Vehicle Formulation Impacts Tolerability and Patient Preference: Comparison of Tretinoin Branded Lotion and Generic Cream

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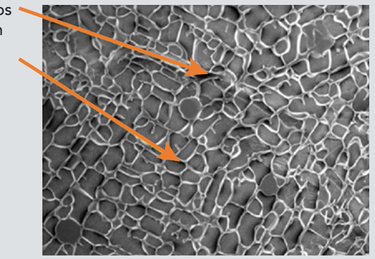
SYNOPSIS

- Vehicle design and optimization of topical formulations are critical to the drug-development process, as product vehicle and active/inactive ingredients can contribute to drug tolerability/efficacy and patient preference/adherence[1,2]
- Retinoids are a mainstay of acne treatment, though topical retinoids—such as tretinoin—can be associated with significant cutaneous irritation and drying, which can lead to poor adherence[3,4]
- To mitigate these issues, tretinoin 0.05% lotion (Altreno®) was formulated using a polymeric honeycomb matrix, which allows for efficient and uniform delivery of micronized tretinoin and moisturizing/hydrating ingredients[5,6] (**Figure 1**)
- Branded topical acne therapies, however, are often substituted at the pharmacy for a generic version, without accounting for the physiochemical differences between formulations and the potential impact of this product substitution

FIGURE 1. **Polymeric Emulsion Technology for Tretinoin 0.05% Lotion**



Micronized tretinoin [Kircik et al. 2019][6]. Cryo scanning electron microscopy imaging of the polymeric matrix (×1000). Micronized tretinoin particles are predominantly <10 microns in diameter.

OBJECTIVE

- To compare the tolerability and participant preference of two tretinoin formulations: a branded 0.05% lotion (Altreno) and a frequently dispensed 0.05% generic cream (Taro)

METHODS

- In this single-center, double-blinded, split-face study, females with acne aged ≥18 years were randomized to apply tretinoin lotion or generic cream once daily to the right or left cheek for 2 weeks
  - First application occurred at the research site under the supervision of a research coordinator
- Assessments were conducted immediately after first use and after two weeks of split-face drug application
- The investigator assessed erythema, scaling, skin dryness, softness, smoothness, radiance, and brightness on a 5-point scale (0=none, 1=minimal, 2=mild, 3=moderate, 4=severe)
- Participants completed a 16-item facial marketing questionnaire assessing their impressions of the products and their skin on a 9-point scale (1=agree completely, 9=disagree completely) for each side of their face

RESULTS

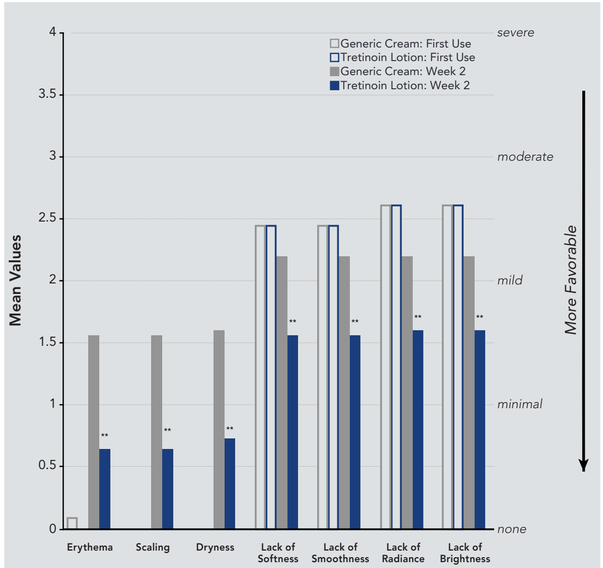
Participants

- Twenty-five female participants with a mean age of 40.6 years (range: 19–69 years) enrolled in and completed the study
- All participants had a Fitzpatrick skin type of 1 or 2 and self-identified as White
- Almost half of participants had combination skin type (48%), followed by dry (32%), normal (12%), and oily (8%)

Investigator Assessments

- After first use, investigator assessments were not significantly different between the lotion- and cream-treated sides of the face, and there was no/minimal erythema, scaling, or dryness with either treatment (**Figure 2**; open bars)
- At week 2, the cream-treated side of the face had significantly more erythema (144%), scaling (144%), and dryness (122%) versus the lotion-treated side ($P<0.01$ each; **Figure 2**; filled bars)
- The lotion-treated side also demonstrated significantly enhanced softness, smoothness, radiance, and brightness (~40% difference, $P<0.01$, each) versus cream at week 2 (**Figure 2**; filled bars)

FIGURE 2. **Investigator Assessments of Irritation and Skin Appearance (N=25)**

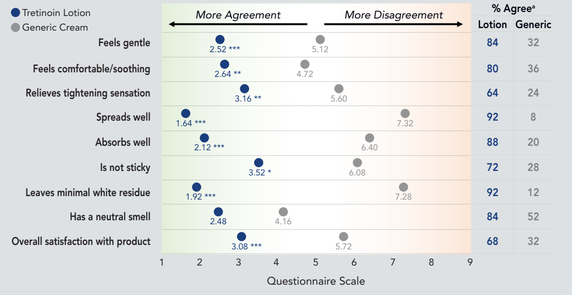


**$P<0.01$ vs generic cream at week 2.

Participant Assessments

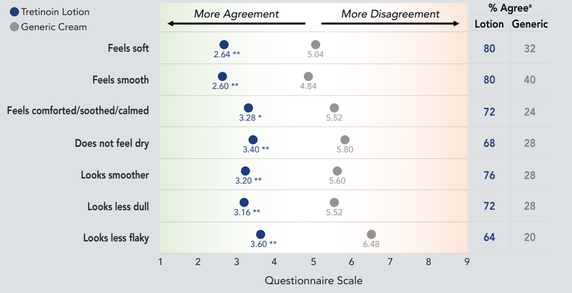
- After 2 weeks of use, average impression rating scores on each of the 16 questionnaire items were better (lower) for lotion versus cream ($P<0.05$ on 15 of 16 items; **Figures 3 and 4**)
  - Similar results were observed immediately after one use ($P<0.05$ on 10 of 16 items; data not shown)
- More than 70% of participants agreed (rating score 1–3) that the tretinoin lotion was gentle, comfortable/soothing, spreadable, absorbent, not sticky, and left a minimal white residue versus <40% for generic cream (**Figure 3**)
- Agreement scores on skin sensation (feels soft, smooth, comforted/soothed/calm, not dry and looks smoother, less dull, less flaky) were similarly higher for lotion versus cream (>60% vs ≤40%; **Figure 4**)
- Overall, approximately 70% of participants preferred to take tretinoin lotion home over cream both after first use and 2 weeks of use (**Figure 5**)

FIGURE 3. **Self-Assessments of Product Properties at Week 2 (N=25)**



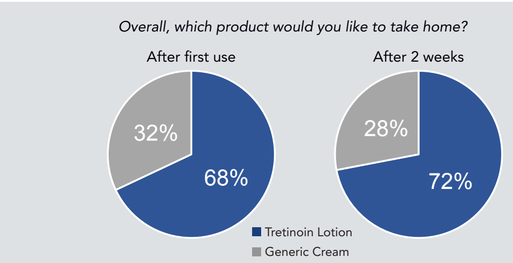
*$P<0.05$, **$P<0.01$, ***$P<0.001$ vs generic cream.
Questions rated on a scale of 1=agree completely to 9=disagree completely.
[a]Defined as a rating of 1, 2, or 3 on the questionnaire scale.

FIGURE 4. **Self-Assessments of Skin Properties at Week 2 (N=25)**



*$P<0.05$, **$P\leq0.01$, ***$P<0.001$ vs generic cream.
Questions rated on a scale of 1=agree completely to 9=disagree completely.
[a]Defined as a rating of 1, 2, or 3 on the questionnaire scale.

FIGURE 5. **Self-Assessment of Product Preference**



CONCLUSIONS

- In this split-face study, tretinoin 0.05% lotion led to significantly less investigator-assessed erythema, scaling, and dryness versus generic cream after 2 weeks of once-daily use, accompanied by a significant improvement in skin appearance (softness, smoothness, radiance, and brightness)
- Participants also significantly preferred properties of the lotion formulation (eg, gentle, spreadable, absorbs well) and skin sensation (eg, soft, soothed, not dry, less dull) with lotion versus cream
- These results demonstrate the importance of a well-designed topical formulation—such as tretinoin 0.05% lotion—on both improved tolerability and patient preference, underscoring the potential negative impact of generic switching at the pharmacy
  - Given the established impact of tolerability and patient preference on drug adherence and treatment success,[2,7] this further underscores the potential negative effect of generic switching at the pharmacy

REFERENCES

1. Piacquadio D, and Kligman A. *J Am Acad Dermatol*. 1998;39(2 Pt 3): S67-73.
2. Eastman WJ, et al. *Cutis*. 2014;94(1):46-53.
3. Zaenglein AL, et al. *J Am Acad Dermatol*. 2016;74(5):945-73.e33.
4. Sevimli Dikicier B. *J Int Med Res*. 2019;47(7):2987-2992.
5. Tyring SK, et al. *J Drugs Dermatol*. 2018;17(10):1084-1091.
6. Kircik LH, Draelos ZD, and Berson DS. *J Drugs Dermatol*. 2019;18(4):s148-154.
7. Dreno B, et al. *Int J Dermatol*. 2010;49(4):448-56.

AUTHOR DISCLOSURES

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