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Efficacy and safety of apremilast in patients with mild-to-moderate plaque psoriasis: Results of a phase 3, multicenter, randomized, double-blind, placebo-controlled trial

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Background: Patients with mild-to-moderate psoriasis may have substantial quality-of-life impairment.

Objective: To evaluate apremilast 30 mg twice daily for mild-to-moderate psoriasis.

Methods: Phase 3, double-blind, placebo-controlled study in adults with mild-to-moderate psoriasis inadequately controlled or intolerant to ≥ 1 topical psoriasis therapy (NCT03721172). The primary endpoint was the achievement of static Physician Global Assessment score of 0 (clear) or 1 (almost clear) and ≥ 2-point reduction at week 16.

Results: Five hundred ninety-five patients were randomized (apremilast: 297; placebo: 298). The primary endpoint was met, with a significantly greater static Physician Global Assessment response rate observed at week 16 in the apremilast group compared with the placebo group (21.6% vs 4.1%; $P < .0001$). All secondary endpoints were met with the achievement of body surface area-75 (33.0% vs 7.4%), body surface area ≤ 3% (61.0% vs 22.9%), ≥ 4-point reduction in Whole Body Itch Numeric Rating Scale (43.2% vs 18.6%), Scalp Physician Global Assessment 0 or 1 and ≥ 2-point reduction (44.0% vs 16.6 %), and changes from baseline in body surface area, Psoriasis Area and Severity Index, and Dermatology Life Quality Index (all $P < .0001$). The most commonly reported adverse events (≥ 5%) with apremilast were diarrhea, headache, nausea, nasopharyngitis, and upper respiratory tract infection, consistent with prior studies.

Limitations: The study lacked an active-comparator arm.

Conclusion: Apremilast demonstrated efficacy in mild-to-moderate psoriasis and safety consistent with the established safety profile of apremilast. (J Am Acad Dermatol 2022;86:77-85.)

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INTRODUCTION

Quality-of-life (QOL) impairment may be substantial in patients with mild-to-moderate psoriasis, even though they have less overall skin involvement than patients with more-severe disease.[1] Psoriasis that affects special areas, such as the scalp or nails, is an example of relatively limited skin lesions associated with moderate-to-high disease burden.[2,3] Because of the limited body surface area involved, these patients may be classified as having mild or moderate disease. Symptoms such as itch also can be extremely bothersome and impactful for patients with all levels of disease severity.[1]

CAPSULE SUMMARY

- Patients with mild-to-moderate psoriasis report high quality-of-life impairment despite limited skin involvement.
- Apremilast demonstrated statistically significant, clinically meaningful efficacy as systemic treatment for mild-to-moderate plaque psoriasis and safety consistent with prior clinical trials.

Patients with mild-to-moderate psoriasis often receive only topical therapy.[1] Several classes of topical treatments are available, including topical corticosteroids, retinoids, vitamin D analogs, calcineurin inhibitors, dithranol, tar-based preparations, and combination treatments.[4,5] Topical treatments have demonstrated efficacy and tolerability for mild-to-moderate psoriasis[6-9] and are the initial treatment for patients with mild-to-moderate psoriasis.[10] However, for some patients, topical treatments may not achieve sufficient disease control or may be impractical to apply.[11]

Tolerability or safety issues may be associated with topical treatments. These include the potential immunosuppressive effects with corticosteroids; teratogenicity with retinoids; effects on calcium metabolism with vitamin D analogs; skin irritation and discoloration with dithranol; and staining and malodor with tar-based treatments.[5,12] These concerns may make topical treatments unsuitable for patients with mild-to-moderate psoriasis.

Timely use of systemic treatment may help treat patients who cannot tolerate topical therapies or have an inadequate response, thus avoiding significant QOL impairment. Systemic therapies are generally used for more-severe psoriasis in accordance with their labels; thus, there is a paucity of data on systemic therapies for milder psoriasis.

Apremilast, an oral phosphodiesterase 4 inhibitor, is indicated for patients with moderate-to-severe plaque psoriasis who are candidates for phototherapy or systemic therapy.[13] In phase 3 and 4 clinical trials, apremilast was efficacious for moderate-to-severe plaque psoriasis, including psoriasis in special areas such as the scalp.[14-18] The Apremilast as a Direct Treatment for Mild-to-Moderate Plaque Psoriasis Versus Placebo trial (ADVANCE; NCT03721172) is the first prospective, phase 3, multicenter, randomized, double-blind, placebo-controlled study of apremilast for mild-to-moderate psoriasis. The objective was to evaluate the efficacy and safety of apremilast 30 mg twice daily versus placebo in patients with mild-to-moderate psoriasis, based on static Physician Global Assessment (sPGA), psoriasis-involved body surface area (BSA), and Psoriasis Area and Severity Index (PASI) assessments.

METHODS

Study design

The ADVANCE study was conducted in the United States and Canada (Supplemental Fig 1; available via Mendeley at https://doi.org/10.17632/djj5s5nyxc.2). The study was registered on October 26, 2018 and the first patient was enrolled on March 19, 2019. Patients were randomized (1:1) to apremilast 30 mg twice daily or placebo for the first 16 weeks by permuted block randomization using centralized interactive response technology. Treatment assignment was stratified by baseline sPGA (mild [sPGA = 2]: approximately 30% of patients; moderate [sPGA = 3]: approximately 70% of patients).

The study drug was administered twice daily (approximately 12 hours apart) without food or drink restrictions and with titration over the first week to mitigate gastrointestinal side effects. All patients received apremilast 30 mg twice daily from weeks 16 to 32, followed by a 4-week post-treatment observational phase for patients who completed the study or discontinued early.

The study sponsor, persons responsible for ongoing study conduct, and patients were blinded to treatment allocation. The study was approved by the institutional review board/ethics committee before commencement and was conducted in compliance with Good Clinical Practice, International Council for Harmonisation Guideline E6, the Declaration of Helsinki, and regulatory

Abbreviations used:

ADVANCE:	Apremilast as a Direct Treatment for Mild-to-Moderate Plaque Psoriasis Versus Placebo: an Analysis of Clinical Safety and Efficacy
AE:	adverse event
BSA:	psoriasis-involved body surface area
BSA-75:	≥75% improvement in psoriasis-involved body surface area
CMH:	Cochran-Mantel-Haenszel
DLQI:	Dermatology Life Quality Index
ITT:	intent to treat
PASI:	Psoriasis Area and Severity Index
QOL:	quality of life
sPGA:	static Physician Global Assessment
ScPGA:	Scalp Physician Global Assessment
TEAE:	treatment-emergent adverse event
WBI-NRS:	Whole Body Itch Numeric Rating Scale

requirements. Patients provided written informed consent before study-related procedures. The protocol was amended twice to clarify inclusion criteria, study assessments, and procedures based on comments from regulatory authorities. No patients were enrolled before these amendments.

Patients

The ADVANCE study enrolled biologic-naive adults (≥ 18 years) with chronic plaque psoriasis for ≥ 6 months before screening. Eligible patients had mild-to-moderate plaque psoriasis (sPGA 2-3, BSA 2%-15%, and PASI 2-15) inadequately controlled with, or intolerant to, 1 or more topical therapies.

Patients with any condition that would present a risk to the patient or confound the ability to interpret study data were excluded. Patients with current or planned concurrent use of topical therapy within 2 weeks of randomization also were excluded, except for unmedicated skin moisturizers, which were permitted for body lesions, but not within 24 hours before the clinic visit. Other exclusion criteria included conventional systemic therapy or phototherapy within 4 weeks of randomization and the use of any investigational drug within 4 weeks before randomization or 5 pharmacokinetic/pharmacodynamic half-lives if known (whichever is longer).

Assessments

The primary efficacy endpoint was the proportion of patients achieving sPGA of 0 (clear) or 1 (almost clear) with a 2-point reduction or more from baseline at week 16. The sPGA is an investigator-rated assessment of overall disease severity, evaluated on a 5-point scale (0 [clear] to 4 [severe]), including an assessment of the severity of erythema, scaling, and plaque elevation.

The predefined secondary endpoints at week 16 were the achievement of ≥ 75% improvement in BSA (BSA-75); change from baseline in BSA; change from baseline in PASI; achievement of BSA ≤ 3% (baseline BSA > 3%); Whole Body Itch Numeric Rating Scale (WBI-NRS) response (≥ 4-point reduction from baseline; baseline score ≥ 4); achievement of Scalp PGA (ScPGA) of 0 (clear) or 1 (almost clear) with a 2-point or greater reduction from baseline (baseline ScPGA ≥ 2); and a change from baseline in Dermatology Life Quality Index (DLQI) total score. The proportion of patients achieving BSA ≤ 1% was a predefined exploratory endpoint. Post hoc analyses evaluated proportions of patients at week 16 who achieved a DLQI total score ≤ 5, a DLQI total score of 0 or 1, and a ≥ 5-point reduction in DLQI total score (baseline score > 5).

Safety was evaluated throughout the study, including adverse events (AEs), discontinuations due to AEs, and clinically significant changes in physical examinations, vital signs, or laboratory findings. Adverse events were recorded from the time of informed consent to 28 days after the last dose; thereafter, reported serious AEs with a suspected relationship to the study drug were recorded.

Statistical analysis

Sample size was calculated by assuming a 15% response rate for placebo and a 20% dropout rate. With approximately 574 patients randomized 1:1, the study would randomize approximately 287 patients to apremilast and approximately 287 to placebo. This provided > 90% power to detect a 15% between-group difference for the primary endpoint (2-sided 0.05 significance level).

Efficacy analyses were conducted in the intent-to-treat (ITT) population (all randomized patients). The safety population comprised all randomized patients who received 1 or more doses of the study drug. Primary and secondary endpoints analyzed at week 16 were hierarchically ranked for testing to control the overall type 1 error rate at the 2-sided 0.05 significance level. The following sequence was used: achievement of sPGA 0 (clear) or 1 (almost clear) with a ≥ 2-point reduction from baseline, achievement of BSA-75, change from baseline in BSA, change from baseline in PASI, achievement of BSA ≤ 3% (baseline BSA > 3%), achievement of ≥ 4-point reduction (improvement) from baseline in WBI-NRS (baseline score ≥ 4), achievement of ScPGA of 0 or 1 with ≥ 2-point reduction from baseline (baseline score ≥ 2), and change from baseline in DLQI total score.

Primary and categorical secondary endpoints were analyzed using the Cochran-Mantel-Haenszel (CMH) test, adjusting for stratification factor at randomization (missing values were imputed using the multiple imputation method). Continuous variables were analyzed using a mixed model for repeated measures, with change from baseline as the response variable. Treatment group, visit time, treatment-by-time interaction, and stratification factor were included as fixed effects, with baseline value as a covariate. Post hoc analyses of DLQI responses were analyzed with CMH tests using nonresponder imputation for missing data.

RESULTS

Patients and baseline characteristics

Patients were recruited between March 19 and November 18, 2019. Five hundred ninety-five patients were randomized and analyzed in the ITT population (apremilast, n = 297; placebo, n = 298). A total of 504 patients completed the double-blind phase (apremilast, n = 258; placebo, n = 246). The safety analysis included 594 patients who received 1 or more doses of the study drug (apremilast, n = 298; placebo, n = 296).

Primary reasons for discontinuation of apremilast versus placebo were withdrawal by patient (6.1% vs 7.7%), lost to follow-up (4.4% vs 5.0%), AEs (2.4% vs 2.3%), lack of efficacy (0% vs 1.3%), noncompliance with study drug (0.3% vs 0%), and other (0% vs 1.0%) (Supplemental Fig 2).

Demographics and baseline characteristics were generally similar between groups (Table I). Mean age was 49.2 years in the apremilast group and 48.3 years in the placebo group. Almost half of the patients were women (apremilast: 41.4%; placebo: 49.3%). In the apremilast and placebo groups, mean WBI-NRS scores were 6.1 and 6.3, respectively. Most patients had ScPGA ≥ 2 (71.4% and 66.8%).

Table I. Baseline demographics and disease characteristics

Parameter	Placebo n = 298	Apremilast n = 297	Total N = 595
Age in years, mean (SD)	48.3 (14.5)	49.2 (14.7)	48.7 (14.6)
Female, n (%)	147 (49.3)	123 (41.4)	270 (45.4)
Body mass index, mean (SD), kg/m^2	30.9 (7.0)	31.2 (7.2)	31.1 (7.1)
Duration of plaque psoriasis in years, mean (SD)	16.9 (13.9)	16.9 (14.3)	16.9 (14.1)
sPGA score, n (%)			
2 (Mild)	91 (30.5)	91 (30.6)	182 (30.6)
3 (Moderate)	207 (69.5)	206 (69.4)	413 (69.4)
BSA percentage, mean (SD)	6.3 (3.3)	6.4 (3.6)	6.4 (3.4)
PASI score, mean (SD)	6.5 (2.9)	6.4 (2.9)	6.5 (2.9)
Whole Body Itch NRS score, mean (SD)	6.3 (2.6)	6.1 (2.4)	6.2 (2.5)
Scalp involvement (ScPGA score ≥ 2), n (%)	199 (66.8)	212 (71.4)	411 (69.1)
DLQI total score, mean (SD)	9.8 (5.9)	9.9 (5.8)	9.9 (5.9)
Prior treatment, n (%)*			
≥1 conventional systemic treatment	30 (10.1)	35 (11.8)	65 (10.9)
≥1 biologic treatment†	0 (0)	1 (0.3)	1 (0.2)

BSA, Psoriasis-involved body surface area; *DLQI*, Dermatology Life Quality Index; *N*, total randomized patients; *n*, patients in each group; *NRS*, numeric rating scale; *PASI*, Psoriasis Area and Severity Index; *ScPGA*, Scalp Physician Global Assessment; *sPGA*, static Physician Global Assessment.

*Per the study inclusion criteria, all patients had received ≥1 topical therapy.

†One patient with prior biologic treatment was enrolled in the study despite not meeting the eligibility criteria. This was a protocol deviation.

Efficacy endpoints

The primary endpoint was met, with statistically significantly greater and clinically meaningful achievement of sPGA scores of 0 (clear) or 1 (almost clear) and ≥ 2-point reduction from baseline with apremilast compared with placebo at week 16 (21.6% vs 4.1%, $P < .0001$). Compared with placebo, the sPGA response rate for apremilast was statistically significantly greater as early as week 2 ($P < .05$, week 2; $P < .0001$, weeks 4 to 16; Fig 1).

Apremilast demonstrated statistically significant and clinically meaningful improvements compared with placebo on all secondary endpoints at week 16 ($P < .0001$). Achievement of BSA-75 response (33.0% vs 7.4%) and BSA ≤ 3% (61.0% vs 22.9%) was significantly greater with apremilast compared with placebo ($P < .0001$ for both; Fig 2). Statistically significantly greater least-squares mean changes from baseline were observed with apremilast compared with placebo for BSA (−3.45% vs −0.07%) and PASI (−3.47 vs −0.54) ($P < .0001$, both). Achievement of BSA ≤ 1% at week 16 was 31.7% in the apremilast group and 7.2% in the placebo group (nominal $P < .0001$). Achievement of ScPGA response was greater with apremilast compared with placebo (44.0% vs 16.6%, $P < .0001$; Fig 2).

Apremilast showed greater achievement of WBI-NRS response compared with placebo at week 16

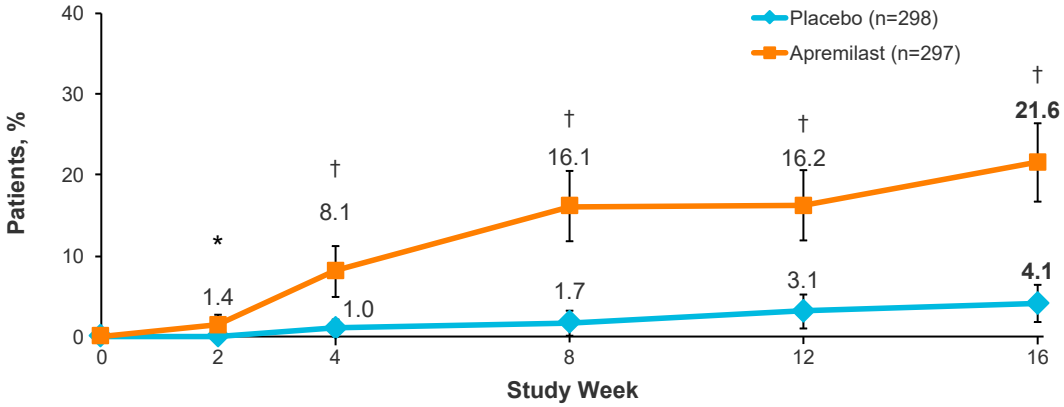


Fig 1. Proportion of patients achieving sPGA response (score of 0 or 1 with ≥ 2-point improvement) over 16 weeks (intent-to-treat population; multiple imputation analysis). The intent-to-treat population includes all randomized patients. Error bars represent 95% confidence interval. *sPGA*, Static Physician Global Assessment. *$P < .05$; †$P < .0001$ versus placebo based on Cochrane-Mantele-Haenszel test (multiple imputation).

(43.2% vs 18.6%, $P < .0001$). Least-squares mean improvement from baseline in DLQI total score was significantly greater with apremilast compared with placebo at week 16 (−5.2 vs −2.4, $P < .0001$). Significantly greater improvement in DLQI score was observed with apremilast compared with placebo as early as week 2 (Fig 3). Greater proportions of patients achieved clinically meaningful DLQI responses with apremilast compared with placebo at week 16, including mean change from baseline exceeding the minimal clinically important difference (minimal clinically important difference, ≥ 4-point reduction from baseline) for DLQI total score,[19] achievement of DLQI score ≤ 5 (56.3% vs 31.5%, nominal $P < .0001$), DLQI score of 0 or 1 (22.3% vs 5.5%, nominal $P < .0001$), and ≥ 5-point DLQI reduction (60.7% vs 33.8%, nominal $P < .0001$).

Safety

During the placebo-controlled period, 195 (65.4%) of 298 patients in the apremilast group and 139 (47.0%) of 296 in the placebo group experienced 1 or more treatment-emergent AEs (TEAEs; Table II). Few patients reported severe TEAEs (apremilast: 8 of 298 [2.7%]; placebo: 2 of 296 [0.7%]; Table II). The most common TEAEs (≥ 5%, either group) with apremilast compared with placebo were diarrhea (49 of 298 [16.4%] vs 15 of 296 [5.1%]), headache (39 of 298 [13.1%] vs 15 of 296 [5.1%]), nausea (38 of 298 [12.8%] vs 13 of 296 [4.4%]), nasopharyngitis (22 of 298 [7.4%] vs 8 of 296 [2.7%]), and upper respiratory tract infection (17 of 298 [5.7%] vs 15 of 296 [5.1%]) (Table II). Most TEAEs were mild-to-moderate. Onset of diarrhea, nausea, headache/tension headache, and vomiting typically occurred within the first month of treatment (Supplemental Table I).

In the apremilast group, 1 of 298 (0.3%) patients had serious TEAEs of angina pectoris and myocardial ischemia. In the placebo group, serious TEAEs occurred in 4 of 296 (1.4%) patients (congestive heart failure and pneumonia [n = 1], pneumococcal pneumonia [n = 1], migraine without aura [n = 1], and ectopic pregnancy [n = 1]). The patient with the TEAEs of angina pectoris and myocardial ischemia had a prior history of hypertension and hypothyroidism and a BMI of 29.9 kg/m^2, bordering on obesity. No serious TEAEs of depression or suicidal behavior were reported during the placebo-controlled period. Few TEAEs led to withdrawal of the study drug (apremilast: 13 of 298 [4.4%]; placebo: 7 of 296 [2.4%]; Table II). No clinically significant changes in physical examinations, vital signs, or laboratory parameters were noted.

DISCUSSION

In this first phase 3 study of the efficacy and safety of apremilast in patients with mild-to-moderate plaque psoriasis, apremilast demonstrated clinically meaningful and statistically significant improvements compared with placebo in overall psoriasis severity, scalp psoriasis, and whole body itch. The safety profile of apremilast in patients with mild-to-moderate psoriasis was consistent with prior clinical trials in moderate-to-severe psoriasis.[14-17]

Unlike prior apremilast studies, the ADVANCE study evaluated patients with mild-to-moderate psoriasis who are commonly seen in clinical practice. In these patients, apremilast treatment was associated with significantly greater achievement of sPGA,

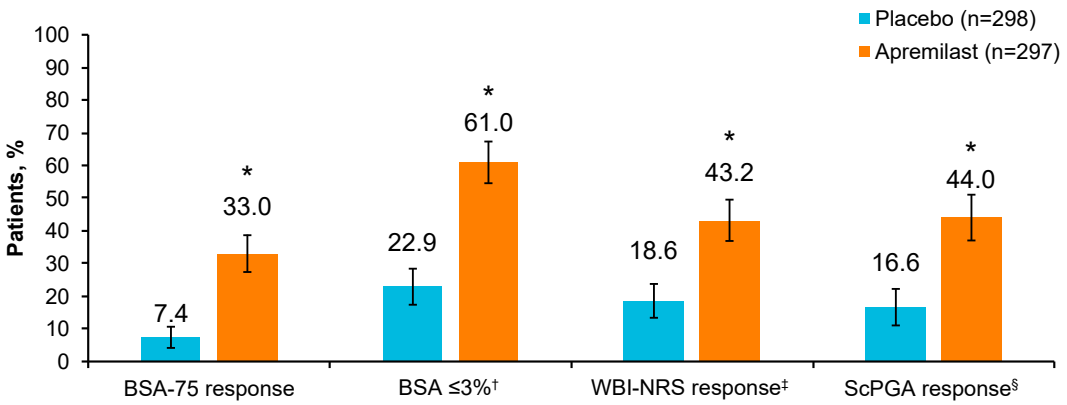
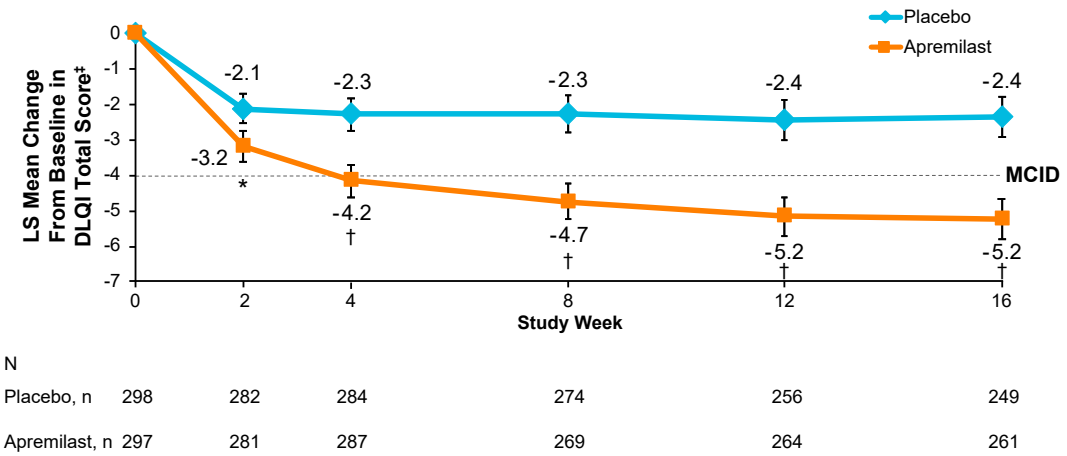


Fig 2. Proportions of patients achieving BSA-75, BSA ≤ 3%, WBI-NRS, and ScPGA responses at week 16 (intent-to-treat population; multiple imputation analysis). Categorical endpoints analyzed by Cochran-Mantel-Haenszel test (multiple imputation); continuous endpoints analyzed by mixed model for repeated measures. The intent-to-treat population represents all randomized patients. Error bars represent 95% confidence interval. *BSA*, Psoriasis-involved body surface area; *BSA-75*, ≥ 75% reduction from baseline in BSA; *ScPGA*, Scalp Physician Global Assessment; *WBI-NRS*, Whole Body Itch Numeric Rating Scale. **P* < .0001 versus placebo for all secondary endpoints; †In patients with BSA > 3% at baseline; ‡In patients with WBI-NRS ≥ 4 at baseline; §In patients with ScPGA ≥ 2 at baseline.



N						
Placebo, n	298	282	284	274	256	249
Apremilast, n	297	281	287	269	264	261

Fig 3. Least-squares mean change from baseline in DLQI total score over 16 weeks (intent-to-treat population, mixed model for repeated measures). The intent-to-treat population represents all randomized patients. A ≥ 4-point improvement from baseline is considered to be the MCID for DLQI improvement.[19] Error bars represent 95% confidence interval. *DLQI*, Dermatology Life Quality Index; *LS*, least squares; *MCID*, minimal clinically important difference. **P* < .001; †*P* < .0001 versus placebo based on mixed model for repeated measures analysis; ‡Data as observed for mean change from baseline in DLQI total score over time.

BSA-75, ScPGA, and WBI-NRS responses and greater achievement of treatment targets based on National Psoriasis Foundation recommendations (ie, BSA ≤ 3% and BSA ≤ 1%)[20] compared with placebo. Improvements in QOL outcomes were observed, including greater achievement of DLQI minimal clinically important difference[19] and DLQI total score ≤ 5 with apremilast compared with placebo at week 16. Greater proportions of patients achieved minimal to no impact of psoriasis on QOL with apremilast compared with placebo at week 16.

Assessments of skin involvement, such as PASI, may not adequately assess disease severity or improvement in patients with mild psoriasis and can be difficult to use in clinical practice.[21] Although patients in the ADVANCE study had mild-to-moderate psoriasis based on baseline sPGA, mean BSA (apremilast: 6.4%; placebo: 6.3%), and mean

Table II. Overview of TEAEs during the placebo-controlled phase in the safety population

Patients, n (%)	Placebo n = 296	Apremilast n = 298
Overview of TEAEs		
Any TEAE	139 (47.0)	195 (65.4)
Any severe TEAEs*	2 (0.7)	8 (2.7)
Any serious TEAEs†	4 (1.4)	1 (0.3)
Any TEAEs leading to drug withdrawal‡	7 (2.4)	13 (4.4)
Any TEAEs leading to death	0 (0)	0 (0)
Most commonly reported (≥ 5% in any group) TEAEs		
Diarrhea	15 (5.1)	49 (16.4)
Headache	15 (5.1)	39 (13.1)
Nausea	13 (4.4)	38 (12.8)
Nasopharyngitis	8 (2.7)	22 (7.4)
Upper respiratory tract infection	15 (5.1)	17 (5.7)

TEAE, Treatment-emergent adverse event.

*TEAE severity was determined based on the investigator's judgment, and severe TEAEs included symptoms that caused severe discomfort or pain; symptoms that required medical or surgical attention or intervention; interference with activities of daily living; or AEs requiring drug therapy.

†Serious TEAEs were determined based on standardized definitions and included AEs that resulted in death; were life-threatening (i.e., in the opinion of the investigator, the patient is at immediate risk for death from the AE); required inpatient hospitalization or prolongation of existing hospitalization (hospitalization is defined as an inpatient admission, regardless of length of stay); resulted in persistent or significant disability/incapacity (a substantial disruption of the patient's ability to conduct normal life functions); were congenital anomalies/birth defects; or constituted an important medical event.

‡This table presents the number of patients who had any TEAEs leading to drug withdrawal. Some of these patients discontinued the study mainly due to the AEs, and these patients are reflected in the patient disposition figure (Supplemental Fig 2) as discontinuations due to AEs. However, some patients decided to withdraw themselves from the study when a mild AE was reported or after AEs that were quickly resolved. Based on the investigator's judgment, the main reason for study discontinuation in those cases was noted as either withdrawal by patient or lost to follow-up. The safety population is defined as all randomized patients who received ≥1 dose of study drug. TEAEs leading to drug withdrawal in the apremilast group were abdominal pain, Crohn's disease, depression, eczema, diarrhea, fatigue, gastritis, gastroenteritis, headache, myalgia, myocardial ischemia, nausea, suicidal ideation, and vomiting. TEAEs leading to drug withdrawal in the placebo group were abdominal pain, cough, diarrhea, ectopic pregnancy, face edema, headache, nausea, pharyngeal edema, pruritus, and psoriasis.

PASI (apremilast: 6.4; placebo: 6.5), rates of scalp involvement (apremilast: 71.4%; placebo: 66.8%), and mean DLQI scores (apremilast: 9.9; placebo: 9.8) reflected substantial disease burden.

Nonetheless, baseline skin severity, scalp involvement (ScPGA ≥ 2), and mean DLQI scores were lower among patients in the ADVANCE study compared with patients with moderate-to-severe psoriasis in the ESTEEM 1 and 2 phase 3 pivotal trials and patients with moderate psoriasis in the UNVEIL trial.[14,15,17] Overall, the ADVANCE population was notably different from the pivotal ESTEEM trials, as mean BSA and PASI were at least 3 times higher in ESTEEM 1 and 2 versus ADVANCE,[14,15] and psoriasis duration and prior use of conventional systemic treatments at baseline were lower in ADVANCE versus ESTEEM 1 and 2.[14,15] Despite these differences, efficacy findings in ADVANCE were generally consistent with those of ESTEEM 1 and 2.[14,15] Safety findings in ADVANCE were consistent with the known safety profile of apremilast.[14,15] The current study demonstrates that apremilast represents an effective systemic treatment option for patients with mild-to-moderate psoriasis.

Topical treatments are commonly used to treat mild-to-moderate psoriasis and have demonstrated efficacy and tolerability in randomized clinical trials.[6,7] However, guidelines suggest that systemic treatment should be considered for patients with mild-to-moderate skin involvement who experience high disease burden or inadequate disease control with topical therapies, including patients with psoriasis in special areas.

One limitation of this study is the lack of an active-comparator arm. This restricts the ability to make direct comparisons with other systemic treatments. The homogeneity of the study population limits its generalizability to patients in the clinical setting. These data should be complemented by real-world data.

CONCLUSION

Apremilast significantly and clinically meaningfully reduced overall psoriasis severity and improved scalp psoriasis, whole body itch, and QOL in patients with mild-to-moderate plaque psoriasis. No new safety findings were observed.[14,15]

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Conflicts of interest

Dr Gold received honoraria, grants, and/or research funding as a speaker, investigator, and/or advisory board member for AbbVie, Amgen Inc, Arcutis, Celgene Corporation, Dermira, Dermavant, Eli Lilly, Galderma, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, UCB, and Valeant. Dr Papp was a steering

committee member for PSLOAR and PURE and received honoraria, grants, and/or research funding as a speaker, investigator, advisory board member, data safety monitoring board member, and/or consultant for AbbVie, Actelion, Amgen Inc, Astellas Pharma US, Boehringer Ingelheim, Bausch Health, Celgene Corporation, Dermira, Dow Pharmaceuticals, Eli Lilly, Frontier, Galderma, Janssen, Kyowa Hakko Kirin Pharma, LEO Pharma, MedImmune, Merck & Co, Inc, Novartis, Pfizer, Regeneron, Roche Laboratories, Sanofi Genzyme, Takeda Pharmaceuticals, UCB, and Valeant. Dr Pariser received honoraria or was an investigator, advisory board member, or data monitoring board member for Amgen Inc, AO Biome, Asana, Brickel Biotech, Celgene Corporation, Dermavant, Dermira, Eli Lilly, Menlo Therapeutics, Merck, Novartis, Ortho, Regeneron, Atacama, Biofrontera, Bristol Myers Squibb, LEO Pharma, Pfizer, Sanofi, and Valeant. Dr Green was an investigator, speaker, and/or consultant for AbbVie, Amgen Inc, Arcutis, Dermavant, MC2, Novartis, Lilly, OrthoDerm, SunPharma, and UCB. Dr Bhatia was an advisor, consultant, investigator, and/or speaker for AbbVie, Actavis, Allergan, Amgen Inc, Aqua, Bayer, Biofrontera, BiopharmX, Castle, Cipher, Dermira, Encore, Exeltis, Ferndale, Foamix, Galderma, Intraderm, ISDIN, LaRoche-Posay, LEO Pharma, Novan, Novartis, PharmaDerm, Pfizer, Promius, Regeneron, Sanofi, Sun Pharma, and Valeant. Dr Sofen received honoraria, grants, and/or research funding as an investigator and/or advisory board member for AbbVie, Amgen Inc, Celgene Corporation, Dermira, Dermavant, Eli Lilly, Galderma, LEO Pharma, Novartis, Pfizer, and UCB. Dr Albrecht received honoraria, grants, and/or research funding as a speaker, investigator, advisory board member, and/or consultant for AbbVie, Amgen Inc, Arcutis, Boehringer Ingelheim, Bausch Health/Valeant, Celgene Corporation, Dermira, Dermavant, Eli Lilly, Galderma, Janssen, LEO Pharma, MedImmune, Merck & Co, Novartis, Pfizer, Regeneron, Roche Laboratories, Sanofi Genzyme, and UCB. Dr Gooderham received honoraria, grants, and/or research funding as a speaker, investigator, advisory board member, data safety monitoring board member, and/or consultant for AbbVie, Amgen Inc, Akros, Arcutis, Bausch/Valeant, Boehringer Ingelheim, Celgene Corporation, Dermira, Dermavant, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin Pharma, LEO Pharma, MedImmune, Merck & Co, Novartis, Pfizer, Regeneron, Roche Laboratories, Sanofi Genzyme, Takeda Pharmaceuticals USA Inc, and UCB. Author Chen and Dr Paris are employees of Amgen Inc. Dr Wang was employed by Amgen Inc at time of the study. Dr Callis Duffin received honoraria, grants, and/or research funding as an investigator, advisory board member, consultant, and/or non-promotional speaker for AbbVie, Amgen Inc, Boehringer Ingelheim, Celgene Corporation, Eli Lilly, Janssen, Novartis, Pfizer, Regeneron, and UCB.

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