# A Comparative Evaluation of Tretinoin Gel Microsphere, 0.1%, versus Tretinoin Cream, 0.025%, in Reducing Facial Shine

Judit Nyirady, MD, Skillman, New Jersey
Margaret Nighland, Skillman, New Jersey
Gregory Payonk, PhD, Skillman, New Jersey
Jeffrey Pote, BS, Skillman, New Jersey
Steven Phillips, MS, Skillman, New Jersey
Rachel Grossman, MD, Skillman, New Jersey

*Tretinoin gel microsphere, 0.1%, is a highly effective anti-acne medication formulated with sponge-like microspheres encapsulating the active ingredient, tretinoin. In addition to minimizing cutaneous irritation, this system may also reduce facial shine. This single-center, double-blind, half-face study evaluated the potential of tretinoin gel microsphere, 0.1%, to reduce the appearance of facial shine compared to tretinoin cream, 0.025%. Thirty-five subjects (ages 12 to 24 years) with moderate acne vulgaris and moderate facial oiliness, were evaluated after 4 consecutive days of product use. On sides treated with tretinoin gel microsphere, 0.1%, investigators found significantly reduced facial shine at 3 and 6 hours post-treatment. Subjects' self-evaluations revealed a significant reduction in facial shine at 3 hours posttreatment. Photographic analyses showed reductions in facial shine for both treatments, but decreases were greater on tretinoin gel microsphere, 0.1%-treated sides. Both therapies were well tolerated, and no adverse events occurred. Tretinoin gel microsphere, 0.1%, has the added benefit of reducing the appearance of facial shine, which is a frequent concern in acne patients.*

Dr. Nyirady is Director, Medical Affairs; M. Nighland is Clinical Project Manager, Medical Affairs; Dr. Payonk is a Research Fellow, Model and Method Development; J. Pote is a Senior Scientist, Model and Method Development; S. Phillips is a Manager, Statistical Services; and Dr. Grossman is Worldwide Medical Director, Research and Development, Johnson & Johnson Consumer Products Worldwide, Skillman, New Jersey. REPRINT REQUESTS to Director, Medical Affairs, Johnson & Johnson Consumer Products Worldwide, 199 Grandview Road, Skillman, NJ 08558-9418 (Dr. Nyirady).

Acne vulgaris, an inflammatory disorder of the pilosebaceous units of the face, neck, and trunk,[1] is the most common skin disorder treated by physicians.[2] Although a variety of topical and systemic prescription medications, as well as topical over-the-counter drugs, are used to treat acne vulgaris,[3] retinoids are the only topical anti-acne agents believed to be effective against the microcomedone, the precursor lesion in acne vulgaris.[4,5] The effectiveness of topical tretinoin, the first of the retinoids to become commercially available, is well established, yet the associated skin irritation may be a limiting factor in some patients.[6,7] Tretinoin gel microsphere, 0.1%, a tretinoin microsponge formulation, was developed with the goal of minimizing cutaneous irritation while maintaining efficacy.[6] In this novel formulation, the active ingredient is entrapped in porous polymeric microspheres that serve as a reservoir, releasing the active ingredient into the vehicle, and thus reducing irritation.[6] The present study evaluated whether the sponge-like quality of tretinoin gel microsphere, 0.1%, reduces the appearance of facial shine compared to tretinoin cream, 0.025%.

## Methods

*Study Sample*—Subjects with moderate facial acne vulgaris [10 to 50 inflammatory lesions (papules and

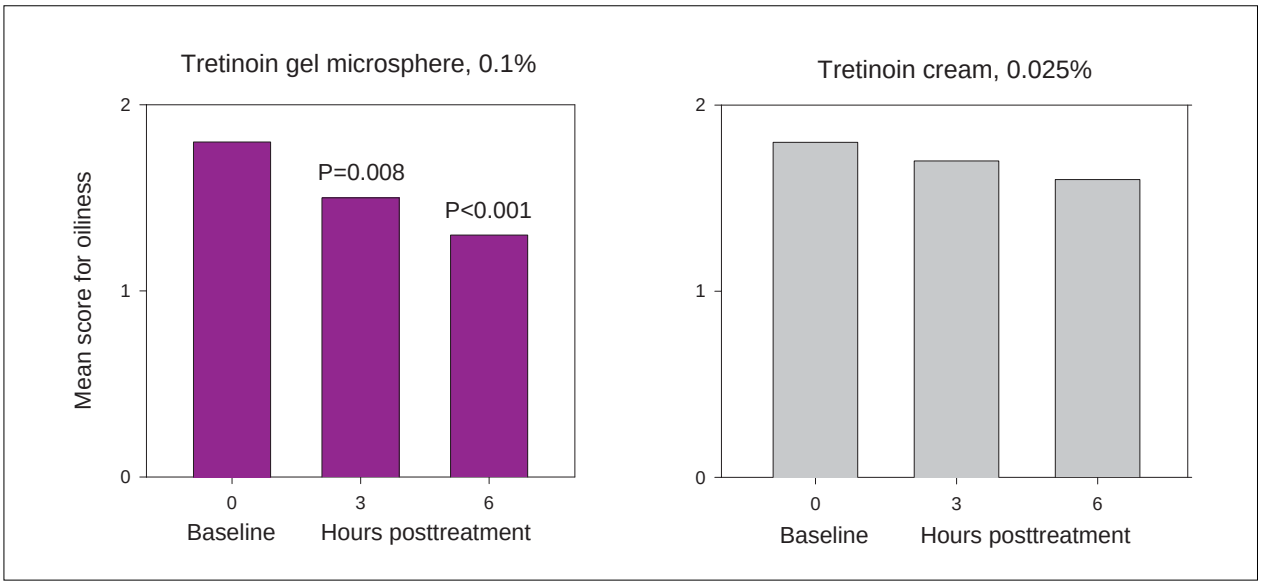


**FIGURE 1.** Study coordinator's assessment of facial oiliness. Tretinoin gel microsphere, 0.1%, showed significant changes from baseline at 3 and 6 hours posttreatment.

pustules, no nodular lesions)] were eligible to enroll in a single-center, double-blind, half-face study to compare the potential of tretinoin gel microsphere, 0.1%, versus tretinoin cream, 0.025%, to reduce the appearance of facial oiliness (shine). Healthy men and women between the ages of 12 and 35 years were eligible for enrollment if their baseline scores for facial oil presence were greater than or equal to 2 on a 4-point grading scale (0=none, 1=mild, 2=moderate, 3=very oily) as assessed by the study coordinator.

Subjects with pre-existing skin disease other than acne vulgaris or with known hypersensitivity to any of the formulation components were excluded. Other exclusion criteria included the use of systemic retinoids within 3 months before study entry, topical retinoids within 2 weeks of study entry, other topical facial medications that could influence the outcome of the study within 1 week of study entry, emollients 12 hours before study entry, or cosmetics on the day of study evaluation, and any known photosensitizing agent. Women who were pregnant, nursing, or of childbearing potential and not using a reliable form of contraception also were excluded.

Prior to initiation of the study, Institutional Review Board approval was obtained and each subject was completely informed according to Informed Consent Guidelines. Written informed consent was obtained from each participant.

*Study Procedures*—Each subject was randomly assigned to apply tretinoin gel microsphere, 0.1%, to one side of the face and tretinoin cream, 0.025%, to the other side of the face. Subjects visited the study site once daily for 3 consecutive days, at which times they cleansed their faces and applied the assigned treatments under the supervision of study personnel. Following facial cleansing on day 4, half-face baseline photographs were taken. At that time, the study coordinator and subjects used a 4-point scale [0=none, 1=mild (very little), 2=moderate, 3=severe (very oily)] to assess facial oiliness on both sides of each patient's face. At 3 and 6 hours following product application, the same photographic procedures and evaluations by the study coordinator and by the subjects were performed. Cutaneous treatment effects and adverse events were noted at each visit by the study coordinator.

*Photographic Methodology*—Photographic images were obtained using a high-resolution digital camera and a visible strobe. Standardized procedures allowed reproducible positioning of the subject, camera, and illumination source over time. The photographs taken on day 4 at baseline and at 3 and 6 hours after application of therapy were analyzed using image analysis software that scans the photographic image and counts the number of "bright" pixels, which are associated with appearance of facial shine. Reductions in the number of "bright" pixels were considered to reflect reduced facial shine.

*Statistical Methodology*—Outcome variables included changes in the study coordinator's and subjects' ratings of facial oiliness between assessments, and change in the number of "bright" pixels in photographs between measurements. Baseline evaluations were made on day 4 after the face had been

washed but before therapies were applied. For each subject and treatment area, changes from baseline at 3 and 6 hours posttreatment were calculated and analyzed separately. The statistical significance of changes within treatments was tested using the two-tailed Wilcoxon matched-pair signed rank test for ordinal ratings and the paired *t* test for "bright" pixel counts.[8] Changes from baseline in outcomes were compared between the two treatments using Wilcoxon matched-pair signed rank tests for ordinal ratings and analysis of variance (subjects, therapies) for "bright" pixel counts; *P* values <0.05 were considered statistically significant.

## Results

Thirty-six subjects met all eligibility criteria and were randomly selected. Overall, 77.8% of subjects were male and 88.9% were Caucasian. Subjects ranged in age from 12 to 24 years, with a mean age of 16.0 years. At the start of the study, all had at least moderate acne vulgaris with between 10 and 47 facial inflammatory lesions. One subject did not present for evaluation on day 4 and was discontinued from the study.

At baseline, the study coordinator's ratings showed 77.2% of facial sides treated with tretinoin gel microsphere, 0.1%, and 80.0% of those treated with tretinoin cream, 0.025%, exhibited moderate or severe oiliness (difference not significant). Mean scores for the two groups were identical at baseline. In contrast, 45.7% and 34.3% of sides receiving tretinoin gel microsphere, 0.1% were rated as moderately or severely oily after 3 and 6 hours, respectively (change from baseline: $P = 0.008$ and $P < 0.001$) (Figure 1). Smaller, not statistically significant declines in oiliness occurred at both time points on the sides treated with tretinoin cream, 0.025%. At 3 hours, the change from baseline oiliness was significantly greater for sides treated with tretinoin gel microsphere, 0.1%, than for sides receiving tretinoin cream, 0.025% ($P = 0.048$). At 6 hours, this trend continued ($P = 0.096$).

Subjects' self-evaluations also showed a statistically significant decrease in facial oiliness for sides treated with tretinoin gel microsphere, 0.1%, at 3 hours posttreatment ($P = 0.023$) and a nearly significant decrease at 6 hours posttreatment ($P = 0.057$). Changes from baseline for sides treated with tretinoin cream, 0.025%, were not significant at either follow-up time. The difference between the effects of the two therapies was significant 3 hours posttreatment ($P = 0.011$) and marginally so after 6 hours ($P = 0.077$).

The number of "bright" pixels counted in the digital photographs decreased significantly in both treatment groups at each follow-up interval. Declines from baseline at 3 and 6 hours posttreatment were 5.3% and 9.1% for sides receiving tretinoin gel microsphere, 0.1% ($P < 0.001$ for both), and 4.5% and 7.1% for sides treated with tretinoin cream, 0.025% ($P = 0.035$ and $P < 0.001$, respectively). Changes in "bright" pixel counts were not significantly different between groups at either time point.

No adverse events were reported at any time during the study. Mild erythema ($n = 7$) and peeling ($n=3$) were observed in some subjects.

## Discussion

Acne vulgaris, a skin disorder common in adolescence, may be considered a rite of passage, but its potentially negative psychosocial consequences, including diminished self-esteem, depression, and social withdrawal, should not be underestimated.[9] Acne is not limited to adolescents, however, and the quality of life of affected adults also has been found to be diminished by the condition.[10] Fortunately, effectively treating acne vulgaris improves patients' psychosocial functioning,[11] and physicians have at their disposal a wide variety of therapies for acne. Substantial patient dissatisfaction with currently available treatments exists, however, and the relative cosmetic effects of various therapies have rarely been compared.

Topical tretinoin, believed to be the most effective topical comedolytic agent,[4] is frequently used in patients with mild to moderate acne vulgaris. Tretinoin acts by reversing the process of abnormal follicular keratinization and reducing microcomedone formation. A reduction in the number of microcomedones, as well as a change in keratinization, may result in a decrease in the number of inflammatory lesions. A microencapsulated form of tretinoin, tretinoin gel microsphere, 0.1%, has been developed to minimize the skin irritation (erythema, peeling, burning) that often accompanies the use of tretinoin.[6]

The present study tested whether the sponge-like quality of tretinoin gel microsphere, 0.1%, also reduces facial oiliness or shine, a condition that often accompanies acne and that may contribute to the psychosocial difficulties experienced by patients with acne vulgaris. Independent but similar ratings of facial oiliness by the study coordinator and by the subjects themselves demonstrated that tretinoin gel microsphere significantly reduces facial shine compared both with baseline values and with the tretinoin cream formulation tested. These subjective evaluations were supported by results of photographic analyses that showed greater reductions in facial shine on sides treated with tretinoin gel microsphere, 0.1%.

In conclusion, tretinoin gel microsphere, 0.1%, which effectively treats mild to moderate acne vulgaris while minimizing cutaneous irritation, also reduces the appearance of facial oiliness or shine. In choosing an anti-acne medication, physicians and patients should consider that the sponge-like quality of this formulation has the added benefit of reducing the appearance of facial shine, a condition that is often a concern among acne vulgaris patients.

**Product Information—**Tretinoin gel microsphere, 0.1%; RETIN-A® MICRO™ (tretinoin gel), microsphere, 0.1%, and tretinoin cream, 0.025%; RETIN-A® (tretinoin) Cream 0.025% are both products of Ortho Dermatological Division Ortho-McNeil Pharmaceutical, Inc.

## REFERENCES


1. Kligman AM, Plewig G: Classification of acne. *Cutis* 17: 520-522, 1976.
2. Pochi PE: The pathogenesis and treatment of acne. *Annu Rev Med* 41: 187-198, 1990.
3. Lever L, Marks R: Current views on the aetiology, pathogenesis and treatment of acne vulgaris. *Drugs* 39: 681- 692, 1990.
4. Brown SK, Shalita AR: Acne vulgaris. *Lancet* 351: 1871-1876, 1998.
5. Gollnick H, Schramm M: Topical drug treatment in acne. *Dermatology* 196: 119-125, 1998.
6. Leyden JJ: Topical treatment of acne vulgaris: retinoids and cutaneous irritation. *J Am Acad Dermatol* 38: S1-S4, 1998.
7. Webster GF: Topical tretinoin in acne therapy. *J Am Acad Dermatol* 39: S38-S44, 1998.
8. Dawson-Saunders B, Trapp RG: Basic and Clinical Biostatistics. Norwalk, CT, Appleton & Lange, 1990.
9. Koo J: The psychosocial impact of acne: patients' perceptions. *J Am Acad Dermatol* 32: S26-S30, 1995.
10. Lasek RJ, Chren M-M: Acne vulgaris and the quality of life in adult dermatology patients. *Arch Dermatol* 134: 454- 458, 1998.
11. Newton JN, Mallon E, Klassen A, *et al*: The effectiveness of acne treatment: an assessment by patients of the outcome of therapy. *Br J Dermatol* 137: 563-567, 1997.