Efficacy and Tolerability of Once-Daily Tazarotene 0.1% Gel Versus Once-Daily Tretinoin 0.025% Gel in the Treatment of Facial Acne Vulgaris: A Randomized Trial

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Tazarotene 0.1% gel and tretinoin 0.025% gel are both effective in the treatment of acne vulgaris. Results of a multicenter, double-blind, randomized, parallel-group study that compared the efficacy and tolerability of these drugs are presented here. A total of 143 patients with mild-to-moderate facial acne vulgaris were randomized to receive tazarotene 0.1% gel or tretinoin 0.025% gel once daily for 12 weeks. Tazarotene 0.1% gel was more effective than tretinoin 0.025% gel in reducing the open comedo count ($P \leq .05$), the total noninflammatory lesion count ($P \leq .05$), and the total inflammatory lesion count (not statistically significant). At some time points, tazarotene was associated with increased irritation, but peeling, erythema, dryness, burning, and itching never exceeded trace levels. We conclude that tazarotene 0.1% gel is more effective than tretinoin 0.025% gel in reducing noninflammatory lesions and similarly effective in reducing inflammatory lesions.

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Anticomedonal therapy is central to long-term control of acne vulgaris.[1] Tretinoin has been the predominant anticomedonal medication, but other products have been introduced in recent years. Tazarotene 0.1% gel was approved by the US Food and Drug Administration for the treatment of mild-to-moderate facial acne vulgaris in 1997 and is effective in the treatment of both noninflammatory and inflammatory acne.[2] Although previous clinical trials have compared tazarotene or tretinoin gels with vehicle[2,3] or other retinoids,[4,5] the only known direct comparison of tazarotene with tretinoin in a controlled setting has been a recent facial tolerability study in healthy volunteers.[6] To provide further comparative data, a multicenter, double-blind, randomized, parallel-group clinical trial has been performed to compare the efficacy and tolerability of once-daily applications of tazarotene 0.1% gel and tretinoin 0.025% gel in patients with facial acne vulgaris.

Methods

Patients—Patients with mild-to-moderate facial acne vulgaris who were at least 12 years of age were eligible for recruitment into this multicenter, double-blind, randomized, parallel-group clinical trial. Mild-to-moderate acne vulgaris was defined as 10 to 60 facial inflammatory lesions (papules and pustules), 10 to 200 facial noninflammatory lesions (open and closed

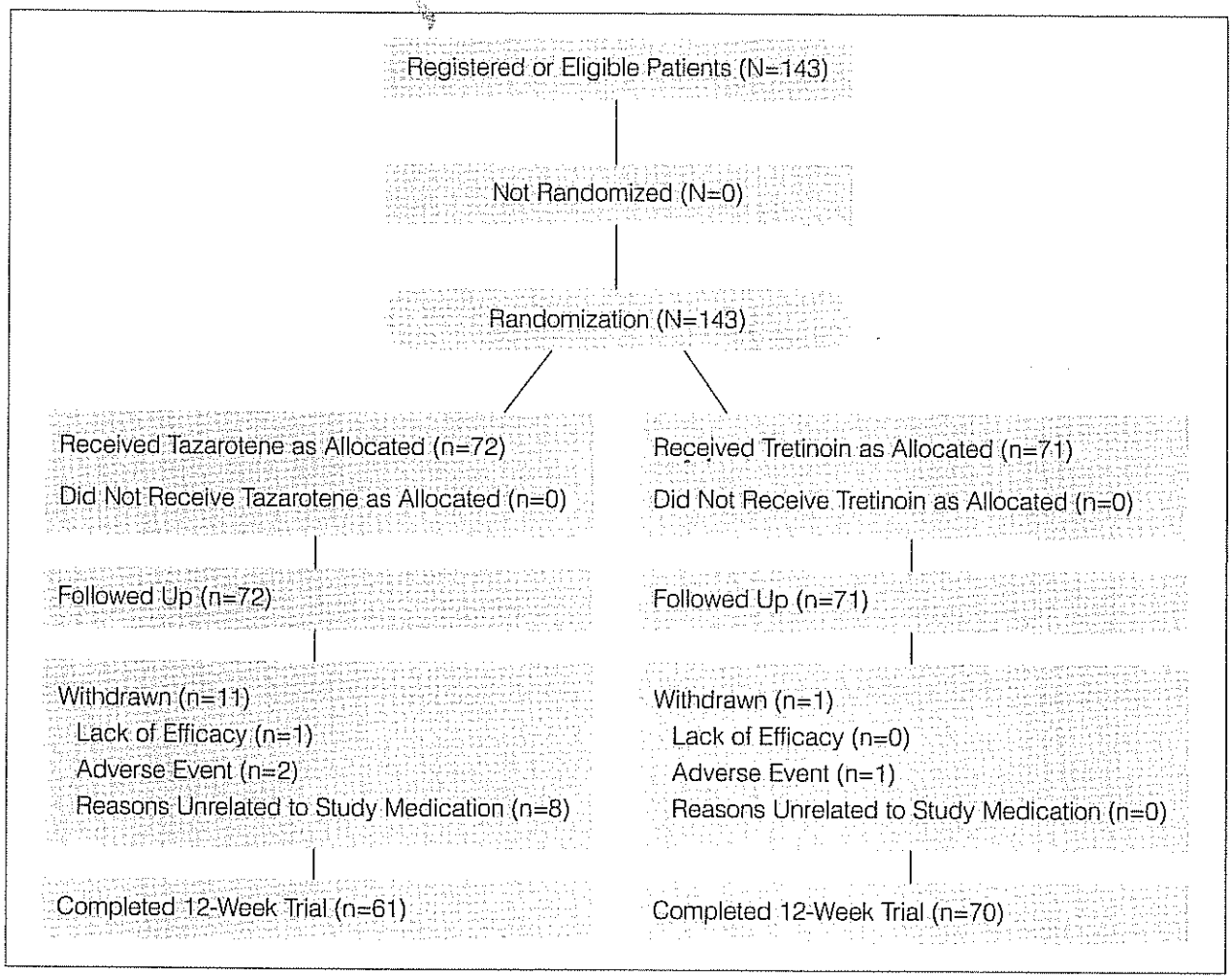

Figure 1. Flow diagram of subjects enrolled in the trial.

comedos), and no more than 2 facial nodular cystic lesions (none >5 mm in diameter).

The following washout periods were required: 14 days for other topical antiacne medications, 30 days for systemic antibiotics, and 2 years for oral retinoids. Exclusion criteria included any uncontrolled systemic disease; known hypersensitivity to any of the components of the study medications; use of any topical medicated creams, lotions, powders, or solutions (other than the study medication) during the study period; acne vulgaris known to be resistant to oral antibiotics; use of estrogens or birth control pills for less than 12 weeks prior to study entry; presence of any skin disease that might interfere with the diagnosis or evaluation of acne vulgaris; participation in another study within 30 days of study entry; and pregnancy, lactation, or intent to become pregnant during the study. Females of childbearing potential were required to use a reliable form of contraception throughout the study.

Approval was obtained from the appropriate internal review boards, and written informed consent was obtained from each patient or legal guardian.

Treatment Regimen—Subjects were randomized to receive 1 of 2 treatments: tazarotene 0.1% gel or tretinoin 0.025% gel. Study medications were applied once a day, in the evening, for a total of 12 weeks.

Prior to each application of study medication, subjects were instructed to wash their faces with a nonmedicated nonsoap cleanser, to rinse thoroughly, and to pat dry with a soft towel. After 15 to 20 minutes, each subject was instructed to apply the study medication to the face by placing a pea-sized amount of the gel on the tip of the finger, and placing a dab of the gel on the forehead, each cheek, and chin. The gel was then spread gently in a thin film over the entire face. Subjects were supplied with, and encouraged to use, a noncomedogenic moisturizer as needed for dryness.

Randomization and Masking Procedures—The statistician of the independent clinical research

Patient Demographics at Baseline

	Tazarotene (N=72)	Tretinoin (N=71)
Age in years, mean±SD	23±10	22±9
Females	71%	63%
Race, n (%)*		
White	42 (60)	43 (61)
Black	21 (30)	21 (30)
Asian	4 (6)	1 (1)
Hispanic	3 (4)	1 (1)
Other	0 (0)	4 (6)
Skin type, n (%)†		
Oily	20 (28)	15 (21)
Normal to oily	26 (36)	41 (59)
Normal	8 (11)	7 (10)
Normal to dry	7 (10)	3 (4)
Dry	2 (3)	1 (1)
Mixed (oily/dry)	9 (13)	3 (4)
Duration of acne, n (%)		
<1 y	3 (4)	6 (9)
1–2 y	16 (22)	13 (18)
3–5 y	21 (29)	17 (24)
6–10 y	11 (15)	15 (21)
>10 y	21 (29)	20 (28)
Total open and closed comedos	36	28
Total papules, pustules, and nodules	22	21

*Data is unavailable for 2 patients in the tazarotene group and 1 patient in the tretinoin group.

†Data is unavailable for 1 patient in the tretinoin group.

organization produced a computer-generated treatment allocation list using software from the SAS Institute, Inc. This randomization code was used to prepare, under Good Manufacturing Practices, one medication kit per subject containing the assigned treatment. Subjects were assigned the medication kits chronologically, as they enrolled in the study.

The randomization code for each subject was kept in tamper-evident sealed envelopes at the clinical research organization for emergency code breaks. No emergency code breaks were requested by the investigators during the trial. A second copy of the randomization code was kept securely with the statistician of the clinical research organization off-site. The investigation sites and all persons working on the study did not have access to the codes at any time during the study.

Blinding was maintained by labeling the study medications with opaque, permanent adhesive labels. Medication was dispensed to each subject periodically throughout the study in presealed cardboard boxes.

Patient Evaluations—The following demographic details were recorded at baseline: age, gender, race, duration of acne, and skin type. Skin type was classified according to the investigator's opinion of the subject's skin type as oily, normal to oily, normal, normal to dry, dry, or mixed.

The numbers of open comedos, closed comedos, papules, pustules, and nodules were counted by the

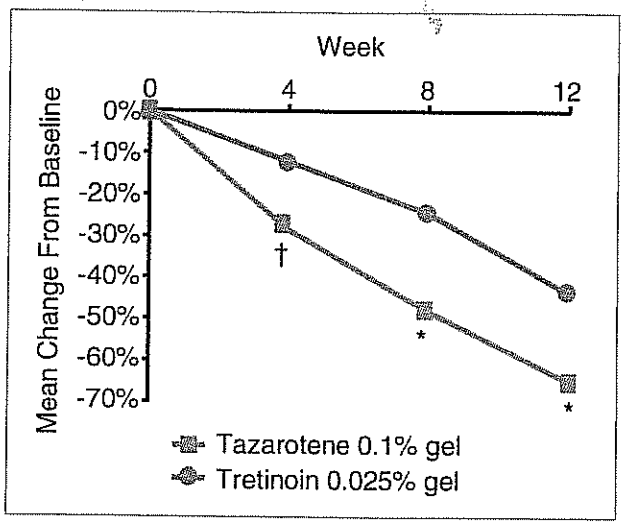

Figure 2. Reduction in number of open comedos following once-daily applications of tazarotene 0.1% gel or tretinoin 0.025% gel. Asterisk indicates $P \leq .05$; dagger, $P \leq .01$ versus tretinoin.

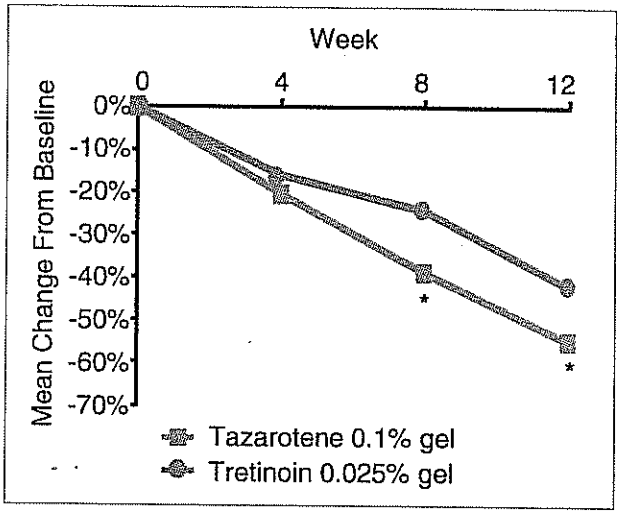

Figure 3. Reduction in total number of noninflammatory lesions (open and closed comedos) following once-daily applications of tazarotene 0.1% gel or tretinoin 0.025% gel. Asterisk indicates $P \leq .05$ versus tretinoin.

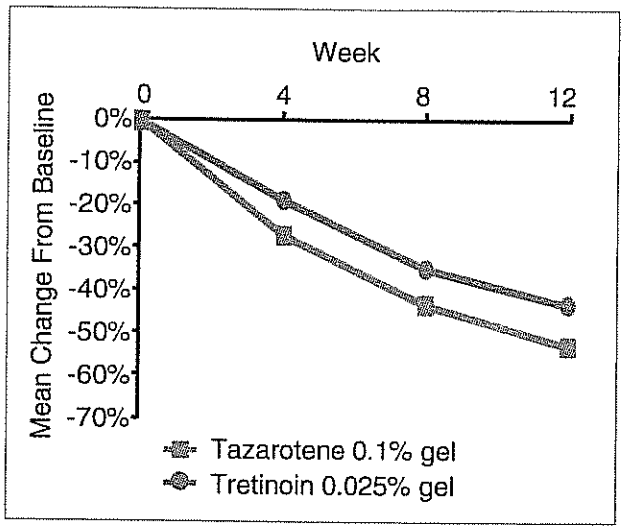

Figure 4. Reduction in total number of inflammatory lesions (papules, pustules, and nodules) following once-daily applications of tazarotene 0.1% gel or tretinoin 0.025% gel (no statistical significance).

investigator at baseline (week 0) and at weeks 4, 8, and 12. In addition, the severity of peeling, erythema, dryness, and burning on the subjects' treated skin was evaluated by the investigator at each visit using the following scale: 0=none (normal), 1=trace (mild and localized), 2=mild (mild and diffuse), 3=moderate (moderate and diffuse), 4=marked (moderate and dense), or 5=severe (prominent and dense).

Statistical Analysis—Analyses were performed on an intent-to-treat basis, and between-group differences were analyzed using the *t* test. A *P* value of ≤.05 was considered to be statistically significant.

Results

Patient Demographics—A total of 143 subjects were enrolled, of whom 131 (92%) completed the 12-week treatment regimen (Figure 1). Subjects ranged in age from 7 to 56 years. Most were female, white or black, and had oily or normal-to-oily skin (Table). Both treatment groups were comparable at baseline with respect to patient demographics and lesions.

Efficacy—Tazarotene achieved significantly greater reductions in open comedo count than tretinoin at all time points (Figure 2). The reductions in open comedo count were also more rapid with tazarotene than with tretinoin. At the end of the treatment period, the mean reduction in open comedo count was 21 percentage points greater with tazarotene than with tretinoin (65% vs 44%; $P=.034$). Tazarotene was also significantly more effective in reducing the total number of noninflammatory lesions (open and closed comedos) at weeks 8 and 12 (Figure 3). At the end of the treatment period, the mean reduction in the total number of noninflammatory lesions was 13 percentage points greater with tazarotene than with tretinoin (55% vs 42%; $P=.042$).

Tazarotene treatment also was associated with a greater reduction in the total number of inflammatory lesions (papules, pustules, and nodules) than tretinoin treatment at all time points (Figure 4). At the end of the treatment period, the mean reduction in total inflammatory count was 10 percentage points greater with tazarotene than with tretinoin (54% vs 44%; not statistically significant).

Mean levels of peeling, erythema, dryness, and burning were similar in both treatment groups and

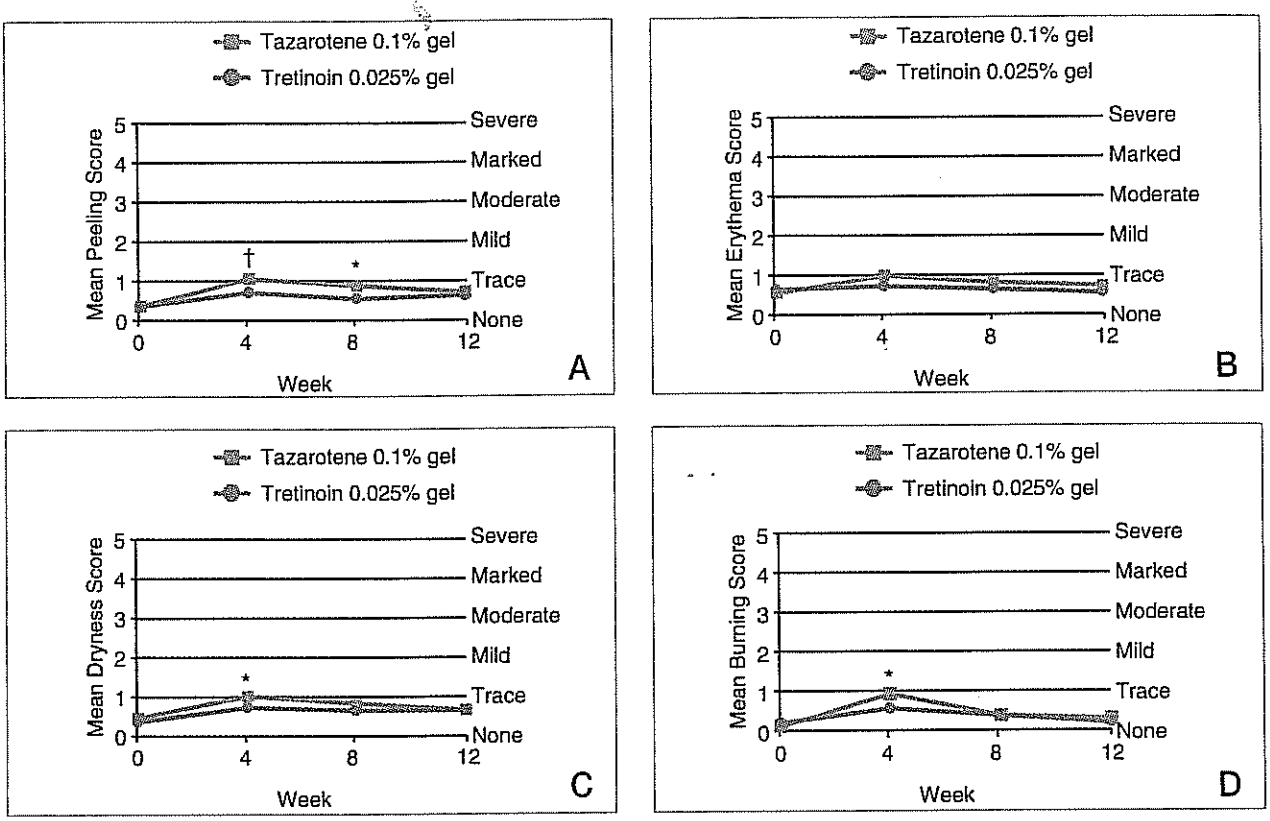

Figure 5. Mean levels of peeling (A), erythema (B), dryness (C), and burning (D) following once-daily applications of tazarotene 0.1% gel or tretinoin 0.025% gel. Asterisk indicates $P \leq .05$; dagger, $P \leq .01$ versus tretinoin.

were never more severe than trace (Figure 5, A through D). Significant but transient increases in peeling, dryness, and burning were evident at week 4 but subsided in subsequent weeks.

Tolerability—The percentage of subjects experiencing adverse events that were probably or definitely treatment related was 21% in the tazarotene group and 7% in the tretinoin group. The most common adverse events in the tazarotene group were a burning sensation (7% of patients), xerosis (6%), irritation (6%), erythema (4%), peeling (1%), and dermatitis (1%). The most common adverse events in the tretinoin group were a burning sensation (3%), xerosis (3%), irritation (3%), and pruritus (1%).

Patient Discontinuations—Three subjects discontinued the study because of treatment-related adverse events: 2 (3%) in the tazarotene group (because of mild erythema, peeling, and irritation in 1 patient and moderate facial dermatitis in the other patient) and 1 (1%) in the tretinoin group (reason for withdrawal unknown).

One patient in the tazarotene group (1%) discontinued due to lack of efficacy, and an additional 8 patients (11%) discontinued for reasons unrelated to the study medication (all in the tazarotene group): missed visits (3), unknown (2), personal reasons (1), relocation (1), and concomitant therapy (1).

Comment

Tazarotene-treated patients achieved a significantly greater reduction in the total number of noninflammatory lesions, and open comedos in particular, compared with tretinoin-treated patients. Tazarotene-treated patients also achieved consistently greater reductions in the total number of inflammatory lesions, although these differences did not attain statistical significance.

The tolerability of tazarotene 0.1% gel was comparable with that of tretinoin 0.025% gel, with levels of peeling, erythema, dryness, and burning reported by the investigators to be no more than trace in both treatment groups throughout the study. The incidence of patients discontinuing treatment early as a result of adverse events (≤3% in both treatment groups) was lower than those previously reported with once-daily applications of tazarotene 0.1% or 0.05% gel.[2] This may be attributable to the fact that only this study specified in the patient instructions that the face should be washed using a gentle nonsoap cleanser; no more than a pea-sized amount of tazarotene gel should be applied; and a noncomedogenic moisturizer should be used, as needed, for dryness. In addition to the data from this and other studies, clinical experience also indicates that, with an appropriate application technique, the facial

tolerability of tazarotene is comparable with other topical retinoids used to treat acne, including tretinoin 0.1% gel microsponge, tretinoin 0.025% gel, and adapalene 0.1% gel.[6]

In summary, this study showed that tazarotene 0.1% gel is more effective than tretinoin 0.025% gel in reducing noninflammatory lesions and also achieves a more rapid improvement in these lesions. Both drugs were similarly effective in reducing inflammatory lesions, and both were well tolerated with the use of a nonsoap cleanser and noncomedogenic moisturizer.

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