Clinical trial results:
A Phase 4, Multi-center, Randomized, Double-blind, Placebo-controlled Study of the Impact of Apremilast (CC-10004) on Quality of Life, Efficacy, and Safety in Subjects With Manifestations of Plaque Psoriasis and Impaired Quality of Life

Summary

EudraCT number	2018-002850-58
Trial protocol	GB DE FR IT
Global end of trial date	03 November 2021

Results information

Result version number	v1 (current)
This version publication date	26 August 2022
First version publication date	26 August 2022

Trial information

Trial identification

Sponsor protocol code	CC-10004-PSOR-020

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03774875
WHO universal trial number (UTN)	U1111-1224-8381

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 November 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 November 2021
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 assess the impact of apremilast 30 mg twice daily (BID), compared to placebo, on health-related quality of life in subjects with manifestations of plaque psoriasis and impaired quality of life at week 16.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines and in accordance with the general ethical principles outlined in the Declaration of Helsinki.
The study protocol and all amendments, the informed consent form, and any accompanying materials provided to the subjects were reviewed and approved by an Independent Ethics Committee (IEC) at each study center.
The investigator or his/her designee informed the subject of all aspects pertaining to the subject's participation in the study before any screening procedures were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 147
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Spain: 47
Country: Number of subjects enrolled	Switzerland: 8
Country: Number of subjects enrolled	United Kingdom: 37
Worldwide total number of subjects	277
EEA total number of subjects	232

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	231
From 65 to 84 years	46
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eligible participants were enrolled at 55 centers in France, Germany, Italy, Spain, Switzerland, and the United Kingdom.
The study consisted of a 16-week placebo-controlled period and a 36-week apremilast extension period.

Pre-assignment

Screening details:

Participants were randomized in a 1:2 ratio to receive placebo or apremilast. Participants were block-randomized to each of the manifestations of psoriasis (scalp psoriasis, nail psoriasis, palmoplantar psoriasis, genital psoriasis, and psoriasis in visible locations).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo tablets orally twice a day for 16 weeks.

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:

Administered twice a day by mouth

Arm title	Apremilast 30 mg

Arm description:

Participants received apremilast 30 mg orally twice a day for 16 weeks.

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:

Administered twice a day by mouth

Number of subjects in period 1	Placebo	Apremilast 30 mg
Started	92	185
Received Study Drug	91	185
Completed	69	152
Not completed	23	33
Consent withdrawn by subject	12	10
Reason Unknown	1	-
Adverse event, non-fatal	8	16
Protocol Deviation	-	1
Lost to follow-up	-	2
Lack of efficacy	2	4

Period 2

Period 2 title	Apremilast Extension Period (Week 16-52)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo / Apremilast 30 mg

Arm description:

At week 16 participants switched to receive apremilast 30 mg orally twice a day up to week 52.

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:

Administered twice a day by mouth

Arm title	Apremilast 30 mg / Apremilast 30 mg

Arm description:

Participants continued to receive apremilast 30 mg orally twice a day from week 16 to week 52.

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:

Administered twice a day by mouth

Number of subjects in period 2	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg
Started	69	152
Completed	53	105
Not completed	16	47
Consent withdrawn by subject	7	20
Non-compliance with Study Drug	-	2
Adverse event, non-fatal	6	9
Protocol Deviation	-	1
Other	1	1
Lost to follow-up	-	3
Lack of efficacy	2	11

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo tablets orally twice a day for 16 weeks.	
Reporting group title	Apremilast 30 mg
Reporting group description:	
Participants received apremilast 30 mg orally twice a day for 16 weeks.	

Reporting group values	Placebo	Apremilast 30 mg	Total
Number of subjects	92	185	277
Age Categorical Units: participants			
< 65 years	73	158	231
≥ 65 years	19	27	46
Age Continuous Units: years			
arithmetic mean	50.9	47.4	
standard deviation	± 13.68	± 14.28	-
Sex: Female, Male Units: participants			
Female	35	79	114
Male	57	106	163
Race/Ethnicity, Customized Units: Subjects			
White	89	179	268
Black or African American	0	2	2
Asian	1	1	2
Not Collected or Unknown	2	3	5
Region of Enrollment Units: Subjects			
France	6	13	19
Germany	45	102	147
Italy	8	11	19
Spain	23	24	47
Switzerland	1	7	8
United Kingdom	9	28	37
Primary Manifestations for Stratifications Units: Subjects			
Scalp Psoriasis	23	45	68
Nail Psoriasis	20	40	60
Palmoplantar Psoriasis	10	22	32
Genital Psoriasis	15	28	43
Psoriasis in Visible Locations	24	50	74
Duration of Plaque Psoriasis Units: years			
arithmetic mean	18.41	16.31	
standard deviation	± 13.350	± 13.116	-

Dermatology Life Quality Index (DLQI) Score			
The DLQI is a 10-item skin disease-specific questionnaire used to evaluate the impact of skin disease on health-related quality of life (QOL). The items address symptoms and feelings, daily activities, leisure, work/school, personal relationships, and issues with treatment. Questions are answered on a 4-point scale from 0 (not at all/not applicable) to 3 (very much). Item scores are added to provide a total score from 0 to 30, with higher scores indicating greater impairment of QOL.			
Units: score on a scale			
arithmetic mean	18.5	18.1	
standard deviation	± 4.94	± 4.86	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo tablets orally twice a day for 16 weeks.	
Reporting group title	Apremilast 30 mg
Reporting group description:	
Participants received apremilast 30 mg orally twice a day for 16 weeks.	
Reporting group title	Placebo / Apremilast 30 mg
Reporting group description:	
At week 16 participants switched to receive apremilast 30 mg orally twice a day up to week 52.	
Reporting group title	Apremilast 30 mg / Apremilast 30 mg
Reporting group description:	
Participants continued to receive apremilast 30 mg orally twice a day from week 16 to week 52.	
Subject analysis set title	All Apremilast 30 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants initially randomized to placebo received apremilast 30 mg orally twice a day from week 16 to week 52. Participants initially randomized to apremilast received apremilast 30 mg orally twice a day for 52 weeks.	

Primary: Percentage of Participants who Achieved a ≥ 4-point Reduction from Baseline in Dermatology Life Quality Index (DLQI) at Week 16

End point title	Percentage of Participants who Achieved a ≥ 4-point Reduction from Baseline in Dermatology Life Quality Index (DLQI) at Week 16
End point description:	
The DLQI is a 10-item skin disease-specific questionnaire used to evaluate the impact of skin disease on health-related quality of life (QOL). The items address symptoms and feelings, daily activities, leisure, work/school, personal relationships, and issues with treatment. Questions are answered on a 4-point scale from 0 (not at all/not applicable) to 3 (very much). Item scores are added to provide a total score from 0 to 30, with higher scores indicating greater impairment of QOL. The analysis includes all randomized participants; missing data at week 16 were imputed using multiple imputation.	
End point type	Primary
End point timeframe:	
Baseline and week 16	

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	185		
Units: percentage of participants				
number (confidence interval 95%)	41.3 (30.0 to 52.6)	73.3 (66.7 to 79.9)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg
Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Response Rates
Point estimate	31.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.6
upper limit	45.2
Variability estimate	Standard error of the mean
Dispersion value	6.78

Notes:

[1] - The CMH (Cochran-Mantel-Haenszel) test adjusting for the stratification of the 5 difficult to treat manifestation types at randomization.

Secondary: Change from Baseline in DLQI at Week 16

End point title	Change from Baseline in DLQI at Week 16

End point description:

The DLQI is a 10-item skin disease-specific questionnaire used to evaluate the impact of skin disease on health-related quality of life. The items address symptoms and feelings, daily activities, leisure, work/school, personal relationships, and issues with treatment. Questions are answered on a 4-point scale from 0 (not at all/not applicable) to 3 (very much). Item scores are added to provide a total score from 0 to 30, with higher scores indicating greater impairment of QOL. A negative change from baseline indicates improvement in quality of life.
The analysis includes all randomized participants; missing data at week 16 were imputed using multiple imputation.

End point type	Secondary

End point timeframe:

Baseline and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	185		
Units: score on a scale				
least squares mean (standard error)	-3.4 (± 0.80)	-8.7 (± 0.54)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	-5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.15
upper limit	-3.43
Variability estimate	Standard error of the mean
Dispersion value	0.95

Notes:

[2] - ANCOVA model with treatment arm and stratification factor as independent variables and baseline value as a covariate.

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

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

End point description:

Body surface area is 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"), which equates to approximately 1% of total BSA.
The analysis includes all randomized participants; missing data at week 16 were imputed using multiple imputation.

End point type	Secondary

End point timeframe:

Baseline and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	185		
Units: percent change				
least squares mean (standard error)	18.5 (± 12.95)	-19.8 (± 6.58)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0085 [3]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-38.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-66.58
upper limit	-10.14
Variability estimate	Standard error of the mean
Dispersion value	14.12

Notes:

[3] - ANCOVA model with treatment arm and stratification factor as independent variables and the baseline value as a covariate variable.

Secondary: Change from Baseline in Itch Numeric Rating Scale (NRS) Score at Week 16

End point title	Change from Baseline in Itch Numeric Rating Scale (NRS) Score at Week 16

End point description:

The Itch Numeric Rating Scale (NRS) asked participants to assess the worst severity of itch experienced over the past 24 hours on an 11-point scale anchored from 0, representing 'no itching' to 10, representing 'worst itch imaginable'.
A negative change from baseline indicates improvement in itch severity.
The analysis includes all randomized participants; missing data at week 16 were imputed using multiple imputation.

End point type	Secondary

End point timeframe:

Baseline and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	185		
Units: score on a scale				
least squares mean (standard error)	-0.9 (± 0.32)	-2.5 (± 0.21)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [4]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.34
upper limit	-0.86
Variability estimate	Standard error of the mean
Dispersion value	0.38

Notes:

[4] - ANCOVA model with treatment arm and stratification factor as independent variables and the baseline value as a covariate.

Secondary: Change from Baseline in Skin Discomfort/Pain Visual Analog Scale (VAS) at Week 16

End point title	Change from Baseline in Skin Discomfort/Pain Visual Analog Scale (VAS) at Week 16

End point description:

Participants were asked to indicate their level of skin discomfort/pain in the past week by placing a vertical stroke on a 100 mm horizontal line on which the left-hand boundary (0) represents no skin discomfort/pain, and the right-hand boundary (100) represents worst possible skin discomfort/pain. The distance from the mark to the left-hand boundary was recorded.
A negative change from baseline indicates improvement in skin discomfort/pain.
The analysis includes all randomized participants; missing data at week 16 were imputed using multiple imputation.

End point type	Secondary

End point timeframe:

Baseline and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	185		
Units: score on a scale				
least squares mean (standard error)	-5.4 (± 3.61)	-21.5 (± 2.36)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003 [5]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-16.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.63
upper limit	-7.6
Variability estimate	Standard error of the mean
Dispersion value	4.31

Notes:

[5] - ANCOVA model with treatment arm and stratification factor as independent variables and the baseline value as a covariate.

Secondary: Percentage of Participants who Achieved a Psoriasis Area Severity Index (PASI) Score < 3 at Week 16

End point title	Percentage of Participants who Achieved a Psoriasis Area Severity Index (PASI) Score < 3 at Week 16

End point description:

The PASI score 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. 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 total qualitative score (sum of erythema, thickness, and scaling scores) is multiplied by the degree of involvement for each anatomic region and then multiplied by a constant and the values for each anatomic region are summed to yield the PASI score. PASI scores range from 0 to 72, with higher scores reflecting greater disease severity.
The analysis includes all randomized participants; missing data at week 16 were imputed using multiple imputation.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	185		
Units: percentage of participants				
number (confidence interval 95%)	26.3 (16.6 to 36.0)	39.7 (32.3 to 47.1)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0328 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Response Rates
Point estimate	13.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	25.8
Variability estimate	Standard error of the mean
Dispersion value	6.3

Notes:

[6] - Cochran-Mantel-Haenszel test adjusted for the stratification of the 5 difficult to treat manifestation types at randomization.

Secondary: Percentage of Participants who Achieved a Patient Benefit Index (PBI) Global Score of ≥ 1 at Week 16

End point title	Percentage of Participants who Achieved a Patient Benefit Index (PBI) Global Score of ≥ 1 at Week 16

End point description:

The PBI is a validated patient-reported instrument to assess patient-relevant benefits of psoriasis treatment. Prior to starting study treatment, participants were asked to assess the importance of a series of treatment goals (from not important to very important) by completing the Patient Needs Questionnaire (PNQ). After a period of treatment (16 weeks), participants were then asked to assess the extent to which these goals were achieved (from not at all to very) by completing the Patient Benefit Questionnaire (PBQ). The Patient Benefit Index represents the benefits realized as a function of most important needs. The PBI score ranges from 0 (no benefit) to 4 (maximum benefit).
The analysis includes all randomized participants; missing data at week 16 were imputed using multiple imputation.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	185		
Units: percentage of participants				
number (confidence interval 95%)	39.9 (28.8 to 51.0)	76.6 (70.2 to 83.1)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Response Rates
Point estimate	37
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.1
upper limit	49.9
Variability estimate	Standard error of the mean
Dispersion value	6.58

Notes:

[7] - Cochran-Mantel-Haenszel test adjusting for the stratification of the 5 difficult to treat manifestation types at randomization.

Secondary: Percent Change from Baseline in European Quality of Life 5-Dimension (EQ-5D) VAS Score at Week 16

End point title	Percent Change from Baseline in European Quality of Life 5-Dimension (EQ-5D) VAS Score at Week 16

End point description:

EQ-5D measures the participant's general health state on a vertical VAS and five quality of life domains. The EQ-5D VAS score ranges from 0 to 100, where a score of 0 indicates the worst imaginable health states and a score of 100 indicates the best imaginable health state. A positive change from baseline indicates improvement.
The analysis includes all randomized participants with available data at baseline and week 16.

End point type	Secondary

End point timeframe:

Baseline and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	160		
Units: percent change				
least squares mean (standard error)	18.9 (± 15.96)	33.8 (± 10.67)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4216 [8]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	14.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.62
upper limit	51.48
Variability estimate	Standard error of the mean
Dispersion value	18.55

Notes:

[8] - ANCOVA model with treatment arm and stratification factor as independent variables and the baseline value as a covariate.

Secondary: Percent Change from Baseline in EQ-5D Index Score at Week 16

End point title	Percent Change from Baseline in EQ-5D Index Score at Week 16

End point description:

EQ-5D measures the participants general health state as a vertical VAS and 5 quality of life domains: mobility, self-care, main activity (work, study, housework, family/leisure activities), pain/discomfort, and anxiety/depression. Each dimension is rated on three levels (no problems, some/moderate problems, extreme problems). An EQ-5D summary index is derived by applying a formula that attaches values (weights) to each of the levels in each dimension.
EQ-5D index values were derived using the UK scoring algorithm, where a higher score indicates a better health state. The range of the score is from −0.224 to 1, with 0 corresponding to death, 1 corresponding to full health, and negative numbers indicate health states worse than death. A positive change from baseline indicates improvement.
The analysis includes all randomized participants with available data at baseline and week 16.

End point type	Secondary

End point timeframe:

Baseline and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	160		
Units: percent change				
least squares mean (standard error)	165.9 (± 89.80)	17.8 (± 59.59)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1559 [9]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-148.024
Confidence interval	
level	95 %
sides	2-sided
lower limit	-352.8793
upper limit	56.8304
Variability estimate	Standard error of the mean
Dispersion value	103.9525

Notes:

[9] - ANCOVA model with treatment arm and stratification factor as independent variables and the baseline value as a covariate.

Secondary: Change from Baseline in WPAI: PSO at Week 16: Percentage Work Impairment

End point title	Change from Baseline in WPAI: PSO at Week 16: Percentage Work Impairment

End point description:

The WPAI: PSO is a self-administered questionnaire designed to address impairment to the work productivity and activity of participants due to psoriasis in the past 7 days. Percent impairment while working was derived from the participant's assessment of the degree to which psoriasis affected their productivity while working. A higher percentage indicates greater impairment and less productivity, and a negative change from baseline indicates improvement.
The analysis includes randomized participants with available data and who had reported being employed at baseline and at week 16.

End point type	Secondary

End point timeframe:

Baseline and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	102		
Units: percent impairment				
least squares mean (standard error)	-11.5 (± 3.82)	-13.9 (± 2.32)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.562 [10]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.83
upper limit	5.91
Variability estimate	Standard error of the mean
Dispersion value	4.23

Notes:

[10] - ANCOVA model with treatment arm and stratification factor as independent variables and the baseline value as a covariate.

Secondary: Change from Baseline in Work Productivity and Activity Impairment Questionnaire: Psoriasis (WPAI: PSO) at Week 16: Percentage Work Time Missed

End point title	Change from Baseline in Work Productivity and Activity Impairment Questionnaire: Psoriasis (WPAI: PSO) at Week 16: Percentage Work Time Missed

End point description:

The WPAI: PSO is a self-administered questionnaire designed to address impairment to the work productivity and activity of participants due to psoriasis in the past 7 days. Percent of work time missed is derived from the number of hours of work missed due to psoriasis symptoms as a percentage of total hours that should have been worked. A higher percentage indicates more hours missed, and a negative change from baseline indicates improvement.
The analysis includes randomized participants with available data and who had reported being employed at baseline and at week 16.

End point type	Secondary

End point timeframe:

Baseline and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	104		
Units: percent impairment				
least squares mean (standard error)	-4.1 (± 2.56)	-0.9 (± 1.54)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2667 [11]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.43
upper limit	8.73
Variability estimate	Standard error of the mean
Dispersion value	2.82

Notes:

[11] - ANCOVA model with treatment arm and stratification factor as independent variables and the baseline value as a covariate.

Secondary: Change from Baseline in WPAI: PSO at Week 16: Percentage Overall Work Impairment

End point title	Change from Baseline in WPAI: PSO at Week 16: Percentage Overall Work Impairment

End point description:

The WPAI: PSO is a self-administered questionnaire designed to address impairment to the work productivity and activity of participants due to psoriasis in the past 7 days. Percent overall work impairment takes into account both hours missed due to psoriasis symptoms and the participant's assessment of the degree to which psoriasis affected their productivity while working. A higher percentage indicates greater impairment and less productivity, and a negative change from baseline indicates improvement.
The analysis includes randomized participants with available data and who had reported being employed at baseline and at week 16.

End point type	Secondary

End point timeframe:

Baseline and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	104		
Units: percent impairment				
least squares mean (standard error)	-13.2 (± 4.35)	-13.8 (± 2.63)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8927 [12]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.16
upper limit	8.86
Variability estimate	Standard error of the mean
Dispersion value	4.81

Notes:

[12] - ANCOVA model with treatment arm and stratification factor as independent variables and the baseline value as a covariate.

Secondary: Change from Baseline in WPAI: PSO at Week 16: Percentage Activity Impairment

End point title	Change from Baseline in WPAI: PSO at Week 16: Percentage Activity Impairment

End point description:

The WPAI: PSO is a self-administered questionnaire designed to address impairment to the work productivity and activity of participants due to psoriasis in the past 7 days. Percent activity impairment is derived from the patient's assessment of the degree to which psoriasis affected their regular daily unpaid activities, measured on a VAS from 1 (no effect on daily activities) to 10 (psoriasis completely prevented daily activities). A higher percentage indicates greater impairment and less productivity, and a negative change from baseline indicates improvement.
The analysis includes all randomized participants with available data at baseline and at week 16.

End point type	Secondary

End point timeframe:

Baseline and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	116		
Units: percent impairment				
least squares mean (standard error)	-13.4 (± 3.66)	-21.2 (± 2.24)		

Statistical analyses

Statistical analysis title	Treatment Comparison
Comparison groups	Placebo v Apremilast 30 mg

Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0572 [13]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-7.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.9
upper limit	0.24
Variability estimate	Standard error of the mean
Dispersion value	4.09

Notes:

[13] - ANCOVA model with treatment arm and stratification factor as independent variables and the baseline value as a covariate.

Secondary: Number of Participants with Treatment-emergent Adverse Events (TEAEs) During the Placebo-controlled Period

End point title	Number of Participants with Treatment-emergent Adverse Events (TEAEs) During the Placebo-controlled Period

End point description:

An adverse event (AE) is any noxious, unintended, or untoward medical occurrence that may appear or worsen in a participant during a 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 of a preexisting condition was considered an AE.
A serious adverse event (SAE) is any AE occurring at any dose that:
- Resulted in death;
- Was life-threatening;
- Required inpatient hospitalization or prolongation of existing hospitalization;
- Resulted in persistent or significant disability/incapacity;
- Was a congenital anomaly/birth defect;
- Constituted an important medical event.

The Investigator assessed the severity/intensity of each event as mild, moderate, or severe based on level of symptoms.
Analysis includes all randomized participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From first dose of study drug to week 16 or up to 28 days after last dose for participants who didn't enter the apremilast extension period.

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	185		
Units: participants				
Any TEAE	54	152		
Drug-related TEAE	26	113		
Severe TEAEs	1	10		
Serious TEAEs	0	8		
Serious drug-related TEAE	0	1		
TEAE leading to drug interruption	0	9		
TEAE leading to drug withdrawal	8	18		

TEAE leading to death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Marked Laboratory Abnormalities During the Placebo-controlled Period

End point title	Number of Participants with Marked Laboratory Abnormalities During the Placebo-controlled Period

End point description:

Marked laboratory abnormalities are defined in the table below for each parameter.
ULN = upper limit of normal
The analysis includes all randomized participants who received at least one dose of study drug with at least one post-baseline measurement.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	162		
Units: participants				
Alanine Aminotransferase > 3 × ULN (N = 80, 161)	0	2		
Albumin < 25 g/L	0	0		
Alkaline Phosphatase > 400 U/L	0	0		
Aspartate Aminotransferase > 3 × ULN (N = 79, 160)	0	1		
Bilirubin > 1.8 × ULN (N = 80, 161)	0	0		
Blood Urea Nitrogen > 15 mmol/L	0	2		
Calcium < 1.8 mmol/L	0	0		
Calcium > 3.0 mmol/L	0	0		
Cholesterol > 7.8 mmol/L	0	1		
Creatinine > 1.7 × ULN	0	1		
Glucose < 2.8 mmol/L	0	0		
Glucose > 13.9 mmol/L	0	3		
Hemoglobin A1C (Fasting) > 9% (N = 35, 97)	0	3		
Lactate Dehydrogenase > 3 × ULN (N = 69, 155)	0	0		
Potassium < 3.0 mmol/L (N = 80, 161)	0	0		
Potassium > 5.5 mmol/L (N = 80, 161)	0	1		
Sodium < 130 mmol/L (N = 80, 161)	0	0		
Sodium > 150 mmol/L (N = 80, 161)	0	0		
Triglycerides > 3.4 mmol/L	6	6		

Hemoglobin: Women <85 g/L; Men <105 g/L (N=79,160)	0	0		
Hemoglobin: Women >170g/L; Men >185 g/L (N=79,160)	0	0		
Leukocytes < 1.5 × 10^9/L (N = 79, 160)	0	0		
Lymphocytes < 0.8 × 10^9/L (N = 79, 159)	1	2		
Neutrophils, Segmented < 1.0 × 10^9/L (N=79, 159)	0	0		
Platelets < 75 × 10^9/L (N = 79, 159)	0	1		
Platelets > 600 × 10^9/L (N = 79, 159)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Blood Pressure During the Placebo-controlled Period

End point title	Change from Baseline in Blood Pressure During the Placebo-controlled Period

End point description:

The analysis includes randomized participants who received at least one dose of study drug and with a baseline value and a post-baseline value at each time point.

End point type	Secondary

End point timeframe:

Baseline, week 2, week 4, and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	185		
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic: Week 2 (N = 88, 174)	-0.5 (± 11.17)	0.1 (± 12.44)		
Systolic: Week 4 (N = 79, 170)	1.9 (± 12.29)	0.4 (± 11.88)		
Systolic: Week 16 (N = 67, 153)	2.2 (± 13.77)	1.0 (± 12.66)		
Diastolic: Week 2 (N = 88, 174)	-0.1 (± 7.89)	-0.6 (± 8.27)		
Diastolic: Week 4 (N = 79, 170)	1.3 (± 7.62)	-1.0 (± 9.51)		
Diastolic: Week 16 (N = 67, 153)	0.8 (± 8.29)	0.6 (± 9.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pulse Rate During the Placebo-controlled Period

End point title	Change from Baseline in Pulse Rate During the Placebo-controlled Period

End point description:

The analysis includes randomized participants who received at least one dose of study drug and with a baseline value and a post-baseline value at each time point.

End point type	Secondary

End point timeframe:

Baseline and week 2, week 4, and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	185		
Units: beats/minute				
arithmetic mean (standard deviation)				
Week 2 (N = 87, 173)	0.3 (± 10.82)	3.4 (± 9.75)		
Week 4 (N = 79, 170)	-0.4 (± 10.17)	3.5 (± 10.43)		
Week 16 (N = 67, 149)	1.0 (± 9.97)	2.0 (± 10.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Body Weight During the Placebo-controlled Period

End point title	Change from Baseline in Body Weight During the Placebo-controlled Period

End point description:

The analysis includes randomized participants who received at least one dose of study drug and with a baseline value and a post-baseline value at each time point.

End point type	Secondary

End point timeframe:

Baseline and week 2, week 4, and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	185		
Units: kg				
arithmetic mean (standard deviation)				
Week 2 (N = 88, 174)	-0.02 (± 1.161)	-0.31 (± 1.188)		
Week 4 (N = 79, 170)	0.04 (± 1.285)	-0.57 (± 2.060)		
Week 16 (N = 67, 153)	0.08 (± 2.337)	-0.98 (± 2.722)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Waist Circumference During the Placebo-controlled Period

End point title	Change from Baseline in Waist Circumference During the Placebo-controlled Period

End point description:

The analysis includes randomized participants who received at least one dose of study drug and with a baseline value and a post-baseline value at each time point.

End point type	Secondary

End point timeframe:

Baseline and week 2, week 4, and week 16

End point values	Placebo	Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	185		
Units: cm				
arithmetic mean (standard deviation)				
Week 2 (N = 88, 174)	-0.2 (± 3.93)	0.2 (± 3.49)		
Week 4 (N = 79, 168)	-0.1 (± 4.89)	-0.3 (± 3.63)		
Week 16 (N = 67, 151)	0.1 (± 6.16)	-0.9 (± 5.06)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved a ≥ 4-point Reduction from Baseline in DLQI at Weeks 32 and 52

End point title	Percentage of Participants who Achieved a ≥ 4-point Reduction from Baseline in DLQI at Weeks 32 and 52

End point description:

The DLQI is a 10-item skin disease-specific questionnaire used to evaluate the impact of skin disease on health-related quality of life (QOL). The items address symptoms and feelings, daily activities, leisure, work/school, personal relationships, and issues with treatment. Questions are answered on a 4-point scale from 0 (not at all/not applicable) to 3 (very much). Item scores are added to provide a total score from 0 to 30, with higher scores indicating greater impairment of QOL.
The analysis includes randomized participants who entered the apremilast extension phase. Missing data were imputed using non-responder imputation.

End point type	Secondary

End point timeframe:

Baseline, week 32 and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	152		
Units: percentage of participants				
number (confidence interval 95%)				
Week 32	68.1 (55.8 to 78.8)	68.4 (60.4 to 75.7)		
Week 52	76.8 (65.1 to 86.1)	79.6 (72.3 to 85.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DLQI at Weeks 32 and 52

End point title	Change from Baseline in DLQI at Weeks 32 and 52

End point description:

The DLQI is a 10-item skin disease-specific questionnaire used to evaluate the impact of skin disease on health-related quality of life. The items address symptoms and feelings, daily activities, leisure, work/school, personal relationships, and issues with treatment. Questions are answered on a 4-point scale from 0 (not at all/not applicable) to 3 (very much). Item scores are added to provide a total score from 0 to 30, with higher scores indicating greater impairment of QOL. A negative change from baseline indicates improvement in quality of life.
The analysis includes randomized participants who entered the apremilast extension phase with available data at baseline and each time point.

End point type	Secondary

End point timeframe:

Baseline, week 32 and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	152		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 32 (N = 62, 127)	-9.8 (± 8.19)	-9.9 (± 7.28)		
Week 52 (N = 55, 112)	-11.3 (± 7.84)	-11.2 (± 7.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Itch NRS Score at Weeks 32 and 52

End point title	Change from Baseline in Itch NRS Score at Weeks 32 and 52

End point description:

The Itch Numeric Rating Scale (NRS) asked participants to assess the worst severity of itch experienced over the past 24 hours on an 11-point scale anchored from 0, representing 'no itching' to 10, representing 'worst itch imaginable'.
A negative change from baseline indicates improvement in itch severity.
The analysis includes randomized participants who entered the apremilast extension phase with available data at baseline and each time point.

End point type	Secondary

End point timeframe:

Baseline, week 32 and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	151		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 32 (N = 62, 127)	-3.2 (± 3.50)	-2.8 (± 3.22)		
Week 52 (N = 54, 112)	-3.9 (± 3.61)	-3.3 (± 3.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Skin Discomfort/Pain VAS at Weeks 32 and 52

End point title	Change from Baseline in Skin Discomfort/Pain VAS at Weeks 32 and 52

End point description:

Participants were asked to indicate their level of skin discomfort/pain in the past week by placing a vertical stroke on a 100 mm horizontal line on which the left-hand boundary (0) represents no skin discomfort/pain, and the right-hand boundary (100) represents worst possible skin discomfort/pain. The distance from the mark to the left-hand boundary was recorded.
A negative change from baseline indicates improvement in skin discomfort/pain.
The analysis includes randomized participants who entered the apremilast extension phase with available data at baseline and each time point.

End point type	Secondary

End point timeframe:

Baseline, week 32 and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	151		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 32 (N = 57, 114)	-28.4 (± 38.40)	-22.6 (± 33.71)		
Week 52 (N = 51, 104)	-35.0 (± 36.76)	-31.0 (± 34.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in BSA Affected by Psoriasis at Weeks 32 and 52

End point title	Percent Change from Baseline in BSA Affected by Psoriasis at Weeks 32 and 52

End point description:

Body surface area is 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"), which equates to approximately 1% of total BSA.
The analysis includes randomized participants who entered the apremilast extension phase with available data at baseline and each time point.

End point type	Secondary

End point timeframe:

Baseline, week 32 and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	152		
Units: percent change				
arithmetic mean (standard deviation)				
Week 32 (N = 57, 114)	-49.5 (± 47.35)	-40.2 (± 51.79)		
Week 52 (N = 51, 104)	-49.9 (± 53.25)	-32.0 (± 93.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved a PBI Score of ≥ 1 at Weeks 32 and 52

End point title	Percentage of Participants who Achieved a PBI Score of ≥ 1 at Weeks 32 and 52

End point description:

The PBI is a validated patient-reported instrument to assess patient-relevant benefits of psoriasis treatment. Prior to starting study treatment, participants were asked to assess the importance of a series of treatment goals (from not important to very important) by completing the Patient Needs Questionnaire (PNQ). After a period of treatment (32 weeks and 52 weeks), participants were then asked to assess the extent to which these goals were achieved (from not at all to very) by completing the Patient Benefit Questionnaire (PBQ). The Patient Benefit Index represents the benefits realized as a function of most important needs. The PBI score ranges from 0 (no benefit) to 4 (maximum benefit). The analysis includes randomized participants who entered the apremilast extension phase. Missing data were imputed using non-responder imputation.

End point type	Secondary

End point timeframe:

Week 32 and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	152		
Units: percentage of participants				
number (confidence interval 95%)				
Week 32	66.7 (54.3 to 77.6)	67.8 (59.7 to 75.1)		
Week 52	65.2 (52.8 to 76.3)	63.8 (55.6 to 71.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved a PASI Score < 3 at Weeks 32 and 52

End point title	Percentage of Participants who Achieved a PASI Score < 3 at Weeks 32 and 52

End point description:

The PASI score is a measure of psoriatic disease severity taking into account qualitative lesion characteristics (erythema, thickness, and scaling) and degree of skin surface area involvement. 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 total qualitative score (sum of erythema, thickness, and scaling scores) is multiplied by the degree of involvement for each anatomic region and then multiplied by a constant and the values for each anatomic region are summed to yield the PASI score, which ranges from 0 to 72, with higher scores reflecting greater disease severity.
The analysis includes randomized participants who entered the apremilast extension phase. Missing data were imputed using non-responder imputation.

End point type	Secondary

End point timeframe:

Week 32 and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	152		
Units: percentage of participants				
number (confidence interval 95%)				
Week 32	58.0 (45.5 to 69.8)	40.1 (32.3 to 48.4)		
Week 52	50.7 (38.4 to 63.0)	37.5 (29.8 to 45.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in EQ-5D Index Score at Week 52

End point title	Percent Change from Baseline in EQ-5D Index Score at Week 52

End point description:

EQ-5D measures the participants general health state as a vertical VAS and 5 quality of life domains: mobility, self-care, main activity (work, study, housework, family/leisure activities), pain/discomfort, and anxiety/depression. Each dimension is rated on three levels (no problems, some/moderate problems, extreme problems). An EQ-5D summary index is derived by applying a formula that attaches values (weights) to each of the levels in each dimension.
EQ-5D index values were derived using the UK scoring algorithm, where a higher score indicates a better health state. The range of the score is from −0.224 to 1, with 0 corresponding to death, 1 corresponding to full health, and negative numbers indicate health states worse than death. A positive change from baseline indicates improvement.
The analysis includes randomized participants who entered the apremilast extension phase with available data at baseline and week 52.

End point type	Secondary

End point timeframe:

Baseline and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	112		
Units: percent change				
arithmetic mean (standard deviation)	214.103 (± 1799.6328)	11.039 (± 224.3001)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in EQ-5D VAS Score at Week 52

End point title	Percent Change from Baseline in EQ-5D VAS Score at Week 52

End point description:

EQ-5D measures the participant's general health state on a vertical VAS and five quality of life domains. The EQ-5D VAS score ranges from 0 to 100, where a score of 0 indicates the worst imaginable health states and a score of 100 indicates the best imaginable health state. A positive change from baseline indicates improvement.
The analysis includes randomized participants who entered the apremilast extension phase with available data at baseline and week 52.

End point type	Secondary

End point timeframe:

Baseline and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	112		
Units: percent change				
arithmetic mean (standard deviation)	51.4 (± 132.13)	33.6 (± 78.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in WPAI: PSO at Week 52: Percentage Work Impairment

End point title	Change from Baseline in WPAI: PSO at Week 52: Percentage

	Work Impairment

End point description:

The WPAI: PSO is a self-administered questionnaire designed to address impairment to the work productivity and activity of participants due to psoriasis in the past 7 days. Percent impairment while working was derived from the participant's assessment of the degree to which psoriasis affected their productivity while working. A higher percentage indicates greater impairment and less productivity, and a negative change from baseline indicates improvement.
The analysis includes randomized participants who entered the apremilast extension phase with available data and who had reported being employed at baseline and at week 52.

End point type	Secondary

End point timeframe:

Baseline and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	64		
Units: percent impairment				
arithmetic mean (standard deviation)	-21.0 (± 29.82)	-24.4 (± 26.78)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in WPAI: PSO at Week 52: Percentage Work Time Missed

End point title	Change from Baseline in WPAI: PSO at Week 52: Percentage Work Time Missed

End point description:

The WPAI: PSO is a self-administered questionnaire designed to address impairment to the work productivity and activity of participants due to psoriasis in the past 7 days. Percent of work time missed is derived from the number of hours of work missed due to psoriasis symptoms as a percentage of total hours that should have been worked. A higher percentage indicates more hours missed, and a negative change from baseline indicates improvement.
The analysis includes randomized participants who entered the apremilast extension phase with available data and who had reported being employed at baseline and at week 52.

End point type	Secondary

End point timeframe:

Baseline and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	64		
Units: percent impairment				
arithmetic mean (standard deviation)	-4.6 (± 17.43)	-3.2 (± 17.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in WPAI: PSO at Week 52: Percentage Overall Work Impairment

End point title	Change from Baseline in WPAI: PSO at Week 52: Percentage Overall Work Impairment

End point description:

The WPAI: PSO is a self-administered questionnaire designed to address impairment to the work productivity and activity of participants due to psoriasis in the past 7 days. Percent overall work impairment takes into account both hours missed due to psoriasis symptoms and the participant's assessment of the degree to which psoriasis affected their productivity while working. A higher percentage indicates greater impairment and less productivity, and a negative change from baseline indicates improvement.
The analysis includes randomized participants who entered the apremilast extension phase with available data and who had reported being employed at baseline and at week 52.

End point type	Secondary

End point timeframe:

Baseline and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	64		
Units: percent impairment				
arithmetic mean (standard deviation)	-21.7 (± 30.12)	-25.3 (± 29.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in WPAI: PSO at Week 52: Percentage Activity Impairment

End point title	Change from Baseline in WPAI: PSO at Week 52: Percentage Activity Impairment

End point description:

The WPAI: PSO is a self-administered questionnaire designed to address impairment to the work productivity and activity of participants due to psoriasis in the past 7 days. Percent activity impairment is derived from the patient's assessment of the degree to which psoriasis affected their regular daily unpaid activities, measured on a VAS from 1 (no effect on daily activities) to 10 (psoriasis completely prevented daily activities). A higher percentage indicates greater impairment and less productivity, and a negative change from baseline indicates improvement.
The analysis includes randomized participants who entered the apremilast extension phase with available data at baseline and week 52.

End point type	Secondary

End point timeframe:

Baseline and week 52

End point values	Placebo / Apremilast 30 mg	Apremilast 30 mg / Apremilast 30 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	75		
Units: percent impairment				
arithmetic mean (standard deviation)	-32.7 (± 33.94)	-30.5 (± 27.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with TEAEs During Apremilast Treatment

End point title	Number of Participants with TEAEs During Apremilast Treatment

End point description:

An AE is any noxious, unintended, or untoward medical occurrence that may appear or worsen in a participant during a 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 of a preexisting condition was considered an AE.
A serious adverse event (SAE) is any AE occurring at any dose that:
- Resulted in death;
- Was life-threatening;
- Required inpatient hospitalization or prolongation of existing hospitalization;
- Resulted in persistent or significant disability/incapacity;
- Was a congenital anomaly/birth defect;
- Constituted an important medical event.

The Investigator assessed the severity/intensity of each event as mild, moderate, or severe based on level of symptoms.

End point type	Secondary

End point timeframe:

From first dose of apremilast up to 28 days after last dose; up to 40 weeks for participants initially randomized to placebo and 56 weeks for participants initially randomized to apremilast.

End point values	All Apremilast 30 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	254			
Units: participants				
Any TEAE	217			
Drug-related TEAE	152			
Severe TEAEs	14			
Serious TEAEs	18			
Serious drug-related TEAE	2			
TEAE leading to drug interruption	19			
TEAE leading to drug withdrawal	31			
TEAE leading to death	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Marked Laboratory Abnormalities During Apremilast Treatment

End point title	Number of Participants with Marked Laboratory Abnormalities During Apremilast Treatment

End point description:

The analysis includes randomized participants who received at least 1 dose of apremilast, ie, participants originally randomized to apremilast and participants originally randomized to placebo who entered the apremilast extension phase with at least 1 treatment of apremilast, and at least 1 post-baseline measurement.

End point type	Secondary

End point timeframe:

From first dose of apremilast up to 28 days after last dose; up to 40 weeks for participants initially randomized to placebo and 56 weeks for participants initially randomized to apremilast.

End point values	All Apremilast 30 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	235			
Units: participants				
Alanine Aminotransferase > 3 × ULN	2			
Albumin < 25 g/L	0			
Alkaline Phosphatase > 400 U/L	0			
Aspartate Aminotransferase > 3 × ULN (N=234)	1			
Bilirubin > 1.8 × ULN	1			
Blood Urea Nitrogen > 15 mmol/L	2			
Calcium < 1.8 mmol/L	1			
Calcium > 3.0 mmol/L	0			
Cholesterol > 7.8 mmol/L	3			
Creatinine > 1.7 × ULN	1			
Glucose < 2.8 mmol/L	0			

Glucose > 13.9 mmol/L	7			
Hemoglobin A1C (Fasting) > 9% (N=142)	3			
Lactate Dehydrogenase > 3 × ULN (N=228)	0			
Potassium < 3.0 mmol/L	0			
Potassium > 5.5 mmol/L	2			
Sodium < 130 mmol/L	0			
Sodium > 150 mmol/L	0			
Triglycerides > 3.4 mmol/L	22			
Hemoglobin: Women < 85 g/L; Men < 105 g/L (N=232)	1			
Hemoglobin: Women >170 g/L; Men >185 g/L (N=232)	0			
Leukocytes < 1.5 × 10^9/L (N=232)	0			
Lymphocytes < 0.8 × 10^9/L (N=232)	3			
Neutrophils, Segmented < 1.0 × 10^9/L (N=232)	0			
Platelets < 75 × 10^9/L (N=232)	2			
Platelets > 600 × 10^9/L (N=232)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pulse Rate at End of Apremilast Extension Period

End point title	Change from Baseline in Pulse Rate at End of Apremilast Extension Period

End point description:

The analysis includes randomized participants who received at least 1 dose of apremilast, ie, participants originally randomized to apremilast and participants originally randomized to placebo who entered the apremilast extension phase with at least 1 treatment of apremilast, with a baseline value and at least 1 post-baseline value.

End point type	Secondary

End point timeframe:

Baseline (defined as the last value measured on or before the day of the first apremilast dose) and end of apremilast extension period; week 52, or earlier for participants who discontinued prior to week 52

End point values	All Apremilast 30 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	246			
Units: beats/minute				
arithmetic mean (standard deviation)	1.0 (± 10.29)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Blood Pressure at End of Apremilast Extension Period

End point title	Change from Baseline in Blood Pressure at End of Apremilast Extension Period

End point description:

The analysis includes randomized participants who received at least 1 dose of apremilast, ie, participants originally randomized to apremilast and participants originally randomized to placebo who entered the apremilast extension phase, with a baseline value and at least 1 post-baseline value.

End point type	Secondary

End point timeframe:

Baseline (defined as the last value measured on or before the day of the first apremilast dose) and end of apremilast extension period; week 52, or earlier for participants who discontinued prior to week 52

End point values	All Apremilast 30 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	246			
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic	0.1 (± 13.68)			
Diastolic	0.1 (± 8.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Waist Circumference at End of Apremilast Extension Period

End point title	Change from Baseline in Waist Circumference at End of Apremilast Extension Period

End point description:

The analysis includes randomized participants who received at least 1 dose of apremilast, ie, participants originally randomized to apremilast and participants originally randomized to placebo who entered the apremilast extension phase with at least 1 treatment of apremilast, with a baseline value and at least 1 post-baseline value.

End point type	Secondary

End point timeframe:

Baseline (defined as the last value measured on or before the day of the first apremilast dose) and end of apremilast extension period; week 52, or earlier for participants who discontinued prior to week 52

End point values	All Apremilast 30 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	246			
Units: cm				
arithmetic mean (standard deviation)	-0.8 (± 4.97)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Body Weight at End of Apremilast Extension Period

End point title	Change from Baseline in Body Weight at End of Apremilast Extension Period

End point description:

The analysis includes randomized participants who received at least 1 dose of apremilast, ie, participants originally randomized to apremilast and participants originally randomized to placebo who entered the apremilast extension phase with at least 1 treatment of apremilast, with a baseline value and at least 1 post-baseline value.

End point type	Secondary

End point timeframe:

Baseline (defined as the last value measured on or before the day of the first apremilast dose) and end of apremilast extension period; week 52, or earlier for participants who discontinued prior to week 52

End point values	All Apremilast 30 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	246			
Units: kg				
arithmetic mean (standard deviation)	-1.20 (± 3.802)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

PPlacebo-controlled period: From first dose of study drug to week 16 or 28 days after last dose for subjects who didn't enter the extension period.
Apremilast extension period: From first in the extension period to 28 days after last dose, 40 weeks.

Adverse event reporting additional description:

Adverse events are reported for all participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Placebo-controlled Period: Placebo

Reporting group description:

Participants received placebo tablets orally twice a day for 16 weeks.

Reporting group title	Apremilast Extension Period: Apremilast 30 mg

Reporting group description:

Participants received apremilast 30 mg tablets orally twice a day from week 16 to week 52 (36 weeks).

Reporting group title	Placebo-controlled Period: Apremilast 30 mg

Reporting group description:

Participants received apremilast 30 mg tablets orally twice a day for 16 weeks.

Serious adverse events	Placebo-controlled Period: Placebo	Apremilast Extension Period: Apremilast 30 mg	Placebo-controlled Period: Apremilast 30 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 92 (0.00%)	12 / 221 (5.43%)	8 / 185 (4.32%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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
Prolactin-producing pituitary tumour			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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
Transitional cell carcinoma			

subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	0 / 92 (0.00%)	0 / 221 (0.00%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 92 (0.00%)	0 / 221 (0.00%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 92 (0.00%)	0 / 221 (0.00%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 92 (0.00%)	0 / 221 (0.00%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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			
Chest pain			

subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Iridocyclitis			
subjects affected / exposed	0 / 92 (0.00%)	0 / 221 (0.00%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 92 (0.00%)	0 / 221 (0.00%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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
Abdominal pain			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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
Inguinal hernia			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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			
Ovarian cyst			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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			
Renal colic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 221 (0.00%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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			
COVID-19 pneumonia			
subjects affected / exposed	0 / 92 (0.00%)	0 / 221 (0.00%)	2 / 185 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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
Abdominal infection			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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
Erysipelas			
subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (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
Erythema migrans			

subjects affected / exposed	0 / 92 (0.00%)	1 / 221 (0.45%)	0 / 185 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo-controlled Period: Placebo	Apremilast Extension Period: Apremilast 30 mg	Placebo-controlled Period: Apremilast 30 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 92 (41.30%)	93 / 221 (42.08%)	113 / 185 (61.08%)
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 92 (5.43%)	19 / 221 (8.60%)	37 / 185 (20.00%)
occurrences (all)	6	34	50
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 92 (1.09%)	4 / 221 (1.81%)	10 / 185 (5.41%)
occurrences (all)	1	4	10
Abdominal pain upper			
subjects affected / exposed	4 / 92 (4.35%)	3 / 221 (1.36%)	12 / 185 (6.49%)
occurrences (all)	4	3	13
Diarrhoea			
subjects affected / exposed	6 / 92 (6.52%)	22 / 221 (9.95%)	61 / 185 (32.97%)
occurrences (all)	7	25	72
Nausea			
subjects affected / exposed	5 / 92 (5.43%)	10 / 221 (4.52%)	37 / 185 (20.00%)
occurrences (all)	5	10	38
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	10 / 92 (10.87%)	20 / 221 (9.05%)	5 / 185 (2.70%)
occurrences (all)	10	20	5
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 92 (4.35%)	12 / 221 (5.43%)	6 / 185 (3.24%)
occurrences (all)	4	12	6
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	11 / 92 (11.96%) 11	25 / 221 (11.31%) 28	18 / 185 (9.73%) 22

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 January 2019	Major changes included: • Added safety endpoints. • Clarified inclusion/exclusion criteria. • Modified Table of Events to include additional vital signs and body weight measures. • Clarified demography data collection, clinical laboratory evaluation, and efficacy assessments. • Added description of safety assessments. • Clarified data collection of permitted concomitant medications and added information on concomitant medications not permitted. • Clarified safety analyses. • Added clarification specifying electronic AE and SAE reporting through database. • Clarified treatment discontinuation.
01 November 2019	Major changes included: • Removed the requirement for equal block-randomization to each of the 5 manifestations of plaque psoriasis. • Updated reporting modalities to reflect the use of an eCRF-based system for reporting of SAEs and clarified expectations for pregnancy reporting.
01 May 2020	Major changes included: • Updated to reflect the change in Sponsor from Celgene to Amgen, as well as key contact and emergency information. • Updated safety reporting and product complaints information to align with Amgen processes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported