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Efficacy and safety of apremilast in paediatric patients with moderate-to-severe plaque psoriasis: 52-week results from the SPROUT randomized controlled trial

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Abstract

Background Oral treatment options for paediatric patients with moderate-to-severe plaque psoriasis are limited. In the 16-week double-blind placebo-controlled phase of the SPROUT trial, apremilast demonstrated efficacy vs. placebo in paediatric patients with psoriasis.

Objectives To evaluate the 52-week efficacy and safety of apremilast in SPROUT.

Methods SPROUT was a phase III multicentre randomized double-blind placebo-controlled parallel-group study (NCT03701763). Patients were randomized 2 : 1 to receive apremilast 20 or 30 mg (for patients weighing 20 to < 50 kg or ≥ 50 kg at baseline, respectively) twice daily or placebo for 16 weeks, after which all patients received apremilast through week 52 (apremilast/apremilast or placebo/apremilast, respectively). Patients were aged 6–17 years and had moderate-to-severe psoriasis that was inadequately controlled by or intolerant to topical therapy.

Results Of 245 patients randomized, 221 (apremilast/apremilast, $n=149$; placebo/apremilast, $n=72$) entered the apremilast extension phase and 186 (apremilast/apremilast, $n=125$; placebo/apremilast, $n=61$) completed 52 weeks. With continued apremilast treatment, rates of static Physician Global Assessment (sPGA) response (score of 0 or 1 with ≥ 2-point reduction from baseline) further improved from week 16 (30.1%) to week 52 (47.7%). In the placebo/apremilast group, sPGA response rates increased from 9.8% at week 16 to 44.4% at week 52. The proportions of patients with ≥ 75% reduction from baseline in Psoriasis Area and Severity Index increased from 42.3% at week 16 to 60.4% at week 52 in the apremilast/apremilast group and from 13.4% to 63.9% in the placebo/apremilast group. No new safety signals were observed.

Conclusions Improvements in clinical outcomes were sustained through 52 weeks with apremilast treatment in paediatric patients with moderate-to-severe psoriasis. Safety findings were consistent with the known safety profile.

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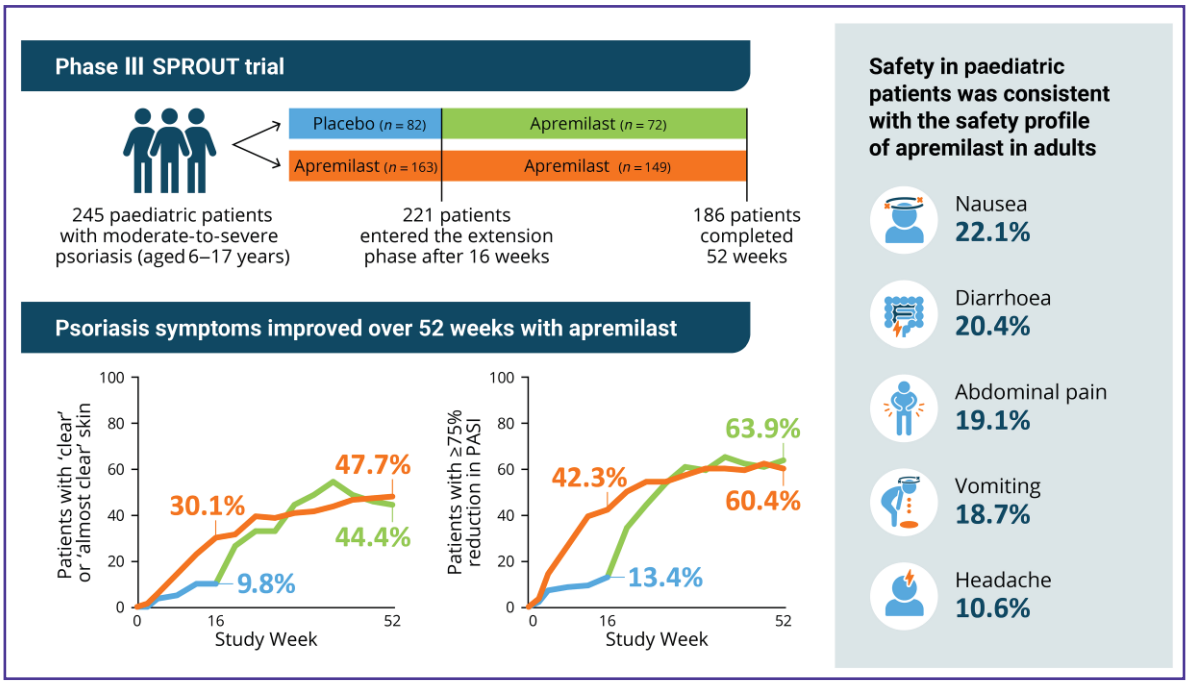
Graphical Abstract



Lay summary

Psoriasis is a skin condition that causes red, scaly rashes, as well as itch and pain. It is estimated to affect around 125 million people worldwide. About 30% of cases of psoriasis develop in childhood. Many treatments approved for use in adults are not approved for children.

In this multinational SPROUT study, we looked at how effective and safe an oral drug called 'apremilast' was in treating psoriasis in children and adolescents for over 1 year. Altogether, 245 patients were given either apremilast or 'placebo' (a dummy drug containing no active ingredients) for 16 weeks. After this, all patients received apremilast until week 52. We looked at how many patients developed clear or almost clear skin. We noted how many patients saw a decrease of at least 75% in the affected area and severity of their psoriasis. We also monitored patients' safety during the study. Previous research showed that apremilast improved the symptoms of psoriasis symptoms after 16 weeks. In this study, we found that these treatment benefits were maintained for 1 year. They even continued to improve up to the end of the study. By week 52, almost half of the patients had clear or almost clear skin. More than half of patients experienced a reduction in their psoriasis by at least 75%. This was true whether they received apremilast from the beginning of the study or switched from the placebo to apremilast at week 16. We also found no new side effects from week 16 to week 52.

In conclusion, our findings suggest that apremilast could improve psoriasis in children and adolescents over 1 year of treatment. There were no major safety concerns.

What is already known about this topic?

- Paediatric patients with moderate-to-severe psoriasis require systemic therapy.
- Oral agents approved in this population are lacking.
- The safety and efficacy of apremilast over 16 weeks have been demonstrated in paediatric patients with moderate-to-severe psoriasis in the phase III placebo-controlled randomized SPROUT trial.

What does this study add?

- Improvements in psoriasis were maintained for 52 weeks with continued apremilast treatment.
- The safety profile of apremilast over 52 weeks was consistent with the 16-week placebo-controlled period and consistent with the safety profile in adults.

Paediatric patients with psoriasis can experience significant burden, with reduced quality of life and many of the same comorbidities as adults.[1–5] Children and adolescents are particularly affected by bullying, stigma and reduced self-esteem due to their psoriasis.[1,2] Experiencing these negative effects on mental health at a young age can have a lifelong impact and put children at greater risk of developing psychiatric disorders such as depression and anxiety.[6,7] Treatment with systemic therapy may be necessary based on disease severity, lack of response to topical or phototherapy, impaired functioning or quality of life, and associated comorbidities.[4] Systemic treatments recommended for paediatric psoriasis include etanercept, ustekinumab, adalimumab, methotrexate, ciclosporin and acitretin.[4] However, paediatric patients may be undertreated, as use of conventional systemic and biologic therapies remains low.[8] In a real-world survey of physicians treating a total of 1919 paediatric patients with psoriasis, conventional systemics were prescribed in 10.8% of patients and biologics in 24.3%, despite 71.8% of the population having moderate-to-severe disease.[8] Even this may be an overestimate of biologic use due to recruiting requirements; dermatologists were asked to recruit their next 10 consulting paediatric patients with psoriasis but were requested to include 2 patients who were currently receiving or had received a biologic in the last 12 months. Furthermore, only 41.3% of physicians treating patients with moderate-to-severe disease were satisfied with the level of disease control achieved.

There are several challenges in treating moderate-to-severe paediatric psoriasis. Most psoriasis therapies are indicated for adults and have not yet been approved for use in children,[9] in part due to the lack of clinical trial data on the efficacy and safety of these systemic therapies in paediatric populations. Some biologic treatments have been approved in the USA for paediatric psoriasis, including etanercept, ustekinumab, ixekizumab and secukinumab.[9] However, due to a fear of needles, paediatric patients may not be willing to use biologic therapies if they require injection.[10] Additionally, there are limitations associated with currently available oral systemic therapies. For example, although methotrexate is one of the most commonly used conventional systemic therapies for paediatric psoriasis, it has shown modest efficacy in clinical practice and is associated with potentially serious adverse effects such as hepatotoxicity and immune suppression.[4,11,12] Owing to these adverse effects, methotrexate requires routine clinical and laboratory monitoring.[4]

Apremilast is an oral phosphodiesterase 4 inhibitor approved for the treatment of plaque psoriasis in adults who are candidates for phototherapy or systemic therapy and moderate-to-severe plaque psoriasis in paediatric patients aged ≥ 6 years and weighing at least 20 kg who are candidates for phototherapy or systemic therapy.[13] Apremilast is the first US Food and Drug Administration-approved oral systemic therapy for paediatric psoriasis. Apremilast may be easier for children to use than biologics, which require injection, particularly because long-term treatment is often required. The phase III SPROUT trial evaluated the efficacy and safety of apremilast in paediatric patients with moderate-to-severe psoriasis. Week-16 results from the SPROUT trial showed significantly greater improvements in clinical outcomes with apremilast compared with placebo and a safety profile in line with studies in adult populations.[14] As one of the goals of systemic therapy for the treatment of psoriasis in children is to maintain treatment benefits once disease control is achieved,[4] it is important to assess the long-term efficacy and safety of a therapy. The objective of this analysis is to report the 52-week efficacy and safety of apremilast in the SPROUT trial.

Materials and methods

Study design

The study design and eligibility criteria for SPROUT have previously been published in detail.[14] In brief, SPROUT was a phase III multicentre randomized double-blind placebo-controlled parallel-group study (NCT03701763). Patients were randomized 2 : 1 to receive apremilast or placebo for 16 weeks. Dose titration occurred on days 1–7. Randomization was stratified by age group (6–11 years or 12–17 years). Apremilast dosage was assigned by baseline bodyweight; patients weighing 20 to < 50 kg received apremilast 20 mg twice daily and patients weighing ≥ 50 kg received apremilast 30 mg twice daily. During weeks 8–16, patients with a Psoriasis Area and Severity Index (PASI) increase ≥ 50% from baseline were eligible for early escape and could begin treatment with moderate-to-high-potency topical steroid preparations, while continuing their randomized treatment. At week 16, patients randomized to apremilast continued their apremilast treatment and those randomized to placebo transitioned to apremilast (20 mg twice daily or 30 mg twice daily, according to baseline weight at randomization; placebo/apremilast group) through week 52 (extension phase).

Patients

Eligible patients were aged 6–17 years and had moderate-to-severe plaque psoriasis [PASI ≥ 12, psoriasis body surface area (BSA) ≥ 10% and static Physician Global Assessment (sPGA) ≥ 3] that was inadequately controlled by or inappropriate for topical therapy.

Assessments

The primary endpoint was sPGA response [score 0 (clear) or 1 (almost clear) with ≥ 2-point reduction from baseline] at week 16. The major secondary endpoint was ≥ 75% reduction from baseline in PASI score (PASI 75) at week 16. Here, we assessed the exploratory endpoints of sPGA response and PASI 75 response at each study visit through week 52, as well as conducting a pharmacokinetic analysis of apremilast at week 24. Safety endpoints included treatment-emergent adverse events (TEAEs) and changes in body mass index (BMI), and were assessed at all study visits.

Statistical analysis

During the placebo-controlled phase, all efficacy endpoints were assessed in the intent-to-treat population, defined as all randomized patients. During the apremilast extension phase, efficacy endpoints were assessed in the population of patients who entered the extension phase. Missing values were imputed using nonresponder imputation. Patients

Table 1 Baseline characteristics of patients who entered the extension phase

Characteristic	Placebo/apremilast (*n*=72)	Apremilast (*n*=149)	Total (*n*=221)
Age (years), mean (SD)	12.3 (3.3)	12.3 (3.3)	12.3 (3.3)
6–11	30 (41.7)	60 (40.3)	90 (40.7)
12–17	42 (58.3)	89 (59.7)	131 (59.3)
Sex			
Male	38 (52.8)	67 (45.0)	105 (47.5)
Female	34 (47.2)	82 (55.0)	116 (52.5)
BMI (kg m^{-2}), mean (SD)	21.2 (5.6)	21.4 (5.3)	21.3 (5.4)
BMI category[a]			
Underweight	4 (5.6)	4 (2.7)	8 (3.6)
Healthy weight	47 (65.3)	93 (62.4)	140 (63.3)
Overweight	7 (9.7)	24 (16.1)	31 (14.0)
Obese	14 (19.4)	28 (18.8)	42 (19.0)
Race			
White	65 (90.3)	130 (87.2)	195 (88.2)
Black or African American	3 (4.2)	3 (2.0)	6 (2.7)
Asian	3 (4.2)	5 (3.4)	8 (3.6)
Native Hawaiian or Other Pacific Islander	0 (0)	0 (0)	0 (0.0)
American Indian or Alaskan Native	0 (0)	1 (0.7)	1 (0.5)
Not collected/unknown	1 (1.4)	10 (6.7)	11 (5.0)
Duration of plaque psoriasis, (years), mean (SD)	4.2 (3.4)	4.4 (3.4)	4.3 (3.4)
sPGA score			
3 (moderate)	57 (79.2)	111 (74.5)	168 (76.0)
4 (severe)	15 (20.8)	38 (25.5)	53 (24.0)
PASI score, mean (SD)	19.7 (8.2)	20.1 (8.0)	20.0 (8.1)
BSA (%), mean (SD)	31.2 (19.5)	32.2 (18.3)	31.9 (18.6)

Data are presented as *n* (%) unless otherwise stated. The number (*n*) reflects the number of patients who entered the apremilast extension phase; the actual number of patients available for each parameter may vary. BMI, body mass index; BSA, body surface area; PASI, Psoriasis Area and Severity Index; SD, standard deviation; sPGA, static Physician Global Assessment. [a]BMI categories were classified as follows: underweight = percentile < 5; healthy weight = percentile ≥ 5 to < 85; overweight = percentile ≥ 85 to < 95; obesity = percentile ≥ 95.

who underwent early escape were considered nonresponders. Results are summarized descriptively. The safety analysis set included all randomized patients who received ≥1 dose of apremilast started from either week 0 or week 16.

Results

Baseline patient characteristics have been reported previously.[14] Of 245 patients randomized (apremilast, *n*=163; placebo, *n*=82), 221 entered the extension phase [90.2% (apremilast/apremilast, *n*=149/163, 91.4%; placebo/apremilast, *n*=72/82, 87.8%)] and 186 completed 52 weeks [75.9% (apremilast/apremilast, *n*=125/163, 76.7%; placebo/apremilast, *n*=61/82, 74.4%] (Figure S1; see Supporting Information). During the placebo-controlled phase, two (2.5%) patients in the placebo group and 5 (3.1%) in the apremilast group added moderate-to-high-potency topical steroid preparations (early escape). During the extension phase, 15.8% (*n*=35/221) of all patients discontinued the study. The most common reasons for discontinuation (> 2 patients) were lack of efficacy (*n*=11/221; 5.0%), withdrawal by parent/guardian (*n*=9; 4.1%), adverse event (*n*=4; 1.8%), withdrawal by the patient (*n*=4; 1.8%) or other reasons (*n*=3; 1.4%). Baseline characteristics for the 221 patients who entered the extension phase were similar to the overall population. Participants' mean (SD) age at baseline was 12.3 (3.3) years, 52.5% (*n*=116) were girls, mean (SD) duration of psoriasis was 4.3 (3.4) years, 76.0% (*n*=168) had an sPGA score of 3 and mean (SD) PASI total score was 20.0 (8.1) (Table 1). Characteristics were mostly balanced between treatment groups except for a greater proportion of girls in the apremilast group than the placebo/apremilast group [55.0% (*n*=82) vs. 47.2% (*n*=34)].

Static Physician Global Assessment response

We reported previously that the primary endpoint and all secondary endpoints were met.[14] sPGA response rates further increased from 30.1% at week 16 to 47.7% at week 52 in the apremilast group (Figure 1a). In the placebo/apremilast group, sPGA response rates increased from 9.8% at week 16 with placebo to 44.4% at week 52 with apremilast.

PASI 75 response

In the apremilast group, PASI 75 response rates increased from 42.3% at week 16 to 60.4% at week 52 (Figure 1b). In the placebo/apremilast group, PASI 75 response rates increased from 13.4% at week 16 with placebo to 63.9% at week 52 with apremilast.

Safety

During the apremilast exposure period (weeks 0–52 for patients who were initially randomized to receive apremilast or weeks 16–52 for patients who transitioned from placebo to apremilast at week 16), TEAEs and tolerability in the 20-mg and 30-mg dose groups were consistent with the placebo-controlled phase and with the known safety

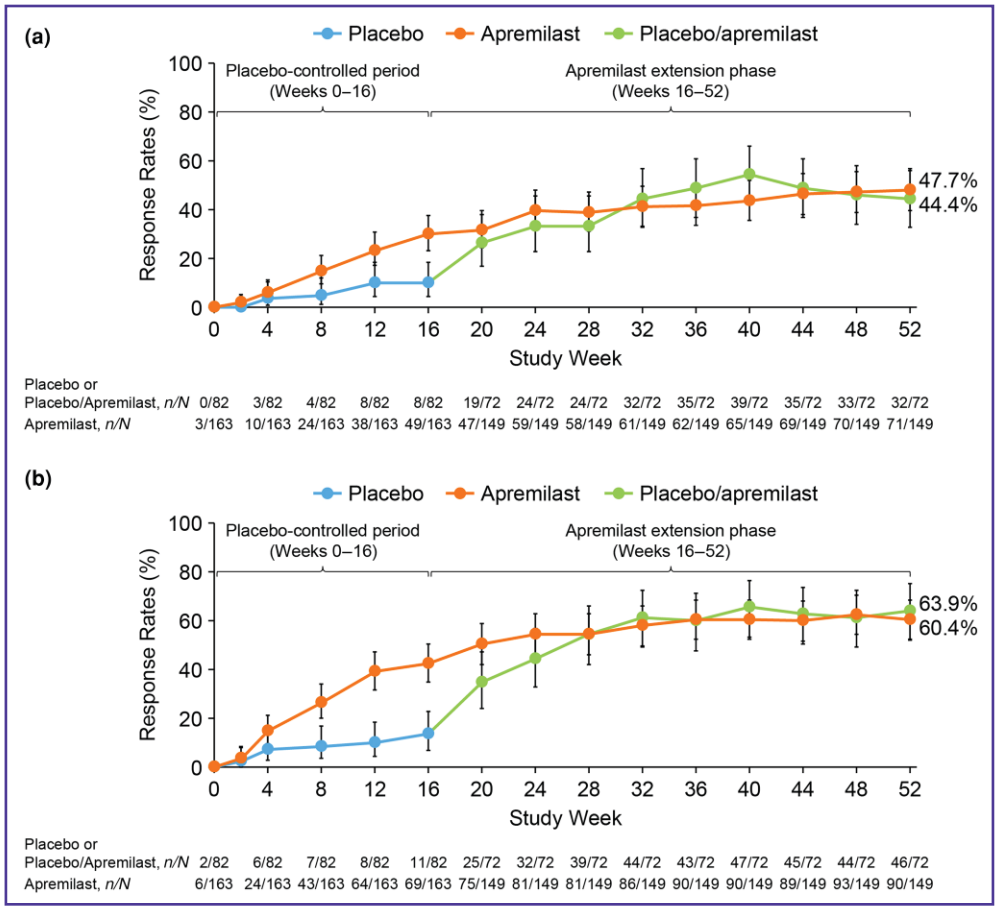


Figure 1 (a) Static Physician Global Assessments (PGA) and (b) ≥75% improvement from baseline in Psoriasis Area and Severity Index (PASI 75) response rates over 52 weeks. sPGA response was defined as a score of 0 or 1 with ≥2-point reduction from baseline. Intent-to-treat population (weeks 0–16) and patients who entered the extension phase (weeks 16–52). Error bars represent the 95% confidence interval. *n/N* indicates the number responders/total number of patients based on nonresponder imputation for missing data.

profile of apremilast in adults. Serious adverse events were reported for 4 of 235 patients (1.7%): psoriasis worsening ($n=1$); appendicitis ($n=1$); iron deficiency anaemia, sinus tachycardia, wandering pacemaker and autonomic nervous system imbalance ($n=1$); and status migrainosus ($n=1$). None of these were considered to be related to treatment by the investigator (Table 2). There were no serious gastrointestinal adverse events. The most common TEAEs (> 5%) in the 20-mg and 30-mg groups combined were nausea (22.1%; $n=52/235$), diarrhoea (20.4%; $n=48/235$), abdominal pain (19.1%; $n=45/235$), vomiting (18.7%; $n=44/235$), headache (10.6%; $n=25/235$), nasopharyngitis (8.5%; $n=20/235$), psoriasis (8.1%; $n=19/235$), pyrexia (6.0%; $n=14/235$), abdominal pain upper (5.5%; $n=13/235$), influenza (5.5%; $n=13/235$) and dyspepsia (5.1%; $n=12/235$) (Table 2). TEAEs of nausea, diarrhoea and vomiting generally decreased during the course of treatment. With regard to nausea, 38.8% of events began in the first month, 12.9% in the second, 9.5% in the third and 3.4% in the fourth. For diarrhoea, 23.5% of events began in the first month, 14.8% in the second, 8.7% in the third and 6.6% in the fourth. For vomiting, 40.5% of events began in the first month, 23.0% in the second, 9.5% in the third and 8.1% in the fourth. Most resolved within 3 days (nausea: 69.8%; diarrhoea: 77.6%; vomiting: 70.3%). TEAEs leading to discontinuation were reported in 9 of 235 (3.8%) patients. The most frequently reported (> 1 patient) TEAEs leading to discontinuation were abdominal pain and vomiting [3 (1.3%) patients each]. No TEAEs of diarrhoea led to discontinuation. The safety profile was generally similar between the 20-mg and 30-mg dose groups, although there was a general trend toward higher rates of some TEAEs such as abdominal pain (27.6% vs. 10.9%), vomiting (23.3% vs. 14.3%) and headache (14.7% vs. 6.7%) in the 20-mg group vs. the 30-mg group. This trend was also seen in the placebo group during the placebo-controlled phase; there were higher rates of diarrhoea (13.2% vs. 7.1%), nausea (5.3% vs. 0%), abdominal pain (15.8% vs. 4.8%) and headache (10.5% vs. 0%) in patients receiving placebo weighing < 50 kg vs. ≥ 50 kg. Additionally, during the apremilast exposure period, abdominal pain (32.0% vs. 10.1%), vomiting (22.7% vs. 15.9%) and headache (16.5% vs. 6.5%) were higher in apremilast-treated patients aged 6–11 years vs. those aged 12–17 years. There was one report of suicidal ideation in the placebo group during the placebo-controlled period that led to treatment discontinuation. There were no reports of suicidal ideation in patients who received apremilast treatment during either the placebo-controlled or extension phases. In 21 patients vaccinated during the study (including COVID-19, influenza, diphtheria, pertussis,

Table 2 Overview of treatment-emergent adverse events (TEAEs) and common (≥ 5%) TEAEs in the apremilast exposure period

	Apremilast exposure					
	Apremilast 20 mg twice daily (*n* = 116, PY = 95.1)		Apremilast 30 mg twice daily (*n* = 119, PY = 93.7)		Total apremilast (*n* = 235, PY = 188.9)	
Event	*n* (%)	EAIR/100 PY	*n* (%)	EAIR/100 PY	*n* (%)	EAIR/100 PY
Any TEAE	88 (75.9)	255.1	80 (67.2)	197.8	168 (71.5)	224.2
Serious TEAEs	2 (1.7)	2.1	2 (1.7)	2.2	4 (1.7)	2.1
Serious treatment-related TEAEs	0 (0.0)	0.0	0 (0.0)	0.0	0 (0.0)	0.0
TEAEs leading to drug withdrawal	5 (4.3)	5.3	4 (3.4)	4.3	9 (3.8)	4.8
Abdominal pain	2 (1.7)	2.1	1 (0.8)	1.1	3 (1.3)	1.6
Vomiting	2 (1.7)	2.1	1 (0.8)	1.1	3 (1.3)	1.6
Abdominal pain, upper	0 (0.0)	0.0	1 (0.8)	1.1	1 (0.4)	0.5
Blood creatinine increased	0 (0.0)	0.0	1 (0.8)	1.1	1 (0.4)	0.5
Guttate psoriasis	1 (0.9)	1.1	0 (0.0)	0.0	1 (0.4)	0.5
Nausea	0 (0.0)	0.0	1 (0.8)	1.1	1 (0.4)	0.5
Tremor	1 (0.9)	1.1	0 (0.0)	0.0	1 (0.4)	0.5
TEAEs occurring in ≥ 5% of patients in any group						
Nausea	29 (25.0)	37.4	23 (19.3)	29.9	52 (22.1)	33.7
Diarrhoea	25 (21.6)	32.3	23 (19.3)	30.6	48 (20.4)	31.5
Abdominal pain	32 (27.6)	44.0	13 (10.9)	15.3	45 (19.1)	28.5
Vomiting	27 (23.3)	34.6	17 (14.3)	20.4	44 (18.7)	27.3
Headache	17 (14.7)	20.3	8 (6.7)	9.2	25 (10.6)	14.6
Nasopharyngitis	12 (10.3)	13.5	8 (6.7)	8.9	20 (8.5)	11.2
Psoriasis	6 (5.2)	6.4	13 (10.9)	14.3	19 (8.1)	10.3
Pyrexia	11 (9.5)	12.6	3 (2.5)	3.3	14 (6.0)	7.8
Abdominal pain, upper	9 (7.8)	10.1	4 (3.4)	4.4	13 (5.5)	7.2
Influenza	9 (7.8)	10.1	4 (3.4)	4.4	13 (5.5)	7.2
Dyspepsia	3 (2.6)	3.3	9 (7.6)	10.4	12 (5.1)	6.7
Abdominal distension	6 (5.2)	6.5	5 (4.2)	5.6	11 (4.7)	6.1
COVID-19[a]	6 (5.2)	6.5	5 (4.2)	5.5	11 (4.7)	6.0

Safety population includes all patients who received at least one dose of apremilast. Exposure-adjusted incidence rate (EAIR) per 100 person-years (PY) is defined as 100 times the number of patients reporting the specific event divided by PY within the phase (up to the first event start date for patients reporting the event). [a]This study was conducted during the COVID-19 pandemic. All cases of COVID-19 resolved.

tetanus, meningococcus and hepatitis B), no new safety findings were reported.

Body mass index changes in the apremilast exposure period

Of 44 patients who were obese at baseline, 27 (61.4%) remained obese, 15 (34.1%) shifted to overweight and 2 (4.5%) shifted to a healthy weight during the apremilast exposure period (Table 3). Of 35 patients who were overweight at baseline, 13 (37.1%) remained overweight, 2 (5.7%) shifted to obese and 20 (57%) shifted to a healthy weight. Of 149 patients who were a healthy weight at baseline, 144 (96.6%) remained a healthy weight, 3 (2.0%) shifted to overweight and 2 (1.3%) shifted to underweight. Of the two patients who shifted from a healthy weight to being underweight, one was a 6-year-old patient who was underweight at screening (BMI 13.7 kg m^{-2}), moved up to a healthy weight at baseline (BMI 14.5 kg m^{-2}) and returned to their original BMI at screening of 13.7 kg m^{-2} by week 52. This patient experienced nausea, suspected by the investigator to be related to apremilast treatment. The other was a 10-year-old patient with a BMI of 15.7 kg m^{-2} at baseline and 14.6 kg m^{-2} at week 52. This patient experienced multiple events of abdominal pain, increased frequency of bowel movements and diarrhoea both suspected and not suspected by the investigator

Table 3 Shift in body mass index (BMI) category from baseline to last measurement up to week 52 in the apremilast exposure period

	BMI category at end of apremilast treatment (*n* = 235)			
Baseline BMI category[a]	Underweight	Healthy weight	Overweight	Obese
Underweight (*n* = 7)	3 (42.9)	4 (57.1)	0 (0.0)	0 (0.0)
Healthy weight (*n* = 149)	2 (1.3)	144 (96.6)	3 (2.0)	0 (0.0)
Overweight (*n* = 35)	0 (0.0)	20 (57.1)	13 (37.1)	2 (5.7)
Obese (*n* = 44)	0 (0.0)	2 (4.5)	15 (34.1)	27 (61.4)

Data are presented as *n* (%). Red = shift toward unhealthy BMI. Green = shift toward healthier BMI. Grey = no change. [a]BMI categories were classified as follows: underweight = percentile < 5; healthy weight = percentile ≥ 5 to < 85; overweight = percentile ≥ 85 to < 95; obesity = percentile ≥ 95.

to be related to apremilast treatment. Seven patients were underweight at baseline, of whom four (57.1%) shifted to a healthy weight during the apremilast exposure period.

Pharmacokinetics

Samples from 195 patients were included in the pharmacokinetic analysis at week 24, including 61 patients who transitioned from placebo to apremilast at week 16. Apremilast plasma concentrations at week 24 were similar between dose groups, and between patients who switched from placebo to apremilast and those who were initially randomized to apremilast (Figure S2; see Supporting Information).

Discussion

Apremilast demonstrated continued efficacy over 52 weeks in paediatric patients with moderate-to-severe psoriasis in SPROUT. Rates of sPGA response and PASI 75 response continued to increase from week 16 through week 52 with continued apremilast treatment. Approximately half of the population achieved sPGA response and PASI 75 response at week 52, whether they were initially randomized to apremilast transitioned from placebo to apremilast at week 16. The dropout rate remained low during the extension phase, with 84.2% of all patients who entered the extension completing the study. No patterns were observed among patients who discontinued due to lack of efficacy.

Safety and tolerability are primary concerns for systemic treatment of paediatric patients. In SPROUT, the safety profile of apremilast in the apremilast exposure period was consistent with the 16-week placebo-controlled period.[14] Rates of serious TEAEs and TEAEs leading to withdrawal were low in the 52-week apremilast exposure period. None of the serious TEAEs was reported to be related to treatment. The most common TEAEs were also in line with the profile observed in adults.[15,16] These occurred at a similar frequency in the 20-mg and 30-mg dose groups, with the exception of higher rates of abdominal pain, vomiting and headache in the 20-mg group than the 30-mg group (weighing 20 to < 50 kg and ≥ 50 kg, respectively). This may have been more related to patient weight and age rather than dose as this trend was also observed in placebo-treated patients weighing 20 to < 50 kg vs. ≥ 50 kg and in younger (6–11 years) vs. older (12–17 years) apremilast-treated patients. Although gastrointestinal adverse events were common, there were no serious gastrointestinal events and no events of diarrhoea that led to discontinuation. Additionally, the majority of gastrointestinal events in the exposure period resolved within 3 days, consistent with results from the placebo-controlled phase. Among patients who experienced a shift in BMI, most were shifts toward healthier BMI categories. Only two patients shifted from a healthy BMI at baseline to below normal for age in the apremilast exposure period. Both patients were at the low end of the healthy BMI range at baseline, suggesting that paediatric patients with borderline normal for age BMI should be closely monitored for weight changes, especially in the presence of gastrointestinal adverse events. In addition, pharmacokinetics remained consistent between the 20-mg and 30-mg dose groups, as well as apremilast/apremilast and placebo/apremilast groups, in the extension phase.

The generalizability of the conclusions from this study are limited by a lack of racial diversity and lack of comparison to other treatments. Additionally, the smaller sample size of patients with severe sPGA scores vs. moderate scores may limit interpretations in patients with severe plaque psoriasis.

Altogether, these results support apremilast as a safe and effective treatment for paediatric patients with moderate-to-severe psoriasis over a 52-week treatment period. Safe, oral treatment options for paediatric patients are valuable in light of challenges to treatment and the significant impact of psoriasis during this critical stage of development.

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Conflicts of interest

A.S.P. has been an investigator for AbbVie, Applied Pharma Research, Biomendics, Dermavant, Eli Lilly, Incyte, Janssen, Krystal, Regeneron, Timber and UCB; a consultant for Abeona, Apogee, Arcutis, ASLAN, BioCryst, Boehringer Ingelheim, Castle Creek, Bristol Myers Squibb, Dermavant, Incyte, Krystal, LEO, L'Oréal, Mitsubishi Tanabe, MoonLake Immunotherapeutics, Procter & Gamble, Regeneron, Sanofi, Seanergy and UCB; and been on the Data Safety Monitoring Board for AbbVie, Abeona and Galderma. L.F. has been an investigator for, has received honoraria from and has been an advisory board member for Pfizer, Amgen, Galderma and LEO Pharma; and a speaker for Pierre Fabre and Galderma. E.B. has been an investigator for Amgen and a speaker for Pfizer, Regeneron and Sanofi. S.A. has been a speaker and advisory board member for Amgen, Janssen, LEO Pharma and Novartis. A.K., R.K.O., W.Z., H.A. and Z.Z. are employees of and stockholders in Amgen Inc. L.A. has received research equipment from Candela; has been an investigator for Celgene and Amgen; and has been a consultant to AbbVie, Amgen, Regeneron and Verrica.

Data availability

Qualified researchers may request data from Amgen clinical studies. Complete details are available at: http://www.amgen.com/datasharing

Ethics statement

The study was approved by an Institutional Review Board/ethics committee at each study centre before commencement and conducted in compliance with Good Clinical Practice, the International Council for Harmonisation Guideline E6, the Declaration of Helsinki and applicable regulatory requirements.

Patient consent

Patients provided written assent and their legal guardians provided written informed consent before study-related procedures. Written patient consent for publication was obtained.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website.

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