Clinical trial results:
A Phase 4, Multicenter, Single-Arm, Open-Label Study to Evaluate the Impact of Apremilast (CC-10004) on MRI Outcomes in Subjects with Psoriatic Arthritis

Summary

EudraCT number	2018-002748-10
Trial protocol	GB DE ES AT DK BE IT
Global end of trial date	11 May 2022

Results information

Result version number	v1 (current)
This version publication date	16 December 2022
First version publication date	16 December 2022

Trial information

Trial identification

Sponsor protocol code	CC-10004-PSA-014

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03783026
WHO universal trial number (UTN)	-
Other trial identifiers	Amgen Study ID: 20200059

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	11 May 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 May 2022
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 efficacy of apremilast 30 mg twice per day (BID) on inflammation indices, assessed by magnetic resonance imaging (MRI) of the hand.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonization (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 Institutional Review Board (IRB) or 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	06 February 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	Canada: 6
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	Switzerland: 8
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	United States: 40
Country: Number of subjects enrolled	Russian Federation: 38
Worldwide total number of subjects	123
EEA total number of subjects	22

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)	111
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 43 centers in Austria, Belgium, Canada, Denmark, Germany, Italy, Russia, Spain, Switzerland, United Kingdom, and the United States.

Pre-assignment

Screening details:

This was a single-arm, open-label study to evaluate the impact of apremilast on magnetic resonance imaging (MRI) outcomes in adults with psoriatic arthritis (PsA). The study consisted of a 48-week treatment phase, and an observational 4-week follow-up phase.

Period 1

Period 1 title	Treatment Phase (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Apremilast

Arm description:

Participants received apremilast 30 mg twice a day for 48 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 orally twice a day

Number of subjects in period 1	Apremilast
Started	123
Received apremilast	122
Completed	80
Not completed	43
Consent withdrawn by subject	6
Adverse event, non-fatal	15
Protocol Deviation	8
Did Not Receive Treatment	1
Lack of efficacy	13

Baseline characteristics

Reporting groups	
Reporting group title	Apremilast
Reporting group description:	
Participants received apremilast 30 mg twice a day for 48 weeks.	

Reporting group values	Apremilast	Total	
Number of subjects	123	123	
Age Categorical Units: participants			
< 65 years	111	111	
≥ 65 years	12	12	
Age Continuous Units: years			
arithmetic mean	46.6		
standard deviation	± 12.89	-	
Sex: Female, Male Units: participants			
Female	68	68	
Male	55	55	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	4	4	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	117	117	
More than one race	0	0	
Unknown or Not Reported	2	2	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	8	8	
Not Hispanic or Latino	111	111	
Unknown or Not Reported	4	4	
Duration of Psoriatic Arthritis			
From time of diagnosis to time the informed consent was signed. Data are reported for the full analysis set; 122 participants. The full analysis set (FAS) includes all participants who were enrolled, and excludes participants who did not receive any study drug.			
Units: years			
arithmetic mean	1.9		
standard deviation	± 1.66	-	
Synovitis Score Assessed by PsAMRIS			
The Psoriatic Arthritis Magnetic Resonance Imaging Score (PsAMRIS) scoring system assesses metacarpophalangeal (MCP), proximal interphalangeal (PIP), and distal interphalangeal (DIP) joints of fingers 2 to 5 of the most affected hand (the hand with the greater inflammatory burden of swollen joints and/or dactylitis). Synovitis was scored from 0 to 3 at MCP, PIP and DIP joints of fingers 2 to 5 (total of 12 joints), where score 0 is normal and 3 is severe. The overall score ranges from 0 (normal) to 36 (severe). Data are reported for subjects in the FAS with available data (115 subjects).			
Units: score on a scale			

arithmetic mean	6.13		
standard deviation	± 5.121	-	
Tenosynovitis Score Assessed by PsAMRIS			
Tenosynovitis is inflammation of the protective sheath (synovial membrane) that surrounds tendons. The PsAMRIS scoring system assesses MCP, PIP, and DIP joints of fingers 2 to 5 of the most affected hand (the hand with the greater inflammatory burden of swollen joints and/or dactylitis). Flexor tenosynovitis was scored from 0 to 3 at 12 joints, where 0: none; 1: < 1/2 tendon thickness; 2: ≥ 1/2 and < 1 tendon thickness; 3: ≥ 1 tendon thickness. The overall score ranges from 0 (none) to 36 (severe). Data are reported for subjects in the FAS with available data (115 subjects).			
Units: score on a scale			
arithmetic mean	1.70		
standard deviation	± 3.268	-	
Composite Score of BME, Synovitis, and Tenosynovitis Assessed by PsAMRIS			
The PsAMRIS scoring system assesses MCP, PIP, and DIP joints of fingers 2 to 5 of the most affected hand. Synovitis, flexor tenosynovitis, and bone edema were each scored from 0 (none/normal) to 3 (severe) at each joint. The total scores for synovitis and tenosynovitis range from 0 to 36 and the total score for BME ranges from 0 to 72. The PsAMRIS composite inflammation score is calculated as: BME score + 2 × synovitis score + 2 × tenosynovitis score. The score ranges from 0 (normal) to 216 (severe). Data are reported for subjects in the FAS with available data (114 subjects).			
Units: score on a scale			
arithmetic mean	18.51		
standard deviation	± 17.849	-	
Bone Marrow Edema Score Assessed by PsAMRIS			
Bone marrow edema (BME) is a buildup of fluid inside the bones. The PsAMRIS scoring system assesses BME at the proximal and distal regions of MCP, PIP, and DIP joints of fingers 2 to 5 of the most affected hand. BME 1s assessed as the proportion of bone with edema, compared to the assessed bone volume (articular surface to a depth of 1 cm), judged on all available images; score 0: no edema; 1: 1–33% of bone edema; 2: 34–66% bone edema; 3: 67–100% bone edema. The overall score ranges from 0 (none) to 72 (severe). Data are reported for subjects in the FAS with available data (114 subjects).			
Units: score on a scale			
arithmetic mean	3.02		
standard deviation	± 4.942	-	
Composite Score of BME and Synovitis Assessed by PsAMRIS			
The PsAMRIS scoring system assesses MCP, PIP, and DIP joints of fingers 2 to 5 of the most affected hand. Synovitis and bone edema were each scored from 0 (none/normal) to 3 (severe) at each joint. The total score for synovitis ranges from 0 to 36 and the total score for BME ranges from 0 to 72 since it is scored at both proximal and distal regions of each joint. The PsAMRIS composite score of BME and synovitis is calculated as: BME score + 2 × synovitis score. The score ranges from 0 (normal) to 144 (severe). Data are reported for subjects in the FAS with available data (114 subjects).			
Units: score on a scale			
arithmetic mean	15.12		
standard deviation	± 13.501	-	
Periarticular Inflammation Score Assessed by PsAMRIS			
The PsAMRIS scoring system assesses MCP, PIP, and DIP joints of fingers 2 to 5 of the most affected hand. Periarticular inflammation was scored 0 (absent) or 1 (present) separately at volar and dorsal aspects of the same 12 joint regions as evaluated for synovitis and flexor tenosynovitis. The score for periarticular inflammation ranges from 0 (absent) to 24 (present at all joints). Data are reported for subjects in the FAS with available data (115 subjects).			
Units: score on a scale			
arithmetic mean	2.47		
standard deviation	± 2.709	-	
Total Inflammation Score Assessed by PsAMRIS			

The PsAMRIS scoring system assesses MCP, PIP, and DIP joints of fingers 2 to 5 of the most affected hand. The PsAMRIS total inflammation score consists of BME, synovitis, tenosynovitis and periarticular inflammation. The total inflammation score is calculated as BME score + 2 × synovitis score + 2 × tenosynovitis + 3 × periarticular inflammation. The total inflammation score ranges from 0 (normal) to 288 (severe). Data are reported for subjects in the FAS with available data (114 subjects).			
Units: score on a scale			
arithmetic mean	25.79		
standard deviation	± 24.191	-	
Bone Erosion Score Assessed by PsAMRIS			
The PsAMRIS scoring system assesses bone erosion at the proximal and distal regions of MCP, PIP, and DIP joints of fingers 2 to 5 of the most affected hand. Bone erosion (loss of bone) was assessed on a scale of 0-10, based on the proportion of eroded bone compared to the assessed bone volume (articular surface to a depth of 1 cm), judged on all available images, where 0: no erosion; 1: 1–10% of bone eroded; 2: 11–20%, etc. The total bone erosion score is from 0 (none) to 240 (severe). Data are reported for subjects in the FAS with available data (115 subjects).			
Units: score on a scale			
arithmetic mean	2.19		
standard deviation	± 4.561	-	
Bone Proliferation Score Assessed by PsAMRIS			
The PsAMRIS scoring system assesses MCP, PIP, and DIP joints of fingers 2 to 5 of the most affected hand. Bone proliferation is abnormal bone formation in the periarticular region, such as at the entheses (enthesophytes) and across the joint (ankylosis). Bone proliferation was scored at each joint as 0 (absent) or 1 (present). The total bone proliferation score is from 0 (none) to 12 (present at all joints). Data are reported for subjects in the FAS with available data (115 subjects).			
Units: score on a scale			
arithmetic mean	2.32		
standard deviation	± 1.608	-	
Total Damage Score Assessed by PsAMRIS			
The PsAMRIS assesses MCP, PIP, and DIP joints of fingers 2 to 5 of the most affected hand. The total damage score consists of the erosion score and the bone proliferation score, calculated as: Erosion score + 20 × Bone Proliferation score, and ranges from 0 to 480 (worst). Data are reported for subjects in the FAS with available data (115 subjects).			
Units: score on a scale			
arithmetic mean	48.51		
standard deviation	± 35.147	-	

End points

End points reporting groups

Reporting group title	Apremilast
Reporting group description:	
Participants received apremilast 30 mg twice a day for 48 weeks.	

Primary: Change From Baseline in the Composite Score of BME, Synovitis, and Tenosynovitis Assessed by PsAMRIS at Week 24

End point title	Change From Baseline in the Composite Score of BME, Synovitis, and Tenosynovitis Assessed by PsAMRIS at Week 24[1]

End point description:

PsAMRIS is a validated MRI scoring system that assesses metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints of fingers 2 to 5 of the most affected hand (the hand with the greater inflammatory burden of swollen joints and/or dactylitis).
Synovitis, flexor tenosynovitis, and bone marrow edema were scored from 0 (none/normal) to 3 (severe) at each joint. The total scores for synovitis and tenosynovitis range from 0 to 36 and the total score for BME ranges from 0 to 72 since both proximal and distal regions of each joint were scored.
The PsAMRIS composite inflammation score is calculated as: BME score + 2 × synovitis score + 2 × tenosynovitis score, and ranges from 0 (normal) to 216 (severe). A negative change from baseline indicates improvement.
This endpoint was analyzed using a mixed-effects model for repeated measures (MMRM) with change from baseline as the dependent variable; baseline value, scanner type and time as independent variables.

End point type	Primary

End point timeframe:

Baseline and week 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not conducted in this single-arm study.

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	98[2]			
Units: score on a scale				
least squares mean (confidence interval 95%)	-2.32 (-4.73 to 0.09)			

Notes:

[2] - Full analysis set participants with available data at baseline and week 24.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Composite Score of BME, Synovitis, and Tenosynovitis Assessed by PsAMRIS at Week 48

End point title	Change from Baseline in the Composite Score of BME, Synovitis, and Tenosynovitis Assessed by PsAMRIS at Week 48

End point description:

PsAMRIS is a validated MRI scoring system that assesses metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints of fingers 2 to 5 of the most affected hand (the hand

with the greater inflammatory burden of swollen joints and/or dactylitis).
Synovitis, flexor tenosynovitis, and bone marrow edema were scored from 0 (none/normal) to 3 (severe) at each joint. The total scores for synovitis and tenosynovitis range from 0 to 36 and the total score for BME ranges from 0 to 72 since both proximal and distal regions of each joint were scored.
The PsAMRIS composite inflammation score is calculated as: BME score + 2 × synovitis score + 2 × tenosynovitis score, and ranges from 0 (normal) to 216 (severe). A negative change from baseline indicates improvement.
This endpoint was analyzed using a MMRM with change from baseline as the dependent variable; baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and week 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	81[3]			
Units: score on a scale				
least squares mean (confidence interval 95%)	-2.91 (-5.45 to -0.37)			

Notes:

[3] - Full analysis set participants with available data at baseline and week 48

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Composite Score of BME and Synovitis Assessed by PsAMRIS at Weeks 24 and 48

End point title	Change from Baseline in the Composite Score of BME and Synovitis Assessed by PsAMRIS at Weeks 24 and 48

End point description:

PsAMRIS is a validated MRI scoring system that assesses metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints of fingers 2 to 5 of the most affected hand (the hand with the greater inflammatory burden of swollen joints and/or dactylitis).
Synovitis and bone marrow edema were each scored from 0 (none/normal) to 3 (severe) at each joint. The total score for synovitis ranges from 0 to 36 and the total score for BME ranges from 0 to 72 since this is scored at both proximal and distal regions of each joint.
The PsAMRIS composite score of BME and synovitis is calculated as: BME score + 2 × synovitis score. The score ranges from 0 (normal) to 144 (severe). A negative change from baseline indicates improvement.
This endpoint was analyzed using a MMRM including change from baseline of composite score of BME and synovitis as dependent variable; baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	98[4]			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 24	-1.19 (-2.89 to 0.50)			
Week 48	-1.54 (-3.53 to 0.46)			

Notes:

[4] - Full analysis set participants with available data at each time point; N = 81 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the PsAMRIS Total Inflammation Score at Weeks 24 and 48

End point title	Change from Baseline in the PsAMRIS Total Inflammation Score at Weeks 24 and 48

End point description:

PsAMRIS is a validated MRI scoring system that assesses metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints of fingers 2 to 5 of the most affected hand. Synovitis, flexor tenosynovitis, and bone marrow edema were each scored from 0 (none/normal) to 3 (severe) at each joint. Periarticular inflammation was scored 0 (absent) or 1 (present) separately at volar and dorsal aspects of the same 12 joints. The scores for synovitis and tenosynovitis range from 0 to 36, the score for BME is from 0 to 72 and the periarticular inflammation score is from 0 to 24.
The PsAMRIS total inflammation score is calculated as: BME score + 2 × synovitis score + 2 × tenosynovitis score + 3 × periarticular inflammation, and ranges from 0 (normal) to 288 (severe). A negative change from baseline indicates improvement.
This endpoint was analyzed using a MMRM with change from baseline score as dependent variable; baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	98[5]			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 24	-3.62 (-7.11 to -0.12)			
Week 48	-4.35 (-8.14 to -0.56)			

Notes:

[5] - Full analysis set participants with available data at each time point; N = 81 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Bone Marrow Edema Assessed by PsAMRIS at Weeks 24 and 48

End point title	Change from Baseline in Bone Marrow Edema Assessed by PsAMRIS at Weeks 24 and 48

End point description:

Bone marrow edema (BME) is a buildup of fluid inside the bones. The OMERACT PsAMRIS scoring system assesses BME at the proximal and distal regions of MCP, PIP, and DIP joints of fingers 2 to 5 of the most affected hand. BME is assessed on a scale of 0-3 based on the proportion of bone with edema, compared to the assessed bone volume (articular surface to a depth of 1 cm), judged on all available images; where 0: no edema; 1: 1–33% of bone edema; 2: 34–66% of bone edema; 3: 67–100% of bone edema. The overall score ranges from 0 (none) to 72 (severe). A negative change from baseline indicates improvement.
This endpoint was analyzed using a MMRM with change from baseline BME score as dependent variable; baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	99[6]			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 24	-0.22 (-0.83 to 0.38)			
Week 48	-0.39 (-1.14 to 0.37)			

Notes:

[6] - Full analysis set participants with available data at each time point; N = 82 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Synovitis Assessed by PsAMRIS at Weeks 24 and 48

End point title	Change from Baseline in Synovitis Assessed by PsAMRIS at Weeks 24 and 48

End point description:

PsAMRIS is a validated MRI scoring system that assesses metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints of fingers 2 to 5 of the most affected hand (the hand with the greater inflammatory burden of swollen joints and/or dactylitis).
Synovitis is inflammation of the synovial membrane, connective tissue that lines the inside of the joint. Synovitis was scored from 0 to 3 at MCP, PIP and DIP joints of fingers 2 to 5 (total of 12 joints), where score 0 is normal, and a score of 1 is mild, 2 is moderate, and 3 is severe. The overall synovitis score ranges from 0 (normal) to 36 (severe). A negative change from baseline indicates improvement.
This endpoint was analyzed using a MMRM including change from baseline in synovitis score as dependent variable; baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	99[7]			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 24	-0.47 (-1.11 to 0.16)			
Week 48	-0.65 (-1.39 to 0.10)			

Notes:

[7] - Full analysis set participants with available data at each time point; N = 82 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Tenosynovitis Assessed by PsAMRIS at Weeks 24 and 48

End point title	Change from Baseline in Tenosynovitis Assessed by PsAMRIS at Weeks 24 and 48

End point description:

PsAMRIS is a validated MRI scoring system that assesses metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints of fingers 2 to 5 of the most affected hand (the hand with the greater inflammatory burden of swollen joints and/or dactylitis).
Tenosynovitis is inflammation of the protective sheath (synovial membrane) that surrounds tendons. Flexor tenosynovitis was scored from 0 to 3 at MCP, PIP and DIP joints of fingers 2 to 5 (total of 12 joints) where a score of 0 is none; 1: < 1/2 tendon thickness; 2: ≥ 1/2 and < 1 tendon thickness; 3: ≥ 1 tendon thickness. The overall tenosynovitis score ranges from 0 (none) to 36 (severe). A negative change from baseline indicates improvement.
This endpoint was analyzed using a MMRM including change from baseline in tenosynovitis score as dependent variable; baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	99[8]			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 24	-0.64 (-1.10 to -0.19)			
Week 48	-0.78 (-1.15 to -0.40)			

Notes:

[8] - Full analysis set participants with available data at each time point; N = 82 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Periarticular Inflammation Assessed by PsAMRIS at Weeks 24 and 48

End point title	Change from Baseline in Periarticular Inflammation Assessed by PsAMRIS at Weeks 24 and 48

End point description:

PsAMRIS is a validated MRI scoring system that assesses metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints of fingers 2 to 5 of the most affected hand (the hand with the greater inflammatory burden of swollen joints and/or dactylitis).
Periarticular inflammation refers to inflammation of the tissues surrounding the joint, including the periosteum and the entheses, but not the tendon sheaths.
Periarticular inflammation was scored 0 (absent) or 1 (present) separately at volar and dorsal aspects of the same 12 joint regions as evaluated for synovitis and flexor tenosynovitis. The score for periarticular inflammation ranges from 0 (absent) to 24 (present at all joints). A negative change from baseline indicates improvement.
This endpoint was analyzed using a MMRM including change from baseline in periarticular inflammation as dependent variable; baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	99[9]			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 24	-0.49 (-0.90 to -0.07)			
Week 48	-0.59 (-1.04 to -0.13)			

Notes:

[9] - Full analysis set participants with available data at each time point; N = 81 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the PsAMRIS Total Damage Score at Weeks 24 and 48

End point title	Change from Baseline in the PsAMRIS Total Damage Score at Weeks 24 and 48

End point description:

PsAMRIS is a validated MRI scoring system that assesses MCP, PIP, and DIP joints of fingers 2 to 5 of the most affected hand.
Bone erosion (loss of bone) was assessed at the distal and proximal regions of each joint on a scale of 0 to 10, based on the proportion of eroded bone compared to the assessed bone volume, where 0 is no erosion; 1: 1–10% of bone eroded; 2: 11–20%, etc. The total erosion score is from 0 (none) to 240 (severe).
Bone proliferation (abnormal bone formation in the periarticular region) was scored at each joint as 0 (absent) or 1 (present). The total proliferation score is from 0 to 12 (present at all joints)
The total damage score includes the erosion and bone proliferation scores, calculated as: Erosion score + 20 × bone proliferation score, and ranges from 0 (none) to 480 (worst). A negative change from baseline indicates improvement.
This endpoint was analyzed using a MMRM with baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	100[10]			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 24	0.22 (-1.10 to 0.53)			
Week 48	0.50 (-0.38 to 1.38)			

Notes:

[10] - Full analysis set participants with available data at each time point; N = 83 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Bone Erosion Assessed by PsAMRIS at Weeks 24 and 48

End point title	Change from Baseline in Bone Erosion Assessed by PsAMRIS at Weeks 24 and 48

End point description:

PsAMRIS is a validated MRI scoring system that assesses metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints of fingers 2 to 5 of the most affected hand.
Bone erosion (loss of bone) was assessed at the distal and proximal regions of each joint on a scale of 0-10, based on the proportion of eroded bone compared to the assessed bone volume, judged on all available images: 0: no erosion; 1: 1–10% of bone eroded; 2: 11–20%, etc. The assessed bone volume is from the articular surface (or its best estimated position if absent) to a depth of 1 cm. The total erosion score ranges from 0 (none) to 240 (severe). A negative change from baseline indicates improvement.
This endpoint was analyzed using a MMRM with baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	100[11]			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 24	-0.01 (-0.06 to 0.05)			
Week 48	0.03 (-0.04 to 0.10)			

Notes:

[11] - Full analysis set participants with available data at each time point; N = 83 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Bone Proliferation Assessed by PsAMRIS at Weeks 24 and 48

End point title	Change from Baseline in Bone Proliferation Assessed by PsAMRIS at Weeks 24 and 48

End point description:

PsAMRIS is a validated MRI scoring system that assesses metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints of fingers 2 to 5 of the most affected hand.
Bone proliferation (abnormal bone formation in the periarticular region such as at the entheses and across the joint) was scored at each joint as 0 (absent) or 1 (present). The total proliferation score ranges from 0 (none) to 12 (present at all joints). A negative change from baseline indicates improvement.
This endpoint was analyzed using a MMRM with baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	100[12]			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 24	0.01 (-0.01 to 0.03)			
Week 48	0.02 (-0.02 to 0.07)			

Notes:

[12] - Full analysis set participants with available data at each time point; N = 83 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Swollen Joint Count (SJC) at Weeks 24 and 48

End point title	Change from Baseline in Swollen Joint Count (SJC) at Weeks 24 and 48

End point description:

A total of 76 joints (including the distal interphalangeal joints of the fingers and toes) were examined for swelling.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	98[13]			
Units: joints				
arithmetic mean (standard deviation)				
Week 24	-5.8 (± 7.11)			
Week 48	-6.3 (± 8.02)			

Notes:

[13] - Full analysis set participants with available data at each time point; N = 81 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Tender Joint Count (TJC) at Weeks 24 and 48

End point title	Change from Baseline in Tender Joint Count (TJC) at Weeks 24 and 48

End point description:

A total of 78 joints (including the distal interphalangeal joints of the fingers and toes) were examined for pain or tenderness.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	98[14]			
Units: joints				
arithmetic mean (standard deviation)				
Week 24	-7.9 (± 9.39)			
Week 48	-8.4 (± 10.97)			

Notes:

[14] - Full analysis set participants with available data at each time point; N = 81 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Clinical Disease Activity Index for Psoriatic Arthritis (c-DAPSA) Score at Weeks 24 and 48

End point title	Change from Baseline in the Clinical Disease Activity Index for Psoriatic Arthritis (c-DAPSA) Score at Weeks 24 and 48

End point description:

The c-DAPSA is a measure of PsA disease activity, associated with functional and structural outcomes. C-DAPSA is calculated as the sum of the following measures:
- Tender joint count 68 (TJC68);
- Swollen joint count 66 (SJC66);
- Patient global assessment of disease activity measured on a numerical rating scale (NRS) from 0 (not active) to 10 (very active); and
- Pain measured on a NRS from 0 (none) to 10 (worst pain imaginable).

The c-DAPSA score ranges from 0 to 154, where a higher score indicates greater disease activity. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	98[15]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24	-15.3 (± 14.04)			
Week 48	-17.2 (± 16.46)			

Notes:

[15] - Full analysis set participants with available data at each time point; N = 81 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index at Weeks 24 and 48 in Participants with Pre-existing Enthesopathy

End point title	Change from Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index at Weeks 24 and 48 in Participants with Pre-existing Enthesopathy

End point description:

Enthesitis is inflammation of the sites where tendons or ligaments insert into the bone. The SPARCC Enthesitis Index assesses 16 unique sites for tenderness recorded as either present (1) or absent (0) for an overall score range of 0 to 16. A higher count represents greater enthesitis burden. A negative change from baseline indicates improvement.
Pre-existing enthesopathy was defined as a baseline SPARCC score greater than 0.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	96[16]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24	-1.8 (± 2.26)			
Week 48	-2.3 (± 2.00)			

Notes:

[16] - FAS participants with baseline enthesopathy (SPARCC > 0) and available data; N = 79 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Leeds Enthesitis Index (LEI) at Weeks 24 and 48 in Participants with Pre-existing Enthesopathy

End point title	Change from Baseline in the Leeds Enthesitis Index (LEI) at Weeks 24 and 48 in Participants with Pre-existing Enthesopathy

End point description:

LEI is a validated tool for the assessment of enthesitis in PsA patients. Tenderness was assessed at 6 sites of tendon insertion (lateral epicondyle, left and right, medial femoral condyle, left and right, and Achilles tendon insertion, left and right). Tenderness was recorded as either present (1) or absent (0) for each of the 6 sites, for an overall score range of 0 to 6. A higher count represents a greater enthesitis burden. A negative change from baseline indicates improvement.
Pre-existing enthesopathy was defined as a baseline LEI score greater than 0.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	78[17]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24	-1.3 (± 1.38)			
Week 48	-1.5 (± 1.19)			

Notes:

[17] - FAS participants with baseline enthesopathy (LEI > 0) and available data; N = 61 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Baseline SPARCC Enthesitis whose Enthesitis Improved to 0 at Weeks 24 and 48

End point title	Percentage of Participants with Baseline SPARCC Enthesitis whose Enthesitis Improved to 0 at Weeks 24 and 48

End point description:

Enthesitis is inflammation of the sites where tendons or ligaments insert into the bone. The SPARCC Enthesitis Index assesses 16 unique sites for tenderness recorded as either present (1) or absent (0) for an overall score range of 0 to 16. A higher count represents greater enthesitis burden. Resolution of SPARCC enthesitis is defined as achieving a SPARCC index score of 0 for participants with baseline SPARCC enthesitis (SPARCC index score > 0).

End point type	Secondary

End point timeframe:

Weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	96[18]			
Units: percentage of participants				
number (confidence interval 95%)				
Week 24	46.9 (36.61 to 57.34)			
Week 48	57.0 (45.33 to 68.06)			

Notes:

[18] - FAS participants with baseline SPARCC enthesitis (SPARCC > 0) and available data; N = 79 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Baseline LEI Enthesitis whose Enthesitis Improved to 0 at Weeks 24 and 48

End point title	Percentage of Participants with Baseline LEI Enthesitis whose Enthesitis Improved to 0 at Weeks 24 and 48

End point description:

LEI is a validated tool for the assessment of enthesitis in PsA patients. Tenderness was assessed at 6 sites of tendon insertion (lateral epicondyle, left and right, medial femoral condyle, left and right, and Achilles tendon insertion, left and right). Tenderness was recorded as either present (1) or absent (0) for each of the 6 sites, for an overall score range of 0 to 6. A higher count represents a greater enthesitis burden. Resolution of LEI enthesitis is defined as a LEI score of 0 for participants with baseline LEI enthesitis (LEI score > 0).

End point type	Secondary

End point timeframe:

Weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	78[19]			
Units: percentage of participants				
number (confidence interval 95%)				
Week 24	56.4 (44.70 to 67.61)			
Week 48	62.3 (48.96 to 74.39)			

Notes:

[19] - FAS participants with baseline LEI enthesitis (LEI > 0) and available data; N = 61 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Leeds Dactylitis Index (LDI) at Weeks 24 and 48 in Participants with Pre-existing Dactylitis

End point title	Change from Baseline in Leeds Dactylitis Index (LDI) at Weeks 24 and 48 in Participants with Pre-existing Dactylitis

End point description:

Dactylitis is characterized by the swelling of the entire finger or toe. Dactylitis was assessed using the Leeds Dactylitis Index (LDI). LDI measures the ratio of the circumference of the affected digit to the circumference of the digit on the opposite hand or foot, using a minimum difference of 10% to define a dactylitic digit. The ratio of circumference is multiplied by a tenderness score from 0 to 3, where 0 = No Tenderness, 1 = Tender, 2 = Tender and wince, 3 = Tender and withdraw. The dactylitis score is the sum of the individual scores for each digit, where 0 indicates no dactylitis and higher scores represent worse dactylitis. A negative change from baseline indicates improvement.
Pre-existing dactylitis is defined as a baseline LDI score greater than 0.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	37[20]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24	-34.38 (± 21.322)			
Week 48	-38.71 (± 21.793)			

Notes:

[20] - FAS participants with baseline dactylitis (LDI > 0) and available data; N = 30 at week 48

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Baseline Dactylitis whose Dactylitis Count Improved to 0 at Weeks 24 and 48

End point title	Percentage of Participants with Baseline Dactylitis whose Dactylitis Count Improved to 0 at Weeks 24 and 48

End point description:

Dactylitis is characterized by the swelling of the entire finger or toe. Dactylitis was assessed using the Leeds Dactylitis Index (LDI). LDI measures the ratio of the circumference of the affected digit to the circumference of the digit on the opposite hand or foot, using a minimum difference of 10% to define a dactylitic digit. The ratio of circumference is multiplied by a tenderness score from 0 to 3 , where 0 = No Tenderness, 1 = Tender, 2 = Tender and wince, 3 = Tender and withdraw). The LDI score is the sum of the individual scores for each digit, where 0 is no dactylitis and higher scores represent worse dactylitis. Resolution of dactylitis is defined as a LDI score of 0 for participants with dactylitis (LDI score > 0) at baseline.

End point type	Secondary

End point timeframe:

Weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	37[21]			
Units: percentage of participants				
number (confidence interval 95%)				
Week 24	89.2 (74.58 to 96.97)			
Week 48	93.3 (77.93 to 99.18)			

Notes:

[21] - FAS participants with baseline dactylitis (LDI > 0) and available data; N = 30 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Psoriatic Arthritis Disease Activity Score (PASDAS) at Weeks 24 and 48

End point title	Change from Baseline in the Psoriatic Arthritis Disease Activity Score (PASDAS) at Weeks 24 and 48

End point description:

PASDAS is a measure of disease activity derived from the following variables:
- Physician and patient global assessment of disease activity (assessed on a 0-10 NRS, then multiplied by 10)
- 68 tender joint count
- 66 swollen joint count
- Short Form-36 Questionnaire (SF-36) physical component summary score (general health status on a scale from 0-100)
- Tender dactylitis count (each digit assessed for tender dactylitis; total score 0-20)
- Leeds enthesitis index (enthesitis assessed at 6 sites; total score of 0-6)
- C-reactive protein (CRP) level (mg/L)

The composite score is a weighted index that ranges from 0 to 10, with worse disease activity represented by higher scores. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	103[22]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24	-1.752 (± 1.3002)			
Week 48	-1.833 (± 1.4146)			

Notes:

[22] - Full analysis set participants with available data at each time point; N = 88 at week 48.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Evaluator’s Global Assessment of Disease Activity at Weeks 24 and 48

End point title	Change from Baseline in the Evaluator’s Global Assessment of Disease Activity at Weeks 24 and 48

End point description:

The Evaluator’s Global Assessment of Disease Activity evaluates how active a participant’s PsA was on the day of the assessment. Disease activity was assessed on a 0 to 10 numeric rating scale (NRS) where 0 represents "no arthritis activity,” and 10 represents "extreme active arthritis". A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	98[23]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24	-2.7 (± 1.99)			
Week 48	-2.8 (± 2.11)			

Notes:

[23] - Full analysis set participants with available data at each time point; N = 81 at week 48

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Patient’s Global Assessment of Disease Activity at Weeks 24 and 48

End point title	Change from Baseline in the Patient’s Global Assessment of Disease Activity at Weeks 24 and 48

End point description:

The Patient's Global Assessment is an assessment of how active a participant's arthritis was on average during the past week. The score ranges from 0 to 10 based on a numerical rating scale, where 0 represents 'Very Well' and 10 represents 'Very Poor'. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	99[24]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24	-1.3 (± 2.09)			
Week 48	-1.6 (± 2.24)			

Notes:

[24] - Full analysis set participants with available data at each time point; N = 82 at week 48

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Subject’s Assessment of Pain at Weeks 24 and 48

End point title	Change from Baseline in the Subject’s Assessment of Pain at Weeks 24 and 48

End point description:

The Subject's Assessment of Pain is an assessment of how much pain a participant had on average during the past week due to psoriatic arthritis. The score ranges from 0-10 based on a numerical rating scale, where 0 represents 'No Pain' and 10 represents 'Pain As Bad As You Can Imagine'. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	99[25]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24	-1.4 (± 2.10)			
Week 48	-2.0 (± 2.13)			

Notes:

[25] - Full analysis set participants with available data at each time point; N = 82 at week 48

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Health Assessment Questionnaire-Disability Index (HAQ-DI) at Weeks 24 and 48

End point title	Change from Baseline in the Health Assessment Questionnaire-Disability Index (HAQ-DI) at Weeks 24 and 48

End point description:

The Health Assessment Questionnaire Disability Index is a patient-reported questionnaire that measures the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and errands and chores) over the past week. Participants assessed their ability to do each task on a scale from 0 (without any difficulty) to 3 (unable to do). Scores were averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 represents very severe, high-dependency disability. A negative change from Baseline in the overall score indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	99[26]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24	-0.293 (± 0.4162)			
Week 48	-0.383 (± 0.4654)			

Notes:

[26] - Full analysis set participants with available data at each time point; N = 82 at week 48

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Whole Body MRI (WB-MRI) Peripheral Enthesitis Inflammation Index at Weeks 24 and 48

End point title	Change from Baseline in Whole Body MRI (WB-MRI) Peripheral Enthesitis Inflammation Index at Weeks 24 and 48

End point description:

Enthesitis was assessed by whole body MRI according to the OMERACT MRI Whole-Body Score for Inflammation in Peripheral Joints and Entheses in Inflammatory Arthritis (MRI-WIPE) scoring system. Thirty-three entheseal sites were assessed for soft tissue inflammation (STI) and 34 sites for osteitis, including the shoulder, pelvis, knees and feet, each on a scale from 0 (none) to 3 (severe).
The Total Peripheral Enthesitis Inflammation score is calculated by adding up all the enthesitis (STI and

osteitis) scores and ranges from 0 to 201, with higher scores reflecting greater disease severity. A negative change from baseline indicates improvement.
WB-MRI endpoints were analyzed using a MMRM including change from baseline as dependent variable; baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	100[27]			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 24	-0.17 (-0.65 to 0.31)			
Week 48	-0.52 (-1.01 to -0.02)			

Notes:

[27] - Full analysis set participants with available data at each time point; N = 84 at week 48

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the WB-MRI Peripheral Joints Inflammation Index at Weeks 24 and 48

End point title	Change from Baseline in the WB-MRI Peripheral Joints Inflammation Index at Weeks 24 and 48

End point description:

Joint inflammation was assessed by whole body MRI according to the OMERACT MRI-WIPE scoring system. Eighty-three peripheral joints were assessed for synovitis and 96 sites for osteitis at the shoulder, hands, pelvis, knees and feet on a semiquantitative scale from 0 (none) to 3 (severe).
The Peripheral Joint Inflammation score is calculated by adding up all the joint (synovitis and osteitis) scores and ranges from 0 to 537, with higher scores reflecting greater disease severity. A negative change from baseline indicates improvement.
WB MRI endpoints were analyzed using a MMRM including change from baseline as dependent variable; baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	100[28]			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 24	-3.38 (-5.10 to -1.66)			

Week 48	-3.58 (-5.66 to -1.51)			

Notes:

[28] - Full analysis set participants with available data at each time point; N = 84 at week 48

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the WB-MRI Total Peripheral Inflammation Index at Weeks 24 and 48

End point title	Change from Baseline in the WB-MRI Total Peripheral Inflammation Index at Weeks 24 and 48

End point description:

Inflammation in joints (arthritis) and at entheses (enthesitis) were assessed separately for soft tissues (synovitis at joints, soft tissue inflammation at entheses) and bone (osteitis) by whole body MRI according to the OMERACT MRI-WIPE scoring system. Each entheseal and joint was scored on a scale from 0 (none) to 3 (severe).
The total peripheral inflammation index is the sum of peripheral enthesitis and peripheral joints inflammation index scores, and ranges from 0 to 738, with higher scores reflecting greater disease severity. A negative change from baseline indicates improvement.
WB MRI endpoints were analyzed using a MMRM including change from baseline as dependent variable; baseline value, scanner type and time as independent variables.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	100[29]			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 24	-3.49 (-5.46 to -1.52)			
Week 48	-4.06 (-6.39 to -1.72)			

Notes:

[29] - Full analysis set participants with available data at each time point; N = 84 at week 48

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Weeks 24 and 48

End point title	Change from Baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Weeks 24 and 48

End point description:

BASDAI is a composite score based on a self-administered survey of six questions with each answered on a 0 to 10 NRS. The 6 questions assess the five major symptoms relevant to spondyloarthropathies:

1) fatigue; 2) spinal pain; 3) peripheral joint pain/swelling; 4) areas of localized tenderness; 5a) morning stiffness severity upon wakening; 5b) morning stiffness duration upon wakening.
To give each of the 5 symptoms equal weighting, the mean of the two scores relating to morning stiffness (questions 5 and 6) is taken. The final BASDAI score is calculated as the mean of the 5 items. The BASDAI score ranges from 0 to 10, with higher scores reflecting greater disease activity. A negative change from baseline indicates improvement.
BASDAI was analyzed in participants deemed to have PsA spondylitis by the investigator and with BASDAI question (Q) 2 score ≥ 4 at baseline).

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	35[30]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24	-1.94 (± 1.935)			
Week 48	-2.01 (± 2.246)			

Notes:

[30] - FAS participants with PsA spondylitis, baseline BASDAI Q2 ≥ 4, and available data; N = 31 at week 48

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Psoriatic Arthritis Impact of Disease 12 domain Questionnaire (PsAID-12) at Weeks 24 and 48

End point title	Change from Baseline in the Psoriatic Arthritis Impact of Disease 12 domain Questionnaire (PsAID-12) at Weeks 24 and 48

End point description:

The PsAID consists of 12 physical and psychological domains: pain, fatigue, skin, work and/or leisure activities, function, discomfort, sleep, coping, anxiety, embarrassment and/or shame, social life, and depression.
Each domain is scored on a NRS rom 0 to 10. The final score is derived as a weighted sum of each domain score, divided by 20, and has a range from 0 (best status) to 10 (worst status). A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and weeks 24 and 48

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	104[31]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24	-1.352 (± 1.8441)			
Week 48	-1.612 (± 1.6613)			

Notes:

[31] - Full analysis set participants with available data at each time point; N = 90 at week 48

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Participants with Treatment-emergent Adverse Events (TEAEs)

End point description:

A TEAE is any adverse event (AE) that began or worsened on or after the first dose of apremilast and no later
than 28 days after the last dose.
A serious adverse event 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.

For each AE, the Investigator assessed the severity/intensity of the event as mild, moderate, or severe (symptoms causing severe discomfort/pain, interference with daily activities, and requiring medical, surgical or drug therapy). The Investigator also assessed whether each event was suspected to be related to study drug based on whether there was evidence to suggest a causal relationship.

End point type	Secondary

End point timeframe:

From first dose of study drug up to 28 days after last dose; up to 52 weeks.

End point values	Apremilast			
Subject group type	Reporting group			
Number of subjects analysed	122[32]			
Units: participants				
Any treatment-emergent adverse event (TEAE)	95			
Any drug-related TEAE	60			
Any severe TEAE	6			
Any serious TEAE	6			
Any serious drug-related TEAE	0			
Any TEAE leading to study drug interruption	12			
Any TEAE leading to study drug withdrawal	15			

Any TEAE leading to death	0			

Notes:

[32] - The safety analysis set includes all participants who received at least 1 dose of study medication.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug up to 28 days after last dose; up to 52 weeks.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	Apremilast
Reporting group description:	
Participants received apremilast 30 mg twice a day for 48 weeks.	

Serious adverse events	Apremilast		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 122 (4.92%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Acetabulum fracture			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic fracture			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Apremilast		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 122 (51.64%)		
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 122 (10.66%)		
occurrences (all)	15		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	41 / 122 (33.61%)		
occurrences (all)	52		
Dyspepsia			

subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	8 / 122 (6.56%) 8 15 / 122 (12.30%) 19		
Skin and subcutaneous tissue disorders Psoriasis subjects affected / exposed occurrences (all)	 7 / 122 (5.74%) 7		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 9 / 122 (7.38%) 11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 September 2018	Major changes included: - deleted 14-3-3η eta biomarker from the protocol as it will no longer be part of the study, due to feasibility issues; - specified the timeframes within which the magnetic resonance imaging (MRI) assessments should be performed.
12 February 2019	Major changes included: - updated exclusion criteria to comply with requests from European Health Authorities; - updated screening period section for consistency with CRF and within the protocol; - clarified clinical disease activity index for psoriatic arthritis (cDAPSA) by adding cut-offs for cDAPSA; - revised safety assessment by deleting the reference to SMT; - added consideration of study treatment discontinuation in the event of unexplained and clinically significant weight loss; - added a recommendation for study treatment discontinuation in the event of new/worsening psychiatric symptoms or suicidal ideation/attempt to comply with European Health Authorities' requests; - added section on diarrhoea, nausea and vomiting to comply with European Health Authorities requests; - revised clinical laboratory evaluations to add creatinine clearance; - added concomitant medications not recommended for consistency with apremilast's label; - revised to reflect subjects' right to withdraw from the study (and proper documentation), as well as the importance of early termination assessments; - updated HAQ-DI questionnaire - added reference to the evaluation of the number of affected digits; - updated the BASDAI questionnaire; - revised text of questions with near the NRS extremes; updated scoring and calculation rules to display PsAID-12 accurate multiplying factors for each domain.
17 May 2019	Major changes included: - removed references to "approved product labeling" and "prescribing information" to clarify that the Investigator’s brochure is the identified RSI for this trial; - updated exclusion criteria to include prior exposure to a tyk2 inhibitor, as prohibited medication.
04 May 2020	Major changes included: - updated to replace references to Celgene Corporation with Amgen Inc. throughout the protocol; - updated monitoring and reporting of adverse events and pregnancy to align with Amgen global drug safety processes; - updated to include instructions for paper reporting of serious adverse events; - added a section on product complaint.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported