Optimized Formulation for Topical Application of a Fixed Combination Halobetasol/Tazarotene Lotion Using Polymeric Emulsion Technology

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SYNOPSIS

- Halobetasol propionate (HP) and tazarotene (TAZ) are both effective treatments for psoriasis but are limited by labelling restrictions or potential for adverse events
- Recently, positive clinical data on a novel halobetasol propionate 0.01%/tazarotene 0.045% (HP/TAZ; Duobrii™) lotion formulation for the treatment of moderate or severe plaque psoriasis have been published[1-3]
- The unique formulation of HP/TAZ lotion utilizes a technology that allows uniform disposition of both active ingredients simultaneously onto the skin surface and has been developed to be a non-greasy lotion that would be well-liked by patients, help adherence, and normalize epidermal barrier function

OBJECTIVES

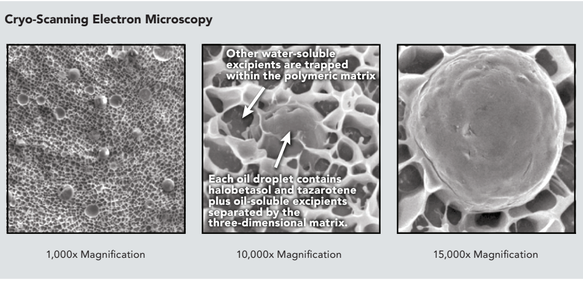
- To detail the unique formulation approach to HP/TAZ lotion development
- To assess the absorption and epidermal barrier effects of the novel formulation of HP/TAZ lotion compared to expected individual results with HP and TAZ

METHODS

Polymeric Emulsion Technology Formulation

- HP and TAZ are encapsulated within the same oil droplet together with moisturizing/hydrating excipients (light mineral oil, diethyl sebacate; **Figure 1**)
- Oil droplets (HP/TAZ plus excipients) are uniformly distributed within the oil-in-water emulsion; additional water-soluble moisturizing excipients (sorbitol) are trapped within the 3-D matrix (mesh)
- On application, the mesh is uniformly distributed on the skin and instantly breaks upon contact with salts commonly present on skin, allowing for uniform absorption of HP/TAZ

FIGURE 1. Oil-in-Water Emulsion Droplet Separated Within a Polymeric Matrix



Percutaneous Absorption

- Percutaneous absorption studies compared the *in vitro* dermal deposition of HP/TAZ lotion (polymeric emulsion technology) versus HP 0.05% cream (Ultravate®) and TAZ 0.1% cream (Tazorac®) individually
  - Approximately 5 mg/cm² of each formulation was applied to the epidermis of dermatomated human cadaver back tissue (one donor)
  - After 24 hours, HP or TAZ concentrations were determined with Liquid Chromatography-Mass Spectrometry
- Another percutaneous absorption study (same methodology as above) compared the permeability of TAZ in a layered application of TAZ 0.1% cream on top of HP 0.05% cream with that of an application of TAZ 0.1% cream only

Epidermal Barrier Function

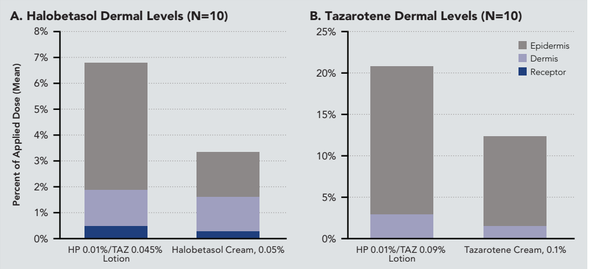
- Skin hydration and epidermal barrier maintenance were assessed through corneometry and transepidermal water loss (TEWL) over 24 hours in healthy female participants with Fitzpatrick Skin Type I-IV
  - Following a 1-week washout with no moisturizing products, vehicle lotion (0.05 mL) was applied to the volar forearm (other forearm served as control)
  - Moisture (corneometry; Corneometer®) and skin barrier function (TEWL; Tewameter®) were evaluated
  - Patient preference to several features (hydrating, moisturizing, skin absorption, aesthetic) of the vehicle lotion were assessed through a questionnaire (18 questions) at the 8-hour evaluation point

RESULTS

Percutaneous Absorption

- The polymeric emulsion technology used to formulate HP/TAZ lotion demonstrated higher percutaneous permeation efficiency of active ingredients into the dermal layers than either HP 0.05% cream (**Figure 2A**) or TAZ 0.1% cream (**Figure 2B**) alone

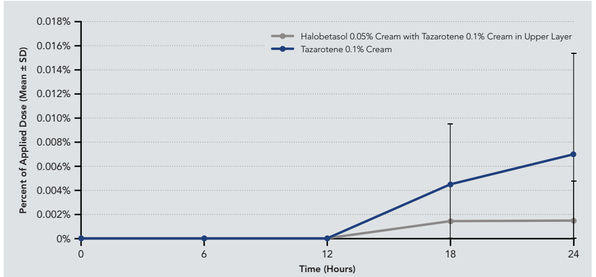
FIGURE 2. Dermal Levels Following 24 Hours of Topical Exposure to Halobetasol/Tazarotene Lotion Versus Halobetasol 0.05% Cream (A) or Tazarotene 0.1% Cream (B)



HP, halobetasol propionate; TAZ, tazarotene.

- The advantage of simultaneous and uniform delivery of HP/TAZ using this formulation was apparent when it was shown that simply layering TAZ 0.1% cream onto HP 0.05% cream decreased the percutaneous permeation of tazarotene (**Figure 3**)

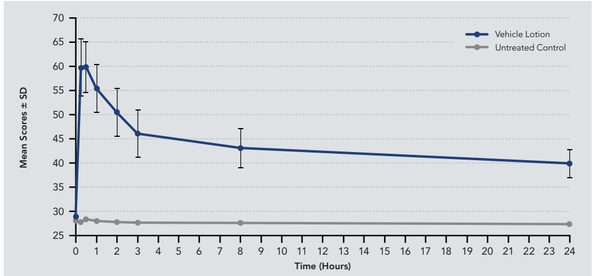
FIGURE 3. Cumulative Receptor Phase Levels of Tazarotene Following 24 Hours of Topical Exposure of Layered Tazarotene 0.1% Cream on Top of Halobetasol 0.05% Cream Versus Tazarotene 0.1% Cream Alone (N=8)



Epidermal Barrier Function

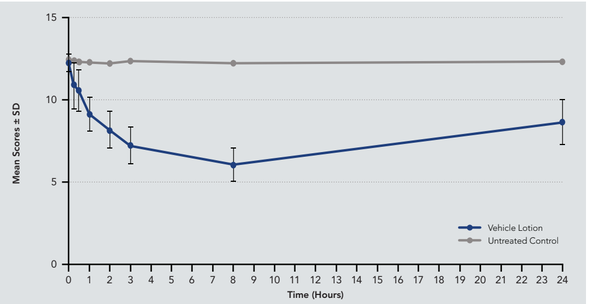
- The vehicle lotion formulation provided rapid and sustained increases in skin moisturization (**Figure 4**) and gradual decreases in TEWL over 24 hours (**Figure 5**)

FIGURE 4. Skin Moisturization Assessment of Vehicle Lotion and Untreated Control Over 24 Hours Using Corneometry (N=30)



*All time points except baseline $P<0.001$ versus untreated control.

FIGURE 5. Skin Barrier Assessment of Vehicle Lotion and Untreated Control Over 24 Hours Using Transepidermal Water Loss (TEWL) (N=30)



*All time points except baseline $P<0.001$ versus untreated control.

- Most participants (93%-100%; 15 total participants) responded favorably (strongly agree or agree) to all questions asked about the various physical attributes (hydrating, moisturizing, skin absorption, aesthetic) of the vehicle lotion

CONCLUSIONS

- A fixed combination HP 0.01%/TAZ 0.045% lotion formulation has been developed that utilizes an innovative polymeric emulsion technology and an optimal selection of solvents, emollients, and humectants which is aesthetically pleasing and provides enhanced barrier to the skin
- Application of this HP/TAZ formulation resulted in a higher permeation efficiency of both active ingredients compared with application of HP or TAZ cream alone
- These results are consistent with data from clinical studies, where HP/TAZ has been shown to provide synergistic activity, with efficacy greater than that which would be predicted from the individual active ingredients[3]
- Taken together, these results suggest that the unique formulation of HP/TAZ lotion may provide a more effective, predictable, and patient-preferred treatment option than use of separate formulations of HP and TAZ

REFERENCES

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3. Kircik LH, et al. *J Drugs Dermatol*. 2019;18(3):279-284.

AUTHOR DISCLOSURES

Dr. Emil Tanghetti has served as speaker for Novartis, Ortho Dermatologics, Sun, Lilly, Galderma, AbbVie, and Dermira; served as a consultant/clinical studies for Hologic, Ortho Dermatologics, and Galderma; and is a stockholder for Accure.
Dr. Linda Stein Gold has served as investigator/consultant or speaker for Ortho Dermatologics, LEO, Dermavant, Incyte, Novartis, AbbVie, and Lilly.
Dr. James Del Rosso has served as a consultant, investigator, and speaker for Ortho Dermatologics.
Dr. Stefan Weiss has served as consultant, speaker, advisor or research honoraria from AbbVie, Ortho Dermatologics, Jansen Biotech, Dermira, Almirall, Brickell Biotech, DermTech, and Scynexis.
Dr. Tina Lin is an employee of Ortho Dermatologics.
Mr. Arturo Angel and Dr. Radhakrishnan Pillai are employees of Bausch Health Americas Inc.

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