Poster 101

Moisturizer Use Enhances Facial Tolerability of Tazarotene 0.1% Cream Without Compromising Efficacy in Patients With Acne Vulgaris

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INTRODUCTION

The use of any topical retinoid can involve a period of "retinization" in the first few weeks of treatment while the skin is adapting to the retinoid. During this period of acclimatization, some patients transiently experience dryness, erythema, stinging, or peeling on treated skin—which potentially reduces patient compliance and, ultimately, efficacy.[1] Importantly, retinization effects can be avoided or minimized by using a moisturizer,[1,2] applying the retinoid sparingly, and initiating therapy slowly (for example, by using the retinoid in the lowest concentration available and/or by starting with applications every 2 or 3 days before gradually increasing to once-daily applications).[1,3,4] It is also important that the patient uses a gentle skin care regimen. For example, they should use only non-soap-based cleansers and avoid the use of abrasive products, peeling agents, astringents, and other drying products including salicylic acid preparations and harsh soaps and gels.[3-5]

Some patients use a moisturizer in conjunction with topical retinoid treatment and yet, to our knowledge, there has been little or no research evaluating whether this has any impact on efficacy. From a theoretical perspective, it could be argued that the adjunctive use of a moisturizer might impair the absorption of a topical retinoid and therefore reduce its efficacy. However, it could also be argued that, by enhancing tolerability, the moisturizer promotes optimal patient compliance and consequently might enhance efficacy.

We therefore performed a multicenter, investigator-blind, randomized study of patients with facial acne vulgaris to compare the efficacy and tolerability of tazarotene 0.1% cream alone with tazarotene 0.1% cream plus moisturizer.

METHODS

Study design

- Multicenter, investigator-blind, randomized, parallel-group study

Key inclusion criteria

- Mild to moderate facial acne vulgaris, defined as:
  - 15-100 papules plus pustules
  - 15-100 comedones
  - ≤ 2 nodules or cysts
- At least 12 years of age

Key exclusion criteria

- Skin disease or disorder that might interfere with the diagnosis or evaluation of acne vulgaris
- Cosmetic or surgical procedure complementary to the treatment of facial acne (cryotherapy, acne surgery etc.) in preceding 14 days
- Participation in investigational drug study in preceding 30 days
- Pregnancy or breastfeeding
- Not using reliable contraception if a female of childbearing potential

Washout periods

- 14 days for over-the-counter acne products and facial use of topical medications (retinoids, corticosteroids, and prescription acne medications)
- 30 days for antibiotics or corticosteroids indicated for acne vulgaris, or for investigational drugs
- 90 days for estrogens/birth control pills (unless they had already been in use for more than 90 days at study entry and their use would continue unchanged during the study)
- 6 months for systemic retinoids

Treatment regimen

- Patients were randomly assigned (on a 1:2 basis) to one of the following regimens* for 16 weeks:
  - Once-daily tazarotene 0.1% cream
  - Once-daily tazarotene 0.1% cream plus twice-daily moisturizing cream.†
- In the tazarotene plus moisturizer group, the use of moisturizer was mandatory. In the tazarotene alone group, patients were allowed to use a moisturizing lotion† but only if absolutely necessary.
- All subjects were instructed to wash their face twice daily with a hydrating cleanser† and then to rinse it thoroughly with warm water and to pat it dry gently with a soft towel before applying their assigned study product(s).
- Tazarotene was applied only in the evening and patients were instructed to wait at least 5 minutes for it to dry before retiring to bed.
- In the tazarotene plus moisturizer group, patients were instructed to apply the evening dose of moisturizer approximately 20 minutes before the tazarotene.
- During the study period, patients were not permitted to use any antibiotic for more than 14 days or to use tetracycline antibiotics.
- The use of acne medications, skin cleansers, and moisturizers was restricted to those provided as part of the study.
- The use of cosmetics that were not oil-based was permitted although no change in cosmetic use was allowed during the study and no facial cosmetics were allowed to be applied prior to study visits.
- Subjects were advised to limit excessive exposure to ultraviolet light and to use a sunscreen or wide-brimmed hat if exposure was unavoidable.

Outcome measures

- Investigator ratings:
  - Inflammatory lesion count (papules plus pustules)
  - Noninflammatory lesion count (open plus closed comedones)
  - Overall disease severity (Table 1)
  - Dryness, peeling, erythema, perception of oiliness (Table 2)
- Patient ratings:
  - Moisturizer use since the last visit—rated as none, a little (once or twice), occasionally (2-3 times per week), frequently (most days), or always (every day)
  - Burning since the last visit (Table 2)
  - Skin comfort—rated as 0 = very comfortable, 1 = comfortable, 2 = somewhat comfortable, 3 = somewhat uncomfortable, 4 = uncomfortable, or 5 = very uncomfortable
  - Compliance—rated as not compliant (< 50% compliant), mostly compliant (50-75% compliant), or very compliant (> 75% compliant)

Statistical analyses

- Between-group differences were evaluated using the following statistical tests: chi-square test or Fisher's exact test for gender and race; ANOVA or Kruskal-Wallis test for age; Kruskal-Wallis test for level of compliance, moisturizer use, and scores for overall disease severity, dryness, peeling, erythema, burning, perception of oiliness, and skin comfort; and ANCOVA or Rank ANCOVA for percent reduction in lesion count.

** The study also included a third regimen but results from this arm are not presented here as they are not relevant to the objective of this poster (i.e. to report whether the adjunctive use of moisturizer affects the efficacy or tolerability of tazarotene).*

† A patented multivesicular emulsion formulation containing ceramides.

Table 1. Scale used to assess overall disease severity.

Score	Overall disease severity
0	None—clear, no inflammatory lesions
1	Sparse comedones, with very few or no inflammatory lesions present
2	Mild comedones, with some small inflammatory lesions present; minimal erythema
3	Comedones with an increasing number of inflammatory lesions compared to grade 2
4	Moderate comedones, a moderate number of small inflammatory lesions extending over a wide area of the face; erythema is increasing
5	Comedones, an increasing number of inflammatory lesions compared to grade 4, with some larger inflamed lesions
6	Severe, numerous comedones, papules and pustules with larger inflamed lesions extending over much of the face; erythema may be pronounced

Table 2. Scales used to assess dryness, peeling, erythema, burning, and perception of oiliness.

Score	Dryness	Peeling	Erythema	Burning (since the last visit)	Perception of oiliness
0	**Absent** None	**Absent** Smooth	**Absent** No redness	**Absent** Normal, no discomfort	**Normal**
1	**Trace** Barely perceivable dryness by palpation with no accentuation of skin markings, skin desquamation (flakes) or fissure formation	**Trace** Fine peeling, barely perceptible	**Trace** Faint red or pink coloration, barely perceptible	**Trace** An awareness, but no discomfort and no intervention required	**Mild and localized**
2	**Mild** Easily perceptible dryness by palpation with accentuation of skin markings but no skin desquamation (flakes) or fissure formation	**Mild** Slight peeling	**Mild** Light red or pink coloration	**Mild** Noticeable discomfort causing intermittent awareness	**Mild and diffuse**
3	**Moderate** Easily noted dryness with accentuation of skin markings and skin desquamation (small flakes) but no fissure formation	**Moderate** Definitely noticeable peeling	**Moderate** Medium red coloration	**Moderate** Noticeable discomfort causing continuous awareness	**Moderate and diffuse**
4	**Severe** Easily noted dryness with accentuation of skin markings, skin desquamation (large flakes) and/or fissure formation	**Severe** Extensive peeling	**Severe** Beet red coloration	**Marked** Definite discomfort causing continuous awareness interfering occasionally with normal daily activities	**Prominent and dense**
5	—	—	—	**Severe** Definite, continuous discomfort interfering with normal daily activities	—

RESULTS

Patients

- 119 patients were enrolled to receive one of the tazarotene regimens (39 tazarotene alone, 80 tazarotene + moisturizer), of whom:
  - 96 (81%) completed
  - 2 (2%) discontinued due to lack of efficacy (1 in each group)
  - 1 (1%) discontinued due to adverse events (peeling, redness, and burning—whose relationship to treatment was considered unknown—in a patient in the tazarotene + moisturizer group)
  - 20 (17%) discontinued due to loss to follow-up (13), withdrawal of consent (6), or other reasons (1).
- There were no significant between-group differences in demographic details.
- At baseline, the mean papule plus pustule count was 22 in both groups and the mean comedo count was 36 (tazarotene group) or 38 (tazarotene + moisturizer group).
- Mean levels of compliance were between "mostly compliant" and "very compliant" in both groups throughout the study. There were no significant between-group differences in the degree of compliance.
- Moisturizer use was significantly greater in the tazarotene + moisturizer group than in the tazarotene alone group (P≤.001). At week 2, mean levels of use were between "frequently" and "always" in the tazarotene + moisturizer group and between "a little" and "occasionally" in the tazarotene alone group.

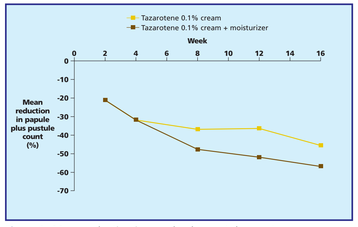

Figure 1. Mean reduction in papule plus pustule count.

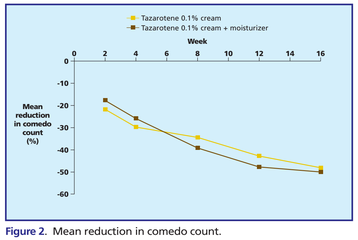

Figure 2. Mean reduction in comedo count.

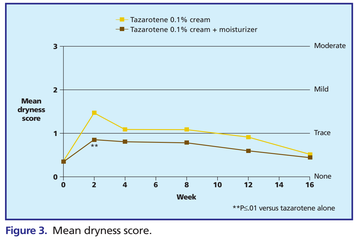

Figure 3. Mean dryness score.

Efficacy

- The reduction in lesion counts with tazarotene + moisturizer was at least as great as that with tazarotene alone at week 16:
  - 57% vs. 46%, respectively, for papules plus pustules (Figure 1)
  - 50% vs. 48%, respectively, for comedones (Figure 2).
- Both regimens were associated with a comparable reduction in mean overall disease severity score.

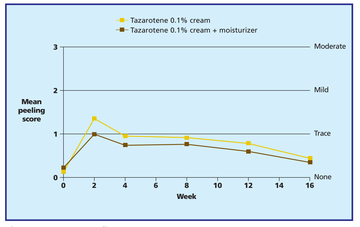

Figure 4. Mean peeling score.

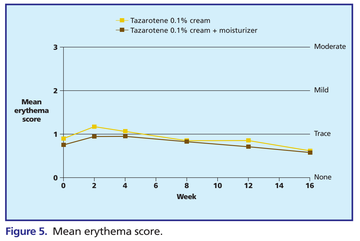

Figure 5. Mean erythema score.

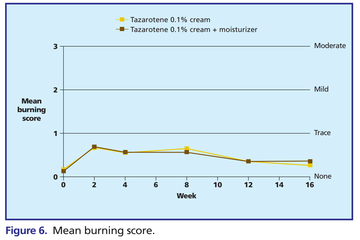

Figure 6. Mean burning score.

Tolerability

- No adverse events considered probably or definitely related to treatment were reported.
- Mean scores for dryness were consistently lower with tazarotene + moisturizer than with tazarotene alone, with the difference being significant at week 2 (P≤.01; Figure 3). The mean level of dryness at week 2 was "none to trace" with tazarotene + moisturizer and "trace to mild" with tazarotene alone.
- Mean scores for peeling and erythema were also consistently lower with tazarotene + moisturizer than with tazarotene alone, although there were no significant between-group differences (Figures 4 and 5).
- Mean scores for burning (Figure 6) were almost identical with both regimens and remained at "none to trace" throughout the study.
- Mean scores for perception of oiliness were reduced similarly with both regimens from "trace" at baseline to "none to trace" at all subsequent timepoints.
- Both regimens showed comparable improvements in skin comfort.

CONCLUSIONS

Treatment with tazarotene 0.1% cream was generally well tolerated, with or without the adjunctive use of a moisturizer. The transient increase in mean dryness levels during the retinization period was small (mean levels peaked at "trace" to "mild" in the tazarotene alone group) and was likely not sufficient to trigger moisturizer use in many patients. Indeed, the average usage of moisturizer in the tazarotene alone group was reported to be no more than occasional, which appears to confirm that the patients in this group did not experience troublesome levels of dryness.

Although the increase in dryness was small, the adjunctive use of a moisturizer was effective in helping to prevent it. Importantly, this enhancement in the tolerability of tazarotene 0.1% cream was achieved without compromising efficacy.

Patients are most likely to discontinue topical retinoid therapy during the initial retinization period and it appears likely that, in everyday clinical practice (i.e. outside the confines of a clinical protocol), the adjunctive use of a moisturizer during this period may help enhance compliance, prevent premature discontinuations, and potentially enhance efficacy.

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DISCLOSURES

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