SUMMARY OF THE STUDY REPORT

STUDY CODE: ACR/GLYCO/1215

EudraCT-No: 2012-002393-32

A monocenter, double-blind, randomized study to assess the antiperspirant efficacy of glycopyrrolate 2% versus placebo after topical applications on axilla of healthy volunteers.

Investigational site :	bioskin GmbH Bergmannstrasse 5 10961 Berlin
Sponsor :	**L'OREAL** 14 rue Royale 75008 Paris for : **L'OREAL RESEARCH & INNOVATION** Advanced Clinical Research Centre d'Aulnay-Chanteloup 1 Avenue Eugène Schueller 93600 Aulnay-sous-Bois
Study responsible:	Benoit Muller Ph.D Head of Clinical Evaluation for Advanced Research Christian TRAN Head of project
Study monitor(s) :	Romain de DORMAEL
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Principal Investigator	Heinrich Siemetzki M.D.	
Study date	**Start date:** 27 September 2012	**End date:** 07 November 2012
Duration of Treatment	10 days	
Study objective(s)	The main objective of this study was to assess the antiperspirant efficacy of Glycopyrrolate 2% on the axillae of healthy volunteers, after topical applications and compare to the placebo. The secondary objective was to assess the safety of the different study products.	
Study design	Monocenter, randomized, double-blind compared to placebo. 33 healthy men and female volunteers, 18 to 45 years old, received the Glycopyrrolate 2% during ten consecutive days after a 21 days wash out period. Volunteers should show a variety of sweating rates. The difference between the highest and lowest sweat output among the subjects should not exceed 600 mg of sweat collected in one 20 min collection per axilla.	
Procedures	Both axillae were treated at 0.4 g per day for 10 days. One axilla received the Glycopyrolate 2%; the other received the vehicle in a randomized manner. Axillae were washed on-site in a standardized manner with a standard soap for 30 seconds, then drying with paper towel before to enter in the warm-up period.	

	Thermal challenge was performed before treatment (baseline), then 24hours, 48hours and 72hours after last treatment, under medical supervision in conditioned room at the study site. Thermal challenge was performed as follow: 1- The subjects sited on a bench in a conditioned room at 38°C ±2°C and 35% ±5% of humidity for a 40 minutes warm-up period. 2- After the warm up, new weighed pads were placed under their axillae. Therefore only freshly secreted sweat was measured. After a time period of 20 minutes in a conditioned room at 38°C ±2°C and 35% ±5% of humidity the pads were removed and the amount of sweat was determined gravimetrically. 3- New weighed pads were placed under the axillae and again the sweat was collected for further 20 minutes in a conditioned room at 38°C ±2°C and 35% ±5% of humidity and determined gravimetrically. The amount of sweat was evaluated by gravimetric measurement of absorbed sweat. Sweat was collected in pads and weighed. Each pad was weighed before and after the thermal challenge in the conditioned room. The relative percentage of reduction of sweat was assessed and calculated by the experimental determination with the study products in comparison to sweat output in an untreated control area. The treated and untreated areas were compared each other.
Population	39 patients were screened and 33 patients were randomized in the study. All the patients were included in the PP population. The 6 screening failure reasons were about some not met inclusion criteria or met non inclusion criteria. Mean age of the 33 adults was 31.5 years (range 20 to 45 years). Overall, there were 87.9% (29) women and 12.1% (4) men. Mean weight was 63.4 kg (range 50 to 85 kg) and mean BMI was 22.1 kg/m^2 (range 20 to 27 kg/m^2) whereas mean height was 168.9 cm (range 159 to 185 cm). 21.2% subjects had phototype II whereas 78.8% subjects had phototype III. Moreover, 6.9% (2) women were not of childbearing potential. For the 27 other women, their contraceptive states were acceptable.
Investigational products	• Glycopyrrolate 2% • Placebo
Investigational areas	Both Axillae
Treatment Allocation	• *Route of administration:* topical administration at the study site by a technician. • *Dose:* application once daily for ten days of 0,4 g on treated areas. • Product was conditioned in a flask of 5 ml and applied with a micropipette. • Application of investigational products was done on treated areas

	(according to randomization), with a rest around 5 minutes at ambient temperature for a complete product penetration.
Evaluation criteria	• Primary criteria **Efficacy:** Antiperspirant efficacy by assessment of the relative reduction % of sweat by the experimental determination with the study products in comparison to sweat output in a placebo treated field. Measurement was done approximately 1 hour after the last washing (done at site) plus 40 min warming period. Collection was done in 2 consecutive times of 20 min. • Secondary criteria **Safety :** Safety was assessed by recording Adverse Events, including cutaneous reactions (local intolerance), from the informed consent signature date until the end of the study.
Statistical methodology	Relative reduction of sweat, Z-value and total amount of sweat were analyzed using two – sided Wilcoxon signed rank tests, in order to assess the antiperspirant efficacy. The general efficacy was calculated based on Z< 80 %. A generalized linear mixed model (on the sweat reduction R) for repeated longitudinal data in a covariance pattern framework, with time as fixed effect, allows studying time effect.
Major Protocol deviations & modifications to the study conduct	No subjects were entered into the trial even though they did not fully satisfy entry criteria (responses that were inconsistent with the protocol inclusion and exclusion criteria were recorded for subjects on the Inclusion/Exclusion Checklist CRFs). A protocol amendment was written before the start of the study (Protocol V 1.1 August 20, 2012) in order to answer to the requests of BfArM and Ethic Committee. No protocol deviation was noted during the study duration.
Efficacy Results	The data analyses were conducted on the 33 randomized subjects. The main objective of this study was to assess the antiperspirant efficacy of the Glycopyrrolate 2% on the axillae of healthy volunteers, after topical applications in comparison with placebo. Z-value, sweat reduction and amount of sweat were computed at each evaluation and evaluated as follow: -The calculated Z - value is the ratio of test axilla to control axilla adjusted for the ratio of right-to-left area sweating rate. In other words, Z-value quantifies the difference between the pre-treatment ratio of test axilla to control axilla and the ratio of test axilla to control axilla at different time points. - R criterion is equal to Z-100. - Amount of sweat sums the amount of sweat of the two warm-up periods, and

	is computed compared to the baseline amount of sweat. Amount of sweat evolution (compare to baseline) showed a decrease in Glycopyrrolate group (Mean: -471mg after 24h, -377mg after 48h and -347mg after 72h) where Placebo group increased in the same time (Mean: +41mg after 24h, +76mg after 48h and +86mg after 72h). The general efficacy was calculated based on Z< 80 %. We can see that after 24h, 48h and 72h the median for Z is inferior to 80. Moreover, the result is always significant for the three time points with p<0.001 (Median: 48.61% after 24h, 53.18% after 48h and 58.07% after 72h). We can see that after 24h, 48h and 72h the mean for R (sweat reduction) is always significant for the three time points with p<0.001 (Mean: 52.45% after 24h, 45.04% after 48h and 40.77% after 72h). In terms of efficacy results, main primary criteria analyses: Z, R and total amount of sweat analyses showed significant statistical results for the treatment effect.
Safety Results	♦ **Safety data :** The safety is based on the thirty three (33) subjects included in the study. During the study, 2 subjects reported an adverse event not related to the investigational products, one "Common cold" and one "Toothache". ♦ **Tolerance data :** No local intolerance was reported during the study duration.
Conclusion	Glycopyrrolate 2% provides a significant higher efficacy in comparison to Placebo on the amount of sweat after warm-up periods.