Efficacy and safety of apremilast in pediatric patients with moderate-to-severe plaque psoriasis: 16-week results from SPROUT, a randomized controlled trial

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Background: Approved systemic treatment options are limited for pediatric patients with moderate to severe plaque psoriasis.

Objective: To assess the efficacy and safety of apremilast over 16 weeks in pediatric patients with plaque psoriasis.

Methods: SPROUT (NCT03701763) was a phase 3, multicenter, randomized, double-blind, placebo-controlled study of apremilast in patients aged 6-17 years with moderate-to-severe psoriasis (Psoriasis Area and Severity Index [PASI] ≥12, body surface area ≥10%, static Physician Global Assessment [sPGA] ≥3) inadequately controlled by/inappropriate for topical therapy. Patients were stratified by age group and randomized (2:1) to apremilast (20 or 30 mg BID based on weight) or placebo for 16 weeks, followed by apremilast extension to 52 weeks.

Results: Of 245 patients randomized (apremilast: 163; placebo: 82), 221 (90%) completed the double-blind phase (apremilast: 149; placebo: 72). Significantly more patients achieved sPGA response and ≥75% reduction in PASI with apremilast than placebo, regardless of baseline age, weight, or disease severity. No new safety signals were observed.

Limitations: Sample size of subgroup analyses.

Conclusions: Improvements in global disease activity and skin involvement were significantly greater in pediatric patients treated with apremilast versus placebo. Adverse events were consistent with the known apremilast safety profile. (J Am Acad Dermatol 2024;90:1232-9.)

Key words: apremilast; oral; pediatric; psoriasis; systemic treatment.

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

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INTRODUCTION

Approximately one-third of psoriasis cases develop during childhood.[1] Psoriasis symptoms can present differently in children than in adults.[2,3] Plaques are often thinner and smaller in pediatric patients and mistaken for eczema.[2-4] The most common sites for psoriasis to develop on children are the scalp, face, and flexural areas.[2,3]

Psoriasis greatly decreases health-related quality of life (QOL) in children and adolescents, as well as in their caregivers.[5,6] Self-image, relationships, and physical activity in particular are affected.[5,6] Onset at a young age may be associated with greater adverse outcomes later in life, such as reduced QOL and greater likelihood of psychiatric disorders, sleep problems, and social discrimination.[7] One study found risk for depression, anxiety, and bipolar disorder increased by 23%, 32%, and 55%, respectively, in pediatric patients with psoriasis.[8] In addition, pediatric psoriasis is associated with increased risk of many of the comorbidities that affect adults with psoriasis, including obesity, cardiovascular disease, metabolic syndrome, diabetes, Crohn's disease, and psoriatic arthritis.[1,2,9] It is therefore critical that children receive appropriate treatment. Approved systemic therapies for moderate-to-severe plaque psoriasis in pediatric patients are limited. Many therapies prescribed for children with psoriasis are used off-label as they are not approved for use in children.[4] The American Academy of Dermatology—National Psoriasis Foundation 2020 guidelines give the strongest recommendations to etanercept, ustekinumab, adalimumab, methotrexate, cyclosporine, and acitretin as systemic treatments for pediatric patients with plaque psoriasis.[1] However, clinical trial data on the efficacy of systemic therapies in pediatric populations are lacking. Additionally, there are barriers to their use, such as cost and insurance coverage limitations.[4] Furthermore, many therapies used in pediatric patients are administered subcutaneously. Children tend to not like injections and can be fearful of them, making biologics difficult to use in pediatric patients. Increasing the number of oral treatment options for this population would be beneficial.

Apremilast, a unique oral phosphodiesterase 4 inhibitor that immunomodulates the inflammatory response, is internationally approved for use in adults with plaque psoriasis, psoriatic arthritis, and oral ulcers associated with Behçet's disease.[10] Since Food and Drug Administration (FDA) approval in 2014, apremilast has demonstrated a favorable benefit-risk profile in more than half a million patients worldwide across approved indications. Exploratory analyses from a phase 2 study of apremilast in pediatric patients with moderate-to-severe psoriasis showed improvements in skin involvement, supporting further evaluation of apremilast in these patients.[11] Here, we report 16-week data from a Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Study to Assess the Efficacy and Safety of Apremilast (CC-10004) in Pediatric Subjects from 6 Through 17 Years of Age with Moderate to Severe Plaque Psoriasis (SPROUT).

CAPSULE SUMMARY

- Pediatric patients with moderate-to-severe psoriasis require treatment with systemic therapies, but current options are limited.
- In this phase 3 study, apremilast was safe and effective in reducing psoriasis severity over 16 weeks in children aged 6-17 years, supporting its use as an oral systemic therapy for pediatric psoriasis.

METHODS

Study design

SPROUT was a phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group study conducted from when the first patient was enrolled in December 2018 to December 2021 (NCT03701763, registered August 2018) (Fig 1). Patients were randomized 2:1 to receive apremilast or placebo for 16 weeks, with dose titration on Days 1−7. Dose titration followed a similar schedule as titration in adults except for omission of a 10 mg placebo dose on Days 4 and 5 to reduce the burden of swallowing extra pills for these pediatric patients. Randomization was stratified by age group (6-11 years or 12-17 years). Dosage was assigned by weight; patients weighing 20 to <50 kg received apremilast 20 mg BID and patients weighing ≥50 kg received apremilast 30 mg BID. During Weeks 8-16, patients with a Psoriasis Area and Severity Index (PASI) increase ≥50% from baseline could commence treatment with moderate-to high-potency topical steroid preparations (early escape). After Week 16, patients entered an extension phase during which all patients received apremilast through Week 52.

The study was approved by the institutional review board (IRB)/ethics committee before commencement and conducted in compliance with Good Clinical Practice, the International Council for

Abbreviations used:

BID:	twice daily
BMI:	body mass index
BSA:	body surface area
CI:	confidence interval
CV:	coefficient of variation
LS:	least squares
PASI:	Psoriasis Area and Severity Index
PASI-75:	a ≥75% reduction from baseline in PASI score
PASI-90:	a ≥90% reduction from baseline in PASI score
QOL:	quality of life
ScPGA:	Scalp Physician Global Assessment
SD:	standard deviation
sPGA:	static Physician Global Assessment
sPGA-G:	modified sPGA of genitalia
SPROUT:	A Phase 3, Multi-center, Randomized, Double-blind, Placebo-controlled Study to Assess the Efficacy and Safety of Apremilast (CC-10004) in Pediatric Subjects from 6 Through 17 Years of Age with Moderate to Severe Plaque Psoriasis
TEAE:	treatment-emergent adverse event
WBI-NRS:	Whole Body Itch Numeric Rating Scale

Harmonisation Guideline E6, the Declaration of Helsinki, and applicable regulatory requirements. Patients provided written assent and their legal guardians provided written informed consent before study-related procedures.

Patients

Patients were aged 6-17 years with moderate-to-severe plaque psoriasis (PASI ≥12, body surface area [BSA] ≥10%, and static Physician Global Assessment [sPGA] ≥3) inadequately controlled by or inappropriate for topical therapy. Exclusion criteria included guttate, erythrodermic, or pustular psoriasis at screening and baseline; topical therapy ≤2 weeks before randomization with the exception of low-potency or weak corticosteroids (class 6 and 7 for North America and Europe) and unmedicated skin moisturizer; and conventional systemic therapy or phototherapy ≤4 weeks before randomization.

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. Other secondary endpoints included percent change from baseline in PASI score and percent change from baseline in BSA at Week 16. Exploratory endpoints evaluated at all time points through Week 16 included ≥90% reduction from baseline in PASI score (PASI-90), Scalp Physician Global Assessment (ScPGA) response (0 [clear] or 1 [almost clear] with ≥2-point reduction from baseline in patients with baseline ScPGA ≥3), modified sPGA of genitalia (sPGA-G) response ([clear] or 1 [almost clear] with ≥2-point reduction from baseline in patients with baseline sPGA-G ≥3), modified Whole Body Itch-Numeric Rating Scale (WBI-NRS) response (≥4-point reduction from baseline), and pharmacokinetic estimates of systemic exposure to apremilast (see the Supplementary Methods, available via Mendeley at https://doi.org/10.17632/bdydt4v6w8.2 for details on pharmacokinetic analysis). sPGA and PASI-75 responses at Week 16 were also assessed in subgroups according to baseline age (6-11 years and 12-17 years), weight (≥20 to <50 kg and ≥50 kg), and psoriasis severity (moderate [sPGA = 3] and severe [sPGA = 4]). Assessment of treatment-emergent adverse events (TEAEs) occurred at all study visits.

Statistical analysis

Sample size was calculated assuming a 15% difference in sPGA response rate between placebo and apremilast (based on phase 3 trials of apremilast in psoriasis). Patients were randomized using a permuted block with centralized interactive response technology. All efficacy endpoints were assessed in the intent-to-treat population, defined as all randomized patients. sPGA, PASI-75, and PASI-90 responses were analyzed using the Cochran-Mantel-Haenszel test adjusting for the stratification factor at randomization. Percentage change from baseline in PASI and BSA were analyzed by analysis of covariance. Subgroup analyses were assessed descriptively. Primary and secondary endpoints were assessed using multiple imputations for missing data. Exploratory endpoints were assessed using last observation carried forward for missing data. Patients who underwent early escape were considered nonresponders.

The safety population comprised all randomized patients who received ≥1 dose of study drug.

RESULTS

In total, 245 patients were randomized (apremilast, 163; placebo, 82) from December 2018 to December 2021. Among patients randomized to apremilast, 80 received 20 mg BID and 83 received 30 mg BID. Mean age was 12 years, with 101 (41.2%) patients aged 6-11 years and 144 (58.8%) aged 12-17 years (Table I). Mean body weight was 52 kg; 120 (49.0%) patients weighed ≥20 to <50 kg and 125 (51.0%) weighed ≥50 kg. Approximately 50% of patients were female and 86.9% were white. Mean duration of plaque psoriasis was 4 years, mean PASI

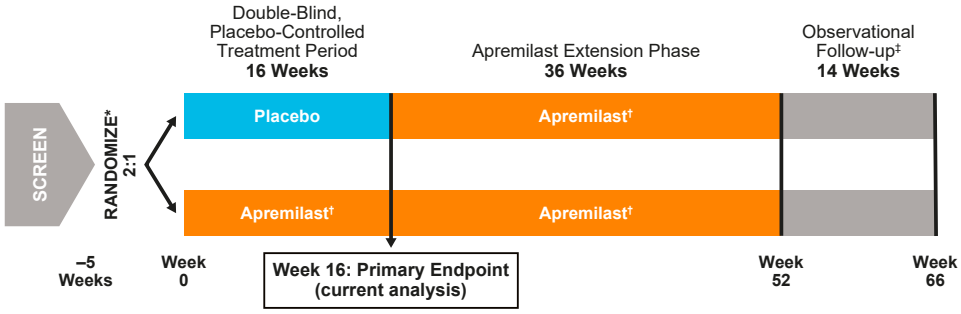

Fig 1. Study design. *Randomization was stratified by age group. †Patients weighing ≥20 to <50 kg received apremilast 20 mg BID and patients weighing ≥50 kg received apremilast 30 mg BID. Titration for the 20 mg dose occurred over 3 days and titration for the 30 mg dose occurred over 5 days. ‡For patients who (1) completed the study and opted not to continue in the long-term study or (2) discontinued the study early. *BID*, Twice daily.

score was 19.8, and 75.5% and 24.5% had an sPGA score of 3 (moderate) or 4 (severe) at baseline, respectively. Patients aged 6-11 years had a mean duration of psoriasis of 2.8 years, and patients aged 12-17 years had a mean duration of 5.2 years. Among younger patients, 73.3% were naive to systemic therapy; in the older population, 60.4% were naive to systemic therapy. Mean PASI and BSA were higher in the older group (20.8 and 34.3%, respectively) than the younger group (18.5 and 27.6%, respectively). A total of 221 (90.2%) patients completed the double-blind phase and 24 discontinued (apremilast, 14 [8.6%]; placebo, 10 [12.2%]) (Supplementary Fig 1, available via Mendeley at https://doi.org/10.17632/bdydt4v6w8.2). Reasons for discontinuation primarily included withdrawal by the patient or parent/guardian (13/245 [5.3%]) and adverse events (6/245 [2.4%]).

Primary endpoint

The sPGA response rate at Week 16 was significantly greater with apremilast (33.1%) versus placebo (11.5%; $P < .0001$) (Fig 2).

PASI response

PASI-75 and PASI-90 response rates were significantly greater with apremilast (45.4% and 25.2%, respectively) versus placebo (16.1% and 4.9%, respectively; both $P \leq .0001$) (Fig 2).

Subgroup analyses

Apremilast showed consistent benefit over placebo for achievement of sPGA response regardless of age or weight (Fig 3). Among patients receiving apremilast, sPGA response rates were greater in younger patients (49.6%) versus older patients (21.5%) and those weighing ≥20 to <50 kg (47.4%) versus ≥50 kg (19.2%). Results for PASI-75 response were similar; consistent treatment differences in favor of apremilast were seen in all age and weight categories, with greater response rates in younger patients and those in the lower weight category (Supplementary Fig 2, available via Mendeley at https://doi.org/10.17632/bdydt4v6w8.2). When efficacy was assessed by baseline disease severity, more patients with moderate disease at baseline achieved sPGA and PASI-75 responses at Week 16 with apremilast versus placebo (Supplementary Fig 3, available via Mendeley at https://doi.org/10.17632/bdydt4v6w8.2). A similar trend was seen in patients with severe disease at baseline; however, sample size was limited. sPGA response rates also tended to be greater in patients with shorter (<5 years) duration of psoriasis versus longer (≥5 years) and in those with no previous use of biologic or systemic therapies (Supplementary Fig 4, available via Mendeley at https://doi.org/10.17632/bdydt4v6w8.2).

Change in PASI and BSA

At Week 16, the percent change from baseline in PASI score was significantly greater with apremilast (−65.3%) versus placebo (−38.3%; $P < .0001$) (Supplementary Fig 5, available via Mendeley at https://doi.org/10.17632/bdydt4v6w8.2). Similarly, BSA decreased by 56.6% in patients receiving apremilast and 21.8% in patients receiving placebo at Week 16 ($P < .0001$) (Supplementary Fig 5, available via Mendeley at https://doi.org/10.17632/bdydt4v6w8.2).

Special areas and itch

At baseline, 81.0% of patients receiving apremilast and 84.1% receiving placebo had moderate-to-severe scalp psoriasis (ScPGA ≥3) (Table I). More patients achieved ScPGA response at Week 16 with apremilast versus placebo (36.4% vs 18.8%; nominal

Table I. Baseline demographics and clinical characteristics

Demographic/characteristic	Placebo (*n* = 82)	Apremilast (*n* = 163)	Total (*N* = 245)
Age, mean (SD), y	12.2 (3.3)	12.3 (3.3)	12.2 (3.3)
Age category, *n* (%)			
6-11 y	34 (41.5)	67 (41.1)	101 (41.2)
12-17 y	48 (58.5)	96 (58.9)	144 (58.8)
Female, *n* (%)	39 (47.6)	89 (54.6)	128 (52.2)
Race, *n* (%)			
American Indian or Alaskan Native	0 (0.0)	2 (1.2)	2 (0.8)
Asian	3 (3.7)	6 (3.7)	9 (3.7)
Black or African American	3 (3.7)	5 (3.1)	8 (3.3)
White	73 (89.0)	140 (85.9)	213 (86.9)
Not collected or unknown	3 (3.7)	10 (6.1)	13 (5.3)
Weight, mean (SD), kg	51.8 (22.2)	52.0 (21.1)	52.0 (21.4)
Weight category, *n* (%)			
≥20-<50 kg	40 (48.8)	80 (49.1)	120 (49.0)
≥50 kg	42 (51.2)	83 (50.9)	125 (51.0)
BMI, mean (SD), kg/m^2	21.3 (5.6)	21.3 (5.2)	21.3 (5.3)
Region, *n* (%)			
Europe	56 (68.3)	108 (66.3)	164 (66.9)
United States	20 (24.4)	38 (23.3)	58 (23.7)
Canada	3 (3.7)	13 (8.0)	16 (6.5)
Rest of world	3 (3.7)	4 (2.5)	7 (2.9)
Duration of plaque psoriasis, mean (SD), y	4.0 (3.4)	4.3 (3.3)	4.2 (3.4)
sPGA score, *n* (%)			
3 (Moderate)	63 (76.8)	122 (74.8)	185 (75.5)
4 (Severe)	19 (23.2)	41 (25.2)	60 (24.5)
ScPGA score, *n* (%)			
0 (Clear)	4 (4.9)	7 (4.3)	11 (4.5)
1 (Almost clear)	3 (3.7)	3 (1.8)	6 (2.4)
2 (Mild)	4 (4.9)	17 (10.4)	21 (8.6)
3 (Moderate)	49 (59.8)	90 (55.2)	139 (56.7)
4 (Severe)	20 (24.4)	42 (25.8)	62 (25.3)
sPGA-G score, *n* (%)			
0 (Clear)	27 (32.9)	65 (39.9)	92 (37.6)
1 (Almost clear)	2 (2.4)	8 (4.9)	10 (4.1)
2 (Mild)	15 (18.3)	12 (7.4)	27 (11.0)
3 (Moderate)	34 (41.5)	60 (36.8)	94 (38.4)
4 (Severe)	2 (2.4)	14 (8.6)	16 (6.5)
PASI, mean (SD)	19.5 (8.0)	20.0 (8.2)	19.8 (8.1)
BSA, mean (SD), %	30.8 (19.0)	31.9 (18.5)	31.5 (18.6)
WBI-NRS score, mean (SD)	5.1 (2.8)	5.4 (2.9)	5.3 (2.9)
≥1 Prior phototherapy, *n* (%)	16 (19.5)	27 (16.6)	43 (17.6)
≥1 Prior conventional systemic therapy, *n* (%)	18 (22.0)	24 (14.7)	42 (17.1)
≥1 Prior biologic therapy, *n* (%)	5 (6.1)	9 (5.5)	14 (5.7)
≥1 Prior systemic therapy, *n* (%)	30 (36.6)	54 (33.1)	84 (34.3)

Intent-to-treat population. Patients in the apremilast arm were assigned to 20 mg BID (baseline weight ≥20 to <50 kg) or 30 mg BID (baseline weight ≥50 kg).

BID, Twice daily; *BMI*, body mass index; *BSA*, body surface area; *PASI*, Psoriasis Area and Severity Index; *ScPGA*, scalp Physician Global Assessment; *sPGA*, static Physician Global Assessment; *sPGA-G*, static Physician Global Assessment of Genitalia; *WBI-NRS*, Whole Body Itch Numeric Rating Scale.

P = .0091) (Supplementary Fig 6, available via Mendeley at https://doi.org/10.17632/bdydt4v6w8.2). A total of 110 patients (44.9%) had moderate-to-severe genital psoriasis (sPGA-G ≥3) at baseline (Table I). Achievement of sPGA-G response at Week 16 was numerically greater with apremilast than placebo (39.2% versus 25.0%), although this did not reach significance, possibly due to small sample size (apremilast, *n* = 74; placebo, *n* = 36) (Supplementary Fig 6, available via Mendeley at https://doi.org/10.17632/

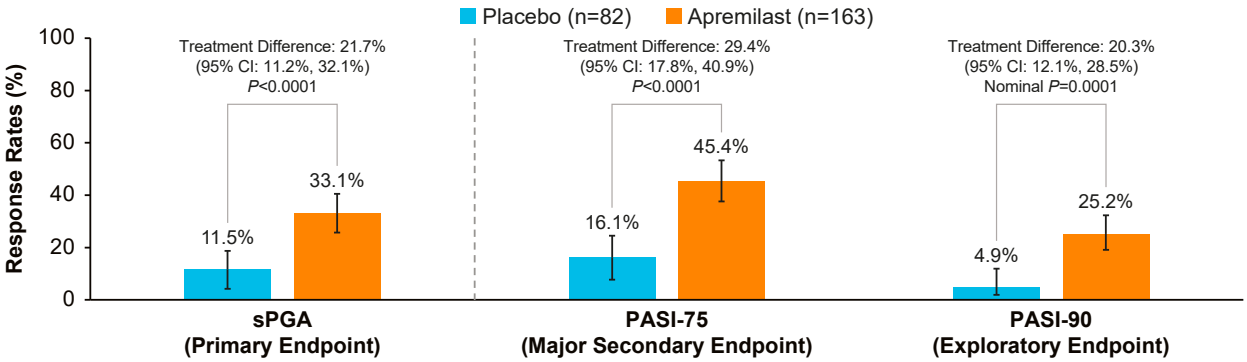

Fig 2. sPGA and PASI Response rates at week 16, Intent-to-treat population. Error bars represent 95% CI. Missing values imputed using multiple imputation for sPGA and PASI-75 response and last observation carried forward for PASI-90 response. Two-sided *P* value is based on the Cochran-Mantel-Haenszel test adjusting for the stratification factors. *PASI*, Psoriasis Area and Severity Index; *PASI-75/90*, ≥75%/90% reduction from baseline in PASI score; *sPGA*, static Physician Global Assessment.

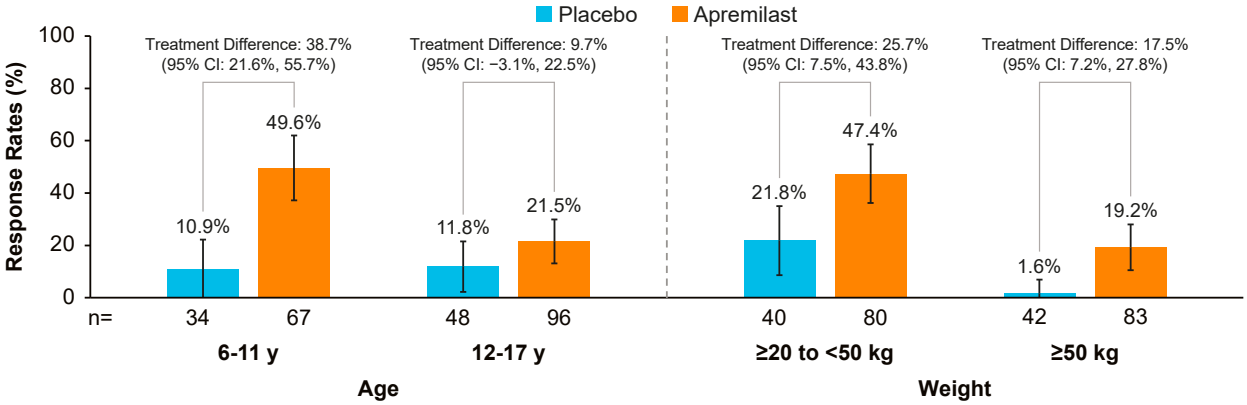

Fig 3. sPGA Response rates at week 16 by age and weight subgroups. Intent-to-treat population. Error bars represent 95% CI. Missing values imputed using multiple imputation. *sPGA*, static Physician Global Assessment.

bdydt4v6w8.2). A greater proportion of patients achieved WBI-NRS response at Week 16 with apremilast versus placebo (52.0% versus 32.1%; nominal P = .0110) (Supplementary Fig 6, available via Mendeley at https://doi.org/10.17632/bdydt4v6w8.2).

Safety

TEAEs were observed in 65.0% of patients in the apremilast group and 41.3% of patients in the placebo group (Table II). Few patients experienced severe (apremilast, 2/163 [1.2%]; placebo, 1/80 [1.3%]) or serious (apremilast, 2/163 [1.2%]; placebo, 1/80 [1.3%]) TEAEs. The most common TEAEs were diarrhea, nausea, and abdominal pain (Table II). For both diarrhea and abdominal pain, 70% of events in the apremilast group resolved within 3 days during the placebo-controlled period. Few TEAEs led to drug withdrawal (apremilast, 5/163 [3.1%]; placebo, 1/80 [1.3%]); these included primarily gastrointestinal disorders for apremilast and suicidal ideation for placebo. No notable differences between treatment groups were observed for changes from baseline in body weight and body mass index (BMI) during the placebo-controlled period.

Pharmacokinetics

At Week 16, there was no apparent difference in the steady-state trough concentrations of apremilast between patients who weighed ≥20 to <50 kg and received 20 mg BID (n = 67), and patients who weighed ≥50 kg and received 30 mg BID (n = 66) (Supplementary Fig 7, available via Mendeley at https://doi.org/10.17632/bdydt4v6w8.2). Apremilast plasma concentrations were similar between the 2 groups with a geometric mean of 51.2 to 81.6 ng/mL

Table II. Overview of TEAEs and most commonly reported TEAEs (weeks 0 to 16; safety population)

Patients, *n* (%)	Placebo (*n* = 80)	Apremilast 20 mg BID (*n* = 80)	Apremilast 30 mg BID (*n* = 83)	Apremilast Total (*n* = 163)
Any TEAE	33 (41.3)	58 (72.5)	51 (61.4)	109 (66.9)
Any drug-related TEAE	12 (15.0)	36 (45.0)	34 (41.0)	70 (42.9)
Any severe TEAE	1 (1.3)	2 (2.5)	0	2 (1.2)
Any serious TEAE	1 (1.3)	2 (2.5)	0	2 (1.2)
TEAE leading to drug withdrawal	1 (1.3)	3 (3.8)	2 (2.4)	5 (3.1)
TEAEs occurring in ≥5% of patients				
Diarrhea	8 (10.0)	15 (18.8)	17 (20.5)	32 (19.6)
Nausea	2 (2.5)	15 (18.8)	17 (20.5)	32 (19.6)
Abdominal pain	8 (10.0)	23 (28.8)	9 (10.8)	32 (19.6)
Vomiting	2 (2.5)	16 (20.0)	13 (15.7)	29 (17.8)
Headache	4 (5.0)	12 (15.0)	5 (6.0)	17 (10.4)
Pyrexia	1 (1.3)	7 (8.8)	3 (3.6)	10 (6.1)
Nasopharyngitis	3 (3.8)	5 (6.3)	5 (6.0)	10 (6.1)
Abdominal pain upper	4 (5.0)	5 (6.3)	4 (4.8)	9 (5.5)
Influenza	1 (1.3)	5 (6.3)	2 (2.4)	7 (4.3)
COVID-19*	5 (6.3)	2 (2.5)	3 (3.6)	5 (3.1)

TEAE, Treatment-emergent adverse event.
*This study was conducted during the COVID-19 pandemic. All cases of COVID-19 resolved.

and a mean of 133 to 173 ng/mL (coefficient of variation: 87% to 107%).

DISCUSSION

The primary endpoint in SPROUT was met, with the rate of sPGA response nearly 3 times greater for patients receiving apremilast than those receiving placebo at Week 16. Apremilast significantly improved generalized skin involvement, scalp psoriasis, which is common in children, and itch, which is often cited as the most burdensome psoriasis symptom.[12] Apremilast showed efficacy regardless of age, weight, or disease severity. However, greater treatment differences between apremilast and placebo tended to be seen in younger patients and in the lower weight group. It should be noted that patients in the younger group had less severe disease as measured by PASI and BSA. In addition, although sample size was limited, a subgroup analysis suggested that patients with shorter disease duration and no prior biologic or systemic treatments may experience greater benefit with apremilast compared to those with longer disease duration and treatment experience. Patients in the older subgroup had longer duration of disease (5.2 years versus 2.8 years) and greater treatment experience (60.4% systemic-naive versus 73.3%) than those in the younger subgroup, which may contribute to the lower treatment effect. Further analysis in a larger population is necessary to understand how these factors affect response to apremilast in the pediatric population.

The baseline PASI score in the SPROUT population (19.8) was similar to ESTEEM 1 and 2 (18.7-20.0), phase 3 trials of apremilast in adults with moderate-to-severe psoriasis. This emphasizes that psoriasis in children can be as severe as psoriasis in adults. SPROUT also indicates that apremilast has a similar safety and efficacy profile in children and adults. Week 16 sPGA response rates in this pediatric population (apremilast, 33.1%; placebo, 11.5%) were similar to those seen in adult populations in ESTEEM 1 (apremilast, 21.7%; placebo, 3.9%) and ESTEEM 2 (apremilast, 20.4%; placebo, 4.4%).[13,14] Likewise, PASI-75 response rates were consistently greater with apremilast treatment in SPROUT (apremilast, 45.4%; placebo, 16.1%), ESTEEM 1 (apremilast, 33.1%; placebo, 5.3%), and ESTEEM 2 (apremilast, 28.8%; placebo, 5.8%). The safety profile in SPROUT was consistent with the ESTEEM trials as well,[13,14] with most events being mild-to-moderate and the most common adverse events being diarrhea, nausea, abdominal pain, and vomiting. Incidence of severe and serious TEAEs was low and balanced across the apremilast and placebo arms. Study discontinuation rates in SPROUT were slightly higher in the placebo group (apremilast, 8.6%; placebo, 12.2%) but consistent with discontinuation rates in the adult studies (apremilast, 10.5% to 12.8%; placebo, 11.7% to 18.2%). Overall, these results suggest that apremilast could be prescribed for children in the

same way it is for adults. The safety profile also indicates that there should not be a need for routine laboratory testing for children taking apremilast.

The lack of racial diversity in this study may limit generalizability of findings. While improvements in sPGA and PASI-75 were seen with apremilast in both moderate and severe subgroups, the smaller sample size of the severe group limits the conclusions drawn from the subgroup analysis. The lack of comparison to other treatments also limits interpretation of efficacy assessments. In addition, this analysis includes 16 weeks of data. Long-term studies with QOL assessments are needed to confirm the viability of apremilast as a long-term systemic treatment for pediatric patients with psoriasis. Such studies are still ongoing.

CONCLUSIONS

Apremilast effectively reduced psoriasis severity compared with placebo in children aged 6-17 years with moderate-to-severe plaque psoriasis inadequately controlled by or inappropriate for topical therapy. Consistent favorable treatment effects were observed in weight and age subgroups. No new safety signals were identified, and TEAEs were consistent with the known apremilast safety profile. These results support apremilast as a safe oral systemic therapy for pediatric patients with moderate-to-severe psoriasis, which may be especially beneficial for children who are reluctant to get injections.

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Conflicts of interest

Dr Fiorillo is an investigator for Pfizer, Amgen, Galderama, and Leo; received honoraria from Pfizer, Amgen, Galderama, and Leo; is an advisory board member for Pfizer, Amgen, Galderama, and Leo; and is a speaker for Pierre Fabre and Galderma. Dr Becker is an investigator for Amgen; and is a speaker for Pfizer, Regeneron, and Sanofi. Dr Belloni-Fortina is a consultant for Sanofi, Janssen, Novartis, AbbVie, and Pfizer and received fees and honorarium. Dr Armesto is a speaker and an advisory board member for Amgen Inc, Janssen, LEO Pharma, and Novartis. Dr Elewski receives research support from AbbVie, Anaptys-Bio, Boehringer Ingelheim, Bristol Myers Squibb (BMS), Incyte, Leo, Lilly, Novartis, Pfizer, UCB, Ortho dermatology, Janssen; is a consultant for Amgen, Arcutis, Boehringer Ingelheim, BMS, Leo, Lilly, Novartis, UCB, Ortho dermatology, Janssen; and received honoraria from Amgen, Arcutis, Boehringer Ingelheim, BMS, Leo, Lilly, Novartis, UCB, Ortho dermatology, Janssen. Authors Maes, Oberoi, Paris, Zhang, and Z. Zhang are employees and stockholders at Amgen Inc. Dr Arkin received research equipment from Candela; is an investigator for Celgene and Amgen; and is a consultant for AbbVie, Amgen, Regeneron, and Verrica. Dr de Lucas has no conflicts of interest to declare.

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