

# Proactive maintenance therapy with a topical corticosteroid for vulvar lichen sclerosus: preliminary results of a randomized study

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## Summary

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**Background** The chronic and relapsing nature of vulvar lichen sclerosus (VLS) represents a challenge for its long-term management after an effective treatment with topical corticosteroids.

**Objectives** To assess the effectiveness of proactive, twice-weekly application of mometasone furoate 0.1% ointment, compared with daily topical vitamin E or cold cream, in keeping VLS in remission and reducing the risk of relapse after 3 months of treatment with topical corticosteroid.

**Methods** In total, 27 patients affected with VLS were enrolled into a 12-week active treatment phase (AP) with topical mometasone furoate 0.1% ointment once daily. Those who achieved disease remission entered a 52-week maintenance phase (MP) in which patients were randomized to apply either mometasone furoate 0.1% ointment twice weekly, a cold cream once daily or topical vitamin E once daily. The primary efficacy parameters were the relapse rate and the mean time to relapse.

**Results** Twenty-five patients considered to have been completely or almost completely healed after the AP entered the MP. By the end of the 52-week MP, 10 patients (40%) experienced a relapse: five in the vitamin E group (56%) and five in the cold cream group (62%), while no patient in the mometasone furoate 0.1% ointment group had a relapse. The occurrence of VLS relapse for patients in therapy with both vitamin E and cold cream was significantly higher than for those in proactive therapy with topical corticosteroid. The median time to relapse was the same (21.6 weeks) for the vitamin E and the emollient groups.

**Conclusions** Once VLS has been stabilized with topical corticosteroids, twice-weekly proactive application of mometasone furoate 0.1% ointment over 56 weeks was found to be an effective and safe therapy option in maintaining VLS remission and in preventing the occurrence of relapse.

Lichen sclerosus (LS) is a chronic inflammatory disease that occurs most commonly on the skin and mucosae of the anogenital area. Among the multiple aetiopathogenetic factors, immunological alterations and chronic inflammatory mechanisms seem to be crucial.<sup>1–4</sup>

Currently, a 3-month topical application of potent or ultra-potent corticosteroids has become the mainstay of medical treatment for vulvar LS (VLS).<sup>4,5</sup> The chronic relapsing nature of VLS is one of its main troublesome features, and recurrence is common when drugs are discontinued.

Once VLS is stabilized with a corticosteroid treatment course, long-term management of the disease is traditionally based on a topical corticosteroid reactively applied on

demand.<sup>5</sup> Nevertheless, there is no consensus on maintenance treatment strategies for controlling the disease in the long term and for extending the relapse-free period after an effective treatment with corticosteroids.<sup>5</sup>

An alternative to the reactive strategy may be a proactive approach. This involves the intensive application of topical corticosteroid therapy until active signs and symptoms are cleared. It is then followed by intermittent, low-dose, long-term application of the same drug to the previously affected areas to both prevent disease exacerbation and maintain clinical remission. To date, no comparative clinical studies have prospectively evaluated the efficacy and safety of a proactive treatment schema in controlling VLS on a long-term basis.

Furthermore, adherence to topical therapies and patient acceptance of them are not well characterized in these patients.

The present randomized, parallel-group, open-label, comparative study was designed to investigate the effectiveness of different long-term therapeutic strategies in managing VLS after a 12-week treatment with a topical corticosteroid. The main objective of the study was to assess whether mometasone furoate 0.1% ointment administered proactively twice weekly as a maintenance therapy was effective and safe in preventing the exacerbation of VLS, compared with daily application of different emollients.

## Patients and methods

### Study design and objectives

The present study was conducted between December 2009 and May 2012 at the Vulva Unit of the Dermatology Section of the University of Ferrara, Italy. In total 93 patients affected by VLS were screened for the study.

The study treatment protocol consisted of two distinct phases: the open-label active treatment phase (AP) of 12 weeks' duration and the maintenance phase (MP) of 52 weeks' duration. The latter was a randomized, parallel-group, open-label, comparative trial. The aims of the study were (i) to compare mometasone furoate 0.1% ointment administered twice weekly with daily application of either topical pure vitamin E oil or a cold cream as a maintenance therapy for VLS previously treated with a topical corticosteroid; (ii) to assess patient adherence to prolonged topical therapies and preferences, comparing daily emollient with biweekly corticosteroid therapy regimens; and (iii) to assess the prognostic significance of demographic and clinical features as potential risk factors for VLS recurrence. The study was approved by the ethics committee of our hospital.

### Study patients

Eligible women with a clinical and, when available, histological diagnosis of VLS were enrolled in the study. Patients were excluded from the study in the presence of the following: systemic treatment with steroids, retinoids or hormonal replacement therapies and oestrogenic drugs during the 4 weeks before enrolment; treatment with topical therapy (e.g. corticosteroids, tacrolimus, pimecrolimus, hormonal therapy) at the affected area during the 4 weeks before enrolment; hypersensitivity to any component of the study drugs; active vulvar infectious diseases or vulvar dermatoses or carcinoma; pregnancy or breastfeeding.

### Study procedures and assessment

After completion of screening, patients entered the study. Subjective evaluation of three symptoms – itching, burning and dyspareunia (the latter only when applicable) – was obtained by interview using a visual analogue scale; a score of 10 was

attributed to the highest intensity of the symptoms, and 0 to their absence. A global subjective score was obtained by summing each symptomatological parameter (highest score = 30).

The following five objective parameters were considered in order to evaluate the clinical features and severity of the disease at baseline: (i) erythema, (ii) leucoderma (pallor), (iii) sclerosis scarring, (iv) hyperkeratosis and (v) purpuric lesions and itching-related excoriations. Objective assessment of each sign was performed by the investigators using the following four-point scale: 0 = absence, 1 = mild, 2 = moderate, 3 = severe. Among these clinical parameters, only the four signs potentially reversible to therapy were considered: erythema, leucoderma (pallor), hyperkeratosis, and purpuric lesions and itching-related excoriations. This was in order to monitor objectively the VLS response to both active and maintenance therapy, at every control visit. For this purpose, a global objective score (OS) was obtained by summing each clinical parameter (highest score = 12).

All the enrolled subjects entered an open-label AP of 12 weeks' duration, in which the patients applied once-daily topical mometasone furoate 0.1% ointment on the affected vulvar surfaces. At 12 weeks, patients who achieved both a score  $\leq 3$  for each evaluable subjective symptom and a global OS  $\leq 4$  were judged as 'treatment responsive' and were eligible for the MP. Subjects who failed to improve at the end of the 12-week AP were discontinued from the study and underwent a further treatment course with topical corticosteroids.

The MP was a randomized, three-branches parallel-group, open-label, comparative study stage. Patients who entered this second 52-week phase of the study were randomized according to a computer-generated simple randomization schedule to apply either mometasone furoate 0.1% ointment twice a week, a cold cream once daily (a dermatological oil-in-water emulsion containing white petrolatum, cetearyl alcohol, paraffinum liquidum, water, propylene glycol and cetareth-20) or a topical oil containing pure 100% vitamin E oil once daily (tocopherol acetate, Veal Olio<sup>®</sup>; Hulka, Rovigo, Italy). The baseline balance of demographic and clinical features among the study treatment groups was assessed by one-way analysis of variance (ANOVA).

Objective and subjective patient assessment was performed by the same two investigators (A.V. and M.C.), not blinded to treatments, at baseline and at all successive 12-week-interval visits. Patients experiencing an exacerbation of their VLS at any time during the MP returned in advance to our Vulva Unit for re-evaluation.

During the MP, relapse was arbitrarily defined by a score  $\geq 5$  for at least one evaluable subjective symptom and/or a score = 3 for any of the four signs considered reversible. Any worsening in sclerosis scarring was arbitrarily also considered as relapse. Patients experiencing a relapse of their VLS discontinued the maintenance protocol and started a further treatment course with daily applications of topical corticosteroid.

The primary efficacy endpoint was the relapse rate at 52-week MP, while the secondary efficacy endpoint was the mean time to relapse, defined as the number of weeks between

entry into the MP and VLS relapse. These data were compared between the three maintenance treatment groups. The adverse events and the causal relationship to medications were assessed.

Patient adherence to treatment regimens, namely daily vs. biweekly topical therapy, and patient satisfaction were assessed at the last visit (at 52-week MP or when relapse occurred). Because of the lack of a gold standard in measuring adherence to topical therapies and satisfaction, these parameters were measured by interview. Adherence to therapy was assessed based on the referred frequency of missing treatment, using a score of 1–4: 1 = never, 2 = sometimes (once or twice a week), 3 = often (three or four times a week), 4 = always/almost always (five or more times a week). Patients were considered 'adherent' when they had missed treatment never (score = 1) or sometimes (score = 2), whereas they were considered 'not adherent' in the other cases.

In order to assess patient satisfaction with topical treatment regimens, each patient was asked to define the treatment protocol as (i) convenient or (ii) inconvenient.

The following demographics and clinical features of the enrolled subjects were statistically elaborated in order to identify factors potentially predisposing to VLS relapse: age at onset and diagnosis of VLS, duration of the disease before entering the study, delay between onset of VLS and diagnosis, and clinical features such as severity of signs and symptoms at both the beginning of the AP and the end of AP, which coincided with the beginning of the MP.

### Statistical analyses

The efficacy analysis was based on the intent-to-treat (ITT) population, defined as all randomized subjects enrolled in the MP. The proportion of patients who experienced a protocol-defined relapse was compared between maintenance treatment groups using a  $\chi^2$  test. The t-test was to compare the mean time of relapse among the three maintenance treatment

groups. Comparison of demographics and clinical features between relapsing and nonrelapsing patients was performed by means of the t-test. Normality of groups was assessed by the Kolmogorov–Smirnov test, and the homoscedasticity of groups was assessed by Levene's test and the Brown–Forsythe test. Comparison of patient adherence between relapsing and nonrelapsing patients and among maintenance treatment groups was performed by means of the exact Fisher's test. The exact Fisher's test was also used to compare the patient satisfaction with the maintenance regimens. For confirmation, the primary analysis was performed on the per-protocol (PP) population composed of all enrolled and randomized patients, except subjects considered not evaluable due to major deviations from the protocol. Moreover, in the case of patients lost during the MP, a further analysis simulating the worst-case scenario was carried out. In this type of analysis all dropouts were assumed as VLS relapses. Statistical significance was defined as  $P < 0.05$ .

## Results

### Patients characteristics

The demographic and clinical data of the 27 women affected with VLS who entered the AP study are reported in Table 1. Diagnosis of VLS was based on clinical features, and in 17 cases it was histopathologically confirmed.

At the end of the AP, 25 patients were considered completely or almost completely healed on the basis of both objective and subjective protocol-defined scores, and entered the MP. Two subjects did not enter this second phase of the study: one patient dropped out, while the second one was discontinued from the study because she discovered she was pregnant.

The 25 patients who entered the MP and were included in the ITT population were randomized to topical vitamin E oil (nine patients), cold cream (eight patients) or mometasone furoate 0.1% ointment (eight patients) (Fig. 1). Demographic

**Table 1** Demographic and clinical data of the patients who entered the active phase (AP) and the maintenance phase (MP) of the study

Patients with vulvar lichen sclerosis (VLS)	Patients entering the AP	Patients entering the MP			
		Total	Mometasone furoate 0.1% ointment	Pure vitamin E oil	Cold cream
Number of patients	27	25	8	9	8
Age (years), mean $\pm$ SD	59.65 $\pm$ 12.30	60.53 $\pm$ 11.89	63.97 $\pm$ 16.34	60.44 $\pm$ 9.84	57.20 $\pm$ 8.98
Age at VLS onset (years), mean $\pm$ SD	55.25 $\pm$ 11.03	55.03 $\pm$ 10.92	60.11 $\pm$ 17.61	54.37 $\pm$ 5.81	50.80 $\pm$ 7.44
Delay in diagnosis of VLS (months), mean $\pm$ SD	32.33 $\pm$ 31.81	33.57 $\pm$ 31.93	27.71 $\pm$ 24.92	34.11 $\pm$ 34.65	38.71 $\pm$ 38.02
Duration of VLS (months), mean $\pm$ SD	56.83 $\pm$ 54.39	59.13 $\pm$ 54.41	34.14 $\pm$ 23.49	72.78 $\pm$ 69.60	66.57 $\pm$ 52.63
Concomitant autoimmune diseases, n (%)	5 (19)	5 (20)	1 (12)	1 (11)	3 (38)
Patients who had used previous therapies, n (%)	18 (67)	17 (68)	5 (62)	6 (67)	6 (75)
Histology, n (%)	17 (63)	16 (64)	6 (75)	4 (44)	6 (75)
Number of relapses, n (%)	10 (37)	10 (40)	0	5 (56)	5 (62)
Mean time to relapse (months)	4.5	4.5	–	4.5	4.5

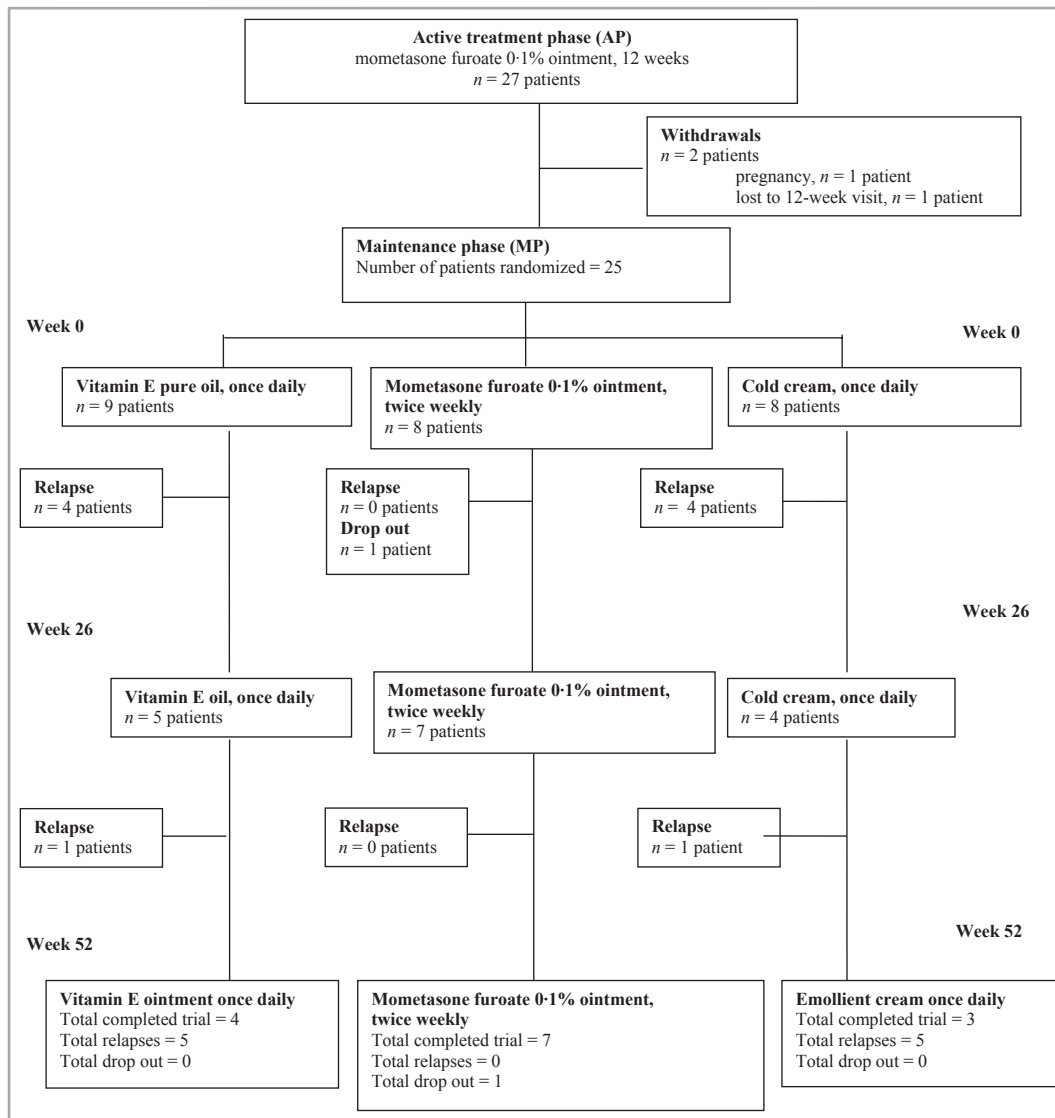


Fig 1. Flow chart of the study.

and disease features were well balanced between the three treatment groups (significance was assessed by one-way ANOVA for each parameter) (Table 1).

### Efficacy evaluations

During the MP, one patient dropped out from the mometasone furoate 0.1% ointment group because she was lost to follow-up (Fig. 1). At the end of the study, overall 10 patients (40%) experienced a protocol-defined relapse and withdrew from the study: five patients in the vitamin E group (5/9, 56%) (Fig. 2), and five patients in the cold cream group (5/8, 62%) (Fig. 3), while no patient in the mometasone furoate 0.1% ointment group had a relapse (Figs 1, 4). These findings show that the incidence of VLS relapse for patients in therapy with both vitamin E ( $P = 0.0204$ , Fisher's test) and cold cream ( $P = 0.0128$ , Fisher's test) was significantly higher

than for those in proactive therapy with topical corticosteroid. The calculation of confidence intervals (CIs) of the odds ratios (ORs) shows that mometasone furoate 0.1% twice a week protects from relapse (OR = 0.0951, 95% CI 0.0177–0.5106). The worst-case scenario analysis confirmed that the rate of VLS relapse was significantly higher in the cold cream group compared with the mometasone furoate 0.1% ointment group ( $P = 0.043$ , Fisher's test). The relapse rate in the vitamin E group was higher than in the mometasone furoate 0.1% ointment group in an almost significant way ( $P = 0.065$ , Fisher's test).

The difference between the rate of VLS relapse in the two nonsteroid maintenance treatment groups was not statistically significant ( $P = 0.5806$ , Fisher's test). Similar efficacy results were found in the PP population. Relapses were observed during the first 6 months of maintenance therapy in 80% of cases (8/10), while only two patients (20%) experienced the



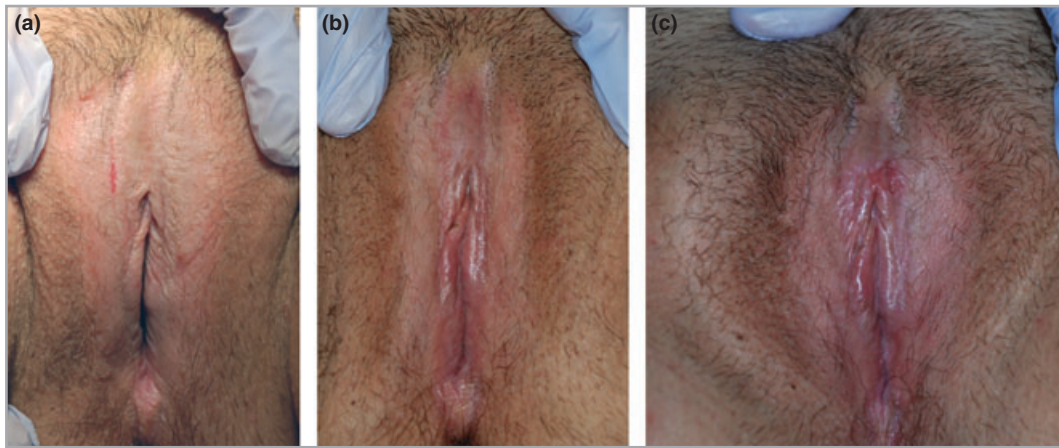


Fig 2. Three-month active treatment phase (AP) with mometasone furoate 0.1% ointment, followed by a maintenance phase (MP) with pure 100% vitamin E oil. (a) Baseline; (b) at the end of the 3-month AP; (c) relapse characterized by worsening of signs and symptoms at week 26 of the MP.

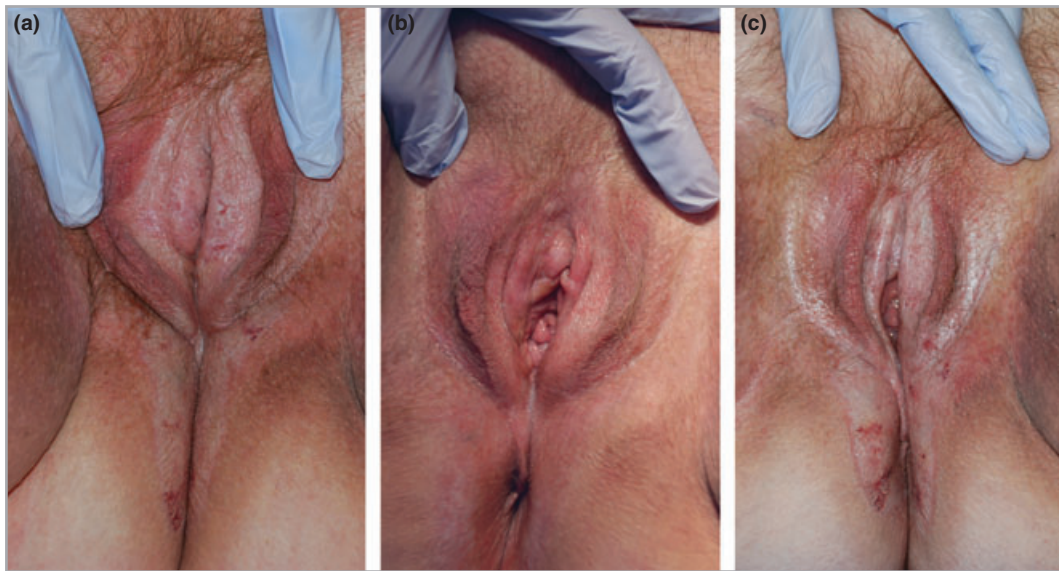


Fig 3. Three-month active treatment phase (AP) with mometasone furoate 0.1% ointment followed by a maintenance phase (MP) with cold cream. (a) Baseline; (b) at the end of the 3-month AP; (c) relapse characterized by worsening of signs and symptoms at week 52 of the MP.



Fig 4. Three-month active treatment phase (AP) with mometasone furoate 0.1% ointment followed by a maintenance phase (MP) with mometasone furoate 0.1% ointment applied proactively twice weekly. (a) Baseline; (b) at the end of the 3-month AP; (c) maintenance of remission of signs and symptoms at week 52 of the MP with proactive therapy.

relapse in the course of the second semester of the MP. The median time to relapse was 21.6 weeks for patients in both the vitamin E and cold cream groups.

Figure 5 shows the changes from baseline in mean global OS (Fig. 5a) and in mean itching and burning scores (Fig. 5b, c, respectively) at each control visit in the three maintenance treatment groups. In Figure 5 the data concern only the patients who did not experience a relapse.

### Demographic and clinical predicting factors for relapse of vulvar lichen SCLEROSUS

The demographics and clinical data of nonrelapsing and relapsing patients are compared in Tables 2 and 3. These data were normally distributed and homoscedastic and thus were analysed by means of t-test in order to predict occurrence of relapse. Neither age at onset ( $P = 0.6246$ ), age at diagnosis of

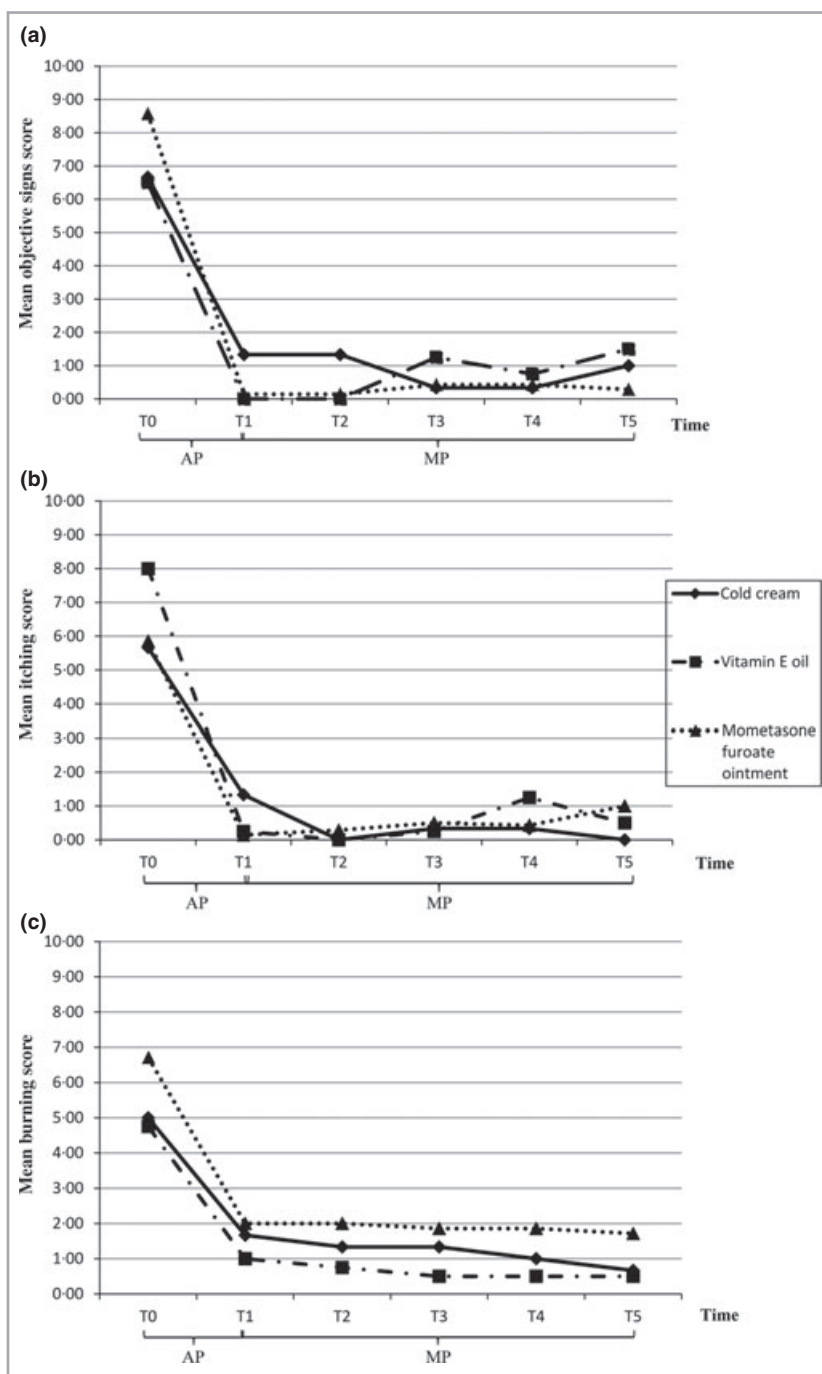


Fig 5. (a) Mean value [visual analogue scale (VAS) 0–10] of objective signs in nonrelapsing patients; (b) mean value (VAS 0–10) of itching in nonrelapsing patients; (c) mean value (VAS 0–10) of burning in nonrelapsing patients. AP, active treatment phase; MP, maintenance phase.

**Table 2** Comparing demographic data and clinical symptoms between relapsing and nonrelapsing patients

	Patients relapsing	Patients not relapsing
Number of patients	10	14
Age (years)	58.8 ± 11.65	60.23 ± 11.34
Age at VLS onset (years)	52.66 ± 7.51	54.79 ± 11.69
Delay in diagnosis of VLS (months)	20.3 ± 17.76	47.08 ± 36.64
Duration of VLS (months)	73.7 ± 71.43	51.4 ± 35.1
Itching, <sup>a</sup> pre-steroid	6.7 ± 3.50	7.6 ± 2.28
Burning, <sup>a</sup> pre-steroid	4.2 ± 4.24	6.4 ± 3.76
Dyspareunia, <sup>a,b</sup> pre-steroid	4.8 ± 4.12	4.1 ± 4.49
Itching, <sup>a</sup> post-steroid	1.0 ± 1.76	0.36 ± 1.08
Burning, <sup>a</sup> post-steroid	0.5 ± 1.08	0.43 ± 1.09
Dyspareunia, <sup>a,b</sup> post-steroid	0.5 ± 0.84	0.5 ± 1.22

Values are the mean ± SD. VLS, vulvar lichen sclerosis. <sup>a</sup>Calculated using a visual analogue scale (VAS) from 0 (none) to 10 (most severe). <sup>b</sup>Dyspareunia VAS was calculated when applicable.

**Table 3** Comparing clinical signs between relapsing and nonrelapsing patients

	Patients relapsing	Patients not relapsing
Number of patients	10	14
Erythema, presteroid	0.8 ± 0.79	1.21 ± 0.97
Leucoderma (pallor), pre-steroid	2.3 ± 0.67	2.21 ± 0.43
Hyperkeratosis, pre-steroid	1.7 ± 1.16	1.21 ± 1.05
Purpura, itching-related excoriations, pre-steroid	0.8 ± 1.03	1.14 ± 1.03
Erythema, post-steroid	0.40 ± 0.7	0.21 ± 0.58
Leucoderma (pallor), post-steroid	1.10 ± 0.88	1.14 ± 0.77
Hyperkeratosis, post-steroid	0.00 ± 0.00	0.07 ± 0.27
Purpura, itching-related excoriations, post-steroid	0.00 ± 0.00	0.21 ± 0.58

Values are the mean ± SD, calculated on a scale from 0 (absence) to 3 (severe).

VLS ( $P = 0.3834$ ) nor duration of the disease before entering the study ( $P = 0.35113$ ) were found to relate significantly to VLS relapse in our study patients. Delay between onset of VLS and diagnosis was found to be the sole factor significantly related to the risk of disease relapse ( $P = 0.04782$ ).

None of the subjective parameters evaluated either at the beginning of the AP (itching  $P = 0.4666$ , burning  $P = 0.1879$ , dyspareunia  $P = 0.7794$ ) or at the end of the AP, which coincided with the beginning of the MP (itching  $P = 0.2799$ , burning  $P = 0.8752$ , dyspareunia  $P = 1.0000$ ) was found to significantly relate to VLS relapse in our population.

Similarly, the severities of the objective clinical signs evaluated both on entering the AP [erythema  $P = 0.2800$ , leucoderma (pallor)  $P = 0.7060$ , hyperkeratosis  $P = 0.2963$ , purpuric lesions and itching-related excoriations  $P = 0.4298$ ] and when patients completed the 12-week corticosteroid therapy [erythema  $P = 0.4846$ , leucoderma (pallor)  $P = 0.9001$ , hyperker-

atosis  $P = 0.3109$ , purpuric lesions and itching-related excoriations  $P = 0.2573$ ] were not statistically different between patients who experienced a relapse and those who did not relapse. On the whole, neither clinical nor demographic parameters were found to predict VLS relapse in our groups.

### Patient adherence and satisfaction

Among the 24 patients who completed the study protocol and underwent the interview, 20 (83%) were considered adherent to maintenance therapy.

Considering all the patients who entered the MP, regardless of the therapies utilized, self-referred adherence to treatment among patients who developed a relapse did not significantly differ from that of patients who had not experienced a relapse ( $P = 0.5632$ , Fisher's test). Similarly, adherence to therapies was not significantly different between relapsing and non-relapsing patients within each maintenance treatment group. The referred adherence of patients who applied the maintenance therapy twice a week (mometasone furoate group) was compared with the adherence of patients who applied topicals every day, namely vitamin E and cold cream considered together, independently from the fact that they did or did not experience a relapse. No statistically significant differences were found ( $P = 0.6719$ , Fisher's test).

Patient satisfaction with topical treatment regimens was assessed in all the patients randomized for the MP, regardless of the clinical outcome of the maintenance treatment. The patients in the proactive corticosteroid maintenance group were found to be more satisfied with treatment (seven out of eight patients) than those in the vitamin E and cold cream groups (eight of seventeen patients), even though the difference did not reach statistical significance ( $P = 0.0967$ , Fisher's test).

### Safety evaluation

During the entire study no side-effects, including contact dermatitis, related to the maintenance topical treatments were noticed and none of the subjects complained about significant local adverse events.

### Discussion

As VLS is a chronic, relapsing disease, a strategy of disease control and suitable management should be pursued. While the efficacy of topical corticosteroids in the treatment of active VLS is well documented, surprisingly there are currently no consensus guidelines for long-term control of symptoms and extension of the relapse-free period after effective treatment with corticosteroids.<sup>5-7</sup> A previous study showed that using clobetasol propionate 0.05% on a regular basis for 6 months was effective and safe in managing VLS in the long term.<sup>8</sup>

The main purpose of the present study was to compare the efficacy and safety of three different maintenance therapies for

VLS. Mometasone furoate was preferred to more potent molecules as it has been reported to be as effective as topical superpotent corticosteroids, like clobetasol, but with fewer side-effects.<sup>9</sup> A cold cream and vitamin E were scheduled for the MP on the basis of several reports in the literature and our previous observations.<sup>10–13</sup>

With regard to the efficacy parameters assessed in the present study, after a 52-week MP the proactive treatment with mometasone furoate 0.1% ointment was shown to be greatly effective in controlling the disease and in preventing VLS exacerbation, as no patients experienced a protocol-defined relapse. Based on these findings, proactive therapy with topical corticosteroid was found to be significantly more effective in preventing the relapse of the disease than the daily application of the two emollients. Vitamin E and cold cream did not significantly differ in the maintenance treatment of VLS on the basis of the relapse incidence.

It is of interest that the majority of the relapses (80%) were observed during the first 6 months of the MP (Fig. 1), while only two patients (20%) experienced relapse in the second semester of the MP. Moreover, all the patients who did not experience a relapse tended to maintain both the objective and subjective severity scores achieved at the end of the AP throughout the entire MP, regardless of the treatment (Fig. 5). Consistent with these features, one could speculate that two different subsets of the disease, which behave differently, may exist. In fact, we observed a group of VLS that exhibited a tendency to relapse and that even had an early relapse; on the other hand, a group of patients was affected with a form of the disease that not only did not relapse but also remained stable in the long term, independently of the type of maintenance treatment. However, it must be stressed that in the study patients the proactive treatment with topical corticosteroid was effective in preventing the exacerbation of the disease in all treated patients, overcoming the hypothetical different behaviours of the disease.

During the MP no adverse events directly connected to the therapies were observed. Among the analysed demographic and clinical features, only a shorter delay in diagnosis was found to be significantly related to VLS relapse. This is an anomalous finding, the opposite of what is generally observed, and needs further investigation.

For patients on long-term therapy for chronic diseases, adherence to treatment is essential for the achievement of optimal outcomes. However, many factors conspire against this, especially in the case of prolonged topical therapies that may be even more cumbersome and time consuming than oral medications.<sup>14–20</sup> In our study, 83% of patients were adherent to maintenance therapy, without significant differences among treatment regimens. Adherence to therapy was not found to relate significantly to the occurrence of relapse. However, among the study patients the adherence to treatment was self-reported and the true level of adherence was not objectively proved. As a consequence, an overestimation of the adherence cannot be excluded.

With regard to patient satisfaction with treatment regimens, the proactive application of a topical twice weekly was judged more convenient than daily application, even though this was not statistically significant.

Limitations of this study are the small number of patients enrolled in each maintenance therapy group and the absence of a control group without maintenance treatment. Furthermore, a univocal method to assess VLS severity and a univocal definition of relapse are not available. Another potential problem is that patients were not initially treated with an ultrapotent topical corticosteroid, which is the recommended first-line treatment for VLS.<sup>5</sup> However, this is the first randomized study of 12 months' duration that has investigated the effectiveness of a proactive corticosteroid therapy as a prevention-flare strategy in the long-term management of VLS, compared with continuous application of noncorticosteroid topicals.

In conclusion, these results provide evidence that maintenance treatment with mometasone furoate 0.1% ointment twice weekly may play an important role in clinical practice and could represent the treatment of choice in the challenging long-term management of VLS. Furthermore this therapy may contribute to improving patients' quality of life. In our opinion, proactive treatment with a corticosteroid should be considered in the guidelines for treating VLS, filling a therapeutic vacuum in the treatment algorithm for VLS.

### What's already known about this topic?

- Despite the chronic relapsing nature of vulvar lichen sclerosis (VLS), to date no guidelines are available for the long-term maintenance of this disease after an effective treatment with corticosteroids.

### What does this study add?

- Our results appear to indicate that proactive treatment with a topical corticosteroid twice weekly may be an effective, safe and reliable therapy for the long-term prevention of relapse in VLS previously treated with topical corticosteroid, and for maintaining VLS remission.

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## References

- 1 Smith YR, Haefner HK. Vulvar lichen sclerosis. Pathophysiology and treatment. *Am J Clin Dermatol* 2004; **5**:105–25.
- 2 Tasker GL, Wojnarowska F. Lichen sclerosis. *Clin Exp Dermatol* 2003; **28**:128–33.



- 3 Carli P, Moretti S, Spallanzani A *et al.* Fibrogenic cytokines in vulvar lichen sclerosis. An immunohistochemical study. *J Reprod Med* 1997; **42**:161–5.
- 4 Funaro D. Lichen sclerosis: a review and practical approach. *Dermatol Ther* 2004; **17**:28–37.
- 5 Neill SM, Lewis FM, Tatnall FM, Cox NH. British Association of Dermatologists' guidelines for the management of lichen sclerosis 2010. *Br J Dermatol* 2010; **163**:672–82.
- 6 Renaud-Vilmer C, Cavelier-Balloy B, Porcher R, Dubertret L. Vulvar lichen sclerosis: effect of long-term topical application of a potent steroid on the course of the disease. *Arch Dermatol* 2004; **140**:709–12.
- 7 Dalziel KL, Millard PR, Wojnarowska F. The treatment of vulval lichen sclerosis with a very potent topical steroid (clobetasol propionate 0.05%) cream. *Br J Dermatol* 1991; **124**:461–4.
- 8 Diakomanolis ES, Haidopoulos D, Syndos M *et al.* Vulvar lichen sclerosis in postmenopausal women: a comparative study for treating advanced disease with clobetasol propionate 0.05%. *Eur J Gynaecol Oncol* 2002; **23**:519–22.
- 9 Cattaneo A, De Magnis A, Botti E *et al.* Topical mometasone furoate for vulvar lichen sclerosis. *J Reprod Med* 2003; **48**:444–8.
- 10 Simonart T, Lahaye M, Simonart JM. Vulvar lichen sclerosis: effect of maintenance treatment with a moisturizer on the course of the disease. *Menopause* 2008; **15**:74–7.
- 11 Thiele JJ, Hsieh SN, Ekanayake-Mudiyanselage S. Vitamin E: critical review of its current use in cosmetic and clinical dermatology. *Dermatol Surg* 2005; **31**:805–13.
- 12 Kuriyama K, Shimizu T, Horiguchi T *et al.* Vitamin E ointment at high dose levels suppresses contact dermatitis in rats by stabilizing keratinocytes. *Inflamm Res* 2002; **51**:483–9.
- 13 Urano S, Iida M, Otani I, Matsuo M. Membrane stabilization of vitamin E; interactions of alpha-tocopherol with phospholipids in bilayer liposomes. *Biochem Biophys Res Commun* 1987; **146**:1413–18.
- 14 Krejci-Manwaring J, McCarty MA, Camacho F *et al.* Adherence with topical treatment is poor compared with adherence with oral agents: implications for effective clinical use of topical agents. *J Am Acad Dermatol* 2006; **54**:S235–6.
- 15 Krejci-Manwaring J, Tusa MG, Carroll C *et al.* Stealth monitoring of adherence to topical medication: adherence is very poor in children with atopic dermatitis. *J Am Acad Dermatol* 2007; **56**:211–16.
- 16 Ali SM, Brodell RT, Balkrishnan R, Feldman SR. Poor adherence to treatments: a fundamental principle of dermatology. *Arch Dermatol* 2007; **143**:912–15.
- 17 Brown KK, Rehmsus WE, Kimball AB. Determining the relative importance of patient motivations for nonadherence to topical corticosteroid therapy in psoriasis. *J Am Acad Dermatol* 2006; **55**:607–13.
- 18 Carroll CL, Feldman SR, Camacho FT *et al.* Adherence to topical therapy decreases during the course of an 8-week psoriasis clinical trial: commonly used methods of measuring adherence to topical therapy overestimate actual use. *J Am Acad Dermatol* 2004; **5**:212–16.
- 19 Feldman SR, Camacho FT, Krejci-Manwaring J *et al.* Adherence to topical therapy increases around the time of office visits. *J Am Acad Dermatol* 2007; **57**:81–3.
- 20 Koehler AM, Maibach HI. Electronic monitoring in medication adherence measurement. Implications for dermatology. *Am J Clin Dermatol* 2001; **2**:7–12.