Sustained Improvement in Patient-Reported Outcomes With Continued Apremilast Treatment Over 104 Weeks in Patients With Moderate to Severe Psoriasis

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INTRODUCTION

- Psoriasis is a chronic, systemic inflammatory disease that is associated with significant impairments in quality of life (QOL), which may include physical discomfort, pruritus, and emotional distress.[1-4]
- Apremilast is an oral, small-molecule phosphodiesterase 4 inhibitor that has demonstrated efficacy and safety vs. placebo (PBO) in the LIBERATE global phase 3b trial in patients with moderate to severe plaque psoriasis.[5]
- Efficacy was maintained for up to 104 weeks in patients who continued treatment with apremilast 30 mg twice daily (APR) in the LIBERATE trial.[6]
- To further understand the clinical profile of APR, the effect of long-term APR treatment on patient-reported outcomes assessed at 104 weeks was evaluated in the LIBERATE patient population.

METHODS

Patients

Key Inclusion Criteria

- Adults ≥18 years of age
- Chronic plaque psoriasis for ≥12 months
- Candidates for phototherapy who had no prior exposure to biologics for the treatment of psoriatic arthritis or psoriasis
- Moderate to severe plaque psoriasis, as defined by Psoriasis Area and Severity Index (PASI) score ≥12, psoriasis-involved body surface area (BSA) ≥10%, and static Physician Global Assessment (sPGA) score ≥3
- Inadequate response, inability to tolerate, or contraindication to ≥1 conventional systemic agent for the treatment of psoriasis

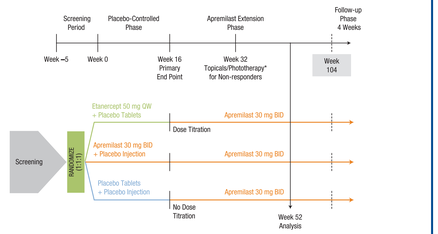
Key Exclusion Criteria

- Prior treatment with >3 systemic agents for the management of psoriasis
- Other clinically significant or major uncontrolled diseases
- Serious infections, including latent, active, or history of incompletely treated tuberculosis

Study Design

- LIBERATE consisted of 2 treatment phases: a 16-week randomized, double-blind, PBO-controlled phase and an 88-week APR extension phase for an overall treatment duration of 104 weeks (**Figure 1**).
  - Patients were randomized (1:1:1) to PBO, APR, or etanercept 50 mg once weekly (ETN).
  - At Week 16, all patients in the PBO and ETN groups switched to APR, and patients in the APR group continued APR. Treatment with APR was maintained from Weeks 16 to 104 (APR extension phase).

Figure 1. Study Design



ClinicalTrials.gov: NCT01690299
Note: LIBERATE was not powered for APR vs. ETN comparisons.
*Starting at Week 32, all non-responders (<PASI-50) had the option of adding topical therapies and/or ultraviolet B phototherapy (excluding oral psoralen combined with ultraviolet A) to their treatment regimen.
PASI-50=50% or greater reduction from baseline in Psoriasis Area and Severity Index score.

METHODS (cont'd)

Patient-Reported Assessments

- At Weeks 16 and 104, the proportion of patients achieving response, defined as the minimal clinically important difference (MCID), was evaluated for the following patient-reported outcomes:
  - Dermatology Life Quality Index (DLQI); MCID defined as a ≥5-point decrease from baseline in patients with baseline DLQI score >5[7]
  - Pruritus visual analog scale (VAS; 0–100 mm); MCID defined as a decrease from baseline ≥20%[8]
  - 36-Item Short Form Health Survey version 2 (SF-36v2) Mental and Physical Component Summary scores (MCS and PCS); both MCIDs defined as an increase of ≥2.5 points from baseline[9]
  - Patient Health Questionnaire-8 (PHQ-8); MCID defined as achievement of score ≤4 (no significant depressive symptoms)[10]

Safety Assessments

- Safety was assessed based on adverse events (AEs), vital signs, clinical laboratory assessments, and physical examinations.

Statistical Analysis

- Achievement of MCID on the DLQI at Week 16 and Week 104 was a prespecified exploratory end point, whereas achievement of MCID on the pruritus VAS, the MCS and PCS, and the PHQ-8 were post hoc analyses.
- All MCID analyses were performed using the modified intent-to-treat (mITT) population, which included all randomized patients who received ≥1 dose of study medication and had an evaluation at baseline and at the specified time point.
- End points were analyzed using descriptive statistics, including proportions of patients achieving each end point by treatment group; associated 95% confidence intervals (CIs) were calculated. All data were analyzed as observed, with no imputation for missing values.
- The safety population consisted of all patients who were randomized and received ≥1 dose of study medication. Descriptive statistics were used for summaries of treatment-emergent AEs and other safety assessments.

RESULTS

Patients

- The mITT population consisted of 250 patients (PBO, n=84; APR, n=83; ETN, n=83).
- Patient demographics and baseline disease characteristics were generally comparable between treatment groups (**Table 1**).

Table 1. Patient Demographics and Baseline Disease Characteristics

	PBO n=84	APR n=83	ETN n=83
Age, mean (SD), years	43.4 (14.9)	46.0 (13.6)	47.0 (14.1)
Male, n (%)	59 (70.2)	49 (59.0)	49 (59.0)
White, n (%)	80 (95.2)	79 (95.2)	75 (90.4)
Body mass index, mean (SD), kg/m^2	29.6 (6.6)	29.1 (5.9)	29.9 (6.9)
Weight, mean (SD), kg	89.5 (23.1)	88.5 (19.8)	88.1 (20.5)
Duration of psoriasis, mean (SD), years	16.6 (12.1)	19.7 (12.7)	18.1 (11.7)
PASI score (0–72), mean (SD)	19.4 (6.8)	19.3 (7.0)	20.3 (7.9)
PASI score >20, n (%)	32 (38.1)	28 (33.7)	34 (41.0)
Body surface area, mean (SD), %	27.3 (16.1)	27.1 (15.6)	28.4 (15.7)
Body surface area >20%, n (%)	42 (50.0)	45 (54.2)	47 (56.6)
sPGA of 4 (severe), n (%)	23 (27.4)	17 (20.5)	13 (15.7)
Prior use of conventional systemic medications, n (%)	70 (83.3)	66 (79.5)	58 (69.9)
VAS scores* (0–100 mm), mean (SD), mm			
Pruritus	62.5 (22.7)	62.6 (25.7)	57.2 (27.7)
Skin discomfort/pain	43.9 (31.2)	51.8 (30.8)	47.3 (32.8)
Patient global assessment of psoriasis disease activity, mean (SD)	53.6 (21.6)	60.9 (24.6)	55.6 (24.2)
DLQI score* (0–30), mean (SD)	11.4 (6.3)	13.6 (6.7)	12.5 (7.0)
PHQ-8* (0–24), mean (SD)	4.8 (4.4)	5.8 (5.0)	5.0 (5.2)
SF-36v2,* mean (SD)			
MCS (0–100)	44.3 (11.0)	42.8 (12.6)	45.6 (10.8)
PCS (0–100)	50.8 (7.8)	46.1 (9.0)	46.2 (9.1)

*n=number of patients randomized; number of patients with scores available at baseline differs from randomized n for the following parameters: VAS (PBO, n=81; APR, n=79; ETN, n=78); DLQI and SF-36v2 MCS and PCS (PBO, n=81; APR, n=81; ETN, n=80); PHQ-8 (PBO, n=81; APR, n=82; ETN, n=80).

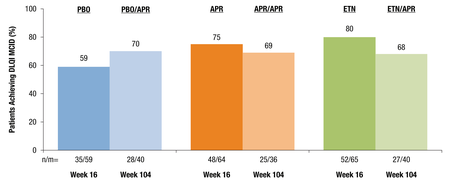
RESULTS (cont'd)

Patient-Reported Outcomes

DLQI MCID Achievement: Week 16 and Week 104

- At Week 16, a higher proportion of patients in the APR and ETN groups achieved DLQI MCID compared with the PBO group; response was generally maintained at Week 104 among patients who continued APR or who were switched at Week 16 from PBO to APR (PBO/APR) or from ETN to APR (ETN/APR) and remained on APR at Week 104 (**Figure 2**).

Figure 2. Achievement of DLQI MCID at Week 16 and Week 104

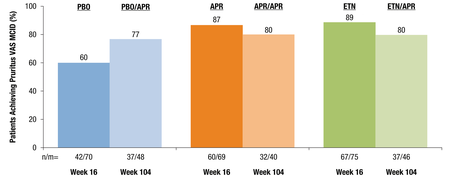


Includes patients in the mITT population with a DLQI score >5 at baseline, with a value at baseline and at the specified time point.
MCID=≥5-point decrease from baseline; n/m=number of patients achieving DLQI MCID/number of patients with evaluable data at the time point.

Pruritus VAS MCID Achievement at Week 16 and Week 104

- At Week 16, a higher proportion of patients in the APR and ETN groups achieved pruritus VAS MCID compared with the PBO group. Response was maintained at Week 104 in the APR/APR group and in patients who switched at Week 16 from ETN or PBO to APR (**Figure 3**).

Figure 3. Achievement of Pruritus VAS MCID at Week 16 and Week 104



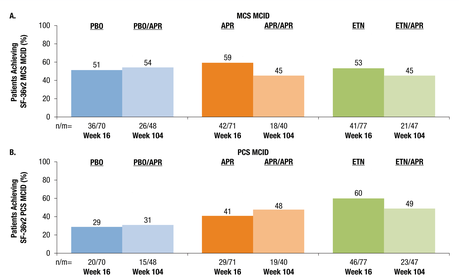
Includes patients in the mITT population with a value at baseline and at the specified time point.
MCID=improvement ≥20% from baseline; n/m=number of patients achieving pruritus improvement ≥20% from baseline/number of patients with evaluable data at the time point.

MCS and PCS MCID Achievement at Week 16 and Week 104

- The proportions of patients achieving the MCID for the MCS were generally similar among the treatment groups at Week 16. At Week 104, MCS response was maintained in PBO/APR patients and was comparable between APR/APR and ETN/APR patients at Week 104 (**Figure 4A**).
- At Week 16, the proportion of patients achieving PCS MCID was lowest in the PBO group. At Week 104, PCS response was comparable between the APR/APR and ETN/APR groups and remained lower in the PBO/APR group (**Figure 4B**).

RESULTS (cont'd)

Figure 4. Achievement of MCID on MCS (A) and PCS (B) at Week 16 and Week 104

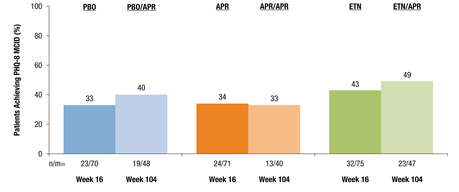


Includes patients in the mITT population with a baseline value and a value at the specified time point.
MCID=improvement ≥2.5 from baseline; n/m=number of patients achieving SF-36v2 MCS or PCS MCID/number of patients with evaluable data at the time point.

PHQ-8 MCID Achievement

- At Week 16 and Week 104, proportions of patients achieving the MCID for PHQ-8 (i.e., score ≤4 [no significant depressive symptoms]) were generally similar among the treatment groups; response was maintained at Week 104 in the APR/APR group and in patients who switched at Week 16 from ETN or PBO to APR (**Figure 5**).

Figure 5. Achievement of PHQ-8 MCID at Week 16 and Week 104



Includes patients in the mITT population with a baseline value and a value at the specified time point.
MCID=score ≤4; n/m=number of patients achieving PHQ-8 score ≤4/number of patients with evaluable data at the time point.

Safety

- During the PBO-controlled period (Weeks 0 to 16), AEs occurring in ≥5% of patients in any treatment group were diarrhea, nausea, upper respiratory tract infection, nasopharyngitis, headache, and tension headache (**Table 2**).
- During the APR extension phase (Weeks 16 to 104), AEs that occurred in ≥5% of patients in any treatment group included those observed during the PBO-controlled period as well as arthralgia, rebound psoriasis, pain in extremity, bronchitis, psoriasis, and sinusitis.
- Most AEs were mild or moderate in severity, did not increase with prolonged APR exposure, and did not lead to study discontinuation.

RESULTS (cont'd)

Table 2. Summary of Safety During Weeks 0 to 16[5]

	PBO-Controlled Phase Weeks 0 to 16*		
	PBO n=84	APR n=83	ETN n=83
Patients, n (%)†			
≥1 AE	45 (53.6)	59 (71.1)	44 (53.0)
≥1 Serious AE	0 (0.0)	3 (3.6)	2 (2.4)
≥1 Severe AE	2 (2.4)	3 (3.6)	3 (3.6)
AE leading to drug withdrawal	2 (2.4)	3 (3.6)	2 (2.4)
AEs reported by ≥5% of patients in any treatment group			
Diarrhea	3 (3.6)	9 (10.8)	1 (1.2)
Nausea	1 (1.2)	9 (10.8)	4 (4.8)
Upper respiratory tract infection	2 (2.4)	6 (7.2)	2 (2.4)
Nasopharyngitis	8 (9.5)	4 (4.8)	8 (9.6)
Headache	3 (3.6)	11 (13.3)	5 (6.0)
Tension headache	4 (4.8)	5 (6.0)	3 (3.6)

*Each patient is counted once for each applicable category.
†Safety population.

- No clinically meaningful changes were reported in laboratory parameters.
- No cases of tuberculosis (new or reactivation) were reported during the trial.

CONCLUSIONS

- In biologic-naive patients with moderate to severe psoriasis, improvements in patient-reported outcomes, including QOL and pruritus, were generally maintained with continued APR treatment up to 104 weeks.
- AEs were consistent with the known safety profile of APR.

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