

# Primary care

## Efficacy and tolerability of topical pimecrolimus and tacrolimus in the treatment of atopic dermatitis: meta-analysis of randomised controlled trials

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### Abstract

**Objective** To determine the efficacy and tolerability of topical pimecrolimus and tacrolimus compared with other treatments for atopic dermatitis.

**Design** Systematic review and meta-analysis.

**Data sources** Electronic searches of Cochrane Library, Medline, and Embase.

**Study selection** Randomised controlled trials of topical pimecrolimus or tacrolimus reporting efficacy outcomes or tolerability.

**Data extraction** Efficacy: investigators' global assessment of response; patients' global assessment of response; proportions of patients with flares of atopic dermatitis; and improvements in quality of life. Tolerability: overall rates of withdrawal, withdrawal due to adverse events, and the proportions of patients with burning of the skin and skin infections.

**Data synthesis** 4186 of 6897 participants in 25 randomised controlled trials received pimecrolimus or tacrolimus. Both drugs were significantly more effective than a vehicle control. Tacrolimus 0.1% was as effective as potent topical corticosteroids at three weeks and more effective than combined treatment with hydrocortisone butyrate 0.1% (potent used on trunk) plus hydrocortisone acetate 1% (weak used on face) at 12 weeks (number needed to treat (NNT) = 6). Tacrolimus 0.1% was also more effective than hydrocortisone acetate 1% (NNT = 4). In comparison, tacrolimus 0.03% was more effective than hydrocortisone acetate 1% (NNT = 5) but less effective than hydrocortisone butyrate 0.1% (NNT = -8). Direct comparisons of tacrolimus 0.03% and tacrolimus 0.1% consistently favoured the higher strength formulation, but efficacy differed significantly between the two strengths only after 12 weeks' treatment (rate ratio 0.80, 95% confidence interval 0.65 to 0.99). Pimecrolimus was far less effective than betamethasone valerate 0.1% (NNT = -3 at three weeks). Pimecrolimus and tacrolimus caused significantly more skin burning than topical corticosteroids. Rates of skin infections in any of the comparisons did not differ.

**Conclusions** Both topical pimecrolimus and topical tacrolimus are more effective than placebo treatments for atopic dermatitis, but in the absence of studies that

show long term safety gains, any advantage over topical corticosteroids is unclear. Topical tacrolimus is similar to potent topical corticosteroids and may have a place for long term use in patients with resistant atopic dermatitis on sites where side effects from topical corticosteroids might develop quickly. In the absence of key comparisons with mild corticosteroids, the clinical need for topical pimecrolimus is unclear. The usefulness of either treatment in patients who have failed to respond adequately to topical corticosteroids is also unclear.

### Introduction

Atopic dermatitis affects 15-20% of children in developed countries,<sup>1</sup> and 1-3% of adults. Traditionally the treatment of atopic dermatitis has included emollients and occasional topical corticosteroids to control flares. Corticosteroids may be associated with several local and systemic adverse events, such as thinning of the skin.

Two new topical agents, pimecrolimus and tacrolimus, were developed to provide alternatives to topical corticosteroids without the adverse events. We undertook a systematic review and meta-analysis of randomised controlled trials of pimecrolimus and tacrolimus in atopic dermatitis to determine whether they offer any advantages over existing treatments for atopic dermatitis in terms of efficacy, improved tolerability, and fewer short term or long term adverse effects.

### Methods

We included randomised controlled trials that compared topical pimecrolimus or topical tacrolimus at a licensed therapeutic dose with vehicle or another active treatment in patients with atopic dermatitis, and reported efficacy outcomes or adverse events.



References w1-w23 are on [bmj.com](http://bmj.com)



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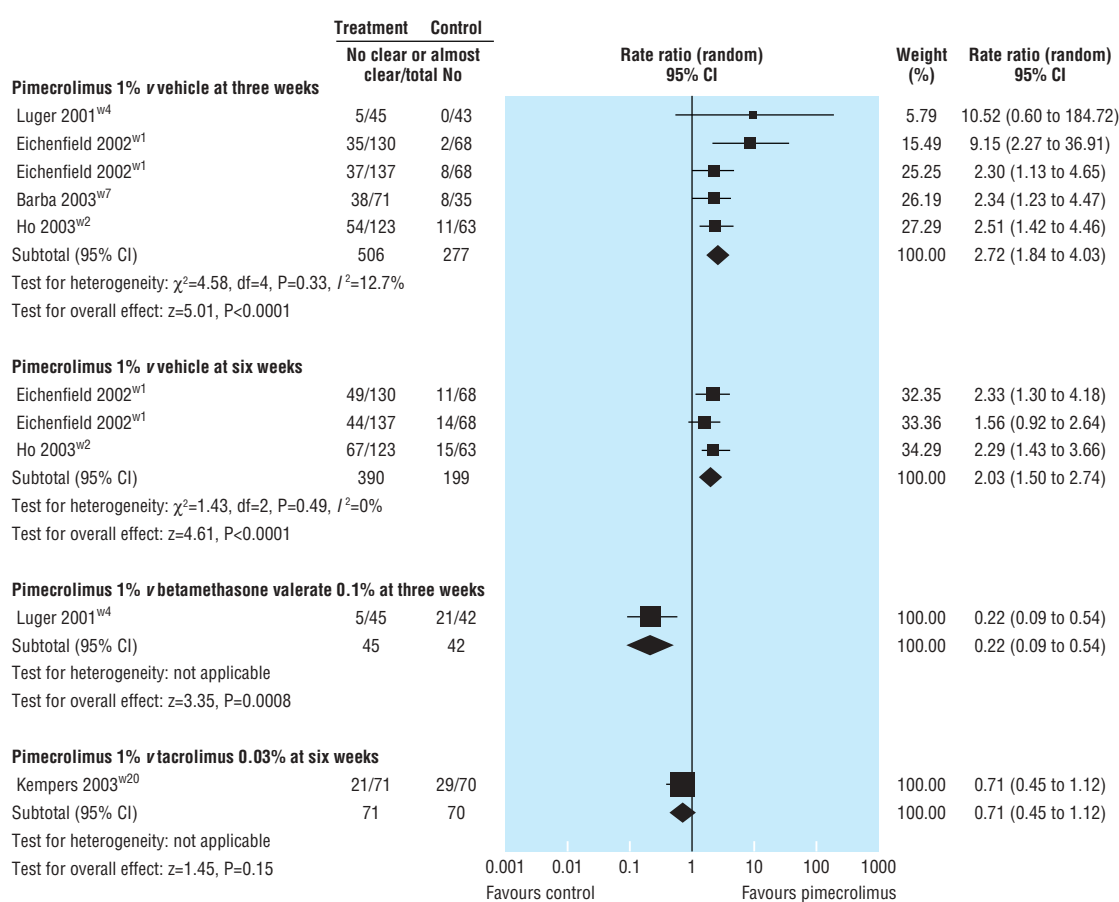


Fig 1 Investigators' global assessment of response (clear or almost clear) with pimecrolimus 1% compared with control

### Outcome measures

For efficacy, we used the investigators' rating of the global degree of improvement. For pimecrolimus, we used the proportion of patients who were rated by the investigator as clear or almost clear as the primary outcome measure, whereas for tacrolimus the primary outcome was the proportion of patients who achieved at least 90% improvement (clear or excellent) from baseline.

Secondary outcome measures included patients' global assessments of feeling better or much better, the proportions of patients with flares, and improvements in quality of life. Tolerability to the drug was assessed from overall rates of withdrawal, withdrawal due to adverse events, and the proportions of patients with burning of the skin and skin infections.

### Search strategy

We searched Medline, Embase, the Cochrane Skin Group specialised register, and the Cochrane central register of controlled trials to December 2004 using the search terms "pimecrolimus", "Elidel", "SDZ ASM 981", "tacrolimus", "Protopic", and "FK506". We also searched the reference lists of all retrieved trials and the websites for the European Agency for the Evaluation of Medicinal Products and the US Food and Drug Administration.

Trial eligibility was determined by two authors (DMA, PD), who also independently extracted the data. Trials were rated for methodological quality using the Jadad scale.

### Data synthesis

Some trials did not report on all the outcomes of interest. For each comparison and outcome we undertook separate meta-analyses. We grouped topical corticosteroids as mild (aclometasone dipropionate 0.1%, hydrocortisone acetate 1%) or potent (betamethasone valerate 0.1%, hydrocortisone butyrate 0.1%, triamcinolone acetonide 0.1%). We also stratified the analysis of efficacy data by the duration of treatment.

We summarised dichotomous data as rate ratios (relative risks) and combined these using a random effects model.<sup>2</sup> We also computed homogeneity statistics to test the agreement of the individual trial results with the combined meta-analytical summary.<sup>3,4</sup>

### Results

Overall, we identified 25 randomised controlled trials, totalling 6897 patients with atopic dermatitis (see [bmj.com](http://bmj.com) for details of trials).<sup>w1-w23</sup> Eleven trials studied the effects of pimecrolimus 1% cream applied twice daily, one trial directly compared pimecrolimus and tacrolimus 0.03% in children,<sup>w20</sup> and 14 trials investigated the effects of tacrolimus 0.1% or tacrolimus 0.03% applied twice daily.

### Vehicle controlled studies

#### *Pimecrolimus 1% versus vehicle*

Five trials (783 patients) reported on the proportion of patients clear or almost clear at three weeks.<sup>w1 w2 w4 w7</sup>

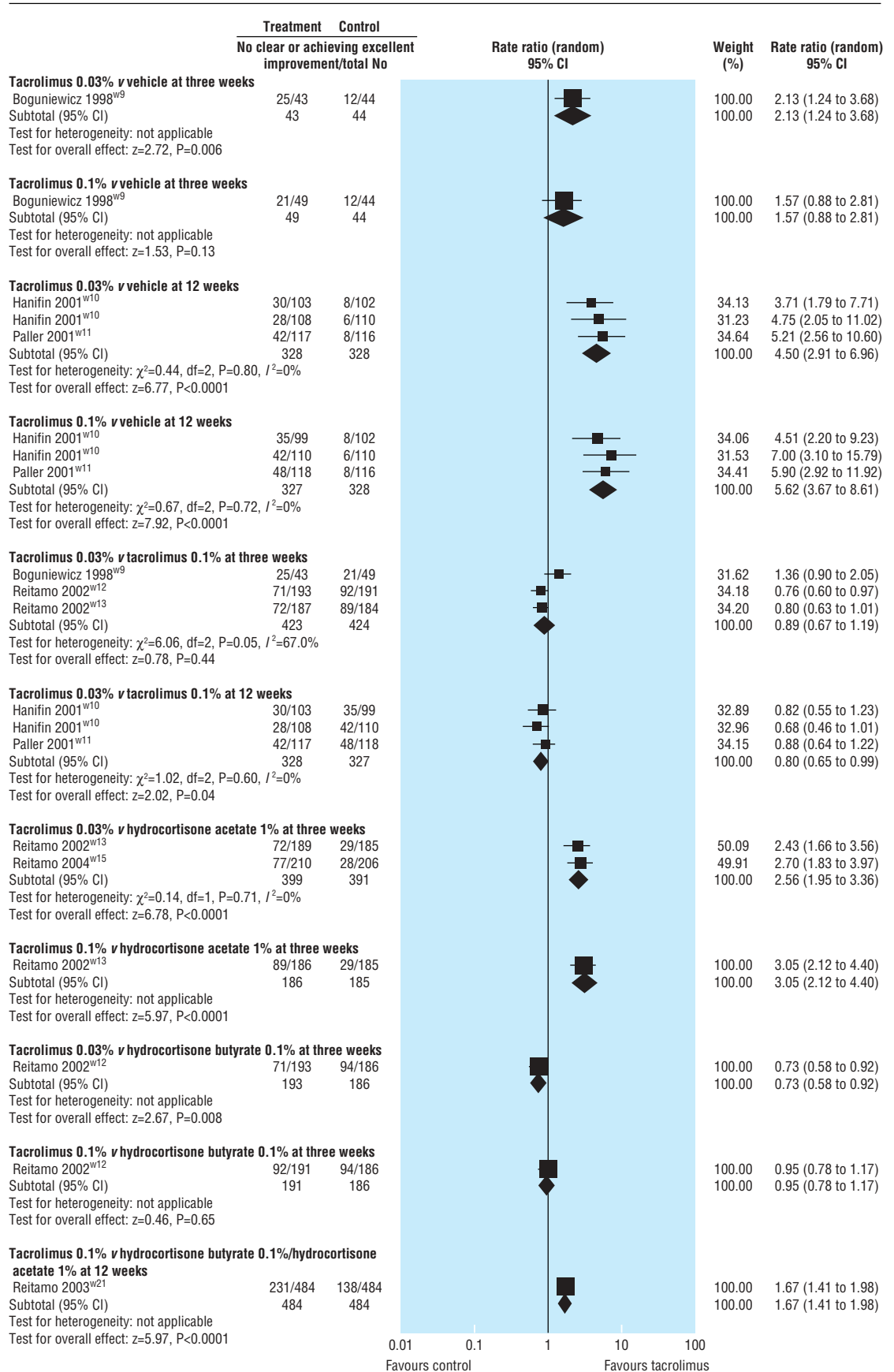


Fig 2 Investigators' global assessment of response (clear or excellent improvement) with tacrolimus (0.03% and 0.1%) compared with control

## Comparison of risk of withdrawals and adverse events in trials of pimecrolimus and tacrolimus for treating atopic dermatitis

Adverse effect	Crude rate	No of studies	Pooled relative risk (95% CI)	Test for homogeneity	
				P value	I <sup>2</sup> (%)
Pimecrolimus 1% v vehicle:					
Withdrawal†	273/1211 v 259/622	7	0.49 (0.38 to 0.64)*	0.042	54.1
Withdrawal‡	9/408 v 15/275	4	0.46 (0.20 to 1.06)	0.887	0
Bacterial skin infections	98/899 v 84/443	4	0.67 (0.28 to 1.60)	0.042	63.5
Viral skin infections	76/776 v 23/380	3	1.53 (0.78 to 2.99)	0.191	39.6
Skin burning	204/1166 v 131/579	6	0.87 (0.70 to 1.09)	0.257	24.6
Pimecrolimus 1% v potent corticosteroid (betamethasone valerate 0.1%):					
Withdrawal†	19/43 v 7/45	1	2.17 (0.60 to 7.69)	—	—
Withdrawal‡	1/43 v 3/45	1	2.78 (0.30 to 25.0)	—	—
Skin burning	1/43 v 2/45	1	5.26 (1.92 to 14.3)*	—	—
Pimecrolimus 1% v triamcinolone acetonide 0.1% (trunk and limbs) and hydrocortisone acetate 1% (face and neck):					
Skin infections (any)	69/328 v 80/330	1	0.87 (0.65 to 1.15)	—	—
Bacterial skin infections	39/328 v 43/330	1	0.91 (0.61 to 1.37)	—	—
Fungal skin infections	1/328 v 4/330	1	0.25 (0.03 to 2.24)	—	—
Viral skin infections	16/328 v 26/330	1	0.62 (0.34 to 1.13)	—	—
Skin burning	85/328 v 36/330	1	2.38 (1.66 to 3.40)*	—	—
Tacrolimus 0.1% v vehicle:					
Withdrawal†	81/430 v 238/426	5	0.35 (0.27 to 0.46)*	0.22	30.6
Withdrawal‡	19/430 v 42/426	5	0.47 (0.28 to 0.80)*	0.714	0
Skin infections	27/327 v 18/330	3	1.48 (0.83 to 2.65)	0.53	0
Skin burning	187/430 v 92/426	5	2.08 (1.35 to 3.18)*	0.010	69.9
Tacrolimus 0.03% v vehicle:					
Withdrawal†	93/425 v 238/426	5	0.40 (0.33 to 0.48)*	0.81	0
Withdrawal‡	20/425 v 42/426	5	0.50 (0.30 to 0.84)*	0.800	0
Skin infections	27/327 v 32/330	3	0.85 (0.52 to 1.39)	0.72	0
Skin burning	173/425 v 92/426	5	1.89 (1.43 to 2.50)*	0.202	32.9
Tacrolimus 0.1% v mild corticosteroid (hydrocortisone acetate 1%):					
Withdrawal†	13/186 v 20/185	1	0.65 (0.33 to 1.27)	—	—
Withdrawal‡	3/186 v 4/185	1	0.75 (0.17 to 3.33)	—	—
Skin infections	4/186 v 4/185	1	0.99 (0.25 to 3.85)	—	—
Skin burning	38/186 v 13/185	1	2.94 (1.61 to 5.26)*	—	—
Tacrolimus 0.1% v potent corticosteroid (betamethasone valerate 0.1%, hydrocortisone butyrate 0.1%):					
Withdrawal†	33/283 v 25/275	2	1.32 (0.80 to 2.13)	0.822	0
Withdrawal‡	8/191 v 3/186	1	2.56 (0.70 to 10.0)	—	—
Skin infections	6/92 v 5/89	1	1.16 (0.37 to 3.70)	—	—
Skin burning	138/283 v 27/275	2	4.76 (3.33 to 7.14)*	0.362	4.9
Tacrolimus 0.1% v hydrocortisone butyrate 0.1% (trunk and extremities) and hydrocortisone acetate 1% (face):					
Withdrawal†	124/488 v 204/487	1	0.61 (0.51 to 0.73)*	—	—
Withdrawal‡	10/488 v 16/487	1	0.63 (0.29 to 1.37)	—	—
Skin infections	18/488 v 21/487	1	0.86 (0.46 to 1.59)	—	—
Skin burning	259/488 v 67/487	1	3.85 (3.03 to 5.00)*	—	—
Tacrolimus 0.03% v mild corticosteroid (hydrocortisone acetate 1%):					
Withdrawal†	42/399 v 61/392	2	0.71 (0.35 to 1.43)	0.022	56.8
Withdrawal‡	11/399 v 10/392	2	1.09 (0.46 to 2.56)	0.529	0
Skin infections	12/399 v 10/392	2	1.18 (0.51 to 2.70)	0.157	36
Skin burning	85/399 v 43/392	2	1.96 (1.25 to 3.13)*	0.203	35.0
Tacrolimus 0.03% v potent corticosteroid (hydrocortisone butyrate 0.1%):					
Withdrawal†	22/193 v 17/186	1	1.03 (0.58 to 1.82)	—	—
Withdrawal‡	7/193 v 3/186	1	0.74 (0.17 to 3.23)	—	—
Skin burning	87/193 v 24/186	1	3.45 (2.33 to 5.26)*	—	—
Tacrolimus 0.1% v tacrolimus 0.03%:					
Withdrawal†	96/807 v 136/807	7	0.75 (0.49 to 1.14)	0.024	58.9
Withdrawal‡	30/807 v 30/807	7	0.99 (0.59 to 1.64)	0.556	0
Skin infections	22/513 v 38/517	4	0.60 (0.35 to 1.02)	0.367	5.2
Skin burning	338/807 v 295/807	7	1.14 (0.95 to 1.35)	0.075	47.6
Tacrolimus 0.1% v oral cyclosporin 3mg/kg:					
Skin burning	4/15 v 0/15	1	9.00 (0.53 to 153.79)	—	—

\*P<0.05. †Any reason. ‡Due to side effects.

Pimecrolimus was significantly more effective than vehicle (pooled rate ratio 2.72, 95% confidence interval 1.84 to 4.03; fig 1). Three of the trials reported on the same outcome after six weeks' treatment and found that pimecrolimus remained significantly more effective (2.03, 1.50 to 2.74). At six months, one trial

(251 patients) found no significant difference (rate ratio 1.46, 0.98 to 2.19).<sup>33</sup> In three vehicle controlled trials (1156 patients), pimecrolimus resulted in significantly fewer patients with flare at six months (pooled rate ratio 1.92, 1.56 to 2.36). At 12 months pimecrolimus remained significantly more effective

than vehicle at preventing flares (two trials: 1.84, 1.50 to 2.24).

#### *Tacrolimus versus vehicle*

One trial (136 children) directly compared tacrolimus 0.03% and tacrolimus 0.1% with vehicle control, and reported on the proportion of children clear or achieving excellent improvement at three weeks.<sup>w9</sup> Tacrolimus 0.03% was significantly more effective than vehicle (rate ratio 2.13, 1.24 to 3.68), but there was no significant differences in response between tacrolimus 0.1% and vehicle (1.57, 0.88 to 2.81). On the basis of the patients' global assessment of response as better or much better, both tacrolimus 0.03% and tacrolimus 0.1% were significantly more effective than vehicle (1.47, 1.06 to 2.04 and 1.76, 1.31 to 2.36, respectively). Three trials (656 patients) also reported on the same outcomes after 12 weeks' treatment and found that tacrolimus 0.03% and tacrolimus 0.1% were significantly more effective than vehicle (pooled rate ratios for proportion of patients clear or achieving excellent improvement 4.50, 2.91 to 6.96 and 5.62, 3.67 to 8.61, respectively; fig 2).

#### **Comparative efficacy of topical pimecrolimus**

##### *Pimecrolimus 1% versus potent corticosteroid*

One trial (87 patients) compared pimecrolimus 1% with betamethasone valerate 0.1% and reported on the proportion of patients clear or almost clear.<sup>w4</sup> Betamethasone valerate 0.1% was significantly more effective than pimecrolimus 1% after three weeks (rate ratio 0.22, 0.09 to 0.54; see fig 2).

##### *Pimecrolimus 1% versus potent corticosteroid (trunk) and mild corticosteroid (face)*

One trial (658 adults; moderate to severe atopic dermatitis) compared pimecrolimus 1% with a combined regimen of triamcinolone acetonide 0.1% (trunk and limbs) and hydrocortisone acetate 1% (face, neck, and intertriginous areas).<sup>w22</sup> On the basis of the proportions of patients moderately clear or better, the combined regimen was significantly more effective than pimecrolimus 1% after treatment for one week, three weeks, and six months, but there were no significant differences between treatment groups at 12 months.

##### *Pimecrolimus 1% versus tacrolimus 0.03%*

One direct comparison of pimecrolimus 1% against tacrolimus 0.03% (141 children; moderate atopic dermatitis) found no significant difference in the proportion of children clear or almost clear at six weeks (0.71, 0.45 to 1.12).<sup>w20</sup>

##### *Pimecrolimus 1% four times daily versus pimecrolimus 1% twice daily*

One crossover trial (49 patients; moderate to severe atopic dermatitis) found no significant difference in the proportion of patients clear or almost clear with four times daily versus twice daily application of pimecrolimus 1% cream at three weeks (0.96, 0.40 to 2.33).<sup>w8</sup>

#### **Comparative efficacy of topical tacrolimus**

##### *Tacrolimus versus mild topical corticosteroids*

Two trials (1183 children; moderate to severe atopic dermatitis) compared tacrolimus with hydrocortisone

acetate 1%.<sup>w13 w15</sup> Both tacrolimus 0.03% and tacrolimus 0.1% were significantly more effective than hydrocortisone acetate 1% on the basis of the proportion of patients clear or achieving excellent improvement at three weeks (2.56, 1.95 to 3.36 and 3.05, 2.12 to 4.40, respectively). Another trial (143 patients; atopic dermatitis of face and neck) compared tacrolimus 0.1% with aclometasone dipropionate 0.1% (mild corticosteroid).<sup>w17</sup> Tacrolimus 0.1% was significantly more effective at treating facial atopic dermatitis than aclometasone dipropionate 0.1% (rate ratio for proportion of patients achieving at least marked improvement (>75%) at one week 3.94, 2.21 to 7.00).

##### *Tacrolimus versus potent topical corticosteroids*

One trial (570 adults; moderate to severe atopic dermatitis) compared tacrolimus (0.03% and 0.1%) with hydrocortisone butyrate 0.1% (potent corticosteroid) and reported on the proportions of patients clear or achieving an excellent improvement at three weeks.<sup>w12</sup> Tacrolimus 0.03% was significantly less effective than hydrocortisone butyrate 0.1% (0.73, 0.58 to 0.92), whereas tacrolimus 0.1% was as effective (0.95, 0.78 to 1.17).

Two trials compared tacrolimus 0.1% with potent topical corticosteroids (betamethasone valerate 0.1%, hydrocortisone butyrate 0.1%) and reported on the proportions of patients achieving at least marked improvement (>75%) at three weeks.<sup>w12 w16</sup> Tacrolimus 0.1% was as effective as the potent topical corticosteroids (pooled rate ratio 1.08, 0.97 to 1.21).

##### *Tacrolimus versus potent corticosteroid (trunk) and mild corticosteroid (face)*

One trial (968 adults; moderate to severe atopic dermatitis) compared tacrolimus 0.1% with a combined regimen of hydrocortisone butyrate 0.1% (trunk and extremities) plus hydrocortisone acetate 1% (head and neck).<sup>w21</sup> At 12 weeks, tacrolimus 0.1% was significantly more effective than the combined regimen on the basis of the proportions of patients clear or achieving an excellent improvement (1.67, 1.41 to 1.98).

##### *Tacrolimus 0.03% versus tacrolimus 0.1%*

Six trials (1502 patients) directly compared tacrolimus 0.03% with tacrolimus 0.1%.<sup>w9-w13</sup> Three trials reported on the proportions of patients clear or achieving excellent improvement at three weeks and found no significant difference in response between strengths of tacrolimus (pooled rate ratio 0.89, 0.67 to 1.19; see fig 2). At 12 weeks in the three remaining trials, however, tacrolimus 0.1% was significantly more effective than tacrolimus 0.03% (0.80, 0.65 to 0.99). On the basis of the participants' global assessment of response of better or much better, there were no significant differences in response between strengths (three weeks: 0.84, 0.69 to 1.00; 12 weeks: 0.93, 0.83 to 1.03).

#### **Quality of life**

Information on quality of life was patchy, with a lack of common outcome measures. In two trials of pimecrolimus compared with vehicle, the parent's index of quality of life in atopic dermatitis was completed for a subset of patients; children who received pimecrolimus were judged to have a significantly improved quality of life than those receiving vehicle.<sup>5</sup> In one trial (192

adults; moderate to severe atopic dermatitis), patients receiving pimecrolimus had a significantly improved quality of life than those receiving vehicle, assessed using the quality of life index—atopic dermatitis and the dermatology life quality index.<sup>5</sup>

In three trials (985 patients), significant improvements in overall quality of life were found separately for infants, children, and adults treated with tacrolimus (0.03% and 0.1%) compared with vehicle.<sup>6</sup> In adults, tacrolimus 0.1% also resulted in a significantly greater improvement in quality of life compared with tacrolimus 0.03%, but no significant differences were found between strengths in infants or children.

#### Withdrawal from treatment

Significantly more patients withdrew from treatment with vehicle than with pimecrolimus 1% or tacrolimus 0.03% or 0.1% (table). No significant differences were found in rates of withdrawals due to adverse events between pimecrolimus 1% and vehicle, but there were significantly higher rates with tacrolimus (0.03% and 0.1%) (pooled rate ratios 0.50, 0.30 to 0.84 and 0.47, 0.28 to 0.80, respectively).

We found no significant differences in rates of withdrawals due to adverse events between any of the comparisons of pimecrolimus or tacrolimus (0.03% and 0.1%) with topical corticosteroids. Direct comparisons of tacrolimus 0.03% against tacrolimus 0.1% also showed no significant differences in withdrawals between the strengths (pooled rate ratio for overall withdrawals 0.75, 0.49 to 1.14 and for withdrawals due to adverse effects 0.99, 0.59 to 1.64).

#### Adverse effects

The most common adverse effects reported related to skin irritation and skin burning. No significant difference was found between pimecrolimus 1% and vehicle in the incidence of skin burning (pooled rate ratio obtained from six trials was 0.87, 0.70 to 1.09). However, we found a significantly higher rate of skin burning with pimecrolimus 1% than with betamethasone valerate 0.1% (5.26, 1.92 to 14.30) or a combined regimen of triamcinolone acetonide 0.1% and hydrocortisone acetate 1% (2.38, 1.66 to 3.40).

Tacrolimus (0.03% and 0.1%) was significantly more likely to cause skin burning than vehicle (pooled rate ratios 1.89, 1.43 to 2.50 and 2.08, 1.35 to 3.18, respectively). Both strengths were also significantly more likely to cause skin burning than mild or potent topical corticosteroids (see table). None of the trials reported on key adverse effects such as thinning of skin.

#### Discussion

Tacrolimus 0.1% is as effective as potent topical corticosteroids and more effective than mild topical corticosteroids, such as hydrocortisone acetate 1%, for treating atopic dermatitis. This means that topical tacrolimus may be useful for resistant atopic dermatitis at sensitive sites such as the face, where the use of more potent topical steroids carries a high risk of thinning of the skin and telangiectasia. Tacrolimus 0.1% may also be useful for patients who depend on the constant use of potent steroids.

#### What is already known on this topic

Atopic dermatitis affects 15-20% of children in developed countries

Topical corticosteroids and emollients have been the mainstay of therapy

Topical pimecrolimus and tacrolimus have been developed as alternative treatments

#### What this study adds

Tacrolimus 0.1% is as effective as potent corticosteroids for treating atopic dermatitis and more effective than mild preparations such as hydrocortisone acetate 1%

Pimecrolimus is less effective than potent corticosteroids; it has not been compared with mild corticosteroids

Both agents caused more burning of the skin than topical corticosteroids, but no differences were observed in rates of skin infections

Pimecrolimus, however, has been found to be less effective than betamethasone valerate 0.1%, a commonly used potent topical corticosteroid. The efficacy of pimecrolimus compared with less potent topical corticosteroids is not known. It prevented more flares than vehicle, but it remains to be seen whether the early use of mild steroids may be as effective.

The main reason for developing new drugs as an alternative to topical steroids is to overcome possible side effects from steroids, such as thinning of the skin. We found no evidence that these newer, more expensive products offer such an advantage when compared with standard practice. No thinning of the skin was found in one preliminary randomised controlled trial of pimecrolimus applied to normal skin for four weeks.<sup>7</sup> Such a study is difficult to generalise to people with atopic dermatitis who apply preparations over the course of a year. A non-randomised prospective study of 119 participants that compared 0.1% topical tacrolimus with conventional steroid based therapy and normal controls found no evidence of decreased skin collagen synthesis or skin thinning at one year in the tacrolimus group.<sup>8</sup>

#### Strengths and limitations of the review

In contrast to an earlier review of 16 studies,<sup>9</sup> we examined 25 clinical trials, using a wider range of clinically relevant outcome measures, and focused on direct comparisons with active treatments, rather than making indirect inferences from placebo controlled trials.

One limitation of our study is that our analysis of rates of withdrawals and adverse events were based on data pooled from trials of different durations. Other potential sources of heterogeneity in the results may include the age of the patient population, the severity of the disease, and the topical corticosteroid. Despite investigators' global assessments of response to treatment being widely used as outcome measures in clinical trials of atopic dermatitis, further research is

needed to fully determine their validity, reliability, and sensitivity to change.<sup>10 11</sup>

Contributors: See bmj.com

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Competing interests: None declared.

Ethical approval: Not required.

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## Commentary: Itching for a solution

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Ashcroft et al<sup>1</sup> illustrate a tension that exists between scientists and patients over the use of topical agents to treat atopic dermatitis, with doctors caught in the middle.

It must be difficult for those without eczema to understand how frustrating and distressing it can be. Having developed atopic eczema in early childhood, I have been living with it for over 60 years. As a boy, the insides of my arms and the backs of my legs itched ferociously and incessantly. My face was dry, flaking, and sore. The area between my upper lip and nose was dry, cracked, and crusted, as was the skin around my ears. I scratched endlessly, and my appearance embarrassed me dreadfully, which suited those who taunted me about it.

In the early days, the only treatment prescribed for me was hydrocortisone cream, which helped but provided no solution over time. Emollients were never mentioned. Slowly, I became more adept at managing my eczema and concealing it from others. The discovery of the benefits of moisturisation helped, as did a switch to cotton clothing. Today my eczema is well managed, but it still takes me about 20 minutes longer to get ready in the morning than it would if I had normal skin. All of which is why those of us who live with eczema are desperate for a cure—or at least for treatments better than those that have been available to date. It is also why we may occasionally be a little impatient with scientists who sometimes seem more preoccupied with the analysis of evidence than with patients' needs.

Non-adherence to treatment regimens is a major cause of treatment failure in the management of atopic eczema. High among the several causes of non-adherence is "corticosteroid phobia."<sup>2</sup>

As chief executive of the National Eczema Society in the late 1990s, I became acutely aware of the large proportion of callers to our helpline who were reluctant to use topical corticosteroids on themselves

or on their children. Their reluctance was caused chiefly by fear of damage to the skin but sometimes by confusion between topical corticosteroids and anabolic steroids.

Ashcroft et al acknowledge the importance of corticosteroid phobia in their paper (see bmj.com) but make no reference to it in their discussion or conclusions, although the paper to which they refer<sup>3</sup> makes clear the extent of such a phobia. And, given that eczema often affects the face and flexures, Ashcroft et al seem to underestimate the implications for patients of the inappropriateness of using topical corticosteroids on those areas.

Their conclusions have clearly been reached through careful and dispassionate analysis of the data, and we agree that more research is needed. Patients, however, long for treatments that are at least as effective as topical corticosteroids, have none of the side effects (real or imagined) that encourage corticosteroid phobia, and can be used safely on the face and flexures.

Tacrolimus and pimecrolimus seem to meet those requirements, which is why patients welcome them. The dilemma, of course, is the doctor's.

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- 1 Ashcroft DM, Dimmock P, Garside R, Stein K, Williams HC. Efficacy and tolerability of topical pimecrolimus and tacrolimus in the treatment of atopic dermatitis: meta-analysis of randomised controlled trials. *BMJ* 2005;330:516-22.
- 2 Beattie PE, Lewis-Jones MS. Parental knowledge of topical therapies in the treatment of childhood atopic dermatitis. *Clin Exp Dermatol* 2003;28:549-53.
- 3 Charman CR, Morris AD, Williams HC. Topical corticosteroid phobia in patients with atopic eczema. *Br J Dermatol* 2000;142:931-6.

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