Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Efficacy and Safety Study of Apremilast (CC-10004) in Subjects with Moderate to Severe Plaque Psoriasis

Summary

EudraCT number	2010-019991-55
Trial protocol	DE BE GB IT
Global end of trial date	22 November 2016

Results information

Result version number	v1 (current)
This version publication date	08 December 2017
First version publication date	08 December 2017

Trial information

Trial identification

Sponsor protocol code	CC-10004-PSOR-008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01194219
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, 01 888-260-1599, ClinicalTrialDisclosure@Celgene.com
Scientific contact	Wendy Zhang, MD, Celgene Corporation, 01 9085149788, WeiZhang@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	22 November 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the clinical efficacy of apremilast 30 mg BID, compared with placebo, in subjects with moderate to severe plaque psoriasis.

Protection of trial subjects:

Patient Confidentiality, Personal Data Protection

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 September 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	66 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 116
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Canada: 317
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Germany: 64
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 294
Worldwide total number of subjects	844
EEA total number of subjects	117

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	772
From 65 to 84 years	72
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 76 study centers in 8 countries

Pre-assignment

Screening details:

Subjects were eligible who had moderate to severe plaque psoriasis.

Period 1

Period 1 title	Placebo-Controlled Phase Weeks 0-16
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

Treatment assignment blinding remained in effect; the blind was broken when all subjects completed their week 52 visit

Arms

Are arms mutually exclusive?	Yes
Arm title	Apremilast

Arm description:

Participants were initially randomized to apremilast (APR) 30 mg tablets twice daily (BID) during the Placebo-controlled Phase (Weeks 0-16)

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

Dosage and administration details:

Apremilast 30 mg tablets BID

Arm title	Placebo

Arm description:

Participants were initially randomized to identically matching placebo (PBO) tablets twice daily BID during the Placebo-controlled Phase (Weeks 0-16)

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:

Identically matching placebo tablets BID

Number of subjects in period 1	Apremilast	Placebo
Started	562	282
Received apremilast	560	282
Completed	503	249
Not completed	59	33
Adverse event, serious fatal	-	1
Consent withdrawn by subject	12	9
Adverse event, non-fatal	23	5
Miscellaneous	1	1
Noncompliance with study drug	7	-
Lost to follow-up	7	9
Lack of efficacy	2	7
Protocol deviation	7	1

Period 2

Period 2 title	Maintenance Phase Weeks 16-32
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

Treatment assignment blinding remained in effect; the blind was broken when all subjects completed their week 52 visit

Arms

Are arms mutually exclusive?	Yes
Arm title	Apremilast-Apremilast

Arm description:

Participants who were initially randomized to apremilast 30 mg tablets BID during the Placebo-controlled Phase (Weeks 0-16) remained on apremilast 30 mg BID during the Maintenance Phase (Weeks 16-32).

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

Dosage and administration details:

Apremilast 30 mg tablets BID

Arm title	Placebo-Apremilast

Arm description:

Participants who were initially randomized to identically matching placebo tablets BID during the Placebo-controlled Phase (Weeks 0-16) were switched after 16 weeks of treatment to apremilast 30 mg tablets BID and continued dosing with apremilast 30 mg BID during the Maintenance Phase (weeks 16-32)

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

Dosage and administration details:

Apremilast 30 mg tablets BID

Number of subjects in period 2[1]	Apremilast-Apremilast	Placebo-Apremilast
Started	494	245
Received apremilast	493	244
Completed	424	215
Not completed	70	30
Non-compliance with Study Drug	2	1
Consent withdrawn by subject	12	3
Adverse event, non-fatal	8	9
Unspecified	2	1
Lost to follow-up	9	-
Lack of efficacy	37	15
Protocol deviation	-	1

Notes:

[1] - 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: The Study PSOR-008 protocol allowed subjects to withdraw from the clinical trial at any time. Of the 752 subjects who completed the Placebo-controlled Phase, 13 subjects withdrew from the study for diverse reasons including adverse events, lack of efficacy, non-compliance and withdrawal by subject. Consequently, a total of 739 subjects entered the Maintenance Phase of the trial.

Period 3

Period 3 title	Randomized Withdrawal Phase-Weeks 32-52
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

Treatment assignment blinding remained in effect; the blind was broken when all subjects completed their week 52 visit

Arms

Are arms mutually exclusive?	Yes

Arm title	APR-APR-Re-randomized to PBO

Arm description:

Participants who were initially randomized to APR 30 mg BID during the 16-week Placebo-controlled Phase (Weeks 0-16) continued dosing with APR 30 mg BID through the Maintenance Phase (Weeks 16-32). At Week 32, those participants who were considered responders [ie, having a ≥ Psoriasis Area and Severity Index score of 75 (PASI-75) response] were re-randomized to PBO during the Randomized Withdrawal Phase (Weeks 32-52). Those participants who retained their ≥PASI-75 response through the Randomized Withdrawal Phase remained on PBO until week 52. Those participants who lost their PASI-75 improvement achieved at week 32, were switched back to APR 30 mg BID at the time loss of effect was observed. All participants who completed the Randomized Withdrawal Phase at week 52 were eligible to participate in the Long-term Extension Phase from weeks 52-260, and received APR 30 mg BID for the remainder of their participation.

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:

Identically matching placebo tablets BID

Arm title	APR-APR-Re-randomized to APR

Arm description:

Participants who were initially randomized to APR 30 mg BID during the 16-week Placebo-controlled Phase (Weeks 0-16) continued dosing with APR 30 mg BID through the Maintenance Phase (Weeks 16-32). At Week 32, those participants who were considered responders (ie, having a ≥PASI-75 response) were re-randomized to APR during the Randomized Withdrawal Phase (Weeks 32-52). Those participants who completed the Randomized Withdrawal Phase at Week 52 were eligible to participate in the Long-term Extension Phase from weeks 52-260 and remained on APR 30 mg BID for the remainder of their participation.

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

Dosage and administration details:

Apremilast 30 mg tablets BID

Arm title	APR-APR-APR + optional topicals/UVB

Arm description:

Participants who were initially randomized to APR 30 mg BID during the 16-week Placebo-controlled Phase (Weeks 0-16) continued dosing with APR 30 mg BID through the Maintenance Phase (weeks 16-32). At week 32, those participants who were considered partial responders (ie, having a response of PASI-50 to PASI-74) and those participants who were considered non-responders (ie, having a response of <PASI-50), remained on APR 30 mg BID and were given the option of adding topical therapies and/or phototherapy to their regimen. Those participants who completed the Randomized Withdrawal Phase at week 52 were eligible to participate in the Long-term Extension (LTE) Phase from Weeks 52-260 and remained on APR 30 mg BID for the remainder of their participation.

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

Dosage and administration details:

Apremilast 30 mg tablets BID

Arm title	PBO-APR-APR + optional topicals/ UVB

Arm description:

Participants who were initially randomized to placebo BID during the 16-week Placebo-controlled Phase (Weeks 0-16) were switched after 16 weeks of treatment to APR 30 mg BID and continued dosing with APR 30 mg BID during the Maintenance Phase (Weeks 16-32). At week 32, all participants continued to receive apremilast 30 mg BID. Those participants who were considered partial responders (ie, having a response of PASI-50 to PASI-74) and non-responders (ie, having a response of < PASI-50), were given the option of adding topical therapies and/or phototherapy to their regimen. All participants who completed the Randomized Withdrawal Phase at week 52 were eligible to participate in the Long-term Extension Phase from Weeks 52-260 and remained on APR 30 mg BID for the remainder of their participation.

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

Dosage and administration details:

Apremilast 30 mg tablets BID

Number of subjects in period 3[2]	APR-APR-Re-randomized to PBO	APR-APR-Re-randomized to APR	APR-APR-APR + optional topicals/UVB
Started	77	77	245
Received topical + light therapy	0 [3]	0 [4]	126 [5]
Completed	73	73	184
Not completed	4	4	61
Non-compliance with Study Drug	1	-	2
Consent withdrawn by subject	1	-	12
Adverse event, non-fatal	-	1	6
Not specified	-	-	1
Lost to follow-up	1	2	5
Lack of efficacy	1	1	35
Protocol deviation	-	-	-

Number of subjects in period 3[2]	PBO-APR-APR + optional topicals/ UVB
Started	208
Received topical + light therapy	91 [6]
Completed	163
Not completed	45
Non-compliance with Study Drug	-
Consent withdrawn by subject	6
Adverse event, non-fatal	5
Not specified	-
Lost to follow-up	-
Lack of efficacy	33

Protocol deviation	1

Notes:

[2] - 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: The Study PSOR-008 protocol allowed subjects to withdraw from the clinical trial at any time. Of the 639 subjects who completed the Maintenance Phase, 32 subjects withdrew from the study for diverse reasons including adverse events, lack of efficacy, non-compliance and withdrawal by subject. Consequently, a total of 607 subjects entered the Randomized Withdrawal Phase of the trial.

[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: Of the 154 subjects who were originally randomized to APR and who achieved a PASI-75 response at Week 32, 77 subjects were re-randomized to placebo and 73 subjects in this group completed the Randomized Withdrawal Phase. Subjects in this treatment group were not permitted to receive topical and/or phototherapy during the Randomization Withdrawal Phase.

[4] - 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: Of the 154 subjects who were originally randomized to APR and who achieved a PASI-75 response at Week 32, 77 subjects were re-randomized to APR and 73 subjects in this group completed the Randomized Withdrawal Phase. Subjects in this treatment group were not permitted to receive topical and/or phototherapy during the Randomization Withdrawal Phase.

[5] - 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: During the Randomization Withdrawal Phase, of the 245 subjects in the APR-APR-APR arm, 126 subjects were treated with topical therapy and/or phototherapy, and 119 subjects did not receive topical and/or phototherapy. A total of 184 subjects completed the Randomized Withdrawal Phase, with 105 subjects in the group receiving topical and/or phototherapy, and 79 subjects in the group which did not receive topical and/or phototherapy.

[6] - 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: During the Randomization Withdrawal Phase, of the 208 subjects in the PBO-APR-APR arm, 91 subjects were treated with topical therapy and/or phototherapy, and 117 subjects did not receive topical and/or phototherapy. A total of 163 subjects completed the Randomized Withdrawal Phase, with 73 subjects in the group receiving topical and/or phototherapy, and 90 subjects in the group which did not receive topical and/or phototherapy.

Period 4

Period 4 title	Long-Term Extension Weeks 52 to 260
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Apremilast (Long-term extension)

Arm description:

Participants who were initially randomized to apremilast 30 mg BID during the 16-week placebo-controlled phase (Weeks 0-16) continued receiving apremilast 30 mg BID through the Maintenance Phase (weeks 16-32) and apremilast 30 mg tablets or placebo during the Randomized Withdrawal Phase then received apremilast 30 mg BID in the Long-term Extension Phase from Weeks 52-260.

Arm type	Experimental

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

Dosage and administration details:

Apremilast 30 mg tablets BID

Arm title	Placebo-Apremilast (Long-term extension)

Arm description:

Participants who were initially randomized to identically matching placebo BID during the placebo-controlled phase (Weeks 0-16) were switched at Week 16 to apremilast 30 mg BID during the Maintenance Phase, received apremilast 30 mg PO BID or placebo during the Randomized Withdrawal Phase and then received apremilast 30 mg tablets BID in the long-term extension phase from weeks 52-260.

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

Dosage and administration details:

Apremilast 30 mg tablets BID

Number of subjects in period 4[7]	Apremilast (Long-term extension)	Placebo-Apremilast (Long-term extension)
Started	306	153
Received Treatment	306	153
Completed	86	41
Not completed	220	112
Adverse event, serious fatal	1	1
Consent withdrawn by subject	66	32
Adverse event, non-fatal	25	14
Miscellaneous	11	2
Noncompliance with IP	9	4
Lost to follow-up	24	10
Lack of efficacy	81	49
Protocol deviation	3	-

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: The Study PSOR-008 protocol allowed subjects to withdraw from the clinical trial at any time. Of the 493 subjects who completed the Randomized Withdrawal Phase, 34 subjects withdrew from the study for diverse reasons including adverse events, lack of efficacy, non-compliance and withdrawal by subject. Consequently, a total of 459 subjects entered the Long-Term Extension of the trial.

Baseline characteristics

Reporting groups	
Reporting group title	Apremilast
Reporting group description:	
Participants were initially randomized to apremilast (APR) 30 mg tablets twice daily (BID) during the Placebo-controlled Phase (Weeks 0-16)	
Reporting group title	Placebo
Reporting group description:	
Participants were initially randomized to identically matching placebo (PBO) tablets twice daily BID during the Placebo-controlled Phase (Weeks 0-16)	

Reporting group values	Apremilast	Placebo	Total
Number of subjects	562	282	844
Age categorical Units: Subjects			
Adults (18-64 years)	514	258	772
From 65-84 years	48	24	72
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	45.8	46.5	
standard deviation	± 13.07	± 12.72	-
Gender, Male/Female Units: Subjects			
Female	183	88	271
Male	379	194	573
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	2	5	7
Asian	28	16	44
Black or African American	18	10	28
Native Hawaiian or Other Pacific Islander	5	1	6
White	507	250	757
Other	2	0	2
Duration of Plaque Psoriasis			
All participants enrolled were required to have a diagnosis of plaque psoriasis at least 12 months prior to screening, but the duration was not required for enrollment. Overall baseline population for duration of plaque psoriasis in the apremilast arm were 562 participants and 282 for those in the placebo arm.			
Units: Subjects			
<10 years	150	85	235
10 to < 20 years	159	73	232
≥ 20 years	253	122	375
Missing	0	2	2

End points

End points reporting groups

Reporting group title	Apremilast

Reporting group description:

Participants were initially randomized to apremilast (APR) 30 mg tablets twice daily (BID) during the Placebo-controlled Phase (Weeks 0-16)

Reporting group title	Placebo

Reporting group description:

Participants were initially randomized to identically matching placebo (PBO) tablets twice daily BID during the Placebo-controlled Phase (Weeks 0-16)

Reporting group title	Apremilast-Apremilast

Reporting group description:

Participants who were initially randomized to apremilast 30 mg tablets BID during the Placebo-controlled Phase (Weeks 0-16) remained on apremilast 30 mg BID during the Maintenance Phase (Weeks 16-32).

Reporting group title	Placebo-Apremilast

Reporting group description:

Participants who were initially randomized to identically matching placebo tablets BID during the Placebo-controlled Phase (Weeks 0-16) were switched after 16 weeks of treatment to apremilast 30 mg tablets BID and continued dosing with apremilast 30 mg BID during the Maintenance Phase (weeks 16-32)

Reporting group title	APR-APR-Re-randomized to PBO

Reporting group description:

Participants who were initially randomized to APR 30 mg BID during the 16-week Placebo-controlled Phase (Weeks 0-16) continued dosing with APR 30 mg BID through the Maintenance Phase (Weeks 16-32). At Week 32, those participants who were considered responders [ie, having a ≥ Psoriasis Area and Severity Index score of 75 (PASI-75) response] were re-randomized to PBO during the Randomized Withdrawal Phase (Weeks 32-52). Those participants who retained their ≥PASI-75 response through the Randomized Withdrawal Phase remained on PBO until week 52. Those participants who lost their PASI-75 improvement achieved at week 32, were switched back to APR 30 mg BID at the time loss of effect was observed. All participants who completed the Randomized Withdrawal Phase at week 52 were eligible to participate in the Long-term Extension Phase from weeks 52-260, and received APR 30 mg BID for the remainder of their participation.

Reporting group title	APR-APR-Re-randomized to APR

Reporting group description:

Participants who were initially randomized to APR 30 mg BID during the 16-week Placebo-controlled Phase (Weeks 0-16) continued dosing with APR 30 mg BID through the Maintenance Phase (Weeks 16-32). At Week 32, those participants who were considered responders (ie, having a ≥PASI-75 response) were re-randomized to APR during the Randomized Withdrawal Phase (Weeks 32-52). Those participants who completed the Randomized Withdrawal Phase at Week 52 were eligible to participate in the Long-term Extension Phase from weeks 52-260 and remained on APR 30 mg BID for the remainder of their participation.

Reporting group title	APR-APR-APR + optional topicals/UVB

Reporting group description:

Participants who were initially randomized to APR 30 mg BID during the 16-week Placebo-controlled Phase (Weeks 0-16) continued dosing with APR 30 mg BID through the Maintenance Phase (weeks 16-32). At week 32, those participants who were considered partial responders (ie, having a response of PASI-50 to PASI-74) and those participants who were considered non-responders (ie, having a response of <PASI-50), remained on APR 30 mg BID and were given the option of adding topical therapies and/or phototherapy to their regimen. Those participants who completed the Randomized Withdrawal Phase at week 52 were eligible to participate in the Long-term Extension (LTE) Phase from Weeks 52-260 and remained on APR 30 mg BID for the remainder of their participation.

Reporting group title	PBO-APR-APR + optional topicals/ UVB

Reporting group description:

Participants who were initially randomized to placebo BID during the 16-week Placebo-controlled Phase (Weeks 0-16) were switched after 16 weeks of treatment to APR 30 mg BID and continued dosing with APR 30 mg BID during the Maintenance Phase (Weeks 16-32). At week 32, all participants continued to receive apremilast 30 mg BID. Those participants who were considered partial responders (ie, having a response of PASI-50 to PASI-74) and non-responders (ie, having a response of < PASI-50), were given the option of adding topical therapies and/or phototherapy to their regimen. All participants who

completed the Randomized Withdrawal Phase at week 52 were eligible to participate in the Long-term Extension Phase from Weeks 52-260 and remained on APR 30 mg BID for the remainder of their participation.

Reporting group title	Apremilast (Long-term extension)

Reporting group description:

Participants who were initially randomized to apremilast 30 mg BID during the 16-week placebo-controlled phase (Weeks 0-16) continued receiving apremilast 30 mg BID through the Maintenance Phase (weeks 16-32) and apremilast 30 mg tablets or placebo during the Randomized Withdrawal Phase then received apremilast 30 mg BID in the Long-term Extension Phase from Weeks 52-260.

Reporting group title	Placebo-Apremilast (Long-term extension)

Reporting group description:

Participants who were initially randomized to identically matching placebo BID during the placebo-controlled phase (Weeks 0-16) were switched at Week 16 to apremilast 30 mg BID during the Maintenance Phase, received apremilast 30 mg PO BID or placebo during the Randomized Withdrawal Phase and then received apremilast 30 mg tablets BID in the long-term extension phase from weeks 52-260.

Subject analysis set title	Number of Subjects with TEAEs During the APR-Exposure Period
Subject analysis set type	Safety analysis

Subject analysis set description:

An AE was any noxious, unintended, or untoward medical occurrence, that may appear or worsen in a participant during the course of study. It may be a new intercurrent illness, a worsening concomitant illness, an injury, or any concomitant impairment of the participant's health, including laboratory test values regardless of etiology. Any worsening (ie, any clinically significant adverse change in the frequency or intensity of a preexisting condition) was considered an AE. A serious AE (SAE) is any untoward adverse event that is fatal, life-threatening, results in persistent or significant disability or incapacity, requires or prolongs existing in-patient hospitalization, is a congenital anomaly or birth defect, or a condition that may jeopardize the patient or may require intervention to prevent one of the outcomes listed above. An AE is a treatment emergent AE if the AE start date is on or after the date of the first dose of study drug and no later than 28 days after the last dose.

Subject analysis set title	Subjects with a Psoriasis Flare During the APR-Exposure Phase
Subject analysis set type	Safety analysis

Subject analysis set description:

Psoriasis flare was defined as a sudden intensification of psoriasis requiring medical intervention, or a diagnosis of new generalized erythrodermic, inflammatory, or pustular psoriasis. Rebound is defined as a severe and sudden worsening of disease that occurs after treatment has been discontinued. Note categories below. [1] Psoriasis adverse events (ie, preferred term as Guttate psoriasis, Psoriasis, Pustular psoriasis) started on or after the first dose date and on or before the last dose date within the phase. [2] Psoriasis adverse events (ie, preferred term as Guttate psoriasis, Psoriasis, Pustular psoriasis, Rebound psoriasis) started after the last dose date for participants who discontinued within the phase. [3] PASI >= 125% of baseline score at any visit after the last dose date for participants who discontinued within the phase and were not included in [1] and/or [2]. Apremilast subjects as treated.

Primary: Percentage of Participants Who Achieved a 75% Improvement (response) in the Psoriasis Area Severity Index (PASI-75) at Week 16 from Baseline

End point title	Percentage of Participants Who Achieved a 75% Improvement (response) in the Psoriasis Area Severity Index (PASI-75) at Week 16 from Baseline

End point description:

The improvement in PASI score was used as a measure of efficacy. PASI was a measure of psoriatic disease severity taking into account qualitative lesion characteristics (erythema, thickness, and scaling) and degree of skin surface area involvement on defined anatomical regions. PASI scores range from 0 to 72, with higher scores = greater disease severity. Erythema, thickness, and scaling are scored on a scale of 0 (none) to 4 (very severe) on 4 anatomic regions of the body: head, trunk, upper limbs, and lower limbs. Degree of involvement on each of the 4 anatomic regions is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement). The Full Analysis Set (FAS) consisted of all participants who were randomized. Participants were included in the treatment group to which they were randomized APR 30 BID or placebo for the FAS. Last observation carried forward (LOCF) imputation was used.

End point type	Primary

End point timeframe:

Baseline to Week 16

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	562	282		
Units: percentage of participants				
number (not applicable)	33.1	5.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Apremilast v Placebo
Number of subjects included in analysis	844
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	27.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.1
upper limit	32.5

Secondary: Percentage of Participants Who Achieved a Static Physician Global Assessment (sPGA) Score of Clear (0) or Almost Clear (1) with At Least 2 Points Reduction from Baseline

End point title	Percentage of Participants Who Achieved a Static Physician Global Assessment (sPGA) Score of Clear (0) or Almost Clear (1) with At Least 2 Points Reduction from Baseline

End point description:

The sPGA was a 5-point scale ranging from 0 (clear), 1 (almost clear), 2 (mild), 3 (moderate), to 4 (severe), incorporating an assessment of the severity of the three primary signs of the disease: erythema, scaling and plaque elevation. When making the assessment of overall severity, the Investigator factored in areas that have already been cleared (ie, have scores of 0) and did not just evaluate remaining lesions for severity, ie, the severity of each sign was averaged across all areas of involvement, including cleared lesions. In the event of different severities across disease signs, the sign that is the predominant feature of the disease should be used to help determine the sPGA score. The Full Analysis Set (FAS) consisted of all participants who were randomized per protocol. Participants were included in the treatment group to which they were randomized APR 30 BID or placebo for the FAS. Last observation carried forward imputation was used.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	562	282		
Units: percentage of participants				
number (not applicable)	21.7	3.9		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Apremilast v Placebo
Number of subjects included in analysis	844
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	17.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.7
upper limit	21.9

Secondary: Percent Change from Baseline in Percent of Affected Body Surface Area (BSA) at Week 16

End point title	Percent Change from Baseline in Percent of Affected Body Surface Area (BSA) at Week 16

End point description:

BSA was a measurement of involved skin. The overall BSA affected by psoriasis was estimated based on the palm area of the participant's hand (entire palmar surface or "handprint" including the fingers), which equates to approximately 1% of total body surface area. BSA percent change from baseline (Visit 2 Week 0) was determined at each visit of the study, which is calculated as 100*(visit BSA – baseline BSA) / baseline BSA (%). The Full Analysis Set (FAS) consisted of all participants who were randomized per protocol. Participants were included in the treatment group to which they were randomized APR 30 BID or placebo for the FAS. Participants with a baseline value and at least 1 postbaseline value were included. Last observation carried forward imputation was used.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	559	278		
Units: percent change				
least squares mean (standard error)	-47.77 (± 1.634)	-6.99 (± 2.317)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Apremilast v Placebo
Number of subjects included in analysis	837
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-40.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.34
upper limit	-35.21

Notes:

[1] - The model included treatment group as a factor and the baseline value as a covariate. The estimation and p-value were adjusted by the covariate.

Secondary: Percent Change from Baseline in the Psoriasis Area Severity Index (PASI) Score at Week 16

End point title	Percent Change from Baseline in the Psoriasis Area Severity Index (PASI) Score at Week 16

End point description:

The improvement in PASI score was used as a measure of efficacy. PASI was a measure of psoriatic disease severity taking into account qualitative lesion characteristics (erythema, thickness, and scaling) and degree of skin surface area involvement on defined anatomical regions. PASI scores range from 0 to 72, with higher scores = greater disease severity. Erythema, thickness, and scaling are scored on a scale of 0 (none) to 4 (very severe) on 4 anatomic regions of the body: head, trunk, upper limbs, and lower limbs. Degree of involvement on each of the 4 anatomic regions is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement). The Full Analysis Set (FAS) consisted of all participants who were randomized. Participants were included in the treatment group to which they were randomized APR 30 BID or placebo for the FAS. Last observation carried forward (LOCF) imputation was used.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	559	278		
Units: percent change				
least squares mean (standard error)	-52.1 (± 1.37)	-16.8 (± 1.94)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Apremilast v Placebo
Number of subjects included in analysis	837
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-35.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.9
upper limit	-30.6

Notes:

[2] - The model included treatment group as a factor and the baseline value as a covariate. The estimation and p-value were adjusted by the covariate.

Secondary: Percentage of Participants Who Achieved a 50% improvement (response) in the PASI score (PASI-50) at Week 16 from Baseline

End point title	Percentage of Participants Who Achieved a 50% improvement (response) in the PASI score (PASI-50) at Week 16 from Baseline

End point description:

A participant was classified as having at least a 50% improvement in PASI score from baseline, which was equivalent to a percent change from baseline ranging from −100% to −50%. PASI score is based on an assessment of erythema (reddening), induration (plaque thickness), desquamation (scaling), and the percent area affected as observed on the day of examination. The Full Analysis Set (FAS) consisted of all participants who were randomized per protocol. Participants were included in the treatment group to which they were randomized APR 30 BID or placebo for the FAS. Last observation carried forward imputation was used.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	562	282		
Units: Percentage of Participants				
number (not applicable)	58.7	17.0		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Apremilast v Placebo
Number of subjects included in analysis	844
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	41.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	35.7
upper limit	47.7

Secondary: Change from Baseline in Pruritus Visual Analog Scale (VAS) Score at Week 16

End point title	Change from Baseline in Pruritus Visual Analog Scale (VAS) Score at Week 16

End point description:

The Pruritus Visual Analog Scores (VAS) were used to measure the amount of itching and discomfort a participant experiences. Participant's Assessment of Pruritus (Itch) asked: On average, how much itch have you had because of your condition in the past week? All VAS values range from 0 to 100. Higher scores correspond to more severe symptom or disease. Change from baseline was calculated for the VAS scale, where change = visit value − baseline value. The Full Analysis Set (FAS) consisted of all participants who were randomized per protocol. Participants were included in the treatment group to which they were randomized APR 30 BID or placebo for the FAS. Last observation carried forward imputation was used. Participants with a baseline value and at least 1 postbaseline value are included.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	559	277		
Units: units on a scale				
least squares mean (standard error)	-31.5 (± 1.30)	-7.3 (± 1.85)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Apremilast v Placebo
Number of subjects included in analysis	836
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Difference in LS Mean
Point estimate	-24.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.7
upper limit	-19.8

Notes:

[3] - Based on an analysis of variance model for the change from baseline at Week 16, with treatment group as a factor (an ANOVA model).

Secondary: Change from Baseline in the Dermatology Life Quality Index (DLQI) total score at Week 16

End point title	Change from Baseline in the Dermatology Life Quality Index (DLQI) total score at Week 16

End point description:

DLQI is a questionnaire that contains 10 items dealing with the subjects skin. With the exception of Item Number 7, the subject responds on a 4-point scale, ranging from Very Much (score 3) to Not at All or Not relevant (score 0). Item Number 7 is a multi-part item, part 1 ascertains whether the subject's skin prevented them from working or studying and if "No," then the subject is asked how much of a problem the skin has been at work or study over the past week, with responses of: A lot, A little, or Not at all (scores 2, 1, or 0 respectively). The DLQI total score is derived by summing scores, which have a possible range of 0 to 30, with 30 corresponding to the worst quality of life, and 0 corresponding to the best. The FAS consisted of all subjects who were randomized. Subjects were included in the treatment group which they were randomized APR 30 BID or placebo for the FAS. LOCF imputation was used. Subjects with a baseline value and at least 1 postbaseline value are included.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	556	274		
Units: units on a scale				
least squares mean (standard error)	-6.6 (± 0.27)	-2.1 (± 0.38)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Apremilast v Placebo
Number of subjects included in analysis	830
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Difference in LS Mean
Point estimate	-4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	-3.6

Secondary: Change from Baseline in the Mental Component Summary (MSC) Score of the Medical Outcome Study Short Form 36-item (SF-36) Health Survey Version 2.0 at Week 16

End point title	Change from Baseline in the Mental Component Summary (MSC) Score of the Medical Outcome Study Short Form 36-item (SF-36) Health Survey Version 2.0 at Week 16

End point description:

The SF-36 was a 36-item general health status instrument consisting of 8 scales: physical function, role limitations–physical, vitality, health perceptions, bodily pain, social function, role limitations–emotional, and mental health. Scale scores range from 0 to 100, with higher scores = better health. 2 overall summary scores were used; a Physical Component Summary (PCS) score and a Mental Component Summary (MSC) score. Scores from the 8 scales, PCS and MCS were transformed to a norm-based scores using weights from the U.S. general population, with 50 as the average and 10 as the standard deviation, higher scores = better health. For norm based scores, change from baseline were calculated for the 8 scales and the 2 summary scales, where change = visit value − baseline value. FAS = all subjects who were randomized. Subjects were included in the treatment to which they were randomized for the FAS. LOCF imputation was used; those with a baseline and 1 postbaseline value were included.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	556	273		
Units: units on a scale				
least squares mean (standard error)	2.28 (± 0.371)	-0.81 (± 0.529)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Apremilast v Placebo
Number of subjects included in analysis	829
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.81
upper limit	4.35

Notes:

[4] - The model included treatment group as a factor and the baseline value as a covariate. The estimation and p-value were adjusted by the covariate.

Secondary: Percentage of Participants Who Achieved both a 75% improvement (response) in the PASI and sPGA Score of Clear (0) or Almost Clear (1) with at Least 2 Points Reduction from baseline at Week 16 from Baseline

End point title	Percentage of Participants Who Achieved both a 75% improvement (response) in the PASI and sPGA Score of Clear (0) or Almost Clear (1) with at Least 2 Points Reduction from baseline at Week 16 from Baseline

End point description:

PASI-75 response was the percentage of participants who achieved at least a 75% reduction (improvement) from baseline in PASI score at Week 16. The improvement in PASI score was used as a measure of efficacy. See Outcome Measure #1 for further description. sPGA is a 5-point scale ranging from 0 (clear), 1 (almost clear), 2 (mild), 3 (moderate), to 4 (severe), incorporating an assessment of the severity of the three primary signs of the disease: erythema, scaling and plaque elevation. See OCM #2 for further description. The Full Analysis Set (FAS) consisted of all participants who were randomized per protocol. Participants were included in the treatment group to which they were randomized APR 30 BID or placebo for the FAS. Last observation carried forward imputation was used.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	562	282		
Units: percentage of participants				
number (not applicable)	20.3	3.5		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Apremilast v Placebo
Number of subjects included in analysis	844
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	16.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.8
upper limit	20.7

Secondary: Kaplan Meier Estimate of Time to loss of PASI-75 response (loss of effect) at Week 32 during the Re-Randomized Treatment Withdrawal Phase

End point title	Kaplan Meier Estimate of Time to loss of PASI-75 response (loss of effect) at Week 32 during the Re-Randomized Treatment Withdrawal Phase

End point description:

Time to loss was the time between the re-randomization date and the date of the first assessment where loss of PASI-75 was observed (event); or the time between the re-randomization date and the date of the last PASI assessment in the Weeks 32-52 interval prior to addition of protocol-prohibited medication/therapy, or resumption of APR 30 BID, or discontinuation, or Week 52 if no loss (censored). Analysis population consisted of participants who were re-randomized to placebo or apremilast 30mg BID at Week 32. "99999" indicates data not available since there were not enough subjects who lost response by the end of the Randomized Withdrawal Phase for the estimation.

End point type	Secondary

End point timeframe:

Week 32 to Week 52

End point values	APR-APR-Re-randomized to PBO	APR-APR-Re-randomized to APR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	77		
Units: Weeks				
median (confidence interval 95%)	17.7 (13.0 to 99999)	5.1 (4.1 to 8.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	APR-APR-Re-randomized to PBO v APR-APR-Re-randomized to APR
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.649
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.768
upper limit	3.969

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:

An AE was any noxious, unintended, or untoward medical occurrence, that may appear or worsen in a subject during the study. It may be a new intercurrent illness, a worsening concomitant illness, an injury, or any concomitant impairment of the subject's health, including laboratory test values regardless of cause. Any worsening (ie, any clinically significant adverse change in the frequency or intensity of a preexisting condition) was considered an AE. A serious AE (SAE) = untoward AE that is fatal, life-threatening, results in persistent disability or incapacity, requires or prolongs existing in-patient hospitalization, is a congenital anomaly or birth defect, or a condition that may jeopardize the subject or require an intervention to prevent one of the outcomes above. A treatment emergent is an AE if the AE start date is on or after the date of the lst dose of IP and no later than 28 days after the last dose. Safety population = subjects randomized; received one dose of IP.

End point type	Secondary

End point timeframe:

Week 0 to Week 16; mean duration of exposure was 14.8 weeks and 15.0 weeks for subjects randomized to placebo and apremilast respectively.

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	560	282		
Units: participants				
Any TEAE	388	157		
Any Drug-Related TEAE	224	58		
Any Severe TEAE	20	9		
Any Serious TEAE	12	8		
Any Serious Drug-Related TEAE	4	0		
Any TEAE leading to Drug Interruption	37	13		
≥ 1 TEAE leading to drug withdrawal	29	9		
Any TEAE Leading to Death	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with TEAEs During the Apremilast-exposure Period Through Week 260

End point title	Number of Participants with TEAEs During the Apremilast-exposure Period Through Week 260

End point description:

The APR-exposure period started on the date of the first dose of APR (Week 0 for participants originally randomized to APR or Wk 16 for subjects originally randomized to placebo) to the last dose of APR. AEs that started after 28 days of initiating PBO and before resuming APR treatment in the Randomized Treatment Withdrawal Phase (Wks 32 to 52) were excluded in the APR-exposure Period. A serious AE (SAE) = untoward AE that is fatal, life-threatening, results in persistent disability or incapacity, requires or prolongs existing in-patient hospitalization, is a congenital anomaly or birth defect, or a condition that may jeopardize the subject or require an intervention to prevent one of the outcomes above. A treatment emergent is an AE if the AE start date is on or after the date of the lst dose of IP and no later than 28 days after the last dose. APR subjects as treated. All subjects randomized to (at Week 0) or treated with (at Wk 16) APR 30 mg BID and received at least 1 dose

End point type	Secondary

End point timeframe:

Week 0 to Week 260; mean exposure to apremilast 30 mg BID during the Apremilast-exposure Period up to Week 260 was 97.83 weeks

End point values	Number of Subjects with TEAEs During the APR-Exposure Period			
Subject group type	Subject analysis set			
Number of subjects analysed	804			
Units: participants				
Any TEAE	675			
Any Drug-Related TEAE	372			
Any Severe TEAE	78			
Any Serious TEAE	74			
Any Serious Drug-Related TEAE	12			

Any TEAE Leading to Drug Interruption	107			
Any TEAE Leading to Drug withdrawal	98			
Any TEAE Leading to Death	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with a Psoriasis Flare or Rebound during the Placebo-Controlled Phase

End point title	Number of Participants with a Psoriasis Flare or Rebound during the Placebo-Controlled Phase

End point description:

Psoriasis flare was defined as a sudden intensification of psoriasis requiring medical intervention, or a diagnosis of new generalized erythrodermic, inflammatory, or pustular psoriasis. Rebound is defined as a severe and sudden worsening of disease that occurs after treatment has been discontinued. Note categories below. [1] Psoriasis adverse events (ie, preferred term as Guttate psoriasis, Psoriasis, Pustular psoriasis) started on or after the first dose date and on or before the last dose date within the phase. [2] Psoriasis adverse events (ie, preferred term as Guttate psoriasis, Psoriasis, Pustular psoriasis, Rebound psoriasis) started after the last dose date for participants who discontinued within the phase. [3] PASI >= 125% of baseline score at any visit after the last dose date for participants who discontinued within the phase and were not included in [1] and/or [2]. Safety population.

End point type	Secondary

End point timeframe:

Weeks 0 to Week 16

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	560	282		
Units: participants				
Participants with any psoriasis flare [1]	6	7		
Participants with any psoriasis rebound [2]	1	1		
PASI ≥ 125% of Baseline score after last dose [3]	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with a Psoriasis Flare or Rebound During the During the Apremilast-exposure Period Through Week 260

End point title	Number of Participants with a Psoriasis Flare or Rebound During the During the Apremilast-exposure Period Through Week 260

End point description:

Psoriasis flare was defined as a sudden intensification of psoriasis requiring medical intervention, or a diagnosis of new generalized erythrodermic, inflammatory, or pustular psoriasis. Rebound is defined as

a severe and sudden worsening of disease that occurs after treatment has been discontinued. Note categories below. [1] Psoriasis adverse events (ie, preferred term as Guttate psoriasis, Psoriasis, Pustular psoriasis) started on or after the first dose date and on or before the last dose date within the phase. [2] Psoriasis adverse events (ie, preferred term as Guttate psoriasis, Psoriasis, Pustular psoriasis, Rebound psoriasis) started after the last dose date for participants who discontinued within the phase. [3] PASI >= 125% of baseline score at any visit after the last dose date for participants who discontinued within the phase and were not included in [1] and/or [2].

End point type	Secondary

End point timeframe:

Week 0 to Week 260

End point values	Subjects with a Psoriasis Flare During the APR-Exposure Phase			
Subject group type	Subject analysis set			
Number of subjects analysed	804			
Units: participants				
Participants with any psoriasis flare [1]	35			
Participants with any psoriasis rebound [2]	12			
PASI ≥ 125% of Baseline score after last dose [3]	26			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs are reported as follows: -16-week PBO-controlled phase -Weeks 32-52 participants re-randomized to PBO at Week 32; re-randomized to PBO at Week 32. -Weeks 0-260 APR exposure period = those randomized or switched to APR at any time during the study

Adverse event reporting additional description:

During the PBO-controlled Phase (Weeks 0-16), the mean duration of treatment for those randomized to APR 30 BID or PBO at Week 0, was 15.0 and 14.8, respectively; for those re-randomized to PBO at Week 32, the mean duration of PBO was 8.1 weeks; during the APR-Exposure Period (Weeks 0-260), the mean duration of exposure to APR was 97.83 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	Placebo (Placebo-Controlled Phase) Weeks 0-16

Reporting group description:

Participants randomized and received identically matching placebo tablets BID during the Placebo-controlled Phase (Weeks 0-16)

Reporting group title	Apremilast (Placebo-Controlled Phase) Weeks 0-16

Reporting group description:

Participants randomized and received apremilast 30 mg tablets BID during the Placebo-Controlled Phase (Weeks 0-16)

Reporting group title	APR-APR-PBO Randomized Withdrawal Phase Weeks 32-52

Reporting group description:

Participants re-randomized and received placebo tablets BID at Week 32. Data from Week 32 up to Week 52 when participants received placebo treatment.

Reporting group title	Apremilast (Apremilast Exposure Period) Weeks 0-260

Reporting group description:

Participants who received apremilast 30 mg tablets BID, regardless of when the apremilast exposure started (at Week 0 or at week 16), up until Week 260. Adverse events associated with apremilast treatment up to Week 260 were included. AEs that started more than 28 days after Placebo treatment and prior to resuming apremilast were excluded for subjects who were re-randomized to Placebo at Week 32.

Serious adverse events	Placebo (Placebo-Controlled Phase) Weeks 0-16	Apremilast (Placebo-Controlled Phase) Weeks 0-16	APR-APR-PBO Randomized Withdrawal Phase Weeks 32-52
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 282 (2.84%)	12 / 560 (2.14%)	2 / 77 (2.60%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			

subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Anal cancer			
subjects affected / exposed	1 / 282 (0.35%)	0 / 560 (0.00%)	0 / 77 (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
Benign neoplasm of thyroid gland			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Conjunctival primary acquired melanosis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Malignant melanoma			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Pituitary tumour benign			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Prostate cancer			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Rectal cancer			

subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 cell carcinoma			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Thyroid cancer			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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			
Orthostatic hypotension			
subjects affected / exposed	0 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (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
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 / 282 (0.00%)	0 / 560 (0.00%)	1 / 77 (1.30%)
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 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Vaginal haemorrhage			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (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
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Completed suicide			
subjects affected / exposed	1 / 282 (0.35%)	0 / 560 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Investigations			
Blood bilirubin increased			

subjects affected / exposed	1 / 282 (0.35%)	0 / 560 (0.00%)	0 / 77 (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
Heart rate increased			
subjects affected / exposed	0 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (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
Oxygen saturation decreased			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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			
Chemical burns of eye			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	1 / 77 (1.30%)
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 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (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
Coronary artery restenosis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Incisional hernia			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Joint dislocation			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Ligament rupture			

subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Multiple injuries			
subjects affected / exposed	0 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Rib fracture			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Road traffic accident			
subjects affected / exposed	0 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (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
Angina unstable			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 arrest			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Mitral valve stenosis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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	1 / 282 (0.35%)	0 / 560 (0.00%)	0 / 77 (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
Supraventricular tachycardia			
subjects affected / exposed	1 / 282 (0.35%)	0 / 560 (0.00%)	0 / 77 (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
Nervous system disorders			
Cerebrovascular accident			

subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Convulsion			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Haemorrhagic stroke			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Presyncope			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Syncope			
subjects affected / exposed	1 / 282 (0.35%)	0 / 560 (0.00%)	0 / 77 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Microcytic anaemia			
subjects affected / exposed	0 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 pain			
subjects affected / exposed	0 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (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
Diverticular perforation			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 282 (0.35%)	1 / 560 (0.18%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Leukoplakia oesophageal			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Umbilical hernia			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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	1 / 282 (0.35%)	0 / 560 (0.00%)	0 / 77 (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
Cholecystitis acute			

subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Ingrowing nail			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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	0 / 282 (0.00%)	1 / 560 (0.18%)	0 / 77 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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			
Goitre			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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			
Muscular weakness			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 chest pain			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Periarthritis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Spinal column stenosis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Bacterial infection			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Brain abscess			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Clostridium difficile colitis			
subjects affected / exposed	1 / 282 (0.35%)	0 / 560 (0.00%)	0 / 77 (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
Diverticulitis			

subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Influenza			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Meningitis viral			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Nasopharyngitis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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			
subjects affected / exposed	1 / 282 (0.35%)	1 / 560 (0.18%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Sepsis			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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			
Hypokalaemia			

subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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
Obesity			
subjects affected / exposed	0 / 282 (0.00%)	0 / 560 (0.00%)	0 / 77 (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	Apremilast (Apremilast Exposure Period) Weeks 0-260		
Total subjects affected by serious adverse events			
subjects affected / exposed	74 / 804 (9.20%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anal cancer			
subjects affected / exposed	0 / 804 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Benign neoplasm of thyroid gland			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	2 / 804 (0.25%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Conjunctival primary acquired melanosis			

subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pituitary tumour benign				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal cancer				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal cell carcinoma				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thyroid cancer				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Orthostatic hypotension				

subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	2 / 804 (0.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vaginal haemorrhage			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			

subjects affected / exposed	2 / 804 (0.25%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Completed suicide			
subjects affected / exposed	0 / 804 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	2 / 804 (0.25%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 804 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Heart rate increased			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oxygen saturation decreased			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Chemical burns of eye			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Concussion			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery restenosis			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Incisional hernia			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ligament rupture			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple injuries			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			

subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute myocardial infarction				
subjects affected / exposed	4 / 804 (0.50%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	2 / 804 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac failure				
subjects affected / exposed	2 / 804 (0.25%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 1			
Cardiac failure congestive				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Coronary artery disease				

subjects affected / exposed	6 / 804 (0.75%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Mitral valve stenosis				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Myocardial infarction				
subjects affected / exposed	2 / 804 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 804 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebrovascular accident				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Convulsion				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic stroke				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	2 / 804 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Syncope				

subjects affected / exposed	0 / 804 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	2 / 804 (0.25%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Microcytic anaemia			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticular perforation			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	2 / 804 (0.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Leukoplakia oesophageal				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	0 / 804 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Ingrowing nail				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urticaria				
subjects affected / exposed	1 / 804 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Nephrolithiasis				

subjects affected / exposed	4 / 804 (0.50%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	3 / 804 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Periarthritis			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rotator cuff syndrome			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal column stenosis			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bacterial infection			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Brain abscess			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	0 / 804 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis viral			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nasopharyngitis			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	2 / 804 (0.25%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 804 (0.25%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Obesity			
subjects affected / exposed	1 / 804 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo (Placebo-Controlled Phase) Weeks 0-16	Apremilast (Placebo-Controlled Phase) Weeks 0-16	APR-APR-PBO Randomized Withdrawal Phase Weeks 32-52
Total subjects affected by non-serious adverse events			
subjects affected / exposed	90 / 282 (31.91%)	260 / 560 (46.43%)	10 / 77 (12.99%)
Vascular disorders			
Hypertension			

subjects affected / exposed	7 / 282 (2.48%)	10 / 560 (1.79%)	0 / 77 (0.00%)
occurrences (all)	7	10	0
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 282 (4.61%)	31 / 560 (5.54%)	0 / 77 (0.00%)
occurrences (all)	16	34	0
Tension headache			
subjects affected / exposed	12 / 282 (4.26%)	41 / 560 (7.32%)	2 / 77 (2.60%)
occurrences (all)	14	49	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	20 / 282 (7.09%)	105 / 560 (18.75%)	0 / 77 (0.00%)
occurrences (all)	23	123	0
Nausea			
subjects affected / exposed	19 / 282 (6.74%)	88 / 560 (15.71%)	0 / 77 (0.00%)
occurrences (all)	21	93	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 282 (1.77%)	9 / 560 (1.61%)	2 / 77 (2.60%)
occurrences (all)	6	11	2
Back pain			
subjects affected / exposed	2 / 282 (0.71%)	14 / 560 (2.50%)	1 / 77 (1.30%)
occurrences (all)	3	14	1
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	6 / 282 (2.13%)	10 / 560 (1.79%)	0 / 77 (0.00%)
occurrences (all)	6	10	0
Nasopharyngitis			
subjects affected / exposed	23 / 282 (8.16%)	41 / 560 (7.32%)	3 / 77 (3.90%)
occurrences (all)	26	48	3
Sinusitis			
subjects affected / exposed	5 / 282 (1.77%)	16 / 560 (2.86%)	1 / 77 (1.30%)
occurrences (all)	6	17	1
Upper respiratory tract infection			
subjects affected / exposed	21 / 282 (7.45%)	57 / 560 (10.18%)	2 / 77 (2.60%)
occurrences (all)	21	64	2

Non-serious adverse events	Apremilast (Apremilast Exposure Period) Weeks 0-260		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	503 / 804 (62.56%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	56 / 804 (6.97%)		
occurrences (all)	57		
Nervous system disorders			
Headache			
subjects affected / exposed	62 / 804 (7.71%)		
occurrences (all)	87		
Tension headache			
subjects affected / exposed	84 / 804 (10.45%)		
occurrences (all)	134		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	163 / 804 (20.27%)		
occurrences (all)	211		
Nausea			
subjects affected / exposed	130 / 804 (16.17%)		
occurrences (all)	153		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	51 / 804 (6.34%)		
occurrences (all)	63		
Back pain			
subjects affected / exposed	50 / 804 (6.22%)		
occurrences (all)	57		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	41 / 804 (5.10%)		
occurrences (all)	50		
Nasopharyngitis			
subjects affected / exposed	131 / 804 (16.29%)		
occurrences (all)	226		

Sinusitis subjects affected / exposed occurrences (all)	45 / 804 (5.60%) 63		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	183 / 804 (22.76%) 326		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 August 2010	1. Updated the Table of Events at Week 34 for Investigational Product (IP) Dispense and Return, which allowed sites to maintain the study blinding during the Randomized Treatment Withdrawal Phase of the study (Weeks 32-52) 2. Clarified procedures for male subjects while on study in the case of a male subject impregnating a female partner 3. Clarified data collection method to be used to subject-reported data 4. Included PHQ-8 quality of life questionnaire within the context of the full protocol 5. Clarified subject signature was required on a separate page of the ICD for PK and photography assessments
04 January 2011	1. Clarified the language regarding contraception methods to ensure that acceptable methods of contraception by subjects were used: added a statement to ensure that appropriate education regarding contraception methods was provided by the investigator to the subjects 2. Clarified procedures for subjects who entered the Randomized Treatment Withdrawal Phase at Week 32 3. Clarified that Arthritis VAS only pertained to subjects with psoriatic arthritis 4. Clarified procedures for VAS Exploratory Endpoint regarding intent to compare the proportion of subjects with 10-mm improvement in symptoms (minimal clinically important difference [MCID]) 5. Deleted annual CXRs allowing local treatment guidelines to dictate when CXRs were performed 6. Corrected the order of Health-Related Quality of Life (HRQoL) and VAS assessments to align with what is actually being done on the SitePad instrument 7. Aligned exclusion criteria related to past malignancies across the entire apremilast Phase 3 program in order to give investigators responsibility for determining subject eligibility for previously successfully treated local lesions 8. Clarified Statistical Efficacy Analysis deleting the "per protocol" analysis 9. Modified the Reasons for Discontinuation to align with what is displayed in the InForm database 10. Clarified protocol definition of permitted therapies for partial responders and nonresponders beginning at Week 32
10 June 2011	1. Clarified the Contraception Education that required the investigator to educate the subject on acceptable birth control any time when a subject's contraceptive measures or ability to become pregnant changed; modified to direct the investigator to Section 7.2 of the protocol where details regarding the acceptable contraception for this study may be found 2. Modified Inclusion Criterion Number 9 (female birth control) to clearly define single or multiple forms of contraception that were acceptable for this study 3. Added a footnote to Inclusion Criterion Number 9 (female birth control) to clarify that the female subject's chosen form of contraception must be fully effective by the time the female subject receives the first dose of IP at randomization 4. Modified Inclusion Criterion Number 10 (male birth control) to clarify that male subjects must use a "male" latex or non-latex condom

19 April 2012	1. Updates made to the contact information for the study medical monitor 2. Clarified in Section 3.2.2, Efficacy, and in Section 3.3, Exploratory Endpoint(s), that the VAS scale endpoints were to be change from baseline rather than percent change 3. Modified Section 4.1, Study Design, to allow the use of topical corticosteroids, retinoids or vitamin D analog preparations and/or phototherapy after the Week 52 visit for partial and nonresponders (< PASI-75) 4. Modified Section 4.1, Study Design, regarding the replacement of the Safety Review Panel with an independent external DMC 5. Added footnote k and h in Table 1 and 2, respectively, to the AEs row that vasculitis assessments and/or psychiatric evaluations were to be performed as needed when AEs were reported 6. Clarification of footnote l and i in Table 1 and 2, respectively, that only subjects with nail disease, scalp psoriasis, palmoplantar psoriasis, and/or psoriatic arthritis at baseline were to be evaluated with the disease activity tools for those respective conditions 7. Revision of the Contraception Education in Section 6.2 and movement of footnote from Section 7.2 to Section 6.2 8. Added Section 6.6.4.1, Vasculitis Assessment 9. Added Section 6.6.4.2, Psychiatric Evaluation, to provide precautionary guidance to physicians for the management of subjects identified as having thoughts of suicide, attempted suicide or having major psychiatric illness 10. Change to the open-label IP package as described in Sections 6.11.1, IP Dispensing and Counting for Compliance, and 8.4, Packaging and Labeling 11. Modified Section 9.1, Permitted Concomitant Medications, and Section 9.2, Prohibited Concomitant Medications, to allow the use of topical corticosteroids, retinoids, or vitamin D analog preparations and/or phototherapy after the Week 52 visit for partial and nonresponders (< PASI-75) 12. Clarified that AE tables were to summarize TEAE only 13. "CRF" changed to "eCRF" to reflect that data captured in the eCRF pages

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported