A proof of concept clinical trial evaluating the safety and efficacy of Eucrisa (crisaborole) in patients with mild to moderate seborrheic dermatitis

Study Protocol & Statistical Analysis Plan

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Boni Elewski, M.D., Principal Investigator
University of Alabama at Birmingham
Birmingham, AL 35294

A proof of concept clinical trial evaluating the safety and efficacy of Eucrisa (crisaborole) in patients with mild to moderate seborrheic dermatitis

Co-Investigators: Boni Elewski, MD, Wendy Cantrell, DNP, and Tiffany Mayo, MD

Site: University of Alabama at Birmingham

Background

Seborrheic dermatitis is a common and recurrent dermatosis that characteristically involves the scalp, nasolabial folds, eyebrows, glabella, and upper eye lids. It presents as an erythematous, thin scaly patch with a greasy sandpaper texture that varies depending on disease severity. While seborrheic dermatitis most frequently occurs on the face, it can involve other areas of the body especially the chest, abdomen, and naval. Overall incidence is thought to be between 2-5% of the general population, though this is likely an underestimation. Pruritus is variable, though the signs and symptoms of this disorder are certainly worsened by certain external conditions especially weather, personal perspiration, stress, and poor hygiene[i],[ii],[iii]. Patients often complain about the red, scaly patches on the face.

Antifungal agents are frequently used as monotherapy or in combination regimens in the treatment of seborrheic dermatitis. Topical corticosteroids are often used for their anti-inflammatory effects. Long term use of topical steroids on the face is not a preferred treatment modality due to the risk of striae development and other textural changes that occur over time. Therefore, topical crisaborole may be an alternative given its non-corticosteroid anti-inflammatory action. Crisaborole is a phosphodiesterase-4 (PDE-4) inhibitor that increases intracellular cyclic AMP (cAMP) levels to exert its anti-inflammatory effects. While it has not previously been investigated for its effects in seborrheic dermatitis, further studies evaluating its role in this disease are warranted.

Therefore, we propose a proof of concept study using topical crisaborole 2% ointment on the face for 4 weeks to evaluate the anti-inflammatory action of this agent and its utility in the treatment of facial seborrheic dermatitis.

Primary Outcome Measure:

- ISGA will be collected via skin examination to evaluate efficacy of Crisaborole 2% topical ointment in the treatment of seborrheic dermatitis. A 0 or 1 (clear or almost clear) on the ISGA would be considered a treatment success

Secondary Outcome Measure:

- The Itch NRS will be collected to assess the percentage of improvement of patient reported itching. This will be calculated as a percent changes from baseline in the Itch NRS scale.

Safety Outcome Measures

- Incidence, severity, and type of treatment-emergent adverse events will be collected via the local tolerability assessment
- Vital signs, clinical assessments, and laboratory test results
- Concomitant medication use
- Adverse events

Primary Objective

- To assess the efficacy of crisaborole ointment 2% (Eucrisa) in the treatment of mild to moderate seborrheic dermatitis.

Statistical Analysis

As this is a proof of concept, open label study, descriptive statistics will be utilized. The goal is for the information to yield data points robust enough to be accepted in a high impact, peer reviewed journal. The sample size was based known patient population and pragmatic considerations and is adequate to characterize anticipated observed effects.

Study Design

40 eligible subjects will be enrolled

Inclusion criteria

1. Capable of understanding and willing to provide signed and dated written voluntary informed consent before any protocol specific procedures are performed.

2. Male or female subjects 18 to 70 years of age.

3. Able to complete the study and to comply with study instructions.

4. Female subjects of childbearing potential must have a negative pregnancy test. Sexually active women of childbearing potential participating in the study must agree to use a medically acceptable form of contraception (which includes oral contraception, injectable or implantable methods, or intrauterine devices) during the entire duration of the study

5. Mild to moderate seborrheic dermatitis on the face with an ISGA of 2 or 3 at baseline.

Exclusion criteria

1. Use of systemic antifungal agents, corticosteroids or other immunosuppressive therapies, or systemic retinoids within 4 weeks prior to the baseline visit.

2. Use of topical antifungal therapy, corticosteroid therapy, or calcineurin inhibitors to the face, within 2 weeks prior to the baseline visit. Topical, over-the-counter antifungal shampoo will be allowed as long as it has remained constant for 4 weeks prior to baseline.

3. Use of any investigational drugs within 4 weeks prior to the baseline visit, or subjects scheduled to receive an investigative drug other than the study product during the period of the study.

4. History of known or suspected intolerance to any of the ingredients of the study product.

5. Female subjects who are pregnant, trying to become pregnant or lactating.

6. Any clinically relevant abnormal vital signs or findings on the physical examination which in the opinion of the investigator might interfere with the study assessments.

7. A clinically relevant history of abuse of alcohol or other drugs.

8. Any major illness within 30 days prior to the baseline visit.

9. Subjects with any clinically significant condition which would, in the opinion of the investigator, compromise the subject's participation in the study.

10. Subjects who are immunocompromised (ex: HIV).

11. Considered unable or unlikely to attend the necessary visits.

12. Currently using any medication, which in the opinion of the investigator may affect the evaluation of the study product

13. Subjects who have significant neurological conditions (Parkinson's disease or Stroke), who in the opinion of the investigator are not eligible for the study due to the severity of neurological condition.

14. Subjects with a history of non-melanoma skin cancer of the face within 6 months

Procedures:

After the informed consent process, the subject will be evaluated for facial seborrheic dermatitis utilizing the Investigator's Static Global Assessment (ISGA). The subject must have a ISGA score of 2 or 3 to qualify for the study.

Patient reported outcomes will be collected at baseline and week 4. We will utilize the SkinDex29 and Itch NRS.

Provider and Patient local tolerability assessment will be collected at Baseline (before medication application) week 1, 2, and 4. We will assess for redness, pain, burning, and scaling at the application site.

Adverse events will be collected from after the informed consent document is signed through week 4.

Concomitant medications will be collected from screening to week 4.

Subjects can continue to use their over-the-counter dandruff shampoo as long as it has remained constant for the past 4 weeks. Subjects will be instructed to avoid the facial area with the shampoo.

Subjects may continue their established makeup, moisturizer and sunscreen regimen.

Other than Urine Pregnancy Tests for women of childbearing potential, no other laboratory evaluations are necessary.

Patients will be instructed to apply a thin layer of medication to the affected area on the face twice daily for 4 weeks, and they will be advised that the medication is not for ophthalmic, oral, or intravaginal use.

Procedures are listed in table below.

Schedule of Events

	Scr	BL	Wk1	Wk 2	Wk 4
Informed Consent	x				
Inclusion/Exclusion Criteria	x	x			
Med History	x				
PE	x				x
Investigator Static Global Assessments (ISGA)	x	x	x	x	x
Seborrheic dermatitis grading scale	x	x	x	x	x
Photography	x	x	x	x	x
UPT	x				x
Con Meds	x	x	x	x	x
AE		x	x	x	x
SkinDex 29		x			x
Itch NRS		x			x
Patient and Provider Tolerability Assessment		x	x	x	x

[i] Katsambas A, Antoniou C, Frangouli E, Avgerinou G, Michailidis D, Stratigos J. A double-blind trial of treatment of seborrhoeic dermatitis with 2% ketoconazole cream compared with 1% hydrocortisone cream. Br J Dermatol. 1989 Sep;121(3):353–7.

[ii] Piérard-Franchimont C, Piérard GE, Arrese JE, De Doncker P. Effect of ketoconazole 1% and 2% shampoos on severe dandruff and seborrhoeic dermatitis: Clinical, squamometric and mycological assessments. Dermatology. 2001;202(2):171–6.

[iii] Stratigos JD, Antoniou C, Katsambas A, Böhler K, Fritsch P, Schmölz A, et al. Ketoconazole 2% cream versus hydrocortisone 1% cream in the treatment of seborrheic dermatitis. A double-blind comparative study. J Am Acad Dermatol. 1988 Nov;19(5 Pt 1):850–3.