

Efficacy and Safety of Apremilast in Patients With Moderate Plaque Psoriasis With Lower BSA: Week 16 Results from the UNVEIL Study

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ABSTRACT

Introduction: Many options are available for patients with moderate to severe plaque psoriasis. Patients with moderate disease, however, are often undertreated and do not achieve satisfactory clearance. UNVEIL (NCT02425826) assessed efficacy and safety of apremilast in patients with chronic moderate plaque psoriasis.

Methods: Patients with psoriasis body surface area (BSA) 5% to 10% and static Physician's Global Assessment (sPGA) score of 3 (moderate) without prior exposure to systemics were randomized (2:1) to apremilast 30 mg twice daily or placebo for 16 weeks. The primary efficacy endpoint was mean percentage change in the product of sPGA and BSA scores (PGAxBSA).

Results: Of 221 patients (placebo, n=73; apremilast, n=148), >80% had received prior topical therapy. At week 16, apremilast yielded a significantly greater percentage change from baseline in PGAxBSA (–48.1%) vs placebo (–10.2^; *P*<0.0001). Dermatology Life Quality Index scores were significantly improved with apremilast (–4.8) vs placebo (–2.4; *P*=0.0008). Mean improvements in the Treatment Satisfaction Questionnaire for Medication, version II, were greater with apremilast vs placebo for global satisfaction (63.2 vs 48.7; *P*<0.0001) and treatment effectiveness (57.3 vs 38.8; *P*<0.0001). Most adverse events were mild or moderate; most common were diarrhea, headache, nausea, upper respiratory tract infection, decreased appetite, and vomiting.

Conclusion: Apremilast was effective and well tolerated, significantly improved quality of life, and was associated with high patient satisfaction in systemic-naive, post-topical patients with moderate plaque psoriasis.

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INTRODUCTION

Treatment of moderate to severe plaque psoriasis has improved substantially with the introduction of treatments that have demonstrated the ability to reduce disease severity and improve quality of life (QOL).[1,2] Despite these advances, management of moderate psoriasis (≥3% to <10% body surface area [BSA] involvement)[3] remains a significant challenge. Patients with moderate psoriasis often do not achieve satisfactory skin clearance with conventional systemic therapy due to undertreatment and/or toxicity concerns.[4-6] In the Multinational Assessment of Psoriasis and Psoriatic Arthritis (MAPP) survey of patient and physician perceptions of satisfaction with current psoriasis therapies, >80% of psoriasis patients with 4 to 10 handprints BSA involvement reported receiving no treatment or topical treatment only.[6] Of psoriasis patients receiving conventional oral medication (cyclosporine, methotrexate, acitretin, fumaric acid esters), 57% reported discontinuing therapy, most often for safety or tolerability reasons and lack/loss of efficacy.[6] Although newer biologics can provide substantially higher clearance rates, their use in more moderate disease has not been studied, and high cost without evidence of clear benefit in this population might be a limiting factor.[7] Clinical studies of biologics typically require patients to have BSA involvement ≥10%, a population that is very different from patients with more moderate disease.[8,9]

Apremilast, an oral, small-molecule phosphodiesterase 4 inhibitor, works intracellularly to regulate inflammatory mediators, including

pathways relevant to the pathogenesis of psoriasis.[10] In the phase III Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis (ESTEEM)[11,12] program, apremilast was effective and demonstrated acceptable tolerability in patients with moderate to severe plaque psoriasis. Patients in the ESTEEM studies were required to have ≥10% BSA involvement and static Physician's Global Assessment (sPGA) score ≥3, and were allowed to have received previous systemic therapy, including biologics.

The current phase IV multicenter, randomized, placebo-controlled, double-blind study (Evaluating Apremilast in a Phase IV Trial of Efficacy and Safety in Patients With Moderate Plaque Psoriasis [UNVEIL]; NCT02425826) was conducted to assess efficacy and safety of apremilast in patients with moderate plaque psoriasis (5% to 10% BSA involvement and sPGA score of 3 [moderate] on a 6-point scale) who were naive to systemic and biologic therapy. UNVEIL is the first randomized, placebo-controlled study to prospectively evaluate the efficacy of a systemic oral therapy exclusively in patients with moderate psoriasis (5% to 10% BSA) using the sPGA and BSA involvement (PGAxBSA) tool. The PGAxBSA tool is a simple alternative for assessing response to therapy that may overcome some limitations of the Psoriasis Area and Severity Index (PASI) with respect to detecting change in disease severity in patients with more moderate disease.[13,14] A post hoc analysis of ESTEEM 1 and 2 demonstrated that PGAxBSA is sensitive to therapeutic response with apremilast.[15]

We report efficacy and safety of apremilast 30 mg twice daily vs placebo through week 16 in patients with moderate plaque psoriasis (5% to 10% BSA) utilizing the PGAxBSA tool.

METHODS

Patients

Patients were adults ≥18 years of age with a diagnosis of chronic plaque psoriasis for ≥6 months and moderate plaque psoriasis, defined by BSA involvement of 5% to 10% and sPGA score of exactly 3 (moderate) based on a 6-point scale (0 [clear] to 5 [very severe]). Patients had no prior exposure to conventional systemics or biologics for treatment of psoriatic arthritis, psoriasis, or any other indication that could affect assessment of psoriasis. Patients with inflammatory or dermatologic conditions which could confound the ability to interpret study data, including forms of psoriasis other than plaque psoriasis (eg, erythrodermic, guttate inverse, pustular) were excluded.

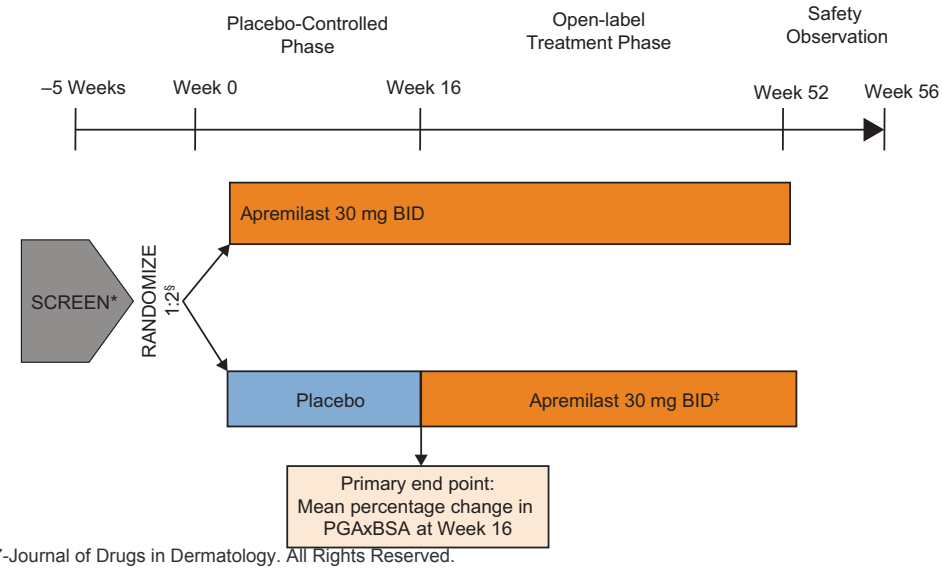
Study Design and Treatment Regimen

Eligible patients were randomized, using a centralized interactive voice response system, to receive apremilast or placebo (2:1) during weeks 0 to 16 (Figure 1). At week 16, placebo patients were switched to apremilast. All patients continued on apremilast through week 52. The institutional review boards of participating medical centers approved the protocol. Patients provided written informed consent before the conduct of study-related procedures.

Efficacy Assessments

The primary efficacy end point was the mean percentage change from baseline in PGAxBSA, which represents the product of sPGA and BSA scores, at week 16. Overall BSA affected by psoriasis is estimated based on the patient's handprint area (entire palmar surface, including fingers), which equates to

FIGURE 1. UNVEIL study design.
*Screening up to 35 days before randomization.
§All doses were titrated over the first week of treatment.
‡At week 16, all placebo patients were switched to open-label apremilast 30 mg BID (with dose titration) through week 52.
BID=twice daily.



approximately 1% of total BSA. For the 6-point sPGA, clinicians score the severity of each of the 3 primary signs of plaques of all involved areas: erythema, scaling, and plaque elevation.[13] Scores for each assessment are averaged and rounded to the nearest whole number for the final sPGA score. Based on eligibility criteria, baseline PGAxBSA values could range from 15 to 30.

Other efficacy end points at week 16 included mean change from baseline in Dermatology Life Quality Index (DLQI) total score; percentage of patients achieving sPGA score of 0 (clear) or 1 (almost clear); percentage of patients achieving score of 0 (clear) or 1 (very mild) on the Patient's Global Assessment (PtGA) scale (0 [clear] to 4 [severe]); mean change from baseline in pruritus visual analog scale (VAS) score; percentage of patients achieving Scalp Physician's Global Assessment (ScPGA) score of 0 (clear) or 1 (minimal) with a ≥2-point reduction from baseline in patients with ScPGA ≥1 at baseline; mean percentage change from baseline in PASI score; percentage of patients achieving ≥75% reduction from baseline in PASI score (PASI-75); percentage of patients achieving an absolute PASI score ≤3; mean percentage change from baseline in Nail Psoriasis Severity Index (NAPSI) score; and percentage of patients with nail psoriasis at baseline who achieved ≥50% reduction from baseline in NAPSI score (NAPSI-50) in the target nail. Patient satisfaction was assessed using the 11-item, patient-completed Treatment Satisfaction Questionnaire for Medication (TSQM), version II.[16]

Safety Assessments

Safety assessments were conducted at screening and weeks 0, 1, 4, 12, and 16 during the placebo-controlled period. Safety was evaluated based on vital signs, weight, waist circumference, adverse events (AEs), clinical laboratory assessments, and complete physical examinations. To better characterize diarrhea, patients reporting diarrhea or similar events (eg, frequent bowel movements, loose bowels) were asked whether they had experienced ≥2 watery/liquid stools in a day. Patients who responded "yes" were asked how often, on average, since their last visit had they experienced ≥2 watery/liquid stools in a day. Patients who responded "no" were not questioned further.

Statistical Analysis

Efficacy assessments were conducted for the intent-to-treat (ITT) population, which included all randomized patients. Approximately 219 patients were planned to be randomized to yield ≥85% power to detect a 15% difference between apremilast and placebo in mean percentage change from baseline in PGAxBSA.

For analysis of the primary end point and other continuous variables at week 16, an analysis of covariance model with treatment and site as a factor and baseline value as a covariate was used. The sPGA 0 or 1 response rates and other categorical variables at week 16 were compared using the Cochran-Mantel-Haenszel test. Last-observation-carried-forward methodology was used to impute missing efficacy measurements. The safety population included all patients who were randomized and received ≥1 dose of study drug. AEs were summarized using descriptive statistics. Statistical analyses were conducted using SAS version 9.2 (SAS Institute Inc, Cary, NC).

RESULTS

Disposition and Baseline Characteristics

A total of 221 patients were randomized and comprised the ITT population (placebo, n=73; apremilast, n=148); 185 (84%) completed the placebo-controlled phase (weeks 0 to 16;

FIGURE 2. Patient disposition. One patient was randomized in error, discontinued prior to receiving any study treatment, and is included in "Other" (placebo).
BID=twice daily.

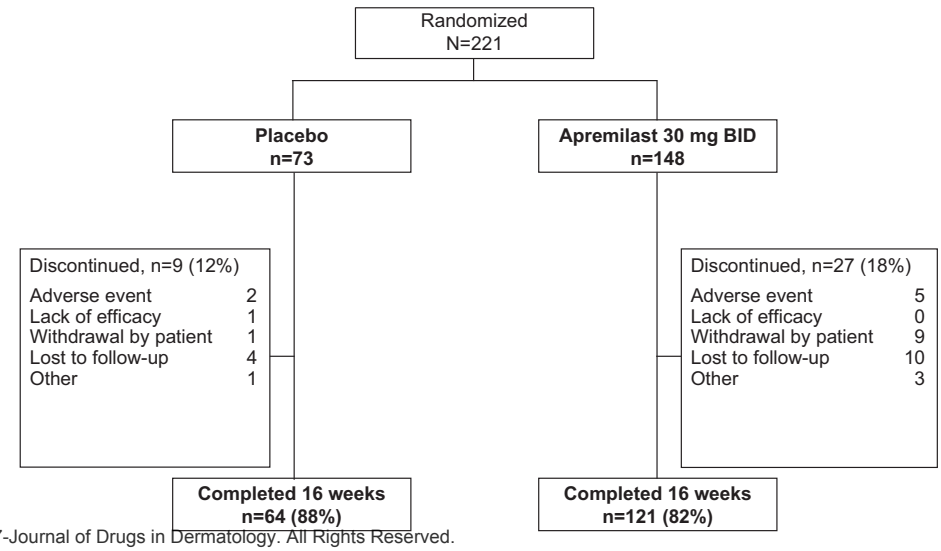


Figure 2). Patient demographics and baseline disease characteristics were comparable between groups (Table 1). At baseline, mean psoriasis duration was 13.9 and 17.5 years in the placebo and apremilast groups, respectively. At baseline, mean BSA was 7.2%, mean PGAxBSA score was 21.8, mean pruritus VAS score was 56.6 mm, and mean DLQI score was 11.0; most patients (82%) reported prior treatment with topical therapy (Table 1). In addition, 76% of patients (n=167) had scalp disease (ScPGA ≥1) at baseline.

Efficacy Assessments

At week 16, the mean percentage change from baseline in PGAxBSA score (primary end point) was significantly greater with apremilast vs placebo (–48.1% vs –10.2%; *P*<0.0001) (Figure 3A; Table 2). At week 16, achievement of ≥75% reduction from baseline in PGAxBSA score (PGAxBSA-75) was significantly greater among patients receiving apremilast (35.1%) vs placebo (12.3%; *P*<0.0001) (Figure 3B; Table 2). An sPGA score of 0 (clear) or 1 (almost clear) at week 16 was achieved by significantly more patients receiving apremilast (30.4%) vs placebo (9.6%; *P*<0.0001) (Table 2); likewise, the proportion of patients achieving a PtGA score of 0 (clear) or 1 (very mild) at week 16 was significantly greater with apremilast (33.8%) vs placebo (20.5%; *P*=0.0365) (Table 2). Figure 3C shows a patient who achieved PGAxBSA-75 at week 16 while receiving apremilast.

Mean percentage change from baseline in PASI score was significantly greater with apremilast (–40.72%) vs placebo (–3.87%; *P*<0.0001) at week 16. PASI-75 response was significantly greater among patients receiving apremilast (21.6%) vs placebo (8.2%; *P*=0.0136). Mean absolute change from baseline in PASI was –3.7 with apremilast vs 0.6 with placebo. Proportions of patients who achieved absolute PASI score ≤3 were 41.22% with apremilast vs 20.55% with placebo.

Other Efficacy End Points

Improvements were observed with apremilast vs placebo at week 16 in pruritus and scalp and nail disease (Table 2). Figure 4 illustrates improvement in scalp psoriasis typically seen at week 16 in a patient receiving apremilast.

Quality of Life Assessments

DLQI scores were significantly improved from baseline at week 16 in patients receiving apremilast (–4.8) vs placebo (–2.4; *P*=0.0008; Table 2); achievement of DLQI response (minimal clinically important difference [MCID], defined as decrease from baseline ≥5 points) was also significantly greater among patients with a DLQI score >5 at baseline receiving apremilast vs placebo (63.8% vs 34.5%; *P*=0.0009; Table 2). TSQM satisfaction scores at week 16 were significantly greater for patients receiving apremilast vs placebo in the Effectiveness and Global Satisfaction domains; no differences in TSQM scores were detected between groups in Convenience and Side Effects domains (Figure 5).

TABLE 1.

Baseline Demographics and Disease Characteristics

	Placebo n=73	Apremilast 30 mg BID n=148
Age, mean (SD), years	51.1 (13.7)	48.6 (15.4)
Male, n (%)	41 (56.2)	74 (50.0)
BMI, mean (SD), kg/m^2	30.8 (6.5)	30.5 (7.4)
Weight, mean (SD), kg	89.6 (19.1)	87.5 (21.1)
Duration of plaque psoriasis, mean (SD), years	13.9 (12.6)	17.5 (13.9)
PGAxBSA score, mean (SD)	21.6 (5.9)	21.8 (5.3)
Body surface area, mean (SD), %	7.1 (1.8)	7.2 (1.6)
PASI score, mean (SD)	8.0 (3.2)	8.2 (4.0)
PASI score ≥10, n (%)	15 (20.5)	34 (23.0)
DLQI total score, mean (SD)	11.1 (6.5)	11.0 (6.5)
Pruritus VAS score, mean (SD), mm	60.0 (22.5)	55.0 (24.3)
ScPGA score ≥1, n (%)	55 (75.3)	112 (75.7)
NAPSI score in target nail, mean (SD)	4.6 (2.1)	3.7 (2.0)
NAPSI score in target nail ≥1, n (%)	27 (37.0)	56 (37.8)
Prior topical therapy for psoriasis, n (%)	59 (80.8)	122 (82.4)

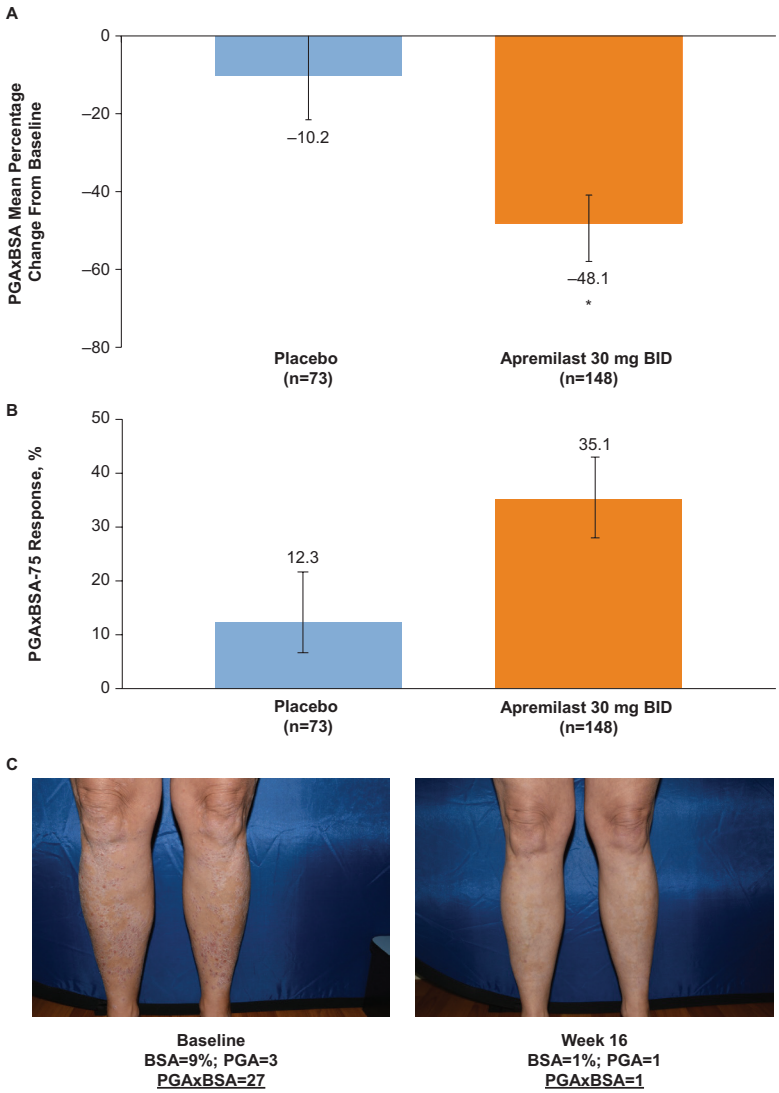
The n reflects the number of randomized patients; the actual number of patients available for each parameter may vary.
BID=twice daily;
BMI=body mass index; DLQI=Dermatology Life Quality Index;
NAPSI=Nail Psoriasis Severity Index;
PASI=Psoriasis Area and Severity Index;
PGAxBSA=product of the static Physician's Global Assessment and percent body surface area with psoriasis involvement;
ScPGA=Scalp Physician Global Assessment;
SD=standard deviation;
VAS=visual analog scale.

Safety

During the placebo-controlled period (weeks 0 to 16), 47.9% of patients receiving placebo and 62.6% receiving apremilast reported ≥1 AE (Table 3); most were mild or moderate. A total of 3 (2.0%) patients receiving apremilast experienced 4 serious AEs; no serious AEs occurred in patients receiving placebo. Serious AEs among apremilast patients included pyelonephritis and nephrolithiasis (both n=1), and cholelithiasis (n=1). A 62-year-old man with medical history of type 2 diabetes mellitus, hyperlipidemia, and peripheral arterial disease had a cerebrovascular accident. No serious AEs were considered treatment related. Discontinuation rates due to AEs were low in both groups (Table 3).

FIGURE 3. PGAxBSA improvements from baseline at week 16 (A) Primary End Point *P<0.0001 for apremilast vs placebo based on 2-way ANCOVA, with treatment and site as factors, and baseline value as covariate; LOCF used to impute missing values; bars indicate 2-sided 95% confidence intervals. (B) PGAxBSA-75 response. *P<0.0001 for apremilast vs placebo based on Cochran-Mantel-Haenszel test stratified by sites; LOCF used to impute missing values; bars indicate 2-sided 95% confidence intervals. (C) Patient with PGAxBSA score of 27.0 at baseline who was randomized to Apremilast; At week 16, PGAxBSA score=1.0

ANCOVA=analysis of covariance; BID=twice daily; LOCF=last observation carried forward; sPGA=static Physician's Global Assessment; PGAxBSA=product of the static Physician's Global Assessment and psoriasis-involved Body Surface Area (%).



Most common AEs (≥5% patients, either group) included diarrhea, headache, nausea, upper respiratory tract infection, decreased appetite, and vomiting (Table 3). Among patients reporting an AE of diarrhea, with follow-up questioning, protocol-defined diarrhea (≥2 loose watery stools in 1 day) was confirmed in 10/73 patients (13.7%) receiving placebo and 28/147 patients (19.0%) receiving apremilast (P=0.1704); 1 patient receiving placebo and 1 receiving apremilast withdrew due to diarrhea.

Significant abnormalities in clinical laboratory parameters were infrequent and comparable between groups. At week 16, mean change from baseline in body weight was +0.42 kg (mean percentage change: +0.58%) in placebo patients and –0.65 kg (mean percentage change: –0.68%) in apremilast patients (P=NS), >5% weight loss from baseline occurred in 13/147 apremilast patients (8.8%), and 3/73 placebo patients (4.1%). No patient had weight loss >10%.

DISCUSSION

UNVEIL is the first prospective, randomized, controlled trial to evaluate the clinical efficacy and safety of a systemic treatment, oral apremilast, in patients with moderate plaque psoriasis with BSA involvement of 5% to 10% who were naive to conventional

TABLE 2.

Summary of Clinical Efficacy End Points at Week 16

	Placebo n=73	Apremilast 30 mg BID n=148	*P*-value
Primary end point			
PGAxBSA score, mean % change (LOCF)	–10.2	–48.1	<0.0001
Secondary end points			
sPGA score 0 (clear) or 1 (almost clear), % (LOCF)	9.6	30.4	<0.0001
PGAxBSA-75, % (LOCF)	12.3	35.1	<0.0001
PtGA score of 0 (clear) or 1 (very mild), % (LOCF)	20.5	33.8	0.0365
Mean change in pruritus VAS score*, mm	–10.2	–19.2	0.0016
ScPGA score 0 (clear) or 1 (minimal) with ≥2 point reduction from baseline§, %	20.0	38.4	0.0178
Mean percentage change in NAPSI score in target nail, %	–10.5	–28.9	0.1215
NAPSI-50‡, %	18.5	26.8	0.5025
Mean change in DLQI score	–2.4	–4.8	0.0008
DLQI response (decrease of ≥5 points)‖, %	34.5	63.8	0.0009

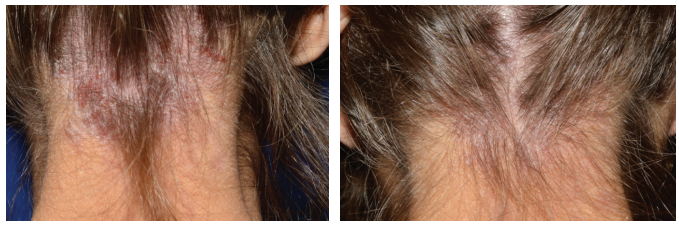
*At baseline, pruritus n=71 and n=144 for placebo and apremilast, respectively.
§Examined in patients with ScPGA score ≥1 at baseline: placebo n=55 and apremilast n=112.
‡Examined in patients with NAPSI score ≥1 at baseline: placebo n=27 and apremilast n=56.
‖Examined in patients with DLQI score >5 at baseline (placebo, n=58; apremilast, n=116).
BID=twice daily;
DLQI=Dermatology Life Quality Index;
LOCF=last observation carried forward;
NAPSI=Nail Psoriasis Severity Index;
NAPSI-50=≥50% reduction from baseline in NAPSI score;
PGAxBSA=product of the static Physician's Global Assessment and psoriasis-involved Body Surface Area (%);
PGAxBSA-75=≥75% reduction from baseline in PGAxBSA score;
PtGA=Patient Global Assessment;
ScPGA, Scalp Physician's Global Assessment;
sPGA=static Physician's Global Assessment;
VAS=visual analog scale.

systemic and biologic therapies. Findings are consistent with the demonstrated efficacy of apremilast in large randomized phase III studies (ESTEEM 1 and 2) in patients with moderate to severe psoriasis (BSA ≥10%).[11,12] Findings from this study, however, illustrate the difficulty in assessing response to therapy in patients with more moderate psoriasis, likely due to the milder disease at baseline compared with patients with moderate to severe disease. In ESTEEM 1, the patient population had more severe disease at baseline with a higher mean PASI score (~19), higher mean BSA (~25%), and more severe disease symptoms (mean pruritus VAS score ~66 mm) compared with the population in the current study.

Despite more moderate disease, DLQI scores at baseline were indicative of significant QOL impairments associated with psoriasis in this population. Baseline DLQI scores in the UNVEIL population (~11.0) were similar to those in ESTEEM 1 (~12.0), which included patients with more severe disease.[11] In the current study, apremilast significantly improved QOL and pruritus.

In line with QOL findings, patients in UNVEIL reported satisfaction with effectiveness, safety, and convenience of apremilast. TSQM assessments showed global satisfaction and effectiveness were significantly better with apremilast compared with placebo; moreover, patient satisfaction as related to convenience and side effects among patients receiving apremilast was similar to that in patients receiving placebo. This is the first time patient satisfaction with apremilast has been assessed in a prospective randomized, controlled trial. Improvement in QOL and patient satisfaction with treatment may be important in treating patients

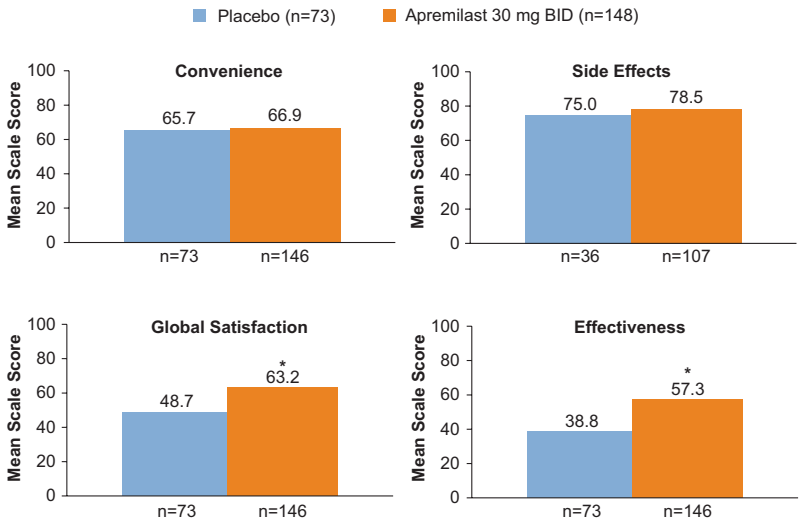
FIGURE 4. Case example of a patient with scalp psoriasis at baseline, at week 16 while receiving apremilast (female, baseline ScPGA=3).
ScPGA=Scalp Physician's Global Assessment.



Baseline
ScPGA=3

Week 16
ScPGA=2

FIGURE 5. Patient satisfaction based on mean TSQM Scale scores at week 16.
Mean TSQM at week 16 (LOCF). Global Satisfaction, *P*<0.0001; Effectiveness, *P*<0.0001; Convenience and Side Effects, both *P*=NS, based on 2-way ANOVA, with treatment and site as factors. ANOVA=analysis of variance; BID=twice daily; TSQM=Treatment Satisfaction Questionnaire for medication, version II (higher scores indicate greater satisfaction).



with moderate disease and should be incorporated into future studies in this patient population.

The safety profile of apremilast in the UNVEIL patient population was similar to that observed previously in phase III trials.[11,12,17-19] Of note, rates of diarrhea (16.4%), headache (11.0%), and nausea (9.6%) in the placebo group in UNVEIL were higher than those in the placebo groups of the ESTEEM studies (diarrhea, ~6.1%; headache, ~2.6%; nausea, ~6.6%). Rates of diarrhea in UNVEIL were higher with apremilast treatment (~29%) than in other randomized, controlled trials of apremilast (15% to 19%).[11,12,17-19]This is likely due to proactive questioning of patients reporting diarrhea in this trial (which was not done in ESTEEM) and the fact that, among physicians, diarrhea is now a widely known AE with apremilast, which may have resulted in hypervigilance in reporting. With follow-up questioning, protocol-defined diarrhea (≥2 loose watery stools in 1 day) was confirmed in 19% of patients receiving apremilast, which is more in line with reported rates.[11,12,17-19] Changes in laboratory parameters were transient and not clinically significant, consistent with previous studies,[11,12] confirming that apremilast does not require regular blood monitoring.

CONCLUSION

Apremilast was effective in the treatment of systemic-naive, post-topical patients with more moderate plaque psoriasis and was generally well tolerated. The efficacy and safety of apremilast demonstrated in UNVEIL are consistent with those seen in patients with moderate to severe plaque psoriasis in randomized phase III trials.[11,12] UNVEIL demonstrated a significantly positive impact of apremilast on QOL and treatment satisfaction in patients with more moderate psoriasis.

DISCLOSURES

Bruce Strober MD PhD has received honoraria for serving as a consultant and advisory board member for AbbVie, Amgen, AstraZeneca, Boehringer Ingelheim, Celgene Corporation, Dermira, Eli Lilly, Forward Pharma, Janssen, LEO Pharma, Maruho, Medac, Novartis, Pfizer, Stiefel/GlaxoSmithKline, Sun Pharma, and UCB; has received payments (to the University of Connecticut) as an investigator for AbbVie, Amgen, Celgene Corporation, Eli Lilly, Janssen, Merck, Novartis, and Pfizer; has received fees as a scientific director for the CORRONA Psoriasis Registry; and has received grant support (to the University of Connecticut for Fellowship Program) from AbbVie and Janssen.

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TABLE 3.

Adverse Events During the Placebo-Controlled Period

Patients	Placebo-Controlled Period 0 to 16 Weeks	
	Placebo n=73	Apremilast 30 mg BID n=148
Overview, n (%)		
≥1 AE	35 (47.9)	92 (62.6)
≥1 serious AE	0 (0.0)	3 (2.0)
≥1 severe AE	1 (1.4)	3 (2.0)
AE leading to drug withdrawal	3 (4.1)	5 (3.4)
Reported by ≥5% of patients in any treatment group, n (%)		
Diarrhea	12 (16.4)	43 (29.3)
Headache	8 (11.0)	30 (20.4)
Nausea	7 (9.6)	26 (17.7)
URTI	3 (4.1)	10 (6.8)
Decreased appetite	4 (5.5)	6 (4.1)
Vomiting	2 (2.7)	9 (6.1)
Select marked laboratory abnormalities,[§] n/m (%)		
ALT >3 x ULN, U/L	0/63 (0.0)	1/130 (0.8)
AST >3 x ULN, U/L	0/62 (0.0)	2/129 (1.6)
Total cholesterol >7.8 mmol/L	0/64 (0.0)	4/130 (3.1)
Triglycerides >3.4 mmol/L	9/64 (14.1)	9/130 (6.9)
Lymphocytes <0.8 × 10^9/L	1/63 (1.6)	0/129 (0.0)

AE=adverse event;
ALT=alanine aminotransferase;
AST=aspartate aminotransferase;
BID=twice daily;
HDL-C=high-density lipoprotein cholesterol;
LDL-C=low-density lipoprotein cholesterol;
ULN=upper limit of normal;
URTI=upper respiratory tract infection.

Joana Goncalves MD, Eugenia Levi PharmD, and Rongdean Chen PhD are employees of Celgene Corporation.

Kristina Callis Duffin MD MS has been a consultant, steering committee member, and/or advisory board member for, and/or has received grants and/or honoraria from AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene Corporation, Centocor/Janssen, Eli Lilly, Novartis, Pfizer, Regeneron, Stiefel, and XenoPort.

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