Apremilast, an Oral Phosphodiesterase 4 Inhibitor, in Patients With Nail, Scalp, and Palmoplantar Psoriasis: 52-Week Results From the ESTEEM 2 Trial

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Disclosures

• Dr. Jeffrey Crowley has been an investigator for AbbVie, Amgen, AstraZeneca, Celgene, Janssen, Merck, Pfizer, and Regeneron; has served on the advisory board for AbbVie, Amgen, and Celgene; and has been a speaker for AbbVie.

• Dr. Melinda Gooderham has been an investigator for AbbVie, Allergan, Amgen, Boehringer Ingelheim, Celgene, Coherus, Eli Lilly, Galderma, Kythera, Kyowa Hakko Kirin Pharma, LEO Pharma, Merck, Novartis, and Pfizer, and has served as a speaker for AbbVie, Amgen, Astellas, Galderma, Janssen, LEO Pharma, Novartis, and Pfizer.

• Dr. Norman Wasel has been an investigator for Celgene.

• Dr. Jamie Weisman has no conflicts of interest to disclose.

• Dr. Stephen Tyring has been an investigator for Celgene.

• Ms. ChiaChi Hu and Dr. Robert M. Day are employees of Celgene Corporation.

• Dr. Carlos Ferrandiz has no conflicts of interest to disclose.
Abstract

**Background:** Apremilast efficacy was assessed in pts with difficult-to-treat nail, scalp, and palmoplantar psoriasis.

**Methods:** Pts with moderate to severe plaque psoriasis (PASI \( \geq 12 \), BSA \( \geq 10\% \), sPGA \( \geq 3 \)) were randomized 2:1 to APR 30 mg BID (APR) or placebo (PBO). At Wk16, PBO pts switched to APR (PBO/APR). At Wk32, APR pts achieving a \( \geq \)PASI-50 response were re-randomized (1:1, blinded) to continue APR or receive PBO. Upon loss of 50% of PASI improvement obtained at Wk32, pts re-randomized to PBO resumed APR. Nail, scalp, and palmoplantar psoriasis were assessed by NAPSI, ScPGA, and PPPGA.

**Results:** The full analysis set included 411 pts (PBO: n=137; APR: n=274) (mean PASI score: 19.3; mean BSA: 26.2%; prior systemic therapy and/or phototherapy: 64.2%). At baseline (BL), 266 (64.7%) pts had nail psoriasis (NAPSI \( \geq 1 \)), 269 (65.5%) had moderate to very severe scalp psoriasis (ScPGA \( \geq 3 \)), and 42 (10.2%) had moderate to severe palmoplantar psoriasis (PPPGA \( \geq 3 \)). At Wk16, significantly more pts receiving APR achieved PASI-75 (28.8%) and PASI-50 (55.5%) vs PBO (5.8% and 19.7%, respectively; \( P < 0.0001 \)). At Wk16, mean percent change from BL in NAPSI was significantly greater with APR (-29.0%) vs PBO (-7.1%; \( P = 0.0052 \)); mean percent changes in PASI were -60.0% (APR/APR) and -47.6% (PBO/APR) for pts at Wk 32. Mean percent change in NAPSI was -59.7% for pts who were re-randomized and continued APR to Wk52 (n=35, APR/APR/APR). At Wk16, NAPSI-50 achievement was significantly greater with APR (44.6%) vs PBO (18.7%; \( P < 0.0001 \)). NAPSI-50 achievement was improved at Wk32 (55.4%, APR/APR; 52.0%, PBO/APR) and at Wk52 (63.2%, n=38, APR/APR/APR). At Wk16, ScPGA 0 (clear) or 1 (minimal) achievement was significantly greater with APR (40.9%) vs PBO (17.2%; \( P < 0.0001 \)). At Wk32, ScPGA 0 or 1 achievement was 32.4% (APR/APR) and 50.7% (PBO/APR). At Wk52 (n=37), ScPGA 0 or 1 achievement was 54.1% (APR/APR/APR). At Wk16, PPPGA 0 (clear) or 1 (almost clear) achievement was significantly greater with APR (65.4%) vs PBO (31.3%; \( P = 0.0315 \)). At Wk32, PPPGA 0 or 1 achievement was 53.8% (APR/APR) and 69.2% (PBO/APR). At Wk52 (n=4), PPPGA 0 or 1 achievement was 100.0% (APR/APR/APR). For all study pts, most common AEs during the APR-exposure period (Wks 0 to 52) were nausea, diarrhea, nasopharyngitis, and URTI.

**Conclusion:** APR significantly reduced the severity of nail, scalp, and palmoplantar psoriasis at Wk16; improvements were observed up to Wk52 for pts continuing APR from BL.
Psoriasis is a chronic inflammatory disease that involves immune dysregulation of pro- and anti-inflammatory signaling.\(^1\)

Psoriasis involvement of the nails, scalp, and palmoplantar surfaces is distressing to patients and often difficult to treat using topical and systemic therapies.\(^2\)

Apremilast, an oral PDE4 inhibitor, works intracellularly to regulate inflammatory mediators.\(^3\)

Apremilast was approved by the FDA in 2014 and by the EC in 2015 for treatment of psoriasis and psoriatic arthritis.\(^4,5\)

ESTEEM is a phase 3 clinical trial program comprising 2 randomized, placebo-controlled studies evaluating the efficacy, safety, and tolerability of apremilast for the treatment of moderate to severe plaque psoriasis.

The objective of the current analysis was to explore the efficacy of apremilast for difficult-to-treat nail, scalp, and palmoplantar psoriasis through 52 weeks of the ESTEEM 2 study.
• Adult patients aged 18 years and older with moderate to severe plaque psoriasis

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*Doses of apremilast were titrated during the first week of administration and at Week 16 when placebo patients were switched to apremilast. §Patients re-started apremilast at the time of loss of effect, defined as time of loss of 50% of the PASI improvement obtained at Week 32 compared with baseline, but no later than Week 52. ‡Patients initially on placebo or randomized to apremilast 30 mg BID who did not attain a PASI-50 were able to add topicals and/or ultraviolet B at Week 32 at the discretion of the investigator.
ESTEEM 2: Study Population

- Diagnosis of chronic plaque psoriasis, with moderate to severe plaque psoriasis at screening and baseline

A priori efficacy analyses included patients with psoriasis in difficult-to-treat areas*

- Nail psoriasis
  - Nail Psoriasis Severity Index (NAPSI) score ≥1§ (n=266, 64.7%)

- Scalp psoriasis, moderate to very severe
  - Scalp Physician Global Assessment (ScPGA) score ≥3 (n=269, 65.5%)

- Palmoplantar psoriasis, moderate to severe
  - Palmoplantar Psoriasis Physician Global Assessment (PPPGA) score ≥3 (n=42, 10.2%)

*At baseline.
§NAPSI score for target nail.
In patients with nail psoriasis at baseline and at least 1 post-baseline NAPSI value,

- NAPSI improvements (i.e., decreases) at Week 16 (Period A) were significantly greater in patients treated with apremilast (-29.0%; n=163, baseline NAPSI=4.2) vs. placebo (-7.1%; n=84, baseline NAPSI=4.4; \(P=0.0052\)).§

- Nail psoriasis continued to improve in the group treated with apremilast for 32 weeks; mean percent NAPSI improvement was -60.0% at Week 32.‡

- In the placebo/apremilast group (treated with apremilast for 16 weeks), mean percent NAPSI improvement at Week 32 was -47.6%.‡
Mean Percent Change in NAPSI Through 52 Weeks*

- Continued improvement in nail psoriasis occurred in patients randomized to apremilast or placebo at baseline who were PASI-50 responders at Week 32 (Period C).

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*In patients with NAPSI score ≥1 at baseline (BL).

§Patients who were initially randomized to apremilast 30 mg BID at Week 0, were PASI-50 responders at Week 32, and were re-randomized to continued apremilast 30 mg BID.

‡Patients who were initially randomized to placebo at Week 0, were PASI-50 responders at Week 32, and entered Period C.

ESTEEM 2
NAPSI-50 Achievement at Weeks 16 and 32

- Among patients with nail psoriasis (NAPSI ≥1) at baseline,
  - NAPSI-50* achievement at Week 16 (Period A) was significantly greater with apremilast (44.6%, 78/175) vs. placebo (18.7%, 17/91; \( P<0.0001 \))§
  - NAPSI-50 achievement continued to increase in the apremilast group; 55.4% of these patients achieved NAPSI-50 at Week 32.‡
  - In the placebo/apremilast group, NAPSI-50 achievement at Week 32 was 52.0%.‡

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*NAPSI-50=≥50% improvement from baseline NAPSI.
§Week 16 findings based on full analysis set having a baseline NAPSI ≥1, with last observation carried forward to impute missing values, \( P<0.0001 \) vs. placebo based on chi-square test.
‡Week 32 findings based on randomized patients with nail psoriasis (NAPSI ≥1) at baseline who received at least 1 dose of study medication; patients without an observation at Week 32 were considered non-responders.
• NAPSI-50 achievement was generally maintained for up to 52 weeks in patients who received apremilast or placebo at baseline who were PASI-50 responders at Week 32.

**In patients with NAPSI score ≥1 at baseline (BL).**

§Patients who were initially randomized to apremilast 30 mg BID at Week 0, were PASI-50 responders at Week 32, and were re-randomized to continued apremilast 30 mg BID in Period C.

‡Patients who were initially randomized to placebo at Week 0, were PASI-50 responders at Week 32, and entered Period C.
Among patients with moderate to very severe scalp psoriasis at baseline,

- ScPGA score of 0 (clear) or 1 (minimal) achievement at Week 16 (Period A) was significantly greater with apremilast (40.9%, 72/176) vs. placebo (17.2%, 16/93; \( P < 0.0001 \)).§

- ScPGA score of 0 or 1 achievement was generally maintained in the apremilast group; 32.4% of these patients achieved ScPGA 0 or 1 at Week 32.‡

- In the placebo/apremilast group, ScPGA 0 or 1 achievement at Week 32 was 50.7%.‡

*In patients with moderate to very severe scalp psoriasis at baseline (ScPGA score ≥3).

§Week 16 findings based on full analysis set having a baseline ScPGA ≥3, with last observation carried forward to impute missing values, \( P < 0.0001 \) vs. placebo based on chi-square test.

‡Week 32 findings based on randomized patients with ScPGA ≥3 at baseline; patients without an observation at Week 32 were considered non-responders.
ScPGA 0 or 1 Achievement Through 52 Weeks*

- ScPGA score of 0 or 1 achievement was generally maintained for up to 52 weeks in patients who received apremilast or placebo at baseline who were PASI-50 responders at Week 32.

*In patients with moderate to very severe scalp psoriasis at baseline (ScPGA score ≥3).

§Patients who were initially randomized to apremilast 30 mg BID at Week 0, were PASI-50 responders at Week 32, and were re-randomized to continued apremilast 30 mg BID in Period C.

‡Patients who were initially randomized to placebo at Week 0, were PASI-50 responders at Week 32, and entered Period C.
PPPGA 0 or 1 Achievement at Weeks 16, 32, and 52*

- Among patients with moderate to severe palmoplantar psoriasis at baseline,
  - PPPGA score of 0 or 1 achievement at Week 16 (Period A) was significantly greater in patients who received apremilast (65.4%, 17/26), vs. placebo (31.3%, 5/16; $P=0.0315$).§
  - PPPGA score of 0 or 1 achievement was generally maintained in the apremilast group; 53.8% of these patients achieved a PPPGA score of 0 or 1 at Week 32.‡
  - In the placebo/apremilast group at Week 32, PPPGA score of 0 or 1 achievement was 69.2%.‡
  - PPPGA score of 0 or 1 achievement was sustained up to Week 52 in patients randomized to apremilast (100%, n=4 of 4 patients) or placebo (75%, n=6 of 8 patients) at baseline who were PASI-50 responders at Week 32 and continued to receive apremilast up to Week 52.

*In patients with moderate to severe palmoplantar psoriasis at baseline (PPPGA ≥3).
§Week 16 findings based on full analysis set having a baseline PPPGA ≥3 with last observation carried forward to impute missing values, $P<0.0001$ vs. placebo based on chi-square test.
‡Week 32 findings based on randomized patients with moderate to severe palmoplantar psoriasis at baseline (PPPGA ≥3) at baseline; patients without an observation at Week 32 were considered non-responders.
The most frequently reported AEs up to Week 52 were nausea, diarrhea, nasopharyngitis, and URTI.

Most AEs were mild or moderate in severity and did not lead to discontinuation.

During Period A (placebo-controlled period):
- Discontinuation rates due to AEs were similar between treatment groups (placebo: 5.1%; apremilast: 5.5%).
- The incidence of serious AEs was low and comparable across treatment groups (placebo: 2.2%; apremilast: 1.8%).

The EAIR§ for serious AEs did not increase with longer apremilast exposure.

No patient reported reactivation of tuberculosis during the study.

Changes in laboratory parameters were transient and not clinically meaningful over time; no trend was observed.

*Safety population includes all randomized patients who received ≥1 dose of study medication. §Exposure-adjusted incidence rate (EAIR) per 100 patient-years is defined as 100 times the number (n) of patients reporting the event divided by patient-years within the phase (up to the first event start date for patients reporting the event).
ESTEEM 2: Conclusions

- Apremilast reduced the severity of nail, scalp, and palmoplantar psoriasis.
  - Over 16 weeks, mean percent improvement in NAPSI, and achievement of NAPSI-50 response, an ScPGA score of 0 (clear) or 1 (minimal), or a PPPGA score of 0 (clear) or 1 (almost clear) was significantly greater with apremilast vs. placebo.
  - Improvements were sustained at Week 52 among PASI-50 responders who were re-randomized to apremilast at Week 32.

- Apremilast demonstrated an acceptable safety profile and was generally well tolerated.

- Apremilast provides healthcare practitioners a therapeutic option with a favorable benefit:risk profile for patients with difficult-to-treat nail, scalp, and palmoplantar psoriasis.