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ORIGINAL RESEARCH

An Emollient PLUS Balm Is Useful for the Management of Xerosis in Patients Treated for Cancer: A Real-World, Prospective, Observational, Multicenter Study

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ABSTRACT

Introduction: Xerosis is a common skin side effect of current anticancer therapies, including chemotherapy, targeted therapy, radiotherapy, and hormonotherapy. We evaluated the effectiveness of an emollient PLUS containing an *Aquaphilus dolomiae* extract (ADE-G1) for the management of xerosis in adult patients treated for cancer.

Methods: This real-world, prospective, observational, multicenter study involved 319 xerotic cancer patients, who were prescribed the study product according to the usual practice of their physician. The practitioner assessed xerosis severity and objective clinical signs, and the patients assessed subjective clinical signs and the impact of their skin condition on their quality of life, at inclusion and after around 4 weeks of use. Overall effectiveness and tolerance were assessed at the end of the study. Clinical success was defined by the combination of several of these effectiveness outcomes.

Results: Daily application of the emollient PLUS reduced xerosis severity in 62.7% of patients ($p < 0.0001$). The mean total severity scores for objective and subjective clinical signs were reduced by 67.7% and 57.4% ($p < 0.0001$), respectively, compared with baseline. The mean Dermatology Life Quality Index (DLQI) score also significantly improved at the end of follow-up (−56.6%, $p < 0.0001$). The product was rated as "effective" or "very effective" by the physician for over 80% of patients, regardless of the initial severity grade of xerosis. Overall clinical success was achieved in 73.7% of patients. A trend toward higher effectiveness and clinical success was observed in patients under hormonotherapy. The study product was well tolerated, regardless of the anticancer therapy being received.

Conclusion: This study shows that the emollient PLUS containing ADE-G1 is an effective treatment for xerosis in cancer patients, regardless of the initial grade of xerosis and the anticancer treatment received.

Keywords: *Aquaphilus dolomiae*; Anticancer therapy; Emollient; Quality of life; Real-world study; Xerosis

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Key Summary Points

Why carry out this study?

Xerosis is a skin condition commonly triggered by anticancer treatments and is associated with significant psychosocial morbidity and quality of life impairment.

An emollient PLUS containing an extract of *Aquaphilus dolomiae* has previously been shown to be efficacious at reducing the severity of xerosis in children with atopic dermatitis and in a population of all ages with a range of dermatologic and systemic diseases.

This real-world study aimed to investigate the effectiveness of this emollient on xerosis severity in adult patients treated for cancer.

What was learned from the study?

This emollient was effective at reducing the severity of xerosis and other clinical symptoms, and at lessening the impact of skin manifestations on patient quality of life, regardless of the anticancer therapy received by the patient.

The product can be useful in the supportive care of patients treated for cancer who develop xerosis, regardless of the anticancer treatment they have received.

INTRODUCTION

Dermatologic adverse events (AEs) are common among patients being treated for cancer. Current anticancer therapies, including chemotherapy, radiotherapy, targeted therapy, hormonotherapy, and immunotherapy, can all induce a wide variety of dermatologic toxicities affecting the skin, oral mucosa, hair, and nails [1]. In particular, anticancer therapy-related cutaneous AEs are linked to skin barrier dysfunction, which generally arises from altered proliferation and differentiation of keratinocytes but can also occur as a result of disturbances to the sebaceous glands and/or cutaneous immune system [1–5]. Xerosis, which is characterized by dry, rough, cracked, and fissured skin, is among the most frequent skin reactions induced by anticancer treatments [6–10]. This skin condition is associated with significant psychosocial morbidity and impaired quality of life (QoL) due to symptoms (itching, sleep disturbance, etc.) and esthetic issues [11–13]. Moreover, onset of this dermatologic AE often causes dose reductions, administration delays, or even interruption of the prescribed anticancer treatment, which can consequently affect patient survival and further impair QoL [3, 14]. Early and effective management of xerosis is therefore an important component of cancer care, with the aim of preventing the exacerbation of symptoms and minimizing the impact of this cutaneous condition on patient QoL and treatment outcomes.

Moisturizers containing both rehydrating and lipid-replenishing components play a major role in the management of xerosis by improving skin hydration and restoring its barrier function [3, 15, 16]. European experts in dermatology and oncology recommend the use of dermocosmetic and cosmetic products to improve the management of cutaneous AEs and enhance QoL in cancer patients [2]. Therefore, the aim of this study was to evaluate the effectiveness and safety of an emollient balm containing an extract of *Aquaphilus dolomiae* (ADE-G1) for the management of xerosis in patients treated for cancer. This emollient was defined as an emollient PLUS in the 2018 consensus-based European guidelines for the treatment of atopic eczema in adults and children [17]. The ADE-G1 component is a purified biomanufactured extract obtained from *A. dolomiae* isolated from the deep aquifer of Avène thermal spring water in the Cévennes mountains (France) [18, 19]. This emollient PLUS has previously been shown to be effective at reducing the severity of xerosis and pruritus in a randomized controlled study in children with atopic dermatitis [20] and in a real-world setting in a wider population with a range of dermatologic and systemic diseases

[21]. However, the effectiveness of this product has not yet been assessed in patients developing xerosis as a result of anticancer therapy.

In this context, we investigated the real-world effectiveness of the emollient PLUS containing ADE-G1 in a population of adult patients with xerosis due to anticancer treatment. The study included evaluations of the effect of the study product on the severity of xerosis and other clinical symptoms, and on the impact of skin manifestations on patient QoL, as well as assessments of safety and tolerance.

METHODS

Study Design

This real-world, prospective, observational, single-arm study was carried out by physicians practicing in oncology centers across three European Union (EU) countries (Spain, France, and Belgium) between September 2017 and July 2020. The study involved two patient visits: an inclusion visit and a follow-up visit after about 4 ± 2 weeks of product use. These visits were part of the systematic follow-up of the patient by the physician usually responsible for their management. No constraints were associated with this study and no additional invasive or specific examinations were carried out.

Ethics

As this was an observational, real-life, phase IV study, it was conducted in a naturalistic setting where the choice of therapy was consistent with approved prescribing information and in line with the usual everyday practice of the physician. The product was prescribed by the practitioners themselves, as per their routine practice. The protocol of this noninterventional study evaluating cosmetic products did not require approval by a local ethics committee or an institutional review board according to Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 (https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf). This clinical study also adhered to Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products (https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:02009R1223-20190813) and complied with the ethical principles of the Declaration of Helsinki (1964, https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/) and good clinical practice guidelines (CPMP/ICH/135/95, https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e-6-r2-guideline-good-clinical-practice-step-5_en.pdf).

Each patient received an information leaflet translated into their native language and including a description of their rights with regard to the processing of their personal data, in accordance with the Regulation (EU) No 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons. All patients provided signed consent before being enrolled in the study.

Participants

Physicians were invited by the sponsor to participate in the study, and those agreeing to participate were asked to recruit at least five patients: adults with xerosis of any severity grade induced by one or several anticancer treatments. All patients enrolled in the study required prescription of an emollient to relieve their symptoms and had been prescribed a cleansing oil (XeraCalm A.D, Eau Thermale Avène, France) along with the study product: an emollient in the form of a balm (XeraCalm A.D, Eau Thermale Avène, France), containing ADE-G1 (I-modulia) as the active nonmedicated substance and Cer-Omega, a complex of omega 6 fatty acids, ceramides, and sterols.

Noninclusion criteria were the presence of xerotic lesions prior to the anticancer treatment, intolerance to any of the components of the test product and participation in interventional clinical studies within 1 month of enrollment in the current study. Pregnant or lactating women were not eligible for prescription of the study product.

Study Procedure

At inclusion, physicians collected patient demographic and clinical data, including the type of anticancer treatment, the localization of xerosis, and details of any concomitant topical or systemic treatments. They then prescribed the study product according to their usual practice in case of xerosis, without any specific instructions or recommendations from the sponsor, with only patients fulfilling all other study criteria being eligible for the study. The physician recorded the prescribed treatment duration and the instructions given to the patient on how to apply the product, i.e., once daily, twice daily, or thrice daily or more, after the skin had been cleansed with the cleansing oil provided and dried. Participants were free to use any of their other usual toiletries during the study period. The physician assessed the severity of xerosis and objective clinical symptoms at the inclusion and follow-up visits, and evaluated the global effectiveness and tolerance of the product at the follow-up visit. Any changes in the anticancer treatments during the study period were also recorded. Patients assessed the severity of subjective clinical symptoms and the impact of skin symptoms on their QoL at the inclusion and follow-up visits. At the follow-up visit, patients were also asked to assess the global effectiveness and ease of use of the product, and to provide details of any improvements in their symptoms.

Outcomes

The primary outcome was evaluation of the effectiveness of the study product on reducing xerosis severity in patients treated for cancer after around 4 weeks of use in a real-life setting. Secondary outcomes were the effectiveness of the emollient PLUS on reducing the severity of clinical symptoms and on lessening the impact of the skin manifestations on patient QoL, and also included the global effectiveness of the product assessed by the physician and the patient. Tolerance was assessed at the end of the study period. The effect of the anticancer treatment received on clinical success and tolerance was also evaluated.

Assessment Methods

Xerosis severity grade was assessed by the physician using the National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI CTCAE, version 4.0) scale for dry skin. The scale comprises three grades ranging from grade 1 (mild) to grade 3 (severe). The physician also assessed the severity of objective clinical symptoms, i.e., xerosis, erythema, and desquamation, using a four-point scale from 0 (no signs) to 3 (severe), and the global effectiveness of the product using a four-point scale from 1 (very effective) to 4 (not effective).

Severity levels of subjective symptoms, i.e., sleep disturbance, pruritus, tightness of the skin, and pain, were assessed by the patients using visual analog scales (VAS), ranging from 0 (absence), > 0 to < 4 (mild), ≥ 4 to < 7 (moderate), ≥ 7 to < 9 (severe), to ≥ 9 (very severe) [22], derived from the SCORing Atopic Dermatitis (SCORAD) index [23]. In addition, patients filled in a questionnaire at the follow-up visit asking them to report the number of days on which they had applied the product during the study period, the global effectiveness of the product, the symptoms that had improved and the time to onset of these improvements. They also reported any acceptability issues they encountered when using the product.

The impact of skin manifestations on patient QoL was evaluated using the Dermatology Life Quality Index (DLQI) patient questionnaire for adults [24]. DLQI index scores were interpreted as described by Hongbo et al. [25], with a total score ranging from 0 to 30 and a higher score meaning a greater impairment of QoL.

Tolerance was ranked by the physician using a scale from 1 (very good) to 4 (very poor) based on the criteria defined previously by Deleuran et al. [21]. Details of any AEs occurring during the course of the study were also recorded.

Finally, overall clinical success was defined according to the combination of the following criteria: $\geq 10\%$ improvement in the total score

for objective clinical signs; ≥ 10% improvement in the total score for subjective clinical signs; ≥ 20% improvement in the DLQI score; and global effectiveness assessed by the physician or by the patient as "very effective" or "effective," or tolerance assessed by the physician as "very good" or "good."

Statistical Analyses

Descriptive data are expressed as the number and percentage, mean and standard deviation (SD), or median and range for each variable as appropriate.

Changes from baseline of xerosis severity grade were analyzed using the Stuart–Maxwell test. Paired data were analyzed using either the parametric *t* test or the nonparametric Wilcoxon test. Between-group analyses were performed using the Chi-square test or Fisher's exact test (when theoretical numbers were < 5) for comparisons of frequencies, or using the Kruskal–Wallis test for comparisons of means. A *p*-value of less than 0.05 was considered as statistically significant. The same statistical methods were used to perform analyses on patient data grouped according to the anticancer treatment received. All statistical analyses were carried out using SAS, version 9.4.

RESULTS

Participants

Participant flow through the study is illustrated in Fig. 1. A total of 41 physicians included 319 cancer patients with xerosis across three EU countries: 188 (58.9%) from Spain, 88 (27.6%) from France, and 43 (13.5%) from Belgium. All patients attended both study visits and were included in the pooled analysis. The mean duration of follow-up was 32.9 ± 31.7 days.

Patient demographics and clinical characteristics at baseline are listed in Table 1. Around half of the patients (50.5%) had grade 2 xerosis. Most patients (75.3%) were not prescribed any treatment other than the emollient PLUS for their xerosis at inclusion. The mean duration of prescription of the product was 30.2 ± 11.6 days (Table 1). The severity of the dermatologic symptoms and their impact on patient QoL as assessed at inclusion are summarized in Table 2. DLQI average score was of 2.7 ± 3.7, indicating a small effect of xerosis on patient QoL.

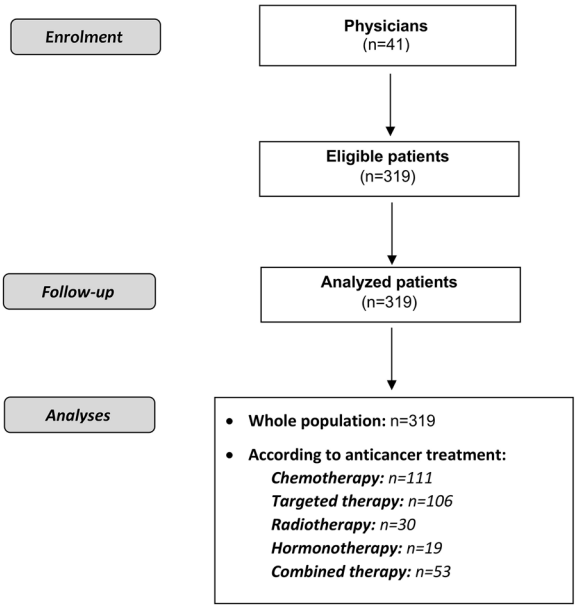


Fig. 1 Participant flow through the study

Effect of the Study Product on Xerosis Severity

The regular use of the emollient PLUS balm led to a reduction in xerosis severity, with a significant decrease in the proportion of patients with grade 2 or grade 3 xerosis between baseline and follow-up ($p < 0.0001$, Stuart–Maxwell test; Fig. 2) and 62.7% (183/292) of the patients being classed as having a lower grade of xerosis at follow-up compared with at baseline (Table S1 Supplementary Material).

Secondary Effectiveness Outcomes

Following the use of the study product, significant decreases in severity scores for objective and subjective clinical signs related to xerosis were observed in the whole population: the

Table 1 Demographic, clinical, and prescription characteristics of the study population at baseline

Demographics	***N* = 319**
Gender, *n* (%)	*n* = 319
Female	189 (59.2)
Males	130 (40.8)
Age, years	*n* = 318
Mean (SD)	63.1 (13.4)
Median (min–max)	64.0 (28.0–92.0)
Clinical characteristics	***N* = 319**
Anticancer treatment, n (%)	*n* = 319
Chemotherapy	111 (34.8)
Targeted therapy	106 (33.2)
Radiotherapy	30 (9.4)
Hormonotherapy	19 (6.0)
Combined therapy[a]	53 (16.6)
Localization of xerosis[b]*, n (%)*	*n* = 319
Lower limbs	191 (59.9)
Upper limbs	173 (54.2)
Trunk	159 (49.8)
Neckline	127 (39.8)
Hands	113 (35.4)
Face/ears	94 (29.5)
Feet	90 (28.2)
Neck	71 (22.3)
Scalp	42 (13.2)
Genitals	28 (8.8)
Xerosis severity grade[c]*, n* (%)	*n* = 301
Grade 1	93 (30.9)
Grade 2	152 (50.5)
Grade 3	56 (18.6)
Prescriptions	***N* = 319**
Study product frequency of application, *n* (%)	*n* = 317
Once daily	126 (39.8)
Twice daily	149 (47.0)
Thrice daily or more	42 (13.2)
Study product duration of prescription, days	*n* = 313
Mean (SD)	30.2 (11.6)
Other topical or systemic treatments[d]*, n (%)*	*n* = 312
Yes	77 (24.7)
No	235 (75.3)

Abbreviations: *N* number of patients in the whole study population, *n* number of patients for whom data were collected, *SD* standard deviation. [a]Combined therapy comprised 31 patients with chemotherapy and targeted therapy; 7 patients with chemotherapy and radiotherapy; 5 patients with hormonotherapy and targeted therapy; 4 patients with chemotherapy and hormonotherapy; 3 patients with hormonotherapy and radiotherapy; 2 patients with chemotherapy, hormonotherapy, and radiotherapy; and 1 patient with chemotherapy, hormonotherapy, and targeted therapy. [b]Patients may have had xerosis on multiple parts of the body. [c]National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI CTCAE, version 4.0) scale for dry skin comprising three grades: grade 1 = covering < 10% of the body surface area (BSA) and no associated erythema or pruritus; grade 2 = covering 10–30% of BSA and associated erythema or pruritus, limiting instrumental activities of daily living (ADL); grade 3 = covering > 30% BSA and associated with pruritus, limiting self-care ADL. [d]Patients may have had more than one concomitant treatment

mean total score decreased by 67.7% (−2.6) for objective clinical signs and by 57.4% (−7.6) for subjective clinical signs ($p < 0.0001$ for between-visit changes in mean total scores and individual symptom scores, *t* test; Fig. 3 and Table S2 in the Supplementary Material). Moreover, the mean total DLQI score showed a significant decrease of 56.6% (−1.5) over the study period ($p < 0.0001$, Wilcoxon test; Fig. 3 and Table S2).

The overall effectiveness of the product was rated by the physicians as "effective" or "very effective" for 88.0% (278/316) of the patients (Fig. 4a and Table S1), with similar results being obtained regardless of the initial grade of xerosis severity (90.3% for patients with grade 1, 88.7% for those with grade 2, and 81.8% for those with grade 3; $p > 0.05$, Chi-square test). Following self-evaluation, most patients (87.3%, 274/314) rated the product as "effective" or "very

Table 2 Severity scores of clinical symptoms related to xerosis and their effect on patient quality of life at baseline

Objective clinical symptoms	***N* = 319**
Severity score[a], mean (SD)	
Xerosis (*n* = 314)	1.7 (0.8)
Desquamation (*n* = 313)	1.3 (0.9)
Erythema (*n* = 313)	1.0 (1.0)
Total score[b] (*n* = 316)	4.0 (2.2)
Subjective clinical symptoms	***N* = 319**
VAS score[c], mean (SD)	
Sleep disturbance (*n* = 315)	2.6 (2.9)
Pruritus (*n* = 318)	4.3 (3.1)
Tightness of the skin (*n* = 316)	4.4 (3.1)
Pain (*n* = 314)	1.8 (2.5)
Total score[d] (*n* = 318)	13.1 (9.5)
Quality of life	***N* = 319**
DLQI score[e], mean (SD)	
Total score (*n* = 319)	2.7 (3.7)

Abbreviations: *DLQI* Dermatology Life Quality Index, *N* number of patients in the whole study population, *n* number of patients for which data were collected, *SD* standard deviation, *VAS* visual analog scale. [a]A four-point severity scale from 0 (no signs) to 3 (severe) was used by the physician to assess each objective clinical symptom. [b]Total score scale ranged from 0 to 9. [c]VAS score was assessed by the patient and the scale of each symptom ranged from 0 (absence) to 10 (very severe). [d]Total VAS score scale ranged from 0 to 40. [e]DLQI total score scale ranged from 0 (no effect at all on patient's life) to 30 (extremely large effect on patient's life)

effective" (Fig. 4b and Table S1), with no significant differences identified according to the initial grade of xerosis severity (89.1% for patients with grade 1, 87.2% for those with grade 2, and 82.1% for those with grade 3; $p > 0.05$, Fisher's exact test). Furthermore, almost all patients (99.7%, 312/313) reported an improvement in at least one symptom (Table S3 Supplementary Material). The mean time to onset of these improvements was 8.0 ± 7.6 days after the first application. This period was significantly longer in patients who had grade 3 xerosis at baseline (9.6 ± 6.3 days; $p < 0.0001$, Kruskall–Wallis test), whereas it was significantly shorter when the product was applied thrice daily or more (5.6 ± 4.4 days; $p < 0.0001$, Kruskall–Wallis test).

Overall clinical success, defined by the combination of several effectiveness criteria, was achieved in 73.7% (235/319) of patients (Table S1).

Tolerance and Safety

Tolerance was rated by physicians as "good" or "very good" in 97.2% (308/317) of cases in the whole population (Table S1).The tolerance was also rated as "good" or "very good" in most patients, regardless of the anticancer treatment received (96.2–100%) or whether the anticancer treatment was changed (89.4% versus 97.7%) during the study period (no significant differences between groups; $p > 0.05$, Fisher's exact test). The incidence of AEs reported by the physicians was 1% (3/307). Moreover, only 9.8% (30/305) patients reported having issues associated with the acceptability of the emollient, mainly related to its texture and odor.

Effect of the Type of Anticancer Treatment on Study Product Effectiveness

As in the whole population, significant reductions in the grade of xerosis severity were observed over the study period across almost all of the anticancer treatment groups ($p < 0.0001$, Stuart–Maxwell test; Fig. 5), except for patients in the radiotherapy group who were already mostly (80%) classed as having grade 1 xerosis at baseline. The anticancer treatment groups with the highest percentages of patients experiencing a reduction in the grade of xerosis severity were the hormonotherapy and the targeted therapy groups (xerosis improvement for 89.5% and 73.0% of patients, respectively, Table S1).

Mean total severity scores for objective and subjective clinical signs decreased between

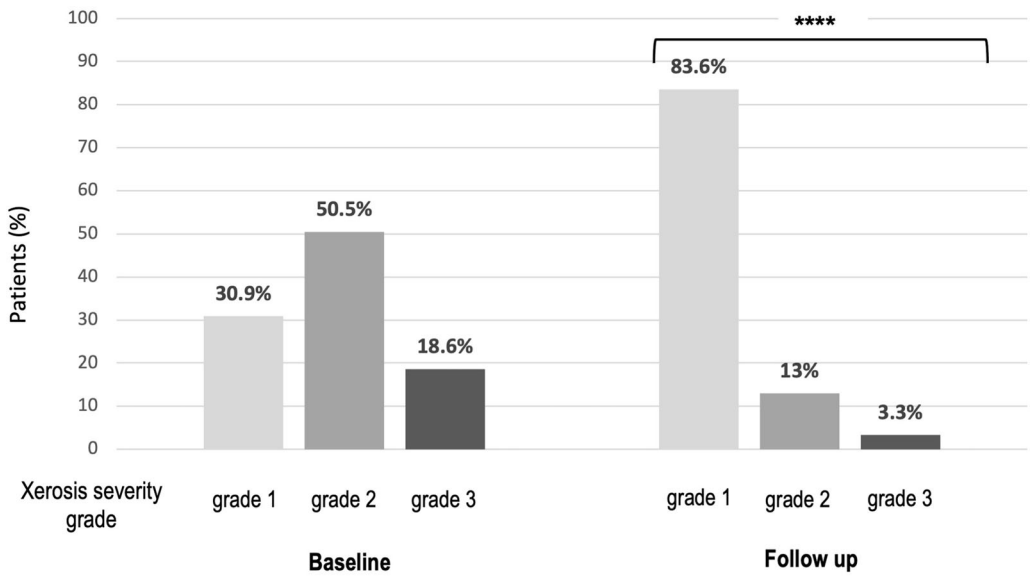


Fig. 2 Effectiveness of the emollient PLUS on xerosis severity in the whole population. Data presented are the percentage of patients with each grade xerosis severity at baseline and at follow-up. ****Indicates $p < 0.0001$ between baseline and follow-up (Stuart–Maxwell test)

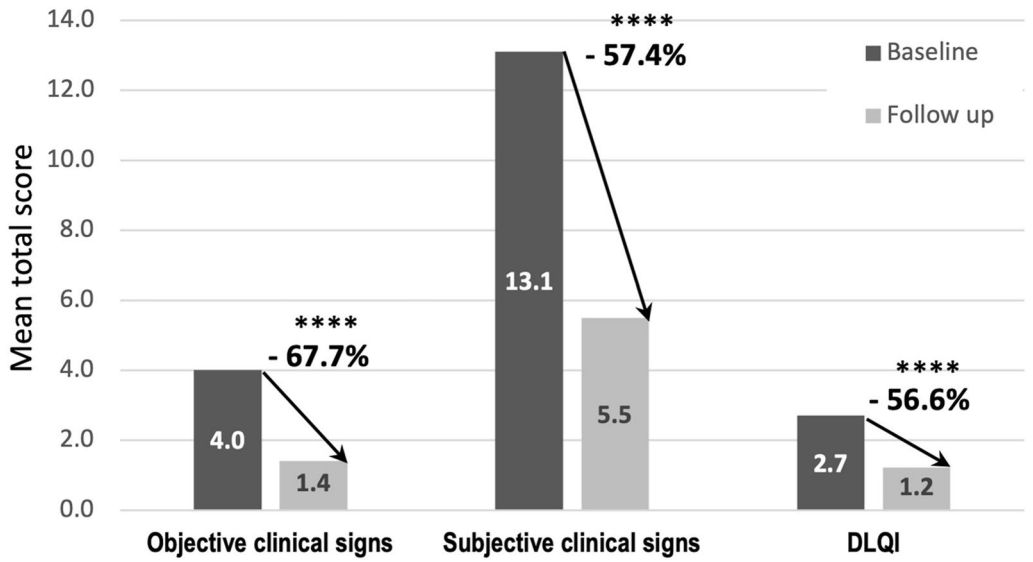


Fig. 3 Absolute and relative changes in mean total scores for objective and subjective clinical signs, and Dermatology Life Quality Index (DLQI) between baseline and follow-up in the whole population. ****Indicates $p < 0.0001$ between baseline and follow-up (t test for clinical signs, and Wilcoxon test for DLQI score)

baseline and follow-up in all of the anticancer treatment groups, with relative changes ranging from −44.8% to −92.4% (−0.4 to −3.5) and from −36.1% to −75.9% (−1.4 to −10.5), respectively (t test on relative changes: $p < 0.05$ for radiotherapy and $p < 0.0001$ for all other anticancer treatments; Fig. 6a and b, and Table S2). DLQI scores decreased by 43.6–87.7% (−1.1 to −2.1) across the anticancer treatment groups (Wilcoxon test on relative changes:

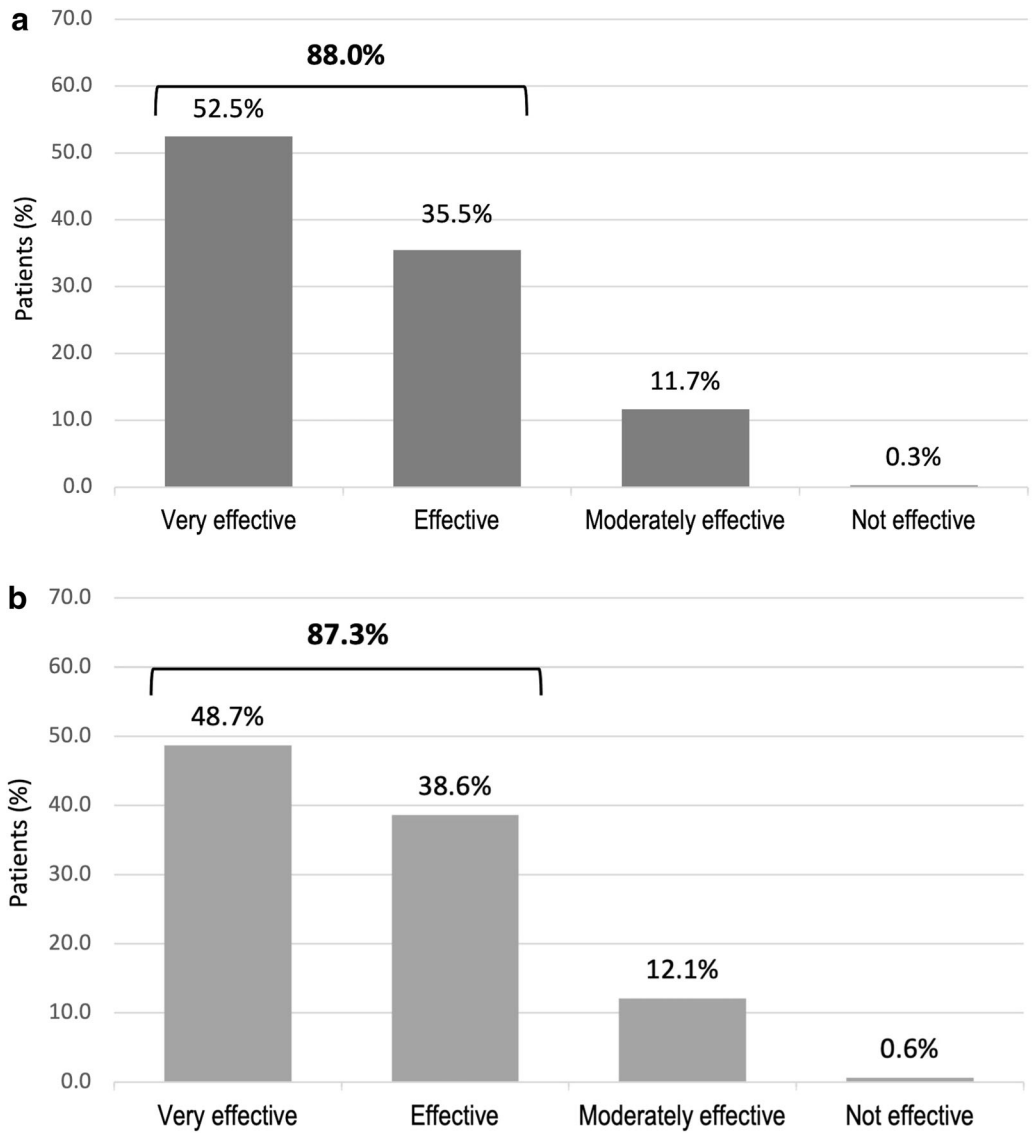


Fig. 4 Overall effectiveness of the product as assessed by the physician (**a**) and the patient (**b**) at follow-up. Data are presented as the percentage of patients in each category

$p < 0.05$ for radiotherapy and $p < 0.0001$ for all other anticancer treatments; Fig. 6c and Table S2).

Regarding the overall effectiveness of the product as assessed by the physician, the accumulated proportion of patients in the "effective" and "very effective" categories ranged from 85.5% to 94.8% according to anticancer treatment (Table S1). This frequency was significantly higher for patients in the hormonotherapy group compared with those in the other anticancer treatment groups (94.8% versus 85.5–93.1%, $p < 0.05$, Fisher's exact test). Moreover, a high proportion of patients evaluated the product as "effective" or "very effective," regardless of their anticancer treatment (83.2–94.7% across groups, $p > 0.05$, Fisher's exact test; Table S1).

Finally, the percentage of patients for whom overall clinical success was achieved was high in all groups, but it was significantly higher in the hormonotherapy group than in the other groups (94.7% versus 60.0–79.2%, $p < 0.05$, Chi-square test; Table S1).

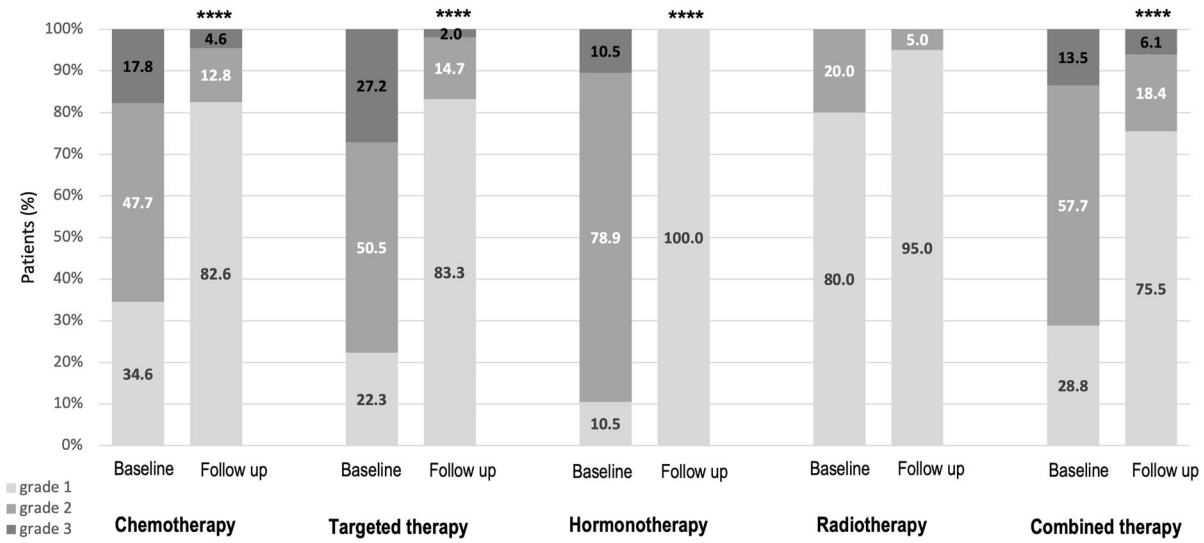


Fig. 5 Effectiveness of the emollient PLUS on xerosis severity according to anticancer treatment. Stacked bars represent the accumulated percentage of patients with each grade of xerosis severity at baseline and follow-up according to anticancer treatment. ****Indicates $p < 0.0001$ between baseline and follow-up (Stuart–Maxwell test)

DISCUSSION

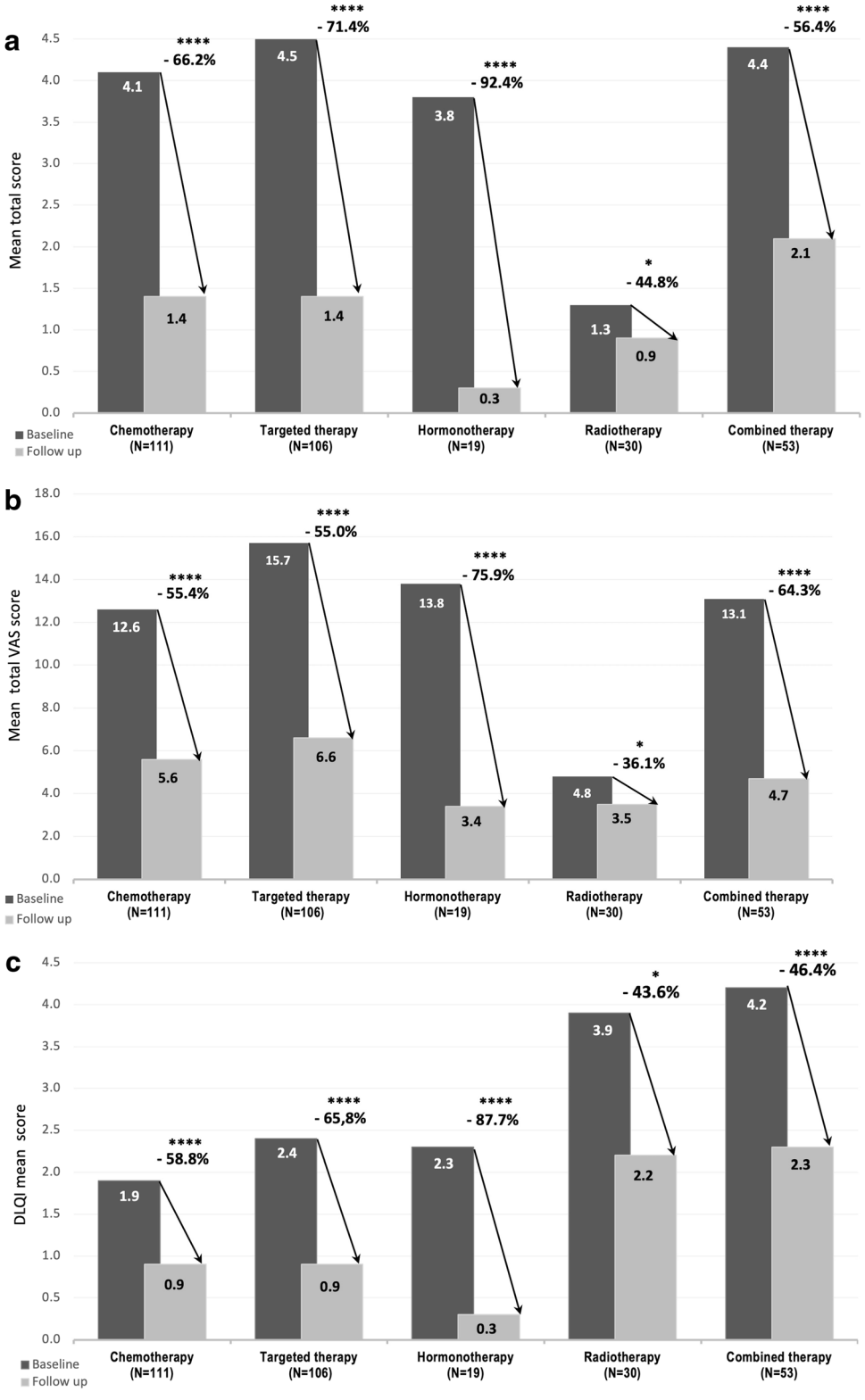
This multicenter, observational study, conducted on a cohort of 319 patients treated for cancer with xerosis, demonstrated that daily use of the emollient PLUS in real-life conditions led to a significant decrease in xerosis severity, regardless of the anticancer therapy received. The study product was also effective at reducing the severity of other dermatologic clinical signs related to xerosis, including desquamation, erythema, pruritus, and tightness of the skin, as well as pain and sleep disturbance. In addition, use of the emollient substantially lessened the impact of the skin symptoms on patient QoL. The vast majority of physicians and patients reported that the effectiveness of the product was good, and overall clinical success was achieved in a high proportion of patients, particularly among those that received hormonotherapy. The product was well tolerated, with no clinically significant AEs reported.

The wide range of available anticancer therapies has greatly improved the management of many malignancies, but these treatments often induce uncomfortable and aesthetically disturbing cutaneous reactions, such as xerosis, that can have a rapid and significant impact on patient self-esteem, social relationships, and QoL [3, 14]. The effectiveness of dermocosmetic products is generally less well documented than that of pharmaceutical treatments and their use is less strictly regulated. However, in recent years, an increasing number of studies have investigated the benefits of skin care products, such as emollients or creams, on the management of cutaneous AEs in various populations, including oncology patients [26–29]. A real-world study in an African population showed that an 8-week regimen with a glycerol-based emollient could lead to reductions in xerosis severity of more than 80% in adults and children, with the effects starting to be observed within the first 4 weeks of treatment [30]. The authors also reported improvements in QoL related to this skin condition. In another study, topical formulations containing glyceryl glucoside and natural moisturizing factors for optimal water distribution, were shown to significantly reduce transepidermal water loss, decrease visible dryness and tactile roughness, and improve skin hydration over 2 weeks of regular use in women over 50 years of age, as compared with a control vehicle [31].

Interestingly, in the regression part of this study, corneometry measurements revealed that the skin remained moisturized for several days after the product had been stopped. Some other dermocosmetic products have been more specifically designed for patients treated for cancer. For instance, two moisturizers have been found to be effective at markedly decreasing the frequency of dry skin (from 69% to 21% of subjects) and skin rash (from 8% to 1% of subjects), as well as the Skindex-16 score (from 25.05 to 16.19), a dermatology-specific QoL instrument, within 1 month of use in patients receiving various anticancer treatments alone or in combination [27]. Similarly, a heparinoid moisturizer has been shown to help mitigate acute dermatitis following whole-breast radiotherapy in women who had previously undergone breast-conserving surgery [29]. The prophylactic application of this moisturizer on irradiated breast skin led to improvements in skin water content and sebum levels, and relieved skin dryness, desquamation, and pain within 2 weeks of use, compared with irradiated breast skin of women who did not apply any moisturizer.

Data from these studies have thus allowed specific guidelines to be generated for both preventive and supportive skin care for patients treated for cancer [2, 32–34]. Indeed, skin hydration with emollients or creams is now an essential part of the general skin care recommendations for patients receiving radiotherapy, targeted therapy, or systemic chemotherapy, as all these treatments can disrupt and compromise skin barrier function [2, 10, 34]. These skin care products can therefore be considered as a first-line management option in these patients, accompanied by early counseling to help patients choose the most appropriate product to prevent worsening of their skin side effects and to minimize the impact of these side effects on their current cancer treatment, as well as on their QoL [2]. As with all forms of xerosis, patients developing xerotic lesions after initiating anticancer therapy are now also advised to initiate treatment for their skin AEs as early as possible, and regularly use clinically tested and hypoallergenic moisturizing products. In mild cases, management with basic emollients is often sufficient [10, 35] but in more severe cases, emollients may need to be used as adjunct therapies alongside systemic or topical pharmacologic treatments to reduce inflammation or treat infections. The recent development of products regarded as emollients PLUS, i.e., those containing active nonmedicated ingredients, allows additional options to be proposed for the management of xerosis. These products may contain saponins, flavonoids, and riboflavins from protein-free oat plantlet extracts, or microbial lysates that can enhance their repairing properties and influence the skin microbiome [17].

The emollient evaluated in our study contains the ADE-G1 extract from the bacteria *Aquaphilus dolomiae*, which has been shown by in vitro studies to display several properties that are relevant for the treatment of xerosis, including immunomodulatory and antiinflammatory activities [18, 19]. In human skin, these properties could help the skin barrier self-repair processes and lessen the cutaneous inflammatory response to triggering agents [21]. The formulation of the ADE-G1 emollient PLUS also contains omega fatty acids, ceramide, and sterols that, in addition to reducing transepidermal water loss, can replenish the lipid composition of the skin and hence strengthen its barrier function [15]. The ADE-G1-containing emollient PLUS has been already shown to be effective in alleviating dry skin and itching symptoms in several clinical studies involving various patient populations [20, 21]. In particular, substantial decreases in xerosis and pruritus severity (−56% and −60% reductions in severity scores, respectively) were found after regular use of the emollient PLUS in real-life conditions in adult and pediatric patients with a range of dermatologic and systemic diseases [21]. The product was also found to be beneficial for improving sleep quality and DLQI scores in these patients. It is noteworthy that the significant improvements in skin symptoms reported in this study were achieved after only a short 1-week period of product use. It is also important to highlight that in our study and in the previous studies mentioned, involving hundreds of subjects, the emollients tested were well tolerated. Overall, clinical studies with


a
Mean total score
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
**** - 66.2%
**** - 71.4%
**** - 92.4%
* - 44.8%
**** - 56.4%
4.1
1.4
4.5
1.4
3.8
0.3
1.3
0.9
4.4
2.1
Baseline
Follow up
Chemotherapy (N=111)
Targeted therapy (N=106)
Hormonotherapy (N=19)
Radiotherapy (N=30)
Combined therapy (N=53)
b
Mean total VAS score
18.0
16.0
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
**** - 55.4%
**** - 55.0%
**** - 75.9%
* - 36.1%
**** - 64.3%
12.6
5.6
15.7
6.6
13.8
3.4
4.8
3.5
13.1
4.7
Baseline
Follow up
Chemotherapy (N=111)
Targeted therapy (N=106)
Hormonotherapy (N=19)
Radiotherapy (N=30)
Combined therapy (N=53)
c
DLQI mean score
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
**** - 58.8%
**** - 65,8%
**** - 87.7%
* - 43.6%
**** - 46.4%
1.9
0.9
2.4
0.9
2.3
0.3
3.9
2.2
4.2
2.3
Baseline
Follow up
Chemotherapy (N=111)
Targeted therapy (N=106)
Hormonotherapy (N=19)
Radiotherapy (N=30)
Combined therapy (N=53)

◀**Fig. 6** Absolute and relative changes in mean total scores of objective (**a**) and subjective (**b**) clinical signs, and Dermatology Life Quality Index (DLQI) (**c**) between baseline and follow-up according to anticancer treatment. ****Indicates $p < 0.0001$ and * indicates $p < 0.05$ between baseline and follow-up (t test for clinical signs, and Wilcoxon test for DLQI score)

emollients and emollients PLUS support the use of these products as part of the regular skin care regime for xerosis patients in multiple populations, including the specific population of patients treated for cancer.

This study provides the first assessment of the effectiveness and tolerance of an emollient PLUS in patients treated for cancer in real-life conditions. Although the observational design of the study has some inherent limitations and did not allow a comparison of the effectiveness of the ADE-G1-containing product with that of a control vehicle, the results of our pre–post analysis gave clear and valuable insights into the benefits of the product for the management of xerosis in general clinical practice. However, the noninterventional nature of the study and its reliance on patient self-assessments may have introduced reporting bias, in particular for assessments of study product use, which was not systematically recorded using a daily diary. Although our analyses indicated that the emollient PLUS was particularly effective for patients in the hormonotherapy group, the level of significance of this finding should perhaps be interpreted with caution as the number of patients in this group was relatively small. Despite these limitations, the main effectiveness outcomes of our study were reliably assessed by the physicians using objective, validated, and noninvasive clinical assessment tools. The multicenter nature of the study also allowed the effectiveness of the product to be investigated in a large number of patients. Moreover, even though the product was not specifically tailored for cancer patients, our before-and-after approach showed it was effective for rapidly relieving xerosis and associated symptoms in these vulnerable and sensitive patients. Contrary to other real-world studies [21, 30, 36], most patients included in our study were prescribed the emollient PLUS without any concurrent medication for xerosis (75.3% of patients), allowing us to make clear assessments supporting the effectiveness of the product as a standalone treatment for mild xerosis. It is also noteworthy that the improvements in dermatological symptoms and QoL were observed in all anticancer treatment groups, demonstrating the generalizability of our findings, regardless of the type of anticancer treatment received.

Future studies could be designed to further determine if the improvements in symptoms resulting from the regular use of the emollient PLUS are sustained over longer periods; this would be especially relevant for oncology patients as their cancer treatments are usually administered over several months. Furthermore, the preventive effect of the study product could also be specifically evaluated in future studies. Indeed, it would be interesting to test our product as a prophylactic treatment as previous studies, such as those evaluating preemptive measures to mitigate the skin toxicities associated with epidermal growth factor receptor inhibitor treatments for metastatic colorectal cancer, have already indicated that this approach could be more effective for cutaneous AEs than reactive treatments [26, 33].

CONCLUSION

This real-world multicenter study demonstrated that the ADE-G1-containing emollient can be useful for alleviating xerosis and associated symptoms in patients treated for cancer. The product was well tolerated and appreciated by most patients, and also helped to maintain a good patient QoL. Although further studies are required to assess the longer-term benefits of the product and investigate its use as a prophylactic measure in these patients, our findings show that this enhanced skin care cosmetic can be used as part of the first-line supportive care strategy for patients with xerosis due to anticancer treatments.

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Compliance with Ethics Guidelines. As this was an observational, real-life, phase IV study, it was conducted in a naturalistic setting where the choice of therapy was consistent with approved prescribing information and in line with the usual everyday practice of the physician. The product was prescribed by the practitioners themselves, as per their routine practice. The protocol of this non-interventional study evaluating cosmetic products did not require approval by a local ethics committee or an institutional review board according to Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 (https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf). This clinical study also adhered to Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products (https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:02009R1223-20190813) and complied with the ethical principles of the Declaration of Helsinki (1964, https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/) and good clinical practice guidelines (CPMP/ICH/135/95, https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e-6-r2-guideline-good-clinical-practice-step-5_en.pdf). Each patient received an information leaflet translated into their native language and including a description of their rights with regard to the processing of their personal data, in accordance with the Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons. All patients provided signed consent before being enrolled in the study. We thank all the patients for their participation to the study.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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