New Formulation Proves Vehicle Matters in Corticosteroid Efficacy

When a dermatologist sought to mimic the legendary efficacy of Skin-Cap in a safe, approvable formulation, he proved the importance of vehicles.

By Paul Winnington, Editor-in-Chief

Almost every dermatologist is familiar with Skin-Cap, the topical formulation that earned mythic status as much for its incredible efficacy as for its infamous withdrawal from the over-the-counter market. Now Charles Crutchfield, III, MD, a Minnesota dermatologist and one of the physicians who uncovered the hidden super-potent steroid behind Skin-Cap's efficacy, has earned a patent for CutiCort, a formulation that he says matches or perhaps surpasses Skin-Cap's efficacy. Unlike its predecessor, the new product is going through the appropriate regulatory channels and has no hidden ingredients. The new prescriptionength formulation could reach the market in about two years, and related research could lead the way to even more therapeutic advancements for psoriasis sufferers.

Proven Efficacy

Dermatologists have always relied on topical corticosteroids to quell flares of inflammatory diseases, such as psoriasis. They've also known the risks of long-term corticosteroid use, including skin atrophy and adrenal axis suppression, among others. Although numerous other treatments provide proven efficacy against psoriasis—including alternative topical agents, systemic retinoids and methotrexate, and now biologics—nothing offers the speed and degree of clearing that topical corticosteroids can.

In fact, when as a resident he saw the incredibly rapid and significant improvement in psoriasis patients treated with Skin-Cap, Dr. Crutchfield likened response to that achieved with class I corticosteroids. He eventually became suspicious of the OTC product, which touted zinc pyrithione as its active ingredient. He suspected undisclosed corticosteroids in the product and worked with colleagues to confirm the source of Skin-Cap's efficacy: clobetasol secretly incorporated into the aerosol product. "Zinc pyrithione had nothing to do with it at all," contends Dr. Crutchfield. "Zinc pyrithione was just a red herring."

Dr. Crutchfield had actually been conducting a research study for the manufacturers of Skin-Cap. Since that experience, he's remained dedicated to protecting unsuspecting patients from dangerous or ineffective products.

Once Skin-Cap's secret was out, the product was pulled from the market. Reports emerged of near-fatal adrenal axis suppression and other serious adverse events in patients who had used the product unaware of its corticosteroid component.

There was no safety threat inherent in Skin-Cap's formulation; the risk was in patients using a class I corticosteroid in great quantities and over long periods of time without appropriate medical supervision.

An Opportunity

Though it's been off the market for years and the original manufacturer has been banned from commerce in the US, patients continue to look for a Skin-Cap substitute. Just do a Google search for "skin cap" and you'll find page after page of products trying to capitalize on the notorious formulation. Dr. Crutchfield continued to wonder why Skin-Cap worked so well—in his estimation, even better than other topical clobetasol formulations—and if he could develop a similarly effective, safe, legal alternative. He realized that the vehicle was key.

"In dermatology, the vehicle can produce a difference in efficacy of 40 percent or even more," Dr. Crutchfield notes. He adds that in his own clinic he has witnessed patients stop responding or fail to respond to treatment when pharmacies swapped branded topical corticosteroids for generic versions made with inferior vehicles.

After two years of tweaking, Dr. Crutchfield developed an aerosol formulation consisting of oil, alcohol, water, and clobetasol that he says surpasses any other topical corticosteroid formulation currently available. "Nothing else works like this," he says. He believes the aerosol vehicle accounts for the remarkable efficacy, which he likens to "a class 0" steroid, though he's not sure exactly why the vehicle is so effective.

Having received a patent for CutiCort earlier this year, Dr. Crutchfield continues to study the formulation and is working to begin FDA review. He says the product is effective

for psoriasis, eczema, lichen planus, and lichen simplex chronicus as well as other steroid-responsive inflammatory dermatoses. He's also developed lower potency formulations of CutiCort. There are three versions: mild-, mid-, and super-potent.

Future Directions

While he's excited about the potential for CutiCort to help psoriasis sufferers safely treat their disease under physician supervision, Dr. Crutchfield is equally optimistic about the scientific findings emerging from his trials. The CutiCort study was a placebo controlled, double-blinded investigation involving 100 patients. As patients enrolled, individuals had the option to agree to biopsies at four to five day intervals from their initial presentation with full-blown inflammation through to clearing. By studying samples through the various stages of the disease, he and his team hope to identify the genes involved in the inflammatory processes of psoriasis.

It's still early in the research, but Dr. Crutchfield suspects they'll find that numerous different genes are "turned on and off" throughout the inflammatory process. As these genes are identified, they may become targets for future therapies. "This will show us different targets to go for in therapeutic development," Dr. Crutchfield says. "Right now the biologics only go after two targets."

But Dr. Crutchfield, who holds a degree in molecular biology, tempers his optimism. "People think of genes as the magic bullet," he notes, but they are actually just the initiators of a complex process. Genes code for proteins that form chains (just as letters in the alphabet form words, then sentences, then paragraphs) that ultimately lead to the clinical presentation of disease. There could be therapeutic targets anywhere along the way, Dr. Crutchfield says.

Current Implications

As noted, CutiCort won't be widely available to patients for some time. But the development of the product has yielded helpful information for clinicians. The efficacy of CutiCort's formulation demonstrates the importance of vehicle on therapeutic efficacy. It also supports the notion that zinc pyrithione had no influence on SkinCap's efficacy and offers no therapeutic benefit in psoriasis.

Finally, the research behind development of CutiCort may provide new information about the pathogenesis of psoriasis and inflammatory processes while pointing the way to new therapies for psoriasis.

New in Your Practice

Dry Spell. For patients suffering from dry skin, SkinMedica recently launched Ceratopic Replenishing Treatment. The company reports Ceratopic's combination of ceramide and other lipids in the same ratio as found in healthy skin provides long-lasting hydration and restores elements essential to a healthy skin barrier. Ceratopic is highly emollient, non-greasy, non-irritating, and fragrance-free.

Oral Update. You may soon have a new treatment option for moderate-to-severe psoriasis, an oral fumarate known as BG-12 ((Biogen Idec/Fumapharm). According to Phase III safety/efficacy studies, patients treated with BG-12 for 16 weeks averaged a 68 percent reduction in baseline PASI, compared to 10 percent of patients receiving placebo. The most common adverse events included flushing and diarrhea.

Spotlight on Safety. Patient safety is taking center stage in Genentech's newest study: RESPONSE [Raptiva (efalizumab) epidemiologic study of psoriasis outcomes and safety events]. Over the next five years, RESPONSE will follow more than 7,500 moderate-to-severe psoriasis patients for adverse events, including malignancies, serious infections, psoriasis-related AEs, thrombocytopenia, hepatic AEs, and congestive heart failure. Five thousand patients will receive Raptiva; 2,500 will receive other biologic therapies.

End of the Road. An unfavorable risk-benefit profile led Serono to discontinue Phase III studies of Onercept (recombinant TNF binding protein) for moderate-to-severe psoriasis. Since initiating the Phase III trial last year, investigators reported two cases of sepsis—one resulting in death. Serono, along with an independent Data and Safety Monitoring Board (DSMB), reviewed efficacy data and determined Onercept is less effective than Phase II studies suggested. The DSMB recommended Serono end clinical development of Onercept.

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percent sensitive but lack specificity. Anti-dsDNA, a confirmatory autoantibody, is highly specific for SLE. Additional assays include Anti-Ro and Anti-La antibodies which correlate with neonatal lupus. Anti-Ro alone is commonly seen with photosensitivity. Anticardiolipin test, lupus anticoagulant test, and B2-glycoprotein antibodies can detect antiphospholipid antibodies present in antiphospholipid syndrome. Histopathology is also confirmatory. Obtained from an active lesion, immunofluorescence reveals deposition of IgG at the dermoepidermal junction—the lupus band test. Erythrocyte sedimentation rate, depletion of complement, and high anti-dsDNA are most reliable in assessing the activity of this disease.

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