Photos Study

Title: Excimer Laser**Ph**ototherapy **O**utcomes in the **T**reatment **O**f P**s**oriasis: A randomized clinical trial to determine whether a novel plaque-based dosimetry strategy can improve the speed of response to treatment in patients with plaque psoriasis (The Photos Study)

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Synopsis	
Objectives	To determine whether a novel plaque-based dosimetry strategy can improve the speed of response to excimer laser treatment (Photomedex XTRAC ® Velocity) in patients with plaque psoriasis.
Methodology	Randomized, assessor-blinded, bilateral comparison clinical trial
Study Period	10 weeks
Number of Subjects	Up to 30
Dosing Regimen	Each patient will receive plaque-based dosing on one side of the body and conventional dosing on the contralateral side. Patients will be treated 1-2 times per week for a maximum of 10 treatments.
Diagnosis and Main Criteria for Inclusion into the Study	Males and females subjects at least 18 years of age with plaque-type psoriasis affecting a body surface area ≤ 10 percent.
Endpoints	**Primary Endpoint**: 1. Change in mPASI of target lesions on each side of the body over time **Secondary Endpoints:** 2. Number of treatments to reach a reduction in mPASI of 75% 3. Percentage of patients reaching a reduction in mPASI of 75% after 10 treatments 4. Change in PGA of each side of the body over time 5. Percentage of patients reaching PGA of 0 or 1 after 10 treatments 6. Number of treatments to reach PGA of 0 or 1 **Safety:** Safety will be assessed by tabulations of adverse events (AE's), with all AE's during the study recorded at each visit.
Statistical Methods	Statistical significance will be based on resulting p-values of 0.05 or less
Ethical Considerations	This study will be conducted in accordance with applicable laws and regulations and according to the recommendations of International Conference on Harmonization Good Clinical Practice (ICH GCP) guidelines and those of the Declaration of Helsinki (Edinburgh, 2000); only after approval for the study has been obtained from the relevant regulatory authority and relevant independent ethics committee (IEC). The institutional review board (IRB)/IEC must review and approve the protocol and informed consent form (ICF) before any subjects are enrolled. The subject must be consented using the approved ICF before any procedures specified in the protocol are performed.

STUDY TITLE: ExcimerLaser **Ph**ototherapy **O**utcomes in the **T**reatment **O**f P**s**oriasis: Arandomized clinical trialto determine whether a novel plaque-based dosimetry strategy can improve the speed of response to treatmentin patients with plaque psoriasis (The Photos Study)

ABSTRACT

Objectives: To determine whether a novel plaque-based dosimetry strategy can improve the speed of response to excimer laser treatment in patients with plaque psoriasis.

Design: Randomized, assessor-blinded, bilateral comparison clinical trial

Subjects: Consecutive sample of patients with generalized plaque type psoriasis seen at the University of California San Francisco Psoriasis and Skin Treatment Center

Variables:

Predictor Variables – plaque-based dosimetry vs. induration and skin type guesstimated dosimetry (Appendix A-1)

Outcome Variables – clearing of target plaque (modified PASI) over time

SPECIFIC AIMS

- To assess the difference in the rate of improvement of plaque psoriasis treated with excimer laser using plaque-based dosimetry compared with current treatment guidelines.

A. BACKGROUND AND RATIONALE:

Psoriasis is a chronic inflammatory condition that is associated with significant morbidityand affects7.5 million Americans.[1]Patients with untreated generalized psoriasis suffer from adecreased quality of life, comparable to patients living with conditions such as congestive heart failure, diabetes mellitus and breast cancer.[2]Further, patients with psoriasis are more likely to be depressed and experience suicidal ideation compared to the general population.

While there are many treatments for psoriasis including topical therapies, oral agents and injectable biologic medications, one of the safest and most widely used is ultraviolet (UV)-B phototherapy.[1]Excimer laser therapy is the most convenient modality of phototherapy, clearing psoriatic plaques in less than half the number of treatments needed with traditional UVB booth phototherapy.[3-5] In contrast to traditional UVB phototherapy, which exposes the whole body, excimer laser therapy targets only lesional plaques. As a result, the clinician is able to dose more aggressively, resulting in faster clearance.

The current standard of care is to determine dosimetry based on skin type and plaque induration (see Appendix A-1). This 'guesstimated' dose is extrapolated from whole body UVB box phototherapy. An alternative method is to use a dose that is 2-4 times higher than the minimal erythema dose (MED) of non-psoriatic skin, a strategy is known as "supra-erythemogenic phototherapy" (see Appendix A-2).[6]However, non-psoriatic skin is much less tolerantto UVB radiation than psoriatic plaques. Thus, a more rational approach

to determining the optimal dosimetry than either of the above strategies can be devised based on direct testing of*psoriatic plaques.*

Prior studies have shown thatthe dose (mj/cm^2) of ultraviolet B administeredis the single most important factor in determining both clearance and duration of therapeutic response of psoriatic plaques to excimer laser phototherapy (5–7). Interestingly, the number of phototherapy sessions is not as critical. Based on these observations, it is best to treat the patient with a dosimetry that is as high as possible, without causing discomfort or blistering to the psoriatic plaques. In order to determine the optimal dosimetry strategy, we propose a head-to-head, bilateral comparison clinical trial that compares plaque-based dosimetryto the current standard of care.

B. STUDY OBJECTIVE

The primary objective of this study is to determine whether a novel plaque-based dosimetry strategy can improve the speed of response toexcimer laser treatment in patients with plaque psoriasis.

C. STUDY DESIGN

This is a randomized, assessor-blindedclinical trial to determine whether a novel plaque-based dosimetry strategy can improve the speed of response to excimer laser treatment (measured by change in Modified Psoriasis Area and Severity Index [mPASI] of target lesion over time) in patients with plaque psoriasis. To minimize the effect of inter-subject variability in response to treatment, this study will use a bilateral comparison

design. Each patient will receive plaque-based dosing on one side of the body and conventional dosing (Appendix A-1) on the contralateral side. This design is based on the assumption that psoriasis usually affects patients in a symmetric distribution (e.g., knees and elbows) and the effect of excimer laser phototherapy is limited to the treated plaque. The side of the body treated with plaque-based dosimetry will be assigned using a table of random numbers. The assessor will be blinded to the treatment group.Each patient will be treated 1-2 times per week at the discretion of the investigator for a maximum of 10 treatments. A summary of study procedures is described in Appendix B.

D. STUDY SUBJECTS

Target Population: Patients with generalized plaque type psoriasis

Accessible Population: Patients with generalized plaque type psoriasis seen at the University of California San Francisco Psoriasis and Skin Treatment Center

Inclusion Criteria:

1) Diagnosis of chronic plaque psoriasis for at least 6 months
2) Age ≥ 18 years
3) Body surface area affected ≤ 10 percent
4) Presence of at least one pair of bilateral target lesions with an area of at least 20 cm^2per target lesion. The bilateral target lesions must be present in the same category of anatomical region (e.g., bilateral lower extremities, bilateral upper extremities or bilateral trunk).

Exclusion Criteria:

1) active or past history of erythrodermic psoriasis, guttate psoriasis, or pustular psoriasis
2) history of photosensitivity disorder
3) history of malignant melanoma
4) active, invasive non-melanoma skin carcinoma
5) Fitzpatrick Skin Type I

6) Subject has received UVB phototherapy or any topical anti-psoriatic therapy within two weeks prior to starting the study.
7) Subject has received systemic or topical psoralen-UVA photochemotherapy within four weeks prior to starting the study.
8) Subject has received biologic therapy within three months of starting the study.

Sampling: Consecutive sample

Recruitment: Eligible patients will be recruited from the Psoriasis and Skin Treatment Center outpatient clinic and from the center's research study hotline.

Ineligible patients or those who decline to participate will be offered the standard of care of psoriasis treatment.

E. STUDY ENDPOINTS

Primary Endpoint:

1. Change in mPASI of target lesions on each side of the body over time

Secondary Endpoints:

2. Number of treatment to reach a reduction in mPASI of 75%
3. Percentage of patients reaching a reduction in mPASI of 75% after 10 treatments
4. Change in PGA of each side of the body over time
5. Percentage of patients reaching PGA of 0 or 1 after 10 treatments
6. Number of treatments to reach PGA of 0 or 1
7. Change in PASI over time for each side of body
8. Percentage of patients reaching a 75% reduction in PASI after 10 treatments
9. Change in Patient's Global Assessment of each side of body over time

The mPASI for each target lesion will be calculated based on erythema, induration, scaling and area scores. Erythema, induration and scaling will be graded on a four-point scale including: [0] none, [1] slight, [2] mild, [3] moderate and [4] severe. The area score will be graded on a six-point scale based on percentage of the target lesion involved: [0] clear, [1] <10%, [2] 10-30%, [3] 30-50%, [4] 50-70%, [5] 70-90%, or [6] 90-100%. This percentage

will be calculated as one minus the proportion of the target lesion cleared compared to the pretreatment baseline.

The PGA is a measurement determined by the investigator that gives an overall clinical impression of the psoriatic lesions of the patient. The PGA is graded on a seven-point scale including: [0] clear, [1] almost clear, [2] mild, [3] mild-to-moderate, [4] moderate, [5] moderate-to-severe and [6] severe. Four characteristics of the patient's psoriatic plaques are considered when determining the PGA including erythema, induration, scaling and total area affected.

F. STUDY TREATMENTS

Control: Dosimetry based on induration and skin type of subject (see Appendix A-1)
Intervention: Dosimetry based on plaque-based testing

Method of Assigning Subjects Treatment

Up to 30 eligible patients will randomly assigned to receive plaque-based dosing on one-half of their body and conventional dosing on the other side. The side of the body treated with plaque-based dosimetry will be assigned using a table of random numbers. Patients will be treated with the Photomedex XTRAC® Velocity, the latest version of the excimer laser.

Blinding

Due to the objectives of the study, the identity of test and control treatments will not be known to investigators or patients. Research staff administering the treatments will know the treatment assignment so they can correctly treat the patients. The following study procedures will be in place to ensure blinding is maintained.

- Access to the randomization code will be strictly controlled.
- The assessor will be blinded to the treatment group
- One investigator will strictly assess the outcome variables while a different investigator will perform the plaque-based testing and administer the excimer treatments.

- Target plaques on both sides of the body will be tested with the new dosimetry device. Therefore, the results of the testing (ink marks, erythema, etc.) will not clue the blinded assessor as to the treatment assignment.

The study blind will be broken on completion of the clinical study and after the study database has been locked. Patients can be made aware of treatment assignments at this time. During the study, the blind may be broken **only** in emergencies when knowledge of the patient's treatment group is necessary for further patient management. The principal investigator will make this determination in consultation with the patient.

G. STUDY PROCEDURES AND GUIDELINES

A Schedule of Events representing the required testing procedures to be performed for the duration of the study is diagrammed in Appendix B.

Prior to conducting any study-related activities, written informed consent and the Health Insurance Portability and Accountability Act (HIPAA) authorization must be signed and dated by the subject. If appropriate, assent must also be obtained prior to conducting any study-related activities.

Determining dosimetry based on plaque-based testing:

Plaque-based testing will be performed in least one but not more than three anatomical areas, namely the trunk, arms and legs. Test lesions need to be at least 2 cm by 2 cm. They will be marked with an inkpad to indicate orientation, photographed and diagrammed in source documentation. These lesions will be treated with a specialized hand piece that can deliver up to 9 different doses of ultraviolet B simultaneously in a 3 by 3 matrix (see Appendix C). The 9 distinct doses are delivered in steps of 10% of the maximum dose (100%, 90%, 80%, etc.). For Fitzpatrick Type II or III skin, this will include doses of 2100milliJoules (mJ), 1890 mJ, 1680 mJ, 1470 mJ, 1260 mJ, 1050 mJ, 840 mJ, 630 mJ, and 420 mJ. For Fitzpatrick Type IV, V or VI skin, this will include doses of 4000 mJ, 3600 mJ, 3200 mJ, 2800 mJ, 2400 mJ, 2000 mJ, 1600 mJ, 1200 mJ, and 800 mJ. The plaque will be inspected and photographed 24-48 hours after the initial doses to determine the minimal

blistering dose (MBD). The MBDis the lowest dose of ultraviolet B that results in clinically perceptible blistering, usually manifest as slight crusting or epidermal erosion. The patient will then be treated with a starting dose that is 20% less the MBD in each respective anatomic area. Subsequent dosing will be determined according to the current standard of care (Appendix A-1, Part B).

Clinical Assessments

Concomitant Medications

All concomitant medication and concurrent therapies will be documented at Screening and at Visits 1, 3, 5, 7, 9, and at early termination when applicable. 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 complete physical examination will be performed by either the investigator or a subinvestigator who is a physician at screening. 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).

H. EVALUATIONS BY VISIT

Screening Visit (Visit 0)

- Review and obtain written informed consent and HIPAA authorization

- Assign subject unique screening number
- Review demographics data
- Review medical history including all medications
- Review inclusion criteria and exclusion criteria
- Perform physical examination, including a careful skin exam
- If patient qualifies, administer test dose to psoriasis plaques

Visits 1-10

- Review any adverse events or side effects from treatment
- Review concomitant medications (only at Screening and Visits 1, 3, 5, 7 and 9)
- Skin assessments
- Treatment with Excimer Laser
- Photograph Psoriasis (only at Visit 1 and Visit 10)

Early Withdrawal Visit

- Record any adverse events
- Record changes to concomitant medications.
- Perform complete physical examination.

I. ADVERSE Experience REPORTING AND DOCUMENTATION

An AE is defined as any undesirable event that occurs to a study participant whether or not it is believed to be related to the study treatment. Examples include:

- Any sign, symptom and/or event that is an undesirable change from the subject's baseline/entry status, e.g. an increase in severity or frequency of a pre-existing abnormality or disorder;
- Any illness, whether apparent to be related or unrelated to the study treatment;
- Injury or accidents.

All AE's, whether observed by the Investigator or reported by the subject, and whether or not thought to be treatment-related, must be fully and completely documented on the

Adverse Event Form or on a Serious Adverse Event Form. Assessment of severity and relationship to the study treatment will be based on specific definitions and reported.

Grading and Severity

The severity of an adverse event should be scored, based on the Investigator's clinical judgment, according to the following scale:

- Mild – the AE does not interfere in a significant manner with the subject's normal activity/functioning level. It may be an annoyance.
- Moderate – the AE produces some impairment of activity/functioning, but is not hazardous to health.
- Severe – the AE produces significant impairment of activity/functioning or incapacitation, and is a definite hazard to the subject's health.

The relationship of an AE to the study treatment should be assessed by the Investigator according to the following definitions:

- Definitely Unrelated – events which occur prior to the administration of study treatment or events which cannot be even remotely related to study treatment.
- Unlikely – there is no reasonable temporal association between the study treatment and the event, and the event could have been produced by the subject's clinical condition or other therapies concomitantly administered to the subject.
- Possible – the event may or may not follow a reasonable temporal sequence from administration of study treatment, but seems to be the type of medical condition that cannot be dismissed as unlikely. The event could have been produced or mimicked by the subject's clinical state or other therapies concomitantly administered to the subject.
- Probable – the event follows a reasonable temporal sequence from administration of study treatment (i.e. abates upon discontinuation of study treatment) and cannot be reasonably explained by the known characteristics of the subject's clinical state.

- Related – events that have no uncertainty in their relationship to the administration of study treatment.

A Serious Adverse Event (SAE) includes, but is not limited to, an event that: (1) is fatal; (2) is life threatening (the subject was at risk of death at the time of the event; this does not refer to an event which might have caused death if it had occurred in a more severe form; (3) requires in-subject hospitalization or prolongs an existing hospitalization; (4) is a persistent or significant disability/incapacity; or (5) is a congenital anomaly/birth defect. Study sites will document all SAEs that occur (whether or not related to study treatment) per UCSF CHR Guidelines. The collection period for all SAEs will begin after informed consent is obtained and end after procedures for the final study visit have been completed. In accordance with the standard operating procedures and policies of the local Institutional Review Board (IRB)/Independent Ethics Committee (IEC), the site investigator will report SAEs to the IRB/IEC.

J. PROTOCOL VIOLATIONS

A protocol violation occurs when the subject or investigator fails to adhere to significant protocol requirements affecting the inclusion, exclusion, subject safety and primary endpoint criteria. Protocol violations for this study include, but are not limited to, the following:

- Failure to meet inclusion/exclusion criteria
- Use of a prohibited concomitant medication

Failure to comply with Good Clinical Practice (GCP) guidelines will also result in a protocol violation. The investigator will determine if a protocol violation will result in withdrawal of a subject.

When a protocol violation occurs, it will be discussed with the investigator and a Protocol Violation Form detailing the violation will be generated. This form will be signed by a Sponsor representative and the Investigator. A copy of the form will be filed in the site's regulatory binder and in the Sponsor's files.

K. STATISTICAL METHODS AND CONSIDERATIONS

The primary outcome variable is Modified Psoriasis Area Severity Index (mPASI) for each target lesionat each study visit. Scores will be compared to Visit 1 in order to calculate change from baseline. The scores for the other outcome variables including Physicians Global Assessment (PGA) of each side of the body, PASI of each side of the body, and Patient's Global assessment will also be compared to baseline.

Statistical significance will be based on resulting p-values of 0.05 or less. Last observation carried forward (LOCF) will be used to impute missing data. Analyses will be conducted on an intent-to-treat (ITT) population (all subjects enrolled and receiving the treatments). Analyses on the per-protocol (PP) population will be considered supportive of the ITT analyses. Subjects will be eligible for the PP analyses if they complete Visit 10 without any noteworthy study protocol violations (i.e. patient or investigator activity that could have possibly interfered with the therapeutic administration of the treatment or the precise evaluation of treatment efficacy).

Sample Size Determination

The primary null hypothesis is that there is no difference in the change in mPASI over time in patients treated with excimer laser using plaque-based dosimetrycompared to conventional dosimetry. The alternative hypothesis is two-sided.

Effect size:

While the change in mPASI over time is not reported in the literature with excimer laser, 20% faster improvementusing plaque-based dosimetry (compared with conventional dosimetry) would be clinically significant. This would lead to a patient achieving a great response of their psoriatic lesions in at least two less treatments, since the average time to response is 10 treatments.

Estimate of Variability (standard deviation):20%, based on published studies using excimer laser to treat plaque psoriasis[4]

E/S ratio: 1

α = 0.05 β = 0.20 (power = 0.80) – minimum sample size = 17 patients *Per group*x 1.2*,* assume 20% loss to follow-up/dropout = 20 patients *per group*

Comment

Effect size and variability were based on prior literature using excimer laser treatment methods in plaque psoriasis [4,6]. This is a two-tailed test because we do not know for certain before hand that the effect size of the novel treatment will increase the change in PGA over time. If it decreased the change in PGA over time, this would be clinically relevant and thus we want to account for this outcome with our statistical test. Alpha and beta were set at 0.05 and 0.20 (power of 0.80). Thus, there is a 5% chance that we would observe a difference in the change in PGA over time based on chance alone, eventhough there is no real difference in the true population. There is an 80% chance we would detect an association of the given effect size or greater if it exists. These are standard α and β values. This particular research question does not require a lower α to avoid potential Type I error - there is no theoretical basis as to why plaque-based dosimetry would result in more harm to the patient. Similarly, since the conventional dosimetry method is safe and well tolerated, there is little reason to require a more stringent β value.

L. DATA COLLECTION, RETENTION AND MONITORING

Data Collection Instruments

The Investigator will prepare and maintain adequate and accurate source documents designed to record all observations and other pertinent data for each treated subject.

Study personnel will enter data from source documents corresponding to a subject's visit into the protocol-specific paper Case Report Form (CRF) when the information corresponding to that visit is available. Subjects will not be identified by name in the study database or on any study documents, but will be identified by a site number, subject number and initials.

If a correction is made on a CRF, the study staff member will line through the incorrect data, write in the correct data and initial and date the change.

The Investigator is responsible for all information collected on subjects enrolled in this study. All data collected during the course of this study must be reviewed and verified for completeness and accuracy by the Investigator. A copy of the CRF will remain at the Investigator's site at the completion of the study.

Data Management

The data will be entered into a Microsoft access database and stored on an encrypted, password-protected research server. Data will be exported from Microsoft access to Stata for analysis. Appropriate backup copies of the database and related software files will be maintained.

Availability and Retention of Investigational Records

The Investigator must make study data accessible to authorized representatives of the Sponsor (or designee), IRB/IEC, and Regulatory Agency (e.g., FDA) inspectors upon request. A file for each subject must be maintained that includes the signed Informed Consent, HIPAA Authorization and Assent Form and copies of all source documentation related to that subject. The Investigator must ensure the reliability and availability of source documents from which the information on the CRF was derived.

All study documents (patient files, signed informed consent forms, copies of CRFs, Study File Notebook, etc.) must be kept secured for a period of two years. There may be other circumstances for which the Sponsor is required to maintain study records and, therefore, the Sponsor should be contacted prior to removing study records for any reason.

Subject Confidentiality

In order to maintain subject confidentiality, only a site number, subject number and subject initials will identify all study subjects on CRFs and other documentation submitted to the Sponsor. Additional subject confidentiality issues (if applicable) are covered in the Clinical Study Agreement.

M. ADMINISTRATIVE, ETHICAL, REGULATORY CONSIDERATIONS

The study will be conducted according to the Declaration of Helsinki, Protection of Human Volunteers (21 CFR 50), Institutional Review Boards (21 CFR 56), and Obligations of Clinical Investigators (21 CFR 312).

To maintain confidentiality, all laboratory specimens, evaluation forms, reports and other records will be identified by a coded number and initials only. All study records will be kept in a locked file cabinet and code sheets linking a patient's name to a patient identification number will be stored separately in another locked file cabinet. Clinical information will not be released without written permission of the subject, except as necessary for monitoring by the FDA. The Investigator must also comply with all applicable privacy regulations (e.g., Health Insurance Portability and Accountability Act of 1996, EU Data Protection Directive 95/46/EC).

Protocol Amendments

Any amendment to the protocol will be written by the investigator. Protocol amendments cannot be implemented without prior written IRB/IEC approval except as necessary to eliminate immediate safety hazards to patients. A protocol amendment intended to eliminate an apparent immediate hazard to patients may be implemented immediately, provided the IRBs are notified within five working days.

Institutional Review Boards and Independent Ethics Committees

The protocol and consent form will be reviewed and approved by the IRB/IEC of each participating center prior to study initiation. Serious adverse experiences regardless of causality will be reported to the IRB/IEC in accordance with the standard operating procedures and policies of the IRB/IEC, and the Investigator will keep the IRB/IEC informed as to the progress of the study. The Investigator will obtain assurance of IRB/IEC compliance with regulations.

Any documents that the IRB/IEC may need to fulfill its responsibilities (such as protocol, protocol amendments, Investigator's Brochure, consent forms, information concerning patient recruitment, payment or compensation procedures, or other pertinent information) will be submitted to the IRB/IEC. The IRB/IECs written unconditional approval of the study protocol and the informed consent form will be in the possession of the Investigator before the study is initiated. The IRB/IECs unconditional approval statement will be transmitted by the Investigator to the Sponsor prior to the shipment of studysupplies to the site. This approval must refer to the study by exact protocol title and number and should identify the documents reviewed and the date of review.

Protocol and/or informed consent modifications or changes may not be initiated without prior written IRB/IEC approval except when necessary to eliminate immediate hazards to the patients or when the change(s) involves only logistical or administrative aspects of the study. Such modifications will be submitted to the IRB/IEC and written verification that the modification was submitted and subsequently approved should be obtained.

The IRB/IEC must be informed of revisions to other documents originally submitted for review; serious and/or unexpected adverse experiences occurring during the study in accordance with the standard operating procedures and policies of the IRB; new information that may affect adversely the safety of the patients of the conduct of the study; an annual update and/or request for re-approval; and when the study has been completed.

Informed Consent Form

Informed consent will be obtained in accordance with the Declaration of Helsinki, ICH GCP, US Code of Federal Regulations for Protection of Human Subjects (21 CFR 50.25[a,b], CFR 50.27, and CFR Part 56, Subpart A), the Health Insurance Portability and Accountability Act (HIPAA, if applicable), and local regulations.

The Investigator will prepare the informed consent form, assent and HIPAA authorization and provide the documents to the Sponsor or designee for approval prior to submission to the IRB/IEC. The consent form generated by the Investigator must be acceptable to the Sponsor and be approved by the IRB/IEC. The written consent document will embody the

elements of informed consent as described in the International Conference on Harmonisation and will also comply with local regulations. The Investigator will send an IRB/IEC-approved copy of the Informed Consent Form to the Sponsor (or designee) for the study file.

A properly executed, written, informed consent will be obtained from each subject prior to entering the subject into the trial. Information should be given in both oral and written form and subjects must be given ample opportunity to inquire about details of the study. If appropriate and required by the local IRB/IEC, assent from the subject will also be obtained. If a subject is unable to sign the informed consent form (ICF) and the HIPAA authorization, a legal representative may sign for the subject. A copy of the signed consent form (and assent) will be given to the subject of the subject and the original will be maintained with the subject's records.

Publications

The preparation and submittal for publication of manuscripts containing the study results shall be in accordance with a process determined by mutual written agreement among the study Sponsor and participating institutions. The publication or presentation of any study results shall comply with all applicable privacy laws, including, but not limited to, the Health Insurance Portability and Accountability Act of 1996.

Investigator Responsibilities

1. Conduct the study in accordance with the protocol and only make changes after notifying the Sponsor (or designee), except when to protect the safety, rights or welfare of subjects.
2. Personally conduct or supervise the study (or investigation).
3. Ensure that the requirements relating to obtaining informed consent and IRB review and approval meet federal guidelines, as stated in § 21 CFR, parts 50 and 56.
4. Report to the Sponsor or designee any AEs that occur in the course of the study, in accordance with §21 CFR 312.64.

5. Ensure that all associates, colleagues and employees assisting in the conduct of the study are informed about their obligations in meeting the above commitments.
6. Maintain adequate and accurate records in accordance with §21 CFR 312.62 and to make those records available for inspection with the Sponsor (or designee).
7. Ensure that an IRB that complies with the requirements of §21 CFR part 56 will be responsible for initial and continuing review and approval of the clinical study.
8. Promptly report to the IRB and the Sponsor (or designee) all changes in the research activity and all unanticipated problems involving risks to subjects or others (to include amendments and IND safety reports).
9. Seek IRB approval before any changes are made in the research study, except when necessary to eliminate hazards to the patients/subjects.
10. Comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements listed in § 21 CFR part 312.

REFERENCES

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2. Rapp SR, Feldman SR, Exum ML, Fleischer AB, Jr., Reboussin DM. Psoriasis causes as much disability as other major medical diseases. *Journal of the American Academy of Dermatology.* 1999;41(3 Pt 1):401-407.
3. Asawanonda P, Anderson RR, Chang Y, Taylor CR. 308-nm excimer laser for the treatment of psoriasis: a dose-response study. *Archives of dermatology.* 2000;136(5):619-624.
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6. Gattu S, Pang ML, Pugashetti R, et al. Pilot evaluation of supra-erythemogenic phototherapy with excimer laser in the treatment of patients with moderate to severe plaque psoriasis. *The Journal of dermatological treatment.* 2010;21(1):54-60.

Appendix A-1: Conventional Excimer Laser Treatment Guidelines

XTRACUltraandXTRACVelocityExcimerLaserProtocol

A.Determiningdoseforfirsttreatmentofpsoriasis

		Fitzpatrickskintype	
Plaque thickness	Induration score	1–3 (mJ/cm^2)	4–6 (mJ/cm^2)
Mild	1	300	400
Moderate	2	500	600
Severe	3	700	900

B.Determiningdoseforsubsequenttreatmentsofpsoriasis

Clinicalobservation

Noeffect	**Minimal effect**	**Goodeffect**	**Considerable improvement**	**Moderate/ severe erythema**
Noerythema at 24hours andandno plaque	Slight erythemaat withplaque nosignificant improvement	Mild-to-moderate blistering response at12–24	Significant improvement 12–24hrbut improvement thinningor reducedscalinesshr orpigmentation occurred	Withor12–without erythema
Increasedose 25%	Increasedose by15%	Maintain dose	Maintaindoseor reducedoseby 15%(reduction intendedto minimize hyperpigmentation effectand/orto avoidincreased erythema)	Reducedose by by25%(treat aroundany blisteredarea; donottreat blisteredarea untilhealed withcrust disappeared)

Source: XTRAC treatment guidelines. 12–95359-01 Rev. C.
Note:Thisdosingguideline isprovided forguidance purposes only.Eachpatientmayreactdifferently,therefore,thephysicianshoulddeterminetheactualtreatmentregimensbasedonpatient historyandtheirownclinicalexperienceand expertise.
XTRAC® clinicalreferenceguide:DosingguidelinefortargetedUVBphototherapyofpsoriasis.

Appendix A-2: Determining Dose for First Treatment of Psoriasis Based on MED and Plaque Characteristics. First Treatment Dose = MED x Multiplier

Plaque Location	Plaque Thickness	Plaque Tan	Multiplier for First Dose
Knees, Elbows, Hands, Feet	Thick, Tough	Tanned	4 (or 400%)
Knees, Elbows, Hands, Feet	Thick, Tough	Not Tanned	3 (or 300%)
Knees, Elbows, Hands, Feet	Thin, Moderate	Tanned	3 (or 300%)
Knees, Elbows, Hands, Feet	Thin, Moderate	Not Tanned	2 (or 200%)
All Other Locations	Thick, Tough	Tanned	3 (or 300%)
All Other Locations	Thick, Tough	Not Tanned	2 (or 200%)
Knees, Elbows, Hands, Feet	Thick, Tough	Tanned	4 (or 400%)

Appendix B: Summary of Study Procedures

Visit Number	0 - Screening	1	2	3	4	5	6	7	8	9	10
Inclusion/Exclusion Criteria	☐										
Informed Consent	☐										
Medical History + Physical Exam	☐										
Fitzpatrick Skin Typing	☐										
Plaque-based Testing	☐										
Physician's Global Assessment, each side		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Patient's Global Assessment, each side		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Modified Psoriasis Area and Severity Index, each side		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Psoriasis Area and Severity Index, target lesion		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Reconcile Concurrent medications		☐		☐		☐		☐		☐	
Adverse Events		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Full body photographs		☐	☐[1]								
Excimer Laser Rx[2]		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Completion Paperwork											☐

[1]Second set of full body photographs will be captured once the patient reaches a PGA or 0 or 1 on one side of the body OR at the last study visit

[2]Patients will be treated excimer laser 1-2x per week at the discretion of the provider for a maximum of 10 treatments over 10 weeks

Appendix C - Matrix Dosimetry Tip for Plaque Based Testing
Matrix Dosimetry Tip includes a series of 9 small reflective filters that reduce the delivered 308 nm UVB by small, controlled, incremental steps of 10%, as shown in the figure below.

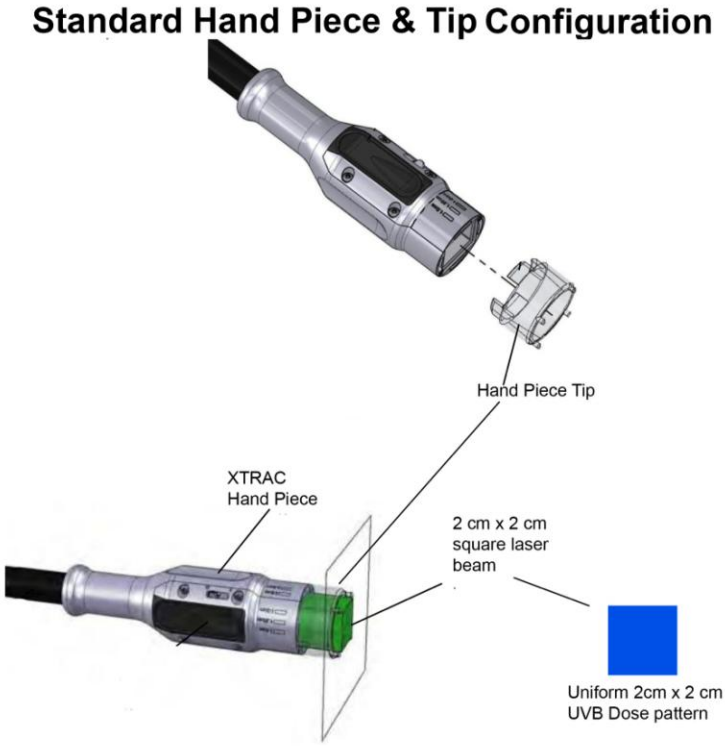

FIG. 1

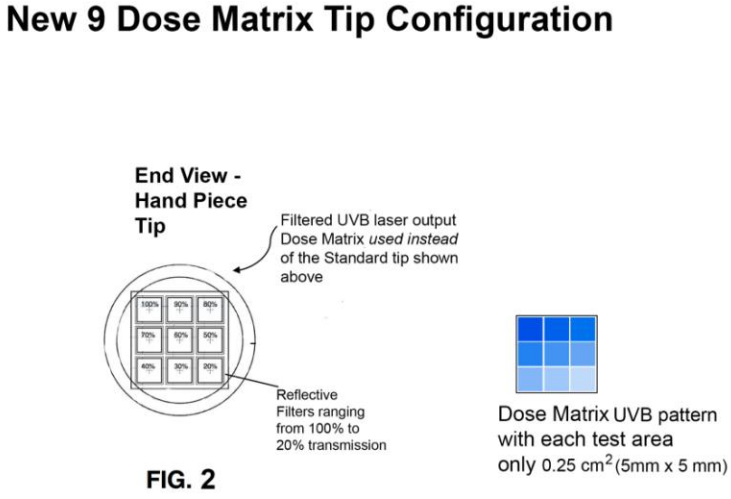

FIG. 2