Investigator-Initiated, Open Label Trial of a Combination of Halobetasol Propionate 0.01% Andtazarotene 0.045% Lotion (Duobrii®) for Plaque Type Psoriasis of the Hands and/or Feet
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NCT04720105
Document Date: Nov 30, 2020

# Clinical Research Protocol

Investigator-Initiated, Open Label Trial of a combination of halobetasol propionate 0.01% and tazarotene 0.045% lotion (Duobrii®) for Plaque Type Psoriasis of the Hands and/or Feet

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| **Version Date** | November 30, 2020<br>(supersedes version date March 31, 2020) |
| **Investigational Product** | Duobrii® (halobetasol propionate 0.01%/tazarotene 0.045% lotion) |
| **Sponsor** | Ortho Dermatologics |
| **Principal Investigator** | Alice Gottlieb, MD, PhD<br>Mount Sinai Downtown Union Square<br><br>212-844-8800<br>alice.gottlieb@mountsinai.org |

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# Protocol Synopsis

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| **Title** | Investigator-initiated, Open Label Trial of Duobrii® for Plaque Type Psoriasis of the Hands and/or Feet |
| **Sponsor** | Ortho Dermatologics |
| **Study Design & Overview** | This is an investigator-initiated, single-arm, open-label study, which will examine the effect of Duobrii® (halobetasol propionate 0.01%/tazarotene 0.045% lotion, HP/TAZ) on plaque type psoriasis of the hands and/or feet. Previous therapies used and failed will be captured for each subject. The findings in this study will result in at least one poster at a conference and at least one publication. |
| **Primary Objective** | Evaluate the percentage of patients achieving Palmoplantar Physician Global Assessment (ppPGA) of 0 (clear) or 1 (almost clear/minimal) after 24 weeks of treatment[1] |
| **Secondary Objectives** | ● Percentage of patients achieving ppPGA of 0 or 1 at weeks 8, 12 and 16<br>● Photography (hands and/or feet only) to assess treatment response at weeks 0, 2, 8, 12, 16 and 24<br>● Patient-reported outcomes to be evaluated by Dermatology Quality of Life Index (DLQI)[2] at weeks 2, 8, 12, 16 and 24 |

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| | ● Treatment satisfaction to be evaluated by Numerical Rating Scale (NRS)[3] at weeks 2, 8, 12, 16 and 24 |
| **Number of Subjects** | 22 |
| **Subject Selection Criteria** | Inclusion Criteria<br>1. Subject is able to provide written, informed consent and comply with the study protocol.<br>2. Subject is at least 18 years of age.<br>3. Subject has a diagnosis of plaque-type palmar and/or plantar psoriasis.<br>4. Patient has at least one psoriatic plaque outside of the palms and soles or psoriatic nail findings.<br>5. Subject has a ppPGA ≥ 3 at screening/baseline visit.<br>6. Subject is using adequate birth control during the study period as defined as follows:<br>○ Option 1: Any one of the following highly effective methods: hormonal contraception (oral, injection, implant, transdermal patch, vaginal ring); intrauterine device (IUD); tubal ligation; or partner's vasectomy;<br>OR<br>○ Option 2: Male or female condom (latex condom or non-latex condom NOT |

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| | made out of natural [animal] membrane [for example, polyurethane]; PLUS one additional barrier method: (a) diaphragm with spermicide; (b) cervical cap with spermicide; or (c) contraceptive sponge with spermicide.<br>OR<br>1. Option 3: Abstinence from sex when it is a lifestyle choice, and not just a social circumstance.<br><br>Exclusion Criteria<br>1. Subject is not able to provide written, informed consent and comply with the study protocol.<br>2. Subject is less than 18 years of age.<br>3. Subject has non-plaque type psoriasis on the hands and/or feet.<br>4. Patient does not have any evidence of psoriasis elsewhere.<br>5. Subject has concurrent cutaneous disease affecting the hands and/or feet that would interfere with assessments.<br>6. Subject has a ppPGA < 3 at screening/baseline visit.<br>7. Subject refuses to discontinue concomitant prescription medications on hands and/or feet.<br>8. Subject has used prescription topical treatments or received phototherapy treatment for psoriasis within 2 weeks of screening/baseline visit. |

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| | 9. Subject has used intralesional kenalog within 4 weeks of screening/baseline visit.<br>10. Subject has taken oral treatments for psoriasis within 4 weeks of screening/baseline visit.<br>11. Subject has received any treatment with biologic medications within 5 half-lives (if known) or 16 weeks prior to screening/baseline, whichever is longer.<br>12. Subject refuses to use adequate birth control during the duration of the study period.<br>13. Subject is currently pregnant or breastfeeding. |

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| **Study Treatment** | Duobrii® (halobetasol propionate 0.01%/tazarotene 0.045% lotion), thin layer applied to affected areas of palms and/or soles once a day |
| **Study Duration** | The total duration of study activities is 24 weeks |
| **Schedule of Efficacy and Safety Assessments** | Screening/Baseline (Week 0), Week 2, Week 8, Week 12, Week 16, Week 24 |
| **Laboratory Work** | None |
| **Safety Evaluations** | Safety and tolerability will be assessed by adverse events, physical examinations (including skin examinations and ppPGA scoring), and concomitant medication review |
| **Statistical Analysis** | Assuming the 40% of patients achieve ppPGA of 0 or 1 (similar to that seen with secukinumab) at week 24, this study requires 22 patients with a statistical power of 0.8 and 5% type one error |
| **Budget Estimate** | $120,845<br><br>88 tubes of Duobrii® (4 tubes of Duobrii® for each subject) supplied by Ortho Dermatologics.<br><br>The medication will be dispensed to the subject at week 0,2,8,16 and returned by the |

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| | subject at week 2,8,16,24.<br><br>Subjects will be compensated $40 per study visit for their time and effort in participating in this study. |

# Brief Summary of Research

The purpose of this research study is to examine the effect of Duobrii® (halobetasol propionate 0.01%/tazarotene 0.045% lotion, HP/TAZ) on plaque type psoriasis of the hands and/or feet. It is an investigator-initiated, single-arm, open-label study that will include 22 subjects. A thin layer of HP/TAZ will be applied to affected areas of palms and/or soles once a day. Treatment response will be clinically evaluated using the Palmoplantar Physician Global Assessment (ppPGA), which is a 5-point scale specifically applied to the hands and/or feet: 0 (clear), 1 (almost clear/minimal), 2 (mild), 3 (moderate), 4 (marked/moderate-to-severe), 5 (severe). The primary objective of the study is to evaluate the percentage of subjects achieving ppPGA of 0 or 1 after 24 weeks of treatment. Secondary objectives include evaluation of treatment response at earlier timepoints (Weeks 2, 8, 12,16 and 24), including serial photography (also taken at week 0), patient-reported outcomes, and treatment satisfaction evaluation throughout the study period. In addition, safety and tolerability will be assessed by physical exam findings, adverse event monitoring, and concomitant medication review. Previous therapies used and failed will be captured for each subject.

# Background

Plaque type psoriasis of the hands and/or feet affects approximately 3-4% of patients with psoriasis.[4] It is characterized by well-defined erythematous desquamative plaques located on the palms and soles, which may be limited to acral involvement or occur in combination with generalized psoriasis.[5] Psoriasis that affects the hands and/or feet has a profound impact on quality of life (QoL) as it contributes to more physical disability and discomfort than patients with other forms of psoriasis, such as difficulty walking or using the hands.[1,6]

Furthermore, psoriasis of the hands and/or feet is generally considered a therapeutic challenge because the thicker stratum corneum reduces the penetration of topical treatment agents. Systemic treatments (retinoids, psoralen–ultraviolet A [PUVA], methotrexate, cyclosporine, and biologic therapy) have shown limited efficacy on psoriasis in acral areas.[5] Unfortunately, patients with hand and/or foot involvement often have too low of body surface area (BSA) to participate in clinical trials for new psoriasis

treatments, resulting in limited studies among this sub-population and no clear treatment algorithm.[1]

The high unmet need for an effective treatment for psoriasis of the hands and/or feet has been addressed in recent years with the development of new medications for generalized psoriasis that may also be effective in treating disease localized to acral areas. In 2015, two multicenter, double-blind, randomized, parallel-group phase 3 studies were conducted to assess the safety, tolerability, and efficacy of lotion containing a combination of halobetasol propionate 0.01% and tazarotene 0.045% (HP/TAZ).[7,8] The study population was subjects with moderate-to-severe psoriasis. The study results found that treatment success (defined as at least a 2-grade improvement from baseline Investigator Global Assessment score and a score of clear or almost clear) was achieved in around 40% of subjects by week 8, with substantial reductions in affected BSA, improvement in QoL, and a significant reduction in signs and symptoms of psoriasis.[7,8]

These phase 3 studies did not include a sub-analysis of the effect of HP/TAZ on psoriasis of the hands and/or feet. Given that topical steroids and topical retinoids are separately recommended as treatment options for psoriasis of the hands and/or feet, an agent that safely combines these medications – and that has demonstrated safety and efficacy in generalized psoriasis – offers a potential treatment for psoriasis of the hands and/or feet.

The purpose of the study described in this protocol is to evaluate the effect of HP/TAZ on plaque type psoriasis of the hands and/or feet after 24 weeks of daily treatment. In addition, given the impact of this variant of psoriasis on QoL and the relative lack of currently available treatment options, this study will also evaluate the impact of HP/TAZ treatment on patient-reported QoL measures and treatment satisfaction scoring.

# Setting of Human Research

All research related activities will take place at Mount Sinai Downtown Department of Dermatology located at 10 Union Square E, New York, NY.

# Study Objectives

**Research Question:** What is the effect of Duobrii® (halobetasol propionate 0.01%/tazarotene 0.045% lotion, HP/TAZ) on plaque type psoriasis of the hands and/or feet?

This study will evaluate the hypothesis that HP/TAZ can improve plaque type psoriasis of the hands and/or feet. The purpose is to evaluate the effect of once daily treatment with HP/TAZ for 24 weeks among 22 subjects. Treatment response will be evaluated using the Palmoplantar Physician Global Assessment (ppPGA) 5-point scale.[1] The primary objective is to determine what percentage of subjects achieve a ppPGA of 0 (clear) or 1 (almost clear/minimal) after 24 weeks of treatment.

# Study Design

The study aims to enroll 22 subjects at a single study site. This number assumes that 40% of subjects with plaque type psoriasis of the hands and/or feet will achieve a ppPGA of 0 or 1 (based on results seen with secukinumab) at week 24. Based on this, the study requires 22 patients to achieve a statistical power of 0.8 and 5% type one error. Based on retrospective data of similar studies conducted at this site, recruitment and enrollment of 22 subjects is feasible and expected to be completed in 12 months.

The study staff includes individuals who are experienced in conducting research and have comprehensive knowledge of the study population, culture, and society. This is a single-site study, so no management of information among sites will be necessary to protect subjects. This study is not classified as Community-Based Participatory Research.

Given that it is a single-arm, open-label study, there will be no randomization.

Study Timeline:

- An individual subject will participate in study activities for a total of 24 weeks from initial screening/baseline visit at Week 0 to the final study visit at Week 24.
- It is anticipated that it will take up to 12 months to enroll all study subjects.

- It is estimated that this study will be completed, including completion of primary analyses, by the end of 2022.

Potential subjects will be screened for eligibility based on the inclusion and exclusion criteria indicated below.

*Inclusion Criteria*

1. Subject is able to provide written, informed consent and comply with the study protocol.
2. Subject is at least 18 years of age.
3. Subject has a diagnosis of plaque-type palmar and/or plantar psoriasis.
4. Patient has at least one psoriatic plaque outside of the palms and soles or psoriatic nail findings.
5. Subject has a ppPGA ≥ 3 at screening/baseline visit.
6. Subject is using adequate birth control during the study period as defined as follows:
    a. Option 1: Any one of the following highly effective methods: hormonal contraception (oral, injection, implant, transdermal patch, vaginal ring); intrauterine device (IUD); tubal ligation; or partner's vasectomy;

    OR

    b. Option 2: Male or female condom (latex condom or nonlatex condom NOT made out of natural [animal] membrane [for example, polyurethane]; PLUS one additional barrier method: (a) diaphragm with spermicide; (b) cervical cap with spermicide; or (c) contraceptive sponge with spermicide.

    OR

    c. Option 3: Abstinence from sex when it is a lifestyle choice, and not just a social circumstance.

*Exclusion Criteria*

1. Subject is not able to provide written, informed consent and comply with the study protocol.
2. Subject is less than 18 years of age.
3. Subject has non-plaque type psoriasis on the hands and/or feet.
4. Patient does not have any evidence of psoriasis elsewhere.

5. Subject has concurrent cutaneous disease affecting the hands and/or feet that would interfere with assessments.
6. Subject has a ppPGA < 3 at screening/baseline visit.
7. Subject refuses to discontinue concomitant prescription medications on hands and/or feet.
8. Subject has used topical prescription treatments or received phototherapy treatment for psoriasis within 2 weeks of screening/baseline visit.
9. Subject has used intralesional kenalog within 4 weeks of screening/baseline visit.
10. Subject has taken oral treatments for psoriasis within 4 weeks of screening/baseline visit.
11. Subject has received any treatment with biologic medications within 5 half-lives (if known) or 16 weeks prior to screening/baseline, whichever is longer.
12. Subject refuses to use adequate birth control during the duration of the study period.
13. Subject is currently pregnant or breastfeeding.

# Criteria for Evaluation

The primary endpoint of this study is an individual subject achieving Palmoplantar Physician Global Assessment (ppPGA) of 0 (clear) or 1 (almost clear/minimal) after 24 weeks of treatment. The ppPGA is based on the Investigators Global Assessment (IGA) modified version 11, specifically applied to the hands and/or feet: 0 (clear), 1 (almost clear/minimal), 2 (mild), 3 (moderate), 4 (marked/moderate-to-severe), 5 (severe). [1]

The secondary endpoints of this study include the following:

- Percentage of patients achieving ppPGA of 0 or 1 at weeks 8, 12 and 16
- Photography (hands and/or feet only) to assess treatment response at weeks 0, 2, 8, 12, 16 and 24
- Patient-reported outcomes evaluated by Dermatology Quality of Life Index (DLQI)[2] to be determined at weeks 2, 8, 12, 16 and 24
- Treatment satisfaction evaluated by a Numerical Rating Scale (NRS)[3] to be determined at weeks 2, 8, 12, 16 and 24

The DLQI is a 10 question dermatology-specific quality of life questionnaire covering the following topics: symptoms, embarrassment, shopping and home care, clothes, social and leisure, sport, work or study, close relationships, sex, treatment. Each question refers

to the impact of the skin disease on the patient's life over the previous week.[2]

The NRS for treatment satisfaction consists of 1 question: “Consider all the good and bad things about this treatment. Overall, how satisfied are you with the treatment?” Answer options: -3 (very dissatisfied), -2 (moderately satisfied), -1 (mildly satisfied), 1 (mildly satisfied), 2 (moderately satisfied), 3 (very satisfied).

There are no anticipated primary or secondary safety endpoints that would cause a study subject’s participation to end due to safety.

# Subject Selection

Potential subjects will be recruited from routine clinical appointments at Mount Sinai dermatology clinics as well as Mount Sinai-affiliated dermatologists and other referring dermatologists.

# Concomitant Therapies

All concomitant therapies must be recorded throughout the study period, from Screening/Baseline through Week 24. Subjects will be asked about concomitant therapies as part of the review of medical history at every study visit. With respect to specific classes of concomitant therapies:

- Topical therapies: Topical therapies that could affect the ppPGA evaluations (eg, corticosteroids, tar, anthralin, calcipotriene, tazarotene, methoxsalen, pimecrolimus, tacrolimus) are not permitted. The only allowable concomitant treatments throughout the study are non-medicated topical moisturizers. However, subjects should not use non-medicated topical moisturizers on the day of a study visit.
- Phototherapy: The use of phototherapy is not permitted at any time during the study.
- Systemic therapy: The use of systemic psoriasis medications is not permitted at any time during the study. These medications include those targeted for reducing TNF (including but not limited to infliximab or etanercept), drugs targeted for reducing IL-12, IL-17, or IL-23 (including but not limited to ustekinumab, tildrakizumab, secukinumab, ixekizumab, or brodalumab), alpha-4 integrin antagonists (including but not limited to natalizumab), systemic steroids, any conventional systemic therapy that could affect ppPGA evaluation (including but

not limited to methotrexate, cyclosporine, acitretin), and any other biological agent or other systemic medication that could affect the ppPGA evaluation.

- Other therapies: Every effort should be made to keep subjects on stable frequency and dosing of concomitant medications for general medical conditions. Such medications should be recorded at Week 0 (Screening/Baseline Visit) and if any changes to frequency or dosing are made during the duration of the study, such changes should be reported by the patient and recorded in the source documents.

# Study Treatments

Upon enrollment in the study, each subject will be given a supply of HP/TAZ at visits 0,2,8,16 to be used over the 24 weeks. Each subject will be instructed to apply a thin layer HP/TAZ to affected areas of palms and/or soles once a day for the duration of the study (i.e. daily treatment for 24 weeks).

All study treatments will be completed by the subject and will occur in the home setting. Subjects will be encouraged to record and report any missed treatments. Patients will be allowed to use OTC moisturizers, but should not apply them the days of their visits.

# Study Procedures & Guidelines

The study is designed to include six study visits over 24 weeks. The procedures performed at each study visit are detailed below. All procedures will be performed at the single study site. They will also be instructed to store the investigational drug at 20 to 25 °C (68 to 77 °F), and to not freeze the drug.

A table detailing the study procedures is found in Appendix 1. All study visits and procedures will be documented in source documents created specifically for this study that will be completed in accordance with Good Clinical Practice (GP) documentation principles (i.e. attributable, legible, contemporaneous, original, accurate, enduring, available and accessible, complete, consistent, credible, and corroborated[9]).

I. Week 0 (Screening/Baseline)
    A. Review Inclusion/Exclusion criteria
    B. Obtain written informed consent
    C. Review medical history and previous failed therapies

D. Review concomitant medications
E. Perform physical examination
F. Obtain urine pregnancy test (for pre-menopausal female subjects only)
G. Evaluate ppPGA
H. Obtain photographs of affected areas
I. Dispense study drug

II. Week 2
A. Review adverse events
B. Review concomitant medications
C. Evaluate ppPGA
D. Administer DQLI
E. Administer NRS for treatment satisfaction
F. Obtain photographs of affected areas
G. Dispense study drug
H. Collect study drug

III. Week 8
A. Review adverse events
B. Review concomitant medications
C. Evaluate ppPGA
D. Administer DQLI
E. Administer NRS for treatment satisfaction
F. Obtain photographs of affected areas
G. Dispense study drug
H. Collect study drug

IV. Week 12
A. Review adverse events
B. Review concomitant medications
C. Evaluate ppPGA
D. Administer DQLI
E. Administer NRS for treatment satisfaction
F. Obtain photographs of affected areas

V. Week 16
A. Review adverse events
B. Review concomitant medications
C. Evaluate ppPGA
D. Administer DQLI

E. Administer NRS for treatment satisfaction
F. Obtain photographs of affected areas
G. Dispense study drug
H. Collect study drug

VI. Week 24
A. Review adverse events
B. Review concomitant medications
C. Evaluate ppPGA
D. Administer DQLI
E. Administer NRS for treatment satisfaction
F. Obtain photographs of affected areas
G. Collect study drug

VII. Early Termination
A. Review adverse events
B. Review concomitant medications
C. Evaluate ppPGA
D. Administer DQLI
E. Administer NRS for treatment satisfaction
F. Obtain photographs of affected areas
G. Collect study drug
H. Physical examination

# Adverse Effects and Reporting

Safety information obtained across two Phase 3 clinical trials of HP/TAZ[5,6] include the following risks:

- The most common adverse reactions are contact dermatitis (7%), application site pain (3%), folliculitis (2%), skin atrophy (2%), and excoriation (2%). No serious treatment-related AEs were reported but would include severe hypersensitivity reactions and anaphylaxis.
- HP/TAZ contains tazarotene, which is a teratogenic substance. Therefore, HP/TAZ is contraindicated in pregnancy and in this study, all pre-menopausal female subjects must have a negative pregnancy test before enrolling.

- HP/TAZ contains halobetasol propionate, which is a steroid. Therefore, reversible hypothalamic-pituitary-adrenal (HPA) axis suppression may occur, with the potential for glucocorticosteroid insufficiency during or after treatment. Systemic effects of topical corticosteroids may also include Cushing's syndrome, hyperglycemia, and glucosuria. Systemic absorption may require evaluation for HPA axis suppression. Use of potent corticosteroids on large areas, for prolonged durations, under occlusive dressings, or on an altered skin barrier may increase systemic exposure. In addition, the use of topical corticosteroids may increase the risk of posterior subcapsular cataracts and glaucoma. Cataracts and glaucoma have been reported postmarketing with the use of topical corticosteroid products. Advise patients to report any visual symptoms and consider referral to an ophthalmologist for evaluation.
- Some individuals may experience atrophy, striae, telangiectasias, and folliculitis at the application site. If these effects occur, discontinue until the integrity of the skin has been restored. Duobrii® should not be used on eczematous skin, as it may cause severe irritation.
- HPT/TAZ can cause photosensitivity and increase the risk of sunburn. Avoid exposure to sunlight, sunlamps, and weather extremes.
- Skin infections

Unexpected fatal or serious adverse events will be reported to the IRB as soon as possible and no later than 7 calendar days after receipt of the information. Any other unanticipated adverse events will be reported no later than 14 days of receipt of the information.

Pregnancies occurring during the study will be reported no later than 7 days of receipt of information and subjects will subsequently be withdraw

# Protocol Violations

Subjects may withdraw from the trial at any time at their request (verbal or written), or they may be withdrawn at any time at the discretion of the Sponsor, PI, or designee for safety, behavioral, or administrative reasons. Subjects may be withdrawn from this study without their consent if the research study is being stopped; or if the instructions of the study team have not been followed.

Any enrolled subject who will not be completing the duration of the study will be asked to complete an Early Termination study visit, consisting of the procedures indicated below. In addition, the reason for Early Termination will be recorded in the source documents.

1) Review medical history
2) Review concomitant medications
3) Perform physical examination
4) Obtain urine pregnancy test (for pre-menopausal female subjects only)
5) Evaluate ppPGA
6) Administer DQLI

7) Administer NRS for treatment satisfaction
8) Obtain photographs of affected areas

If a subject is unable or unwilling to complete an Early Termination visit, this will be documented in the source documents.

# Statistical Methods & Considerations

Assuming the 40% of patients achieve ppPGA of 0 or 1 (similar to that seen with secukinumab) at week 24, this study requires 22 patients with a statistical power of 0.8 and 5% type one error.

Post-trial statistics of the data will be assessed by an individual that's not part of the study staff.

# Data Collection, Retention, & Monitoring

Data collected during this study will include: patient demographic information, past medical history, adverse events, concomitant medication, physical exam findings, urine pregnancy test results (for pre-menopausal female subjects only), ppPGA evaluations, DLQI evaluations, NRS for treatment satisfaction evaluations, and serial photography of affected areas. These data will be stored on-site, with the source documents in a secure, locked physical location and the electronic data in a password-protected format.

Access to this data will be limited to study staff. All study staff will be trained on how to maintain the security of the data via limited authorization of access, password protection, encryption, physical controls, and separation of identifiers and data.

This data will be stored on-site for a minimum of 10 years following completion of all study activities.

# Ethical & Regulatory Considerations

**Consent process:** Consent discussions will occur in a private setting. The consent process will be initiated well in advance to ensure that subjects have sufficient opportunity to consider participation.

The consent process will be enforced per SOP HRP-090 Informed Consent Process for Research. Individuals listed in the application are authorized to obtain consent. However, to minimize undue influence and to allocate ample time for discussion, the consent responsibility will be delegated to the dermatology clinical trial research team.
No children (i.e. subjects under the age of 18) or cognitively impaired adults (i.e. adults who may be unable to consent) will be enrolled in this study.

Consent of the subjects will be documented in writing per the standard PPHS consent template.

**Sharing of results:** Results of this study will not be shared with subjects or others who are not directly involved in the study (e.g. subjects' primary care physicians).

**Specimen banking:** No specimens will be banked in association with this study.

**External IRB Review History:** This protocol has not been previously submitted to an external IRB.

**Control of drugs:** The investigational drug will be stored at 20 to 25 °C (68 to 77 °F) in a secure, locked on-site location that is accessible only by authorized investigators involved in the study.

**Publication of study findings:** The findings in this study will result in at least one poster at a conference and at least one publication.

# References


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# Figure 1: Patient-Reported Outcomes instrument

**DERMATOLOGY LIFE QUALITY INDEX (DLQI)**

**The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please check one box for each question.**

| | | | | |
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| 1. | Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been? | Very much<br>A lot<br>A little<br>Not at all | ☐<br>☐<br>☐<br>☐ | |
| 2. | Over the last week, how **embarrassed** or **self conscious** have you been because of your skin? | Very much<br>A lot<br>A little<br>Not at all | ☐<br>☐<br>☐<br>☐ | |
| 3. | Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **yard?** | Very much<br>A lot<br>A little<br>Not at all | ☐<br>☐<br>☐<br>☐ | Not relevant ☐ |
| 4. | Over the last week, how much has your skin influenced the **clothes** you wear? | Very much<br>A lot<br>A little<br>Not at all | ☐<br>☐<br>☐<br>☐ | Not relevant ☐ |
| 5. | Over the last week, how much has your skin affected any **social** or **leisure** activities? | Very much<br>A lot<br>A little<br>Not at all | ☐<br>☐<br>☐<br>☐ | Not relevant ☐ |
| 6. | Over the last week, how much has your skin made it difficult for you to do any **sport**? | Very much<br>A lot<br>A little<br>Not at all | ☐<br>☐<br>☐<br>☐ | Not relevant ☐ |

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| 7. | Over the last week, has your skin prevented you from **working** or **studying**? | yes<br>no | ☐<br>☐ | Not relevant ☐ |
| | If "No", over the last week how much has your skin been a problem at **work** or **studying**? | A lot<br>A little<br>Not at all | ☐<br>☐<br>☐ | |
| 8. | Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**? | Very much<br>A lot<br>A little<br>Not at all | ☐<br>☐<br>☐<br>☐ | Not relevant ☐ |
| 9. | Over the last week, how much has your skin caused any **sexual difficulties**? | Very much<br>A lot<br>A little<br>Not at all | ☐<br>☐<br>☐<br>☐ | Not relevant ☐ |
| 10. | Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time? | Very much<br>A lot<br>A little<br>Not at all | ☐<br>☐<br>☐<br>☐ | Not relevant ☐ |

**Please check you have answered EVERY question. Thank you.**

Source: Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. Clin Exp Dermatol. 1994;19(3):210-216.

# Figure 2: Treatment Satisfaction instrument

**NUMERICAL RATING SCALE (NRS) FOR TREATMENT SATISFACTION**

**Consider all the good and bad things about this treatment. Overall, how satisfied are you with the treatment?**

**(circle one)**

| | |
|---|---|
| -3 | Very dissatisfied |
| -2 | Moderately dissatisfied |
| -1 | Mildly dissatisfied |
| 1 | Mildly satisfied |
| 2 | Moderately satisfied |
| 3 | Very satisfied |

Source: Salame N, Perez-Chada LM, Singh S, Garg KA, Gottlieb AB, Latella J, Merola, JF, Armstrong AW. International Dermatology Outcome Measures (IDEOM) Annual Meeting. Washington, DC. May 2019.

# Appendix 1: Evaluation Schedule

| Visit | Wk 0 Screening/ Baseline | Wk 2 | Wk 8 | Wk 12 | Wk 16 | Wk 24/ Early Termination |
|---|---|---|---|---|---|---|
| Inclusion/Exclusion criteria | X | | | | | |
| Informed consent | X | | | | | |
| Review medical history, including previous and concomitant therapies | X | | | | | |
| Adverse events | | X | X | X | X | X |
| Review con meds | X | X | X | X | X | X |
| Physical examination | X | | | | | X** |
| Urine pregnancy test* | X | | | | | |
| ppPGA | X | X | X | X | X | X |
| DLQI | | X | X | X | X | X |
| NRS for treatment satisfaction | | X | X | X | X | X |
| Photography | X | X | X | X | X | X |
| Dispense drug | X | X | X | | X | |
| Collect Drug | | X | X | | X | X |

*Urine pregnancy test is required for pre-menopausal female subjects only.
**Physical examination is only required for early termination

ppPGA: Palmoplantar Physician Global Assessment is based on the Investigators Global Assessment (IGA) modified version 2011, specifically applied to the palms and soles and consisting of a 5-point scale: 0 (clear), 1 (almost clear/minimal), 2 (mild), 3 (moderate), 4 (marked/moderate-to-severe), 5 (severe).

DLQI: Dermatology Quality of Life Index is a 10 question dermatology-specific quality of life questionnaire.

NRS for treatment satisfaction: Numerical Rating Scale consisting of 1 question: “Consider all the good and bad things about this treatment. Overall, how satisfied are you with the treatment?” Answer options: -3 (very dissatisfied), -2 (moderately satisfied), -1 (mildly satisfied), 1 (mildly satisfied), 2 (moderately satisfied), 3 (very satisfied)