CLINICAL STUDY REPORT

Open-label, single group clinical trial evaluating the effect of moisturization and safety of ® Silveray-II in adult patients with mild atopic dermatitis

Clinical trial institution	**:**	Gachon University Gil Medical Center
Principal Investigator	**:**	Department of Dermatology Associate Professor Jin Ok Baek
Sponsor	**:**	Silverex Co., Ltd.

Overview of the Clinical Trial

Title of Clinical Trial	Open-label, single group clinical trial evaluating the effect of moisturization and safety of ®Silveray-II in adult patients with mild atopic dermatitis
Protocol No.	Silveray-01
Sponsor	Silverex Co., Ltd. 134, Seunggicheon-ro, Namdong-gu, Incheon
Clinical Trial Institution	Gachon University Gil Medical Center 21, Namdong-daero 774beon-gil, Namdong-gu, Incheon
Principal Investigator and Sub-investigator	1. Principal Investigator Gachon University Gil Medical Center Department of Dermatology Associate Professor Jin Ok Baek M.D., Ph.D. 2. Co-investigator Gachon University Gil Medical Center Department of Dermatology Jung Soo Kim, Sae Ha Park, Seul Ki Lee M.D. 3. Clinical Research Coordinator Gachon University Gil Medical Center Clinical Research Coordinator Soon Sub Hwang * Co-investigators were responsible for the management of investigational device products.
Indications	Mild atopic dermatitis patients with EASI score of 5 points and above to 10 points and less
Duration of Clinical Trial	January 9th, 2018 ~ June 30th, 2018

This clinical trial has been conducted in accordance with the Clinical Trial Protocol approved by the Institutional Review Board (IRB) as well as by relevant regulations including Bioethics & Biosafety Law, Phgroupaceutical Affairs Law, and Korea Good Clinical Practice (KGCP).

· Summary of Clinical Study Report

Title of Clinical Trial	Open-label, single group clinical trial evaluating the effect of moisturization and safety of ®Silveray-II in adult patients with mild atopic dermatitis
Phase	Prospective clinical trial
Clinical Trial Institution	Gachon University Gil Medical Center
Investigational Device	Investigational Device: ®Silveray-II (Silverex Co., Ltd.)
Purpose	Evaluation of the change in moisturization measured with Corneometer before and after using ®Silveray-II in patients with mild atopic dermatitis
Design	Open-label, Single group design study
Targeted sample size	Targeted sample size: 36 subjects - Sample size calculation As this study was conducted to measure the change in moisturization before and after using ®Silveray-II in a single group, its efficacy was confirmed by independent one-sample comparison test of the mean (superiority). With reference to the study evaluating the moisturization before and after using makeup mist, assuming that the expected difference between the groups is 7.5 Arbitrary Capacitance Unit (AU), which is 70% of the mean value of difference in moisturization in the above study, and assuming that the estimated standard deviation of the difference is 15 AU, a total of 31 subjects was calculated by applying significance level of 5% and statistical power of 80%. $n = \frac{(z_{\alpha/2} + z_{\beta})^2 \sigma^2}{d^2}$ Assuming a dropout rate of 15%, the total targeted sample size is 36 subjects.
Inclusion Criteria and Exclusion Criteria	**1. Inclusion Criteria** 1) Adult subjects aged 19 years and older to 65 years and younger. 2) Mild atopic dermatitis patients with EASI score of 5 points and above to 10 points and less. 3) Patients with atopic dermatitis symptoms in the facial area. 4) Patients who have fully heard and understood detailed explanations regarding this clinical trial, and have provided

	written consent to following the precautions with voluntary consent to participation. **2. Exclusion Criteria** 1) Patients who have administered systemic corticosteroids within the last 4 weeks. 2) Patients who have administered antipruritic agents and central nervous system agents within the last week. 3) Patients whose treatment sites are infected or patients who are confirmed with another concurrent skin disorder. 4) Patients with systemic disease. 5) Patients who are pregnant or lactating. 6) Other patients determined by the investigator as not qualifiable for the trial.
M e t h o d s	Investigators were to provide detailed explanations regarding this clinical trial and to receive voluntary written consent from adult patients with mild atopic dermatitis, the subjects of this clinical trial. Subjects determined appropriate for this clinical trial were then selected by confirming the inclusion/exclusion criteria. ®Silveray-II was used 10 minutes after adding 50ml of purified water prior to its use. **1. Primary evaluation** The effect of moisturization was measured in all subjects at the same location, and subjects were to take rest for 10 minutes and above at the location prior to measurement. VAS2) score for the extent of pruritus felt by the subject was measured prior to the evaluation of moisturization. Moisturization was measured with Corneometer, and the mean value calculated using 2 measurements conducted by a single investigator was used to decrease the risk of error. The site of measurement was the U zone of both right and left side of the face (point where the lower area straight down from the lateral end of the eye and the area horizontal from the tip of the nose meet), sites highly prone to dryness. For the control group, the left side without application of the ®Silveray-II was measured, and for the experimental group, the right side that applied the ®Silveray-II was measured. After allowing the subjects to take rest for 10 minutes,

	®Silveray-II was sprayed at the right U zone area for a total of 3 times with a 10-minute interval between each time. Application of ®Silveray-II took approximately 30 minutes including the time of rest. 10 minutes after the final spray, moisturization was measured using Corneometer. Occurrence of any adverse events was monitored after measurement. **2. Secondary evaluation** All subjects who have completed the primary evaluation were provided with the investigational device and were instructed to use the device at any time they felt dryness for a 1-week period. Subjects were also instructed to use the device at least 10 times each day. At the follow-up visit after the 1-week period, subjects who used the investigational device for the entire week were selected by checking the mist usage, and moisturization was measured with Corneometer. After the evaluation of moisturization, VAS score was measured for the extent of pruritus, which was then compared with the VAS score measured prior to the primary evaluation. The subjective satisfaction level of ®Silveray-II was also evaluated using subject satisfaction survey.
Evaluation item and its method	**1. Items for evaluation of efficacy** (1) Primary endpoint: Change in moisturization measured with Corneometer before and after using ®Silveray-II (2) Secondary endpoint: ・ Change in moisturization measured with Corneometer after using ®Silveray-II for a week ・ Change in VAS score for pruritus after using ®Silveray-II for a week ・ Satisfaction survey after using ®Silveray-II for a week **2. Items for evaluation of safety** Adverse events such as erythema, edema, pruritus, burning sensation, pricking sensation, etc.
Statistical analysis	**1. Items for evaluation of efficacy**

	(1) Primary endpoint By comparing the mean measurement value of moisturization in the area that applied the ®Silveray-II and the area that did not apply the ®Silveray-II, the difference in moisturization between the 2 groups was analyzed at a significance level of 0.05. (2) Secondary endpoint ・ Change in moisturization measured with Corneometer after using ®Silveray-II for a week : The difference in the measurement value of moisturization before and after the use of ®Silveray-II for a week was analyzed at a significance level of 0.05. ・ Change in VAS score for pruritus after using ®Silveray-II for a week : The difference in the VAS score before and after the use of ®Silveray-II for a week was analyzed at a significance level of 0.05. ・ Satisfaction survey after using ®Silveray-II for a week : The response rate was presented for each item. **2. Items for evaluation of safety** Each resulting value such as the characteristics of adverse events was reviewed for the evaluation of safety and if necessary, compared.
Results of evaluation of efficacy	**Primary endpoint** ・ Change in moisturization measured with Corneometer before and after using ®Silveray-II The mean±standard deviation of the moisturization measured before the use of ®Silveray-II and at 10 minutes after spraying the device 3 times was 62.76±10.73 and 70.75±12.99, respectively, which indicated that the increase in moisturization after its use was statistically significant ($p<0.00001$). **Secondary endpoint** ・ Change in moisturization measured with Corneometer after using ®Silveray-II for a week

	The mean±standard deviation of the moisturization measured before the use of ®Silveray-II and after using the device for a week was 62.76±10.73 and 69.90±7.48, respectively, which indicated that the increase in moisturization after its use for a week was statistically significant (p<0.0001). Change in VAS score for pruritus after using ®Silveray-II for a week The mean±standard deviation of the VAS score for pruritus measured before the use of ®Silveray-II and after using the device for a week was 4.86±2.20 and 3.22±2.03, respectively, which indicated that the decrease in VAS score for pruritus after its use for a week was statistically significant (p<0.0001). · Satisfaction survey after using ®Silveray-II for a week A. Satisfaction in skin improvement Moisturization: Very satisfied (32.4%), Satisfied (52.9%), Neutral (11.8%), Dissatisfied (2.9%), Very dissatisfied (0.0%) Improvement in skin texture: Very satisfied (26.5%), Satisfied (47.0%), Neutral (26.5%), Dissatisfied (0.0%), Very dissatisfied (0.0%) Hydration: Very satisfied (41.2%), Satisfactory (38.3%), Average (17.6%), Dissatisfied (2.9%), Very dissatisfied (0.0%) B. Improvement in area of atopic dermatitis Decreased pruritus: Highly agree (26.5%), Agree (44.1%), Neutral (23.5%), Disagree (5.9%), Highly disagree (0.0%) Decreased burning sensation: Highly agree (11.8%), Agree (64.7%), Neutral (11.8%), Disagree (8.8%), Highly disagree (2.9%) Improvement in erythema and redness: Highly agree (11.8%), Agree (41.2%), Neutral (35.3%), Disagree (8.8%), Highly disagree (2.9%) C. Satisfaction

	Overall satisfaction regarding the investigational device: Very satisfied (20.6%), Satisfied (55.9%), Neutral (23.5%), Dissatisfied (0.0%), Very dissatisfied (0.0%)
Results of evaluation of safety	Among 36 subjects, there was 1 case of adverse event (1 subject, 2.9%), and acute contact dermatitis occurred in 1 subject. The corresponding adverse event was mild, and was determined to be most likely associated with the investigational device. There were no serious adverse events or adverse event resulting in fatal consequences reported in this clinical trial.
Conclusion	Upon application of ®Silveray-II mist product in the facial area of subjects with mild atopic dermatitis, the results of this clinical trial demonstrate that the skin moisturization was increased and subjects' pruritus improved in comparison with that of prior to use. The investigational device was determined to be effective in improvement of skin and affected area of atopic dermatitis, and the overall satisfaction level was also high. Additionally, the absence of any serious adverse events has demonstrated that this is moisturization device is both safe and convenient.