A Comparison of 15% Azelaic Acid Gel and 0.75% Metronidazole Gel in the Topical Treatment of Papulopustular Rosacea

Results of a Randomized Trial

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Objective: To compare the efficacy and safety of a novel formulation of 15% azelaic acid gel (Finacea; Berlex Laboratories, Inc, Montville, NJ) with 0.75% metronidazole gel (MetroGel; Galderma Laboratories LP, Fort Worth, Tex) as topical therapy for moderate, papulopustular facial rosacea.

Design: Multicenter, double-blind, randomized, parallel-group study.

Setting: Thirteen US centers.

Patients: A total of 251 patients with papulopustular rosacea with persistent erythema and telangiectasia.

Interventions: Patients were randomized to receive azelaic acid gel or metronidazole gel twice daily for 15 weeks.

Main Outcome Measures: Nominal and percent change in inflammatory lesion count, change in erythema and telangiectasia severity ratings, investigator’s global assessment of rosacea, and investigator’s and patient’s overall improvement ratings.

Results: Azelaic acid gel was superior to metronidazole gel in reduction of mean nominal lesion count (−12.9 vs −10.7, respectively) (P = .003) and mean percent decrease in inflammatory lesions (−72.7% vs −55.8%, respectively) (P < .001). With respect to erythema severity, 56% of azelaic acid gel–treated patients were rated improved vs 42% of metronidazole gel–treated patients (P = .02). The effectiveness of metronidazole gel on these variables seemed to plateau after week 8, whereas azelaic acid gel demonstrated progressive improvement through week 15. Neither treatment had a clinically appreciable effect on telangiectasia. Both the investigator’s global assessment (P = .02) and overall assessment of improvement (P = .005) showed a significant therapeutic advantage for azelaic acid gel. Azelaic acid gel also scored higher on the patient’s overall assessment of efficacy. Both treatments were rated as having high cosmetic acceptability. No serious or systemic treatment–related adverse events were reported in either group.

Conclusion: Use of 15% azelaic acid gel twice daily for 15 weeks demonstrated significant superiority over using 0.75% metronidazole gel in improving principal signs of rosacea (inflammatory lesions and erythema).

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OSACEA IS a chronic dermatosis characterized by facial flushing, erythema, telangiectasia, inflammatory episodes with papules and pustules, and, in severe cases, rhinophyma. It most commonly becomes manifest in patients between the ages of 30 and 60 years. Previously, 3 stages of rosacea were described: stage 1, characterized by transient erythema lasting several hours or days and early telangiectasia; stage 2, characterized by papules, pustules and persistent erythema, and telangiectasia; and stage 3, characterized by large inflammatory nodules and tissue hyperplasia, including phymas. Recently, another classification system of rosacea has been introduced that distinguishes 4 different subtypes (erythematotelangiectatic, papulopustular, phymatous, and ocular rosacea), describing the most common patterns of signs. The etiology of rosacea is not understood; pathophysiologic findings include lack of tissue support and widening of dermal vessels, inflammation, and fibromatous proliferation in the dermis.

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Whereas no pharmacologic treatment of the vascular component of rosacea is known, inflammatory papules and pustules and, to some extent, persistent erythema of stage 2 rosacea react favorably to select topical antimicrobials. Their mechanism of action in rosacea is not known, since no microbiologic cause of rosacea has conclusively been identified.
Metronidazole preparations are most commonly used as monotherapy or in combination with oral tetracyclines. Additionally, other topical antibiotics and sulfaacetamide have been used to treat stage 2 rosacea. Due to the chronic nature of rosacea, there is a continuing need for efficacious treatments that provide sustained relief of its principal signs.

Azelaic acid is a naturally occurring dicarboxylic acid (HOOC-[CH2]7-COOH). It is currently used as a topical 20% cream to treat mild to moderate forms of acne vulgaris; its antibacterial and comedolytic activity is responsible mainly for its beneficial effects. However, controlled comparisons with either placebo or topical metronidazole have indicated that 20% azelaic acid cream also has therapeutic effects in rosacea. A direct anti-inflammatory effect of azelaic acid, by inhibition of neutrophil-generated reactive oxygen radicals, may account for this beneficial effect.

A novel 15% gel formulation of azelaic acid has recently been developed that optimizes galenical properties for greater drug delivery and improved bioavailability. The scope of the present study was to investigate the efficacy, safety, and tolerability of the newly developed 15% azelaic acid gel (Finacea; Berlex Laboratories, Inc, Montville, NJ) in the treatment of papulopustular rosacea (stage 2 rosacea) by comparison with 0.75% metronidazole gel (MetroGel; Galderma Laboratories LP, Fort Worth, Tex).

STUDY DESIGN AND PATIENTS

This 15-week, randomized, double-blind, parallel-group study was conducted at 13 centers in the United States. Male and female patients, 18 years and older, with moderate facial papulopustular rosacea (stage 2 rosacea) were eligible for inclusion in the study if they exhibited 10 to 50 inflamed facial papules and/or pustules, persistent erythema, and telangiectasia. Patients were excluded if they met the following criteria: mild rosacea (stage 1 disease) with only transient erythema and/or absence of lesions, severe rosacea (stage 3 disease, with phymas, rosacea conglobata, and rosacea fulminans), marked ocular manifestations, steroid rosacea, dermatoses that may interfere with the evaluation or diagnosis of rosacea, or a history of hypersensitivity to any ingredient of the study medication. In addition, due to label restrictions on infant exposure to metronidazole, breastfeeding mothers were excluded from study participation. Before enrollment, all patients provided written informed consent, and institutional review board approval was obtained from each participating center.

Patients were required to complete a washout period of 2 weeks for topical therapy with antibiotics, retinoids, corticosteroids, or nonsteroidal anti-inflammatory drugs (NSAIDs); 4 weeks for systemic therapy with antibiotics, corticosteroids, or NSAIDs; 6 weeks for facial laser or light therapy; and at least 6 months for oral isotretinoin. A total of 251 patients were randomly assigned to receive 15 weeks of treatment with either azelaic acid gel (n=124) or metronidazole gel (n=127), applied twice daily, in the morning and evening, to the entire face. A computer-generated blockwise randomization method was used to ensure balance between the 2 treatment groups. Assignment occurred by the physician in ascending order, with each newly accepted patient receiving study medication with the lowest randomization number available in the center. A minimum of 12 patients was enrolled in each center. To preserve blinding, study medication was dispensed and collected only by a study nurse or assistant not involved with selection and assessment of patients. Patients were not permitted to receive any concurrent therapy that could potentially affect the course of rosacea during the study.

Efficacy and safety variables were evaluated at baseline and every 4 weeks until the final 15-week visit. To ensure consistency, patient assessments were conducted by the same investigator throughout the entire treatment period.

EFFICACY VARIABLES

Efficacy variables were aimed at assessing the effect of treatment on the 3 principal symptoms of facial papulopustular rosacea and providing overall assessment of treatment effect. The primary efficacy end point was the change in inflammatory lesion count (sum of facial inflammatory papules and pustules) from baseline to last available visit. Secondary efficacy variables included percent change in inflammatory lesion count and change in severity rating for erythema and telangiectasia. In addition, an investigator’s global assessment (IGA) of rosacea and investigator’s and patient’s overall improvement ratings were evaluated, and patients’ opinions of the cosmetic acceptability of the treatments were recorded.

The severity of erythema was rated on a 4-point scale (none, mild, moderate, severe) (Table 1). Improvement in erythema severity was defined as a decrease of at least 1 point. Telangiectasia was assessed with the same method. The IGA was performed using a recently developed 7-point, static scoring system, ranging from 0 (clear) to 6 (severe) (Table 2). This descriptive score provides an integrated assessment of stage 2 rosacea based on the severity of the principal symptoms: inflammatory lesions, erythema, and telangiectasia.

The investigator’s and patient’s ratings of overall improvement were based on a comparison of the rosacea severity from baseline to each visit (investigator only) and at the last available visit. The investigator’s rating was measured on a 6-point scale, reflecting the degree of clearance of disease signs and symptoms, from 1 (complete remission) to 6 (deterioration). The patient’s rating reflected a subjective impression of improvement based on a 5-point score, with 1 indicating excellent improvement and 5 denoting a worsening of rosacea severity. Additionally, patients rated the cosmetic acceptability of the study medications on a scale from 1 to 4, with 1 being very good and 4 being poor.

SAFETY AND TOLERABILITY

Rosacea patients frequently report highly sensitive skin and lack of tolerance to cosmetic products. Therefore, pretreatment signs and symptoms of any untoward cutaneous events, such as burning, stinging, or dryness, were recorded at baseline in all eligible patients who completed the study.
patients. Treatment emergent adverse events (AEs) were recorded throughout the entire study period, including all cutaneous and systemic events observed by the investigator and all subjective skin symptoms reported by patients. For all AEs, the duration, intensity, seriousness, and causal relationship to the study medication were assessed by the investigator. Adverse events were classified into 3 groups: facial skin signs and symptoms similar to pretreatment skin signs and symptoms (burning, stinging, itching, dry skin, rash, facial edema), other cutaneous AEs, and systemic AEs by body system. The pattern of facial skin signs and symptoms (every dose, intermittent, continuous) was also assessed. The term transient was used to describe events that were reported as every dose. In addition, patient opinion of local tolerability of therapy was evaluated at the last visit based on 4 possible ratings (good, acceptable despite minor irritation, less acceptable due to continuous irritation, and nonacceptable).

STATISTICAL ANALYSIS

Efficacy and safety analyses were performed on the intent-to-treat (ITT) population, which included all randomized patients who received study medication. Analysis of efficacy end points was based on the last observation carried forward method, in which data from the last available visit of each patient were used to evaluate each efficacy variable. All statistical tests were 2-sided using a .05 level of significance.

Analysis of mean and percent change in inflammatory lesion count was performed using an analysis of covariance model, which included factors for treatment and study center and the covariate number of lesions at baseline. For all other end points, treatment differences were compared using an extended Mantel-Haenszel test, controlling for centers and using modified ridit scores (van Elteren test). SAS statistical software (SAS Institute Inc, Cary, NC) was used to perform these analyses.

The incidence of all treatment-related AEs reported in the ITT population was tabulated and classified by intensity, duration, and pattern. Differences in the patient's overall rating of tolerability between the 2 treatments were analyzed using the same method as for other secondary end points (ie, extended Mantel-Haenszel test controlling for centers and using modified ridit scores [van Elteren test]).

The sample size calculation was based on results for the lesion count. A difference of 5 lesions in mean lesion count for the 2 treatments was considered to be medically relevant. Assuming a common SD of 12 for the number of inflammatory lesions at the end of treatment, 92 patients per group would be sufficient to detect a difference of 5 in mean lesion count between the 2 treatments with a power of 80% and a .05 2-sided significance level. Accounting for dropouts, it was planned to include a total of 204 patients (102 per treatment) in this study.

**RESULTS**

**PATIENT CHARACTERISTICS AND DISPOSITION**

Study enrollment occurred from October 29, 2001, to January 31, 2002. Because of the fast enrollment rate, the study overenrolled 47 patients before all recruiting efforts in the centers could be stopped. At baseline, patient demographic characteristics and signs and symptoms of rosacea were comparable in the azelaic acid gel and metronidazole gel groups (Table 3).

### Table 2. Investigator's Global Assessment of Rosacea: 7-Point Static Score

<table>
<thead>
<tr>
<th>Numerical Score</th>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Clear</td>
<td>Almost no rosacea (ie, no papules and/or pustules); no or residual erythema; mild to moderate degree of telangiectasia may be present</td>
</tr>
<tr>
<td>1</td>
<td>Minimal</td>
<td>Rare papules and/or pustules; residual to mild erythema; mild to moderate degree of telangiectasia may be present</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
<td>Few papules and/or pustules; mild erythema; mild to moderate degree of telangiectasia may be present</td>
</tr>
<tr>
<td>3</td>
<td>Mild to moderate</td>
<td>Distinct number of papules and/or pustules; mild to moderate erythema; mild to moderate degree of telangiectasia may be present</td>
</tr>
<tr>
<td>4</td>
<td>Moderate</td>
<td>Pronounced number of papules and/or pustules; moderate erythema; mild to moderate degree of telangiectasia may be present</td>
</tr>
<tr>
<td>5</td>
<td>Moderate to severe</td>
<td>Many papules and/or pustules, occasionally with large inflamed lesions; moderate erythema; moderate degree of telangiectasia may be present</td>
</tr>
<tr>
<td>6</td>
<td>Severe</td>
<td>Numerous papules and/or pustules, occasionally with confluent areas of inflamed lesions; moderate to severe erythema; moderate to severe degree of telangiectasia may be present</td>
</tr>
</tbody>
</table>

### Table 3. Patient Demographics and Baseline Characteristics (Intent-to-Treat Population)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Azelaic Acid Gel* (n = 124)</th>
<th>Metronidazole Gel† (n = 127)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), y</td>
<td>49 (23-83)</td>
<td>46 (18-82)</td>
<td>.15</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>68</td>
<td>66</td>
<td>.79</td>
</tr>
<tr>
<td>Ethnicity, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>94</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>2</td>
<td>3</td>
<td>.79</td>
</tr>
<tr>
<td>Hispanic</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Mean previous duration of rosacea, y</td>
<td>7.8</td>
<td>7.5</td>
<td>.75</td>
</tr>
<tr>
<td>Mean inflammatory lesion count</td>
<td>18</td>
<td>19</td>
<td>.25</td>
</tr>
<tr>
<td>Erythema intensity, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>28</td>
<td>26</td>
<td>.78</td>
</tr>
<tr>
<td>Moderate</td>
<td>65</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>8</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Telangiectasia intensity, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>53</td>
<td>49</td>
<td>.17</td>
</tr>
<tr>
<td>Moderate</td>
<td>45</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>2</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

*Finacea; Berlex Laboratories, Inc, Montville, NJ.
†MetroGel; Galderma Laboratories LP, Fort Worth, Tex.
The disposition of patients is summarized in Figure 1. Overall, approximately 90% of patients completed the study, with a slightly higher completion rate in the metronidazole gel group. The discontinuation rates were 11% and 8% in the azelaic acid gel and metronidazole gel groups, respectively.

Efficacy

Inflammatory Lesion Count

Patients in the azelaic acid gel group experienced a continuous decline in mean inflammatory lesion counts throughout 15 weeks of treatment, from 18.1 lesions at baseline to 4.5 lesions at week 15 (Figure 2). In the metronidazole gel group, the mean number of lesions also decreased from baseline (19.4 lesions) through week 8 (7.7 lesions). However, after week 8, lesion counts leveled off, with no further reduction seen through week 15 (7.6 lesions). No such leveling off in efficacy was observed in the azelaic acid gel group. At the last available visit, the mean inflammatory lesion counts with azelaic acid gel and metronidazole gel were 5.1 and 8.7, respectively.

The mean decrease in the number of facial inflammatory papules and pustules from baseline to the last available visit was significantly greater with azelaic acid gel (−12.9) than metronidazole gel (−10.7) (P = .003). Also, a significantly greater mean percent reduction in inflammatory lesions from baseline to last available visit was achieved with azelaic acid gel (−72.7%) compared with metronidazole gel (−55.8%) (P < .001) (Table 4).

Erythema

Overall facial erythema improved over time in both treatment groups. However, at the last available visit, azelaic acid gel demonstrated a statistically significantly greater reduction in overall facial erythema than metronidazole gel (P = .02). An improvement in erythema severity was observed in 56% of patients in the azelaic acid gel group vs 42% of patients in the metronidazole gel group. Erythema continued to improve during the 15 weeks of treatment in the azelaic acid gel group but remained steady after week 8 in the metronidazole gel group (Figure 3).

Telangiectasia

No clinically relevant improvement in telangiectasia severity occurred in either treatment group. The telangiectasia rating remained unchanged in 73% and 76% of patients in the azelaic acid gel and metronidazole gel groups, respectively. A total of 6% of patients in each group experienced a worsening of telangiectasia during the study.
Investigator's Global Assessment

Before treatment, approximately 92% of all patients in both treatment groups were classified as having a mild, mild-to-moderate, or moderate rating of rosacea on the IGA static score of stage 2 papulopustular rosacea. (No patients were rated clear or minimal.) At the last available visit, success, as defined by an IGA rating of clear, minimal, or mild, was achieved in a significantly greater proportion of patients treated with azelaic acid gel (69%) compared with metronidazole gel (55%) \((P = .02)\) \((\text{Table 5})\). Nearly twice as many azelaic acid–treated patients (11%) received an IGA score of clear at the last available visit compared with metronidazole gel (6%). By contrast, more than twice as many patients in the metronidazole gel group (19%) had a score of moderate, moderate to severe, or severe disease compared with the azelaic acid gel group (9%).

Investigator's Rating of Overall Improvement

An overall improvement in rosacea occurred over time in both treatment groups. Nearly half of azelaic acid gel–treated patients (48%) experienced excellent remission or complete remission, whereas slightly more than one third (35%) of metronidazole gel–treated patients received these ratings. More patients in the metronidazole gel group (6%) experienced deterioration of their rosacea compared with the azelaic acid gel group (1%). At the last available visit, the difference between treatment groups was statistically significant \((P = .005)\). This difference reached statistical significance at week 12 \((P = .006)\).

Table 5. Investigator’s Global Assessment of Rosacea Scores at Baseline and Last Available Visit

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline, No. (%)</th>
<th>Last Available Visit (LOCF), No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azelaic acid gel* ((n = 124))</td>
<td>Clear 0 14 (11.3)</td>
<td>Minimal 0 37 (29.6) Mild 11 (8.9) Mild to moderate 62 (50.0) Moderate 42 (33.9) Moderate to severe 9 (7.3) Severe 0 0</td>
</tr>
<tr>
<td>Metronidazole gel† ((n = 127))</td>
<td>Clear 0 8 (6.3) Minimal 0 38 (29.9) Mild 14 (11.0) Mild to moderate 50 (39.4) Moderate 53 (41.7) Moderate to severe 8 (6.3) 7 (5.5) Severe 2 (1.6) 2 (1.6)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: LOCF, last observation carried forward.
*Finacea; Berlex Laboratories, Inc, Montville, NJ.
†MetroGel; Galderma Laboratories LP, Fort Worth, Tex.

Patient’s Overall Rating of Improvement

The patient’s subjective impression of the overall improvement achieved with study medications was consistent with that seen in the investigator’s rating. Excellent improvement was noted in 40% of patients receiving azelaic acid gel vs 34% of patients receiving metronidazole gel. In the azelaic acid gel group, 78% of patients rated their improvement as excellent or good compared with 64% of patients in the metronidazole gel group.

Patient’s Opinion’s of Cosmetic Acceptability

There was no significant difference in patient’s opinion of the cosmetic acceptability of the study medications, with both receiving favorably high ratings at the end of the study. A rating of very good or good was given by 75% and 82% of patients in the azelaic acid gel and metronidazole gel groups, respectively.

SAFETY AND TOLERABILITY

Pretreatment, untoward facial skin signs and symptoms, such as burning, stinging, itching, scaling, and dry skin, were observed in most patients in both treatment groups (85% and 91% with azelaic acid gel and metronidazole gel, respectively). Skin dryness was reported by approximately two thirds of patients, and more than half complained of scaling. Other events cited by at least one third of all patients were itching, edema, burning, and stinging, in descending order of frequency.

No serious or systemic AEs were reported in either treatment group. There were no reports of phototoxic or photoallergic reactions. The investigators determined that most AEs causally related to the study medication were facial or involved other cutaneous signs and symptoms.
In total, 32 of 124 azelaic acid gel–treated patients (26%) experienced facial skin signs and symptoms. In most of these patients (25/32), these events were transient in nature. Furthermore, these events were of mild-to-moderate severity in most patients (25/32). In the metronidazole gel group, 9 (7%) of 127 patients experienced facial skin signs and symptoms. In 3 of these 9 patients, the events were transient. In all 9 patients, the severity was mild to moderate. In addition, 1 incident of acne was reported in the azelaic acid gel group.

In the azelaic acid gel group, 4 patients discontinued treatment and 5 patients had their dose reduced due to a treatment-related AE. In the metronidazole gel group, treatment-related AEs resulted in a dose reduction in 2 patients.

At the end of treatment, patients gave both treatments favorable local tolerability ratings. In the patient's opinion of local tolerability, the treatments were evaluated as good or acceptable despite minor irritation by 89% and 96% of patients in the azelaic acid gel and metronidazole gel groups, respectively.

This randomized, double-blind study compared the efficacy and safety of a novel formulation of azelaic acid (15% gel) with a widely used topical therapy (0.75% metronidazole gel) over 15 weeks of twice-daily treatment in 251 patients with moderate, facial papulopustular rosacea. Efficacy as assessed by nominal and percent change of inflammatory lesion count from baseline to last available visit in the ITT population was statistically significantly superior for azelaic acid gel. Thus, azelaic acid gel proved superior to metronidazole gel in reducing both the mean nominal lesion count (–12.9 vs –10.7, respectively) (P = .003) and the mean percent decrease in inflammatory lesions (–72.7% vs –55.8%, respectively) (P < .001). Also, in the azelaic acid gel group, a higher number of patients showed improvement of the erythema severity score (P = .02). In the azelaic acid gel group, 56% of patients were rated improved at the last available visit compared with 42% of patients in the metronidazole gel group. Likewise, the IGA, a static score describing the overall severity of rosacea, and the investigator's overall assessment of improvement showed a significant advantage for azelaic acid gel at the last available visit. According to patient's overall assessment, azelaic acid gel scored numerically higher than metronidazole gel. Neither treatment had a clinically appreciable effect on telangiectasia. Thus, in this study, azelaic acid gel demonstrated consistently and significantly superior efficacy over metronidazole gel on the primary and most secondary efficacy end points.

During the first 4 weeks of treatment, there was a greater mean decrease in the number of inflammatory lesions with azelaic acid gel, from 18.1 to 9.6 compared with a decrease of 19.4 to 11.9 with metronidazole gel. This suggests that azelaic acid gel may have a more rapid onset of action. The signs and symptoms of stage 2 rosacea continued to improve during the 15-week treatment course with azelaic acid gel. In contrast, in this study, the effect of metronidazole gel showed a plateau that occurred from week 8 on with regard to inflammatory lesion count and a slight worsening between weeks 8 and 15 of the erythema severity score. Given the chronic nature of rosacea, further studies with longer treatment durations are needed to investigate the long-term effects of azelaic acid gel.

The safety of topical azelaic acid has been established through many years of worldwide clinical use, including use during pregnancy (pregnancy category B). Likewise, metronidazole gel is considered to be a safe topical treatment. The safety and tolerability of azelaic acid gel and metronidazole gel were confirmed by this study. No serious or systemic AEs considered to be drug related by the investigator were reported for either treatment, and no phototoxic or photoallergic reactions occurred. The cutaneous AEs observed with both treatments were similar to those recorded as pretreatment, untoward skin signs and symptoms. Some degree of burning, stinging, itching, scaling, and dry skin was present in more than 85% of the patients at baseline, perhaps a result of the sensitive skin associated with rosacea. The most frequent treatment-related AEs reported in both treatment groups were facial skin signs and symptoms. In most patients, these events were of mild-to-moderate severity and transient in nature. However, a higher incidence of these events was seen in patients treated with azelaic acid gel. Overall, these events did not seem to be of great concern to the patients in either treatment group. Patients expressed overall satisfaction with the local tolerability of both azelaic acid gel and metronidazole gel, with 89% of the patients rating their treatment as good or acceptable despite minor irritation in the azelaic acid gel group and 96% of the patients in the metronidazole gel group.

In conclusion, this study evaluated the efficacy, safety, and tolerability of a novel 15% azelaic acid gel compared with 0.75% metronidazole gel. Results showed that azelaic acid gel was consistently superior to metronidazole gel in improving principal signs of rosacea (ie, reducing inflammatory papules and pustules and reducing erythema intensity). In addition, azelaic acid gel was superior to metronidazole gel in improving or resolving rosacea signs as measured by 2 distinct investigators’ assessments. Although the effectiveness of metronidazole gel plateaued after week 8, azelaic acid gel continued to show progressive improvement through 15 weeks. Thus, these results suggest a beneficial effect of azelaic acid during prolonged treatment periods, warranting further investigation of long-term treatment of rosacea with azelaic acid gel. The high safety of both topical azelaic acid and metronidazole was confirmed. This study establishes 15% azelaic acid gel to be a promising, new, safe, and tolerable therapy option for patients with moderate papulopustular rosacea.

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REFERENCES


Congratulations to the winner of our August quiz, Pij B. Marko, MD, Department of Dermatology, Maribor Teaching Hospital, Maribor, Slovenia. The correct answer to our August challenge was desmoplastic melanoma. For a complete discussion of this case, see the Off-Center Fold section in the September ARCHIVES (Calista D. Dome-shaped lesion of the nose. Arch Dermatol. 2003;139:1209-1214).

Be sure to visit the Archives of Dermatology World Wide Web site (http://www.archdermatol.com) to try your hand at the Interactive Quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month’s print edition of the ARCHIVES. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also receive a free copy of the The Art of JAMA II.