Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group, Efficacy and Safety Study of Two Doses of Apremilast (CC-10004) in Subjects with Active Psoriatic Arthritis and a Qualifying Psoriasis Lesion

Summary

EudraCT number	2010-019941-24
Trial protocol	LT SK FI GB DE ES IT
Global end of trial date	09 February 2017

Results information

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

Trial information

Trial identification

Sponsor protocol code	CC-10004-PSA-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01212770
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Celgene Corporation
Sponsor organisation address	86 Morris Avenue, Summit, United States, 07901
Public contact	Clinical Trial Disclosure, Celgene Corporation, 01 8882601599, ClinicalTrialDisclosure@Celgene.com
Scientific contact	Nikolay Delev, Celgene Corporation, 01 18882601599, ndelev@celgene.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	16 June 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the clinical efficacy of 2 doses of apremilast (20 mg or 30 mg orally twice daily [BID]), compared with placebo (PBO), on the signs and symptoms of psoriatic arthritis (PsA) after 16 weeks administration.

Protection of trial subjects:

Patient Confidentiality, Personal Data Protection and Biomarker Consent. This study was conducted in accordance with the guidelines of current Good Clinical Practice including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 September 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Ethical reason, Regulatory reason, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 7
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Lithuania: 27
Country: Number of subjects enrolled	Poland: 111
Country: Number of subjects enrolled	Romania: 25
Country: Number of subjects enrolled	Slovakia: 9
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	Switzerland: 6
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 130
Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	Australia: 44
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Russian Federation: 53

Worldwide total number of subjects	505
EEA total number of subjects	226

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)	459
From 65 to 84 years	46
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 78 study centers in 16 countries.

Pre-assignment

Screening details:

This study consisted of a 24-week randomized, double-blind, placebo-controlled phase, a 28-week randomized, double-blind active treatment phase and a 4-year open-label safety phase, for an overall study duration of 5 years.

Period 1

Period 1 title	Placebo-controlled Phase (Week 0 - 24)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

Blinding to treatment assignment was maintained at all sites until after the Week 52 database lock at Year 1, after all Week 52 analyses were completed and the results were released. At that time, active medication was provided. The blind was otherwise not to be broken during the study unless, in the opinion of the doctor, it was necessary to safely treat the subject.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants initially randomized to receive placebo tablets twice daily (BID) in the 24-week placebo-controlled phase. Participants who did not have at least 20% improvement in swollen and tender joint counts at Week 16 were re-randomized to either 20 mg or 30 mg apremilast twice daily (early escape).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets (identical in appearance to apremilast) twice daily.

Arm title	Apremilast 20 mg

Arm description:

Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 20 mg tablets twice daily

Arm title	Apremilast 30 mg

Arm description:

Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-

controlled phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 30 mg tablets twice daily

Number of subjects in period 1	Placebo	Apremilast 20 mg	Apremilast 30 mg
Started	169	169	167
Received Treatment	169	169	167
Completed Week 16	156	157	156
Early Escape at Week 16	97 [1]	76 [2]	53 [3]
Completed	146	147	145
Not completed	23	22	22
Consent withdrawn by subject	3	4	1
Adverse event, non-fatal	10	12	8
Miscellaneous	3	1	2
Lost to follow-up	1	-	3
Lack of efficacy	6	5	7
Protocol deviation	-	-	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: For all the arms, the number of subjects starting the subsequent periods were less than or equal to the number completing the preceding period, this is because not all subjects who completed the preceding period would enter the subsequent period.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: For all the arms, the number of subjects starting the subsequent periods were less than or equal to the number completing the preceding period, this is because not all subjects who completed the preceding period would enter the subsequent period.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: For all the arms, the number of subjects starting the subsequent periods were less than or equal to the number completing the preceding period, this is because not all subjects who completed the preceding period would enter the subsequent period.

Period 2

Period 2 title	Active Treatment Phase (Weeks 25 - 52)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

Blinding to treatment assignment was maintained at all sites until after the Week 52 database lock at Year 1, after all Week 52 analyses were completed and the results were released. At that time, active medication was provided. The blind was otherwise not to be broken during the study unless, in the opinion of the doctor, it was necessary to safely treat the subject.

Arms

Are arms mutually exclusive?	Yes
Arm title	Apremilast 20 mg

Arm description:

Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase continued receiving 20 mg apremilast tablets twice daily in the active treatment / long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otzela
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 20 mg tablets twice daily

Arm title	Apremilast 30 mg

Arm description:

Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-controlled phase continued receiving 30 mg apremilast tablets twice daily in the active treatment / long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 30 mg tablets twice daily

Arm title	Placebo / Apremilast 20 mg EE

Arm description:

Participants initially randomized to placebo twice daily were re-randomized due to early escape (EE) at Week 16 to receive 20 mg apremilast twice daily in the active treatment phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 20 mg tablets twice daily

Arm title	Placebo / Apremilast 20 mg XO

Arm description:

Participants initially randomized to receive placebo twice daily were re-randomized at Week 24 (XO) to receive 20 mg apremilast tablets twice daily in the active treatment phase.

Arm type	Experimental

Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 20 mg tablets twice daily

Arm title	Placebo / Apremilast 30 mg EE

Arm description:

Participants initially randomized to placebo twice daily were re-randomized due to early escape at Week 16 to receive 30 mg apremilast tablets twice daily in the active treatment phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 30 mg tablets twice daily

Arm title	Placebo / Apremilast 30 mg XO

Arm description:

Participants initially randomized to placebo twice daily in the 24-week placebo-controlled phase were re-randomized at Week 24 to receive 30 mg apremilast twice daily in the active treatment phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 30 mg tablets twice daily

Number of subjects in period 2[4]	Apremilast 20 mg	Apremilast 30 mg	Placebo / Apremilast 20 mg EE
Started	139	138	43
Completed	120	126	32
Not completed	19	12	11
Consent withdrawn by subject	6	3	3
Adverse event, non-fatal	6	2	2
Unspecified	-	1	1
Lost to follow-up	-	1	-
Lack of efficacy	7	5	4
Protocol deviation	-	-	1

Number of subjects in period 2[4]	Placebo / Apremilast 20 mg XO	Placebo / Apremilast 30 mg EE	Placebo / Apremilast 30 mg XO

Started	25	47	25
Completed	23	44	23
Not completed	2	3	2
Consent withdrawn by subject	1	1	1
Adverse event, non-fatal	-	-	1
Unspecified	-	-	-
Lost to follow-up	-	-	-
Lack of efficacy	1	2	-
Protocol deviation	-	-	-

Notes:

[4] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: For all the arms, the number of subjects starting the subsequent periods were less than or equal to the number completing the preceding period, this is because not all subjects who completed the preceding period would enter the subsequent period.

Period 3

Period 3 title	Long-term Safety Phase (Year 2)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Apremilast 20 mg

Arm description:

Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase continued receiving 20 mg apremilast tablets twice daily in the active treatment / long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 20 mg tablets twice daily

Arm title	Apremilast 30 mg

Arm description:

Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-controlled phase continued receiving 30 mg apremilast tablets twice daily in the active treatment / long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 30 mg tablets twice daily

Arm title	Placebo/Apremilast 20 mg

Arm description:	
Participants initially randomized to placebo tablets twice daily during the 24-week placebo-controlled phase were re-randomized to 20 mg apremilast tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 20 mg tablets twice daily in active treatment / long-term safety phase.	
Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Apremilast 20 mg tablets twice daily	
Arm title	Placebo/Apremilast 30 mg
Arm description:	
Participants initially randomized to placebo tablets BID during the 24-week placebo-controlled phase were re-randomized to apremilast 30 mg tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 30 mg tablets twice daily in the active treatment / long-term safety phase.	
Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Apremilast 30 mg tablets twice daily	

Number of subjects in period 3[5]	Apremilast 20 mg	Apremilast 30 mg	Placebo/Apremilast 20 mg
Started	111	121	51
Completed	88	106	42
Not completed	23	15	9
Consent withdrawn by subject	9	3	4
Adverse event, non-fatal	3	3	-
Miscellaneous	2	1	-
Non-compliance	1	-	-
Lost to follow-up	2	1	1
Lack of efficacy	6	7	4

Number of subjects in period 3[5]	Placebo/Apremilast 30 mg
Started	64
Completed	50
Not completed	14
Consent withdrawn by subject	4
Adverse event, non-fatal	2
Miscellaneous	1

Non-compliance	-
Lost to follow-up	1
Lack of efficacy	6

Notes:

[5] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: For all the arms, the number of subjects starting the subsequent periods were less than or equal to the number completing the preceding period, this is because not all subjects who completed the preceding period would enter the subsequent period.

Period 4

Period 4 title	Long-term Safety Phase (Year 3)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Apremilast 20 mg

Arm description:

Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase continued receiving 20 mg apremilast tablets twice daily in the active treatment/long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 20 mg tablets twice daily

Arm title	Apremilast 30 mg

Arm description:

Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-controlled phase continued receiving 30 mg apremilast tablets twice daily in the active treatment/long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 30 mg tablets twice daily

Arm title	Placebo/Apremilast 20 mg

Arm description:

Participants initially randomized to placebo tablets twice daily during the 24-week placebo-controlled phase were re-randomized to 20 mg apremilast tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 20 mg tablets twice daily in active treatment/long-term safety phase.

Arm type	Experimental

Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 20 mg tablets twice daily

Arm title	Placebo/Apremilast 30 mg

Arm description:

Participants initially randomized to placebo tablets BID during the 24-week placebo-controlled phase were re-randomized to apremilast 30 mg tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 30 mg tablets twice daily in the active treatment/long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 30 mg tablets twice daily

Number of subjects in period 4[6]	Apremilast 20 mg	Apremilast 30 mg	Placebo/Apremilast 20 mg
Started	87	105	42
Completed	76	94	35
Not completed	11	11	7
Consent withdrawn by subject	3	4	1
Adverse event, non-fatal	2	2	2
Miscellaneous	2	1	1
Lost to follow-up	1	-	-
Lack of efficacy	3	4	2
Protocol deviation	-	-	1

Number of subjects in period 4[6]	Placebo/Apremilast 30 mg
Started	49
Completed	44
Not completed	5
Consent withdrawn by subject	1
Adverse event, non-fatal	1
Miscellaneous	1
Lost to follow-up	-
Lack of efficacy	2
Protocol deviation	-

Notes:

[6] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: For all the arms, the number of subjects starting the subsequent periods were less than or equal to the number completing the preceding period, this is because not all subjects who completed the preceding period would enter the subsequent period.

Period 5

Period 5 title	Long-term Safety Phase (Year 4)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Apremilast 20 mg

Arm description:

Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase continued receiving 20 mg apremilast tablets twice daily in the active treatment/long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 20 mg tablets twice daily

Arm title	Apremilast 30 mg

Arm description:

Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-controlled phase continued receiving 30 mg apremilast tablets twice daily in the active treatment/long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 30 mg tablets twice daily

Arm title	Placebo/Apremilast 20 mg

Arm description:

Participants initially randomized to placebo tablets twice daily during the 24-week placebo-controlled phase were re-randomized to 20 mg apremilast tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 20 mg tablets twice daily in active treatment / long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 20 mg tablets twice daily

Arm title	Placebo/Apremilast 30 mg

Arm description:

Participants initially randomized to placebo tablets BID during the 24-week placebo-controlled phase were re-randomized to apremilast 30 mg tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 30 mg tablets twice daily in the active treatment/long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 30 mg tablets twice daily

Number of subjects in period 5	Apremilast 20 mg	Apremilast 30 mg	Placebo/Apremilast 20 mg
Started	76	94	35
Completed	71	83	32
Not completed	6	11	3
Consent withdrawn by subject	2	3	-
Adverse event, non-fatal	1	1	-
Miscellaneous	1	-	-
Non-compliance with study drug	1	1	1
Lost to follow-up	-	1	-
Lack of efficacy	1	5	2
Joined	1	0	0
1 subject not counted in year 4	1	-	-

Number of subjects in period 5	Placebo/Apremilast 30 mg
Started	44
Completed	42
Not completed	2
Consent withdrawn by subject	-
Adverse event, non-fatal	1
Miscellaneous	1
Non-compliance with study drug	-
Lost to follow-up	-
Lack of efficacy	-
Joined	0
1 subject not counted in year 4	-

Period 6

Period 6 title	Long-term Safety Phase (Year 5)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Apremilast 20 mg

Arm description:

Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase continued receiving 20 mg apremilast tablets twice daily in the active treatment / long-term safety phase. (After 30 mg apremilast BID was identified as the optimal dose, all participants receiving 20 mg apremilast BID were switched to the 30 mg apremilast BID dose).

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 20 mg tablets twice daily

Arm title	Apremilast 30 mg

Arm description:

Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-controlled phase continued receiving 30 mg apremilast tablets twice daily in the active treatment / long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 30 mg tablets twice daily

Arm title	Placebo/Apremilast 20 mg

Arm description:

Participants initially randomized to placebo tablets twice daily during the 24-week placebo-controlled phase were re-randomized to 20 mg apremilast tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 20 mg tablets twice daily in active treatment/long-term safety phase. (After 30 mg apremilast BID was identified as the optimal dose, all participants receiving 20 mg apremilast BID were switched to the 30 mg apremilast BID dose).

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 20 mg tablets twice daily

Arm title	Placebo/Apremilast 30 mg

Arm description:

Participants initially randomized to placebo tablets BID during the 24-week placebo-controlled phase were re-randomized to apremilast 30 mg tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 30 mg tablets twice daily in the active treatment / long-term safety phase.

Arm type	Experimental
Investigational medicinal product name	CC-10004
Investigational medicinal product code	
Other name	Otezla
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Apremilast 30 mg tablets twice daily

Number of subjects in period 6[7]	Apremilast 20 mg	Apremilast 30 mg	Placebo/Apremilast 20 mg
Started	70	83	32
Completed	68	72	30
Not completed	2	11	2
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	2	1	1
Adverse event, non-fatal	-	2	-
Miscellaneous	-	3	-
Missing	-	1	-
Lack of efficacy	-	4	-

Number of subjects in period 6[7]	Placebo/Apremilast 30 mg
Started	42
Completed	41
Not completed	1
Adverse event, serious fatal	-
Consent withdrawn by subject	-
Adverse event, non-fatal	1
Miscellaneous	-
Missing	-
Lack of efficacy	-

Notes:

[7] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: For all the arms, the number of subjects starting the subsequent periods were less than or equal to the number completing the preceding period, this is because not all subjects who completed the preceding period would enter the subsequent period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants initially randomized to receive placebo tablets twice daily (BID) in the 24-week placebo-controlled phase. Participants who did not have at least 20% improvement in swollen and tender joint counts at Week 16 were re-randomized to either 20 mg or 30 mg apremilast twice daily (early escape).	
Reporting group title	Apremilast 20 mg
Reporting group description:	
Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase.	
Reporting group title	Apremilast 30 mg
Reporting group description:	
Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-controlled phase.	

Reporting group values	Placebo	Apremilast 20 mg	Apremilast 30 mg
Number of subjects	169	169	167
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	155	152	152
From 65-84 years	14	17	15
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	49.5	49.6	49.9
standard deviation	± 11.64	± 12.10	± 11.38
Gender, Male/Female Units: Subjects			
Female	91	90	88
Male	78	79	79
Duration of psoriatic arthritis Units: years			
arithmetic mean	6.78	7.74	7.48
standard deviation	± 6.463	± 7.690	± 7.646

Reporting group values	Total		
Number of subjects	505		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	459		
From 65-84 years	46		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female			
Units: Subjects			
Female	269		
Male	236		
Duration of psoriatic arthritis			
Units: years			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants initially randomized to receive placebo tablets twice daily (BID) in the 24-week placebo-controlled phase. Participants who did not have at least 20% improvement in swollen and tender joint counts at Week 16 were re-randomized to either 20 mg or 30 mg apremilast twice daily (early escape).	
Reporting group title	Apremilast 20 mg
Reporting group description:	
Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase.	
Reporting group title	Apremilast 30 mg
Reporting group description:	
Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-controlled phase.	
Reporting group title	Apremilast 20 mg
Reporting group description:	
Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase continued receiving 20 mg apremilast tablets twice daily in the active treatment / long-term safety phase.	
Reporting group title	Apremilast 30 mg
Reporting group description:	
Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-controlled phase continued receiving 30 mg apremilast tablets twice daily in the active treatment / long-term safety phase.	
Reporting group title	Placebo / Apremilast 20 mg EE
Reporting group description:	
Participants initially randomized to placebo twice daily were re-randomized due to early escape (EE) at Week 16 to receive 20 mg apremilast twice daily in the active treatment phase.	
Reporting group title	Placebo / Apremilast 20 mg XO
Reporting group description:	
Participants initially randomized to receive placebo twice daily were re-randomized at Week 24 (XO) to receive 20 mg apremilast tablets twice daily in the active treatment phase.	
Reporting group title	Placebo / Apremilast 30 mg EE
Reporting group description:	
Participants initially randomized to placebo twice daily were re-randomized due to early escape at Week 16 to receive 30 mg apremilast tablets twice daily in the active treatment phase.	
Reporting group title	Placebo / Apremilast 30 mg XO
Reporting group description:	
Participants initially randomized to placebo twice daily in the 24-week placebo-controlled phase were re-randomized at Week 24 to receive 30 mg apremilast twice daily in the active treatment phase.	
Reporting group title	Apremilast 20 mg
Reporting group description:	
Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase continued receiving 20 mg apremilast tablets twice daily in the active treatment / long-term safety phase.	
Reporting group title	Apremilast 30 mg
Reporting group description:	
Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-controlled phase continued receiving 30 mg apremilast tablets twice daily in the active treatment / long-term safety phase.	
Reporting group title	Placebo/Apremilast 20 mg
Reporting group description:	
Participants initially randomized to placebo tablets twice daily during the 24-week placebo-controlled phase were re-randomized to 20 mg apremilast tablets twice daily at Week 16 or Week 24 and	

continued receiving apremilast 20 mg tablets twice daily in active treatment / long-term safety phase.

Reporting group title	Placebo/Apremilast 30 mg

Reporting group description:

Participants initially randomized to placebo tablets BID during the 24-week placebo-controlled phase were re-randomized to apremilast 30 mg tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 30 mg tablets twice daily in the active treatment / long-term safety phase.

Reporting group title	Apremilast 20 mg

Reporting group description:

Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase continued receiving 20 mg apremilast tablets twice daily in the active treatment/long-term safety phase.

Reporting group title	Apremilast 30 mg

Reporting group description:

Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-controlled phase continued receiving 30 mg apremilast tablets twice daily in the active treatment/long-term safety phase.

Reporting group title	Placebo/Apremilast 20 mg

Reporting group description:

Participants initially randomized to placebo tablets twice daily during the 24-week placebo-controlled phase were re-randomized to 20 mg apremilast tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 20 mg tablets twice daily in active treatment/long-term safety phase.

Reporting group title	Placebo/Apremilast 30 mg

Reporting group description:

Participants initially randomized to placebo tablets BID during the 24-week placebo-controlled phase were re-randomized to apremilast 30 mg tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 30 mg tablets twice daily in the active treatment/long-term safety phase.

Reporting group title	Apremilast 20 mg

Reporting group description:

Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase continued receiving 20 mg apremilast tablets twice daily in the active treatment/long-term safety phase.

Reporting group title	Apremilast 30 mg

Reporting group description:

Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-controlled phase continued receiving 30 mg apremilast tablets twice daily in the active treatment/long-term safety phase.

Reporting group title	Placebo/Apremilast 20 mg

Reporting group description:

Participants initially randomized to placebo tablets twice daily during the 24-week placebo-controlled phase were re-randomized to 20 mg apremilast tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 20 mg tablets twice daily in active treatment / long-term safety phase.

Reporting group title	Placebo/Apremilast 30 mg

Reporting group description:

Participants initially randomized to placebo tablets BID during the 24-week placebo-controlled phase were re-randomized to apremilast 30 mg tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 30 mg tablets twice daily in the active treatment/long-term safety phase.

Reporting group title	Apremilast 20 mg

Reporting group description:

Participants initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase continued receiving 20 mg apremilast tablets twice daily in the active treatment / long-term safety phase. (After 30 mg apremilast BID was identified as the optimal dose, all participants receiving 20 mg apremilast BID were switched to the 30 mg apremilast BID dose).

Reporting group title	Apremilast 30 mg

Reporting group description:

Participants initially randomized to 30 mg apremilast tablets twice daily during the 24-week placebo-controlled phase continued receiving 30 mg apremilast tablets twice daily in the active treatment / long-term safety phase.

Reporting group title	Placebo/Apremilast 20 mg

Reporting group description:

Participants initially randomized to placebo tablets twice daily during the 24-week placebo-controlled phase were re-randomized to 20 mg apremilast tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 20 mg tablets twice daily in active treatment/long-term safety phase. (After 30 mg apremilast BID was identified as the optimal dose, all participants receiving 20 mg apremilast BID were switched to the 30 mg apremilast BID dose).

Reporting group title	Placebo/Apremilast 30 mg

Reporting group description:

Participants initially randomized to placebo tablets BID during the 24-week placebo-controlled phase were re-randomized to apremilast 30 mg tablets twice daily at Week 16 or Week 24 and continued receiving apremilast 30 mg tablets twice daily in the active treatment / long-term safety phase.

Subject analysis set title	Placebo /Apremilast 20 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects initially randomized to placebo tablets twice daily during the 24-week placebo-controlled phase were re-randomized to apremilast 20 mg twice daily at Week 16 or Week 24 and continued receiving apremilast 20 mg twice daily in the active treatment/long-term safety phase.

Subject analysis set title	Placebo/Apremilast 30 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects initially randomized to placebo tablets twice daily during the 24-week placebo-controlled phase were re-randomized to apremilast 30 mg twice daily at Week 16 or Week 24 and continued receiving apremilast 30 mg twice daily in the active treatment/long-term safety phase.

Subject analysis set title	Apremilast 20 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects initially randomized to 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase continued receiving 20 mg apremilast twice daily in the active treatment/long-term safety phase.

Subject analysis set title	Apremilast 30 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Participants initially randomized to 30 mg apremilast tablets twice daily in the 24-week placebo-controlled phase continued receiving 30 mg apremilast twice daily in the active treatment/long-term safety phase.

Subject analysis set title	Apremilast 20 mg (Pre-switch)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects who received apremilast 20 mg twice daily regardless of when the apremilast exposure started (at Week 0, 16 or 24). Only the TEAEs that occurred during apremilast 20 mg BID treatment (before the switch to 30 mg apremilast) were included

Subject analysis set title	Apremilast 20 mg/30 mg (Post-switch)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects who switched from apremilast 20 mg twice daily to apremilast 30 mg twice daily. Only the TEAEs that occurred during APR 30 mg BID treatment were included.

Subject analysis set title	Apremilast 30 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects who received apremilast 30 mg twice daily, regardless of when the apermilast-exposure started (at Week 0, 16 or 24).

Subject analysis set title	Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who received placebo tablets twice daily in the 24-week placebo-controlled phase.

Subject analysis set title	Apremilast 20 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who received 20 mg apremilast tablets twice daily in the 24-week placebo-controlled phase.

Subject analysis set title	Apremilast 30 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who received 30 mg apremilast tablets twice daily in the 24-week placebo-controlled phase.

Primary: Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 16

End point title	Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 16

End point description:

A subject was a responder if the following 3 criteria for improvement from Baseline were met: • ≥ 20% improvement in 78 tender joint count; • ≥ 20% improvement in 76 swollen joint count; and • ≥ 20% improvement in at least 3 of the 5 following parameters: ◦ Patient's assessment of pain (measured on a 100 mm visual analog scale [VAS]); ◦ Patient's global assessment of disease activity (measured on a 100 mm VAS); ◦ Physician's global assessment of disease activity (measured on a 100 mm VAS); ◦ Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index (HAQ-DI)); ◦ C-Reactive Protein. Full analysis set (FAS) = subjects randomized as specified per protocol; subjects who were randomized in error and did not receive any dose of study drug were excluded. Subjects who withdrew early who did not have sufficient data for a determination of response status at Week 16 were counted as non-responders

End point type	Primary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	169	167	
Units: percentage of participants				
number (not applicable)	18.3	28.4	40.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	22.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	13
upper limit	31.6

Notes:

[1] - The percentage of participants with an ACR20 response was compared using a Cochran-Mantel-Haenszel (CMH) test. The Hochberg procedure was used to maintain the Type 1 error at the 0.05 significance level. The results were considered statistically significant if both the 30 mg apremilast dose versus placebo comparison and the 20 mg versus placebo comparison were statistically significant at the 0.05 significance level, or one of the comparisons was statistically significant at the 0.025 level.
[2] - 2-sided p-value is based on the CMH test adjusting for baseline disease modifying antirheumatic drug (DMARD) use and ≥ 3% body surface area (BSA) psoriasis involvement at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	338
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.0295 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	9.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	18.6

Notes:

[3] - In order to maintain the Type 1 error at the 0.05 significance level, the Hochberg procedure was to be used. The results of the endpoint were to be considered statistically significant if both the 30 mg apremilast dose versus placebo comparison and the 20 mg versus placebo comparison were statistically significant at the 0.05 significance level, or one of the comparisons was statistically significant at the 0.025 level.
[4] - 2-sided p-value is based on the CMH test adjusting for baseline disease modifying antirheumatic drug (DMARD) use and ≥ 3% body surface area (BSA) psoriasis involvement at baseline.

Secondary: Change From Baseline in Health Assessment Questionnaire- Disability Index (HAQ-DI) at Week 16

End point title	Change From Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) at Week 16

End point description:

The Health Assessment Questionnaire - Disability Index is a patient-reported questionnaire consisting of 20 questions referring to eight domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and usual activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task are summed and averaged to provide an overall score ranging from 0 to 3, where zero represents no disability and three very severe, high-dependency disability. Negative mean changes from Baseline in the overall score indicate improvement in functional ability. FAS population. Subjects with a baseline value and at least 1 post-baseline value at or prior to Week 16 are included; LOCF imputation was used.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	163	163	160	
Units: units on a scale				
least squares mean (standard error)	-0.065 (± 0.0335)	-0.131 (± 0.0337)	-0.192 (± 0.0339)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.0073 [6]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.127
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	-0.034

Notes:

[5] - Pairwise comparisons (30 mg vs placebo and 20 mg vs placebo) were conducted conditional on the primary endpoint results. If the primary endpoint was statistically significant for both apremilast dose groups, pairwise comparisons for the HAQ-DI were to be evaluated at the 0.05 level using the Hochberg procedure. If only one apremilast dose was statistically significant, then only the comparison between that apremilast dose and placebo was conducted for the HAQ-DI score, at the 0.025 level.
[6] - Based on an analysis of covariance (ANCOVA) model with treatment group and baseline DMARD use and ≥ 3% BSA psoriasis involvement as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Apremilast 20 mg v Placebo
Number of subjects included in analysis	326
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.1619 [8]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.066
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.158
upper limit	0.027

Notes:

[7] - Pairwise comparisons (30 mg vs placebo and 20 mg vs placebo) were conducted conditional on the primary endpoint results. If the primary endpoint was statistically significant for both apremilast dose groups, pairwise comparisons for the HAQ-DI were to be evaluated at the 0.05 level using the Hochberg procedure. If only one apremilast dose was statistically significant, then only the comparison between that apremilast dose and placebo was conducted for the HAQ-DI score, at the 0.025 level.

[8] - Based on an analysis of covariance (ANCOVA) model with treatment group and baseline DMARD use and ≥ 3% BSA psoriasis involvement as factors and the baseline value as a covariate

Secondary: Percentage of Participants With an ACR 20 Response at Week 24

End point title	Percentage of Participants With an ACR 20 Response at Week 24

End point description:

Percentage of participants with an American College of Rheumatology 20% (ACR20) response. A participant was a responder if the following 3 criteria for improvement from Baseline were met: • ≥ 20% improvement in 78 tender joint count; • ≥ 20% improvement in 76 swollen joint count; and • ≥ 20% improvement in at least 3 of the 5 following parameters: ◦ Patient's assessment of pain (measured on a 100 mm visual analog scale [VAS]); ◦ Patient's global assessment of disease activity (measured on a 100 mm VAS); ◦ Physician's global assessment of disease activity (measured on a 100 mm VAS); ◦ Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index (HAQ-DI)); ◦ C-Reactive Protein. FAS population; subjects who discontinued early, escaped early at Week 16 or who did not have sufficient data for a definitive determination of response status at Week 24 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	169	167	
Units: percentage of participants				
number (not applicable)	15.4	26.6	31.1	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.0007 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	15.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.7
upper limit	24.3

Notes:

[9] - Secondary endpoints from the placebo-controlled period (Weeks 16 and 24) were analyzed in a hierarchical fashion to control the Type I error rate as described above. Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.
[10] - Two-sided p-value is based on the Cochran-Mantel-Haenszel test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	338
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.011 [12]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	11.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.7
upper limit	19.5

Notes:

[11] - Secondary endpoints from the placebo-controlled period (Weeks 16 and 24) were analyzed in a hierarchical fashion to control the Type I error rate as described above. Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.
[12] - 2-sided p-value is based on the Cochran-Mantel-Haenszel test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Change From Baseline in Health Assessment Questionnaire- Disability Index (HAQ-DI) at Week 24

End point title	Change From Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) at Week 24

End point description:

The HAQ-DI is a patient-reported questionnaire consisting of 20 questions referring to eight domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and usual activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task are summed and averaged to provide an overall score ranging from 0 to 3, where zero represents no disability and three very severe, high-dependency disability. Negative mean changes from Baseline in the overall score indicate improvement in functional ability. Subjects with a baseline value and at least 1 post-baseline value at or prior to Week 24 are included; LOCF imputation was used. The Week 16 value was carried over to Week 24 for participants who escaped early at Week 16

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	163	164	161	
Units: units on a scale				
least squares mean (standard error)	-0.053 (± 0.0350)	-0.137 (± 0.0351)	-0.192 (± 0.0353)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	324
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.005 [14]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.139
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.236
upper limit	-0.042

Notes:

[13] - Secondary endpoints from the placebo-controlled period (Weeks 16 and 24) were analyzed in a hierarchical fashion to control the Type I error rate as described above.
[14] - Based on an ANCOVA model with treatment group, baseline DMARD use and ≥ 3% BSA psoriasis involvement as factors and the baseline value as a covariate

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	327
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.086 [16]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.084
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.181
upper limit	0.012

Notes:

[15] - Secondary endpoints from the placebo-controlled period (Weeks 16 and 24) were analyzed in a hierarchical fashion to control the Type I error rate as described above.
[16] - Based on an ANCOVA model with treatment group, baseline DMARD use and ≥ 3% BSA psoriasis involvement as factors and the baseline value as a covariate.

Secondary: Change From Baseline in 36-item Short Form Health Survey (SF-36) Physical Functioning Domain at Week 16

End point title	Change From Baseline in 36-item Short Form Health Survey (SF-36) Physical Functioning Domain at Week 16

End point description:

The Medical Outcome Study Short Form 36-Item Health Survey, Version 2 (SF-36) is a self-administered instrument that measures the impact of disease on overall quality of life and consists of 36 questions in eight domains (physical function, pain, general and mental health, vitality, social function, physical and emotional health). Norm-based scores were used in analyses, calibrated so that 50 is the average score and the standard deviation equals 10. Higher scores indicate a higher level of functioning. The physical functioning domain assesses limitations in physical activities because of health problems. A positive change from Baseline score indicates an improvement. Full analysis set; participants with a baseline value and at least 1 post-baseline value at or prior to Week 16 are included; LOCF was used.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	162	162	160	
Units: units on a scale				
least squares mean (standard error)	1.14 (± 0.589)	2.29 (± 0.592)	3.47 (± 0.594)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.0053 [18]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	3.95

Notes:

[17] - Secondary endpoints from the placebo-controlled period (Weeks 16 and 24) were analyzed in a hierarchical fashion to control the Type I error rate as described above.

[18] - Based on an analysis of covariance model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg

Number of subjects included in analysis	324
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	= 0.1658 [20]
Method	ANCOVA
Parameter estimate	LS mean Difference
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	2.77

Notes:

[19] - Secondary endpoints from the placebo-controlled period (Weeks 16 and 24) were analyzed in a hierarchical fashion to control the Type I error rate as described above.
[20] - Based on an analysis of covariance model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Secondary: Percentage of Participants With a Modified Psoriatic Arthritis Response Criteria (PsARC) Response at Week 16

End point title	Percentage of Participants With a Modified Psoriatic Arthritis Response Criteria (PsARC) Response at Week 16

End point description:

Modified PsARC response is defined as improvement in at least 2 of the 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: • 78 tender joint count, • 76 swollen joint count, • Patient 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 global assessment of disease activity, measured on a 100 mm VAS, where 0 mm = lowest disease activity and 100 mm = highest. Improvement or worsening in joint counts is defined as decrease or increase, respectively, from baseline by ≥ 30%, and improvement or worsening in global assessments is defined as decrease or increase, respectively, from baseline by ≥ 20 mm VAS. Full analysis set; Participants who discontinued early, or who did not have sufficient data for a definitive determination of response status at Week 16 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	169	167	
Units: percentage of participants				
number (not applicable)	27.2	37.9	52.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	< 0.0001 [22]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	25.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.5
upper limit	35.3

Notes:

[21] - Secondary endpoints from the placebo-controlled period (Weeks 16 and 24) were analyzed in a hierarchical fashion to control the Type I error rate as described above.
[22] - The 2-sided p-value is based on the CMH test adjusting for baseline DMARD use and ≥ 3% BSA psoriasis involvement at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	338
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	= 0.0372 [24]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	10.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	20

Notes:

[23] - Secondary endpoints from the placebo-controlled period (Weeks 16 and 24) were analyzed in a hierarchical fashion to control the Type I error rate as described above.
[24] - The 2-sided p-value is based on the CMH test adjusting for baseline DMARD use and ≥ 3% BSA psoriasis involvement at baseline.

Secondary: Percentage of Participants Achieving a ≥ 75% Improvement in Psoriasis Area and Severity Index Score (PASI75) at Week 16

End point title	Percentage of Participants Achieving a ≥ 75% Improvement in Psoriasis Area and Severity Index Score (PASI75) at Week 16

End point description:

The percentage of participants with Baseline psoriasis body surface area (BSA) involvement ≥ 3% who achieved 75% or greater improvement from Baseline in Psoriasis Area and Severity Index (PASI) score after 16 weeks of treatment. The Psoriasis Area and Severity Index (PASI) score is a combination of the intensity of psoriasis, assessed by erythema (reddening), induration (plaque thickness) and desquamation (scaling) scored on a scale from 0 (none) to 4 (very severe), together with the percentage of the area affected, rated on a scale from 0 (no involvement) to 6 (90% to 100% involvement). PASI scoring is performed at four body areas, the head, arms, trunk, and legs. The total PASI score ranges from 0 to 72. The higher the total score, the more severe the disease. FAS population with BSA ≥3%; LOCF was used. Participants who did not have sufficient data for a definitive

determination of response status at Week 16 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	91	90	
Units: percentage of participants				
number (not applicable)	7.9	20.9	22.2	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 2 strata of baseline DMARD with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	= 0.0062 [26]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	14.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.5
upper limit	24.8

Notes:

[25] - Secondary endpoints from the placebo-controlled period (Weeks 16 and 24) were analyzed in a hierarchical fashion to control the Type I error rate as described above.

[26] - The 2-sided p-value is based on the CMH test adjusting for baseline DMARD use.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 2 strata of baseline DMARD with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg

Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	= 0.0134 [28]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	13
Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	23.1

Notes:

[27] - Secondary endpoints from the placebo-controlled period (Weeks 16 and 24) were analyzed in a hierarchical fashion to control the Type I error rate as described above.
[28] - The 2-sided p-value is based on the CMH test adjusting for baseline DMARD use.

Secondary: Change from Baseline in Patient's Assessment of Pain at Week 16

End point title	Change from Baseline in Patient's Assessment of Pain at Week 16

End point description:

The participant was asked to place a vertical line on a 100-mm visual analog scale on which the left-hand boundary (score = 0 mm) represents "no pain," and the right-hand boundary (score = 100 mm) represents "pain as severe as can be imagined." The distance from the mark to the left-hand boundary was recorded in millimeters. Full analysis set; participants with a baseline value and at least 1 postbaseline value at or prior to Week 16 are included; LOCF was used.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	164	163	161	
Units: mm				
least squares mean (standard error)	-4.9 (± 1.79)	-8.6 (± 1.80)	-12.7 (± 1.81)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	= 0.0021 [30]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-7.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.8
upper limit	-2.9

Notes:

[29] - Secondary endpoints from the placebo-controlled period (Weeks 16 and 24) were analyzed in a hierarchical fashion to control the Type I error rate as described above.
[30] - Based on an ANCOVA model with treatment group, baseline DMARD use and ≥ 3% BSA psoriasis involvement as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	327
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	= 0.1482 [32]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.6
upper limit	1.3

Notes:

[31] - Secondary endpoints from the placebo-controlled period (Weeks 16 and 24) were analyzed in a hierarchical fashion to control the Type I error rate as described above.
[32] - Based on an ANCOVA model with treatment group, baseline DMARD use and ≥ 3% BSA psoriasis involvement as factors and the baseline value as a covariate.

Secondary: Change From Baseline in Maastricht Ankylosing Spondylitis Entheses Score (MASES) at Week 16

End point title	Change From Baseline in Maastricht Ankylosing Spondylitis Entheses Score (MASES) at Week 16

End point description:

The Maastricht Ankylosing Spondylitis Enthesitis Score quantitates inflammation of the entheses (enthesitis) by assessing pain at the following entheses (sites where tendons or ligaments insert into the bone): 1st costochondral joints left/right; 7th costochondral joints left/right; posterior superior iliac spine left/right; anterior superior iliac spine left/right; iliac crest left/right; 5th lumbar spinous process; and the proximal insertion of the Archilles tendon left/right. The MASES, ranging from 0 to 13, is the number of painful entheses out of 13 entheses. Full analysis set; participants with a baseline MASES > 0 (i.e., pre-existing enthesopathy) and at least 1 postbaseline value at or prior to Week 16 are included; LOCF was used.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	106	93	107	
Units: units on a scale				
least squares mean (standard error)	-0.7 (± 0.27)	-0.7 (± 0.29)	-1.0 (± 0.27)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5349 [33]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.5

Notes:

[33] - Based on an ANCOVA model with treatment group, baseline DMARD use and ≥ 3% BSA psoriasis involvement as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8231 [34]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.9

Notes:

[34] - Based on an ANCOVA model with treatment group, baseline DMARD use and ≥ 3% BSA psoriasis involvement as factors and the baseline value as a covariate.

Secondary: Change From Baseline in Dactylitis Severity Score at Week 16

End point title	Change From Baseline in Dactylitis Severity Score at Week 16

End point description:

Dactylitis is characterized by swelling of the entire finger or toe. Each digit on the hands and feet was rated as zero for no dactylitis or 1 for dactylitis present. The dactylitis severity score is the sum of the individual scores for each digit. The dactylitis severity score, ranging from 0 to 20, is the number of

digits on the hands and feet with dactylitis present. Participants with a baseline dactylitis severity score > 0 (i.e., pre-existing dactylitis) and at least 1 postbaseline value at or prior to Week 16 are included. LOCF was used.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	70	76	
Units: units on a scale				
least squares mean (standard error)	-1.3 (± 0.34)	-1.7 (± 0.33)	-2.1 (± 0.32)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.072 [35]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.1

Notes:

[35] - Based on an analysis of covariance model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3641 [36]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.5

Notes:

[36] - Based on an analysis of covariance model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Secondary: Change From Baseline in Clinical Disease Activity Index (CDAI) at Week 16

End point title	Change From Baseline in Clinical Disease Activity Index (CDAI) at Week 16

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 10 cm visual analog scale (VAS), where 0 cm = lowest disease activity and 10 cm = highest; • Physician's Global Assessment of Disease Activity -measured on a 10 cm VAS, where 0 cm = lowest disease activity and 10 cm = highest. The CDAI score ranges from 0-76 where lower scores indicate less disease activity. The following thresholds of disease activity have been defined for the CDAI: Remission: ≤ 2.8 Low Disease Activity: > 2.8 and ≤ 10 Moderate Disease Activity: > 10 and ≤ 22 High Disease Activity: > 22. Full analysis set; participants with a baseline value and at least 1 postbaseline value at or prior to Week 16 are included. LOCF was used.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	154	156	
Units: units on a scale				
least squares mean (standard error)	-2.76 (± 0.869)	-4.61 (± 0.886)	-7.70 (± 0.881)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001 [37]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-4.94

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.34
upper limit	-2.53

Notes:

[37] - Based on an analysis of covariance model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1325 [38]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.27
upper limit	0.56

Notes:

[38] - Based on an analysis of covariance model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Secondary: Change From Baseline in the Disease Activity Score (DAS28) at Week 16

End point title	Change From Baseline in the Disease Activity Score (DAS28) at Week 16

End point description:

The DAS28 measures the severity of disease at a specific time and is derived from the following variables: • 28 tender joint count • 28 swollen joint count, which do not include the distal interphalangeal (DIP) joints, the hip joint, or the joints below the knee; • C-reactive protein (CRP) • Patient's global assessment of disease activity. DAS28(CRP) scores range from 0 to approximately 10, with the upper bound dependent on the highest possible level of CRP. A DAS28 score higher than 5.1 indicates high disease activity, a DAS28 score less than 3.2 indicates low disease activity, and a DAS28 score less than 2.6 indicates clinical remission. Full analysis set; participants with a baseline value and at least 1 post-baseline value at or prior to Week 16 are included. LOCF was used.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	163	160	160	
Units: units on a scale				
least squares mean (standard error)	-0.28 (± 0.084)	-0.54 (± 0.085)	-0.74 (± 0.085)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001 [39]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.24

Notes:

[39] - Based on an analysis of covariance model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0237 [40]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.04

Notes:

[40] - Based on an analysis of covariance model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate

Secondary: Change From Baseline in the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Score at Week 16

End point title	Change From Baseline in the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Score at Week 16

End point description:

The FACIT-Fatigue scale is a 13-item self-administered questionnaire that assesses both the physical and functional consequences of fatigue. Each question is answered on a 5-point scale, where 0 means "not at all," and 4 means "very much." The FACIT-Fatigue scale score ranges from 0 to 52, with higher

scores denoting lower levels of fatigue. Full analysis set; participants with a baseline value and at least 1 post-baseline value at or prior to Week 16 are included. LOCF was used.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	160	160	160	
Units: units on a scale				
least squares mean (standard error)	1.18 (± 0.640)	1.86 (± 0.643)	3.72 (± 0.641)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0049 [41]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	4.3

Notes:

[41] - Based on an analysis of covariance model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4505 [42]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	2.44

Notes:

[42] - Based on an analysis of covariance model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Secondary: Change From Baseline in 36-item Short Form Health Survey (SF-36) Physical Functioning Domain at Week 24

End point title	Change From Baseline in 36-item Short Form Health Survey (SF-36) Physical Functioning Domain at Week 24

End point description:

The Medical Outcome Study Short Form 36-Item Health Survey, Version 2 (SF-36) is a self-administered instrument that measures the impact of disease on overall quality of life and consists of 36 questions in eight domains (physical function, pain, general and mental health, vitality, social function, physical and emotional health). Norm-based scores were used in analyses, calibrated so that 50 is the average score and the standard deviation equals 10. Higher scores indicate a higher level of functioning. The physical functioning domain assesses limitations in physical activities because of health problems. A positive change from Baseline score indicates an improvement. Full analysis set; participants with a baseline value and at least 1 post-baseline value at or prior to Week 24 are included; LOCF imputation was used. The Week 16 value was carried over to Week 24 for participants who escaped early at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	162	163	161	
Units: units on a scale				
least squares mean (standard error)	1.03 (± 0.581)	2.71 (± 0.582)	3.37 (± 0.585)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0043 [43]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	3.94

Notes:

[43] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0404 [44]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	3.27

Notes:

[44] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Secondary: Percentage of Participants With a Modified Psoriatic Arthritis Response Criteria (PsARC) Response at Week 24

End point title	Percentage of Participants With a Modified Psoriatic Arthritis Response Criteria (PsARC) Response at Week 24

End point description:

Modified PsARC response is defined as improvement in at least 2 of the 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: • 78 tender joint count, • 76 swollen joint count, • Patient 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 global assessment of disease activity, measured on a 100 mm VAS, where 0 mm = lowest disease activity and 100 mm = highest. Improvement or worsening in joint counts is defined as decrease or increase, respectively, from baseline by ≥ 30%, and improvement or worsening in global assessments is defined as decrease or increase, respectively, from baseline by ≥ 20 mm VAS. Full analysis set; Participants who discontinued early, escaped early at Week 16 or who did not have sufficient data for a definitive determination of response status at Week 24 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	169	167	
Units: percentage of participants				
number (not applicable)	23.1	32.0	44.3	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline

DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [45]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	21.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.5
upper limit	30.9

Notes:

[45] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	338
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0661 [46]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	8.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	18

Notes:

[46] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants Achieving a ≥ 75% Improvement in Psoriasis Area and Severity Index Score (PASI75) at Week 24

End point title	Percentage of Participants Achieving a ≥ 75% Improvement in Psoriasis Area and Severity Index Score (PASI75) at Week 24

End point description:

The percentage of participants with Baseline psoriasis body surface area (BSA) involvement ≥ 3% who achieved 75% or greater improvement from Baseline in Psoriasis Area and Severity Index (PASI) score after 24 weeks of treatment. The Psoriasis Area and Severity Index (PASI) score is a combination of the intensity of psoriasis, assessed by erythema (reddening), induration (plaque thickness) and desquamation (scaling) scored on a scale from 0 (none) to 4 (very severe), together with the percentage of the area affected, rated on a scale from 0 (no involvement) to 6 (90% to 100% involvement). PASI scoring is performed at four body areas, the head, arms, trunk, and legs. The total PASI score ranges from 0 to 72. The higher the total score, the more severe the disease. FAS population with BSA ≥3%; LOCF was used. Participants who did not have sufficient data for a definitive determination of response status at Week 24 were counted as non-responders

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	91	90	
Units: percentage of participants				
number (not applicable)	11.2	22.2	25.6	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 2 strata of baseline DMARD use with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0099 [47]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	14.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.8
upper limit	25.7

Notes:

[47] - Two-sided p-value is based on the Cochran-Mantel-Haenszel test adjusting for baseline DMARD use.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 2 strata of baseline DMARD use with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0515 [48]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	10.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	21.4

Notes:

[48] - Two-sided p-value is based on the Cochran-Mantel-Haenszel test adjusting for baseline DMARD use

Secondary: Change From Baseline in Patient's Assessment of Pain at Week 24

End point title	Change From Baseline in Patient's Assessment of Pain at Week 24

End point description:

The participant was asked to place a vertical line on a 100-mm visual analog scale on which the left-hand boundary (score = 0 mm) represents "no pain," and the right-hand boundary (score = 100 mm) represents "pain as severe as can be imagined." The distance from the mark to the left-hand boundary was recorded in millimeters. Full analysis set; participants with a baseline value and at least 1 post-baseline value at or prior to Week 24 are included; LOCF imputation was used. The Week 16 value was carried over to Week 24 for participants who escaped early at Week 16.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	164	164	162	
Units: mm				
least squares mean (standard error)	-4.4 (± 1.75)	-8.2 (± 1.76)	-10.9 (± 1.77)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	326
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008 [49]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.4
upper limit	-1.7

Notes:

[49] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	328
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1218 [50]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.6
upper limit	1

Notes:

[50] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Secondary: Change From Baseline in Maastricht Ankylosing Spondylitis Entheses Score (MASES) at Week 24

End point title	Change From Baseline in Maastricht Ankylosing Spondylitis Entheses Score (MASES) at Week 24

End point description:

The Maastricht Ankylosing Spondylitis Enthesitis Score quantitates inflammation of the entheses (enthesitis) by assessing pain at the following entheses (sites where tendons or ligaments insert into the bone): 1st costochondral joints left/right; 7th costochondral joints left/right; posterior superior iliac spine left/right; anterior superior iliac spine left/right; iliac crest left/right; 5th lumbar spinous process; and the proximal insertion of the Archilles tendon left/right. The MASES, ranging from 0 to 13, is the number of painful entheses out of 13 entheses. Full analysis set; participants with a baseline MASES > 0 (i.e., pre-existing enthesopathy) and at least 1 post-baseline value at or prior to Week 24 are included; LOCF imputation was used. The Week 16 value was carried over to Week 24 for participants who escaped early at Week 16.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	106	93	107	
Units: units on a scale				
least squares mean (standard error)	-0.7 (± 0.29)	-1.0 (± 0.31)	-1.1 (± 0.29)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2761 [51]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.4

Notes:

[51] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5012 [52]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.6

Notes:

[52] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Secondary: Change From Baseline in Dactylitis Severity Score at Week 24

End point title	Change From Baseline in Dactylitis Severity Score at Week 24

End point description:

Dactylitis is characterized by swelling of the entire finger or toe. Each digit on the hands and feet will be rated as zero for no dactylitis or 1 for dactylitis present. The dactylitis severity score is the sum of the individual scores for each digit. The dactylitis severity score, ranging from 0 to 20, is the number of digits on the hands and feet with dactylitis present. Full analysis set. Participants with a baseline dactylitis severity score > 0 (i.e., pre-existing dactylitis) and at least 1 postbaseline value at or prior to Week 24 are included. LOCF was used. The Week 16 value was carried over to Week 24 for participants who escaped early at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	71	77	
Units: units on a scale				
least squares mean (standard error)	-1.3 (± 0.35)	-1.7 (± 0.34)	-2.3 (± 0.32)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0399 [53]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0

Notes:

[53] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4413 [54]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.6

Notes:

[54] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Secondary: Change From Baseline in Clinical Disease Activity Index (CDAI) at Week 24

End point title	Change From Baseline in Clinical Disease Activity Index (CDAI) at Week 24

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 10 cm visual analog scale (VAS), where 0 cm = lowest disease activity and 10 cm = highest; • Physician's Global Assessment of Disease Activity -measured on a 10 cm VAS, where 0 cm = lowest disease activity and 10 cm = highest. The CDAI score ranges from 0-76 where lower scores indicate less disease activity. The following thresholds of disease activity have been defined for the CDAI: Remission: ≤ 2.8; Low Disease Activity: > 2.8 and ≤ 10; Moderate Disease Activity: > 10 and ≤ 22; High Disease Activity: > 22. Full analysis set; participants with a baseline value and at least 1 postbaseline value at or prior to Week 24 are included; LOCF imputation was used. The Week 16 value was carried over to Week 24 for participants who escaped early at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	156	158	
Units: units on a scale				
least squares mean (standard error)	-2.53 (± 0.889)	-5.18 (± 0.900)	-7.81 (± 0.895)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	317
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [55]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-5.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.73
upper limit	-2.82

Notes:

[55] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg

Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0349 [56]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.11
upper limit	-0.19

Notes:

[56] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Secondary: Change From Baseline in the Disease Activity Score (DAS28) at Week 24

End point title	Change From Baseline in the Disease Activity Score (DAS28) at Week 24

End point description:

The DAS28 measures the severity of disease at a specific time and is derived from the following variables: • 28 tender joint count • 28 swollen joint count, which do not include the DIP joints, the hip joint, or the joints below the knee; • C-reactive protein (CRP) • Patient's global assessment of disease activity. DAS28(CRP) scores range from 0 to approximately 10, with the upper bound dependent on the highest possible level of CRP. A DAS28 score higher than 5.1 indicates high disease activity, a DAS28 score less than 3.2 indicates low disease activity, and a DAS28 score less than 2.6 indicates clinical remission. Full analysis set; participants with a baseline value and at least 1 postbaseline value at or prior to Week 24 are included; LOCF imputation was used. The Week 16 value was carried over to Week 24 for participants who escaped early at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	163	161	161	
Units: units on a scale				
least squares mean (standard error)	-0.27 (± 0.087)	-0.57 (± 0.088)	-0.75 (± 0.087)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	324
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001 [57]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	-0.24

Notes:

[57] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	324
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0147 [58]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	-0.06

Notes:

[58] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Secondary: Change From Baseline in the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Score at Week 24

End point title	Change From Baseline in the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Score at Week 24

End point description:

The FACIT-Fatigue scale is a 13-item self-administered questionnaire that assesses both the physical and functional consequences of fatigue. Each question is answered on a 5-point scale, where 0 means "not at all," and 4 means "very much." The FACIT-Fatigue scale score ranges from 0 to 52, with higher scores denoting lower levels of fatigue. A positive change from baseline score indicates an improvement. Full analysis set; participants with a baseline value and at least 1 postbaseline value at or prior to Week 24 are included; LOCF imputation was used. The Week 16 value was carried over to Week 24 for participants who escaped early at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	161	163	161	
Units: units on a scale				
least squares mean (standard error)	0.83 (± 0.652)	2.01 (± 0.651)	3.27 (± 0.654)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0078 [59]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	4.24

Notes:

[59] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	324
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1936 [60]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	2.98

Notes:

[60] - Based on an analysis of covariance model for the change from baseline at Week 24, with treatment group, baseline DMARD use, and involvement of >= 3% BSA with psoriasis at baseline as factors and the baseline value as a covariate.

Secondary: Percentage of Participants With MASES Improvement ≥ 20% at Week 16

End point title	Percentage of Participants With MASES Improvement ≥ 20% at Week 16

End point description:

Percentage of participants with pre-existing enthesopathy whose MASES improved by ≥ 20% from

Baseline after 16 weeks of treatment. The Maastricht Ankylosing Spondylitis Enthesitis Score quantitates inflammation of the entheses (enthesitis) by assessing pain at the following entheses (sites where tendons or ligaments insert into the bone): 1st costochondral joints left/right; 7th costochondral joints left/right; posterior superior iliac spine left/right; anterior superior iliac spine left/right; iliac crest left/right; 5th lumbar spinous process; and the proximal insertion of the Archilles tendon left/right. The MASES, ranging from 0 to 13, is the number of painful entheses out of 13 entheses. Full analysis set; participants with a baseline MASES > 0 (i.e., pre-existing enthesopathy) are included; LOCF was used. Participants who did not have sufficient data (observed or imputed) for a determination of response status at Week 16 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	97	112	
Units: percentage of participants				
number (not applicable)	53.2	48.5	54.5	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	221
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7585 [61]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.9
upper limit	15

Notes:

[61] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg

Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5808 [62]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	-3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.4
upper limit	9.7

Notes:

[62] - 2-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants With Dactylitis Improvement ≥ 1 Point at Week 16

End point title	Percentage of Participants With Dactylitis Improvement ≥ 1 Point at Week 16

End point description:

Percentage of participants with pre-existing dactylitis whose dactylitis severity score improved by ≥ 1 after 16 weeks of treatment. Dactylitis is characterized by swelling of the entire finger or toe. Each digit on the hands and feet was rated as zero for no dactylitis or 1 for dactylitis present. The dactylitis severity score is the sum of the individual scores for each digit. The dactylitis severity score, ranging from 0 to 20, is the number of digits on the hands and feet with dactylitis present. Full analysis set; participants with a baseline dactylitis severity score > 0 (i.e., pre-existing dactylitis) are included; LOCF was used. Participants who did not have sufficient data (observed or imputed) for a determination of response status at Week 16 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	71	80	
Units: percentage of participants				
number (not applicable)	59.2	66.2	71.3	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1303 [63]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	27

Notes:

[63] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.361 [64]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.3
upper limit	23.2

Notes:

[64] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants With Good or Moderate European League Against Rheumatism (EULAR) Response at Week 16

End point title	Percentage of Participants With Good or Moderate European League Against Rheumatism (EULAR) Response at Week 16

End point description:

A EULAR response reflects an improvement in disease activity and an attainment of a lower degree of disease activity based on the DAS-28 score. A Good Response is defined as an improvement (decrease) in the DAS28 of more than 1.2 compared with Baseline and attainment of a DAS28 score less than or equal to 3.2. A Moderate Response is defined as either: • an improvement (decrease) in the DAS28 of greater than 0.6 and less than or equal to 1.2 and attainment of a DAS28 score of less than or equal to 5.1 or, • an improvement (decrease) in the DAS28 of more than 1.2 and attainment of a DAS28 score of greater than 3.2. Full analysis set; Participants who discontinued early, or who did not have sufficient data for a definitive determination of response status at Week 16 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	169	167	
Units: percentage of participants				
number (not applicable)	29.0	40.2	51.5	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [65]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	22.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.4
upper limit	32.6

Notes:

[65] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	338
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0309 [66]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	11

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	20.9

Notes:

[66] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants With MASES Improvement ≥ 20% at Week 24

End point title	Percentage of Participants With MASES Improvement ≥ 20% at Week 24

End point description:

Percentage of participants with pre-existing enthesopathy whose MASES improved by ≥ 20% from Baseline after 24 weeks of treatment. The Maastricht Ankylosing Spondylitis Enthesitis Score quantitates inflammation of the entheses (enthesitis) by assessing pain at the following entheses (sites where tendons or ligaments insert into the bone): 1st costochondral joints left/right; 7th costochondral joints left/right; posterior superior iliac spine left/right; anterior superior iliac spine left/right; iliac crest left/right; 5th lumbar spinous process; and the proximal insertion of the Archilles tendon left/right. The MASES, ranging from 0 to 13, is the number of painful entheses out of 13 entheses. FAS; participants with a baseline MASES > 0 are included; LOCF was used. The Week 16 value was carried over to Week 24 for participants who EE at Week 16. Participants who did not have sufficient data for a determination of response status at Week 24 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	97	112	
Units: percentage of participants				
number (not applicable)	51.4	51.5	54.5	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	221
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5731 [67]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	3.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.1
upper limit	16.7

Notes:

[67] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8876 [68]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.6
upper limit	14.6

Notes:

[68] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants With Dactylitis Improvement ≥ 1 Point at Week 24

End point title	Percentage of Participants With Dactylitis Improvement ≥ 1 Point at Week 24

End point description:

Percentage of participants with pre-existing dactylitis whose dactylitis severity score improved by ≥ 1 after 24 weeks of treatment. Dactylitis is characterized by swelling of the entire finger or toe. Each digit on the hands and feet was rated as zero for no dactylitis or 1 for dactylitis present. The dactylitis severity score is the sum of the individual scores for each digit. The dactylitis severity score, ranging from 0 to 20, is the number of digits on the hands and feet with dactylitis present. Full analysis set; participants with a baseline dactylitis severity score > 0 are included; LOCF was used. The Week 16 value was carried over to Week 24 for participants who escaped early at Week 16. Participants who did not have sufficient data (observed or imputed) for a determination of response status at Week 24 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	71	80	
Units: percentage of participants				
number (not applicable)	60.6	67.6	73.8	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1172 [69]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	12.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	26.9

Notes:

[69] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3695 [70]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	7.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.2
upper limit	22.6

Notes:

[70] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants With Good or Moderate EULAR Response at Week 24

End point title	Percentage of Participants With Good or Moderate EULAR Response at Week 24

End point description:

EULAR response reflects an improvement in disease activity and an attainment of a lower degree of disease activity based on the DAS-28 score. A Good Response is defined as an improvement (decrease) in the DAS28 of more than 1.2 compared with Baseline and attainment of a DAS28 score less than or equal to 3.2. A Moderate Response is defined as either: • an improvement (decrease) in the DAS28 of greater than 0.6 and less than or equal to 1.2 and attainment of a DAS28 score of less than or equal to 5.1 or, • an improvement (decrease) in the DAS28 of more than 1.2 and attainment of a DAS28 score of greater than 3.2. Full analysis set; Participants who discontinued early, escaped early at Week 16 or who did not have sufficient data for a definitive determination of response status at Week 24 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	169	167	
Units: percentage of participants				
number (not applicable)	20.1	32.0	42.5	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [71]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	22.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	13
upper limit	32.1

Notes:

[71] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	338
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0123 [72]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	11.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.7
upper limit	20.7

Notes:

[72] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants With a ACR 50 Response at Week 16

End point title	Percentage of Participants With a ACR 50 Response at Week 16

End point description:

Percentage of participants with an American College of Rheumatology 50% (ACR50) response. A participant was a responder if the following 3 criteria for improvement from Baseline were met: • ≥ 50% improvement in 78 tender joint count; • ≥ 50% improvement in 76 swollen joint count; and • ≥ 50% improvement in at least 3 of the 5 following parameters: ◦ Patient's assessment of pain (measured on a 100 mm visual analog scale [VAS]); ◦ Patient's global assessment of disease activity (measured on a 100 mm VAS); ◦ Physician's global assessment of disease activity (measured on a 100 mm VAS); ◦ Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index (HAQ-DI)); ◦ C-Reactive Protein. Full analysis set; Participants who discontinued early, or who did not have sufficient data for a definitive determination of response status at Week 16 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	169	167	
Units: percentage of participants				
number (not applicable)	8.3	12.4	15.0	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.052 [73]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	13.5

Notes:

[73] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	338
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2052 [74]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	10.6

Notes:

[74] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants With an ACR 70 Response at Week 16

End point title	Percentage of Participants With an ACR 70 Response at Week 16

End point description:

Percentage of participants with an American College of Rheumatology 70% (ACR70) response. A participant was a responder if the following 3 criteria for improvement from Baseline were met: • ≥ 70% improvement in 78 tender joint count; • ≥ 70% improvement in 76 swollen joint count; and • ≥ 70% improvement in at least 3 of the 5 following parameters: ◦ Patient's assessment of pain (measured on a 100 mm visual analog scale [VAS]); ◦ Patient's global assessment of disease activity (measured on a 100 mm VAS); ◦ Physician's global assessment of disease activity (measured on a 100 mm VAS); ◦

Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index (HAQ-DI)); ◦ C-Reactive Protein. Full analysis set; Participants who discontinued early, or who did not have sufficient data for a definitive determination of response status at Week 16 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	169	167	
Units: percentage of participants				
number (not applicable)	2.4	4.7	3.6	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5154 [75]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	4.8

Notes:

[75] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg

Number of subjects included in analysis	338
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2527 [76]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	6.2

Notes:

[76] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants With an ACR 50 Response at Week 24

End point title	Percentage of Participants With an ACR 50 Response at Week 24

End point description:

Percentage of participants with an American College of Rheumatology 50% (ACR50) response. A participant was a responder if the following 3 criteria for improvement from Baseline were met: • ≥ 50% improvement in 78 tender joint count; • ≥ 50% improvement in 76 swollen joint count; and • ≥ 50% improvement in at least 3 of the 5 following parameters: ◦ Patient's assessment of pain (measured on a 100 mm visual analog scale [VAS]); ◦ Patient's global assessment of disease activity (measured on a 100 mm VAS); ◦ Physician's global assessment of disease activity (measured on a 100 mm VAS); ◦ Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index (HAQ-DI)); ◦ C-Reactive Protein. Full analysis set; Participants who discontinued early, escaped early at Week 16 or who did not have sufficient data for a definitive determination of response status at Week 24 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	169	167	
Units: percentage of participants				
number (not applicable)	7.7	13.6	16.2	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018 [77]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	15.1

Notes:

[77] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	338
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0807 [78]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	5.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	12.3

Notes:

[78] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants With a ACR 70 Response at Week 24

End point title	Percentage of Participants With a ACR 70 Response at Week 24

End point description:

Percentage of participants with an American College of Rheumatology 70% (ACR70) response. A participant was a responder if the following 3 criteria for improvement from Baseline were met: • ≥ 70% improvement in 78 tender joint count; • ≥ 70% improvement in 76 swollen joint count; and • ≥ 70% improvement in at least 3 of the 5 following parameters: ◦ Patient's assessment of pain (measured on a 100 mm visual analog scale [VAS]); ◦ Patient's global assessment of disease activity (measured on a 100 mm VAS); ◦ Physician's global assessment of disease activity (measured on a 100 mm VAS); ◦ Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index (HAQ-DI)); ◦ C-Reactive Protein. Full analysis set; Participants who discontinued early, escaped early at Week 16 or who did not have sufficient data for a definitive determination of response status at Week 24 were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	169	167	
Units: percentage of participants				
number (not applicable)	3.6	4.1	5.4	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.423 [79]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	6.2

Notes:

[79] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	338
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.787 [80]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	4.6

Notes:

[80] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants Achieving a MASES Score of Zero at Week 16

End point title	Percentage of Participants Achieving a MASES Score of Zero at Week 16

End point description:

Percentage of participants with pre-existing enthesopathy whose MASES improves to 0 after 16 weeks of treatment. The Maastricht Ankylosing Spondylitis Enthesitis Score quantitates inflammation of the entheses (enthesitis) by assessing pain at the following entheses (sites where tendons or ligaments insert into the bone): 1st costochondral joints left/right; 7th costochondral joints left/right; posterior superior iliac spine left/right; anterior superior iliac spine left/right; iliac crest left/right; 5th lumbar spinous process; and the proximal insertion of the Archilles tendon left/right. The MASES, ranging from 0 to 13, is the number of painful entheses out of 13 entheses. Full analysis set; participants with a baseline MASES > 0 (i.e., pre-existing enthesopathy) are included; LOCF was used. Participants who did not have sufficient data (observed or imputed) for a determination of response status at Week 16 were counted as non-responders.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	97	112	
Units: percentage of participants				
number (not applicable)	24.8	19.6	20.5	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	221
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4707 [81]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	-4.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.8
upper limit	6.5

Notes:

[81] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3547 [82]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	-5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.6
upper limit	5.7

Notes:

[82] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants Achieving a Dactylitis Score of Zero at Week 16

End point title	Percentage of Participants Achieving a Dactylitis Score of Zero at Week 16

End point description:

Percentage of participants with pre-existing dactylitis whose dactylitis severity score improves to zero after 16 weeks of treatment. Dactylitis is characterized by swelling of the entire finger or toe. Each digit on the hands and feet was rated as zero for no dactylitis or 1 for dactylitis present. The dactylitis severity score is the sum of the individual scores for each digit. The dactylitis severity score, ranging from 0 to 20, is the number of digits on the hands and feet with dactylitis present. Full analysis set; participants with a baseline dactylitis severity score > 0 (i.e., pre-existing dactylitis) are included; LOCF was used. Participants who did not have sufficient data (observed or imputed) for a determination of response status at Week 16 were counted as non-responders.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	71	80	
Units: percentage of participants				
number (not applicable)	35.2	40.8	41.3	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4175 [83]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.6
upper limit	21.8

Notes:

[83] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.437 [84]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	6.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.1
upper limit	21.8

Notes:

[84] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants Achieving a MASES Score of Zero at Week 24

End point title	Percentage of Participants Achieving a MASES Score of Zero at Week 24

End point description:

Percentage of participants with pre-existing enthesopathy whose MASES improves to 0 after 24 weeks of treatment. The Maastricht Ankylosing Spondylitis Enthesitis Score quantitates inflammation of the entheses (enthesitis) by assessing pain at the following entheses (sites where tendons or ligaments insert into the bone): 1st costochondral joints left/right; 7th costochondral joints left/right; posterior superior iliac spine left/right; anterior superior iliac spine left/right; iliac crest left/right; 5th lumbar spinous process; and the proximal insertion of the Archilles tendon left/right. The MASES, ranging from 0 to 13, is the number of painful entheses out of 13 entheses. Full analysis set; participants with a baseline MASES > 0 are included; LOCF was used. The Week 16 value was carried over to Week 24 for participants who escaped early at Week 16. Participants who did not have sufficient data for a determination of response status at Week 24 were counted as non-responders.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	97	112	
Units: percentage of participants				
number (not applicable)	28.4	20.6	27.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2032 [85]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	-7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.3
upper limit	3.8

Notes:

[85] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	221
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9463 [86]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.1
upper limit	11.3

Notes:

[86] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants Achieving a Dactylitis Score of Zero at Week 24

End point title	Percentage of Participants Achieving a Dactylitis Score of Zero at Week 24

End point description:

Percentage of participants with pre-existing dactylitis whose dactylitis severity score improves to zero after 24 weeks of treatment. Dactylitis is characterized by swelling of the entire finger or toe. Each digit on the hands and feet was rated as zero for no dactylitis or 1 for dactylitis present. The dactylitis severity score is the sum of the individual scores for each digit. The dactylitis severity score, ranging from 0 to 20, is the number of digits on the hands and feet with dactylitis present. Participants who did not have sufficient data for a determination of response status at Week 24 were counted as non-responders.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	71	80	
Units: percentage of participants				
number (not applicable)	36.6	45.1	46.3	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2321 [87]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	9.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	25.4

Notes:

[87] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted difference is the weighted average of the treatment differences across 4 strata of baseline DMARD use by ≥ 3% BSA psoriasis involvement at baseline with the CMH weights. The 95% CI is based on a normal approximation to the weighted average.

Comparison groups	Placebo v Apremilast 20 mg
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.252 [88]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	9.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	25.3

Notes:

[88] - Two-sided p-value is based on the CMH test adjusting for baseline DMARD use and involvement of >= 3% BSA with psoriasis at baseline.

Secondary: Percentage of Participants With an ACR 20 Response at Week 52

End point title	Percentage of Participants With an ACR 20 Response at Week 52

End point description:

Percentage of participants with an ACR response. A participant was a responder if the following 3 criteria for improvement from Baseline were met: • ≥ 20% improvement in 78 tender joint count; • ≥ 20% improvement in 76 swollen joint count; and • ≥ 20% improvement in at least 3 of the 5 following parameters: ◦ Patient's assessment of pain (measured on a 100 mm VAS); ◦ Patient's global assessment of disease activity (measured on a 100 mm VAS); ◦ Physician's global assessment of disease activity (measured on a 100 mm VAS); ◦ Patient's self-assessment of physical function (HAQ-DI); ◦ C-Reactive Protein. 2 sided 95% confidence interval (CI) is based on the Clopper-Pearson method. The Apremilast

Subjects as Randomized/Re-randomized (AAR) Population consisted of all participants who were randomized or re-randomized to apremilast at any time during the study; only subjects who had sufficient data for a definitive determination of response at Week 52 are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	54	67	116	127
Units: percentage of participants				
number (confidence interval 95%)	59.3 (45.0 to 72.4)	58.2 (45.5 to 70.2)	56.0 (46.5 to 65.2)	63.0 (54.0 to 71.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) at Week 52

End point title	Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) at Week 52

End point description:

The HAQ-DI is a patient-reported questionnaire consisting of 20 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and usual activities. Participants assessed their ability to do each task over the past week using the following response categories: without any difficulty (0); with some difficulty (1); with much difficulty (2); and unable to do (3). Scores on each task are summed and averaged to provide an overall score ranging from 0 to 3, where zero represents no disability and three very severe, high-dependency disability. Negative mean changes from Baseline in the overall score indicate improvement in functional ability. Apremilast Subjects as Randomized/Re-randomized (AAR) Population consisted of subjects who were randomized or re-randomized to apremilast at any time during the study. Only those participants who had sufficient data for a definitive determination of response status at Week 52 are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	55	67	122	127
Units: units on a scale				
arithmetic mean (standard deviation)	-0.34 (± 0.407)	-0.34 (± 0.491)	-0.33 (± 0.505)	-0.35 (± 0.505)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the SF-36 Physical Functioning Scale Score at Week 52

End point title	Change From Baseline in the SF-36 Physical Functioning Scale Score at Week 52

End point description:

The Medical Outcome Study Short Form 36-Item Health Survey, Version 2 (SF-36) is a self-administered instrument that measures the impact of disease on overall quality of life and consists of 36 questions in eight domains (physical function, pain, general and mental health, vitality, social function, physical and emotional health). Norm-based scores were used in analyses, calibrated so that 50 is the average score and the standard deviation equals 10. Higher scores indicate a higher level of functioning. The physical functioning domain assesses limitations in physical activities because of health problems. A positive change from Baseline score indicates an improvement. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; participants with a Baseline value and a Week 52 value are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	55	66	121	127
Units: units on a scale				
arithmetic mean (standard deviation)	7.76 (± 8.236)	6.87 (± 7.241)	5.68 (± 8.467)	5.87 (± 8.008)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Modified PsARC Response at Week 52

End point title	Percentage of Participants With a Modified PsARC Response at Week 52

End point description:

Modified PsARC response is defined as improvement in at least 2 of the 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: • 78 tender joint count, • 76 swollen joint count, • Patient global assessment of disease activity, measured on a 100 mm VAS, where 0 mm = lowest disease activity and 100 mm = highest; • Physician global assessment of disease activity, measured on a 100 mm VAS, where 0 mm = lowest disease activity and 100 mm = highest. Improvement or worsening in joint counts is defined as decrease or increase, respectively, from baseline by ≥ 30%, and improvement or worsening in global assessments is defined as decrease or increase, respectively, from baseline by ≥ 20 mm VAS. 2-sided 95% CI is based

on the Clopper-Pearson method. Apremilast Subjects as Randomized/Re-randomized (AAR) population; only subjects who had sufficient data for a definitive response status at Week 52 are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	53	66	116	124
Units: percentage of participants				
number (confidence interval 95%)	81.1 (68.0 to 90.6)	75.8 (63.6 to 85.5)	71.6 (62.4 to 79.5)	79.0 (70.8 to 85.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving a ≥ 75% Improvement in Psoriasis Area and Severity Index Score (PASI75) at Week 52

End point title	Percentage of Participants Achieving a ≥ 75% Improvement in Psoriasis Area and Severity Index Score (PASI75) at Week 52

End point description:

The percentage of participants with Baseline psoriasis body surface area (BSA) involvement ≥ 3% who achieved 75% or greater improvement from Baseline in Psoriasis Area and Severity Index (PASI) score after 52 weeks. The Psoriasis Area and Severity Index (PASI) score is a combination of the intensity of psoriasis, assessed by erythema (reddening), induration (plaque thickness) and desquamation (scaling) scored on a scale from 0 (none) to 4 (very severe), together with the percentage of the area affected, rated on a scale from 0 (no involvement) to 6 (90% to 100% involvement). PASI scoring is performed at four body areas, the head, arms, trunk, and legs. The total PASI score ranges from 0 to 72. The higher the total score, the more severe the disease. 2-sided 95% confidence interval is based on the Clopper-Pearson method. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; participants with a Baseline Psoriasis Body Surface Area ≥ 3% and a Week 52 value are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	35	63	64
Units: percentage of participants				
number (confidence interval 95%)	33.3 (15.6 to 55.3)	28.6 (14.6 to 46.3)	28.6 (17.9 to 41.3)	39.1 (27.1 to 52.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Patient Assessment of Pain at Week 52

End point title	Change From Baseline in the Patient Assessment of Pain at Week 52

End point description:

The participant was asked to place a vertical line on a 100-mm visual analog scale on which the left-hand boundary (score = 0 mm) represents "no pain," and the right-hand boundary (score = 100 mm) represents "pain as severe as can be imagined." The distance from the mark to the left-hand boundary was recorded in millimeters. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; participants with a Baseline value and a Week 52 value are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	55	66	122	127
Units: mm				
arithmetic mean (standard deviation)	-19.9 (± 24.54)	-19.1 (± 26.95)	-14.9 (± 24.86)	-18.7 (± 27.01)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maastricht Ankylosing Spondylitis Entheses Score (MASES) at Week 52

End point title	Change From Baseline in Maastricht Ankylosing Spondylitis Entheses Score (MASES) at Week 52

End point description:

The Maastricht Ankylosing Spondylitis Enthesitis Score quantitates inflammation of the entheses (enthesitis) by assessing pain at the following entheses (sites where tendons or ligaments insert into the bone): 1st costochondral joints left/right; 7th costochondral joints left/right; posterior superior iliac spine left/right; anterior superior iliac spine left/right; iliac crest left/right; 5th lumbar spinous process; and the proximal insertion of the Archilles tendon left/right. The MASES, ranging from 0 to 13, is the number of painful entheses out of 13 entheses. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; participants with a baseline value > 0 (i.e., pre-existing enthesopathy) and a Week 52 value are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	34	48	66	87
Units: units on a scale				
arithmetic mean (standard deviation)	-2.5 (± 3.10)	-2.2 (± 3.01)	-2.2 (± 2.98)	-1.9 (± 2.99)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Dactylitis Severity Score at Week 52

End point title	Change From Baseline in the Dactylitis Severity Score at Week 52

End point description:

Dactylitis is characterized by swelling of the entire finger or toe. Each digit on the hands and feet will be rated as zero for no dactylitis or 1 for dactylitis present. The dactylitis severity score is the sum of the individual scores for each digit. The dactylitis severity score, ranging from 0 to 20, is the number of digits on the hands and feet with dactylitis present. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; participants with a baseline value > 0 (i.e., pre-existing dactylitis) and a Week 52 value are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	26	52	61
Units: units on a scale				
arithmetic mean (standard deviation)	-3.1 (± 4.26)	-3.8 (± 4.52)	-2.9 (± 3.67)	-3.6 (± 4.30)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the CDAI Score at Week 52

End point title	Change From Baseline in the CDAI Score at Week 52

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 10 cm visual analog scale (VAS), where 0 cm = lowest disease activity and 10 cm = highest; •Physician's Global Assessment of Disease Activity -measured on a 10 cm VAS, where 0 cm = lowest disease activity and 10 cm = highest. The CDAI score ranges from 0-76 where lower scores indicate less disease activity. The following thresholds of disease activity have been defined for the CDAI: Remission: ≤ 2.8 Low Disease Activity: > 2.8 and ≤ 10 Moderate Disease Activity: > 10 and ≤ 22 High Disease Activity: > 22. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; participants with a baseline value and a Week 52 value are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	53	66	116	124
Units: units on a scale				
arithmetic mean (standard deviation)	-13.54 (± 10.689)	-12.38 (± 10.308)	-12.86 (± 12.654)	-14.14 (± 11.354)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the DAS28 at Week 52

End point title	Change From Baseline in the DAS28 at Week 52

End point description:

The DAS28 measures the severity of disease at a specific time and is derived from the following variables: •28 tender joint count •28 swollen joint count, which do not include the DIP joints, the hip joint, or the joints below the knee; •C-reactive protein (CRP) •Patient's global assessment of disease activity. DAS28(CRP) scores range from 0 to approximately 10, with the upper bound dependent on the highest possible level of CRP. A DAS28 score higher than 5.1 indicates high disease activity, a DAS28 score less than 3.2 indicates low disease activity, and a DAS28 score less than 2.6 indicates clinical remission. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; participants with a Baseline value and a Week 52 value are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	54	67	121	127
Units: units on a scale				
arithmetic mean (standard deviation)	-1.28 (±	-1.29 (±	-1.21 (±	-1.41 (±

1.102)	1.156)	1.063)	1.204)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the FACIT-Fatigue Scale Score at Week 52

End point title	Change From Baseline in the FACIT-Fatigue Scale Score at Week 52

End point description:

The FACIT-Fatigue scale is a 13-item self-administered questionnaire that assesses both the physical and functional consequences of fatigue. Each question is answered on a 5-point scale, where 0 means "not at all," and 4 means "very much." The FACIT-Fatigue scale score ranges from 0 to 52, with higher scores denoting lower levels of fatigue. A positive change from baseline score indicates an improvement. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; participants with a baseline value and a Week 52 value are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	54	65	121	127
Units: units on a scale				
arithmetic mean (standard deviation)	6.72 (± 8.996)	5.66 (± 8.738)	4.78 (± 8.526)	6.20 (± 8.679)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With MASES Improvement ≥ 20% at Week 52

End point title	Percentage of Participants With MASES Improvement ≥ 20% at Week 52

End point description:

Percentage of participants with pre-existing enthesopathy whose MASES improved by ≥ 20% from Baseline after 52 weeks. The MASES quantitates inflammation of the entheses (enthesitis) by assessing pain at the following entheses (sites where tendons or ligaments insert into the bone): 1st costochondral joints left/right; 7th costochondral joints left/right; posterior superior iliac spine left/right; anterior superior iliac spine left/right; iliac crest left/right; 5th lumbar spinous process; and the proximal insertion of the Archilles tendon left/right. The MASES, ranging from 0 to 13, is the number of painful entheses out of 13 entheses. Two-sided 95% confidence interval is based on the Clopper-Pearson method. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; only those participants with a baseline MASES > 0 and who had sufficient data for a definitive response at Week 52.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	34	48	66	87
Units: percentage of participants				
number (confidence interval 95%)	73.5 (55.6 to 87.1)	75.0 (60.4 to 86.4)	77.3 (65.3 to 86.7)	71.3 (60.6 to 80.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Dactylitis Improvement ≥ 1 Point at Week 52

End point title	Percentage of Participants With Dactylitis Improvement ≥ 1 Point at Week 52

End point description:

Percentage of participants with pre-existing dactylitis whose dactylitis severity score improved by ≥ 1 after 52 weeks. Dactylitis is characterized by swelling of the entire finger or toe. Each digit on the hands and feet was rated as zero for no dactylitis or 1 for dactylitis present. The dactylitis severity score is the sum of the individual scores for each digit. The dactylitis severity score, ranging from 0 to 20, is the number of digits on the hands and feet with dactylitis present. Two-sided 95% confidence interval is based on the Clopper-Pearson method. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; Participants with a baseline dactylitis severity score > 0 (i.e., pre-existing dactylitis) and who had sufficient data for a definitive determination of response status at Week 52 are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	26	52	61
Units: percentage of participants				
number (confidence interval 95%)	95.5 (77.2 to 99.9)	92.3 (74.9 to 99.1)	88.5 (76.6 to 95.6)	91.8 (81.9 to 97.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Good or Moderate EULAR Response at Week 52

End point title	Percentage of Participants Achieving Good or Moderate EULAR Response at Week 52

End point description:

A EULAR response reflects an improvement in disease activity and an attainment of a lower degree of disease activity based on the DAS-28 score. A Good Response is defined as an improvement (decrease) in the DAS28 of more than 1.2 compared with Baseline and attainment of a DAS28 score less than or equal to 3.2. A Moderate Response is defined as either: • an improvement (decrease) in the DAS28 of greater than 0.6 and less than or equal to 1.2 and attainment of a DAS28 score of less than or equal to 5.1 or, • an improvement (decrease) in the DAS28 of more than 1.2 and attainment of a DAS28 score of greater than 3.2. 2-sided 95% confidence interval is based on the Clopper-Pearson method. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; only those participants who had sufficient data for a definitive determination of response status at Week 52 are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	54	67	121	127
Units: percentage of participants				
number (not applicable)	64.8	73.1	69.4	74.8

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With an ACR 50 Response at Week 52

End point title	Percentage of Participants With an ACR 50 Response at Week 52

End point description:

Percentage of participants with an ACR 50 response. A participant was a responder if the following 3 criteria for improvement from Baseline were met: • ≥ 50% improvement in 78 tender joint count; • ≥ 50% improvement in 76 swollen joint count; and • ≥ 50% improvement in at least 3 of the 5 following parameters: ◦ Patient's assessment of pain (measured on a 100 mm visual analog scale [VAS]); ◦ Patient's global assessment of disease activity (measured on a 100 mm VAS); ◦ Physician's global assessment of disease activity (measured on a 100 mm VAS); ◦ Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index (HAQ-DI)); ◦ C-Reactive Protein. 2-sided 95% confidence interval is based on the Clopper-Pearson method. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; only those participants who had sufficient data for a definitive determination of response status at Week 52 are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	53	66	119	126
Units: percentage of participants				
number (confidence interval 95%)	28.3 (16.8 to 42.3)	31.8 (20.9 to 44.4)	25.2 (17.7 to 34.0)	30.2 (22.3 to 39.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With an ACR 70 Response at Week 52

End point title	Percentage of Participants With an ACR 70 Response at Week 52

End point description:

Percentage of participants with an ACR70 response. A participant was a responder if the following 3 criteria for improvement from Baseline were met: • ≥ 70% improvement in 78 tender joint count; • ≥ 70% improvement in 76 swollen joint count; and • ≥ 70% improvement in at least 3 of the 5 following parameters: ◦ Patient's assessment of pain (measured on a 100 mm visual analog scale [VAS]); ◦ Patient's global assessment of disease activity (measured on a 100 mm VAS); ◦ Physician's global assessment of disease activity (measured on a 100 mm VAS); ◦ Patient's self-assessment of physical function (Health Assessment Questionnaire - Disability Index (HAQ-DI)); ◦ C-Reactive Protein. Two-sided 95% confidence interval is based on the Clopper-Pearson method. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; only those participants who had sufficient data for a definitive determination of response status at Week 52 are included.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	53	67	120	125
Units: percentage of participants				
number (confidence interval 95%)	20.8 (10.8 to 34.1)	14.9 (7.4 to 25.7)	9.2 (4.7 to 15.8)	10.4 (5.7 to 17.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving a MASES Score of Zero at Week 52

End point title	Percentage of Participants Achieving a MASES Score of Zero at Week 52

End point description:

Percentage of participants with pre-existing enthesopathy whose MASES improves to 0 after 24 weeks.

The Maastricht Ankylosing Spondylitis Enthesitis Score quantitates inflammation of the entheses (enthesitis) by assessing pain at the following entheses (sites where tendons or ligaments insert into the bone): 1st costochondral joints left/right; 7th costochondral joints left/right; posterior superior iliac spine left/right; anterior superior iliac spine left/right; iliac crest left/right; 5th lumbar spinous process; and the proximal insertion of the Archilles tendon left/right. The MASES, ranging from 0 to 13, is the number of painful entheses out of 13 entheses. 2-sided 95% confidence interval is based on the Clopper-Pearson method. Apremilast Subjects as Randomized/Re-randomized Population; subjects with a baseline value > 0 and who had sufficient data for a definitive response at Week 52 are included.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	34	48	66	87
Units: percentage of participants				
number (confidence interval 95%)	44.1 (27.2 to 62.1)	43.8 (29.5 to 58.8)	33.3 (22.2 to 46.0)	36.8 (26.7 to 47.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving a Dactylitis Score of Zero at Week 52

End point title	Percentage of Participants Achieving a Dactylitis Score of Zero at Week 52

End point description:

Percentage of participants with pre-existing dactylitis whose dactylitis severity score improves to zero after 52 weeks. Dactylitis is characterized by swelling of the entire finger or toe. Each digit on the hands and feet was rated as zero for no dactylitis or 1 for dactylitis present. The dactylitis severity score is the sum of the individual scores for each digit. The dactylitis severity score, ranging from 0 to 20, is the number of digits on the hands and feet with dactylitis present. Two-sided 95% confidence interval is based on the Clopper-Pearson method. The Apremilast Subjects as Randomized/Re-randomized (AAR) Population; Participants with a baseline dactylitis severity score > 0 (i.e., pre-existing dactylitis) and who had sufficient data for a definitive determination of response status at Week 52 are included.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo /Apremilast 20 mg	Placebo/Apremilast 30 mg	Apremilast 20 mg	Apremilast 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	26	52	61
Units: percentage of participants				
number (confidence interval 95%)	68.2 (45.1 to 86.1)	80.8 (60.6 to 93.4)	75.0 (61.1 to 86.0)	68.9 (55.7 to 80.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent Adverse Events (TEAEs) During the Placebo-Controlled Phase

End point title	Number of Participants with Treatment Emergent Adverse Events (TEAEs) During the Placebo-Controlled Phase

End point description:

TEAE is an adverse event (AE) with a start date on or after the first dose of IP and no later than 28 days after the last dose; an AE is any noxious, unintended, or untoward medical occurrence that may appear or worsen in a subject during the course of a study; a serious AE= an AE that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability, is a congenital anomaly or constitutes an important medical event. The investigator assessed severity of an AE by a grading scale: Mild: asymptomatic or with mild symptoms, Moderate-symptoms causing moderate discomfort or Severe- symptoms causing severe discomfort or pain. 1 subject randomized to 30 mg APR who received PBO in error is counted in the PBO group;1 subject randomized to PBO who received 30 mg APR in error is counted in the 30 mg group;1 subject randomized to PBO who received 20 mg APR in error is counted in the 20 mg group

End point type	Secondary

End point timeframe:

Week 0 to Week 16 for placebo participants who entered EE at Week 16 and up to Week 24 for all other participants (placebo participants who remained on placebo through week 24 and participants randomized to the APR 20 mg BID or APR 30 mg BID)

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	168	170	167	
Units: participants				
Any TEAE	83	100	104	
Any Drug-Related TEAE	33	50	62	
Any Severe TEAE	8	5	10	
Any Serious TEAE (SAE)	9	3	6	
Any Serious Drug-Related TEAE	2	0	0	
Any TEAE Leading to Drug Interruption	4	20	16	
Any TEAE Leading to Drug Withdrawal	10	13	12	
Any TEAE Leading to Death	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent Adverse Events During

the Apremilast Exposure Period

End point title	Number of Participants with Treatment Emergent Adverse Events During the Apremilast Exposure Period

End point description:

A TEAE is an adverse event (AE) with a start date on or after the date of the first dose of investigational product (IP) and no later than 28 days after the last dose of IP. An adverse event (AE) is any noxious, unintended, or untoward medical occurrence that may appear or worsen in a subject during the course of a study. A serious AE is any AE that results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; or constitutes an important medical event. For both AEs and SAEs the investigator assessed the severity of the event according to the grading scale: Mild: asymptomatic or with mild symptoms, Moderate: symptoms causing moderate discomfort or Severe: symptoms causing severe discomfort or pain. Apremilast subjects as treated population.

End point type	Secondary

End point timeframe:

Week 0 to Week 260; median duration of exposure to apremilast 20 mg BID was 121.71 weeks and 232.50 weeks for apremilast 30 mg BID

End point values	Apremilast 20 mg (Pre-switch)	Apremilast 20 mg/30 mg (Post-switch)	Apremilast 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	241	97	242	
Units: participants				
Any TEAE	194	64	209	
Any Drug-Related TEAE	98	11	111	
Any Severe TEAE	21	0	30	
Any Serious TEAE (SAE)	38	4	54	
Any Serious Drug-Related TEAE|	5	0	3	
Any TEAE Leading to Drug Interruption	48	4	53	
Any TEAE Leading to Drug Withdrawal	30	0	30	
Any TEAE Leading to death	0	1	0	

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

AEs are reported for the PBO-controlled phase: Weeks 0 -16 for PBO subjects who entered EE at Week 16 and up to Week 24 for all others; AE's are reported for the APR Exposure Period: Weeks 0 - 260

Adverse event reporting additional description:

Median duration: APR 20 mg BID = 121.71 weeks; APR 30 mg BID = 232.50 weeks; 1 subject randomized to 30 mg APR who received PBO in error is counted in the PBO group; 1 subject randomized to PBO who received 30 mg APR in error is counted in the 30 mg group; 1 subject randomized to PBO who received 20 mg APR in error is counted in the 20 mg group

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	V14.0

Reporting groups

Reporting group title	Weeks 0-24: Placebo (Placebo-Controlled Phase)

Reporting group description:

Participants received placebo tablets twice daily during the placebo-controlled phase. Includes data through Week 16 for participants who escaped early, and through Week 24 for all other participants.

Reporting group title	Weeks 0-24: Apremilast 20 mg (Placebo- Controlled Phase)

Reporting group description:

Participants received 20 mg apremilast tablets twice daily during the 24-week placebo-controlled phase.

Reporting group title	Weeks 0-24: Apremilast 30 mg (Placebo- Controlled Phase)

Reporting group description:

Participants received 30 mg apremilast tablets PO twice daily during the 24-week placebo-controlled phase.

Reporting group title	APR Exposure Period Up to 5 Years: Apremilast 20 mg

Reporting group description:

Participants who received apremilast 20 mg twice daily regardless of when the apremilast exposure started (at Week 0, 16 or 24). Only TEAEs that occurred during apremilast 20 mg BID treatment (before the switch to 30 mg apremilast) were included.

Reporting group title	APR Exposure Period Up to 5 Years: Apremilast 20mg/30 mg

Reporting group description:

Participants who switched from apremilast 20 mg twice daily to apremilast 30 mg BID. Only the TEAEs that occurred during apremilast 30 mg twice daily treatment were included.

Reporting group title	APR Exposure Period Up to 5 Years: Apremilast 30 mg

Reporting group description:

Participants who received apremilast 30 mg twice daily throughout the study regardless of when the apremilast-exposure started (at Week 0, 16, or 24).

Serious adverse events	Weeks 0-24: Placebo (Placebo-Controlled Phase)	Weeks 0-24: Apremilast 20 mg (Placebo- Controlled Phase)	Weeks 0-24: Apremilast 30 mg (Placebo- Controlled Phase)
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 168 (5.36%)	4 / 170 (2.35%)	6 / 167 (3.59%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 168 (0.00%)	1 / 170 (0.59%)	0 / 167 (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
Breast cancer stage III			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipoma			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oncocytoma			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroid tumour benign			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Uterine leiomyoma			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial thrombosis limb			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	1 / 168 (0.60%)	0 / 170 (0.00%)	0 / 167 (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
Thrombophlebitis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Alcohol rehabilitation			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			

subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast enlargement			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial hyperplasia			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian haemorrhage			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine haemorrhage			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nasal polyps			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal septum deviation			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal turbinate hypertrophy			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar hypertrophy			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental disorder			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 168 (0.00%)	1 / 170 (0.59%)	0 / 167 (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
Investigations			

Blood pressure increased			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	0 / 168 (0.00%)	1 / 170 (0.59%)	0 / 167 (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
Ankle fracture			
subjects affected / exposed	1 / 168 (0.60%)	0 / 170 (0.00%)	0 / 167 (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
Cerebral haemorrhage traumatic			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	1 / 167 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Meniscus lesion			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural complication			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Snake bite			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	1 / 168 (0.60%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic haematoma			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Whiplash injury			

subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	1 / 167 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arteriovenous fistula			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	1 / 167 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac failure			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sick sinus syndrome			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial aneurysm			

subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	1 / 167 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			

Meniere's disease			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic polyp			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal polyp			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	2 / 168 (1.19%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis chronic			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cholelithiasis			
subjects affected / exposed	1 / 168 (0.60%)	0 / 170 (0.00%)	1 / 167 (0.60%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 168 (0.60%)	0 / 170 (0.00%)	0 / 167 (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
Psoriasis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	1 / 168 (0.60%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Acromegaly			

subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Finger deformity			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyarthritis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriatic arthropathy			

subjects affected / exposed	2 / 168 (1.19%)	1 / 170 (0.59%)	1 / 167 (0.60%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis infective			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			

subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	1 / 167 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinitis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic shock syndrome			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 168 (0.00%)	0 / 170 (0.00%)	0 / 167 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	APR Exposure Period	APR Exposure Period	APR Exposure Period

	Up to 5 Years: Apremilast 20 mg	Up to 5 Years: Apremilast 20mg/30 mg	Up to 5 Years: Apremilast 30 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 241 (15.77%)	4 / 97 (4.12%)	54 / 242 (22.31%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Breast cancer			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer stage III			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Lipoma			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Lung adenocarcinoma			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oncocytoma			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroid tumour benign			

subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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 skin			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Vascular disorders			
Arterial thrombosis limb			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Hypertension			
subjects affected / exposed	2 / 241 (0.83%)	0 / 97 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Alcohol rehabilitation			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration			

site conditions			
Chest pain			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast enlargement			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Endometrial hyperplasia			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian haemorrhage			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
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 haemorrhage			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
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			
Interstitial lung disease			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal polyps			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal septum deviation			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal turbinate hypertrophy			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 241 (0.00%)	1 / 97 (1.03%)	0 / 242 (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
Tonsillar hypertrophy			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
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			
Anxiety			
subjects affected / exposed	0 / 241 (0.00%)	1 / 97 (1.03%)	0 / 242 (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
Mental disorder			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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

Suicidal ideation			
subjects affected / exposed	2 / 241 (0.83%)	0 / 97 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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			
Alcohol poisoning			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Cerebral haemorrhage traumatic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Head injury			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus lesion			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural complication			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Snake bite			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic haematoma			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			

subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Whiplash injury			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arteriovenous fistula			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	2 / 241 (0.83%)	0 / 97 (0.00%)	2 / 242 (0.83%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrioventricular block complete			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 241 (0.41%)	1 / 97 (1.03%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Sick sinus syndrome			
subjects affected / exposed	0 / 241 (0.00%)	1 / 97 (1.03%)	0 / 242 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Intracranial aneurysm			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Loss of consciousness			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Polyneuropathy			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic polyp			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal polyp			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis chronic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholecystitis			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriasis			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Urticaria			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endocrine disorders			
Acromegaly			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Finger deformity			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 241 (0.00%)	1 / 97 (1.03%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	3 / 241 (1.24%)	0 / 97 (0.00%)	2 / 242 (0.83%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyarthritis			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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

Psoriatic arthropathy			
subjects affected / exposed	2 / 241 (0.83%)	0 / 97 (0.00%)	7 / 242 (2.89%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Cholecystitis infective			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Chronic sinusitis			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			

subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 241 (0.83%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Rhinitis			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic shock syndrome			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Urosepsis			
subjects affected / exposed	1 / 241 (0.41%)	0 / 97 (0.00%)	0 / 242 (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
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 241 (0.00%)	0 / 97 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Weeks 0-24: Placebo (Placebo-Controlled Phase)	Weeks 0-24: Apremilast 20 mg (Placebo- Controlled Phase)	Weeks 0-24: Apremilast 30 mg (Placebo- Controlled Phase)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 168 (20.83%)	66 / 170 (38.82%)	71 / 167 (42.51%)
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 168 (2.98%)	3 / 170 (1.76%)	4 / 167 (2.40%)
occurrences (all)	6	3	4
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 168 (4.76%)	16 / 170 (9.41%)	20 / 167 (11.98%)
occurrences (all)	10	19	21
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 168 (1.19%)	3 / 170 (1.76%)	8 / 167 (4.79%)
occurrences (all)	2	3	8
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 168 (1.79%)	26 / 170 (15.29%)	26 / 167 (15.57%)
occurrences (all)	3	29	27
Nausea			
subjects affected / exposed	9 / 168 (5.36%)	19 / 170 (11.18%)	23 / 167 (13.77%)
occurrences (all)	12	21	26
Vomiting			
subjects affected / exposed	1 / 168 (0.60%)	5 / 170 (2.94%)	8 / 167 (4.79%)
occurrences (all)	1	6	9
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 168 (0.00%)	4 / 170 (2.35%)	5 / 167 (2.99%)
occurrences (all)	0	5	6
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 168 (2.38%)	1 / 170 (0.59%)	2 / 167 (1.20%)
occurrences (all)	4	1	2

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 168 (1.79%)	2 / 170 (1.18%)	4 / 167 (2.40%)
occurrences (all)	3	2	4
Back pain			
subjects affected / exposed	3 / 168 (1.79%)	1 / 170 (0.59%)	0 / 167 (0.00%)
occurrences (all)	3	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 168 (1.19%)	3 / 170 (1.76%)	1 / 167 (0.60%)
occurrences (all)	2	3	1
Nasopharyngitis			
subjects affected / exposed	2 / 168 (1.19%)	7 / 170 (4.12%)	4 / 167 (2.40%)
occurrences (all)	2	8	4
Pharyngitis			
subjects affected / exposed	1 / 168 (0.60%)	1 / 170 (0.59%)	1 / 167 (0.60%)
occurrences (all)	2	1	1
Sinusitis			
subjects affected / exposed	3 / 168 (1.79%)	4 / 170 (2.35%)	4 / 167 (2.40%)
occurrences (all)	3	4	4
Upper respiratory tract infection			
subjects affected / exposed	3 / 168 (1.79%)	11 / 170 (6.47%)	12 / 167 (7.19%)
occurrences (all)	3	12	14
Urinary tract infection			
subjects affected / exposed	1 / 168 (0.60%)	2 / 170 (1.18%)	5 / 167 (2.99%)
occurrences (all)	1	2	5

Non-serious adverse events	APR Exposure Period Up to 5 Years: Apremilast 20 mg	APR Exposure Period Up to 5 Years: Apremilast 20mg/30 mg	APR Exposure Period Up to 5 Years: Apremilast 30 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	142 / 241 (58.92%)	36 / 97 (37.11%)	164 / 242 (67.77%)
Vascular disorders			
Hypertension			
subjects affected / exposed	17 / 241 (7.05%)	3 / 97 (3.09%)	22 / 242 (9.09%)
occurrences (all)	20	3	24
Nervous system disorders			

Headache			
subjects affected / exposed	30 / 241 (12.45%)	4 / 97 (4.12%)	39 / 242 (16.12%)
occurrences (all)	142	24	49
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 241 (2.49%)	1 / 97 (1.03%)	16 / 242 (6.61%)
occurrences (all)	6	1	17
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	40 / 241 (16.60%)	1 / 97 (1.03%)	44 / 242 (18.18%)
occurrences (all)	58	1	66
Nausea			
subjects affected / exposed	28 / 241 (11.62%)	3 / 97 (3.09%)	47 / 242 (19.42%)
occurrences (all)	31	3	59
Vomiting			
subjects affected / exposed	10 / 241 (4.15%)	1 / 97 (1.03%)	14 / 242 (5.79%)
occurrences (all)	11	1	15
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 241 (2.49%)	1 / 97 (1.03%)	18 / 242 (7.44%)
occurrences (all)	8	1	21
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 241 (0.83%)	0 / 97 (0.00%)	14 / 242 (5.79%)
occurrences (all)	2	0	16
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 241 (3.73%)	0 / 97 (0.00%)	19 / 242 (7.85%)
occurrences (all)	10	0	23
Back pain			
subjects affected / exposed	12 / 241 (4.98%)	4 / 97 (4.12%)	18 / 242 (7.44%)
occurrences (all)	16	4	22
Infections and infestations			
Bronchitis			
subjects affected / exposed	17 / 241 (7.05%)	3 / 97 (3.09%)	20 / 242 (8.26%)
occurrences (all)	26	3	31

Nasopharyngitis			
subjects affected / exposed	34 / 241 (14.11%)	12 / 97 (12.37%)	36 / 242 (14.88%)
occurrences (all)	61	14	61
Pharyngitis			
subjects affected / exposed	14 / 241 (5.81%)	1 / 97 (1.03%)	14 / 242 (5.79%)
occurrences (all)	22	1	14
Sinusitis			
subjects affected / exposed	12 / 241 (4.98%)	1 / 97 (1.03%)	18 / 242 (7.44%)
occurrences (all)	16	1	33
Upper respiratory tract infection			
subjects affected / exposed	34 / 241 (14.11%)	6 / 97 (6.19%)	36 / 242 (14.88%)
occurrences (all)	65	7	58
Urinary tract infection			
subjects affected / exposed	19 / 241 (7.88%)	3 / 97 (3.09%)	22 / 242 (9.09%)
occurrences (all)	27	4	41

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 January 2011	1. Modification of protocol language for clarification. 2. Clarified the language around contraception methods to ensure precise description of acceptable methods of contraception given the global nature of Celgene's trial. In addition, a statement was added into the protocol to ensure that appropriate education regarding contraception methods was provided by the investigator to the subject. 3. Modification to protocol deleting annual chest radiographs allowing local treatment guidelines to dictate when chest radiographs were performed. 4. BSA involved by psoriasis added as study assessment. 5. Alignment of exclusion criteria related to past malignancies across the entire APR Phase 3 program that gave investigators responsibility for determining subject eligibility for previously successfully treated local lesions. 6. Modification of Reasons for Discontinuation to align with what was displayed in the InForm database.
10 June 2011	1. Provided correction regarding the Celgene Therapeutic Area Head of the study. 2. Addition of a serum pregnancy test at baseline for FCBP. 3. A clarification in Section 6.2, Contraception Education, which directed the investigator to Section 7.2 of the protocol where the specific details regarding acceptable contraception for this study were found. 4. A clarification in Section 6.6.4, Clinical Laboratory Evaluations, to indicate that a microscopic evaluation was to be performed on all urine samples. 5. Modification to Inclusion Criterion Number 14 – The Female Birth Control Inclusion Criterion was updated to clearly define single or multiple forms of contraception that were acceptable for this study. 6. Addition of a footnote to Inclusion Criterion Number 14 – The Female Birth Control Inclusion Criteria, which clarified that the female subject's chosen form of contraception must be fully effective by the time the female subject received the first dose of study medication at randomization. 7. Modification to Inclusion Criterion Number 13 – Male Birth Control Inclusion Criteria, which clarified that male subjects must use a "male" latex or non-latex condom. 8. Descriptive text on how to record onset and end dates of SAEs on the SAE Report Form was deleted because it was no longer applicable
20 April 2012	1. Provided updates to the contact information for the Medical Monitor of the study. 2. Modification of Section 4.1 Study Design, Section 8.2 Treatment Administration and Schedule, and Section 10.1 Overview regarding site and subject blinding until completion of the 52 Week double-blind phase. 3. Revision of Section 4.1 regarding the replacement of the Safety Review Panel with an independent external DMC. 4. Modification of Section 4.2 Study Design Rationale, Section 9.1 Permitted Concomitant Medications and Procedures, and Section 9.2 Prohibited Concomitant Medications and Procedures to allow the use of topical therapy and/or phototherapy after the Week 52 study visit for worsening skin psoriasis. 5. Addition of a footnote to the Adverse Events row in Table of Events, Section 5, (Tables 1 and 2) which reminded investigators to perform vasculitis assessments and/or psychiatric evaluations as appropriate, when AEs were reported. 6. A revision of the Contraception Education in Section 6.2 and movement of footnote from Section 7.2 to Section 6.2. 7. Addition of Section 6.6.3.1 Vasculitis Assessment providing guidance to investigators. 8. Addition of Section 6.6.3.2 Psychiatric Evaluation to provide guidance to investigators for the management of subjects identified as having thoughts of suicide, attempted suicide, or having a major psychiatric illness. 9. Addition of Section 6.6.3.3 Risk Benefit for Long-term Active Treatment providing guidance to investigators regarding radiographs of symptomatic joints. 10. A change to the open-label IP packaging is described in Sections 6.9.1 and 8.4. 11. A note was added to Section 7.2, Inclusion Criterion 14, to refer investigators to Section 6.2, Contraception Education. 12. AE tables will summarize TEAEs only.12. The term "CRF" (case report form) was changed to "eCRF" globally throughout the document to reflect that data is captured in this study in electronic case report form pages (eCRF).

12 July 2012	1. The assessment of the primary efficacy endpoint (ACR 20) was changed to Week 16 instead of Week 24. 2. Assessments of enthesitis and dactylitis (in subjects who present with these manifestations of PsA at baseline) were elevated to be secondary rather than exploratory outcome measures. 3. The secondary endpoints were to be assessed at Week 16, in addition to Weeks 24 and 52. 4. The order of secondary endpoints at Weeks 16, 24 and 52 was modified to coincide with the planned sequence of statistical testing. 5. The modified PsARC and EULAR response were added as secondary efficacy endpoints. 6. The ACR-N was added as an exploratory endpoint. The health-related quality of life endpoints were to be assessed at Week 16, in addition to Weeks 24 and 52. 7. Modification of Section 9.1 Permitted Concomitant Medications to allow use of systemic corticosteroids and DMARDs after the Week 52 study visit for worsening arthritic symptoms of PsA. 8. The statistical approaches for analysis of secondary endpoints were updated. 9. The statistical approaches for subgroup analyses were updated. 10. Citations were included to provide references for the modified PsARC and EULAR response that were added as secondary efficacy outcome measures in this amendment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26792812