	1 / 159 (0.63%)	2 / 158 (1.27%)	2 / 158 (1.27%)
occurrences (all)	1	2	2
Diarrhoea infectious			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Diverticulitis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 159 (0.00%)	3 / 158 (1.90%)	2 / 158 (1.27%)
occurrences (all)	0	3	2
Fungal skin infection			
subjects affected / exposed	0 / 159 (0.00%)	2 / 158 (1.27%)	2 / 158 (1.27%)
occurrences (all)	0	2	2
Eyelid infection			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	3 / 159 (1.89%)	3 / 158 (1.90%)	1 / 158 (0.63%)
occurrences (all)	3	3	1
Gastroenteritis viral			
subjects affected / exposed	0 / 159 (0.00%)	3 / 158 (1.90%)	0 / 158 (0.00%)
occurrences (all)	0	3	0
Gastroenteritis aeromonas			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0

Gastrointestinal infection			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Helicobacter gastritis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Genital infection fungal			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Helicobacter infection			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	1
Hordeolum			
subjects affected / exposed	0 / 159 (0.00%)	2 / 158 (1.27%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Influenza			
subjects affected / exposed	2 / 159 (1.26%)	1 / 158 (0.63%)	2 / 158 (1.27%)
occurrences (all)	2	1	2
Laryngitis			
subjects affected / exposed	2 / 159 (1.26%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	2	0	0
Laryngitis viral			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Lyme disease			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Lower respiratory tract infection			
subjects affected / exposed	2 / 159 (1.26%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	2	0	0
Nasopharyngitis			
subjects affected / exposed	16 / 159 (10.06%)	25 / 158 (15.82%)	22 / 158 (13.92%)
occurrences (all)	22	28	25

Oral candidiasis			
subjects affected / exposed	2 / 159 (1.26%)	0 / 158 (0.00%)	2 / 158 (1.27%)
occurrences (all)	2	0	2
Oral herpes			
subjects affected / exposed	4 / 159 (2.52%)	0 / 158 (0.00%)	4 / 158 (2.53%)
occurrences (all)	4	0	4
Oral infection			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Otitis media			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 159 (0.00%)	2 / 158 (1.27%)	2 / 158 (1.27%)
occurrences (all)	0	2	2
Pharyngitis			
subjects affected / exposed	3 / 159 (1.89%)	4 / 158 (2.53%)	2 / 158 (1.27%)
occurrences (all)	3	4	2
Pneumonia			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Pulpitis dental			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	2 / 158 (1.27%)
occurrences (all)	1	0	2

Respiratory tract infection viral			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	6 / 159 (3.77%)	0 / 158 (0.00%)	4 / 158 (2.53%)
occurrences (all)	6	0	5
Sinusitis			
subjects affected / exposed	7 / 159 (4.40%)	2 / 158 (1.27%)	2 / 158 (1.27%)
occurrences (all)	8	3	2
Skin bacterial infection			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Sinusitis bacterial			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	0 / 159 (0.00%)	2 / 158 (1.27%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Skin candida			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Subcutaneous abscess			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	2
Tinea pedis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	1	1	1
Tooth abscess			
subjects affected / exposed	2 / 159 (1.26%)	2 / 158 (1.27%)	1 / 158 (0.63%)
occurrences (all)	2	2	1
Upper respiratory tract infection			
subjects affected / exposed	10 / 159 (6.29%)	8 / 158 (5.06%)	7 / 158 (4.43%)
occurrences (all)	12	9	9

Tooth infection			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	4 / 159 (2.52%)	1 / 158 (0.63%)	3 / 158 (1.90%)
occurrences (all)	4	1	3
Viral infection			
subjects affected / exposed	1 / 159 (0.63%)	1 / 158 (0.63%)	2 / 158 (1.27%)
occurrences (all)	1	1	2
Viral sinusitis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	2
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
Electrolyte imbalance			

subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Fructose intolerance			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Gout			
subjects affected / exposed	1 / 159 (0.63%)	3 / 158 (1.90%)	0 / 158 (0.00%)
occurrences (all)	1	3	0
Hypercalcaemia			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	1 / 159 (0.63%)	2 / 158 (1.27%)	1 / 158 (0.63%)
occurrences (all)	1	2	1
Hyperkalaemia			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Hyperlipidaemia			
subjects affected / exposed	0 / 159 (0.00%)	3 / 158 (1.90%)	1 / 158 (0.63%)
occurrences (all)	0	3	1
Hypertriglyceridaemia			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	1	0	1
Hyperuricaemia			
subjects affected / exposed	1 / 159 (0.63%)	2 / 158 (1.27%)	1 / 158 (0.63%)
occurrences (all)	1	2	1
Impaired fasting glucose			
subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Lactose intolerance			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
Type 2 diabetes mellitus			

subjects affected / exposed	0 / 159 (0.00%)	0 / 158 (0.00%)	1 / 158 (0.63%)
occurrences (all)	0	0	1
Vitamin D deficiency			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 March 2014	Based on the identification, from other studies of suicidal behavior and suicidal ideation reported in brodalumab psoriasis studies, the Columbia Suicide Severity Rating (C-SSRS) and the Patient Health Questionnaire depression scale (PHQ-8) were added as instruments to assess subject eligibility and monitor subject safety (ie, stopping rules). Other minor editorial were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported