

# A New Use of the Antacid Drug Esomeprazole to Treat Morphea, a Chronic Connective Tissue Disease



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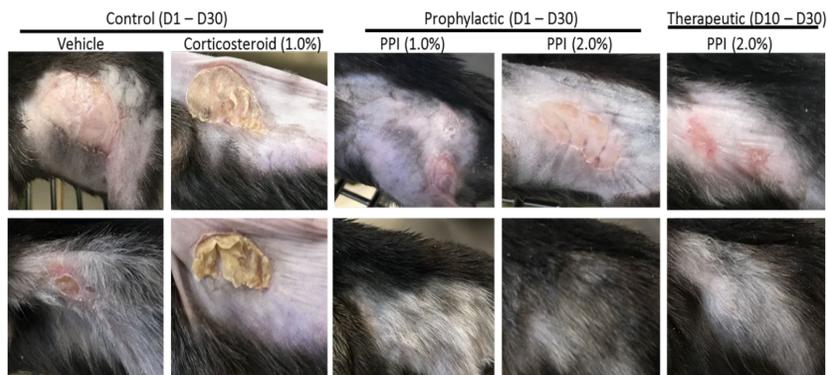
## PROPOSED TREATMENT

Evaluating the safety/tolerability and efficacy of topically-formulated esomeprazole in patients with morphea.

Morphea (localized scleroderma) is characterized by inflammation and excessive collagen deposition in the skin and muscles. Recently, our research team conducted high throughput drug screening of over 130,000 small molecules to identify compounds that regulate processes involved in tissue inflammation and fibrosis. We discovered that proton pump inhibitors (PPIs), FDA-approved for gastroesophageal reflux disease (GERD), are potent inhibitors of inflammation and fibrosis, with esomeprazole as the most potent. Therefore, a topical formulation esomeprazole may be a potential treatment option for morphea patients.

Our mouse model shows that topical esomeprazole improves radiation-induced dermal inflammation and fibrosis.

We hypothesize that topical esomeprazole will be safe and well-tolerated in patients with morphea and may even slow or reverse the disease process.



Day 16

Day 30

## SUMMARY STATEMENT

Using a topical formulation of esomeprazole, an anti-inflammatory and antifibrotic drug, to slow or reverse the pathological features of morphea

## DISEASE/CONDITION

Scleroderma is a rare autoimmune connective tissue disorder characterized by profound thickening and scarring of the skin and internal organs and vascular pathology. Morphea is a localized form of scleroderma, generally restricted the skin and muscle.

Morphea has an incidence of up to 3 cases per 100,000 and a prevalence of up to 9 per 100,000 – with women disproportionately affected. It causes functional and cosmetic impairment, including pigmentary changes, superficial and deep tissue atrophy, impaired mobility of joints or deformity, as well as significant disfigurement of the hands, head and neck or other areas of the body.



## CURRENT TREATMENT

Morphea has no curative treatment options. Immunosuppressive drugs such as cyclophosphamide, mycophenolate, or methotrexate and UV light, are used to manage morphea and alleviate symptoms. Anti-inflammatory medications, such as topical corticosteroids, are also sometimes used. Unfortunately, many of these treatments are associated with considerable side effects, including toxicity, cutaneous atrophy, allergy, and secondary skin infection.

## PROJECT

A pilot Phase I/IIA clinical trial will evaluate the safety / tolerability and preliminary efficacy of topical esomeprazole.

This study will enroll 6 healthy volunteers and at least 15 morphea patients in a modified “3+3” design. Initially, two dose levels of topical esomeprazole (1% and 2%) will be evaluated in a “patch test” by applying to small area of the skin in healthy volunteers for 6 weeks. This study will assess adverse reactions including burning, itching, tenderness, rash, and any other local or systemic allergic reactions. If no adverse reactions are observed, topical esomeprazole will be applied in patients with active morphea in a 6-week patch test in an unaffected area of the skin, and subsequently, in the area affected by morphea for another 12 weeks to assess safety and preliminary efficacy. All the patients will be followed for 4 weeks post-treatment.

We will use the Localized Skin Severity Index (LoSSI) test to assess preliminary efficacy (i.e., disease activity), and the SkinDex-16 test to evaluate the impact of the disease/intervention on patients’ quality of life (by scoring emotional, symptom, and functional variables) on a weekly basis.

This treatment has the potential to impact clinical practice by significantly slowing or potentially reversing many of the pathological features of morphea. If topical esomeprazole is proven to be safe in this first-in-human clinical trial, we plan to quickly proceed to a multisite Phase II clinical trial.



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