An investigator initiated open label study evaluating the efficacy and tolerability of application of Metaderm product for the treatment of psoriasis

Study Protocol & Statistical Analysis Plan

NCT03597620

November 5, 2018

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

An investigator initiated open label study evaluating the efficacy and tolerability of application of Metaderm product for the treatment of psoriasis

PI: Boni Elewski, MD

Sponsor : Procter & Gamble

Introduction:

Psoriasis vulgaris is a common inflammatory condition of the skin that results in well-demarcated, scaly, erythematous, itchy plaques. In the United States, psoriasis remains a common, immune-mediated disease, affecting 7.4 million adults. (1) Often topical prescription medications are used as first line treatment for moderate psoriasis. Some topical medications have side effects and risk with long time use, thus not ideal for extensive and indefinite amount of time. Conversely, over- the-counter emollient treatments are readily available, safe and potentially efficacious. This study is design to test the safety and efficacy of topical application of the Metaderm product cream. The Metaderm cream is non-prescription, natural product.

Study objectives

Primary objective

The Primary efficacy and end point will be the mean percentage change in the product of sPGA and BSA (PGAxBSA) from baseline to week 12. The PGA x BSA is an assessment tools used to calculating disease severity and maybe more likely to differentiate among people with less disease severity (Walsh)

Secondary objective

The secondary efficacy and end point will be the percentage improvement in DLQI

Study Design

Study Outline

This is an open-label pilot study aimed at evaluating the efficacy and safety of treating psoriasis using the Metaderm product. The inclusion and exclusion criteria as listed below. Study designed into 3 subgroups:

1) 5 patients with plaque psoriasis 3-10% BSA
2) 5 patients with stable dose of biologic treatment and have plaque psoriasis with 3-10% BSA
3) 5 patients with scalp psoriasis

Number of subjects:

Total of 15 eligible patients will be enrolled. Patients will be treated for duration of 12 weeks. During the treatment phase patients will be evaluated every 4 weeks. All patients will be treated with the active medication, there will be no placebo arm in the study.

Visit Schedule

Screening Period

Patient eligibility will be determined within 28 days prior to enrollment in the study. Subjects who meet the inclusion and exclusion criteria may proceed to the baseline visit.

Study Visits

Subjects will report to the investigational site for disease and safety assessments every 4 weeks for total of 12 Weeks. Patients will have photos taken of 1-3 target lesions at baseline , W4 , W8, and W12 . Patient will complete the Itch Severity Scale (ISS, Visual Analogue Scale (VAS) and Dermatology Quality of Life Index (DLQI) questionnaires at every visit. Patient will have a Psoriasis Area and Severity Index (PASI), Static Physicians Global Assessment (sPGA) and Body Surface Area (BSA) evaluation at every visit.

Dosing schedule

15 eligible patients will be enrolled. Patient will be treated for 12 weeks. There will be a total of five visits: screening, baseline, w4, w8 and w12. Metaderm cream will be applied topically twice a day to all active lesions. The metaderm scalp spray will be applied daily to the affected areas on the scalp. Patients will be provided with metaderm cleanser, can be use daily. For the subgroup for scalp psoriasis, patient will use the shampoo Head & Shoulders formula with 1% Pyrithione Zinc as the active ingredient

Discontinuation of the Study

The study may be discontinued at the discretion of the investigator at any time without replacement

STUDY ENTRY CRITERIA

Patients will be recruited from the university hospital clinic as well as resident's continuity clinics

Inclusion Criteria for patients with plaque psoriasis 3-10% BSA

Subjects must satisfy the following criteria to be enrolled in the study:

1. Must be in general good health (except for disease under study) as judged by the Investigator, based on medical history, physical examination, clinical laboratories, and urinalysis. (NOTE: The definition of good health means a subject does not have uncontrolled significant co-morbid conditions).
2. Patients 18 and older
3. Give written informed consent prior to any study procedures being conducted, and candidates will authorize the release and use of protected health information (PHI)
4. Be willing and consent to having photos taken of their skin
5. Diagnosis of chronic plaque psoriasis that has been present for at least 6 months prior to baseline

6. Plaque psoriasis involving at least 3-10% of the patient's body surface area
7. Must have discontinued all systemic therapies for the treatment of psoriasis or psoriatic arthritis at least 4 weeks or 5 half-lives, and biologics 6 months) prior to baseline visit
8. Must have discontinued all topical therapies for the treatment of psoriasis at least 2 weeks prior to baseline visit
9. Subjects must have discontinued UV therapy at least 2 weeks prior to baseline and PUVA at least 4 weeks prior to baseline.
10. Subjects must be in good general health without significant uncontrolled comorbidities, other than psoriasis, as determined by the investigator based on exam findings, medical history, and clinical laboratories. Patients with stable mild renal insufficiency are eligible for enrolling in this trial.
11. Females of childbearing potential must use an approved birth control method while receiving treatment and for 28 days following the investigational product and there must be a documented negative pregnancy tests prior to initiating treatment. Approved birth control methods include hormonal contraception (oral, injection, implant, transdermal patch, vaginal ring), intrauterine device, tubal ligation (tying your tubes), partners vasectomy, or male or female condoms that are not made of natural materials PLUS a diaphragm with spermicide, cervical cap with spermicide, or a contraceptive sponge with spermicide. Females not of child bearing potential are defined as being at least 1 year postmenopausal or surgically sterile (bilateral tubal ligation, bilateral oophorectomy and/or hysterectomy).

Inclusion Criteria with stable dose of biologic treatment and have plaque psoriasis 3-10 %BSA

Subjects must satisfy the following criteria to be enrolled in the study:

1. Must be in general good health (except for disease under study) as judged by the Investigator, based on medical history, physical examination, clinical laboratories, and urinalysis. (NOTE: The definition of good health means a subject does not have uncontrolled significant co-morbid conditions).
2. Patients 18 and older
3. Give written informed consent prior to any study procedures being conducted, and candidates will authorize the release and use of protected health information (PHI)
4. Be willing and consent to having photos taken of their skin

5. Diagnosis of chronic plaque psoriasis that has been present for at least 6 months prior to baseline
6. Stable dose of biologic therapy for the last 6 months prior to screening visit
7. Plaque psoriasis involving at least 3-10% of the patient's body surface area
8. Must have discontinued all topical therapies for the treatment of psoriasis at least 2 weeks prior to baseline visit
9. Subjects must have discontinued UV therapy at least 2 weeks prior to baseline and PUVA at least 4 weeks prior to baseline.
10. Subjects must be in good general health without significant uncontrolled comorbidities, other than psoriasis, as determined by the investigator based on exam findings, medical history, and clinical laboratories. Patients with stable mild renal insufficiency are eligible for enrolling in this trial.
11. Females of childbearing potential must use an approved birth control method while receiving treatment and for 28 days following the investigational product and there must be a documented negative pregnancy tests prior to initiating treatment. Approved birth control methods include hormonal contraception (oral, injection, implant, transdermal patch, vaginal ring), intrauterine device, tubal ligation (tying your tubes), partners vasectomy, or male or female condoms that are not made of natural materials PLUS a diaphragm with spermicide, cervical cap with spermicide, or a contraceptive sponge with spermicide. Females not of child bearing potential are defined as being at least 1 year postmenopausal or surgically sterile (bilateral tubal ligation, bilateral oophorectomy and/or hysterectomy).

Inclusion Criteria for patients with scalp psoriasis

Subjects must satisfy the following criteria to be enrolled in the study:

1. Must be in general good health (except for disease under study) as judged by the Investigator, based on medical history, physical examination, clinical laboratories, and urinalysis. (NOTE: The definition of good health means a subject does not have uncontrolled significant co-morbid conditions).
2. Patients 18 and older
3. Give written informed consent prior to any study procedures being conducted, and candidates will authorize the release and use of protected health information (PHI)

4. Be willing and consent to having photos taken of their skin
5. Diagnosis of chronic plaque psoriasis that has been present for at least 6 months prior to baseline
6. Plaque psoriasis involving the scalp
7. Body plaque psoriasis cannot exceed 10 %BSA
8. Must have discontinued all systemic therapies for the treatment of psoriasis or psoriatic arthritis at least 4 weeks or 5 half-lives, and biologics 6 months) prior to baseline visit
9. Must have discontinued all topical therapies for the treatment of psoriasis at least 2 weeks prior to baseline visit
10. Subjects must have discontinued UV therapy at least 2 weeks prior to baseline and PUVA at least 4 weeks prior to baseline.
11. Subjects must be in good general health without significant uncontrolled comorbidities, other than psoriasis, as determined by the investigator based on exam findings, medical history, and clinical laboratories. Patients with stable mild renal insufficiency are eligible for enrolling in this trial.
12. Females of childbearing potential must use an approved birth control method while receiving treatment and for 28 days following the investigational product and there must be a documented negative pregnancy tests prior to initiating treatment. Approved birth control methods include hormonal contraception (oral, injection, implant, transdermal patch, vaginal ring), intrauterine device, tubal ligation (tying your tubes), partners vasectomy, or male or female condoms that are not made of natural materials PLUS a diaphragm with spermicide, cervical cap with spermicide, or a contraceptive sponge with spermicide. Females not of child bearing potential are defined as being at least 1 year postmenopausal or surgically sterile (bilateral tubal ligation, bilateral oophorectomy and/or hysterectomy).

Exclusion Criteria

The presence of any of the following will exclude a subject from enrollment:

13. Other than disease under study, any clinically significant (as determined by the Investigator) cardiac, endocrinologic, pulmonary, neurologic, psychiatric, hepatic, renal, hematologic, immunologic disease, or other major disease that is currently uncontrolled.

14. Any condition, including the presence of laboratory abnormalities, which would place the subject at unacceptable risk if he/she were to participate in the study.
15. Prior history of suicide attempt at any time in the subject's life time prior to screening or randomization, or major psychiatric illness requiring hospitalization within the last 3 years.
16. Pregnant or breast feeding.
17. Active substance abuse or a history of substance abuse within 6 months prior to Screening.
18. Use of any investigational drug within 4 weeks prior to randomization, or 5 pharmacokinetic/pharmacodynamic half lives, if known (whichever is longer).
19. Prior treatment with the investigational product
20. Unable to comply with the protocol (as defined by the Investigator; i.e. drug or alcohol abuse or history of noncompliance)
21. Any other dermatologic conditions that prohibit or confound the ability of the investigator to interpret skin and/or nail exam findings.
22. Patients who will be unable to avoid the use of systemic steroids, excluding intranasal or inhaled steroids that will be permitted, for the duration of the trial

STUDY PROCEDURES & TREATMENT PLAN GUIDELINES

Informed Consent:

A written, signed informed consent form (ICF) and written authorization to release and use PHI, will be obtained prior to performing any tests or evaluations under this protocol. Patients will have the option to ask questions and will be given at least 24 hours to review the ICF before signing. Patients may request the 24 hour review to be waived due to work or travel constraints.

See Protocol Flowchart for detailed timing of tests and evaluations.

General Concomitant Therapy:

Subjects should advise the investigator if they start taking any new medications, including over the counter and complementary and alternative medications.

Concomitant Therapy

Concomitant medications for psoriasis will not be permitted

SAFETY PLAN

Clinical Safety Assessments

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

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

Laboratory Safety Assessments

The following laboratory tests will be performed at screening, baseline:

- Urine pregnancy test, if applicable.

Test / Evaluation	Screening	Visit 1 W k 0	Visit 2 Wk 4	Visit 3 Wk 8	Visit 4 Wk 12
Informed Consent	X				
Inclusion/exclusion criteria reviewed	X	X			
Medical History	X				
Concomitant medications	X	X	X	X	X
Physical Exam	X				
Vital Signs	X	X	X	X	X
Urine pregnancy test	X	X			
Adverse Events	X	X	X	X	X
Photos of Target lesions	x	X	x	x	X
PASI	x	X	x	x	x
BSA	x	X	x	x	x
sPGA	x	x	x	x	x
ISS	X	X	X	X	X
PSSI	X	X	X	X	X
VAS	X	X	X	X	X
DLQI	X	X	X	X	X
IP dispensing		X	X	X	X
IP accountability			X	X	X

SAFETY REPORTING

Adverse Event

An adverse event (AE) is any noxious, unintended, or untoward medical occurrence occurring at any dose that may appear or worsen in a subject during the course of a study. It may be a new intercurrent illness, a worsening concomitant illness, an injury, or any concomitant impairment of the subject's health, including laboratory test values (as specified by the criteria below), regardless of etiology. Any medical condition that was present prior to study treatment and that remains unchanged or improved should not be recorded as an AE. If there is a worsening of that medical condition this should be considered an AE. A diagnosis or syndrome should be recorded on the AE page of the Case Report Form rather than the individual signs or symptoms of the diagnosis or syndrome.

All AEs will be recorded by the Investigator(s) from the time of signing the informed consent through the end of the designated follow-up period.

Serious adverse event

A serious adverse event (SAE) is any AE which:

- Results in death
- Is life-threatening (i.e., in the opinion of the Investigator(s) the subject is at immediate risk of death from the AE)
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity (a substantial disruption of the subject's ability to conduct normal life functions)
- Is a congenital anomaly/birth defect
- Constitutes an important medical event

Important medical events are defined as those occurrences that may not be immediately life threatening or result in death, hospitalization, or disability, but may jeopardize the subject or require medical or surgical intervention to prevent one of the other outcomes listed above. Medical and scientific judgment should be exercised in deciding whether such an AE should be considered serious.

Events not considered to be SAEs are hospitalizations which: were planned before entry into the clinical study; are for elective treatment of a condition unrelated to the studied indication or its treatment; occur on an emergency outpatient basis and do not result in admission (unless fulfilling other criteria above); are part of the normal treatment or monitoring of the studied indication and are not associated with any deterioration in condition.

If an AE is considered serious, both the AE pages of the CRF and the SAE Report Form must be completed.

For each SAE, the Investigator(s) will provide information on severity, start and stop dates, relationship to study drug, action taken regarding study drug, and outcome.

Classification of severity

For both AEs and SAEs, the investigator(s) must assess the severity of the event. The AEs will be evaluated for severity according to the following scale:

Grade 1 = Mild

Grade 2 = Moderate

Grade 3 = Severe

Classification of Relationship/Causality of adverse events (SAE/AE) to study drug

The Investigator(s) must determine the relationship between the administration of study drug and the occurrence of an AE/SAE as Not Suspected or Suspected as defined below:

Not suspected:	The temporal relationship of the adverse event to study drug administration makes **a causal relationship unlikely or remote**, or other medications, therapeutic interventions, or underlying conditions provide a sufficient explanation for the observed event
Suspected:	The temporal relationship of the adverse event to study drug administration makes **a causal relationship possible,** and other medications, therapeutic interventions, or underlying conditions do not provide a sufficient explanation for the observed event.

Immediate reporting of serious adverse events

Any AE that meets the any criterion for a SAE requires the completion of an SAE Report Form in addition to being recorded on the AE pages of the CRF. The Investigator(s) is required to ensure that the data on these forms is accurate and consistent. This applies to all SAEs, regardless of relationship to study drug, that occur during the study, those made known to the Investigator(s) within 30 days after a subject's last dose of study drug, and those made known to the investigator(s) at anytime that are suspected of being related to study drug.

The SAE must be reported immediately (i.e., within 24 hours of the Investigators' knowledge of the event)

The Investigator(s) is responsible for informing the Institutional Review Board/Ethics Committee (IRB/IEC) of the SAE and providing them with all relevant initial and follow-up information about the event. The Investigator(s) must keep copies of all SAE information, including correspondence with Celgene and the IRB/IEC, on file. All SAEs that have not resolved upon discontinuation of the subject's participation in the study must be followed until either the event resolves completely, stabilizes/resolves with sequelae, or returns to baseline (if a baseline value is available).

Citations

1. Rachakonda, Tara D. et al. Psoriasis prevalence among adults in the United States. Journal of the American Academy of Dermatology , Volume 70 , Issue 3 , 512 - 516
2. Walsh JA, McFadden M, Woodcock J, et al. Product of the Physician Global Assessment and body surface area: a simple static measure of psoriasis severity in a longitudinal cohort. J Am Acad Dermatol. 2013;69(6):931-937.