Clinical trial results:
A Phase 3, Multi-Center, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Apremilast (CC-10004) in Pediatric Subjects From 6 Through 17 Years of Age With Moderate to Severe Plaque Psoriasis

Summary

EudraCT number	2018-002918-12
Trial protocol	FR NL CZ HU BE IT
Global end of trial date	27 March 2023

Results information

Result version number	v1 (current)
This version publication date	07 October 2023
First version publication date	07 October 2023

Trial information

Trial identification

Sponsor protocol code	CC-10004-PPSO-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03701763
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States,
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	Study Director, Amgen Inc., medinfo@amgen.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 March 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the clinical efficacy of apremilast compared with placebo in children and adolescents (ages 6 through 17 years) with moderate to severe plaque psoriasis.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines and in accordance with the general ethical principles outlined in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 December 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Czechia: 5
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Russian Federation: 103
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	United States: 58
Worldwide total number of subjects	245
EEA total number of subjects	61

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	101
Adolescents (12-17 years)	144
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled into this study at sites in Belgium, Canada, Czech Republic, France, Israel, Italy, Russia, Spain, and the United States.

Pre-assignment

Screening details:

Screening tests and procedures were performed up to 35 days preceding randomization.

Period 1

Period 1 title	Placebo-controlled Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

In the placebo-controlled phase, participants who were randomized to placebo received placebo twice daily (BID) for 16 weeks. At Week 16, participants in the placebo group were switched to apremilast based on baseline weight. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

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:

Tablets

Arm title	Apremilast

Arm description:

In the placebo-controlled phase, participants who were randomized to apremilast who were 20 to < 50 kg received apremilast 20 mg twice daily (BID) for 16 weeks, and participants >/= 50 kg received apremilast 30 mg BID for 16 weeks. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

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

Dosage and administration details:

Tablets

Number of subjects in period 1	Placebo	Apremilast
Started	82	163
Took Investigational Product (IP)	80	163
Completed	72	149
Not completed	10	14
Consent withdrawn by subject	2	3
Adverse event, non-fatal	1	5
Miscellaneous	2	-
Withdrawal by Parent/Guardian	3	5
Lost to follow-up	-	1
Lack of efficacy	2	-

Period 2

Period 2 title	Apremilast Extension Phase
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Apremilast

Arm description:

At Week 16, participants in the placebo group during the placebo-controlled phase were switched to apremilast based on baseline weight. Participants 20 to < 50 kg received apremilast 20 mg BID for 36 weeks, and participants >/= 50 kg received apremilast 30 mg BID for 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

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

Dosage and administration details:

Tablets

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

Dosage and administration details:

Tablets

Arm title	Apremilast/Apremilast

Arm description:

At Week 16, participants in the apremilast group during the placebo-controlled phase continued to receive their original dosing assignment for an additional 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

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

Dosage and administration details:

Tablets

Number of subjects in period 2	Placebo/Apremilast	Apremilast/Apremilast
Started	72	149
Apremilast 20mg Apremilast Exposure Prd	36 [1]	80 [2]
Apremilast 30mg Apremilast Exposure Prd	36 [3]	83 [4]
Took at Least 1 Dose of IP	72	149
Completed	61	125
Not completed	11	24
Non-compliance with Study Drug	1	1
Consent withdrawn by subject	1	3
Adverse event, non-fatal	3	1
Miscellaneous	2	1
Withdrawal by Parent/Guardian	1	8
Lost to follow-up	-	2
Lack of efficacy	3	8

Notes:

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

Justification: Includes participants who received apremilast 20mg during the apremilast exposure period.

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

Justification: Includes participants who received apremilast 20mg during the apremilast exposure period.

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

Justification: Includes participants who received apremilast 30mg during the apremilast exposure period.

[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: Includes participants who received apremilast 30mg during the apremilast exposure period.

Period 3

Period 3 title	14-Week Observational Follow-up Phase
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

In the placebo-controlled phase, participants who were randomized to placebo received placebo twice daily (BID) for 16 weeks. At Week 16, participants in the placebo group were switched to apremilast based on baseline weight. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

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:

Tablets

Arm title	Apremilast

Arm description:

In the placebo-controlled phase, participants who were randomized to apremilast who were 20 to < 50 kg received apremilast 20 mg twice daily (BID) for 16 weeks, and participants >/= 50 kg received apremilast 30 mg BID for 16 weeks. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

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

Dosage and administration details:

Tablets

Arm title	Placebo/Apremilast

Arm description:

At Week 16, participants in the placebo group during the placebo-controlled phase were switched to apremilast based on baseline weight. Participants 20 to < 50 kg received apremilast 20 mg BID for 36 weeks, and participants >/= 50 kg received apremilast 30 mg BID for 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

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

Dosage and administration details:

Tablets

Investigational medicinal product name	Apremilast
Investigational medicinal product code	
Other name	Otezla®

Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets

Arm title	Apremilast/Apremilast

Arm description:

At Week 16, participants in the apremilast group during the placebo-controlled phase continued to receive their original dosing assignment for an additional 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

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

Dosage and administration details:

Tablets

Number of subjects in period 3[5]	Placebo	Apremilast	Placebo/Apremilast
Started	1	4	14
Completed	1	3	11
Not completed	0	1	3
Consent withdrawn by subject	-	-	-
Miscellaneous	-	-	1
Withdrawal by Parent/Guardian	-	1	1
Study Terminated by Sponsor	-	-	1
Lost to follow-up	-	-	-

Number of subjects in period 3[5]	Apremilast/Apremilast
Started	26
Completed	23
Not completed	3
Consent withdrawn by subject	2
Miscellaneous	-
Withdrawal by Parent/Guardian	-
Study Terminated by Sponsor	-
Lost to follow-up	1

Notes:

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

Justification: Includes participants who completed the study or discontinued the study early who opted to enter the 14-week observational follow up.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
In the placebo-controlled phase, participants who were randomized to placebo received placebo twice daily (BID) for 16 weeks. At Week 16, participants in the placebo group were switched to apremilast based on baseline weight. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.	
Reporting group title	Apremilast
Reporting group description:	
In the placebo-controlled phase, participants who were randomized to apremilast who were 20 to < 50 kg received apremilast 20 mg twice daily (BID) for 16 weeks, and participants >/= 50 kg received apremilast 30 mg BID for 16 weeks. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.	

Reporting group values	Placebo	Apremilast	Total
Number of subjects	82	163	245
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	34	67	101
Adolescents (12-17 years)	48	96	144
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	12.2	12.3	
standard deviation	± 3.25	± 3.32	-
Sex: Female, Male Units: participants			
Female	39	89	128
Male	43	74	117
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	2	2
Asian	3	6	9
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	5	8
White	73	140	213
More than one race	0	0	0
Unknown or Not Reported	3	10	13
Ethnicity (NIH/OMB) Units: Subjects			

Hispanic or Latino	8	24	32
Not Hispanic or Latino	71	129	200
Unknown or Not Reported	3	10	13

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

In the placebo-controlled phase, participants who were randomized to placebo received placebo twice daily (BID) for 16 weeks. At Week 16, participants in the placebo group were switched to apremilast based on baseline weight. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

Reporting group title	Apremilast

Reporting group description:

In the placebo-controlled phase, participants who were randomized to apremilast who were 20 to < 50 kg received apremilast 20 mg twice daily (BID) for 16 weeks, and participants >/= 50 kg received apremilast 30 mg BID for 16 weeks. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

Reporting group title	Placebo/Apremilast

Reporting group description:

At Week 16, participants in the placebo group during the placebo-controlled phase were switched to apremilast based on baseline weight. Participants 20 to < 50 kg received apremilast 20 mg BID for 36 weeks, and participants >/= 50 kg received apremilast 30 mg BID for 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

Reporting group title	Apremilast/Apremilast

Reporting group description:

At Week 16, participants in the apremilast group during the placebo-controlled phase continued to receive their original dosing assignment for an additional 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

Reporting group title	Placebo

Reporting group description:

In the placebo-controlled phase, participants who were randomized to placebo received placebo twice daily (BID) for 16 weeks. At Week 16, participants in the placebo group were switched to apremilast based on baseline weight. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

Reporting group title	Apremilast

Reporting group description:

In the placebo-controlled phase, participants who were randomized to apremilast who were 20 to < 50 kg received apremilast 20 mg twice daily (BID) for 16 weeks, and participants >/= 50 kg received apremilast 30 mg BID for 16 weeks. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

Reporting group title	Placebo/Apremilast

Reporting group description:

At Week 16, participants in the placebo group during the placebo-controlled phase were switched to apremilast based on baseline weight. Participants 20 to < 50 kg received apremilast 20 mg BID for 36 weeks, and participants >/= 50 kg received apremilast 30 mg BID for 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

Reporting group title	Apremilast/Apremilast

Reporting group description:

At Week 16, participants in the apremilast group during the placebo-controlled phase continued to receive their original dosing assignment for an additional 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

Subject analysis set title	Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

In the placebo-controlled phase, participants who were randomized to placebo received placebo twice daily (BID) for 16 weeks. At Week 16, participants in the placebo group were switched to apremilast

based on baseline weight. Participants 20 to < 50 kg received apremilast 20 mg BID for 36 weeks, and participants >/= 50 kg received apremilast 30 mg BID for 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up. The arms for this endpoint are different to those in the overall study reporting group. Due to constraints of the EudraCT system, these arms have had to be added as subject analysis sets.

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

Subject analysis set description:

In the placebo-controlled phase, participants who were randomized to apremilast who were 20 to < 50 kg received apremilast 20 mg twice daily (BID) for 16 weeks, and participants >/= 50 kg received apremilast 30 mg BID for 16 weeks. At Week 16, participants in the apremilast group continued to receive their original dosing assignment for an additional 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up. The arms for this endpoint are different to those in the overall study reporting group. Due to constraints of the EudraCT system, these arms have had to be added as subject analysis sets

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

Subject analysis set description:

In the placebo-controlled phase, participants who were randomized to apremilast who were 20 to < 50 kg received apremilast 20 mg twice daily (BID) for 16 weeks, and participants >/= 50 kg received apremilast 30 mg BID for 16 weeks. At Week 16, participants in the apremilast group continued to receive their original dosing assignment for an additional 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up. The arms for this endpoint are different to those in the overall study reporting group. Due to constraints of the EudraCT system, these arms have had to be added as subject analysis sets.

Subject analysis set title	Apremilast-extension Phase: Apremilast 20 mg BID
Subject analysis set type	Safety analysis

Subject analysis set description:

At Week 16, participants 20 to < 50 kg received apremilast 20 mg BID for 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up. The arms for this endpoint are different to those in the overall study reporting group. Due to constraints of the EudraCT system, these arms have had to be added as subject analysis sets.

Subject analysis set title	Apremilast-extension Phase: Apremilast 30 mg BID
Subject analysis set type	Safety analysis

Subject analysis set description:

At Week 16, participants >/= 50 kg received apremilast 30 mg BID for 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up. The arms for this endpoint are different to those in the overall study reporting group. Due to constraints of the EudraCT system, these arms have had to be added as subject analysis sets.

Subject analysis set title	Apremilast Exposure Period: Apremilast 20 mg BID
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who were randomized to apremilast during the placebo-controlled phase and received apremilast 20 mg BID for 16 weeks during the placebo-controlled phase. At Week 16, participants in the placebo group during the placebo-controlled phase were switched to apremilast 20mg BID for 36 weeks based on baseline weight. Participants who received apremilast 20 mg BID during the placebo-controlled phase continued to receive their original dosing assignment for an additional 36 weeks during the apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

Subject analysis set title	Apremilast Exposure Period: Apremilast 30 mg BID
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who were randomized to apremilast during the placebo-controlled phase and received apremilast 30 mg BID for 16 weeks during the placebo-controlled phase. At Week 16, participants in the placebo group during the placebo-controlled phase were switched to apremilast 30mg BID for 36 weeks based on baseline weight. Participants who received apremilast 30 mg BID during the placebo-controlled phase continued to receive their original dosing assignment for an additional 36 weeks during the

apremilast-extension phase. Participants who completed the study or discontinued the study early could have opted to enter the 14-week observational follow up.

Subject analysis set title	Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who received placebo in the placebo-controlled phase who entered the 14-week observational follow up.

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

Subject analysis set description:

Participants who received apremilast 20 mg in either the placebo-controlled phase or apremilast extension phase who entered the 14-week observational follow up.

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

Subject analysis set description:

Participants who received apremilast 30 mg in either the placebo-controlled phase or apremilast extension phase who entered the 14-week observational follow up.

Primary: Percentage of Participants with a Static Physician Global Assessment (sPGA) Response at Week 16

End point title	Percentage of Participants with a Static Physician Global Assessment (sPGA) Response at Week 16

End point description:

The sPGA is the assessment by the Investigator of the overall disease severity of plaque psoriasis at the time of evaluation. The sPGA is a 5-point scale ranging from 0 (clear) to 4 (severe), incorporating an assessment of the severity of the three primary signs of the disease: erythema, scaling and plaque elevation. The results presented are for the percentage of participants with a sPGA response. An sPGA response was defined as a score of clear (0) or almost clear (1) with at least a 2-point reduction from baseline at Week 16. Measured in the intent-to-treat (ITT) population, which included all participants who were randomized.

End point type	Primary

End point timeframe:

Baseline to Week 16

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	163		
Units: percentage of participants				
number (not applicable)	11.5	33.1		

Statistical analyses

Statistical analysis title	Placebo vs. Apremilast
Comparison groups	Placebo v Apremilast

Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Adjusted Difference
Point estimate	21.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.2
upper limit	32.1

Secondary: Percentage of Participants who Achieved At Least 75% Reduction in Psoriasis Area Severity Index (PASI-75) from Baseline at Week 16

End point title	Percentage of Participants who Achieved At Least 75% Reduction in Psoriasis Area Severity Index (PASI-75) from Baseline at Week 16

End point description:

The Psoriasis Area Severity Index (PASI) is 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. The PASI scores range from 0 to 72, with higher scores reflecting greater disease severity. The results presented are for the percentage of participants with PASI-75. PASI-75 was defined as at least a 75% reduction in PASI score from baseline. Measured in the intent-to-treat (ITT) population, which included all participants who were randomized.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	163		
Units: percentage of participants				
number (not applicable)	16.1	45.4		

Statistical analyses

Statistical analysis title	Placebo vs. Apremilast
Comparison groups	Placebo v Apremilast
Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Adjusted Difference
Point estimate	29.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	17.8
upper limit	40.9

Secondary: Percentage of Participants who Achieved At Least 50% Reduction in Psoriasis Area Severity Index (PASI-50) from Baseline at Week 16

End point title	Percentage of Participants who Achieved At Least 50% Reduction in Psoriasis Area Severity Index (PASI-50) from Baseline at Week 16

End point description:

The PASI is 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. The PASI scores range from 0 to 72, with higher scores reflecting greater disease severity. The results presented are for the percentage of participants with PASI-50. PASI-50 was defined as at least a 50% reduction in PASI score from baseline. Measured in the intent-to-treat (ITT) population, which included all participants who were randomized.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	163		
Units: percentage of participants				
number (not applicable)	32.1	70.5		

Statistical analyses

Statistical analysis title	Placebo vs. Apremilast
Comparison groups	Placebo v Apremilast
Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Adjusted Difference
Point estimate	38.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.6
upper limit	51.2

Secondary: Percentage Change from Baseline in Total PASI Score at Week 16

End point title	Percentage Change from Baseline in Total PASI Score at Week 16

End point description:

The PASI is 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. The PASI scores range from 0 to 72, with higher scores reflecting greater disease severity. Positive percentage change from baseline scores indicate a worsening of disease severity, and negative percentage change from baseline scores indicate an improvement in disease severity. Measured in the intent-to-treat (ITT) population, which included all participants who were randomized.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	163		
Units: percentage change				
arithmetic mean (standard error)	-37.49 (± 3.866)	-64.52 (± 2.543)		

Statistical analyses

Statistical analysis title	Placebo vs. Apremilast
Comparison groups	Placebo v Apremilast
Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Difference in Least Squares Mean
Point estimate	-26.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.93
upper limit	-18
Variability estimate	Standard error of the mean
Dispersion value	4.572

Secondary: Percentage Change from Baseline in Body Surface Area (BSA) Affected by Psoriasis at Week 16

End point title	Percentage Change from Baseline in Body Surface Area (BSA) Affected by Psoriasis at Week 16

End point description:

BSA is a measurement of involved skin of the whole body affected by psoriasis, which ranges from 0% to 100%. Positive percentage change from baseline indicates that a greater BSA was affected by psoriasis. A negative percentage change from baseline indicates that a lesser BSA was affected by psoriasis. Measured in the intent-to-treat (ITT) population, which included all participants who were randomized.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	163		
Units: percentage change in affected BSA				
arithmetic mean (standard error)	-20.56 (± 5.441)	-55.44 (± 3.428)		

Statistical analyses

Statistical analysis title	Placebo vs. Apremilast
Comparison groups	Placebo v Apremilast
Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Difference in Least Squares Mean
Point estimate	-34.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.99
upper limit	-22.55
Variability estimate	Standard error of the mean
Dispersion value	6.229

Secondary: Percentage of Participants who Achieved a Children’s Dermatology Life Quality Index (CDLQI) Score of 0 or 1 at Week 16

End point title	Percentage of Participants who Achieved a Children’s Dermatology Life Quality Index (CDLQI) Score of 0 or 1 at Week 16

End point description:

The CDLQI is designed to measure the impact of skin disease on children’s quality of life. The CDLQI measures how much the participant’s psoriasis has affected them over the last week, and includes 10

questions with possible answers ranging from not at all (score of 0) to very much (score of 3). The CDLQI total score ranged from 0 (no effect on the participant's life) to 30 (extremely large effect on the participant's life). The results presented are for the percentage of participants who achieved a total CDLQI score of 0 or 1 at Week 16. Measured in participants in the intent-to-treat (ITT) population (which included all participants who were randomized), with a baseline CDLQI Score >/= 2.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	148		
Units: percentage of participants				
number (not applicable)	31.3	35.4		

Statistical analyses

Statistical analysis title	Placebo vs. Apremilast
Comparison groups	Placebo v Apremilast
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5616
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Adjusted Difference
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.8
upper limit	18

Secondary: Change from Baseline in CDLQI Score at Week 16

End point title	Change from Baseline in CDLQI Score at Week 16

End point description:

The CDLQI is designed to measure the impact of skin disease on children’s quality of life. The CDLQI measures how much the participant’s psoriasis has affected them over the last week, and includes 10 questions with possible answers ranging from not at all (score of 0) to very much (score of 3). The CDLQI total score ranged from 0 (no effect on the participant's life) to 30 (extremely large effect on the participant's life). A positive change from baseline score indicates that a participant's quality of life has worsened. A negative change from baseline score indicates that a participant’s quality of life has improved. Measured in the intent-to-treat (ITT) population, which included all participants who were randomized.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	163		
Units: scores on a scale				
arithmetic mean (standard error)	-2.7 (± 0.56)	-5.3 (± 0.44)		

Statistical analyses

Statistical analysis title	Placebo vs. Apremilast
Comparison groups	Placebo v Apremilast
Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0009
Method	ANCOVA
Parameter estimate	Difference in Least Squares Mean
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.55

Secondary: Number of Participants who Experienced a Treatment-emergent Adverse Event (TEAE) During the Placebo-controlled Phase

End point title	Number of Participants who Experienced a Treatment-emergent Adverse Event (TEAE) During the Placebo-controlled Phase

End point description:

An adverse event (AE) was defined as any noxious, unintended, or untoward medical occurrence that may appear or worsen in a participant during the course of the study. A TEAE is any AE that occurred after first dose of the investigational product. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product. As pre-specified, data are presented per treatment received and adverse event data collected by apremilast dose.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	80	80	83	
Units: participants	33	58	48	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a TEAE During the Apremilast Exposure Period

End point title	Number of Participants who Experienced a TEAE During the Apremilast Exposure Period

End point description:

An AE was defined as any noxious, unintended, or untoward medical occurrence that may appear or worsen in a participant during the course of the study. A TEAE is any AE that occurred after first dose of the investigational product. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product. As pre-defined in the statistical analysis plan, data are presented per treatment received and adverse event data collected by apremilast dose.

End point type	Secondary

End point timeframe:

52 weeks

End point values	Apremilast Exposure Period: Apremilast 20 mg BID	Apremilast Exposure Period: Apremilast 30 mg BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	116	119		
Units: participants	88	80		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a Treatment-emergent Serious Adverse Event (TESAE) During the Placebo-controlled Phase

End point title	Number of Participants who Experienced a Treatment-emergent Serious Adverse Event (TESAE) During the Placebo-controlled Phase

End point description:

A TESAE is any AE occurring at any dose after first dose that results in death, is life-threatening (ie, in the opinion of the Investigator, the participant is at immediate risk of death from the AE), requires inpatient hospitalization or prolongation of existing hospitalization (hospitalization is defined as an inpatient admission, regardless of length of stay), results in persistent or significant disability/incapacity (a substantial disruption of the participant's ability to conduct normal life functions), is a congenital

anomaly/birth defect, or constitutes an important medical event. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product. As pre-specified, data are presented per treatment received and adverse event data collected by apremilast dose.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	80	80	83	
Units: participants	1	2	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a TESAE During the Apremilast Exposure Period

End point title	Number of Participants who Experienced a TESAE During the Apremilast Exposure Period

End point description:

A TESAE is any AE occurring at any dose after first dose that results in death, is life-threatening (ie, in the opinion of the Investigator, the participant is at immediate risk of death from the AE), requires inpatient hospitalization or prolongation of existing hospitalization (hospitalization is defined as an inpatient admission, regardless of length of stay), results in persistent or significant disability/incapacity (a substantial disruption of the participant's ability to conduct normal life functions), is a congenital anomaly/birth defect, or constitutes an important medical event. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product. As pre-defined in the statistical analysis plan, data are presented per treatment received and adverse event data collected by apremilast dose.

End point type	Secondary

End point timeframe:

52 weeks

End point values	Apremilast Exposure Period: Apremilast 20 mg BID	Apremilast Exposure Period: Apremilast 30 mg BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	116	119		
Units: participants	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a Treatment-related Adverse Event (TRAE) During the Placebo-controlled Phase

End point title	Number of Participants who Experienced a Treatment-related Adverse Event (TRAE) During the Placebo-controlled Phase

End point description:

A TREAE is any AE that is determined by the Investigator to have a possibly causal relationship to the investigational product. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product. As pre-specified, data are presented per treatment received and adverse event data collected by apremilast dose.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Placebo	Apremilast 20 mg	Apremilast 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	80	80	83	
Units: participants	12	36	32	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a TRAE During the Apremilast Exposure Period

End point title	Number of Participants who Experienced a TRAE During the Apremilast Exposure Period

End point description:

A TREAE is any AE that is determined by the Investigator to have a possibly causal relationship to the investigational product. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product. As pre-defined in the statistical analysis plan, data are presented per treatment received and adverse event data collected by apremilast dose.

End point type	Secondary

End point timeframe:

52 weeks

End point values	Apremilast Exposure Period: Apremilast 20 mg BID	Apremilast Exposure Period: Apremilast 30 mg BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	116	119		
Units: participants	45	47		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Diarrhea During the Placebo-controlled Phase

End point title	Number of Participants with Diarrhea During the Placebo-controlled Phase

End point description:

Diarrhea was defined as having 3 or more liquid or watery stools in a day. Participants and their parent/guardian were supplied with diaries (either paper or electronic) that were filled out daily to record and describe any diarrhea and associated symptoms. Measured in participants in the Safety Population (which included all randomized participants who received at least 1 dose of investigational product), who had diary entries at each specified time point.

End point type	Secondary

End point timeframe:

Up to approximately 113 days

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	163		
Units: participants				
Day 1 to 28 (n=77,156)	25	67		
Day 29 to 56 (n=73,155)	20	51		
Day 57 to 84 (n=73,147)	14	41		
Day 85 to 112 (n=69,142)	10	29		
Day >/= 113 (n=46,105)	2	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Diarrhea During the Apremilast Exposure Period

End point title	Number of Participants with Diarrhea During the Apremilast Exposure Period

End point description:

Diarrhea was defined as having 3 or more liquid or watery stools in a day. Participants and their parent/guardian were supplied with diaries (either paper or electronic) that were filled out daily to record and describe any diarrhea and associated symptoms. Measured in participants in the Safety Population (which included all randomized participants who received at least 1 dose of investigational product), who had diary entries at each specified time point.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 365 days

End point values	Apremilast Exposure Period: Apremilast 20 mg BID	Apremilast Exposure Period: Apremilast 30 mg BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	116	119		
Units: participants				
Day 1 to 28 (n=109, 114)	36	47		
Day 29 to 56 (n= 108,103)	30	36		
Day 57 to 84 (n=101, 110)	22	32		
Day 85 to 112 (n=100,106)	17	19		
Day 113 to 140 (n=99,106)	21	17		
Day 141 to 168 (n=98,104)	16	21		
Day 169 to 196 (n=96,102)	19	17		
Day 197 to 224 (n=93,102)	19	12		
Day 225 to 252 (n=92,98)	20	12		
Day 253 to 280 (n=76,69)	18	16		
Day 281 to 308 (n=61,60)	13	9		
Day 309 to 336 (n=62,59)	12	5		
Day 337 to 364 (n=59,58)	7	5		
Day >= 365 (n=24,22)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Diarrhea Symptoms During the Placebo-controlled Phase

End point title	Number of Participants with Diarrhea Symptoms During the Placebo-controlled Phase

End point description:

Diarrhea symptoms were nausea, vomiting, abdominal cramps, abdominal pain, fever, bloating, and other symptoms. Participants and their parent/guardian were supplied with diaries (either paper or electronic) that were filled out daily to record and describe any diarrhea and associated symptoms. Measured in participants in the Safety Population (which included all randomized participants who received at least 1 dose of investigational product), who had diary entries at each specified time point.

End point type	Secondary

End point timeframe:

Up to approximately 113 days

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	163		
Units: participants				
Day 1 to 28|Nausea (n=77,156)	3	32		
Day 29 to 56|Nausea (n=80,163)	2	22		
Day 57 to 84|Nausea (n=80,163)	1	12		
Day 85 to 112|Nausea (n=80,163)	2	8		
Day >/= 113|Nausea (n=80,163)	0	2		
Day 1 to 28|Vomiting (n=77,156)	2	13		
Day 29 to 56|Vomiting (n=80,163)	2	6		
Day 57 to 84|Vomiting (n=80,163)	0	7		
Day 85 to 112|Vomiting (n=80,163)	1	3		
Day >/= 113|Vomiting (n=80,163)	0	1		
Day 1 to 28|Abdominal cramps (n=77,156)	3	16		
Day 29 to 56|Abdominal cramps (n=80,163)	3	7		
Day 57 to 84|Abdominal cramps (n=80,163)	1	9		
Day 85 to 112|Abdominal cramps (n=80,163)	1	5		
Day >/= 113|Abdominal cramps (n=80,163)	0	1		
Day 1 to 28|Abdominal pain (n=77,156)	9	28		
Day 29 to 56|Abdominal pain (n=80,163)	9	17		
Day 57 to 84|Abdominal pain (n=80,163)	5	13		
Day 85 to 112|Abdominal pain (n=80,163)	2	7		
Day >/= 113|Abdominal pain (n=80,163)	0	2		
Day 1 to 28|Fever (n=77,156)	1	5		
Day 29 to 56|Fever (n=80,163)	0	1		
Day 57 to 84|Fever (n=80,163)	0	2		
Day 85 to 112|Fever (n=80,163)	0	2		
Day >/= 113|Fever (n=80,163)	0	0		
Day 1 to 28|Bloating (n=77,156)	1	8		
Day 29 to 56|Bloating (n=80,163)	4	12		
Day 57 to 84|Bloating (n=80,163)	2	6		
Day 85 to 112|Bloating (n=80,163)	3	5		
Day >/= 113|Bloating (n=80,163)	1	1		
Day 1 to 28|Other symptoms (n=77,156)	5	21		
Day 29 to 56|Other symptoms (n=80,163)	4	17		
Day 57 to 84|Other symptoms (n=80,163)	6	11		
Day 85 to 112|Other symptoms (n=80,163)	5	8		
Day >/= 113|Other symptoms (n=80,163)	0	2		
Day 1 to 28|No symptoms (n=77,156)	53	33		
Day 29 to 56|No symptoms (n=80,163)	56	81		
Day 57 to 84|No symptoms (n=80,163)	65	103		

Day 85 to 112|No symptoms (n=80,163)	66	125		
Day >/= 113|No symptoms (n=80,163)	79	154		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Diarrhea Symptoms During the Apremilast Exposure Period

End point title	Number of Participants with Diarrhea Symptoms During the Apremilast Exposure Period

End point description:

Diarrhea symptoms were nausea, vomiting, abdominal cramps, abdominal pain, fever, bloating, and other symptoms. Participants and their parent/guardian were supplied with diaries (either paper or electronic) that were filled out daily to record and describe any diarrhea and associated symptoms. Measured in participants in the Safety Population (which included all randomized participants who received at least 1 dose of investigational product), who had diary entries at each specified time point.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 365 days

End point values	Apremilast Exposure Period: Apremilast 20 mg BID	Apremilast Exposure Period: Apremilast 30 mg BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	116	119		
Units: participants				
Day 1 to 28|Nausea (n=109,114)	17	21		
Day 1 to 28|Vomiting (n=109,114)	10	4		
Day 1 to 28|Abdominal cramps (n=109,114)	7	9		
Day 1 to 28|Abdominal pain (n=109,114)	21	14		
Day 1 to 28|Fever (n=109,114)	2	3		
Day 1 to 28|Bloating (n=109,114)	3	7		
Day 1 to 28|Other symptoms (n=109,114)	11	13		
Day 1 to 28|No symptoms (n=109,114)	38	43		
Day 29 to 56|Nausea (n=108,113)	14	10		
Day 29 to 56|Vomiting (n=108,113)	4	3		
Day 29 to 56|Abdominal cramps (n=108,113)	4	4		
Day 29 to 56|Abdominal pain (n=108,113)	13	8		
Day 29 to 56|Fever (n=108,113)	1	0		
Day 29 to 56|Bloating (n=108,113)	4	9		
Day 29 to 56|Other symptoms (n=108,113)	9	9		

Day 29 to 56|No symptoms (n=108,113)	59	70		
Day 57 to 84|Nausea (n=101,110)	6	8		
Day 57 to 84|Vomiting (n=101,110)	6	4		
Day 57 to 84|Abdominal cramps (n=101,110)	8	3		
Day 57 to 84|Abdominal pain (n=101,110)	10	6		
Day 57 to 84|Fever (n=101,110)	1	1		
Day 57 to 84|Bloating (n=101,110)	1	6		
Day 57 to 84|Other symptoms (n=101,110)	10	6		
Day 57 to 84|No symptoms (n=101,110)	59	76		
Day 85 to 112|Nausea (n=100,106)	3	5		
Day 85 to 112|Vomiting (n=100,106)	3	0		
Day 85 to 112|Abdominal cramps (n=100,106)	4	2		
Day 85 to 112|Abdominal pain (n=100,106)	6	3		
Day 85 to 112|Fever (n=100,106)	1	2		
Day 85 to 112|Bloating (n=100,106)	2	4		
Day 85 to 112|Other symptoms (n=100,106)	5	4		
Day 85 to 112|No symptoms (n=100,106)	76	86		
Day 113 to 140|Nausea (n=99,106)	6	2		
Day 113 to 140|Vomiting (n=99,106)	5	1		
Day 113 to 140|Abdominal cramps (n=99,106)	4	0		
Day 113 to 140| Abdominal pain (n=99,106)	7	3		
Day 113 to 140|Fever (n=99,106)	1	0		
Day 113 to 140|Bloating (n=99,106)	3	2		
Day 113 to 140|Other symptoms (n=99,106)	5	3		
Day 113 to 140|No symptoms (n=99,106)	68	95		
Day 141 to 168|Nausea (n=98,104)	5	2		
Day 141 to 168|Vomiting (n=98,104)	3	1		
Day 141 to 168|Abdominal cramps (n=98,104)	2	1		
Day 141 to 168|Abdominal pain (n=98,104)	4	2		
Day 141 to 168|Fever (n=98,104)	0	0		
Day 141 to 168|Bloating (n=98,104)	2	2		
Day 141 to 168|Other symptoms (n=98,104)	3	1		
Day 141 to 168|No symptoms (n=98,104)	79	95		
Day 169 to 196|Nausea (n=96,102)	3	4		
Day 169 to 196|Vomiting (n=96,102)	2	1		
Day 169 to 196|Abdominal cramps (n=96,102)	1	2		
Day 169 to 196|Abdominal pain (n=96,102)	7	5		
Day 169 to 196|Fever (n=96,102)	0	2		
Day 169 to 196|Bloating (n=96,102)	0	1		

Day 169 to 196|Other symptoms (n=96,102)	7	0		
Day 169 to 196|No symptoms (n=96,102)	76	87		
Day 197 to 224|Nausea (n=93,102)	5	2		
Day 197 to 224|Vomiting (n=93,102)	5	0		
Day 197 to 224|Abdominal cramps (n=93,102)	1	0		
Day 197 to 224|Abdominal pain (n=93,102)	3	1		
Day 197 to 224|Fever (n=93,102)	2	0		
Day 197 to 224|Bloating (n=93,102)	1	1		
Day 197 to 224|Other symptoms (n=93,102)	4	1		
Day 197 to 224|No symptoms (n=93,102)	72	97		
Day 225 to 252|Nausea (n=92,98)	9	3		
Day 225 to 252|Vomiting (n=92,98)	3	0		
Day 225 to 252|Abdominal cramps (n=92,98)	2	1		
Day 225 to 252|Abdominal pain (n=92,98)	7	1		
Day 225 to 252|Fever (n=92,98)	0	0		
Day 225 to 252|Bloating (n=92,98)	3	1		
Day 225 to 252|Other symptoms (n=92,98)	4	0		
Day 225 to 252|No symptoms (n=92,98)	64	92		
Day 253 to 280|Nausea (n=76,69)	5	4		
Day 253 to 280|Vomiting (n=76,69)	1	0		
Day 253 to 280|Abdominal cramps (n=76,69)	3	1		
Day 253 to 280|Abdominal pain (n=76,69)	6	3		
Day 253 to 280|Fever (n=76,69)	1	0		
Day 253 to 280|Bloating (n=76,69)	2	1		
Day 253 to 280|Other symptoms (n=76,69)	3	2		
Day 253 to 280|No symptoms (n=76,69)	55	58		
Day 281 to 308|Nausea (n=61,60)	2	3		
Day 281 to 308|Vomiting (n=61,60)	1	2		
Day 281 to 308|Abdominal cramps (n=61,60)	1	2		
Day 281 to 308|Abdominal pain (n=61,60)	4	2		
Day 281 to 308|Fever (n=61,60)	0	0		
Day 281 to 308|Bloating (n=61,60)	0	1		
Day 281 to 308|Other symptoms (n=61,60)	1	1		
Day 281 to 308|No symptoms (n=61,60)	52	49		
Day 309 to 336|Nausea(n=62,59)	2	1		
Day 309 to 336|Vomiting(n=62,59)	2	0		
Day 309 to 336|Abdominal cramps(n=62,59)	1	0		
Day 309 to 336|Abdominal pain(n=62,59)	4	0		

Day 309 to 336|Fever(n=62,59)	1	0		
Day 309 to 336|Bloating(n=62,59)	1	0		
Day 309 to 336|Other symptoms(n=62,59)	4	1		
Day 309 to 336|No symptoms(n=62,59)	47	57		
Day 337 to 364|Nausea(n=59,58)	2	1		
Day 337 to 364|Vomiting(n=59,58)	1	0		
Day 337 to 364|Abdominal cramps(n=59,58)	0	0		
Day 337 to 364|Abdominal pain(n=59,58)	2	2		
Day 337 to 364|Fever(n=59,58)	0	0		
Day 337 to 364|Bloating(n=59,58)	1	0		
Day 337 to 364|Other symptoms(n=59,58)	1	1		
Day 337 to 364|No symptoms(n=59,58)	52	54		
Day >= 365|Nausea (n=24,22)	0	0		
Day >= 365|Vomiting (n=24,22)	0	0		
Day >= 365|Abdominal cramps (n=24,22)	0	1		
Day >= 365|Abdominal pain (n=24,22)	0	0		
Day >= 365|Fever (n=24,22)	0	0		
Day >= 365|Bloating (n=24,22)	0	0		
Day >= 365|Other symptoms (n=24,22)	0	0		
Day >= 365|No symptoms (n=24,22)	24	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Suicidal Ideation or Behavior per the Columbia-Suicide Severity Rating Scale (C-SSRS) During the Placebo-controlled Phase

End point title	Number of Participants with Suicidal Ideation or Behavior per the Columbia-Suicide Severity Rating Scale (C-SSRS) During the Placebo-controlled Phase

End point description:

The C-SSRS is a questionnaire that is used to assess suicidal ideation and behavior. The C-SSRS questionnaire measures suicidal ideation, intensity of ideation, and suicidal behaviors. Results presented are for the number of participants who recorded suicidal ideation or behavior on the C-SSRS. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	163		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Suicidal Ideation or Behavior per the C-SSRS During the Apremilast-extension Phase

End point title	Number of Participants with Suicidal Ideation or Behavior per the C-SSRS During the Apremilast-extension Phase

End point description:

The C-SSRS is a questionnaire that is used to assess suicidal ideation and behavior. The C-SSRS questionnaire measures suicidal ideation, intensity of ideation, and suicidal behaviors. Results presented are for the number of participants who recorded suicidal ideation or behavior on the C-SSRS. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product who had available C-SSRS data.

End point type	Secondary

End point timeframe:

Week 16 to Week 52

End point values	Apremilast-extension Phase: Apremilast 20 mg BID	Apremilast-extension Phase: Apremilast 30 mg BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	110	111		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Female Participants at Stage I-V of Sexual Development per Tanner Staging of Sexual Development

End point title	Number of Female Participants at Stage I-V of Sexual Development per Tanner Staging of Sexual Development

End point description:

The Tanner Staging of sexual development is a scale of physical development as children transition into adolescence and then adulthood. The scale defines physical measurements of development based on characteristics, such as the size of the breasts, genitals, testicular volume, and growth of pubic hair. The scale ranges from stage I (pre-adolescent) to stage V (adult development). The results presented are for the number of participants at stage I-V of development. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product and had available data for the endpoint. As pre-specified, results are presented based on initial treatment received.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	89		
Units: participants				
Breast Growth|Stage 1	8	17		
Pubic Hair Growth|Stage 1	8	18		
Other Changes|Stage 1	8	18		
Breast Growth|Stage 2	3	9		
Pubic Hair Growth|Stage 2	3	9		
Other Changes|Stage 2	3	9		
Breast Growth|Stage 3	3	9		
Pubic Hair Growth|Stage 3	3	9		
Other Changes|Stage 3	3	12		
Breast Growth|Stage 4	6	20		
Pubic Hair Growth|Stage 4	6	18		
Other Changes|Stage 4	4	16		
Breast Growth|Stage 5	12	27		
Pubic Hair Growth|Stage 5	12	28		
Other Changes|Stage 5	12	26		
Breast Growth|Missing	5	7		
Pubic Hair Growth|Missing	5	7		
Other Changes|Missing	7	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Male Participants at Stage I-V of Sexual Development per Tanner Staging of Sexual Development

End point title	Number of Male Participants at Stage I-V of Sexual Development per Tanner Staging of Sexual Development

End point description:

The Tanner Staging of sexual development is a scale of physical development as children transition into adolescence and then adulthood. The scale defines physical measurements of development based on characteristics, such as the size of the breasts, genitals, testicular volume, and growth of pubic hair. The scale ranges from stage I (pre-adolescent) to stage V (adult development). The results presented are for the number of participants at stage I-V of development. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product and had available data for the endpoint. As pre-specified, results are presented based on initial treatment received.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	74		
Units: participants				
Testes Growth|Stage 1	11	15		
Penis Growth|Stage 1	11	15		
Pubic Hair Growth|Stage 1	10	15		
Other Changes|Stage 1	9	15		
Testes Growth|Stage 2	5	5		
Penis Growth|Stage 2	5	5		
Pubic Hair Growth|Stage 2	5	6		
Other Changes|Stage 2	5	5		
Testes Growth|Stage 3	4	10		
Penis Growth|Stage 3	4	11		
Pubic Hair Growth|Stage 3	5	8		
Other Changes|Stage 3	4	8		
Testes Growth|Stage 4	5	12		
Penis Growth|Stage 4	5	10		
Pubic Hair Growth|Stage 4	6	14		
Other Changes|Stage 4	4	11		
Testes Growth|Stage 5	14	27		
Penis Growth|Stage 5	14	28		
Pubic Hair Growth|Stage 5	13	26		
Other Changes|Stage 5	14	26		
Testes Growth|Missing	4	5		
Penis Growth|Missing	4	5		
Pubic Hair Growth|Missing	4	5		
Other Changes|Missing	7	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Body Weight of Participants During the Placebo-controlled Phase

End point title	Mean Body Weight of Participants During the Placebo-controlled Phase

End point description:

The participants' body weight in kilograms (kg) was recorded. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	163		
Units: kg				
arithmetic mean (standard deviation)				
Baseline	52.36 (± 22.177)	52.04 (± 21.123)		
Week 16	54.18 (± 22.581)	51.95 (± 20.945)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Body Weight of Participants During the Apremilast Exposure Period

End point title	Mean Body Weight of Participants During the Apremilast Exposure Period

End point description:

The participants' body weight in kilograms (kg) was recorded. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Apremilast Exposure Period: Apremilast 20 mg BID	Apremilast Exposure Period: Apremilast 30 mg BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	116	119		
Units: kg				
arithmetic mean (standard deviation)				
Baseline	36.81 (± 8.954)	67.94 (± 19.053)		
Week 52	39.04 (± 9.823)	67.79 (± 18.889)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Height of Participants During the Placebo-controlled Phase

End point title	Mean Height of Participants During the Placebo-controlled Phase

End point description:

The participants' height in centimeters (cm) was recorded. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	163		
Units: cm				
arithmetic mean (standard deviation)				
Baseline	153.29 (± 18.435)	153.33 (± 18.069)		
Week 16	154.54 (± 17.839)	154.40 (± 17.683)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Height of Participants During the Apremilast Exposure Period

End point title	Mean Height of Participants During the Apremilast Exposure Period

End point description:

The participants' height in centimeters (cm) was recorded. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Apremilast Exposure Period: Apremilast 20 mg BID	Apremilast Exposure Period: Apremilast 30 mg BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	116	119		
Units: cm				
arithmetic mean (standard deviation)				
Baseline	140.86 (± 14.159)	166.13 (± 11.416)		
Week 52	144.90 (± 13.944)	167.84 (± 10.814)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Body Mass Index (BMI) of Participants During the Placebo-controlled Phase

End point title	Mean Body Mass Index (BMI) of Participants During the Placebo-controlled Phase

End point description:

The participants' BMI was calculated as body weight (kg)/height (m^2). Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	163		
Units: kg/m^2				
arithmetic mean (standard deviation)				
Baseline	21.41 (± 5.652)	21.33 (± 5.197)		
Week 16	21.87 (± 5.883)	20.98 (± 5.067)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean BMI of Participants During the Apremilast Exposure Period

End point title	Mean BMI of Participants During the Apremilast Exposure Period

End point description:

The participants' BMI was calculated as body weight (kg)/height (m^2). Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Apremilast Exposure Period: Apremilast 20 mg BID	Apremilast Exposure Period: Apremilast 30 mg BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	116	119		
Units: kg/m^2				
arithmetic mean (standard deviation)				
Baseline	18.32 (± 2.641)	24.52 (± 5.655)		
Week 52	18.30 (± 2.480)	23.95 (± 5.539)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a Psoriasis Flare During the Placebo-controlled Phase

End point title	Number of Participants who Experienced a Psoriasis Flare During the Placebo-controlled Phase

End point description:

A psoriasis flare was defined as a sudden intensification of psoriasis (new generalized erythrodermic, inflammatory or pustular psoriasis) requiring medical intervention beyond allowable medications. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Placebo	Apremilast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	163		
Units: participants	3	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a Psoriasis Flare During the Apremilast Exposure Period

End point title	Number of Participants who Experienced a Psoriasis Flare

	During the Apremilast Exposure Period

End point description:

A psoriasis flare was defined as a sudden intensification of psoriasis (new generalized erythrodermic, inflammatory or pustular psoriasis) requiring medical intervention beyond allowable medications. Measured in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product. As pre-defined in the statistical analysis plan, safety data for the apremilast-extension phase are presented per treatment received.

End point type	Secondary

End point timeframe:

52 weeks

End point values	Apremilast Exposure Period: Apremilast 20 mg BID	Apremilast Exposure Period: Apremilast 30 mg BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	116	119		
Units: participants	7	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a Psoriasis Rebound

End point title	Number of Participants who Experienced a Psoriasis Rebound

End point description:

A psoriasis rebound was defined as an adverse event of psoriasis that started after the last dose date for participants who received treatment in the study. Measured in participants in the Safety Population (which included all randomized participants who received at least 1 dose of investigational product) who entered the 14-week observational follow up.

End point type	Secondary

End point timeframe:

14 weeks post last dose (max mean treatment duration in placebo-controlled phase was 15.3 weeks, and 41.9 weeks in the apremilast-exposure period)

End point values	Placebo	Apremilast 20 mg BID	Apremilast 30 mg BID	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	14	30	
Units: participants	0	0	4	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to a maximum of 52 weeks

Adverse event reporting additional description:

All-cause mortality is reported for all enrolled participants. Serious and other adverse events are reported in the Safety Population, which included all randomized participants who received at least 1 dose of investigational product. As pre-specified, data are presented per treatment received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Placebo-Controlled Phase: Placebo BID
Reporting group description: -	
Reporting group title	Placebo-Controlled Phase: Apremilast 20 mg BID
Reporting group description: -	
Reporting group title	Placebo-Controlled Phase: Apremilast 30 mg BID
Reporting group description: -	
Reporting group title	Apremilast Extension Phase: Apremilast 20 mg or 30 mg BID
Reporting group description: -	
Reporting group title	Apremilast Extension Phase: Apremilast 20 mg BID
Reporting group description: -	
Reporting group title	Apremilast Extension Phase: Apremilast 30 mg BID
Reporting group description: -	
Reporting group title	Placebo-Controlled Phase: Apremilast 20 mg or 30 mg BID

Reporting group description: -

Serious adverse events	Placebo-Controlled Phase: Placebo BID	Placebo-Controlled Phase: Apremilast 20 mg BID	Placebo-Controlled Phase: Apremilast 30 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 80 (1.25%)	2 / 80 (2.50%)	0 / 83 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 80 (1.25%)	0 / 83 (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
Wandering pacemaker			

subjects affected / exposed	0 / 80 (0.00%)	1 / 80 (1.25%)	0 / 83 (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
Nervous system disorders			
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 80 (0.00%)	1 / 80 (1.25%)	0 / 83 (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
Status migrainosus			
subjects affected / exposed	0 / 80 (0.00%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 80 (1.25%)	0 / 83 (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			
Testicular appendage torsion			
subjects affected / exposed	1 / 80 (1.25%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 80 (1.25%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 80 (0.00%)	0 / 83 (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 Extension Phase:	Apremilast Extension Phase: Apremilast	Apremilast Extension Phase:

	Apremilast 20 mg or 30 mg BID	20 mg BID	Apremilast 30 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 221 (0.90%)	0 / 110 (0.00%)	2 / 111 (1.80%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 221 (0.00%)	0 / 110 (0.00%)	0 / 111 (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
Wandering pacemaker			
subjects affected / exposed	0 / 221 (0.00%)	0 / 110 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 221 (0.00%)	0 / 110 (0.00%)	0 / 111 (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
Status migrainosus			
subjects affected / exposed	1 / 221 (0.45%)	0 / 110 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 221 (0.00%)	0 / 110 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Testicular appendage torsion			
subjects affected / exposed	0 / 221 (0.00%)	0 / 110 (0.00%)	0 / 111 (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			

Psoriasis			
subjects affected / exposed	0 / 221 (0.00%)	0 / 110 (0.00%)	0 / 111 (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	1 / 221 (0.45%)	0 / 110 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo-Controlled Phase: Apremilast 20 mg or 30 mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 163 (1.23%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 163 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wandering pacemaker			
subjects affected / exposed	1 / 163 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Autonomic nervous system imbalance			
subjects affected / exposed	1 / 163 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Status migrainosus			
subjects affected / exposed	0 / 163 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			

Iron deficiency anaemia			
subjects affected / exposed	1 / 163 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Testicular appendage torsion			
subjects affected / exposed	0 / 163 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 163 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 163 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo-Controlled Phase: Placebo BID	Placebo-Controlled Phase: Apremilast 20 mg BID	Placebo-Controlled Phase: Apremilast 30 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 80 (32.50%)	50 / 80 (62.50%)	41 / 83 (49.40%)
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 80 (5.00%)	12 / 80 (15.00%)	5 / 83 (6.02%)
occurrences (all)	4	16	5
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 80 (1.25%)	7 / 80 (8.75%)	3 / 83 (3.61%)
occurrences (all)	1	7	8
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	2 / 80 (2.50%)	15 / 80 (18.75%)	17 / 83 (20.48%)
occurrences (all)	2	29	31
Diarrhoea			
subjects affected / exposed	8 / 80 (10.00%)	15 / 80 (18.75%)	17 / 83 (20.48%)
occurrences (all)	24	35	44
Abdominal pain			
subjects affected / exposed	8 / 80 (10.00%)	23 / 80 (28.75%)	9 / 83 (10.84%)
occurrences (all)	20	54	13
Abdominal pain upper			
subjects affected / exposed	4 / 80 (5.00%)	5 / 80 (6.25%)	4 / 83 (4.82%)
occurrences (all)	12	6	4
Vomiting			
subjects affected / exposed	2 / 80 (2.50%)	16 / 80 (20.00%)	13 / 83 (15.66%)
occurrences (all)	3	28	15
Dyspepsia			
subjects affected / exposed	0 / 80 (0.00%)	3 / 80 (3.75%)	7 / 83 (8.43%)
occurrences (all)	0	7	7
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	3 / 80 (3.75%)	0 / 80 (0.00%)	2 / 83 (2.41%)
occurrences (all)	3	0	2
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 80 (1.25%)	5 / 80 (6.25%)	2 / 83 (2.41%)
occurrences (all)	1	5	2
Nasopharyngitis			
subjects affected / exposed	3 / 80 (3.75%)	5 / 80 (6.25%)	5 / 83 (6.02%)
occurrences (all)	3	5	5
COVID-19			
subjects affected / exposed	5 / 80 (6.25%)	2 / 80 (2.50%)	3 / 83 (3.61%)
occurrences (all)	5	2	3

Non-serious adverse events	Apremilast Extension Phase: Apremilast 20 mg or 30 mg BID	Apremilast Extension Phase: Apremilast 20 mg BID	Apremilast Extension Phase: Apremilast 30 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	90 / 221 (40.72%)	52 / 110 (47.27%)	38 / 111 (34.23%)

Nervous system disorders			
Headache			
subjects affected / exposed	12 / 221 (5.43%)	7 / 110 (6.36%)	5 / 111 (4.50%)
occurrences (all)	18	9	9
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 221 (2.26%)	4 / 110 (3.64%)	1 / 111 (0.90%)
occurrences (all)	5	4	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	28 / 221 (12.67%)	18 / 110 (16.36%)	10 / 111 (9.01%)
occurrences (all)	56	34	22
Diarrhoea			
subjects affected / exposed	33 / 221 (14.93%)	20 / 110 (18.18%)	13 / 111 (11.71%)
occurrences (all)	104	53	51
Abdominal pain			
subjects affected / exposed	19 / 221 (8.60%)	14 / 110 (12.73%)	5 / 111 (4.50%)
occurrences (all)	35	24	11
Abdominal pain upper			
subjects affected / exposed	5 / 221 (2.26%)	5 / 110 (4.55%)	0 / 111 (0.00%)
occurrences (all)	5	5	0
Vomiting			
subjects affected / exposed	22 / 221 (9.95%)	15 / 110 (13.64%)	7 / 111 (6.31%)
occurrences (all)	31	23	8
Dyspepsia			
subjects affected / exposed	4 / 221 (1.81%)	2 / 110 (1.82%)	2 / 111 (1.80%)
occurrences (all)	6	2	4
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	16 / 221 (7.24%)	5 / 110 (4.55%)	11 / 111 (9.91%)
occurrences (all)	16	5	11
Infections and infestations			
Influenza			
subjects affected / exposed	6 / 221 (2.71%)	4 / 110 (3.64%)	2 / 111 (1.80%)
occurrences (all)	7	4	3
Nasopharyngitis			

subjects affected / exposed	11 / 221 (4.98%)	8 / 110 (7.27%)	3 / 111 (2.70%)
occurrences (all)	14	11	3
COVID-19			
subjects affected / exposed	7 / 221 (3.17%)	4 / 110 (3.64%)	3 / 111 (2.70%)
occurrences (all)	7	4	3

Non-serious adverse events	Placebo-Controlled Phase: Apremilast 20 mg or 30 mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	91 / 163 (55.83%)		
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 163 (10.43%)		
occurrences (all)	21		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	10 / 163 (6.13%)		
occurrences (all)	15		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	32 / 163 (19.63%)		
occurrences (all)	60		
Diarrhoea			
subjects affected / exposed	32 / 163 (19.63%)		
occurrences (all)	79		
Abdominal pain			
subjects affected / exposed	32 / 163 (19.63%)		
occurrences (all)	67		
Abdominal pain upper			
subjects affected / exposed	9 / 163 (5.52%)		
occurrences (all)	10		
Vomiting			
subjects affected / exposed	29 / 163 (17.79%)		
occurrences (all)	43		
Dyspepsia			
subjects affected / exposed	10 / 163 (6.13%)		
occurrences (all)	14		

Skin and subcutaneous tissue disorders Psoriasis subjects affected / exposed occurrences (all)	 2 / 163 (1.23%) 2		
Infections and infestations Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) COVID-19 subjects affected / exposed occurrences (all)	 7 / 163 (4.29%) 7 10 / 163 (6.13%) 10 5 / 163 (3.07%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 April 2019	- Added an inclusion criterion for baseline minimum allowable body mass index - Added a specific body mass index parameter as a reason for mandatory participant withdrawal - Revised hemoglobin ranges for participant eligibility - Added a note to contraception options to clarify options considered "highly effective contraception" may differ per local guidelines/regulations
23 September 2019	- Replaced depictions of investigational product blister card packaging to align with redesigned packaging - Added text informing of switch from blister card investigational product to bottles during the apremilast-extension phase - Revised platelet ranges for participant eligibility - Removed requirement for reporting of pregnancies of partners of male participants
01 May 2020	- References to Celgene were replaced with Amgen - Updated to align with Amgen Global Drug Safety and Amgen Product Complaint Reporting processes - Updated to include instructions for paper reporting of serious adverse events - Added Sample Serious Adverse Event Form, Pregnancy Notification Form, and Lactation Notification Form to align with Amgen processes
26 August 2021	- Reduced the study sample size from at least 230 randomized participants to at least 180 randomized participants - Updated the power calculations based on the change in sample size - Added language regarding reporting of serious adverse events
17 December 2021	- Reverted the study sample size from at least 180 randomized participants to the original protocol goal of at least 230 randomized participants - Updated the power calculations based on the change in sample size

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
19 March 2020	Effective 19 March 2020, screening and enrollment were temporarily paused at all participating countries/sites to limit potential COVID-19 exposure for study participants, sponsor employees, and staff at clinical study sites. In June 2020, Amgen made a decision to lift the pause on screening and enrollment, based on an assessment that took into account the state of the pandemic, the study design, participant safety, public health risks, the benefit-risk balance, and the burden on healthcare systems. After the pause was lifted, enrollment resumed over the following months in a staggered fashion across countries and study sites, depending on the status of COVID-19 regionally as well as local restrictions and guidance.	01 June 2020

Notes:

Limitations and caveats

None reported