# Evaluation of the PGAxBSA Composite Tool in Patients With Moderate vs. Moderate to Severe Plaque Psoriasis

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## INTRODUCTION

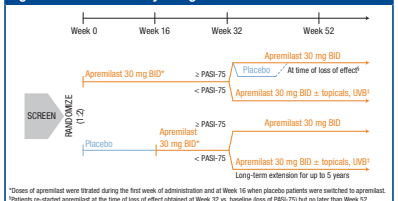
- The Physician Global Assessment and Body Surface Area (PGAxBSA) composite tool is simple to use for the assessment of both severity and extent of psoriasis and correlates with the product of the more complex Psoriasis Area and Severity Index (PASI) tool.[1-3]
- In prior retrospective analyses of the Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis (ESTEEM; NCT01194219 and NCT01232283) phase III clinical trial data, the PGAxBSA and PASI demonstrated ≥79% response concordance and achieved Cohen's effect sizes >0.8, indicating sensitivity to therapeutic change.[4]
- PGAxBSA has also demonstrated sensitivity to small changes from baseline in body surface area (BSA), unlike the non-linear PASI tool,[1,5] and thus may be a more sensitive tool for assessing response in patients with moderate psoriasis.
- The phase IV randomized, placebo (PBO)-controlled, double-blind study Evaluating Apremilast in a Phase IV Trial of Efficacy and Safety in Patients With Moderate Plaque Psoriasis (UNVEIL) (NCT02425826) is the first prospective trial to evaluate the efficacy and safety of oral apremilast 30 mg twice daily (APR) in patients with moderate plaque psoriasis (psoriasis-involved BSA of 5% to 10%) who are naive to systemic and biologic therapy.
- This analysis compared correlations between PGAxBSA and PASI in 2 distinct populations of patients with moderate plaque psoriasis from ESTEEM 1 and UNVEIL.

## METHODS

- Data were collected from patients with moderate plaque psoriasis who were randomly assigned to receive APR at baseline in the ESTEEM 1 trial (n=562) and the UNVEIL trial (n=148).
- ESTEEM 1 was a phase III, multicenter, randomized, double-blind, PBO-controlled study (**Figure 1**).
  - Eligible patients were randomized (2:1) to receive APR or PBO, titrated over the first week of treatment, through Week 16.
  - At Week 16, PBO patients were switched to APR, with titration. Dosing was maintained from Weeks 16 to 32 (maintenance phase).
  - The maintenance phase was followed by a blinded, randomized treatment withdrawal phase through Week 52.
- UNVEIL was a phase IV randomized, double-blind, PBO-controlled study (**Figure 2**).
  - Eligible patients were randomized (2:1) to receive APR or PBO, titrated over the first week of treatment.
  - At Week 16, all PBO patients were switched to open-label APR (with titration) through Week 52.

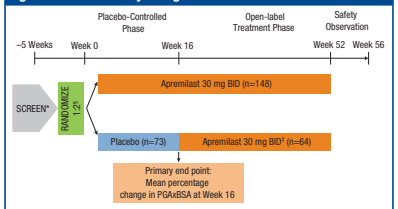
## METHODS (cont'd)

### Figure 1. ESTEEM 1 Study Design




*Doses of apremilast were titrated during the first week of administration and at Week 16 when placebo patients were switched to apremilast.
[6]Patients re-started apremilast at the time of loss of effect obtained at Week 32 vs. baseline (loss of PASI-75) but no later than Week 52.
[7]Patients initially on placebo or randomized to apremilast 30 mg BID who did not attain PASI-75 were able to add topicals and/or UVB light therapy at Week 32 at the discretion of the investigator.
BID=twice daily; PASI=Psoriasis Area and Severity Index; PASI-75=a ≥75% reduction from baseline in PASI score; UVB=ultraviolet B.

### Figure 2. UNVEIL Study Design



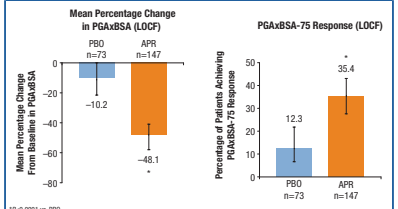

*Screening up to 35 days before randomization.
[5]All doses were titrated over the first week of treatment.
[6]At Week 16, all placebo patients were switched to open-label apremilast 30 mg BID (with dose titration) through Week 52.
BID=twice daily; PGAxBSA=product of the static Physician's Global Assessment and body surface area involvement.

- In these 2 studies, psoriasis severity was defined as follows:
  - **ESTEEM 1:** PASI ≥12, BSA ≥10%, static Physician Global Assessment (sPGA) ≥3.
  - **UNVEIL:** BSA=5% to 10%, sPGA=3.
- Agreement between PGAxBSA and PASI at baseline and Week 16 was evaluated using Spearman correlation (*r*) and intra-class correlation coefficients (ICC).
- Effect size (mean change from baseline/standard deviation of baseline) was calculated for both PGAxBSA and PASI in the APR treatment group in each trial.

## RESULTS

- Patients in UNVEIL who received APR had a significantly greater improvement (reduction) in mean percentage change from baseline in PGAxBSA vs. the PBO group at Week 16 ($P<0.0001$) (**Figure 3**).
- In addition, 35.4% of APR patients in UNVEIL achieved a ≥75% reduction from baseline in PGAxBSA score (PGAxBSA-75) vs. 12.3% of PBO patients ($P<0.0001$) (**Figure 3**).

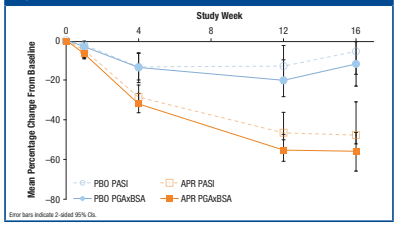
### Figure 3. Mean Percentage Change in PGAxBSA at Week 16 in UNVEIL




*P<0.0001 vs. PBO.
LOCF=last observation carried forward. Error bars indicate 2-sided 95% confidence intervals (CIs).

- Mean percentage changes from baseline in PGAxBSA and PASI scores over the course of the 16-week PBO-controlled period are shown in **Figure 4**; improvement from baseline was greater with PGAxBSA vs. PASI at each time point.

### Figure 4. Mean Percentage Change in PGAxBSA and PASI Scores in UNVEIL




Error bars indicate 2-sided 95% CIs.

## RESULTS (cont'd)

- Correlation between PASI and PGAxBSA at baseline was lower in UNVEIL than it was in ESTEEM 1 (**Table 1**).

**Table 1. Spearman Correlations, ICC, and Effect Sizes: PASI and PGAxBSA at Baseline**

| | PASI Mean (SD) | PGAxBSA Mean (SD) | Spearman Correlation: PASI vs. PGAxBSA | ICC (95% CI): Standardized PASI vs. PGAxBSA | Effect Size | |
|---|---|---|---|---|---|---|
| **Baseline** | | | | | **PASI** | **PGAxBSA** |
| **ESTEEM 1 n=562** | 18.7 (7.2) | 81.8 (54.9) | 0.757* | 0.89 (0.87, 0.90) | NA | NA |
| **UNVEIL n=147** | 8.2 (4.0) | 21.8 (5.3) | 0.395* | 0.42 (0.30,0.56) | NA | NA |

*P<0.0001.
Effect size=(mean change at time point)/$SD_{baseline}$; N=patients with value at the time point indicated; NA=not applicable; standardized=(score-mean)/SD.

- At Week 16, the correlation between PASI and PGAxBSA was lower in UNVEIL as compared with ESTEEM 1 (**Table 2**).
- The effect size was larger for PGAxBSA than for PASI in UNVEIL, whereas in ESTEEM 1 the effect size was larger for PASI than for PGAxBSA (**Table 2**).

**Table 2. Spearman Correlations, ICC, and Effect Sizes: PASI and PGAxBSA at Week 16**

| | PASI Mean (SD) | PGAxBSA Mean (SD) | Spearman Correlation: PASI vs. PGAxBSA | ICC (95% CI): Standardized PASI vs. PGAxBSA | Effect Size | |
|---|---|---|---|---|---|---|
| **Change from baseline at Week 16** | | | | | **PASI** | **PGAxBSA** |
| **ESTEEM 1 Week 16 n=499[8]** | −10.2 (7.3) | −46.5 (45.8) | 0.807* | 0.83 (0.81, 0.86) | −1.41 | −0.85 |
| **UNVEIL Week 16 n=120[8]** | −3.9 (3.8) | −12.3 (9.4) | 0.685* | 0.67 (0.57, 0.76) | −0.97 | −2.51 |

*P<0.0001. [8]n=501 for mean change from baseline in PASI score; n=117 for mean change from baseline in PGAxBSA.
Effect size=(mean change at time point)/$SD_{baseline}$; N=patients with value at the time point indicated; NA=not applicable; standardized=(score-mean)/SD.

## CONCLUSIONS

- Correlation between PASI and PGAxBSA at baseline and Week 16 was lower in UNVEIL (baseline $r$=0.395, Week 16 $r$=0.685) than it was in ESTEEM 1 (baseline $r$=0.757, Week 16 $r$=0.807).
- The larger effect size for PGAxBSA compared with PASI in UNVEIL suggests that PASI may be less sensitive to change in patients with more moderate disease.
- Further study is warranted to demonstrate the robustness of this efficacy measurement.
- PGAxBSA is a simple alternative to PASI, and may be more sensitive for assessing the response to treatment in patients with moderate (BSA=5% to 10%) plaque psoriasis.

## REFERENCES

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## DISCLOSURES

**KCD:** AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene Corporation, Centocor/Janssen, Eli Lilly, Novartis, Pfizer, Regeneron, Stiefel, and XenoPort – consultant, steering committee member, advisory board member, has received grants, and/or has received honoraria. **JMJ:** AbbVie, Amgen, Celgene, Dermira, Galderma, Genentech, Janssen, Lilly, Medimetriks, Merck, Novartis, Pfizer, Promius, and TopMD – research, honoraria, consulting and/or other support. **JG & EL:** Celgene Corporation – employment. **JB:** AbbVie, Amgen, Boehringer Ingelheim, Janssen, LEO Pharma, Eli Lilly, Novartis, Pfizer, and Valeant – speaker board member, consultant, and/or research support.

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