Adapalene 0.3% for the Treatment of Acne in Women

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ABSTRACT

Setting: Acne vulgaris is characterized by comedones, papules, pustules, and secondary lesions. Historically, it has been considered a disease primarily affecting adolescents, but recent reports over the past three decades suggest an increasing prevalence in adults, particularly women. Adapalene was developed for the topical treatment of acne. Adapalene (6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoic acid) is a synthetic naphthoic acid derivative with potent retinoid activity including the reversal of the abnormal follicular keratinization and microcomedo formation and decreasing inflammatory lesions. **Design/objective:** In this analysis, data from two studies comparing adapalene gel 0.3% to vehicle gel were combined and evaluated for change in lesion counts and Investigator's Global Assessment of success rates in adult female subjects ages 18 to 41 years with acne vulgaris. **Results:** The results showed a statistically significant difference favoring adapalene gel 0.3% for reduction in total lesion count at Week 12 (P=0.045). Additionally, median reduction for inflammatory lesions (-61%) and noninflammatory lesions (-51%) also favored adapalene. In addition, adapalene gel, 0.3% was well tolerated with similar tolerability compared to adapalene gel 0.1%; the most common treatment-related adverse events were skin discomfort and dry skin. There were no reported serious adverse events in any group. **Conclusion:** In this subgroup analysis, adapalene gel 0.3% proved effective and well tolerated in adult women with acne vulgaris. (*J Clin Aesthet Dermatol.* 2013;6(10):32–35.)

Acne vulgaris is a chronic skin disease characterized by comedones, papules, and pustules and is associated with negative sequelae including scarring and pigmentation. It affects approximately 30 to 85 percent of adolescents, and literature reviews over the past three decades suggest an increasing prevalence in adults.[1–5] Recent reports suggest this increase to be particularly true for adult women, with more than 50 percent of female patients with acne being over the age of 20.[6–9] Dermatologists see an increasing number of women seeking acne treatment.[7] The variability in response to treatment and the nature of the disease itself can make management of acne challenging, which is particularly true of adult women. The forms described for female acne are identified as nonresponsive or low responding to local or systematic antibiotic treatment, with as high as 82 percent being unresponsive.[10–12,13] Furthermore, oral antibiotic treatment may be less desirable by this patient type due to the association with vaginal candidiasis overgrowth. Women, in general, are very concerned with appearances, and acne has been shown to affect quality of life for those affected.[14,15] Currently, there is an interest to see if adult female acne is different pathophysiologically or clinically from the more frequent form, adolescent acne, to determine if the same treatment strategies will be effective.[7]

Adapalene is a naphthoic acid derivative with potent retinoid and anti-inflammatory properties that was developed for the topical treatment of acne vulgaris. In addition to these properties, adapalene treats acne by modulating cellular differentiation and stabilizing abnormal desquamation.[16–18] Clinical studies have shown adapalene to be safe and effective in treating acne vulgaris, reducing inflammatory and noninflammatory lesions, and being better tolerated than several tretinoin formulations as well as tazarotene.[15,19–24] Adapalene gel 0.3% is also a highly effective comedolytic and anti-inflammatory agent, reversing the abnormal follicular keratinization and microcomedo formation, and decreasing inflammatory lesions, thereby minimizing the risk of negative sequelae.

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TABLE 1. Patient demographics for subjects in *post hoc* analysis of adult females with acne vulgaris treated with adapalene gel 0.3% or vehicle gel

	ADAPALENE GEL 0.3% n=74	VEHICLE GEL n=43
Age, years Mean±SD Median (range)	 27.2±5.99 27 (18–41)	 25.2±6.17 23 (18–37)
Gender, female, n (%)	74 (100%)	43 (100%)
Race, n (%) Caucasian Black Asian Hispanic	 52 (70%) 14 (19%) 2 (3%) 6 (8%)	 31 (72%) 3 (7%) 1 (2%) 8 (19%)

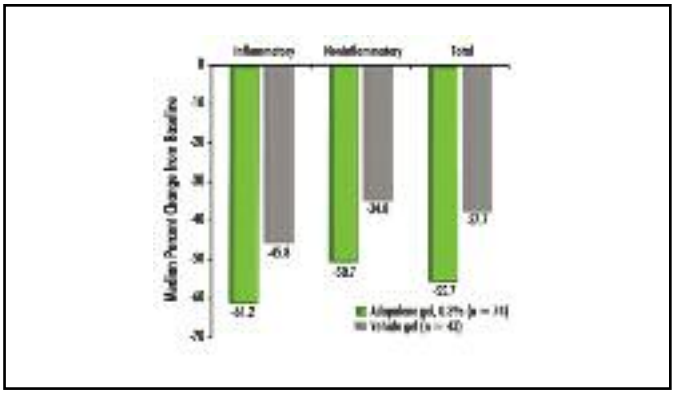


Figure 1. Adult females from the pivotal studies for adapalene 0.3% gel were analyzed separately for efficacy. Median percent change from baseline for inflammatory, noninflammatory, and total lesion counts from this subgroup are shown. Treatment with adapalene gel, 0.3% produced a greater reduction in all lesion counts compared to vehicle. The overall population of the Phase 3 study included 258 patients and showed similar median lesion reductions to what was seen in the adult female subgroup (e.g., total lesion reduction from Phase 3 was -55.6%).

Phase 2 and 3 studies assessed the efficacy, safety, and tolerability of adapalene 0.3% gel compared to adapalene 0.1% gel and vehicle in patients with acne vulgaris.[13,25] This *post hoc* analysis assessed the efficacy and safety of adapalene gel 0.3% in the adult female subgroup from these studies.

METHODS

The subgroup analysis data was obtained from two previously conducted studies that compared the efficacy, safety, and tolerability of adapalene 0.3% gel to vehicle gel and to adapalene 0.1% gel in subjects with acne vulgaris. Study number 1, a Phase 2, dose-assessment, multicenter, randomized, investigator-blind comparison, evaluated male and female adult subjects ages 12 to 40 with moderately severe acne vulgaris.[25] Study number 2, a Phase 3, multicenter, randomized, double-blind comparison, looked at male and female patients with acne vulgaris age 12 years and older.[13] Both studies used success rate, measured by the Investigator's Global Assessment (IGA), and percent reduction in lesion counts from baseline as their primary efficacy endpoints. Subjects were instructed to apply treatment once daily at night for 12 weeks. Study number 1 used the Leeds scale as an overall assessment of acne, and these were collapsed into the standard IGA scale of clear, almost clear, mild, moderate, and severe/very severe. Treatment success using the standard IGA scale was defined to be either a score of clear or almost clear. Safety and tolerability were assessed through local facial tolerability evaluations and evaluation of adverse events (AEs). Investigators rated erythema, scaling, dryness, and stinging/burning along with AEs at each visit.

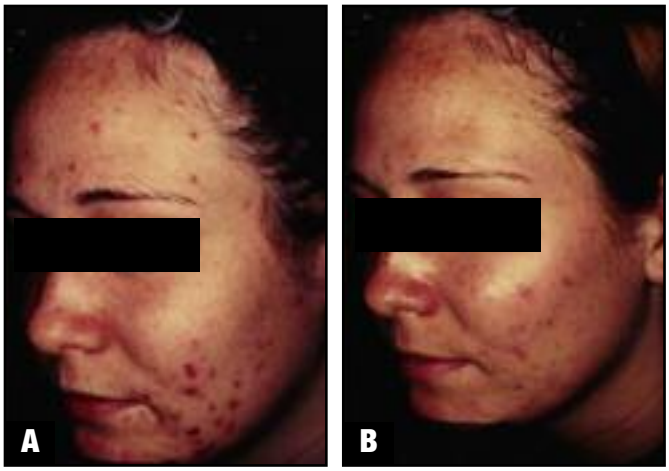
ANALYSIS

The results presented here are combined data analyzed from the Week 12 data from both studies for women 18 years or older. In this subgroup analysis, for the IGA success rate the Cochran-Mantel-Haenszel (CMH) test was used to assess differences between treatment groups. In addition, an analysis of covariance model was used with the number of baseline lesions and the treatment as the only two independent variables to determine treatment differences.

RESULTS

Patient demographics. The study subpopulation consisted of 117 female subjects (n=74 for adapalene gel 0.3%, n=43 for vehicle gel). The subject composition for this subgroup analysis was primarily Caucasian (70% for adapalene gel 0.3%, 72% for vehicle gel) with representation from Black, Hispanic, and Asian subjects as well (Table 1). The median range of subjects was 27 for adapalene gel 0.3% and 23 for vehicle and ranged between 18 and 41 years and 18 and 37 years, respectively (Table 1).

Efficacy. There was a statistically significant difference favoring adapalene gel 0.3% for the mean percent reduction in total lesion count at Week 12 (P=0.045) compared to vehicle. The median results also favored adapalene gel 0.3% for noninflammatory, inflammatory, and total lesion counts compared to vehicle (Figure 1). The decrease in total lesion counts seen in this *post hoc* analysis was similar to the decreases seen from the pivotal Phase 3 study that included male and female subjects. Figure 2 depicts the results seen at baseline and Week 12 in one subject treated with adapalene gel 0.3%. The IGA scale showed a greater percent of female subjects with a



Figures 2A and 2B. Photos, at baseline (A) and Week 12 (B), of adult female patient receiving adapalene gel 0.3% treatment

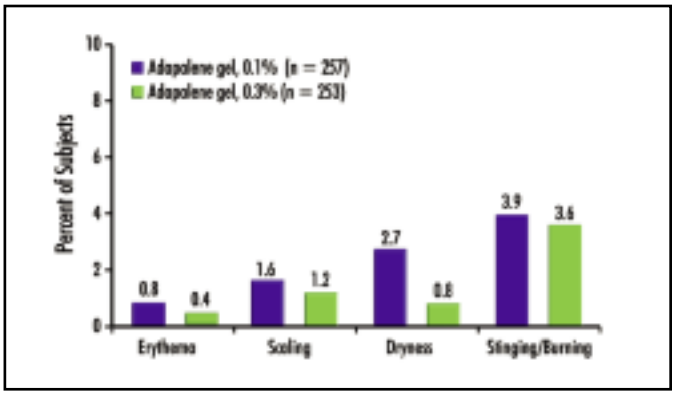


Figure 3. Percent of subjects with severe irritation in the adapalene 0.3% gel and adapalene 0.1% gel groups in the Phase 3 study (N=253, 257, respectively).

rating of clear or almost clear after 12 weeks of treatment with adapalene gel 0.3% (data not shown).

Tolerability/safety. The local tolerability symptoms reported for adapalene gel 0.3% in the Phase 3 study were similar to those observed with adapalene gel 0.1% (Figure 3). There were no statistically significant differences between adapalene 0.1% gel and adapalene 0.3% gel for AEs. In the adapalene gel 0.3% group, the most common treatment-related AEs (occurring in more than 5% of the subjects) were skin discomfort and dry skin; the same was reported for adapalene 0.1%. There were no reported serious AEs in either group.

DISCUSSION

Adapalene gel, 0.3% was shown in this *post hoc* analysis to be an effective treatment option for adult female subjects with acne vulgaris compared to vehicle. Dermatologists have reported an increasing number of female patients seeking acne therapy that require effective and tolerable treatment options.[7] Acne in adult women has shown a propensity to be antibiotic resistant and generally difficult to treat.[10–13] Additionally, research shows that more than half of female patients with acne are over the age of 20 years, a subpopulation that has not been extensively studied and requires an effective treatment option.[11,12,26,27] Inflammatory lesions are a common symptom of the two clinical forms described for adult female acne.[27,28] Adapalene gel 0.3% was effective in reducing acne lesions in this subset analysis including the inflammatory lesions. Women are often more concerned than other subjects about tolerability treatment results. Therefore, it is of particular note that the tolerability profiles for adapalene gel 0.3% were similar to that of adapalene gel 0.1% and both were safe and well tolerated from the subjects' perspective.

This was a *post hoc* analysis combining studies not specifically designed to evaluate women subjects. These limitations lend themselves to areas for further research. The conduct of trials with identified specific populations (i.e., adult women) would serve to confirm and expand the findings presented here for adapalene gel 0.3% in treating acne vulgaris.

In summary, based on this *post hoc* analysis, adapalene gel 0.3% was effective, safe, and well tolerated for treating acne vulgaris in adult women, which, to date, has been understudied, but contributes to a significant proportion of subjects with acne.

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