Sir,
Rosacea is a chronically relapsing inflammatory skin disease that is estimated to affect at least 5% of the US population (1, 2). It is particularly common in fair-skinned people and affects mainly the central face. Based on patterns of physical findings, a classification in four broad subtypes (erythematotelangiectatic, papulopustular, phymatous, ocular) has been proposed (3). The precise aetiology and pathomechanism of rosacea is still unclear (1). Although rosacea is in principle a treatable disorder, none of the established therapies are fully satisfactory and there are cases that do not respond to standard therapies (1, 2, 4). Here we present a patient with granulomatous rosacea, unresponsive to corticosteroids and antibiotics, who was treated with pimecrolimus cream 1% with excellent results.

CASE REPORT
A 58-year-old Caucasian woman had been exposed to hormonal replacement on a steady basis for 3 years prior to the first appearance of rosaceaform lesions on the central face (Fig. 1A). As a potential provoking factor, hormonal replacement was discontinued on the advice of her gynaecologist and treatment with a topical corticosteroid (betamethasone valerate) was prescribed by a dermatologist. As lesions worsened, topical corticosteroid treatment was stopped and replaced by a combination of topical metronidazole gel 0.75 mg b.i.d. and oral tetracycline 500 mg twice daily, for 45 days. However, this treatment resulted in no clinical improvement. The patient was referred to our dermatological specialists. Granulomatous rosacea was diagnosed clinically and confirmed by the results of the histopathological analysis of a biopsy: lymphocytic inflammatory infiltrate in the superficial and deep dermis with rare plasmocytes, some neutrophilic agglomerates and epithelioid histiocyte proliferation forming granulomas with a vast number of multinuclear giant cells (Fig. 2A–C); in the superficial dermis dilation of lymphatic and blood vessels (Fig. 2D).

Treatment with pimecrolimus cream 1% (Elidel®, Novartis Pharma) twice daily was started and the patient was advised to avoid caffeine, spicy food, alcohol and hot liquids. The patient agreed not to use any other medication, topical or oral, during the treatment period. The therapeutic effect was evaluated on the basis of erythema severity, number of papulonodular lesions and overall clinical assessment of the rosacea, and was documented photographically on visits 16, 56, 88, 112 days after the start of treatment. The cream was applied twice a day for the first 180 days. After this period the patient reduced her applications to once a day and continued this use until 211 days after treatment commencement. A steady improvement of the disease over time was observed (Fig. 1B–E). After a slow onset of efficacy in the first weeks, a dramatic clearing of symptoms was observed between the 37th and 56th day of treatment and a complete resolution of all signs and symptoms was achieved after 112 days. The follow-up examination on day 211 showed the patient to be 100% cured with no rebounds observed after the initial clearing. Six months after the 211-day follow-up, the patient was completely lesion- and symptom-free even after stopping pimecrolimus applications.

DISCUSSION
Pimecrolimus is a non-steroid calcineurin inhibitor that acts specifically on T cells and mast cells, preventing the production and release of cytokines and other inflammatory mediators (5, 6). Pimecrolimus cream 1% has proven to be well-tolerated, safe and effective in atopic dermatitis (atopic eczema), especially on delicate skin areas such as the face, a location that is primarily affected by rosacea (6–8). Apart from the wide experience with pimecrolimus cream 1% in the treatment of atopic dermatitis with more than 5000 patients treated...
to date, there is also evidence for a therapeutic potential of pimecrolimus in other inflammatory skin diseases (7). Here we report on the successful treatment of a case of rosacea with a history of worsening due to corticosteroid treatment, leading to complete clearance of symptoms after 4.5 months with no rebound observed. Onset of efficacy was noticed already within the first weeks, whereas the previous treatment with a combination of topical metronidazole and systemic tetracycline had resulted in no improvement within 45 days. Topical tacrolimus (Protopic® ointment), another calcineurin inhibitor, has recently been reported to be effective in an open-label study in patients with erythrotelangiectatic and papulopustular rosacea as well as in three cases of steroid-induced rosacea (9, 10). Interestingly, there is a report of six cases in which patients treated with tacrolimus ointment 0.1% for atopic dermatitis or other inflammatory skin conditions developed rosaceaform dermatitis (11). One case of atopic dermatitis with a similar complication under pimecrolimus treatment was published by the same group (12). However, at least in the case of pimecrolimus, this appears to be a rare event, considering the large number of patients treated with pimecrolimus cream 1% without complications so far. In the case of rosacea described here, pimecrolimus cream 1% was well tolerated and the use of a cream might be preferable to an ointment in the treatment of inflamed facial skin.

Although the precise pathomechanism of rosacea is still unclear, involvement of T cells has been discussed (13), and one might speculate that the therapeutic effects observed with pimecrolimus and tacrolimus are due to the anti-inflammatory activity based on inhibition of T-cell or mast cell activation.

In conclusion, the results reported here suggest that pimecrolimus cream 1% might have the potential for a safe and effective treatment of rosacea. The scope of the therapeutic potential has, however, to be explored in various subtypes of the disease and clinical efficacy confirmed in controlled clinical studies.

No conflict of interest reported.

REFERENCES