

TITLE PAGE

Protocol Number: C-17-ML02

Protocol Title: Open-label, Prospective, Multicenter Study to Evaluate the Cutera enlighten™ Laser and a Micro-Lens Array Handpiece Attachment for the Treatment of Moderate and Severe Acne Scars

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[REDACTED]

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Version, Date: Version 1.0- Dated: July 17, 2017

Statement of Compliance

The study will be conducted in accordance with the design and specific provisions of this IRB approved protocol, in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with Good Clinical Practice (GCP) and the applicable regulatory requirement(s).

NOTE: The confidential information in the following document is provided to you as an Investigator, potential Investigator, or consultant for review by you, your staff, and applicable Institutional Review Board. By accepting this document, you agree that the information contained herein will not be disclosed to others, without written authorization from Cutera, Inc. except to the extent necessary to obtain informed consent from those persons to whom the device will be administered.

Protocol Signature Sheet – Principal Investigator

PROTOCOL C-17-ML02

Study Title: Open-label, Prospective, Multicenter Study to Evaluate the Cutera enlighten™ Laser and a Micro-Lens Array Handpiece Attachment for the Treatment of Moderate and Severe Acne Scars

Protocol Version 1.0, Date: 17JUL2017

I have received and read the protocol dated **July 17, 2017** and agree to adhere to the requirements. I am aware that my adherence to the above protocol is mandatory and that any changes in the protocol or informed consent form must first be approved by Cutera, Inc. and the Institutional Review Board, except those changes necessary to eliminate apparent immediate hazards to subjects. I will provide copies of this protocol and all pertinent information to the study personnel under my supervision. I will discuss this material with them and ensure they are fully informed regarding their role in the study. I will ensure that the study is conducted in compliance with the protocol, Good Clinical Practice (GCP), and all applicable regulatory requirements, and with the reviewing Institutional Review Board (IRB) requirements. I agree to commence this study only after documented IRB approval is obtained.

Principal
Investigator

Signature

Date

Printed Name

Date

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Protocol Summary

Title	Open-label, Prospective, Multicenter Pivotal Study to Evaluate the Cutera enlighten Laser and a Micro-Lens Array Handpiece Attachment for the Treatment of Acne Scars
Objective	<p>a. To evaluate the safety of the Cutera enlighten laser with a Micro-Lens Array handpiece attachment in the improvement of acne scars.</p> <p>b. To evaluate the efficacy of the Cutera enlighten laser with a Micro-Lens Array handpiece attachment in the improvement of acne scars.</p>
Study Design	Open-label, Prospective, Multicenter Pivotal Study to Evaluate the Cutera enlighten multi-wavelength 532 nm and 1064 nm Nd:YAG picosecond duration laser with a Micro-Lens Array handpiece attachment for the Improvement of Moderate and Severe Acne Scars.
Enrollment	Approximately 45 subjects will be treated
Primary Endpoint	<ul style="list-style-type: none"> Correct identification of the 12 weeks post final treatment photographs from the baseline by at least two of the three blinded reviewers in 75% of the patients and an improvement of one point in the ASAS.
Safety Endpoint	<ul style="list-style-type: none"> Safety of the Cutera enlighten laser with a Micro-Lens Array handpiece attachment assessed by the frequency and severity of device related adverse events
Secondary Endpoints	<ul style="list-style-type: none"> [REDACTED] [REDACTED]
Exploratory Analysis	<ul style="list-style-type: none"> [REDACTED]
Subject Population	Female or male subjects, age 18 to 65 years, Fitzpatrick skin types I-VI
Planned Schedule	<p>First subject enrolled: August 2017</p> <p>Last subject last visit: September 2018</p>

1. PURPOSE

The purpose of this pivotal investigation is to evaluate the efficacy and safety of the Cutera enlighten multi-wavelength 532 nm and 1064 nm Nd:YAG picosecond pulse duration laser and an investigational micro-lens array (MLA) handpiece attachment for improvement of acne scars.

2. BACKGROUND INFORMATION

Affecting nearly 40 to 50 million people annually, acne is the most common skin condition in the United States.¹ Acne lesions typically begin to appear in puberty and persist throughout adolescence. Approximately 85% of people between the ages of 12 and 24 have experienced acne.² This wide spread skin condition predominantly affects teens and young adults, but can occur in older adults as well. Countless treatment modalities exist for acne sufferers, however even with effective treatment moderate and severe lesions can result in scarring. Post-acne scarring is estimated to occur in 95% of patients and is a common cosmetic concern for many patients.³ Furthermore, in some patient groups acne scarring is especially devastating and may be a risk factor for suicide.⁴

Scar formation occurs as a result of damage to the layers and substructures of the skin. Following injury to the skin from the acne infection and more severe lesions, a multi-stage healing process begins, which includes inflammation, proliferation and maturation. Unsightly scars result from an abnormal healing process. While the exact cause of abnormal skin healing is unknown, it is thought that excessive collagen and fibrotic tissue forms and a lack of elastic fibers contributes to tough, stiff, nodular scar tissue.⁵⁻⁶ Certain factors increase the likelihood of an abnormal skin healing process, such as patient age or racial/ethnic background, depth of injury and extent of infection.⁷⁻⁸

Acne scars are atrophic scars, with subtypes classified based on scar appearance and skin depth. Ice pick scars are narrow in width at the surface (<2mm) and typically taper in width as the scar extends vertically deep into the dermis. Box car scars are round or oval indentations in the skin surface, with well-defined edges, that may be shallow or deep. Rolling scars are atrophic scars that occur as a result of abnormal fibrous anchoring of the dermis to the subcutis and create a rolling or rippling appearance of the skin surface.⁹

Treatment modalities for acne scarring include ablative laser skin resurfacing, dermabrasion, chemical peels, or a combination of modalities.¹⁰ These traditional, highly effective treatment options are accompanied by undesirable side effects such as significant pain and post-procedure downtime. There is a demand for effective, noninvasive treatment methods for patients suffering from acne scars such as non-ablative laser and light-based therapy to devices that utilize radiofrequency waves.¹¹⁻¹³ Treatment with non-ablative, non-invasive devices cause heat production and heat-induced wound healing within the dermis that over time causes a cascade of cellular events leading to new collagen production.¹⁴⁻¹⁵ Dermal collagen remodeling leads to an improved texture and appearance of the skin, which should also improve the appearance of facial acne scars.

Histology of fractionated laser delivery has demonstrated the formation of vacuoles, or areas of laser induced optical breakdown (LIOB).¹⁶ LIOB occurs when the intensity of the pulse is sufficiently high to generate plasma. Plasma is caused by electrons being stripped from the target material. The resulting electrons continue to absorb the laser heat, creating a vapor plume which forms a cavitation bubble that is observed as an LIOB in histological preparations.

In 2012, Habbema et al., demonstrated that highly focused, fractionated 1064 nm picosecond pulses could create subsurface LIOBs in the upper dermis and 30 days post treatment, they showed new collagen in the areas of the LIOBs, a natural wound healing process as a response to this type of injury.¹⁷

Subsequently, picosecond lasers utilizing 755nm wavelength and a fractionated delivery system have been shown to improve the appearance of facial acne scars.¹⁸ Histological samples taken from the acne scar patients demonstrated improvements in the dermal elastic fibers, collagen and mucin. No severe side effects were observed and the patients tolerated the procedures without complications. The LIOBs observed in the facial acne study were located in the epidermis due to the higher absorption characteristics of 755nm in melanin as compared to 1064 nm used in Habbema's study.

Fractionated delivery of picosecond lasers on humans has been demonstrated to be safe. A similar device to MLA, utilizing 755nm wavelength and a fractionated delivery system, has obtained FDA 510K clearance (K143105) and has been shown to improve the appearance of facial acne scars.¹⁸

Recently, a holographic diffractive beam-splitter technology delivering fractionated picosecond 532 nm and 1064 nm wavelengths has also been described and is available commercially outside of the US (Syneron Candela), but to date, no FDA clearance exists for this device. The company reports the device is able to focus the LIOBs in the epidermis with the 532 nm wavelength and in the upper papillary dermis with the 1064 nm wavelength safely.¹⁹

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]		
[REDACTED]	[REDACTED]	[REDACTED]

4. STUDY OBJECTIVES

The objectives of this pivotal study are:

- a. To evaluate the safety of the Cutera enlighten laser with a Micro-Lens Array handpiece attachment in the improvement of acne scars.
- b. To evaluate the efficacy of the Cutera enlighten laser with a Micro-Lens Array handpiece attachment in the improvement of acne scars.

5. STUDY DESIGN

This is an open-label, prospective, multicenter, pivotal study in up to 45 male or female subjects, age 18 to 65 years who desire laser treatment for the improvement of acne scars. Subjects will receive up to [REDACTED] apart with the Cutera enlighten laser with the Micro-Lens Array handpiece attachment. [REDACTED]

[REDACTED] Subjects will return to the site after all study treatments have been delivered for follow-up visits: [REDACTED] and 12 weeks [REDACTED] following their final study treatment.

5.1 Study Endpoints

5.1.1 Primary Efficacy Endpoint

The primary endpoint is correct identification of the 12 weeks post final treatment photographs from the baseline by at least two of the three blinded reviewers in 75% of the patients and an improvement of one point in the ASAS.

[REDACTED]

[REDACTED]

5.1.3 Safety Endpoints

- Safety of the Cutera enlighten laser with Micro-Lens Array handpiece attachment as assessed by the frequency and severity of device related adverse events.

[REDACTED]

[REDACTED]

5.2 Study Duration

[REDACTED]

The screening and first laser treatment may be combined into one visit provided that the subject has signed the IRB-approved Informed Consent Form prior to the commencement of any study-related procedures and has met all criteria to be enrolled in the study.

5.3 Study Effectiveness Assessments

5.3.1 Blinded Evaluators and Investigator's Global Assessment of Improvement

Blinded improvement assessments will be performed 12 weeks post the [REDACTED] or final laser treatment. Blinded Evaluators will be asked to assess the subject's before (baseline) and after photographs in one and/or both of the below methods:

- Determine the temporal order (before and after) of each photograph pair.

- Rate the degree of improvement observed from baseline using the Acne Scar Assessment Scale (ASAS)

A. Acne Scar Assessment Scale (ASAS): The ASAS is a static assessment scale that allows the Investigator to measure his/her impression of acne scar severity within the treatment area. The treatment area on each side of the face will be assessed separately, then will be averaged to obtain a global score.

Term	Grade	Description
Clear	1	No depressions are seen in the treatment area. Macular discoloration may be seen.
Very Mild	2	A single depression is easily noticeable with direct lighting (deep). Most or all of the depressions seen are only readily apparent with tangential lighting (shallow).
Mild	3	A few to several, but less than half of all the depressions are easily noticeable with direct lighting (deep). Most of the depressions seen are only readily apparent with tangential lighting (shallow).
Moderate	4	More than half of the depressions are apparent with direct lighting (deep).
Severe	5	All or almost all the lesions can be seen with direct lighting (deep).

□

5.3.2 Investigator Assessments

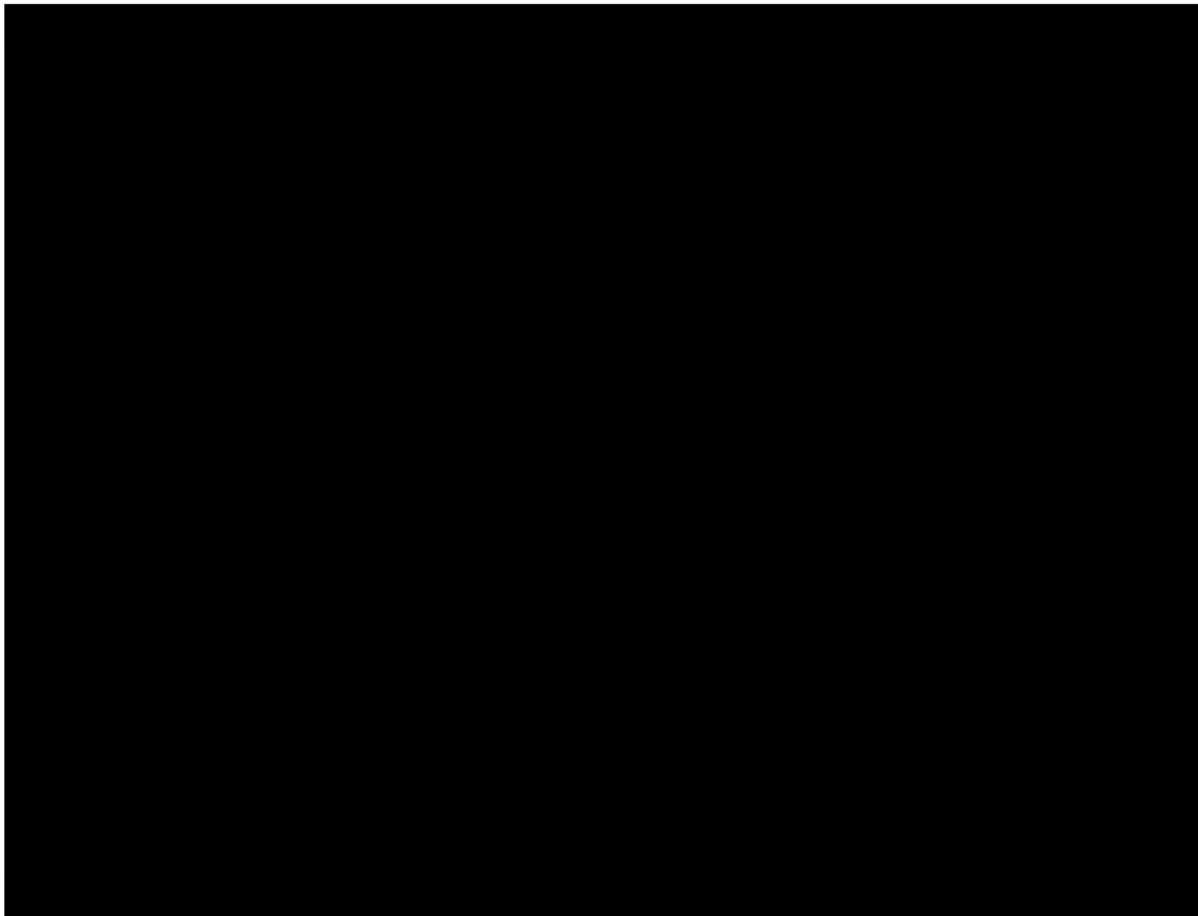
At baseline, [REDACTED], the Investigator will assess the efficacy of the Cutera enlighten laser with the MLA handpiece attachment treatment using the ASAS, GAIS, and Skin Quality Rating Scale. Baseline photos of subjects may be used while assessing the ASAS, GAIS, and Skin Quality Rating Scale.

A. Acne Scar Assessment Scale (ASAS): The ASAS is a static assessment scale that allows the Investigator to measure his/her impression of acne scar severity within the treatment area. The treatment area on each side of the face will be assessed separately, then will be averaged to obtain a global score.

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Moderate	4	More than half of the depressions are apparent with direct lighting (deep).
Severe	5	All or almost all the lesions can be seen with direct lighting (deep).

□

[REDACTED]	[REDACTED]



5.3.3 Subject Satisfaction Assessment



5.4 Study Safety Assessments

5.4.1 Incidence and Severity of Adverse Events:

Following the first laser treatment, adverse effects (AEs) will be assessed post-treatment and at each subsequent visit using the following scale:

- 1= mild: requires minimal or no treatment and does not interfere with the subject's daily activities.
- 2= moderate: may cause some interference with functioning.
- 3= severe: interrupts subject's usual daily activity and may require treatment.

5.4.2 Treatment-related Discomfort

After each laser treatment, subjects will be asked to rate the average amount of discomfort experienced during treatment and immediately after laser treatment using the Pain Rating Scale (VAS Scale) Appendix 2.

5.4.3 Phone Follow-up



5.5 Photographs

Standardized digital photographs will be taken of each subject's treatment area at baseline, prior to and post all laser treatments and at each follow-up visit. Treatment area will be cleansed and any jewelry and make-up will be removed from the area being photographed. For facial photographs, hair will be pulled away from the face with a headband.

Facial photographs will be obtained from at least 3 angles: with the subject facing forward, 45° to the right and 45° to the left. Photographs will be taken in the same windowless room equipped with adequate lighting. The room lighting, camera positioning and subject positioning should be consistent for all study visit photographs. Digital camera settings should remain the same for all photographs and the highest resolution settings should be utilized.

5.6 Study Discontinuation

Cutera, Inc. (the sponsor) has the right to terminate this study at any time. Reasons for terminating the study may include, but are not limited to, the following: incidence or severity of adverse events in this or other studies indicates a potential health hazard to subjects; subject enrollment is unsatisfactory; number of protocol deviations is unacceptable; data recording is inaccurate or incomplete; or questionable study site compliance with ICH-E6, Good Clinical Practice²³.

5.7 Investigator Selection

The Investigator(s) will be invited to participate in the study based on his or her medical specialty, experience conducting clinical research studies and experience in the use of light-based devices for aesthetic indications. Access to potential study subjects and the Investigator's sincere interest in this study along with expressed willingness to cooperate with the study process and requirements was also considered.

6. STUDY POPULATION

6.1 Study Subject Recruitment and Selection

Approximately 45 male or female subjects, ages 18 to 65, with Fitzpatrick Skin Type I-VI who desire laser treatment for moderate to severe facial acne scars. Subjects will be recruited to participate from the local population. Subjects may also be recruited from the Investigator's existing patient database or from patients who present themselves to the study site requesting treatment. Only subjects who meet all eligibility criteria and who provide written informed consent will be enrolled into the study.

Each subject will be evaluated by the Investigator to assess his/her suitability for entry into the study according to the following inclusion and exclusion criteria.

6.1.1 Inclusion Criteria

To be included in the study, subjects must meet all of the following Inclusion Criteria:

1.	Subject must be able to read, understand and sign the Informed Consent Form.
2.	Female or Male, 18 to 65 years of age (inclusive).
3.	Fitzpatrick Skin Type I – VI (Appendix 6).
4.	Subject desires treatment for acne scars and wishes to undergo laser treatments for improvement.
5.	Subject has bilateral moderate to severe signs of facial acne scarring.
6.	Must be willing to have Cutera enlighten laser with the Micro-Lens Array handpiece attachment treatments and able to adhere to the treatments, follow-up visit schedule, and post-treatment care instructions.
7.	Willing to have very limited sun exposure and use sunscreen on the treatment area every day for the duration of the study, including the follow-up period.
8.	Willing to have digital photographs taken of the treatment area and agree to use of photographs for presentation (educational and/or marketing), publications, and any additional marketing purposes.
9.	Agree to not undergo any other procedure(s) or treatment(s) for acne scars during the study and has no intention of having such procedures performed during the course of the study.
10.	For female subjects: not pregnant or lactating and is either post-menopausal, surgically sterilized, or using a medically acceptable form of birth control at least 3 months prior to enrollment and during the entire course of the study.,

6.1.2 Exclusion Criteria

Subjects will be excluded from the study if they meet any of the following Exclusion Criteria:

1.	Participation in a clinical trial of another drug, or device administered to the treatment area, within 6 months prior to enrollment or during the study.
2.	Any type of prior cosmetic treatment to the target area within 6 months of study participation, such as laser procedures, facial fillers, i.e. (Bellafill) and those used for general aesthetic correction, facial peel, lightening creams, or facial surgery.
3.	Use of prescription topicals in the treatment area within one month prior to treatment or use of topical agents one week prior to treatment that may cause facial sensitivity.
4.	Suffering from significant skin conditions in the treated areas or inflammatory skin conditions, including but not limited to, open lacerations or abrasions, hidradenitis, rash, infection, or dermatitis of the treatment area prior to treatment (duration of resolution as per the Investigator's discretion).
5.	Pregnant and/or breastfeeding, or planning to become pregnant.

6.	Significant concurrent illness, such as diabetes mellitus, immunosuppression/immune deficiency disorders (including HIV infection or AIDS) or using immunosuppressive medication.
7.	Hypersensitivity to light exposure.
8.	Any use of medication that is known to increase sensitivity to light according to the Investigator's discretion.
9.	History of keloid scarring, hypertrophic scarring or abnormal wound healing or prone to bruising.
10.	Has a history of squamous cell carcinoma or melanoma in the treatment area.
11.	History of epidermal or dermal disorders (particularly if involving collagen or microvascularity), including collagen vascular disease or vasculitic disorders.
12.	A history or active skin condition that in the opinion of the Investigator may interfere/confound with the treatment.
13.	History of connective tissue disease, such as systemic lupus erythematosus or scleroderma.
14.	History of disease stimulated by heat, such as recurrent herpes simplex and/or herpes zoster (shingles) in the treatment area, unless treatment is conducted following a prophylactic regimen.
15.	History of pigmentary disorders, particularly tendency for hyper- or hypopigmentation, or any that are considered not acceptable by the study investigator.
16.	Has used oral isotretinoin (Accutane or therapeutic vitamin A supplements of \geq 10,000 units per day) within 12 months of initial treatment or plans on using during the course of the study (note: skin must regain its normal degree of moisture prior to treatment, e.g. lack of noticeable skin flaking and peeling).
17.	Excessively tanned or active sun tan in facial area to be treated, or unable/unlikely to refrain from tanning during the study.
19.	Excessive facial hair in the area to be treated (beards, sideburns, and/or moustache,) that would interfere with diagnosis, assessment, and treatment.
20.	As per the Investigator's discretion, any physical or mental condition which might make it unsafe for the subject to participate in this study, including excessive alcohol or drug abuses, or a condition that would compromise the subject's ability to comply with the study requirements.

6.2 Subject Numbering

If a subject completes the Informed Consent Form, meets the study eligibility criteria and is willing to participate, the subject will be assigned a study subject identification number. This number is comprised of a site number (which is provided by the sponsor) and a sequential subject number and the subject initials (first and last names).

6.3 Subject Discontinuation Criteria

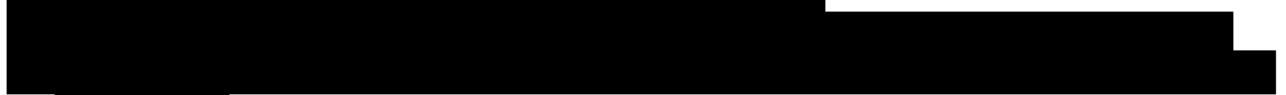
If possible, every subject should remain in the study until completion of the required follow-up period. However, participation in this study is completely voluntary and a subject can choose to withdraw from the study at any time. Decision to withdraw will not affect or prejudice the subject's continued medical care in any way. In those instances, the investigator will attempt to obtain a final clinical assessment and an adverse device effect evaluation for the subject prior to this withdrawal. A subject will be considered

lost to follow-up only after three unsuccessful, documented attempts to contact the subject have been made.

In addition, a subject can be discontinued for any of the following reasons: the Principal Investigator decides that continuing in the study would not be in the subject's best interest, a subject is noncompliant with the protocol, a subject has a serious reaction to the treatment, a subject develops any of the exclusion criteria during the study period or the study is stopped by the study sponsor.

7. STUDY PROCEDURES

A summary of all study required procedures and assessments can be found in Appendix 1.



7.2 Laser Treatment 1 to 6 – Visit Window and Pre-Treatment Procedures



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7.4 Phone and Follow-Up Visits

There are [REDACTED] follow-up visits at [REDACTED] and 12 weeks [REDACTED] () following the final laser treatment.

The following procedures will be performed during the phone and follow-up visits:

1. Assessment of Concomitant Medications: Assess and record any additions, changes and/or deletions in prescription and nonprescription concomitant medications since the previous study visit.
2. Assess for any ongoing, previously reported, and/or new adverse events and expected adverse device effects.

During the follow-up visits:

1. Cleanse subject's treated area with a mild cleanser to remove any cosmetics, lotions, or perfumes.
2. Photographs of the treated area(s) will be taken at the same pre-defined angles (Section 5.5).
3. Investigator will assesses the efficacy of the Cutera enlighten laser with the Micro-Lens Array handpiece attachment treatment using the ASAS, [REDACTED]

8. ADVERSE EVENTS and ADVERSE DEVICE EFFECTS

8.1 Definitions

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

Cutera, Inc.

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"Open-label, Prospective, Multicenter Study to Evaluate the Cutera enlighten™ Laser and a Micro-Lens Array Handpiece Attachment for the Treatment of Moderate and Severe Acne Scars"

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

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8.2 Recording AEs, ADEs and SADEs

All AEs/SAEs or ADEs/SADEs will be: (1) evaluated and must be recorded in the subject's medical chart and in the study case report forms (CRFs); (2) monitored and tracked from the time of the first treatment with the Cutera Enlighten laser system.

At each contact with the subject, the investigator must seek information on AEs/ADEs/SADEs by specific questioning and, as appropriate, by examination. AEs/ADEs/SADEs may be observed by the investigator and/or clinical research staff, elicited from the subject and/or family member or volunteered by the subject. All observed and volunteered adverse signs and symptoms, anticipated or unanticipated, regardless of severity or frequency, will be recorded in the case histories (medical chart and CRFs). Included in the description should be the nature of the sign or symptom, the date of onset, date of resolution (duration), the severity, anticipated or unanticipated, the relationship to study treatment or other therapy, the action taken (if any), and the outcome.

All SAEs/SADEs, anticipated or unanticipated, must be reported to Cutera immediately but not later than 5 working days. The SADE must be recorded in: (1) the AE CRF and (2) a written report must be submitted to Cutera within five (5) working days after the investigator first learns of the event and is to include a full description of the event and sequelae, in the format detailed by the Cutera Serious Adverse Event Form.

8.3 Follow-up of subjects after AEs/ADEs and SAEs/SADEs:

All reported AEs/ADEs/SAEs/SADEs should be followed until resolution or until the subject's participation in the study ends. Resolutions of AEs/ADEs/SAEs/SADEs are to be documented on the appropriate CRFs. All ADEs that result in permanent discontinuation from this clinical trial, whether serious or not, should also be reported on the subject Non-Completion of Study Form.

9. POTENTIAL RISKS / BENIFITS

A 10x4 grid of black and white blocks. The first column contains a large black block with white borders on the left and bottom, and white blocks above and to its right. The other three columns are entirely black.

For more information, contact the Office of the Vice President for Research and the Office of the Vice President for Student Affairs.

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9.2 Potential Benefits

The subjects may or may not benefit from the treatment with the study device. Potential benefit of laser treatment for acne scars is improved appearance of treated area. There is no guarantee of success.

10. RISK MANAGEMENT

The investigator participating in this study was chosen based on extensive and safe experience with the use of lasers in dermatology applications. This is the most critical element in managing subject risk. In addition, study investigators will be trained on the use of the Cutera Enlighten laser system by a representative of Cutera.

11. DATA ANALYSIS PLAN

11.1 Sample Size

The primary objective is to show that the response rate (as defined below) is significantly greater than 50%. Under the assumption that the true population response rate is 75%, 40 subjects will provide 80% power to reject the primary hypothesis. To allow for up to a 10% dropout rate, 45 subjects will be treated.

11.2 Demographics and Subject Characteristics at Baseline

Subject demographics, medical history, concomitant medications will be tabulated and summarized descriptively.

11.3 Statistical Analysis Methods

This is a study to evaluate safety and efficacy of the Cutera enlighten laser with the Micro-Lens Array handpiece attachment. Outcome measures will be assessed around multiple endpoints. These measures will be: degree of improvement as assessed by the Investigator, blinded evaluators, [REDACTED] and safety. Additional assessments may also be performed but are not considered part of the analysis (i.e. Subject post-treatment questionnaire).

11.3.1 Analysis Sets

The efficacy analysis set will include all subjects who received one facial laser treatment session and complete at least one follow-up visit. The safety analysis set will include all subjects enrolled in the study who had at least one laser treatment session.

Missing data will not be imputed for efficacy or safety endpoints.

11.3.2 Primary Efficacy Analysis

The primary endpoint is a responder, where a clinical response is defined as at least two of the three blinded reviewers selecting the correct order of treatment with at least a one-point improvement in the ASAS from baseline to 12 weeks. The primary hypothesis is as follows:

$H_0: \Pi = 0.5$

vs.

$H_A: \Pi \neq 0.5$,

where Π is the population response rate. The primary analysis will place an exact two-sided 95% confidence interval around the observed response rate and compare the lower bound to 50%. If the lower bound exceeds 50% the primary hypothesis will be rejected in favor of the response rate being greater than 50%.

11.3.3 Analysis of Secondary Endpoints

[REDACTED]

[REDACTED]

[REDACTED]



11.3.4 Safety Analyses

Safety variables will be analyzed descriptively. The safety variables for this study are:

- Incidence and severity of adverse effects during study duration (to be displayed descriptively as counts and frequency distributions)

Enrolled subjects who received at least one treatment will be included in the safety analyses. Device-related and procedure-related adverse effects (AEs) and subjects who prematurely terminate from the study due to an adverse device effect, including the treatment-related pain ratings, as reported on case report forms will be tabulated and analyzed. For a given AE term, counting will be done by subject, not by event, i.e. for a subject reporting the same AE more than once, the event will be counted only once, at the most severe and most-related occurrence. The number and percentage of subjects experiencing each AE Term will be descriptively summarized. Statistical hypothesis testing will not be performed for safety data.

12. SUBJECT PAYMENT

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13. STUDY MANAGEMENT AND ADMINISTRATIVE PROCEDURES

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13.2 Informed Consent

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13.3 Protocol Compliance

The principal investigator must comply with all terms of the protocol.

13.4 Protocol Amendments

Neither the principal investigator nor the sponsor will modify or alter this protocol without first obtaining the concurrence of the other party (with the exception of amendments which involves mitigating a medical emergency or immediate health risk to the subject). The party initiating an amendment must confirm it clearly in writing and it must be signed and dated by the sponsor and the principal investigator. IRB approval must be obtained before implementation of an amendment.

13.5 Protocol Deviations

All protocol deviations must be clearly described on the case report form (i.e., Cutera Protocol Deviation Form). Deviations from the protocol may include but are not limited to subject's failure to attend scheduled visit during a visit window, use of out of range treatment parameters and incomplete or incorrect study procedures. Any medical emergency or immediate health risk to the subject which results in a protocol deviation and must be reported to the sponsor within 5 working days

Significant protocol deviations must be reported to IRB according to their policies.

13.6 Study Personnel

The investigator must supply the sponsor with a list of the names and curricula vitae that describe the professional backgrounds of the clinically responsible study investigators (principal, sub-investigators), research nurses, and other possible participants (e.g. medical doctor, nurse, etc.).

13.7 Disclosure of Financial Interest

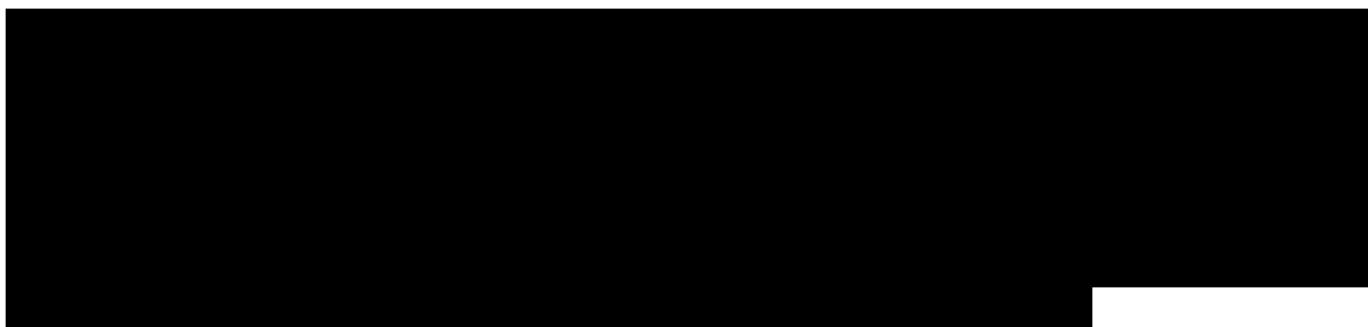
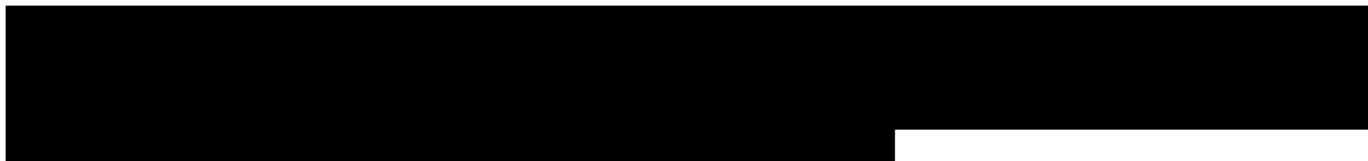
Each investigator [principal and sub-investigator(s)] is required to disclose sufficient accurate financial information to the sponsor, to allow sponsor to submit complete and accurate certification or disclosure statements.

13.8 Data Collection, Record Keeping and Storage



14. SUBJECT CONFIDENTIALITY

This study preserves the confidentiality of all subjects under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule. The following safeguards will be in place to protect the privacy of the individuals who are the subjects of the health information to be used in the research and the confidentiality of that information:



15. PUBLICATION POLICY

The investigator shall have the right to publish the results of the study. Unless mutually agreed upon in writing, prior to submission for publication of any manuscript, poster, presentation, abstract or other written or oral material describing the results of the study, the investigator shall allow sponsor to review manuscript, poster presentation, abstract or other written or oral material which describes the results of the study for the purpose only of determining if any patentable information is disclosed. At the sponsor's request, the investigator shall withhold any publication or presentation to permit sponsor to seek patent protection and to remove any confidential information from all publications.

The International Committee of Medical Journal Editors (ICMJE) member journals have adopted a trials registration policy as a condition for publication. This policy requires that all clinical trials be registered in a public trials registry such as ClinicalTrials.gov, which is sponsored by the National Library of Medicine. It is the responsibility of the sponsor to register this trial in ClinicalTrials.gov. Any clinical trial starting enrollment after September 27, 2007 must be registered either on or before the onset of patient enrollment.

REFERENCES

Cutera, Inc.

Protocol # C-17-ML02

"Open-label, Prospective, Multicenter Study to Evaluate the Cutera enlighten™ Laser and a Micro-Lens Array Handpiece Attachment for the Treatment of Moderate and Severe Acne Scars"



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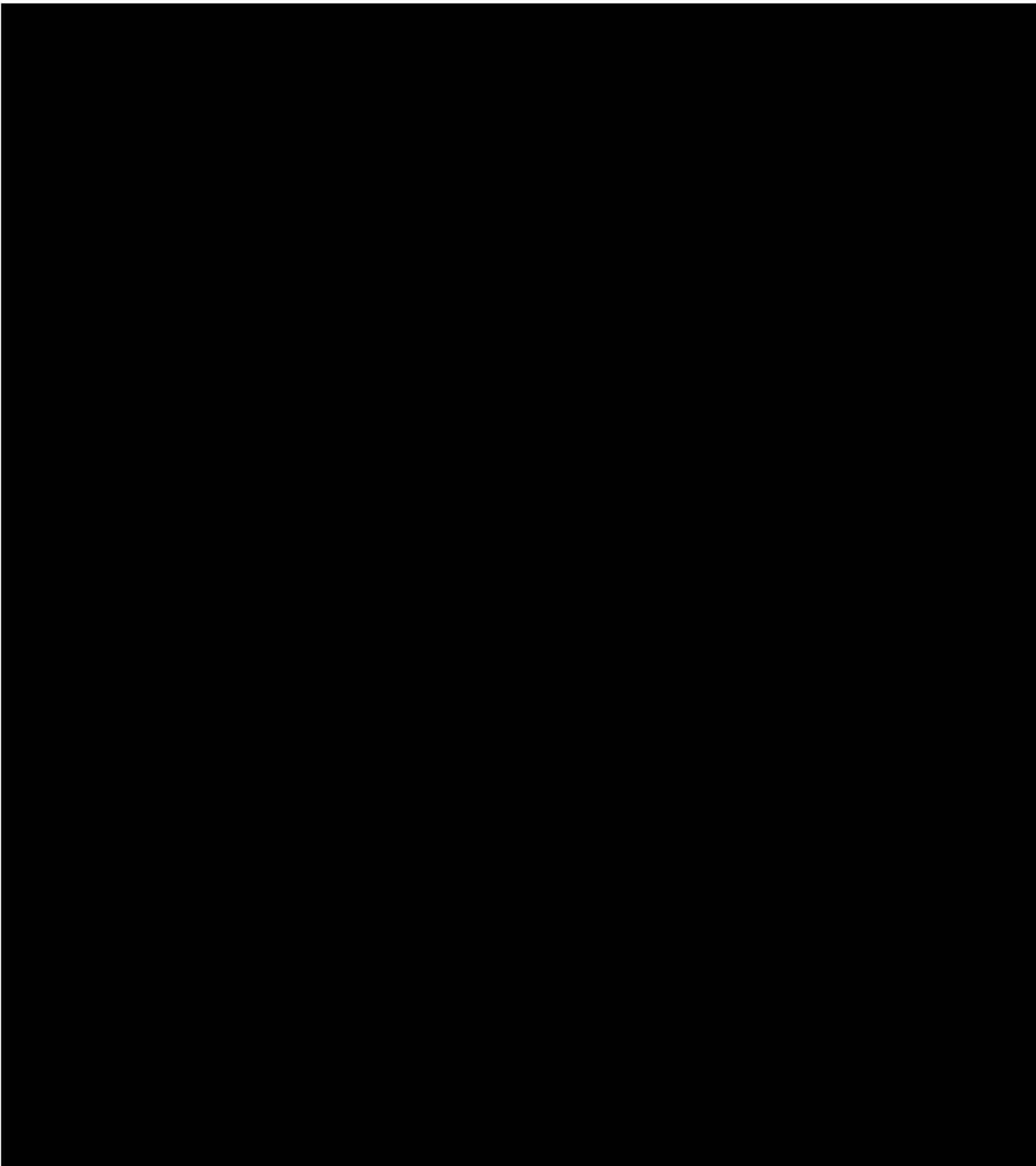
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