

## ORIGINAL ARTICLE

# Control of atopic eczema with pimecrolimus cream 1% under daily practice conditions: results of a > 2000 patient study

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## Keywords

adults, atopic dermatitis, atopic eczema, children, eczema, infants, naturalistic, open-label, pimecrolimus

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## Abstract

**Background** Pimecrolimus cream 1% has been shown to effectively control atopic eczema (AE) when applied twice daily from the first signs or symptoms of AE until clearance. Moreover, pimecrolimus cream 1% has a favourable safety profile, lacking topical corticosteroid-related side-effects such as skin atrophy, making it particularly useful to treat delicate body regions (e.g. the face).

**Objective** The objective of this naturalistic study was to monitor the safety, tolerability and efficacy of pimecrolimus when used in the long-term management of AE in a real-life setting.

**Methods** A multicentre, open-label study was conducted in 2034 patients aged  $\geq 3$  months with mild to moderate AE for up to 12 months' duration. Patients applied pimecrolimus cream twice daily, initiating treatment at first signs or symptoms of AE, continuing until clearance.

**Results** Patients ( $n = 1847$ ; 91%) completed 3 months of the study. Treatment success (clear or almost clear AE) after 3 months of treatment was observed on the whole body in 59% of patients and on the face in 81% of patients. Disease improvement of whole body and face was seen in 77% and 63% of patients, respectively. Pruritus was absent or mild in 79% of patients. Pimecrolimus cream was well tolerated throughout the study.

**Conclusion** In a daily practice setting, pimecrolimus cream 1% effectively and safely controls AE.

## Introduction

Atopic eczema (AE), also known as eczema or atopic dermatitis, is a chronic, recurrent inflammatory skin disease characterized by distressing pruritus, signs of

inflammation and persistent dry skin.<sup>1</sup> All body surfaces can be affected; however, the face and great flexures, such as neck, antecubital and popliteal folds, wrists as well as hands are among the most commonly involved. The disease affects both genders and starts mostly during

infancy and childhood but is also prevalent in adults.<sup>2</sup> Since the 1950s, the mainstay of treatment for AE has been emollients for dry skin, avoidance measures, ultraviolet (UV) therapy and the use of topical corticosteroids (TCS) for acute eczema flares.<sup>3,4</sup> In a 16-week study, it was shown that fluticasone propionate significantly decreased time to relapse compared with placebo.<sup>5</sup> Although potent corticosteroids effectively resolve flares, their use is normally limited to short-term intervention, as their long-term use may be associated with side-effects, such as skin atrophy, vulnerability to infection and, rarely, systemic effects such as suppression of the hypothalamic–pituitary axis.<sup>6–10</sup> A recent study has found a disruption of the skin barrier after the use of TCS, which may lead to an increased permeability of the skin to allergens.<sup>11</sup>

Pimecrolimus cream 1% is a topical calcineurin inhibitor that has been specifically developed for the short-term relief and long-term control of inflammatory skin diseases.<sup>12</sup> Pimecrolimus is a non-steroid compound that selectively inhibits the activation of T cells via the calcineurin pathway by suppressing the release of inflammatory cytokines and other mediators of the allergic inflammatory reaction<sup>13,14</sup> involved in the development of acute and chronic AE.

Previous randomized controlled trials in infants, children and adults with AE have shown that when used at the first signs or symptoms of a recurrence, pimecrolimus prevents the progression of exacerbations to a severity that requires potent TCS treatment (severe/major flares).<sup>15–17</sup>

These studies were conducted under strictly controlled clinical trial settings and had frequently scheduled patient visits, strict inclusion and exclusion criteria for the study population and for treatment modalities as well as careful control of concomitant medications and treatments. This resulted in minimal flexibility in treatment modalities, a practice not reflected in real-life settings. The present study was, therefore, designed to explore the use of pimecrolimus cream in the long-term management of AE under naturalistic conditions reflective of daily practice worldwide, including populations from different ethnic backgrounds. Here, we report the main analysis of results observed after 3 months, the shortest treatment period allowed under the study protocol.

## Patients and methods

### Study design

This was a naturalistic, open-label study conducted at 248 centres in 28 countries in Europe, Asia and South America, with a planned recruitment of 2000 patients. Clinic visits at baseline, 1 week, 1 month and 3 months

**Table 1** Patient demographics at baseline

|                                         | Age (years) |      |       |      | Total |
|-----------------------------------------|-------------|------|-------|------|-------|
|                                         | < 2         | 2–12 | 13–17 | ≥ 18 |       |
| Total (n)                               | 312         | 900  | 199   | 623  | 2034  |
| Male (n)                                | 193         | 410  | 97    | 260  | 960   |
| Female (n)                              | 119         | 490  | 102   | 363  | 1074  |
| Whole-body IGA                          |             |      |       | n    | %     |
| 0 (clear)                               |             |      |       | 4    | 0.2   |
| 1 (almost clear)                        |             |      |       | 102  | 5.0   |
| 2 (mild)                                |             |      |       | 685  | 33.7  |
| 3 (moderate)                            |             |      |       | 1050 | 51.6  |
| 4 (severe)                              |             |      |       | 168  | 8.3   |
| 5 (very severe disease)                 |             |      |       | 25   | 1.2   |
| Facial IGA                              |             |      |       |      |       |
| 0 (clear)                               |             |      |       | 465  | 22.9  |
| 1 (almost clear)                        |             |      |       | 353  | 17.4  |
| 2 (mild)                                |             |      |       | 591  | 29.1  |
| 3 (moderate)                            |             |      |       | 496  | 24.4  |
| 4 (severe)                              |             |      |       | 111  | 5.5   |
| 5 (very severe disease)                 |             |      |       | 18   | 0.9   |
| Pruritus score                          |             |      |       |      |       |
| 0 (absent)                              |             |      |       | 32   | 1.6   |
| 1 (mild)                                |             |      |       | 524  | 26.0  |
| 2 (moderate)                            |             |      |       | 1029 | 51.1  |
| 3 (severe)                              |             |      |       | 429  | 21.3  |
| Patients' assessment of disease control |             |      |       |      |       |
| Complete                                |             |      |       | 12   | 0.6   |
| Good                                    |             |      |       | 441  | 21.7  |
| Limited                                 |             |      |       | 1233 | 60.6  |
| Uncontrolled                            |             |      |       | 347  | 17.1  |

were made. Visits at week 1 and longer study durations of 6, 9 or 12 months were optional for the participating centres and are not discussed further in this report. Ethics committee approval was acquired for all centres prior to study implementation. All patients or legal guardians provided signed informed consent.

### Patients

Male and female patients of all age groups over 3 months of age were eligible for inclusion, after diagnosis of mild to moderate AE was confirmed, and had a baseline Investigators' Global Assessment (IGA) ≥ 1. Patient demographics and baseline disease characteristics are listed in Table 1. Patients were excluded if they had active viral infections at the treatment site, were receiving phototherapy or immunosuppressive therapy, had used a topical calcineurin inhibitor within 2 weeks prior to study entry or had known or suspected hypersensitivity to pimecrolimus or any component of the cream.

## Treatment

Treatment with pimecrolimus cream 1% (Elidel®; Novartis, Basel, Switzerland) was initiated at the first signs or symptoms of eczema (slight redness, skin thickening, papules, persistent itching/scratching) and used continuously twice daily, for as long as signs and/or symptoms persisted. Thereafter, subjects were treated with pimecrolimus cream twice daily on an 'as-needed' basis. A major (severe) flare was considered to be an unacceptable increase in severity of symptoms (itching) or clinical signs (e.g. severe erythema with oozing/crusting). In the event of a major flare, the patient was permitted to use a potent topical steroid after discussion with the investigator. Emollients, systemic antihistamines and other non-medicated interventions were allowed as per normal practice. The use of tacrolimus, cyclosporin A, other immunosuppressant drugs, psoralene plus UVA, UVA and UVB was prohibited throughout the study. The use of pimecrolimus, emollients and concomitant medication was recorded throughout the study.

## Evaluations

Evaluations were done at baseline and after 1 and 3 months of treatment. Investigators ranked disease severity using IGA, an overall static evaluation of the disease state on a 6-point scale (0 = clear: no inflammatory signs of eczema; 1 = almost clear: just perceptible erythema and papulation/infiltration; 2 = mild disease; 3 = moderate disease; 4 = severe disease; 5 = very severe disease: severe erythema and severe papulation/infiltration with oozing/crusting). This index refers exclusively to the disease state at the time of evaluation, with no comparison to prior disease.<sup>18</sup>

Evaluations included an IGA of the whole body, an IGA specifically of the face, pruritus assessment [on a 4-point scale ranging from 0 (absent) to 3 (severe) in the preceding 24 h], and patients' global satisfaction of disease control [on a 4-point scale ranging from 0 (complete disease control) to 3 (uncontrolled disease)]. Because not all patients did have facial involvement at baseline, a secondary analysis, including the subgroup of 1202 patients with facial involvement (facial IGA  $\geq 1$ ) at baseline, was done. Safety and tolerability assessments consisted of monitoring adverse events on an ongoing basis.

## Statistical methods

Study endpoints were based on the IGA; treatment success was defined as an IGA score of 0 or 1 for all four parameters (whole body, face, pruritus and disease control), and disease improvement was defined as any reduction in

IGA score from baseline of at least one point. The efficacy of pimecrolimus cream was considered in relation to the patients' age, level of disease severity and use of other therapies, particularly TCS. Descriptive statistics were used to summarize the results. The safety population included all patients exposed to study drug, and the efficacy population [intention-to-treat (ITT) population] included all patients with at least one post-baseline efficacy measurement. The last observation carried forward value (LOCF) was used for the 3-month analysis. The month 3 assessments were prospectively defined to be the main analyses for the study.

## Results

### Patients

In total, 2034 patients received treatment; 2014 were treated and had at least one post-baseline evaluation endpoint (ITT population); 1847 patients (90.8%) completed 3 months of treatment. A total of 187 patients (9.2%) discontinued the study prematurely. The reasons for discontinuation were unsatisfactory therapeutic effect (3.5%), lost to follow-up (2.3%), withdrew consent (1.3%), adverse events (1.2%) and others (0.8%). All efficacy analyses were done on the ITT population.

### Efficacy

#### Treatment success

##### *Whole-body IGA*

The use of a pimecrolimus-based regimen resulted in treatment success and disease improvement in a high percentage of the patients that was sustained over the course of the study. By the end of the first month of treatment, 46.8% of patients had achieved treatment success [clear or almost clear (IGA 0 or 1); figs 1 and 2]. By the end of month 3, this figure had increased to 59.0% (fig. 2).

##### *Facial IGA*

Treatment success was observed more frequently for the face than for the whole body. At baseline, 40.3% of patients were clear or almost clear (IGA 0 or 1). Based on all patients that had facial involvement at baseline (facial IGA 1–5 at baseline), 76.2% of patients showed a clear or almost clear IGA at 1 month. By the end of 3 months of treatment, 81.3% of patients had facial treatment success (fig. 2). Of the 1202 patients with facial involvement at baseline (IGA  $\geq 2$ ), treatment success (facial IGA 0 or 1) was achieved in 63.9% and 72.6% of patients by the end of 1 and 3 months of treatment, respectively.

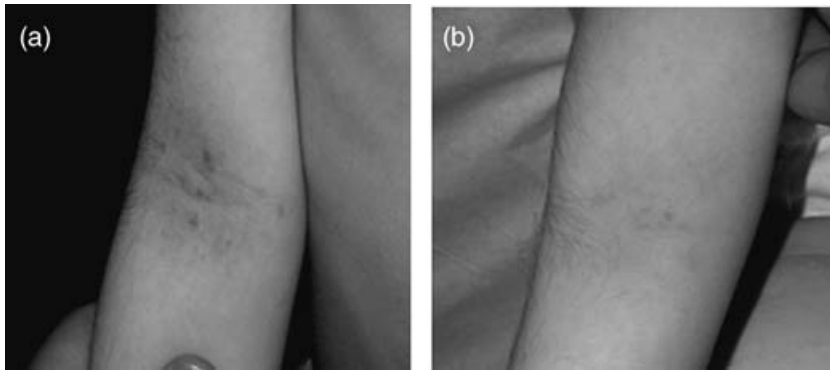


**fig. 1** AE in the right arm fold of a 4-year-old boy. (a) At baseline, moderate erythema, mild excoriation and mild lichenification were present. (b) After 1 month of treatment with pimecrolimus cream 1%, the patient was almost clear, with only mild erythema. No excoriation was present.

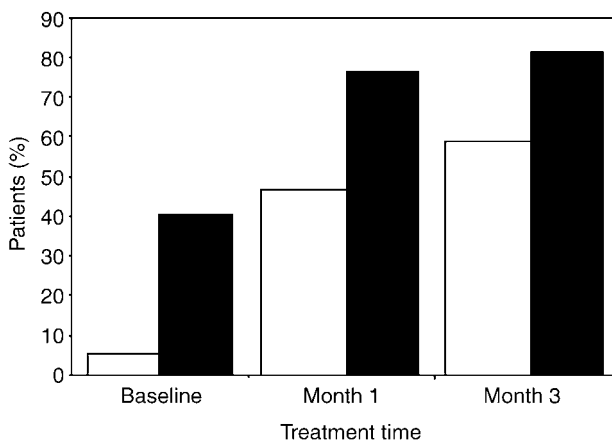


**fig. 2** Treatment success (IGA 0 or 1). Treatment success based on whole-body IGA (white columns) and treatment success based on facial IGA (black columns) show that treatment with pimecrolimus has a high success rate after 1 month of treatment and further increases with treatment time.

### Treatment success by age group

#### Whole-body IGA

The pimecrolimus-based regimen was effective across all ages, and particularly effective in younger patients (fig. 3). At 1 month of treatment, whole-body treatment success (IGA 0 or 1) was seen in 46.8% of patients overall. Treatment success was achieved in 64.6% of infants < 2 years of age, 46.4% of children aged 2 to 12 years, 48.5% of adolescents aged 13 to 17 years and 38.0% of adults (fig. 3). By the end of 3 months of treatment, whole-body treatment success in terms of IGA was achieved in 59.0% of patients overall (in 73.8% of infants, 57.7% of children, 60.6% of adolescents and 53.2% of adults; fig. 3).

#### Facial IGA

Facial treatment success after 1 month of treatment was observed in 79.7% of infants < 2 years of age, 83.0% of children aged 2 to 12 years, 74.7% of adolescents aged 13

to 17 years and 65.0% of adults (fig. 3). After 3 months of treatment, treatment success was achieved in 84.9% of infants, 86.2% of children, 85.4% of adolescents and 71.1% of adults (fig. 3).

### Disease improvement

Disease improvement (a reduction by at least 1 point of the IGA score) regarding the whole body was observed in 71.4% of patients by the end of 1 month of treatment, and after 3 months of treatment, 77.2% of patients experienced an improvement in their AE. Facial disease improvement was observed in 58.9% of patients after 1 month of treatment and in 63.1% of patients after 3 months.

### Pruritus

Pruritus was present in nearly all patients at baseline (98.4%) and was classified as absent in 1.6%, mild in 26.0%, moderate in 51.0% and severe in 21.4% of the patients. After 1 month of treatment with pimecrolimus, pruritus was absent in 25.6% of patients and mild in 49.4% of patients (fig. 4). By the end of 3 months of treatment, pruritus was absent in nearly one third of patients (32.5%) and mild in 46.0% of patients (fig. 4).

### Patients' global satisfaction with treatment

At baseline, 22.3% of patients or their caregivers rated their disease control as 'complete' or 'good'. By the end of the first month of treatment, this value increased to 75.2% and, by the end of month 3, to 78.1% (fig. 5).

### Treatment success and disease improvement by concomitant TCS use

Concomitant steroids were used at the discretion of the investigator to treat severe flares either at the beginning or during the course of this study. Throughout the study, 34.8% of patients used concomitant topical steroids, and

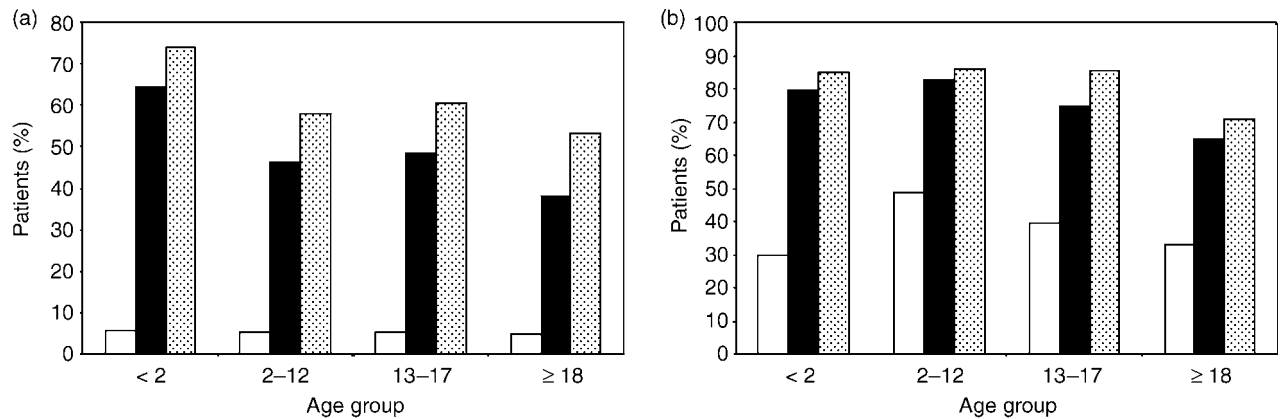


**fig. 3** Clear or almost clear IGA by age group. Treatment success (IGA 0 or 1) based on whole-body IGA (a) and facial IGA (b) shows greatest success in infants and children, compared with adults. *White columns*, baseline; *black columns*, 1 month of treatment; *dotted columns*, 3 months of treatment.

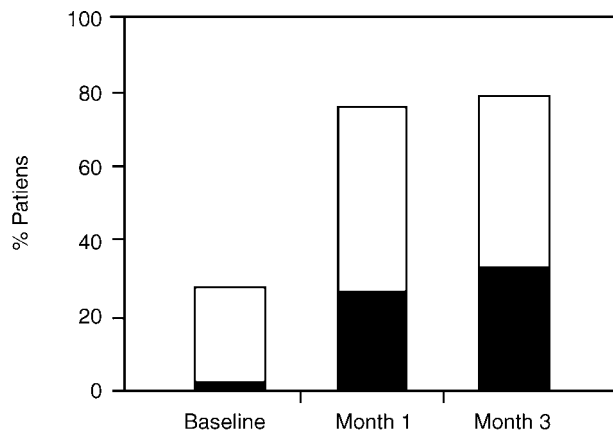


**fig. 4** Percentage of patients with absent or mild pruritus by visit. Pruritus clearly diminished over the course of the treatment. *Black columns*, no pruritus; *white columns*, mild pruritus.

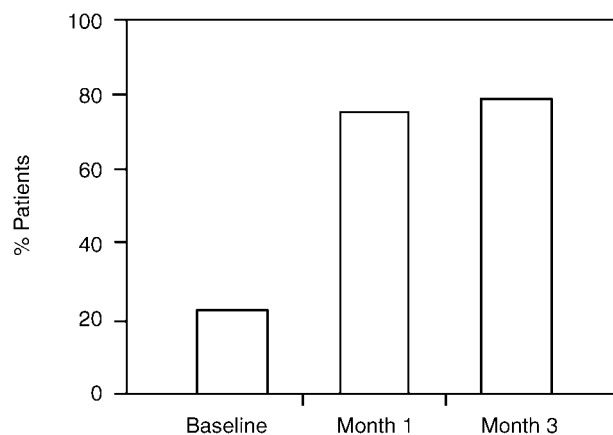


**fig. 5** Patient's global satisfaction with treatment. Disease control increased during the study and most notably after the first month of treatment.

3.3% of patients used concomitant systemic steroids. Patients with severe or very severe disease at baseline were more likely to require corticosteroids than those with mild or moderate disease (47.4% vs. 39.5% used corticosteroids, respectively). Within the group of patients who did not use corticosteroids ( $n = 1213$ ), 6% were clear or almost clear of disease at baseline, 37.2% had mild disease, 48.4% had moderate disease, and 8.4% had severe/very severe disease (Table 2). Disease improvement across the whole body was more pronounced in those patients who did not need to use corticosteroids. Of the patients who did not use corticosteroids, 81.8% improved and 68.1% achieved treatment success at month 3, compared with 69.8% and 44.4% of patients, respectively, who used corticosteroids (Table 2).

Similar results were obtained for the facial region; of the patients who did not use corticosteroids, 64.6% improved and 85.1% achieved treatment success, compared with 60.8% and 75.3% of patients, respectively, who used corticosteroids (Table 2).

Patients who did not use concomitant steroids assessed their rate of improvement and treatment success (75.6% and 83.7%, respectively) higher than those who used steroids (61.3% improved and 69.2% success; Table 2).

In addition, pruritus was decreased to a higher degree in patients who did not use concomitant steroids (74.2% improved and 83.5% had treatment success: pruritus score 0 or 1) compared with patients who used steroids (63.1% improved and 70.5% had treatment success; Table 2).

## Safety

Among all patients ( $n = 2034$ ), 35.2% did not experience any adverse events; 64.8% ( $n = 1318$ ) of patients experienced an adverse event. The event was suspected

**Table 2** Improvement of eczema skin lesions from baseline in patients treated with pimecrolimus and with/without use of topical steroids ( $n = 2014$ )

|                         | Concomitant steroid |        |
|-------------------------|---------------------|--------|
|                         | Yes (%)             | No (%) |
| Whole body IGA baseline |                     |        |
| Clear                   | 0.0                 | 0.3    |
| Almost clear            | 3.8                 | 5.7    |
| Mild                    | 28.4                | 37.2   |
| Moderate                | 56.5                | 48.4   |
| Severe                  | 10.1                | 7.2    |
| Very severe             | 1.3                 | 1.2    |
| Whole body IGA          |                     |        |
| Improved                | 69.8                | 81.8   |
| Success                 | 44.4                | 68.1   |
| Facial IGA              |                     |        |
| Improved                | 60.8                | 64.6   |
| Success                 | 75.3                | 85.1   |
| Patient's assessment    |                     |        |
| Improved                | 61.3                | 75.6   |
| Success                 | 69.2                | 83.7   |
| Pruritus                |                     |        |
| Improved                | 63.1                | 74.2   |
| Success                 | 70.5                | 83.5   |

**Table 3** Occurrence of adverse events ( $> 5\%$ ; population  $n = 2034$ )

|                                         | %    |
|-----------------------------------------|------|
| Patients with adverse event(s)          | 64.8 |
| Adverse event related to study drug     | 15.1 |
| Discontinuation due to adverse event(s) | 1.2  |
| Adverse event                           |      |
| Nasopharyngitis                         | 15.5 |
| Pyrexia                                 | 10.0 |
| Headache                                | 8.2  |
| Cough                                   | 7.3  |
| Application-site burning                | 6.8  |
| Pruritus                                | 5.9  |

by the investigator to be related to study drug in only 15.1% ( $n = 307$ ) of patients. The most frequent adverse events ( $> 5\%$ ) are shown in Table 3; in the majority, they were mild or moderate in severity, with maximum severity being graded 'mild' in 9.8% of patients, 'moderate' in 3.9% and 'severe' in 1.4%.

Of the patients ( $n = 151$ ) who experienced local reactions of any type at the application site, 107 patients (68.6%) reported mild events. All application-site reactions were classified as transient (defined as occurring within the first three days of treatment and resolving within 7 days) and resolved within less than 2 days. Application-site reactions suspected to be related to treatment occurred in

**Table 4** General occurrence of treatment-associated infections and infestations (population  $n = 2034$ )

|                                   | %    |
|-----------------------------------|------|
| Total                             | 40   |
| Nasopharyngitis                   | 15.5 |
| Bronchitis                        | 4.7  |
| Influenza                         | 3.9  |
| Upper respiratory tract infection | 2.9  |
| Herpes simplex                    | 2.3  |
| Impetigo                          | 2.3  |
| Pharyngitis                       | 1.9  |
| Tonsillitis                       | 1.5  |
| Gastroenteritis                   | 1.4  |
| Ear infection                     | 1.4  |
| Otitis media                      | 1.3  |
| Varicella                         | 1.3  |
| Folliculitis                      | 1.2  |
| Viral infection                   | 1.2  |
| Skin infection                    | 1.1  |

**Table 5** Occurrence of treatment-associated infections suspected to be related to study drug (population  $n = 2034$ )

|                        | %    |
|------------------------|------|
| Total                  | 2.3  |
| Folliculitis           | 0.4  |
| Herpes simplex         | 0.4  |
| Molluscum contagiosum  | 0.3  |
| Impetigo               | 0.2  |
| Herpes virus infection | 0.05 |
| Others                 | 1    |

7.4% of patients, with application-site 'burning' reported by 6.8% of patients, the majority being mild to moderate (4.7% reported mild, 1.5% moderate and 0.5% severe application-site burning).

The profile of infections and infestations with an incidence  $> 1\%$  is shown in Table 4. The total number of infections was 814 (40%). The number of infections suspected to be related to study drug was 46 (2.3%), and most of these events were mild (1.3%) to moderate (0.9%) in severity (Table 5). The bacterial infections, related to study drug, were similar to those commonly seen in patients with AE, who are at increased risk of skin infections, and included folliculitis, cellulitis and impetigo/streptococcal impetigo. Seven patients developed molluscum contagiosum. Among the patients with herpes simplex, 2 (0.1% of safety population) experienced clinically diagnosed eczema herpeticum during the first 3 months of treatment. One of these two cases was suspected to be related to study drug. Patients recovered under adequate therapy and continued in the study, without recurrence.

Discontinuation due to adverse events occurred only in 28 (1.4%) patients, mainly due to skin disorders (0.9% of patients) such as pruritus and skin irritation or application-site reactions (0.5% of patients). Four patients discontinued following serious adverse events such as exacerbation of AE, impetigo contagiosa, lack of improvement of AE and asthma exacerbation, of which only the first was considered to be related to the study drug. The overall incidence of serious adverse events was low (1.7%).

## Discussion

This naturalistic study has been so far the largest clinical study done using pimecrolimus cream 1% to date. Naturalistic studies enable the efficacy and safety of a treatment to be verified in a realistic clinical setting that reflects the use and expectation of both the physician and patient in daily practice. Intermittent use of pimecrolimus cream in AE can provide disease control over longer time periods when applied at first signs and symptoms of an exacerbation (such as mild erythema, desquamation and/or pruritus) and continued until exacerbation clears. Pimecrolimus cream offers an alternative treatment to many patients who avoid or under-use TCS due to fear of side-effects and thereby do not manage their disease effectively.<sup>19,20</sup> In addition, most corticosteroids are not indicated in areas of delicate skin such as face, neck and flexural areas, as these are most susceptible for corticosteroid-dependent side-effects (e.g. skin atrophy or striae).<sup>21</sup>

In this naturalistic setting, only 35% of patients required the use of concomitant TCS for flares not controlled by pimecrolimus; this is in line with the proportion of patients requiring corticosteroids in randomized controlled clinical trials in infants and children.<sup>16,17</sup> In a 1-year double-blind controlled study with pimecrolimus plus steroids or vehicle plus steroids, fewer infant patients in the pimecrolimus group required steroids (36.3% vs. 65.2% in the control arm).<sup>16</sup> Similar results were seen at 6 months in a study with children treated with pimecrolimus or vehicle (35% of pimecrolimus patients required steroids vs. 62.9% in the control arm).<sup>17</sup> A significant reduction regarding steroid usage could also be observed in adults (over 6 months). Corticosteroids were required only for 14.2% of study days in the pimecrolimus group vs. 37.2% of study days in the control group.<sup>15</sup> The better efficacy in the patients who did not apply corticosteroids in the naturalistic setting could be due to the fact that patients who used TCS showed a higher disease severity at baseline than non-TCS users but points out that even when TCS are applied, the disease may not be completely controlled.

For both whole-body and facial assessments, treatment success was greatest in infants and children, compared with adults. These findings are important because

paediatric patients have the highest need for an effective and safe alternative to topical steroids for the long-term control of AE.<sup>20</sup> The whole-body treatment success rate (complete or almost complete clearance) reported here (59.0%) is comparable with the results from long-term, double-blind, vehicle-controlled clinical trials in infants and children with mild to severe disease.<sup>16,17</sup> As no significant differences in severity of the disease between children and adults were observed at baseline, this better efficacy may be attributed to the age of the patients.

Disease improvement of the face was less prominent than of the whole body, because a considerable number of patients (40.3%) had a facial IGA of 0 or 1 at baseline; therefore, no further improvement could be achieved, whereas only 5.2% of the patients were clear or almost clear (IGA of 0 or 1) regarding the whole body at study inclusion.

Itch (pruritus) is the major symptom of AE. The relief of pruritus (absent or mild in 78.5% of patients at month 3) reported here is consistent with results from randomized clinical trials. In the clinical trial setting, in which more frequent assessments were carried out, the proportion of patients with absent or mild pruritus has been significantly greater in the pimecrolimus arm than the vehicle/control arm at day 43 in infants (76.5% vs. 58.7%)<sup>16</sup> and already at day 8 in children/adolescents (44.2% vs. 25.7%).<sup>18</sup> Similarly, in adult patients, a significant decrease in pruritus was achieved already after 48 h of treatment with pimecrolimus vs. control and persisted to up to 24 weeks of treatment.<sup>15,22</sup>

As shown in this study, compliance with pimecrolimus-based treatment was excellent, with very few discontinuations due to unsatisfactory therapeutic effect or adverse events. Patient satisfaction with pimecrolimus-based treatment was also high, with 'good' or 'complete' disease control reported by approximately three quarters of patients at both the 1-month and 3-month time points. Treatment was well tolerated across all age ranges and on delicate facial skin; this confirms a previous naturalistic study in which the incorporation of pimecrolimus into individual daily skin care regimens resulted in rapid and sustained disease improvement, with pruritus relief combined with a good safety profile.<sup>23–25</sup>

In line with previous clinical trials, the present study confirmed the favourable safety profile of pimecrolimus cream.<sup>15–18,26,27</sup> However, patients with AE are at increased risk of developing skin infections, including the types reported here.<sup>24,25,28</sup> Viral infections such as herpes simplex are more likely to have a severe course in patients with AE.<sup>29</sup> The two cases observed during this study indicate a low incidence of eczema herpeticum.<sup>29</sup> Application-site burning was reported by only 6.8% of patients and generally resolved within 2 days. Noticeably, this incidence was lower than previously reported in clinical trials.<sup>15–17</sup>

In conclusion, the results of this study indicate that in treatment schemes reflecting real-life usage, the incorporation of pimecrolimus cream into individual daily skin care regimens is effective, well tolerated and accepted by patients. Treatment resulted in high rates of pruritus relief, improvement of skin lesions for both the face and the whole body. Overall, these results confirm the efficacy and safety profiles shown in previous controlled clinical studies of pimecrolimus in the treatment of infants, children and adults with AE. This study shows that AE can be well controlled by a treatment regimen that includes pimecrolimus usage from the first signs or symptoms of an AE recurrence, until complete resolution of lesions, and reserves steroids for severe exacerbations (major flares) of the disease that cannot be controlled by pimecrolimus cream. Consequently, the risk of adverse events related to the frequent or prolonged use of TCS is minimized. Taken together, the negligible systemic absorption and the lack of any atrophogenic potential in contrast to TCS make pimecrolimus cream 1% particularly useful to treat lesions on skin that is thin and thus more vulnerable to atrophy, such as the face and the skin folds.

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