Final Report
August 13, 2012

A pilot practical use evaluation of a novel bio-enriched polymer gel to safely improve treatment outcomes in atopic eczema patients

ACCEPTANCE OF FINAL REPORT
SIGNATURE PAGE

PROTOCOL NUMBER: **SII-001**

PROTOCOL TITLE: *A* **pilot practical use evaluation of *a* novel bio-enriched polymer gel to safe improve treatment outcomes in atopic dermatitis patients**

Signatures below indicate that this is the agreed upon final report.

Sponsor:

Robert Kuhn
Silipos Inc.
4 Brig!"tton Road Suite 302
C!lftor., NJ 07012

Signature _____ Date _____

Principal Investigator:

Zoe Diana Draelos, MD
Dermatology Consulting Services
2444 North Main Street
High Point, NC 27262

Signature _____ Date 08/16/19

Study Manager:

Gregory Biancone
Gregory Biancone Consulting LLC
73 Grove Avenue
Verona, NJ 07044

Sigr.Je _____ Date _____

1. BACKGROUND

Atopic Eczema or Atopic dermatitis (AD) is caused by hypersensitivity in the skin, and is characterized by long-term inflammation, and can be either acute or chronic. The pathogenesis of atopic dermatitis (ID) has been attributed largely to abnormalities in the adaptive immune system, resulting in the ruritic, inflammatory dermatitis that characterizes AD.[1] Often the inflammation causes the skin to become ruritic and scaly and chronic irritation and scratching can cause the skin to thicken and lichenify. Addi onally, there is emerging evidence that inflammation in AD results first from inherited and acquired insults that converge to alter epidermal structure and function, followed by immune system activation, which in turn has negative consequences for skin-barrier function.[2] Quality of life is often impaired for patients with atopic dermatitis due to sleep disturbance, pruritus and the physical impairment of visible skin ifsions.[3] Treatment of AD has been focused on reducing inflammation and pruritus while maintaining pptimal hydration of the affected area.[4]

2. STUDY OBJECTIVES

It is proposed that given the treatment objectives described, a drug free device which may meel these objectives for the treatment of eczema would be of significant interest to the treating physiciaf The Silipos Gel care Advanced product is formulated to reduce inflammation and pruritus and to rest0re and maintain healthy skin barrier function. The GCA device can be applied for short periods of time by the patient so as to not be completely occlusive. Use of the product can keep the skin moist and provide a mechanical barrier to prevent scratching during the treatment period. Thirdly, the drug free device can be used to potentiate low potency corticosteroids for short periods of time, thereby reducing the need for the more potent steroid treatments often used to treat AD.

The purpose of this study was to examine the efficacy and tolerability of the Gel care Advanced device in improving treatment outcomes in eczema patients as a stand-alone treatment or adjunctively with topically applied hydrocortisone.

2.1 Outcome Assessments

2.1.1 Primary Assessments

Treatment outcome success was based on a statistically significant reduction in subjective asse♦sments pertaining to atopic eczema.

2.1.2 Secondary Assessments

Secondary endpoints were the Investigator Global Assessment (IGA) and Patient Global Ass]ssment (PGA) of Treatment Outcome.

2.2 Safety

The incidences of all adverse *events* reported during the study were summarized by treatment, group. Comparison of the test and reference with regard to safety of treatment related adverse events were evaluated by comparing the nature, severity and frequency of their adverse event profiles.

3. STUDY DESIGN

[1] Leung DY, Bieber T. Atopic dermatitis. Lancet. 2003;361:151-160

[2] Elias PM, Schmuth M. Abnormal skin barrier in the etiopathogenesis of atopic dermatitis. Curr Opin Allergy Clin Immunol. 2009;9:437---446

[3] Kemp AS. Cost of illness of atopic dermatitis in children: a societal perspective. Pharmacoeconomics 2003;21:105-13.

[4] Hanifin JM, Cooper KO, Ho VC, et al. Guidelines of care for atopic dermatitis, developed in accordance With the American Academy of Dermatology (AAD)/American Academy of Dermatology Association "Administrative Re4ulations for Evidence-Based Clinical Practice Guidelines." J Am Acad Dermatol. 2004;50:391-404

3.1 Type/Design of Study

This was a 28-day, two arm, evaluator-blinded, pilot evaluation of adult patients age 18 or older who have been diagnosed with atopic dermatitis (AD). The study will evaluate a drug free device for the treatment of AD used alone or in *combination* with topical corticosteroids. Patients enrolled in the evaluation had a target area identified at the time of enrollment for treatment under this protocol.

3.2 Study Device

The Silipos Gel care Advanced (GCA) device is a bio enriched polymer gel (product numben,80584') that was worn over the affected area to be treated. It is drug free, l tex free, and reusable. In the asf of A involvement of the hands, the device tested was a glove. For involvement elsewhere, a three me or six inch wide elastic wrap was used at the discretion of the investigator.

3.3 Study Treatments

Patients who met all study eligibility criteria were enrolled at baseline to receive one of the following two treatment regimens:

3.3.1 Gel Care Advanced {GCA) Group

A group of patients were designated by the investigator at baseline for treatment of the target area with the Gel care Advanced (GCA) device only for the duration of the study. The GCA device was worn on the target area for a minimum of 4 and a maximum of 12 hours per day.

3.3.2 Gel Care Advanced and Hydrocortisone (GCA +HC} Group

A second group of patients was designated by the investigator at baseline for treatment of the target area with the Gel Care Advanced (GCA) device and topical hydrocortisone (HC) for the duration of th study. The GCA device was worn for a minimum of 4 and a maximum of 12 hours per day. Hydrocortisofe (HC) was applied immediately following the use of the device and applied to the target area once only.

Hereafter in this study protocol, all treatments (GCA or HC) distributed to the patients under this protocol will be referred to as "study product(s)". This will include the GCA device, hydrocortisone tubes or oth.

3.4 Study Population

atients of either sex, who_have satisfied all inclusion and exclusion criteria and who have providedlwritten informed co sent were assigned to one of the two treatment groups for evaluation. All patients un erwent treatment with Gel care Advanced (GCA) for 28 days. A subset of patients received both GCA an1 topical hydrocortisone as described above.

Patients were able to give both verbal and written information, including informed consent, regar ing the study. They also agreed to present at the investigational site for three visits over a 28 day period a d were able to maintain and provide written diaries for the duration of the study. Signed informed consrnt was obtained for all patients prior to screening.

4. SELECTION OF PATIENTS

4.1 Inclusion Criteria

Patients were enrolled and received study product based on the following criteria. Patients met all of the following criteria for inclusion at baseline and at subsequent study visits for continuation in the evaluation:

- Diagnosis of moderate to severe atopic dermatitis
- Age 18 years or older.
- Ability to provide informed written consent for participation in the evaluation
- Presence of at least one lesion of atopic dermatitis at the time of baseline enrollment
- Disease limited to less than 100 cm^2 body surface area

4.2 Exclusion Criteria

Patients were excluded from the evaluation if any of the following criteria existed at baseline or at any time during the evaluation:

- Allergy to any ingredient in either the GCA device or corticosteroids
- Usage of oral corticosteroids within the 2 weeks prior to study initiation or during the study
- Use of any concomitant medication that may interfere with the study related activities or assessment of efficacy
- Patients who are pregnant or breast-feeding, or who plan to become pregnant during the course of the study
- Any serious medical condition which, in the opinion of the investigator, may interfere with the evaluation of the results
- Any patient related factor suggesting potential poor compliance with study procedures (e.g. psychiatric disorders, history of alcohol or substance abuse)
- Inability to comply with the study protocol as determined by the investigator
- Clinical diagnosis of bacterial infections of the skin, including impetigo or abscesses.
- Current participation in any other interventional clinical trial.

5. PROCEDURES

5.1 Diagnosis and Assignment of Patient ID Number

Patients were required to *have* a diagnosis of atopic dermatitis at baseline, with the diagnosis recorded on the patient CRF. A **target area for treatment was identified by the principal investigator at baseline and was the only area to be treated and evaluated under this protocol for** their **entire** 28 **day treatment period.**

Patients who signed the informed consent and were enrolled into the evaluation were assigned at baseline a unique two digit Patient Identification (PID) Number. Numbers were assigned sequentially in ascending order with running numbers beginning with PID 01. The PID number uniquely identified every patient enrolled into the study, and was included on all study documents. Patients were also required to provide initials as part of the patient identification process. The investigator kept an enrollment log to identify all patients enrolled into the evaluation.

The investigator determined whether or not hydrocortisone was to be included in the treatment, and this was recorded on the patient CRF.

5.2 Patient Diary

A Patient Diary was distributed to all patients at the baseline visit. Training was conducted by the investigator or qualified designee on the correct completion of the patient diary. Patients were asked to bring the diary at all visits for review by the clinical research staff. Included in the Patient Diary were:

- Patient Instructions
- Visit Schedule
- Study Device Usage Log

53 Study Product Use and Patient Instructions

The GCA device was worn for a minimum of 4 and a maximum of 12 hours per day. If hydrocortisone (HC) was to be applied, the application took place immediately following the use of the device and was applied to the target area once only. HC should be applied once after the GCA device is removed. Patient instructions pertaining to use of the study product(s) will be provided in the patient diary. To standardize treatment and to facilitate training of the patient, the principal investigator or designee will apply the first dose of study product at the baseline study visit.

Patients documented all study product usage in the Patient Diary.

54 Patient Background {Demographics/Medical History)

Patient demographics were collected at the baseline visit only and recorded on the patient CRF. Demographic information was collected as follows:

- Gender
- Race
- Skin Type (Fitzgerald type I-VII)
- Age (Date of Birth)
- Diagnosis
- Hydrocortisone Use (If applicable)
- Additional Comments

55 Concomitant Medications

All concomitant medications were recorded by the principal investigator in the patient CRF. Other treatments for eczema were not permitted while the patient was enrolled in the study under this protocol. Patients were allowed to continue taking stable doses of medications that in the opinion of the investigator would not interfere with the treatment or assessments outlined in this protocol.

5.6 Outcome Assessments

Outcome assessments were performed at baseline and at all study visits unless otherwise noted to evaluate treatment efficacy and tolerability. Assessments were made either by the investigator or trained designee or by the patient as self-reported data and were based on an eleven point (0-10) visual analog ordinal scale unless otherwise noted. **Investigator assessments were blinded with regard to treatment group.**

5.6.1 Pain/Burning

Assessments of pain and/or burning were reported by the patient at each study visit and recorded in the patient CRF, and were measured subjectively according to a visual analog scale (VAS) with 0 being no pain or burning and 10 being the worst pain or burning imaginable.

5.6.2 Pruritus

Assessments of pruritus (itching) were reported by the patient at each study visit and included in the patient CRF, and were measured subjectively according to a visual analog scale (VAS) with O being no itch and 10 being the worst itch imaginable.

5.6.3 Erythema

Assessments of erythema was recorded by the principal investigator or a trained designee at each visit and included in the patient CRF. Erythema was measured subjectively according to a visual analog scale (VAS) with O being no erythema and 10 being extreme erythema.

5.6.4 Edema

Assessments of edema were recorded by the principal investigator or a trained designee at each visit and included in the patient CRF. Edema was measured subjectively according to a visual analog scale (VAS) with O being no edema and 10 being extreme edema.

5.6.5 Crusting and Scaling

Assessments of crusting/scaling were recorded by the principal investigator or a trained designee at each visit and included in the patient CRF. Crusting and scaling were measured subjectively according to a visual analog scale (VAS) with O being no crusting/scaling and 10 being extreme crusting/scaling.

5.6.6 Hydration {Subjective Dryness Scoring)

Assessments of dryness (skin hydration) was recorded by the principal investigator or a trained designee at each visit and included in the patient CRF. Dryness was measured subjectively according to a visual analog scale (VAS) with O being no dryness and 10 being extreme dryness.

5.6.7 Investigator Global Assessment (IGA) of Treatment Outcome

The investigator reported an Investigator Global Assessment (IGA) of overall treatment outcome at each post baseline study visit and results were recorded on the CRF. Grading was on a VAS 10 mm scoring system (O= Very Poor, 10 = Very Good) in response to the question: "How would you rate the overall treatment performed under this protocol?" **The IGA was not obtained at baseline.**

5.6.8 Patient Global Assessment (PGA) of Treatment Outcome

Patients were required to report a Patient Global Assessment (PGA) of overall treatment outcome at each post baseline study visit and results were recorded on the CRF. Grading was on a VAS 10 mm scoring system (O= Very Poor, 10= Very Good) in response to the question: "How would you rate the overall treatment performed under this protocol?" **The PGA was not obtained at baseline.**

5.6.9 Patient Quality of Life Assessment

The impact of treatment on the patient's quality of life as it is related to the condition being treated under this protocol was assessed at each study visit. Skindex 16 (© The Regents of the University of California, 2001), a validated dermatologic quality of life survey was utilized. Skindex 16 was designed to assess patients quality of life based on answers to questions pertaining to the impact on daily activities of the patient due to their skin condition.5'[5]

[5] Chren MM, Lasek RJ, Quinn LM, Mostow EN, Zyzansl<i SJ. Sl<index, a quality-of-life measure for patients with skin disease: reliability, validity and responsiveness. J Invest Dermatol. 1996 Nov;107(5):707-13

[6] Chren MM, Lasek RJ, Sahay AP, Sands LP. Measurement of properties of skindex-16, a brief quality-of-life measure for patients with skin diseases. J Cutan Med Surg. 2001 Mar-Apr;5(2):105-10. Epub 2001 Mar 21.

5.6.10 Patient Device Satisfaction Survey

The satisfaction by the patient with regard to treatment with the GCA device was assessed by each patient at the completion of the study. **The satisfaction survey was given once only at Day 28.**

5.6.11 Photography

High resolution digital photography was performed at each study visit to evaluate overall appearance of the skin. Photographs were taken so that assessments can be made of the entire treatment area.

5.7 Visit Specific Procedures

The following sections outline the procedures required at each visit. The patients visited the study center and were examined by the Investigator. **All visits were within 3 days of the visit schedule defined by this protocol.**

5.7.1 Baseline Visit (Day 0, Visit 1)

The purpose of the baseline visit was to determine potential eligibility for study participation, to perform baseline assessments, and to distribute study product. Potential patients were evaluated for participation based on the inclusion and exclusion criteria detailed in section 4 of this study protocol. Patients signed a written informed consent form to be considered for randomization into the evaluation. The following procedures were completed as part of the baseline visit:

- Obtain written informed consent
- Obtain patient medical history and demographics
- Verify inclusion and exclusion criteria
- Outcome assessments (Investigator and Patient reported)
- Dispense and review procedure for completing Patient Diary
- Review concomitant medication
- Complete CRF (Demographics and Baseline Assessments)

5.7.2 Day 14 (Visit 2)

Visit 2 occurred at day 14, with a window period of ±3 days. The patients visited the study center and were examined by the Investigator. The following procedures and assessments were performed at Day 14:

- Inclusion and Exclusion criteria
- Review patient diary
- Outcome assessments
- Review concomitant medication
- Assess adverse events
- Collect or dispense study product
- Complete CRF

5.7.3 Day 28 (Visit 3)

Visit 3 occurred at day 28, with a window period of ±3 days. The patients visited the study center and were examined by the Investigator. The following procedures and assessments were performed at Day 28 or early termination:

- Review Inclusion and Exclusion criteria
- Review Patient Diary
- Collect unused study product(s)
- Outcome Assessments
- Patient Satisfaction
- Review concomitant medications
- Assess adverse events
- Complete CRF

5.8 Schedule of Study Procedures

The schedule of visits and procedures conducted at each visit are summarized in the following Schedule of Study Procedures.

Visit	Enrollment/ Baseline	Interim Visit	Termination
Day of Evaluation	**Day0**	**Day14**	**Day28**
Window Period	**N/A**	**± 3 Days**	**± 3 Days**
Written Informed Consent	X		
Background Information (Demographics/Diagnosis/Tx)	X		
Inclusion/Exclusion Criteria Review	X	X	X
Outcome Assessments•	X	X	X
Global Assessments (PGA, IGA)	X	X	X
Patient Device Satisfaction			X
Dispense Study Product	X	X	
Collect Unused Study Product		X	X
Concomitant Medication Review	X	X	X
Review Patient Diary	X	X	X
Complete Case Report Forms	X	X	X
Adverse Event Reporting	X	X	X

*All outcome assessments were performed by a blinded evaluator, except pain/burning and pruritus which was reported by the patient

5.9 Protocol Deviations

This study was conducted as described in this protocol. No protocol deviations or protocol violations occurred.

5.10 Patient/Treatment Compliance

Study device use and treatment with HC was documented by the patient and included in the Patient Diary. All study products remaining were collected and inventoried by the investigator at each visit.

5.11 Discontinuation/Withdrawal of Patients

No subject prematurely discontinued or was withdrawn from the study.

6. MATERIALS AND SUPPLIES

6.1 Study Supplies

The patient supplies consisted of enough study devices and/or topical hydrocortisone to be used or applied until the next visit. Study products were distributed as described below, depending on which treatment group the patient in which the patient was enrolled.

For patients designated by the investigator to be enrolled in the GCA only treatment group, one unit of GCA was dispensed at the baseline (Day 0) visit and returned at the interim visit (Day 14). Patients in this group received only one unit of GCA at day 14, and returned it at the termination visit (Day 28).

For patients designated by the investigator to be receiving hydrocortisone and enrolled in the GCA + hydrocortisone treatment group, one unit of GCA and one tube of HC were dispensed at the baseline (Day 0) visit and the GCA device was returned at the interim visit (Day 14). Patients in this group received one unit of Gel care Advanced at day 14, and returned it at the termination visit (Day 28).

The hydrocortisone ointment (1%) was supplied in tubes and provided by Silipos Inc.

The investigator performing the clinical evaluations and assessments did not dispense or collect study product. An independent third-party dispenser who was not performing the clinical evaluations was assigned to dispense and collect study product.

6.2 Product Management

6.2.1 Storage and Test Article Accountability

Study product used to conduct this study was maintained under adequate security by the investigator. Study test articles were stored at 25°C (77°F); excursions permitted between 15 - 30° C (59 - 86° F). The investigator did not supply study product to any person not enrolled in this study.

The investigator kept a running inventory of study product dispensed that included patient numbers assigned and the date each was dispensed and used. A study medication accountability form was maintained by the investigator to document all medications received, dispensed and used by each patient. At the conclusion of the study all unused, partially used, and empty containers were inventoried by the investigator and stored until notified by Silipos.

6.2.2 Procedure for Breaking the Blind

The investigator performing the assessments, study monitors, and data analysis/management personnel were blinded to the patient assignment. The blind was not broken.

7. ADVERSE EVENTS

No adverse events or adverse experiences occurred during the administration of the study.

8. STATISTICAL ANALYSIS PLAN

Dermatology consulting Services performed the statistical analysis on the investigator and subject ordinal data. A Mann Whitney Hest variant was used based on the nonparametric nature of the data. Statistical significance was set at $p<0.05$. The Skindex was analyzed both individually and utilizing an aggregate score of all sixteen components of the Skindex.

9. RESULTS

The results are summarized in the attached tables.

1. Investigator Assessments (Direct Comparison, Longitudinal, Difference from Baseline)
   A. Individual Assessments (Sections 5.6.1 through 5.6.6)
   B. Investigator Global Assessment (IGA) (Section 5.6.7)

2. Subject Assessments (Direct Comparison, Longitudinal, Difference from Baseline)
   A. Patient Global Assessment (PGA) (Section 5.6.8)
   B. Quality of Life Assessment (Skindex 16) (Section 5.6. 9)
   C. Patient Device Satisfaction Survey (Section 5.6.10) - Summary provided separately (See Appendix A)

Three methods of evaluation were performed. The groups that were compared were those that used 1% hydrocortisone and those who did not. Direct comparison examines the difference between the raw ordinal data at each time point. The longitudinal analysis examines the improvement over time of each group separately as compared to baseline. Finally, difference from baseline examines the change over time between the two groups by subtracting each ordinal rating from the baseline rating. Each analysis provides a little different look at the data.

A total of 24 patients completed the evaluation after being treated with either the GCA wrap or the GCA glove with or without hydrocortisone once daily.

9.1 Investigator Assessments

The following analyses represent assessments obtained by the investigator by direct observation or by inquiry with the patient. Table 10.1 below reflects a complete tabulation based on percentage improvement from baseline at days 14 and 28 of treatment of assessments for Pain, Pruritus, Erythema, Edema, Scaling, and Dryness. Data shown are tabulated based on use of the device alone or in conjunction with hydrocortisone l X daily (HC). All assessments were statistically significant ($p<.05$) at each time point.

Table 9.1.1 Individual Investiaator Assessments: Percentage Improvement

	Subiect #	
Data	**Percent Imorovement - HC**	**Percent Imorovement - No HC**
Pain - Dav 14	76%	73%
Pain- Dav 28	90%	98%
Pruritus- Dav 14	51%	43%
Pruritus- Dav 28	81%	74%
Ervthema - Dav 14	48%	49%
Erythema - Dav 28	75%	85%
Edema - Day 14	75%	67%
Edema - Dav 28	86%	87%
Scaling - Dav 14	53%	44%
Scaling - Dav 28	64%	73%

Drvness- Dav 14	s3%	29%
Dryness - Dav 28	67%	76%

A global assessment of treatment outcome (IGA) on a scale of 1-10 was also obtained by the inve◆◆igator al each post baseline study visit. Results are shown below for both treatment groups.

Table 9.1.2 Investigator Global Assessment (IGA) of Treatment Outcome

IGA Day 14 (HC)								
Response (1-10)	2	3	4	5	6	7	8	Total
Frequency(N)	1/14 (7%)	1/14 (7%)	4/14 (28%)	4/14 (28%)	2/14 (14%)	1/14 (7%)	1/14 (7%)	14

IGA_Day 14 (No HC)						
Response (1-10)	2	3	4	6	7	Total
Frequency(N)	1/10 (10%)	3/10 (30%)	3/10 (30%)	1/10 (10%)	2/10 (20%)	10

IGA_Day 28 (HC)								
Response (1-10)	3	4	5	6	7	8	10	Total
Frequency(N)	2/14 (14%)	1/14 (7%)	2/14 (14%)	3/14 (21%)	3/14 (21%)	1/14 (7%)	2/14 (14%)	14

IGA_Day 28 (No HC)							
Response (1-10)	1	5	6	7	8	9	Total
Frequency(N)	1/10 (10%)	1/10 (10%)	1/10 (10%)	5/10 (50%)	1/10 (10%)	1/10 (10%)	10

9.2 Subject Reported Assessments

Subject reported responses to the Skindex 16 questionnaire are shown below for both treatment gr◆ups at each time pont. A reduction in aggregate scoring indicates improvement. Individual assessments Df each component of Skindex 16 were analyzed and are attached separately.

Table 9.2.1: Subiect Reoorted Oualitv of Life Assessments: Skindex 16®

Data (Treatment Group)	Aggregate BL	Aggregate Dav14	Aggregate Dav28
Mean Score (HC)	60.07	24.43	17.79
0/oImprovement (HC)		59%	70%
Mean Score (NO HC)	58.90	30.90	18.40
0/oImprovement (No HC)		48%	69%

A global assessment of treatment outcome (PGA) on a scale of 1-10 was also reported by the su ::,ject al each post baseline study visit. Results are shown below for both treatment groups.

PGA_Day 14 (HC)							
Response (1-10'\	2	4	5	6	7	8	Total
Frequency(N)	1/14 (7%)	4/14 (28%)	4/14 (28%)	3/14 (21%)	1/14 (7%)	1/14 (7%)	14

PGA_Day 14 (No HC)						
Response (1-10)	2	3	4	6	7	Total
Frequency(N)	1/10 (10%)	3/10 (30%)	3/10 (30%)	1/10 (10%)	2/10 (20%)	10

PGA_Day 28 (HC)								
Response (1-10'\	2	3	5	6	7	8	10	Total
Frequency(N}	2/14 (14%)	1/14 (7%)	2/14 (14%)	3/14 (21%)	3/14 (21%)	1/14 (7%)	2/14 (14%)	14

PGA_Day 28 (No HC}							
Response {1-10)	0	4	5	7	9	10	Total
Frequency(N)	1/10 (10%)	1/10 (10%)	1/10 (10%)	4/10 (40%)	2/10 (20%)	1/10 (10%)	10

10. DISCUSSION

The results are discussed for each data set.

Investigator Assessments (Direct Comparison, Longitudinal, Difference from Baseline)

The investigator assessments overall demonstrated the ability of the study product to improve the condition of skin afflicted with atopic dermatitis. The direct comparison analysis showed parity between thEf device alone group and the device plus 1% hydrocortisone group. Both products demonstrated improvemernt in the atopic dermatitis that was statistically significant at day 14 and day 28. Highly statistically siqnificant improvement was seen in both groups in terms of pain, itching, erythema, edema, and scaling. The 1% hydrocortisone group did seem to show faster improvement in dryness probably due to the moisturizing effect of the vehicle. This was also a statistically significant data point in the difference from baseline comparison.

Subject Assessments (Direct Comparison, Longitudinal, Difference from Baseline)

The subject direct comparison and difference from baseline analyses demonstrated parity between the device alone and the device with 1% hydrocortisone treatment arms. Both treatments showed improvement as reported by the subjects in the longitudinal analysis, but the 1% hydrocortisone group reportf more statistically significant data points. Statistically significant improvement in itching, burning, hurting, irritation, persistence, worry/ appearance, frustration, embarrassment, annoyance, depression, an social problems was noted by the subjects using the device plus the 1% hydrocortisone cream at day 14. Similar results were seen at day 28, but additional statistically significant improvement was seen in daily activities and work. Fewer statistically significant data points were seen with the device alone group. At day 14, statistically significant improvement was seen in irritation, persistence, worry, appearance, frustration, embarrassment, annoyance, and depression. The day 28 results showed statistically significant improvement in the same criteria in the device alone group as in the group using the device plus 1%

hydrocortisone. Thus, the 1% hydrocortisone combined with the device led to quicker improvement than the device alone.

11. SUMMARY

Primary efficacy endpoint:
The primary efficacy endpoint was the investigator-assessed improvement in atopic dermatitis at day 28 as compared to baseline based on the use of the study product. **The primary efficacy endpoint was met.**

Secondary efficacy endpoint:
The primary efficacy endpoint was the subject-assessed improvement in atopic dermatitis at day 28 as compared to baseline based on the use of the study product. **The secondary efficacy endpoint was met.**

Safety endpoint:
The safety endpoint was the absence of adverse events related to the study product over the 28 day test period. **The safety endpoint was met.**

12. APPENDIX A: PATIENT SATISFACTION SUMMARY

Silipos Eczema Study (SIL01} Patient Satisfaction Questionnaire
Summary o fResults

Background I Methods

This summary contains an analysis based on questions related to the satisfaction of the patient with the GeI Care Advanced (GCA) device, either glove or wrap, for the treatment of atopic eczema. Data was collected under protocol SILOOl for patients enrolled under the direction of Dr. Zoe Diana Draelos (Dermatology Consultants Inc., High Point NC). Assessments of patient satisfaction were reported by the patient at Day 28 of the study treatment period. See Appendix A (attached) for the questionnaire that was administered under the above reference protocol. A total of 24 patients completed the evaluation after being treated with either the GCA wrap or the GCA *glove* with or without hydrocortisone once daily, with nine (9) being treated with the glove and fifteen (15) being treated with the wrap. Cohort analyses were performed overall and also based on the following patient groups:

A. Device plus hydrocortisone or device only
B. Treatment using the glove or wrap.

1.0 Overall Patient Satisfaction

Patients were asked to report overall satisfaction with the device in response to the following question: "Please rate your overall satisfaction with the GCA device". Responses were limited to the following: 1= Very Satisfied, 2= Somewhat Satisfied, 3 = Neutral, 4 =Somewhat Dissatisfied, 5 = Very Dissatisfied. Mean of ail patient reported overall device satisfaction ratings were 1.6 (N=24). A total of 58% (14/24) patients reported being very satisfied with the device. Frequencies of responses are tabulated below.

1.1 Overall Patient Satisfaction -Analysis by Device Type (Glove or Wrap)

44% (4/9) of patients reported being very satisfied with the glove and 67% (10/15) reported being ve satisfied with the wrap. No patients reported being very dissatisfied with either device. Only one patient reported any dissatisfaction with the device overall (wrap).

Table 1.1: Analysis by Device Type

Overall Satisfaction Rating	Glove	Wrap	Total
1- Very Satisfied	44% (4/9)	67% (10/15)	58% (14/24)
2- Somewhat Satisfied	44% (4/9)	20% (3/15)	29% (7/24)
3- Neutral	11% (1/9)	7% (1/15)	8% (2/24)
4- Somewhat Dissatisfied	0% (0/9)	7% (1/15)	4% (1/24)
5- Very Dissatisfied	0% (0/9)	0% (0/15)	0% (0/24)
Grand Total	**9**	**15**	**24**

1.2 Overall Patient Satisfaction - Analysis by Hydrocortisone Use

57% (8/14) of patients reported being very satisfied with treatment that included administration with hydrocortisone, while 60% (6/10) reported being very satisfied with treatment with the device by itself.

Table 1.2: Analysis by Hydrocortisone Use

Overall Satisfaction Rating	HC	NoHC	Total
1- Very Satisfied	57% (8/14)	60% (6/10)	58% (14/24)
2- Somewhat Satisfied	36% (5/14)	20% (2/10)	29% (7/24)
3- Neutral	7% (1/14)	10% (1/10)	8% (2/24)
4- Somewhat Dissatisfied	0% (0/14)	10% (1/10)	4% (1/24)
5- Very Dissatisfied	0% (0/14)	0% (0/10)	0% (0/24)
Grand.Total	**14**	**10**	24

2.0 Purchase Interest:

Patients were asked to rate their purchase interest for the device in response to the following question: "After using this product, how interested would you be in buying this product if it were available in a store at which you normally shop?" Answers were limited to the following: 1 = Definitely will buy, 2= Probably will buy, 3 = Might or might not buy, 4= Probably will not buy, 5= Definitely will not buy. Mean of patient reported purchase interest ratings was 2.1 at day 28. Of all patients treated, 33% (8/24) reported that they definitely will buy the device, and no patients treated under the protocol reported that they will definitely not buy the device.

2.1 Purchase Interest - Analysis by Device Type

33% (3/9) of patients treated with the glove and 33% (5/15) of patients treated with the wrap reported that they would definitely buy the device. Only 2 patients reported that they probably will not buy the device, both being patients treated with the wrap.

Table 2.1 - Analysis by Device

Purc◆ase Interest Rating	Glove	Wrap	Total
1- Definitely Will Buy	33% (3/9)	33% (5/15)	33% (8/24)
2- Probably Will Buy	22% (2/9)	33% (5/15)	29% (7/24)
3- Might or Might Not Buy	44% (4/9)	20% (3/15)	29% (7/24)
4- Probably Will Not buy	0% (0/9)	13% (2/15)	8% (2/24)
5- Definitely Will ◆ot Buy	0% (0/9)	0% (0/15)	0% (0/24)
Grand Total	**9**	15	**24**

2.2 Purchase Interest - Analysis by Hydrocortisone Use

36% (5/14) of patients treated with hydrocortisone responded that they would definitely by the device and 30% (3/10) patients treated with the device alone responded that they would definitely buy the device. Only 2 patients reported that they probably will not buy the product, both being patients who did not receive HQ.

Table 2.2 - Analysis by HC Use

Purchase Interest Rating	HC	NoHC	Total
1- Definitely Will Buy	36% (5/14)	30% (3/10)	33% (8/24)
2- Probably Will Buy	28% (4/14)	30% (3/10)	29% (7/24)
3- Might or Might Not Buy	36% (5/14)	20% (2/10)	29% (7/24)
4- Probably Will Not buy	0% (0/14)	20% (2/10)	8% (2/24)
5- Definitely Will Not Buy	0% (0/14)	0% (0/10)	0% (0/24)
Grand Total	**14**	**10**	**24**

3.0 Product Effectiveness:

Patients were asked to report overall effectiveness in response to the following question: "How effective was the product in reducing and/or eliminating your eczema?" Answers were limited to the following: 1 = Extremely effective, 2 = Somewhat Effective, 3= Neutral, 4= Not that effective, 5 = Not effective at all Mean of patient reported product effectiveness ratings was 1.7 at day 28. 46% (11/24) of all patients responded that treatment with the device was extremely effective.

3.1 Effectiveness -Analysis by Device Type

56% (5/9) of oatients treated with alove and 40% (6/15) of oatients treated with the wrao resoonded that

the device was extremely effective. Only one patient reported any that the device was ineffective to any extent overall {wrap).

Table 3.1 Effectiveness Rating	Column Labels Glove	Wrap	Total
1- Extremely Effective	56% (5/9)	40% (6/15)	46% (11/24)
2- Somewhat Effective	44% (4/9)	40% (6/15)	42% (10/24)
3- Neutral	0% (0/9)	13% (2/15)	8% (2/24)
4- Not that effective	0% (0/9)	7% (1/15)	4% (1/24)
5- Not effective at all	0% (0/9)	0% (0/15)	0% (0/24)
Grand Total	**9**	15	**24**

3.2 Effectiveness -Analysis by Hydrocortisone Use

50% (7/14) of patients treated with the device and hydrocortisone reported that the treatment wcs extremely effective. 40% (4/10) of patients treated with the device alone reported that the treatment w,s extremely effective.

Table 3.2 Effectiveness Rating	HC	NoHC	Total
1- Extremely Effective	50% (7/14)	40% (4/10)	46% (11/24)
2- Somewhat Effective	50% (7/14)	30% (3/10)	42% (10/24)
3- Neutral	0% (0/14)	20% (2/10)	8% (2/24)
4- Not that effective	0% (0/14)	10% (1/10)	4% (1/24)
5- Not effective at all	0% (0/14)	0% (0/10)	0% (0/24)
Grand Total	**14**	**10**	**24**

4.0 Comfort Rating:

Patients were asked to rate their comfort level with the device in response to the following question1 "How would you describe the comfort of the product?" 1 :;: Extremely comfortable, 2 :;: Somewha: comfortable, 3 = Neutral, 4 = Not that comfortable, 5 :;: Not comfortable at all. Mean of patient reported product comfort ratings was 2.0 at day 28.

4.1 Comfort Rating-Analysis by Device Type

22% (2/9) of patients responded that they felt the glove was extremely comfortable, and 47% (7/15) of patients felt that the wrap was extremely comfortable.

Table 4.1 Comfort Rating	Glove	Wrap	Total
1 - Extremely comfortable	22% (2/9)	47% (7/15)	37% (9/24)
2 - Somewhat comfortable	44% (4/9)	33% (5/15)	37% (9/24)
3 - Neutral	22% (2/9)	13% (2/15)	17% (4/24)
4 - Not that comfortable	11% (1/9)	7% (1/15)	8% (2/24)
5 - Not comfortable at all	0% (0/9)	0% (0/15)	0% (0/24)
Grand Total	**9**	15	**24**

4.2 Comfort Rating- Analysis by Hydrocortisone Use

21% (3/14) of patients treated concomitantly with HC responded that they felt the device was extremely comfortable, and 60% (6/10) of patients treated with the device alone responded that it was extremely comfortable.

Table 4,2 Comfort Rating

	HC	NoHC	Total
1 - Extremely comfortable	21% (3/14)	60% (6/10)	37% (9/24)
2 - Somewhat comfortable	43% (6/14)	30% (3/10)	37% (9/24)
3 - Neutral	28% (4/14)	0% (0/10)	17% (4/24)
4 - Not that comfortable	7% (1/14)	10% (1/10)	8% (2/24)
5 - Not comfortable at all	0% (0/14)	0% (0/10)	0% (0/24)
Grand Total	**14**	**10**	**24**

5.0 Product Comparison Rating:

Patients were asked to describe the comfort of the device in response to the following question: After using the GCA device, how do you feel it compares to other products you have used to treat your eczema? Answers were limited to the following: 1 = Much better, 2 = Somewhat better, 3 = About the same, 4= Not that much better, 5 = Not better at all. Mean of all responses (n=24) was 2.1 at day 28. Overall 33% (8/24) of patients responded that treatment with the device was much better than other products that they have used to treat eczema in the past.

5.1 Product Comparison Rating -Analysis by Device Type

33% (3/9) of patients responded that the glove was much better than other products they have used to treat their eczema, and 33% (5/15) patients responded that the wrap was much better than other products they have used to treat eczema.

Table 5.1 Product Comparison	**Column Labels**		
	Glove	**Wrap**	**Total**
1- Much Better	33% (3/9)	33% (5/15)	33% (8/24)
2- Somewhat Better	33% (3/9)	33% (5/15)	33% (8/24)
3- About the Same	33% (3/9)	13% (2/15)	21% (5/24)
4- Not That Much Better	0% (0/9)	7% (1/15)	4% (1/24)
5- Not Better at All	0% (0/9)	7% {1/15)	4% (1/24)
N/A	0% (0/9)	7% (1/15)	4% (1/24)
Grand Total	**9**	**15**	**24**

5.2 Product Comparison Rating - Analysis by Hydrocortisone Use

36% (5/14) of patients treated with the device plus hydrocortisone felt that the device was much better than other products used to treat their eczema, and 30% (3/10) of patients treated with the device alone responded that the device was much better than other products that they have used in the past to treat eczema.

Table 5.2 Comparison			
	HC	**NoHC**	**Total**
1- Much Better	36% (5/14)	30% (3/10)	33% (8/24)
2- Somewhat Better	43% (6/14)	20% (2/10)	33% (8/24)
3- About the Same	21% (3/14)	20% (2/10	21% (S/24)
4- Not That Much Better	0% (0/14)	10% (1/10)	4% (1/24)
5- Not Better at All	0% (0/14)	10% (1/10)	4% (1/24)
N/A	0% (0/14)	10% (1/10)	4% (1/24)
Grand Total	**14**	**10**	**24**

6.0 Product Usability

Patients were asked to report on the overall ease of use and maintenance of the device based on a yes or no response to the following question: "Did you find that the GCA device was easy to wash and reuse?" A total of 24 patients were evaluated, with 20 indicating that the question was not applicable since washing was not necessary. 27% (4/15) of patients (all wrap devices) felt that the device was easy to wash and reuse. No patients responded that the device was not easy to wash and reuse.

Table 6.0 Usability

(Y/N}	Glove	Wrap	Total
Yes	0% (0/9)	27% (4/15)	17% (4/24)
No	0% (0/9)	0% (0/15)	0% (0/24)
N/A	10Q% (9/9)	73% (IJ/15)	8.3% (20/24)
Grand Total	**9**	15	24

7.0. Product Comfort:

Patients were asked to provide a yes or no response to the question: "Do you believe that the GCA devi1e was comfortable to wear?" (Yes or No). Overall, 92% (22/24) of patients reported that the device was comfortable to wear, and 8% (2/22) reported that it was not comfortable.

Table 7.0 Comfort

(YI!D	Glove	Wrap	Total
Yes	89% {8/9)	93% (14/15)	92% (22/24)
No	11_0% (1/9)	7% (1/15)	8% (2/24)
Grand Total	**9**	15	**24**

8.0 Past Product Usage:

Patients were asked to list examples of products that they have used to treat eczema in the past, in answer to the following question: "Please fist below type of product(s) have you used to treat your eczema in the past." Answers are shown below. No patients reported as to using any similar devices t,, treat eczema in the past.

Vaseline

Cream, Lotion

HC

HC, Moisturizer

Clinique

OTC Cream

Nivea

Moisturizer

Lotion (oatmeal, VaseUne, cocoa butter, shea butter, Gold Bond)

Cetaphil cream

Moisturizer, HC

Gold Bond
Baby lotion/oil
HC
HC
Moo cream, Eucerin, Curel, Dove clanser, Aveeno products
HC
Cream hydro
Eucerin
HC

9.0. Flare Frequency

Patients were asked to describe the frequency of their eczema flares in response to the following question: "Please indicate how many days per week that you experience a flare up of your eczema (1-7)". One patient did not respond.

9.0 Frequency of Flare	**Column Labels**		
Days/Week	**Glove**	**Wrap**	**Grand Total**
0	12% (1/8)	0% (0/15)	4% (1/23)
1	37% (3/8)	13% (2/15)	22% (5/23)
1.5	0% (0/8)	7% (1/15)	4% (1/23)
2	25% (2/8)	33% (5/15)	30% (7/23)
3	12% (1/8)	13% (2/15)	13% (3/23)
3.5	0% (0/8)	7% (1/15)	4% (1/23)
4	12% (1/8)	7% (1/15)	9% (2/23)
5	0% (0/8)	7% (1/15)	4% (1/23)
6	0% (0/8)	7% (1/15)	4% (1/23)
7	0% (0/8)	7% (1/15)	4% (1/23)
Grand Total	**8**	**15**	**23**

10.0 Likes

Patients were asked to describe what they liked about the device that was evaluated. Individual responses are listed below.

Reduced dryness and Itching
Cool, moist, felt great
Easy To Apply
Cooling
Felt nice
Easy To Apply
Felt nice
Softens skin
Easy To Apply, Comfortable
Felt nice, Comfortable

Easy to apply

Cooling

Cool, Comfortable

Comfortable, Soothing

Moistness

Softens skin, Stopped itch

Not messy

Improved condition of skin

Softens skin

Easy to use

Softens and smoothes skin

Softens

Comfortable, Soothing

11.0 Dislikes

Patients were asked to describe what they disliked about the device that was evaluated. Individual responses are listed below. Dislikes were largely focused around the fit of the device which was noted to be in some cases too small (glove) and difficult to remove and associated discomfort related to sweating/warmth.

Sweating

Sticky and made itching worse

Would not stay up and came unwrapped

Hard to remove (glove)

Not as effective as expected

Hard to remove (glove)

Sweating, Hard to remove

Very hot

Coating separated, difficulty removing, strong odor (gloves)

Itchy

Small glove

Small olove

12.0 Flare Reduction

Patients were asked to evaluate the device with respect to the duration of their flares of eczema in answer to the question "Did this product reduce the length of time of your eczema flare-up?" Answers were limited to the following: 1= Yes it was shorter, 2= No it was longer, 3:: About the same time as usual

Patient responses are tabulated below. One patient treated under the protocol (1/24) did not respond and left the response blank. Overall, 65% (15/23) of patients reported that the device tested reduced the length of time of their eczema flare, while 13% (3/23) reported a longer flare than usual and 22% (5/2) reported that their flare duration was about the same.

12.1 Flare Reduction -Analysis by Device Type

55% (5/9) of patients treated with the glove reported that their flare duration was shorter than usual, and 71% (10/14) of patients treated with the wrap reported that their eczema flare was shorter than usual.

Table 12.1 Flare Reduction - By Device Type

Response	Glove	Wrap	Total
Shorter	55% (5/9)	71% (10/14)	65% (15/23}
Longer	22% (2/9)	7% (1/14)	13% (3/23)
Same	22% (2/9)	21%(3/11)	22% (5/23)
Grand Total	**9**	**14**	**23**

12.2 Flare Reduction - Analysis by Hydrocortisone Use

77% (10/13) of patients treated concomitantly with the device and hydrocortisone reported that their eczema flare was shorter than usual, and 50% (5/10) of patients treated with the device alone reportEd shorter flare duration.

Table 12.2 Flare Reduction - By HC Use

Response	HC	NoHC	Total
Shorter	77% (10/13)	50% (5/10)	65% (15/23)
Longer	8% (1/13)	20% (2/10)	13% (3/23)
Same	15% (2/13)	30% (3/10)	22% (5/23)
Grand Total	**13**	**10**	**23**

13.0 Device Attribute Ranking:

Patients were asked to evaluate device attributes based on a ranking of the following potential attributes that may be offered by a device such as this. Patients ranked the following nine attributes of the produ:t on a scale of 1-9, with 1 being the most important attribute and 9 being viewed as the least importa i t attribute in the opinion of the patient.

"Please rank each of the following device attributes based on how important the specific attribute is to ye u as a patient. Place a 1 next to the attribute that is the most important to you, a 2 next to the second mo;t important attribute etc." Proposed device attributes are provided below.

A. Easy to Apply/Use
B. Comfortable to wear
C. Works effectively
D. Reduced Itching
E. Reduced Redness
F. Reduced Swelling
G. Reduced Pain/Burning
H. Reduced Skin Dryness
I. Flexibility of product (ie: moved easily with your skin)

Resolved rankings are listed below in order of most important through least important.

Table 13.1 Patient Reported Device Attribute Rankinas

Attribute	Ranking (Average)
Reduced Itching	**1 (1.46)**

Silipos Eczema Study {SIL01) Patient satisfaction Questionnaire Summary of Results

Reduced Skin Dryness	**2 (1.75)**
Works effectively	**3 (1.83)**
Easy to Apply/Use	**4 (1.88)**
Comfortable to wear	**S (2.25)**
Reduced Pain/Burning	**6 (2.75)**
Reduced Redness	**7 (2.88)**
Reduced Swelling	**8 (3.26)**
Flexibility of product (ie: moved easily with your skin)	**9 (3.38)**

Patient reported rankings clearly reflected the importance of those attributes associated with reduction M symptoms of eczema namely in itching and dryness, as well as overall effectiveness. Device flexibility w,is seen as least important in the opinion of the patient being treated, as were symptoms related to reduction in redness and pain, redness and swelling.

Discussion

Overall satisfaction with the GCA device was high for both the glove and the wrap. While concomitant hydrocortisone use on average contributed to greater satisfaction as well as a shorter eczema flare duration, there was no significant difference between responses from patients treated with or without HC. Since topical applications of HC were limited to once per day, this finding will enable treatment with the devi,e alone or with a lower dosage of HC than typically utilized.

Purchase interest generally was well correlated with device satisfaction. A majority of patients indicatid that they will definitely/probably buy the GCA device, whether or not concomitant HC was used.

Product effectiveness as evaluated by the patient was also well correlated with overall treatment efficacy ,as determined by the investigator.

Comfort of either device was also very high. The device was in some cases observed to be too hot or causing sweating at the treatment site, and this particular phenomenon was mitigated by limiting the daily wear time to four hours per day without limiting treatment efficacy. The glove device, while being effecti'e for treating eczema, was observed in some cases to be too small as well as being warm to wear, often causing sweating at the treatment site.

Patients on average reported that the duration of the flare of their eczema was reduced following treatment.

In conclusion, the Silipos GCA glove and wrap devices were observed by the patient to be satisfactory for treatment of eczema, either with or without once daily hydrocortisone ointment.

Appendix A: Patient Satisfaction Questionnaire

This form contains questions pertaining to the satisfaction of the patient with the Gel Care Advanced (GG◆) device only, regardless of whether or not hydrocortisone was applied as part of the treatment regimen. Assessments of patient satisfaction will be reported by the patient at week 4 of the study period or at the completion of the study, if the patient terminates early. ***This questionnaire is not to be used 11t baseline or at the day 14 visit.***

1. Patient Satisfaction Please rate your overall satisfaction with the GCA device. (Circle one)

1	2	3	4	5
Very Satisfied	Somewhat satisfied	Neutral	Somewhat dissatisfied	Very Dissatisfied

2. Purchase Interest: After using the GCA device, how interested would you be in buying this product if t were available in a store at which you normally shop? (Circle one)

1	2	3	4	5
Definitely will buy	Probably will buy	Might or might not buy	Probably will not buy	Definitely will not buy

3. Product Effectiveness: How effective was the GCA device in reducing or eliminating your eczema? (Circle one)

1	2	3	4	5
Extremely effective	Somewhat Effective	Neutral	Not that effective	Not effective at all

4. Comfort Rating: How would you describe the comfort of the GCA device (circle one)?

1	2	3	4	5
Extremely comfortable	Somewhat comfortable	Neutral	Not that comfortable	Not comfortable at all

5. Product Comparison Rating: After using the GCA device, how do you feel it compares to other products you have used to treat your eczema? (circle one)

1	2	3	4	5
Much better	Somewhat better	About the same	Not that much better	Not better at all

6. Product Usability: Did you find that the GCA device was easy to wash and reuse?

Yes_____; No_ _ _ _

7. Product Comfort: Do you believe that the GCA device was comfortable to wear?

Yes_____; No_ _ _ _

8. Past Product Usage: Please list below type of product(s) have you used to treat your eczema in the past.

Silipos Eczema Study (SIL01) Patient Satisfaction Questionnaire summary of Results

9. Please indicate how many days per week that you experience a flareup of your eczema (1-7)

_____

10. Please describe what you liked about the GCA device.

11. Please describe what you disliked about the GCA device.

12. Did this product reduce the length of time of your eczema flare-up? (circle one)

1. Yes it was shorter
2. No it was longer
3. About the same time as usual

13. Device Attribute Ranking: Please rank each of the following product attributes based on how important the attribute is to you as a patient. Place a 1 next to the attribute that is the most important to you, a 2 next to the second most important attribute etc.

Attribute	Ranking
A. Easy to Apply/Use	
B. comfortable to wear	
C. Works effectively	
D. Reduced Itching	
E. Reduced Redness	
F. Reduced Swelling	
G. Reduced Pain/Burning	
H. Reduced Skin Dryness	
I. Flexibility of product (ie: moved easily with your skin)	