**Materials and Methods**

This prospective randomized controlled study was conducted in patients with acne attending the Unit of Dermatology, Department of Clinical Medicine and Surgery, University Federico II of Naples (Italy), from October 2017 to September 2018. The study was approved by the Local Ethical Committee (No. 104/17) and carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The purpose of the protocol was clearly explained to all the study participants, and a written informed consent was obtained.

The study had been conducted on 126 subjects with moderate to severe acne vulgaris (IGA scores 3 and 4).

They were randomized into 3 groups of 42 patients each. The first group (G1) was trained on the gel application. In particular, to apply the gel every day about 3 h before going to bed to allow the topical drug to be absorbed properly and avoid moving in sensitive areas such as the perioral region and around the eyes. In addition, a brochure containing pictures and information on the physiological redness in the first days followed by treatment start was delivered to the patients.

The second group (G2) received the same instructions as group 1 and also received a daily SMS to remind them of the application of the product. The third group (G3) received only standard instructions for using the product, without receiving text messages (SMS) or the instruction leaflet.

However, all patients applied a moisturizer with SPF 30 in the morning and cleansed their face twice a day with a specific cleanser for acne skin.

*Inclusion Criteria*

• Subjects aged between 14 and 28 years included

• Subjects with moderate to severe symmetrical facial acne vulgaris: IGA 3 and 4, assessed on a 5-point scale ranging from 0 (clear) to 4

• Owning a mobile phone capable of receiving text messages (SMS)

*Exclusion Criteria*

• Subjects unable to understand the information given (for linguistic or psychiatric reasons) and to give his/her consent in writing to participate

• Subjects unable to understand the study procedures (for linguistic or psychiatric reasons) and to report the required information in writing in his/her diary

For women: subjects pregnant or breastfeeding or planning to get pregnant during the study

*Evaluation Criteria*

Evaluations were carried out at the beginning of treatment (T0) and after 12 weeks (T1):

• Assessment of acne severity using the Investigator’s Global Assessment Scale for Acne Severity [14]

• Photographic evaluation with digital images (Reveal Photo Imager, Canfield Scientific Inc., Parsippany, NJ, USA, with 15 megapixel resolution, auto focus, and flash cross-polarized light)

• Assessment of acne patient’s quality of life by the Cardiff Acne Disability Index which ranges from 0 to 15: the higher the score, the more the quality of life is impaired [15]

• Relationship between doctor and patient assessed by the Patient-Doctor Relationship Depth-of-Relationship Scale which ranges from 0 (no relationship) to 32 (very strong relationship) [16]

• Evaluation of skin pH (pHmeter®, Courage & Khazaka Electronic GmbH, Cologne, Germany) [17]

• Stratum corneum hydration by capacitance method (Corneometer®, Courage & Khazaka Electronic GmbH, Cologne, Germany) [18]

• Adherence to treatment, assessed by asking patients to complete a 84-day diary marking the days during the last week when they had been adherent to the treatment [3]

• A satisfaction questionnaire regarding treatment (choosing between “very much satisfied,” “somewhat satisfied,” “not much satisfied” and “not at all satisfied”)

*Statistical Analysis*

Sample size was calculated considering a continuous variable and 1-way ANOVA to compare the means of 3 groups. The total sample of 126 subjects (42 subjects per group) achieved 80% power to detect differences among the means versus the alternative of equal means using an *F* test with a 0.05 significance level and assuming a variation in the means calculated in terms of effect size of 0.28.

Continuous variables were reported as either mean and standard deviation or median and interquartile range according to their distribution, as assessed by the Shapiro-Wilk test. Categorical variables were reported as absolute number and percentage. For continuous variables, differences of patient characteristics among the 3 groups were tested by means of 1-way ANOVA or Kruskal-Wallis test (according to their distribution). For categorical variables, differences of patient characteristics among the 3 groups were tested by means of the Pearson χ2 test or the exact Pearson χ2 test where appropriate. Multiple comparison analyses were also performed. The association between continuous variables was estimated by the Spearman linear correlation coefficient and 95% confidence interval. A 2-tailed *p* value <0.05 was considered significant. Data were analyzed using SAS version 9.2 (SAS Inc., Cary, NC, USA).