Evaluating treatment resistant dermatitis

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Background, Rationale and Context

Psoriasis and atopic dermatitis are chronic inflammatory disease that account for a significant amount of patients in most dermatological practices. Topical corticosteroid agents are often prescribed for treatment of both these conditions, especially when they are localized rather than wide spread. Prolonged treatment with corticosteroids occasionally results in resistance to treatment. The development of resistance to treatment is termed tachyphylaxis. Tachyphylaxis has been thought to be a result of down regulation of target receptors, resulting is a decreased metabolic effect of the compound.

Poor adherence, rather than down regulation of receptors, may be the primary cause of tachyphylaxis to topical corticosteroids. Patients' use of topical medications decrease over time. The messiness of ointment and other topical preparations are a hurdle to good adherence. Topical spray vehicles have become increasingly more popular because of their rapid application and ease of use. Desoximetasone 0.25% spray is a well-tolerated, potent topical corticosteroid that rapidly and successfully treats inflammatory skin diseases.[1]

Lots of treatment options exist for psoriasis; however, some patients do not get better using these medications. These patients are said to have resistant disease. In this study, we define resistant disease by failure of previous topical steroid treatment. Poor adherence is a barrier to positive clinical outcomes. Failure to respond to medication may be a result of poor adherence rather than resistance to the topical therapy. The purpose of this study is to delineate between the two.

Objectives

The primary objective of the study is to determine, under conditions designed to assure good adherence, whether topical 0.25% desoximetasone spray improves clinical outcomes in patients who have resistant inflammatory skin disease defined by failure of previous topical steroid treatment.

Methods and Measures

Design

This is an opened label, randomized, single centered clinical study. Subjects with atopic dermatitis and psoriasis, whom previously failed adequate topical corticosteroid therapy, will be recruited, including subjects who may have been prescribed Topicort in the past with no response. Twenty-four subjects will be enrolled; 12 subjects with psoriasis and 12 with atopic dermatitis, with disease that is amenable to topical therapy. Screening data will be reviewed to determine subject eligibility. Subjects who meet all inclusion and exclusion criteria be offered enrollment into the study. At the baseline visit subjects will be randomized to either receive twice a day phone calls to discuss their medication use or no call, standard of care, for the one or two weeks they are in the research study.

Subjects with atopic dermatitis will be treated for 1 week; subjects with psoriasis will be treated for 2 weeks with topical 0.25% desoximetasone spray. Each visit, disease severity will be measured by Total Lesion Severity Score (TLSS), Eczema Area and Severity Index/Psoriasis Body surface area (EASI) and

(PASI) scoring. Investigator Global Assessment Score (IGA) and Pruritus Visual Analog Scale (VAS) will be determined for both diseases. Visits will take place at baseline, 3 days, 1 week, and in the case of psoriasis, 2 weeks. We will complete a chart review to determine and/or contact each patient via phone to determine which topical medications they were considered resistant to prior to completing the study.

Subjects selection criteria

Subjects with a diagnosis of plaque-type psoriasis or atopic dermatitis who meet the inclusion and exclusion criteria will be eligible for participation in this study. Safety and effectiveness of Topicort Topical Spray in patients younger than 18 years of age have not been studied; therefore use in pediatric patients is not recommended. Patients will be recruited in the dermatology clinic during their regular clinic visit. In clinic, if the patient is eligible for the study they will be asked whether they would be interested in the research study. If they reply yes, further information will be given about the research study. At this time if the patient still agrees to participate, after the patient is complete with checkout they will be taken to the clinical studies research center, located upstairs from the dermatology clinic to read the research study consent form. A study team member will answer any questions they may have about the research study. Once the patient has signed the consent, we will begin the baseline/screening evaluation.

Inclusion Criteria

Male or female ≥18 years of age at baseline visit.

Documentation of plaque-type psoriasis or atopic dermatitis diagnosis as evidenced by one or more clinical features

Written informed consent (and assent when applicable) obtained from subject or subject's legal representative and ability for subject to comply with the requirements of the study

Exclusion Criteria

Pregnant, breastfeeding, or unwilling to practice birth control during participation in the study.

Presence of a condition or abnormality that in the opinion of the Investigator would compromise the safety of the patient or the quality of the data.

No access to a phone throughout the day

Subject is diagnosed with a disease that is known to effect adherence and would otherwise bias our results (Such as Alzheimer's or dementia)

Patient had a history of allergy or sensitivity to corticosteroids or history of any drug hypersensitivity or intolerance that, in the opinion of the Investigator, would compromise the safety of the patient or the results of the study.

Interventions and Interactions

All study subjects will be treated with Topicort (desoximetasone spray 0.25%), an FDA approved drug for the treatment of plaque-type psoriasis.[2] Topicort 100mL sprays will be provided to the subjects, at no cost to the subject, throughout the study.

Supply of Study Drug at the Site

The Sponsor will ship Study Drug to the investigational site. The initial study drug shipment will be shipped after site activation (i.e., all required regulatory documentation has been received by the Sponsor

and a contract has been executed). Subsequent study drug shipments will be made after site request for resupply.

Dosage/Dosage Regimen

Study subjects will be provided with one 100 ml bottle of study medication along with instructions for dosing. Subjects will be asked to apply the drug twice daily on effected sites. Each application is approximately 0.5mL of solution.[2]

Storage

Study drug should be stored by the study site at controlled room temperature, 15 to 30ºC (59 to 86ºF). If the temperature of study drug storage in the clinic/pharmacy exceeds or falls below this range, this should be reported to the Sponsor or designee and captured as a deviation. Subjects will be instructed to store the medication in original packaging at room temperature according to the instructions outlined on the Drug Administration Instructions.[2]

Study Drug Accountability

An accurate and current accounting of the dispensing and return of study drug for each subject will be maintained on an ongoing basis by a member of the study site staff.

Clinical Assessments

Concomitant Medications

All concomitant medication and concurrent therapies will be documented at every visit, including baseline. Dose, route, unit frequency of administration, and indication for administration and dates of medication will be captured.

Demographics

Demographic information (date of birth, gender, race) will be recorded at Screening.

Medical History

Relevant medical history, including history of current disease, other pertinent respiratory history, and information regarding underlying diseases will be recorded at Screening.

Physical Examination

A physical examination will be performed by qualified health professional at the baseline visit. Qualified staff (MD, NP, RN, and PA) may complete the abbreviated physical exam at all other visits. New abnormal physical exam findings must be documented and will be followed by a physician or other qualified staff at the next scheduled visit.

Adverse Events

Information regarding occurrence of adverse events will be captured throughout the study. Duration (start and stop dates), severity/grade, outcome, treatment and relation to study drug will be recorded on the case report form (CRF).

Clinical Laboratory Measurements

Pregnancy Test

A urine pregnancy test will be obtained from female subjects who are of childbearing age prior to their participation in the study.

EVALUATIONS BY VISIT

Visit 1 (Baseline/Screening)

1. Review the study with the subject (subject's legal representative) and obtain written informed consent.
2. Assign the subject a unique screening number.
3. Record demographics data.
4. Record medical history, including smoking and alcohol use.
5. Record concomitant medications.
6. Perform a physical examination of the skin, which includes measuring and recording modified Eczema Area and Severity Index/Psoriasis Body surface area (EASI/PASI), Total Lesion Severity Score (TLSS), Investigator Global Assessment Score (IGA), and Pruritus Visual Analog Scale (VAS).
7. Perform and record vital signs.
8. Perform and record urinary test (for female subjects).
9. Schedule subject for Visit 2 in 3 days.
10. Dispense study drug with instructions on use and under supervision the patient will apply the medication

Visit 2 (Day 3)

1. Record any Adverse Experiences
2. Concomitant medications review.
3. Perform abbreviated physical examination, which includes measuring and recording subjects TLSS, EASI/PASI, IGA, and Pruritus VAS.

Visit 3 (Week 1)

1. Record any Adverse Experiences
2. Concomitant medications review.
3. Perform abbreviated physical examination, which includes measuring and recording subjects TLSS, EASI/PASI, IGA, and Pruritus VAS.

Visit 4 (Week 2)

1. Record any Adverse Experiences
2. Concomitant medications review.

3. Perform abbreviated physical examination, which includes measuring and recording subjects TLSS, EASI/PASI, IGA, and Pruritus VAS.

Outcome Measure(s)

The primary efficacy endpoint is the change in IGA, TLSS, from baseline. Other measures will include, EASI or PASI (for atopic dermatitis and psoriasis, respectively), target lesions severity score (TLSS), and Pruritus VAS scores from baseline

Analytical Plan

Results will be analyzed initially using descriptive statistics. Comparison between groups will be done using chi square tests for proportions, and t-tests or ANOVA procedures for continuous variables. Regression analysis will be performed to identify independent outcome predictors. Other inferential statistical analysis will be conducted as appropriate.

Human Subjects Protection

Subject Recruitment Methods

Subjects with a diagnosis of plaque-type psoriasis or atopic dermatitis who meet the inclusion and exclusion criteria will be eligible for participation in this study. Patients will be recruited via phone or in the dermatology clinic by staff members that are included in the IRB protocol. If recruited via phone, subjects will be invited to make an appointment for baseline visit. During the baseline visit, formal informed consent will be obtained. In clinic, if the patient is eligible for the study they will first be asked whether they would be interested in joining a research study pertaining to their plaque-type psoriasis or atopic dermatitis. If they reply yes, they will be given more information about the research study. If the patient agrees to participate, after the patient is complete with checkout they will be taken to the clinical studies research center. Women and minorities will be included. Women of childbearing potential will have to agree to practice birth control during their participation in the study. All recruitment conversations will take place over the phone, in an exam room, either in the clinic or the research center in order to maintain privacy and confidentiality.

Informed Consent

Signed informed consent will be obtained from each subject. A study team member will obtain informed consent from the subject in the exam room in the clinical studies research center.

Confidentiality and Privacy

Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. To help ensure subject privacy and confidentiality, only a unique study identifier will appear on the data collection form. Any collected patient identifying information corresponding to the unique study identifier will be maintained on a linkage file, store separately from the data. The linkage file will be kept secure, with access limited to designated study personnel. Following data collection subject identifying information will be destroyed (state the anticipated time the data will be destroyed, e.g. three years after closure of the study, and the method of destruction), consistent with data validation and study design, producing an anonymous analytical data set. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

Data and Safety Monitoring

The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

Reporting of Unanticipated Problems, Adverse Events or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

Early Discontinuation of Study Drug

A subject may be discontinued from study treatment at any time if the subject, the investigator, sub-investigator, or staff that are approved by the IRB, or the Sponsor feels that it is not in the subject's best interest to continue. The following is a list of possible reasons for study treatment discontinuation:

- Subject withdrawal of consent (or assent)
- Subject is not compliant with study procedures
- Adverse event that in the opinion of the investigator, sub-investigator, or staff that are approved by the IRB would be in the best interest of the subject to discontinue study treatment
- Protocol violation requiring discontinuation of study treatment
- Lost to follow-up
- Sponsor request for early termination of study
- Positive pregnancy test (females)

If a subject is withdrawn from treatment due to an adverse event, the subject will be followed and treated by the research study team until the abnormal parameter or symptom has resolved or stabilized.

All subjects who discontinue study treatment should come in for an early discontinuation visit as soon as possible and then should be encouraged to complete all remaining scheduled visits and procedures.

All subjects are free to withdraw from participation at any time, for any reason, specified or unspecified, and without prejudice.

Reasonable attempts will be made by the staff to provide a reason for subject withdrawals. The reason for the subject's withdrawal from the study will be specified in the subject's source documents.

References:
1. Data on file. Taro Pharmaceuticals U.S.A., Inc.
2. Topicort® Topical Spray Prescribing Information.Taro Pharmaceuticals U.S.A., Inc