An investigator initiated study evaluating the efficacy and tolerability of Enstilar Foam (calcipotriene and betamethasone dipropionate) in patients with nail psoriasis

Study Protocol

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Sponsor: Investigator Initiated

Introduction

Psoriasis is a chronic, incurable skin disease affecting millions of people worldwide. Nail abnormalities occur concomitantly in 50% of patients with psoriasis, with a lifetime incidence of 80% to 90%.(1) In patients with psoriatic arthritis the incidence of nail disease is greater than 80%.(2) Nail psoriasis significantly impacts quality of life. In a survey of 1728 patients, 93% considered it a significant cosmetic handicap, 52% reported pain as a symptom and 58% reported difficulty carrying out their job.(3) Treatment of nail bed psoriasis poses a challenge to the clinician as there is a lack of controlled clinical trials and no gold standard for therapy to date. When nail bed psoriasis is not associated with widespread skin disease or psoriatic arthritis, topical treatment should be the initial approach. The choice of treatment depends on the type of disease present. Many physicians use topical and intralesional corticosteroids or a vitamin D analog for treatment of nail bed disease (eg onycholysis and subungual hyperkeratosis) (4). There are published reports demonstrating the increased tolerability of calcitriol ointment as compared to calciprotriol cream in the treatment of the sensitive intertriginous areas (5, 6)

In a study by Tosti et al. calcipotriol was as effective as a corticosteroid preparation at reducing subungual hyperkeratosis. (7) Adverse events with vitamin D analog therapy were limited to erythema and burning irritation. The nail unit is a sensitive area that might benefit from a less irritating vitamin D topical medication. In a pilot study by Kole, Cantrell, and Elewski, it was demonstrated that calcitriol ointment was as effective as betamethasone diproprionate ointment for the treatment of nail thickness in nail psoriasis. (8) Furthermore, in a study by Park et al. the fixed combination formulation of calcipotriol/betamethasone dipropionate ointment was safe and effective in the treatment of trachyonychia, which may be associated with psoriasis. (9) Lind et al demonstrated that the fixed combination calcipotriene/betamethasone dipropionate foam had greater skin penetration than the ointment formulation. (10) As such we propose that the combination product of vitamin D and topical steroids in the foam formulation (specifically, Cal/BD Foam), with increased penetration, will be an effective and safe option in the topical treatment of nail psoriasis.

The aim of the proposed study is to evaluate the efficacy and safety of Enstilar Foam (calcipotriene and betamethasone dipropionate) for the treatment of nail psoriasis.

STUDY OBJECTIVES

Primary Objective

To compare the efficacy of a 24-week regimen of twice daily Enstilar Foam (calcipotriene and betamethasone dipropionate) in the treatment of nail bed psoriasis. The primary efficacy outcome measure is the proportion of subjects achieving clinical improvement as measured by the nail thickness (hyperkeratosis) measurement.

Secondary Objectives

1. modified NAPSI (mNAPSI) score of target nail at Baseline, wk 12 and wk 24
2. NAPSI score of target nail at Baseline, wk 12 and wk 24
3. Physician global assessment (PGA) of nail disease.
4. Determine the most optimal method of assessing nail psoriasis (mNAPSI or NAPSI).

Additional Objectives

To assess the safety of a 24-week regimen of twice daily Enstilar Foam (calcipotriene and betamethasone dipropionate) in the treatment of nail bed psoriasis.

STUDY DESIGN

Study Outline

This is open label investigator initiated study to examine the efficacy and safety of twice daily Enstilar Foam (calcipotriene and betamethasone dipropionate) in a population of nail bed psoriasis subjects who are eligible for topical treatment as deemed by the investigator.

Number of Subjects

Up to 20 eligible subjects will be provided twice daily daily Enstilar Foam (calcipotriene and betamethasone dipropionate). Subjects will be instructed to apply a thin layer on the nail plate, around the nail plate and under the nail plate. The patient will be instructed to apply one application at night immediately before bed and not wash their hands before morning. At week 12, those patients with a mNAPSI50 or less may elect to discontinue study treatment. All subjects who completed the 6-month treatment will be followed for 1 month after discontinuation.

Visit Schedule

<u>Screening Period</u>

Patient eligibility will be determined within 28 days prior to study entry. Subjects who meet the entry criteria may proceed to the first dosing visit.

<u>Dosing Visit</u>

Subjects will report to the investigational site to receive twice daily Enstilar Foam (calcipotriene and betamethasone dipropionate)

<u>Study Visit</u>

Subjects will report monthly to the investigational site for nail assessments.

Follow-Up Visits
Subjects will return to the investigational site for follow-up visit at 4 weeks after the last study visit.

Discontinuation of the Study
The study may be discontinued at the discretion of the investigator at any time.

STUDY ENTRY CRITERIA

Study Inclusion Criteria
To be eligible to participate in this study, candidates will meet the following eligibility criteria at the time of enrollment:

1. Give written informed consent prior to any study procedures being conducted, and candidates will authorize the release and use of protected health information (PHI)
2. Between the ages of 18 and 85 years old
3. Have a diagnosis of nail psoriasis in either fingernails or toenails.
4. Candidate for topical therapy in the opinion of the investigator.
5. History of plaque psoriasis or psoriatic arthritis
6. Target nail will be KOH negative for dermatophyte fungus

Study Exclusion Criteria
Candidates will be excluded from study entry if any of the following exclusion criteria exist at the time of enrollment:

1. Males and females unable to practice effective contraception throughout study treatment
2. Unable to comply with the protocol (as defined by the Investigator; i.e. drug or alcohol abuse or history of noncompliance)
3. The presence of skin or nail conditions that might interfere with patient status assessments, as determined by the study investigator.
4. Nursing mothers, pregnant women, and women planning to become pregnant while in this study.
5. Patients with erythrodermic or pustular psoriasis.
6. Other sustained treatment to target fingernail within 6 months prior to screening.
7. History of trauma or surgery to target fingernail.
8. History of any disease known to affect nails (e.g., lichen planus, onychomycosis)
9. History of systemic psoriasis therapy for less than 6 months

Drug Accountability
The investigational site will maintain accurate records demonstrating dates and amount of study medication received, and accounts of any study medication accidentally or deliberately destroyed.

STUDY PROCEDURES & TREATMENT PLAN GUIDELINES

Informed Consent:

A written, signed informed consent form (ICF) and, in the US, written authorization to release and use PHI, will be obtained prior to performing any tests or evaluations under this protocol.

See Protocol Flowchart (Section 1.0) for detailed timing of tests and evaluations.

General Concomitant Therapy:
For subjects on any prescription medications, every attempt should be made to keep the patient on a stable dose of that medication for at least 14 days prior to the first dose of study medication and throughout the study

Subjects should advise the investigator if they start taking any new medications, including non-prescribed drugs.

Concomitant Psoriasis Therapy
Patients will be allowed to use the study medication to treat psoriatic skin lesions, if present. The study medication will be applied once daily on areas other than nails, to remain consistent with the prescribing information

Patients will be allowed to use systemic therapy to treat psoriatic lesions. The regimen should be stable for at least 6 months prior to study entry.

SAFETY PLAN

Clinical Safety Assessments
The following clinical safety assessments will be performed: (See study flowchart)

- Physical examinations
- Vital signs (temperature, heart rate, and blood pressure)
- Monitoring for adverse events
- Monitoring for concomitant therapy

Laboratory Safety Assessments
The following laboratory tests will be performed at screening:

- Urine pregnancy test, if applicable.

STUDY FLOWCHART:

Vectical vs. Betamethasone	Screening	Treatment							Follow Up
	Within 28	Visit 1	2	3	4	5	6	7	8
	Days Prior	W k 1	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 28
Test / Evaluation	to Day 1	Day 1	22	50	78	106	134	162	
Informed Consent	X								
Medical History	X								
Physical Exam	X						X		
Psoriasis Nail Assessment (mNapsi, NAPSI)	X	X	X	X	X	X	X	X	X
Nail Thickness Measurement	X	X	X	X	X	X	X	X	X

Vital Signs	X	X	X	X	X	X	X	X	X
Urine Pregnancy Test[1]		X						X	
Photography		X	X	X	X	X	X	X	X
Adverse Events		X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X

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