RESEARCH LETTER

Effectiveness and Safety of Delgocitinib Cream in Pustulosis Palmoplantaris: A Case Series

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To the Editor,

Palmoplantar pustulosis (PPP) is a chronic immune-mediated skin disease characterized by recurrent erythema, scaling, and eruption of sterile pustules on palms and soles (1, 2). PPP can be subclassified based on co-occurrence of plaque psoriasis according to the European Rare And Severe Psoriasis Expert Network (ERASPEN) (2). Treatment of PPP is challenging, and only 12–27% of patients respond, i.e., achieving PPP Area and Severity Index (PPPASI) reduction of minimum 75%, to biologics approved for plaque psoriasis (3). Interestingly, recent case reports have shown effectiveness of the oral Janus kinase (JAK) inhibitors tofacitinib (4) and upadacitinib (5, 6) in treatment refractory PPP cases (7). However, PPP is associated with smoking and due to the black box of JAK inhibitors, other treatments should be investigated. As PPP in most cases affects an area limited to palms or soles, topical treatment might be a viable treatment option. Indeed, delgocitinib (8), a topical pan JAK inhibitor recently approved for chronic hand eczema, could theoretically be efficacious.

Four patients with treatment refractory PPP without plaque psoriasis were treated with delgocitinib (20 mg/g) cream twice daily, according to recommendations for the treatment of hand eczema. PPPASI (ranging from 0–72) and Dermatology Life Quality Index (DLQI) (ranging from 0–30) were assessed at baseline and after 4 weeks.

- *Patient 1:* A 63-year-old female previously treated with 17.5 mg methotrexate (MTX) orally every week, 25 mg acitretin daily, and 20 mg MTX subcutaneously (SC) every week, both as monotherapy and in combination with 10 mg acitretin daily, all without sufficient effectiveness. At baseline, she had involvement of hands and feet with PPPASI 31.2 and DLQI 17. No effectiveness of treatment was observed (**Table I**).
- *Patient 2:* A 75-year-old female previously treated with 25 mg acitretin daily, 15 mg MTX every week both orally and SC, and lastly with 0.5 mg tablet roflumilast daily, all without sufficient effectiveness. At baseline, she had involvement of hands and feet with PPPASI 13.9 and DLQI 16. No effectiveness of treatment was observed (see Table I).
- *Patient 3:* A 46-year-old female previously treated with 25 mg acitretin daily and 15 mg tablet MTX every week, which were both stopped due to side effects but had had some effectiveness on her disease. At baseline, she had involvement of the feet with baseline PPPASI of 8.4 and DLQI of 3 (see Table I). A burning sensation was described in association with the application of cream. No effectiveness of treatment was observed (**Fig. 1**).
- *Patient 4:* A 29-year-old male previously treated with 25 mg acitretin daily, 15 mg tablet MTX every week and 0.5 mg tablet roflumilast (Daxas®, an oral phosphodiesterase-4 inhibitor) daily, all with insufficient effectiveness. At baseline, PPPASI was 19.8 and DLQI 13. At 4 weeks, he had improvement in the skin of both hands and feet with a PPPASI of 8.3 corresponding to a 58% reduction. No side-effects were observed following treatment.

In this case series, treatment with delgocitinib cream twice daily for 4 weeks was well tolerated, but for 3 of 4 patients with PPP the treatment showed no effectiveness on their disease. One patient showed marked improvement. The findings illustrate that although most of the patients had no response, certain patients with PPP might benefit from treatment with delgocitinib. Indeed, the included patients had very difficult-to-treat PPP and in this population only around 25% of patients respond to biologics inhibiting interleukin-23 (3). Interestingly, as PPP show a Th17/Th2 signature (9) and as some patients share clinical features with that of palmoplantar eczema, JAK inhibition might be more favourable in certain subgroups of patients with PPP.

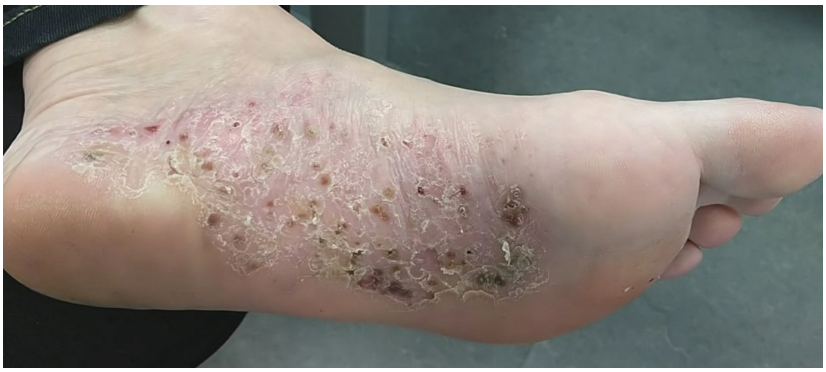
An important limitation to the findings is that patients were treated for only 4 weeks, and a clinical response might occur later. However, due to the off-label use, the exploratory nature of the treatment, and as some patients experienced worsening, we did not continue therapy in those without effectiveness beyond this point. Furthermore, as PPP is a relapsing-remitting disease we cannot

Table I. Characteristics of patients treated with delgocitinib cream twice daily for 4 weeks

Patient no.	Age	Sex	Previous systemic treatments	Smoking status	Plaque psoriasis	Involvement	PPPASI Week 0	DLQI Week 0	PPPASI Week 4	DLQI Week 4
1	63	F	MTX, acitretin, combination of MTX and acitretin	Current	No	Hands and feet	31.2	17	30.0	22
2	75	F	Acitretin, roflumilast, MTX	Previous	No	Hands and feet	13.9	16	20.7	N/A
3	46	F	MTX, acitretin	Previous	No	Feet	8.4	3	8.4	2
4	29	M	MTX, acitretin, roflumilast	Current	No	Hands and feet	19.8	13	8.3	9

DLQI: Dermatology Life Quality Index (range 0–30); F: female: M: male; MTX: methotrexate; N/A: not applicable; PPPASI: Palmoplantar Pustulosis Area and Severity Index (range 0–72).

(A)



(B)

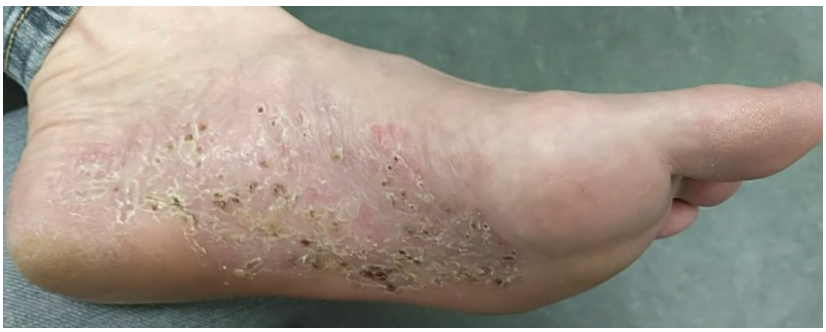


Fig. 1. **Photos of skin involvement of patient 3 at** (A) baseline and (B) after 4 weeks of treatment.

refute the response achieved by patient 4 being part of the natural disease course. Nevertheless, this was a patient with several prior failed systemic treatments for PPP and considered to have difficult-to-treat PPP.

In conclusion, while most patients did not respond, delgocitinib might benefit certain patients with PPP but more case reports in addition to controlled studies are needed.

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Ethics statement: The patient pictured in this manuscript has given written informed consent to publication of photographs and case details.

Conflicts of interest: NL has been a paid speaker for Eli Lilly, Janssen Cilag, and Sandoz and received research funding from the LEO Foundation. CZ has been a paid speaker for Leo Pharma and UCB and been consultant for Leo Pharma, Takeda, Galderma, and UCB. MG has been a paid speaker for Galderma Nordic AB. LS has received research funding from Novartis, Bristol-Myers Squibb, AbbVie, Janssen Pharmaceuticals, the Danish National Psoriasis Foundation, the LEO Foundation, and the Kgl. Hofbundtmager Aage Bang Foundation and received honoraria as consultant and/or speaker for AbbVie, Eli Lilly, Novartis, Pfizer, LEO Pharma, Janssen, UCB, Almirall, Galderma, Stada, Myers Squibb, and Sanofi. FA and DKK have no conflicts of interest to declare.

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