ESTEEM 2: Apremilast Significantly Reduced Psoriasis Severity Throughout 16 Weeks

Written by Toni Rizzo

Apremilast, an oral phosphodiesterase 4 inhibitor that works intracellularly to regulate inflammatory mediators, has been tested in the Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis (ESTEEM) program, which consists of 2 trials: ESTEEM 1 [NCT01194219] and ESTEEM 2 [NCT01232283]. Carle Paul, MD, Toulouse University, Toulouse, France, presented the 52-week results of the ESTEEM 2 trial.

Patients with moderate-to-severe plaque psoriasis, defined as Psoriasis Area and Severity Index (PASI) ≥ 12, body surface area ≥ 10%, and Static Physician's Global Assessment (sPGA) ≥ 3, were randomized 2:1 to treatment with apremilast 30 mg BID (n = 274) or placebo (n = 137). At week 16, placebo patients switched to apremilast, and all patients received apremilast through week 32. At week 32, patients receiving apremilast from baseline who achieved PASI-50 response were rerandomized to continue apremilast or receive placebo. On loss of 50% of PASI improvement achieved at week 32, patients who had been rerandomized to placebo were switched back to apremilast. The primary end point was PASI-75 at week 16.

The included patients were aged ≥ 18 years and had moderate-to-severe chronic plaque psoriasis for ≥ 12 months. The full analysis set included 411 patients. At week 16, significantly more patients treated with apremilast achieved PASI-75 (28.8% vs 5.8%; $P < .0001$) when compared with placebo. Significant findings were also noted in PASI-50 (55.5% vs 19.7%; $P < .0001$) and sPGA 0 or 1 (20.4% vs 4.4%; $P < .0001$; Figure 1).

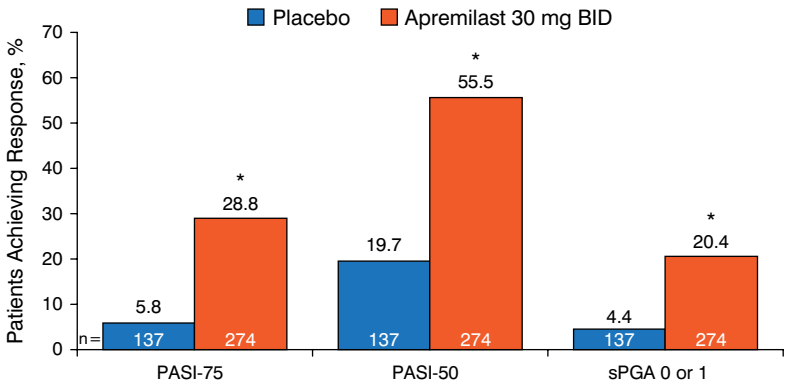
PASI responses generally were maintained through week 32 (Figure 2).

Among patients randomized at baseline to apremilast, the mean percent change from baseline PASI at week 52 was –45.7% in week 32 PASI-50 nonresponders and –74.4% in week 32 PASI-50 responders. Among patients randomized at baseline to placebo and switched to apremilast at week 16, the mean percent change from baseline PASI at week 52 was –24.7% in week 32 PASI-50 nonresponders and –71.8% in week 32 PASI-50 responders.

The mean improvement in PASI generally remained stable from week 32 (77%) to 52 (74%) in patients with PASI-50 rerandomized to apremilast at week 32. The median time to loss of 50% of PASI improvement at week 32 was 12.4 weeks for patients rerandomized to placebo. Approximately 66% of patients rerandomized to placebo regained PASI-50 response after reinitiation of treatment with apremilast (duration of retreatment ranged from 2.6 to 18.3 weeks).

Most adverse events (AEs) were mild or moderate and did not lead to discontinuation. The serious AE rate was low and comparable among treatment arms. AEs occurring in ≥ 5% of patients exposed to apremilast from weeks 0 to 52 were nausea (16.6%), diarrhea (14.5%), nasopharyngitis (14.5%), upper respiratory tract infection (9.2%), tension headache (7.6%), vomiting (6.3%), headache (5.8%), and back pain (5.3%). Changes in laboratory parameters were transient with no trends observed.

Figure 1. PASI-75, PASI-50, and sPGA Responses at Week 16



Data are the full analysis set, last observation carried forward (N = 411). PASI, Psoriasis Area and Severity Index; sPGA, Static Physician's Global Assessment.

*$P < .0001$ vs placebo; sPGA score of 0 (clear) or 1 (almost clear) with ≥ 2-point reduction from baseline.

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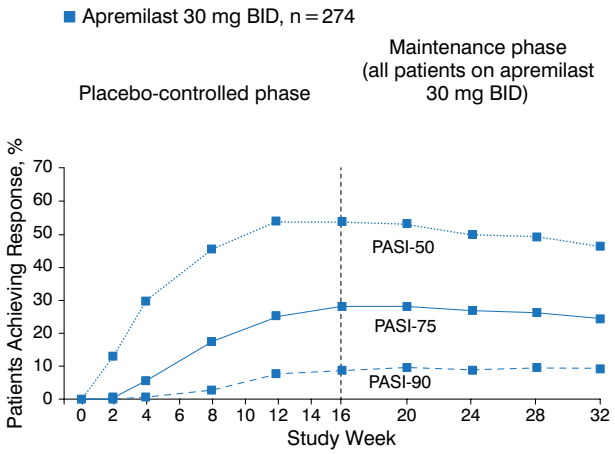
Figure 2. PASI-50, PASI-75, and PASI-90 Throughout 32 Weeks in Patients Receiving Apremilast From Baseline[a]



PASI, Psoriasis Area and Severity Index.

[a]Data using nonresponder imputation at each time point.

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Apremilast 30 mg BID significantly reduced ($P < .0001$) the severity of moderate-to-severe psoriasis throughout 16 weeks, with responses generally maintained to 52 weeks. The results of ESTEEM 2 confirm the efficacy of apremilast in patients with psoriasis, as reported in ESTEEM 1. Apremilast was generally well tolerated up to 52 weeks. Prof Paul concluded that apremilast represents a novel therapeutic option for patients with moderate-to-severe plaque psoriasis.

Adapalene-BPO Reduces Acne Lesions and Scars

Written by Emma Hitt Nichols, PhD

Adapalene-benzoyl peroxide (BPO) fixed-dose combination resulted in a decrease in the number of lesions and new scars but had no effect on preexisting scars in patients with moderate acne vulgaris over 24 weeks. Philippe Martel, MD, Galderma Research and Development, Sophia Antipolis, France, presented data from a study that evaluated the effect of fixed-dose adapalene-BPO for the prevention and treatment of atrophic acne scars.

The current treatment of acne includes topical retinoids, which promote fibroblasts to produce more procollagen. Therefore, it is feasible that topical retinoids may improve preexisting atrophic acne scars or be used for scar prevention. The purpose of this study was to determine if adapalene-BPO treatment could prevent acne scarring and to determine the relationship between primary and secondary acne lesions.

In this international, multicenter, investigator-blinded study, 38 patients with moderate acne vulgaris were randomly assigned in a split-face fashion to receive adapalene-BPO or placebo gel 5 to 7 days per week for 24 weeks. A total of 31 patients completed the study. Moderate acne was defined as 20 to 40 inflammatory lesions (except the nose), ≥10 atrophic acne scars (except the nose), and ≤1 acne nodule. Treatment compliance was measured by an at-home video camera via the Clinical Compliance Control System, which also guided patients during drug application to avoid errors. The mean compliance rate was 77.4%. In addition, patients recorded application of the study treatment in a diary, which was reviewed by the study dispenser at each follow-up visit. End points were the lesion count at 24 weeks, inflammatory and noninflammatory lesion count, the number of scars, the Scar Global Assessment (SGA) of the clearance of scars, and scar volume.

The mean total lesion count was lower with adapalene-BPO compared with placebo (16.1 vs 8.5; $P < .001$). The number of inflammatory and noninflammatory lesions was significantly reduced from baseline with adapalene-BPO compared with placebo (change of 4 and 3.6 lesions, respectively; $P < .001$ for both).

The mean number of scars ≥2 mm using a clinical grading scale decreased by 1.96 at 24 weeks in the adapalene-BPO group compared with the placebo group. In addition, the area that was clear and almost clear of scars as measured by the SGA increased from baseline with adapalene-BPO treatment compared with placebo at week 24, whereas the proportion of skin with mild scars decreased in the adapalene-BPO–treated skin. The proportion of skin that had moderate scarring decreased at similar levels from baseline in both groups; however, the proportion with severe scarring remained the same. Scar volume, as measured by a 3-dimensional analysis, did not change over the study period of 24 weeks, suggesting that treatment with adapalene-BPO does not affect preexisting scars.

During the study, scars formed continuously, with 36% resolved by 24 weeks (mean duration of 41 days) and 64% remaining. Papules and postinflammatory lesions resulted in 98% of scars, and the probability of scar occurrence from inflammatory lesions was 5.7%.

In conclusion, Prof Martel stated that treatment with adapalene-BPO fixed-dose combination compared with placebo was superior for the treatment of acne scars, with a reduction of 1.96 in the number of scars ≥2 mm at 24 weeks. The number of scars continued to increase with placebo, whereas the number was stabilized with treatment. The duration of the papules appeared to be the main contributor to the risk of scarring.