


EARLY CLINIC	
Study Report – 4th February 2014 Final version N° 1.0	

SUMMARY OF THE STUDY REPORT

STUDY CODE: ACR/GLYCALCH/1220

EudraCT-No: 2012-002807-17

A monocenter, double-blind, randomized study to assess the antiperspirant efficacy of glycopyrrolate 2% versus Aluminium chlorohydrate 15% 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
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Report date and version :	04 th February 2014 – Version 1.0

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Study title	A monocenter, double-blind, randomized study to assess the antiperspirant efficacy of Glycopyrrolate 2% versus Aluminium chlorohydrate 15% after topical applications on axilla of healthy volunteers	
Study code	ACR/GLYCALCH/1220 EudraCT-No. 2012-002807-17	
Sponsor L'OREAL 14 rue Royale 75008 Paris for : L'OREAL RESEARCH & INNOVATION Advanced Clinical Research (ACR) Centre d'Aulnay-Chanteloup 1 Avenue Eugène Schueller 93600 Aulnay-sous-Bois <u>Director of ACR:</u> Benoît MULLER Head of Clinical Evaluation for Advanced Research <u>Head of projects:</u> Christian TRAN <u>Study manager:</u> Romain de DORMAEL	Investigational center bioskin GmbH Bergmannstrasse 5 10961 Berlin Tel +49 (0)30 28 04 39 0 web: www.bioskin.de Co-investigators: Saskia Christine KERSCHISCHNIK, M.D.	
Principal Investigator	Heinrich Siemetzki M.D.	
Study date	Start date: 20 December 2012	End date: 13 February 2013
Duration of Treatment	10 days	
Study objective(s)	<p>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 positive control Aluminium chlorohydrate 15%.</p> <p>The secondary objective was to assess the safety of the different study products.</p>	
Study design	<p>Monocenter, randomized, double-blind compared to placebo.</p> <p>33 healthy men and female volunteers, 18 to 45 years old, received the glycopyrrolate 2% on one axillae and the Aluminium chlorohydrate 15% on the other axilla (following randomization) 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.</p>	
Procedures	Both axillae were treated at 0.4 g per day for 10 days. One axilla received the Glycopyrrolate 2%; the other received the Aluminium chlorohydrate 15% in a randomized manner.	

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	<p>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.</p> <p>Thermal challenge was performed before treatment (baseline V2), 24hours after the fourth (V6) and the seventh (V9) treatment, then 24hours, 48hours and 72hours after last treatment, under medical supervision in conditioned room at the study site.</p> <p>Thermal challenge was performed as follow:</p> <ol style="list-style-type: none"> 1- The subjects sited on a bench in a conditioned room at 38°C \pm2°C and 35% \pm5% 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 \pm2°C and 35% \pm5% 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 \pm2°C and 35% \pm5% of humidity and determined gravimetrically. <p>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.</p> <p>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 a positive control area.</p> <p>The areas were compared each other.</p>
Population	<p>39 patients were screened and 33 patients were randomized in the study. 32 patients were included in the PP population (Subject RD025 withdrawn at D25 due to protocol deviation). The 6 screening failure reasons were about some not met inclusion criteria or met non inclusion criteria.</p> <p>Mean age of the 33 adults was 31.5 years (range 18 to 45 years). Overall, there were 78.8% (26) women and 21.2% (7) men. Mean weight was 66.4 kg (range 51 to 87 kg) and mean BMI was 22.7 kg/m² (range 20 to 27 kg/m²) whereas mean height was 170.7 cm (range 159 to 185 cm). 21.2% subjects had phototype II whereas 78.8% subjects had phototype III. Moreover, 1 woman was not of childbearing potential. For the 25 other women, their contraceptive states were acceptable.</p>
Investigational products	<ul style="list-style-type: none"> • Glycopyrrolate 2% • Aluminium chlorohydrate 15%
Investigational areas	Both Axillae
Treatment Allocation	<ul style="list-style-type: none"> • <i>Route of administration:</i> topical administration at the study site by a technician.

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	<ul style="list-style-type: none"> • Dose: application once daily for ten days of 0.4g 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	<ul style="list-style-type: none"> • <u>Primary criteria</u> Efficacy: Antiperspirant efficacy by assessment of the percentage of relative reduction of sweat in comparison to sweat output in an Aluminium chlorohydrate 15% 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. • <u>Secondary criteria</u> 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	<p>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 $Z < 100\%$.</p> <p>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.</p>
Major Protocol deviations & modifications to the study conduct	<p>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 eCRFs).</p> <p>A protocol amendment was written before the start of the study (Protocol V1.1 October 04th, 2012) in order to answer to the requests of BfArM and Ethic Committee.</p> <p>One protocol deviation was noted during the study duration (missing treatments and evaluation)</p>
Efficacy Results	<p>The data analyses were conducted on the 33 randomized subjects. In this report, results were displayed on ITT population. All results with more details and results of Per-Protocol population were given on the Statistical Analysis Report and showed similar results as ITT population.</p> <p>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 Aluminium chlorohydrate 15%.</p>

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	<p>Z-value, sweat reduction and amount of sweat were computed at each evaluation and evaluated as follow:</p> <ul style="list-style-type: none"> -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. <p>Amount of sweat percentage change (compare to baseline) showed a decrease in Glycopyrrolate group (Mean: -50.9% 24h after the fourth treatment, -54.4% 24hours after the seventh treatment, -45.3% 24 hours after the last treatment, -41.4% after 48h and -19.7% 72hours after) where Aluminium chlorohydrate 15% group decreased 24 hours after the fourth, seventh and last treatment (Mean: -14.5%; -14.8% and -13.5% respectively) and increased 48hours and 72hours after the last treatment (Mean: +5.3% and +37.3% respectively). Furthermore the Glycopyrrolate 2% is more efficient than AlCh 15% versus baseline at each evaluation time with $p < 0.001$</p> <p>The general efficacy was calculated based on $Z < 100$ %. We can see that 24hours after the fourth and the seventh treatment and after 24h, 48h and 72h of the last treatment, the median for Z is inferior to 80. Moreover, the result is always significant for the five time points with $p < 0.05$ (Median: 59.54% 24hours after the fourth treatment, 54.45% 24hours after the seventh treatment, 62.03% 24h after the last treatment, 55.47% 48h after the last treatment and 57.54% 72h after the last treatment).</p> <p>We can see that 24hours after the fourth and seventh treatment and 24h, 48h and 72h after the last treatment, the mean for R (sweat reduction) compare to baseline is always significant for the five time points with $p < 0.001$ (Mean: -41.21% 24hours after the fourth treatment, -44.26% 24hours after the seventh treatment, -33.18% 24h after the last treatment, -40.88% 48h after the last treatment and -38.10% 72h after the last treatment).</p> <p>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.</p>
Safety Results	<p>♦ Safety data :</p> <p>The safety is based on the thirty three (33) subjects included in the study.</p> <p>During the study, 7 subjects reported an adverse event not related to the investigational products, three "Common cold", one "Gastroenteritis", one</p>

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	<p>“bronchitis” and two “headaches”.</p> <p>♦ Tolerance data :</p> <p>No local intolerance was reported during the study duration.</p>
Conclusion	<p>Glycopyrrolate 2% provides a significant higher efficacy in comparison to Aluminium hydrohydrate 15% on the amount of sweat after warm-up periods.</p>

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