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Reply to: Successful treatment of recalcitrant nodular prurigo with tofacitinib

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Dear Editor,

We read with interest Molloy *et al's* letter describing a patient with recalcitrant nodular prurigo (NP) responding to tofacitinib.[1] While we recognise the IL-31 and IL-4 mediated therapeutic potential of tofacitinib to inhibit pruritus, our experience has been disappointing. We present three further cases that highlight the heterogeneity in the response of NP to tofacitinib.

Case 1:

A 29-year old male with severe facial atopic dermatitis (AD) and NP was commenced on 2.5mg tofacitinib in combination with ongoing topical corticosteroids (TCS). Though AD severity and pruritis had improved at 6-month review, there was no improvement in his facial AD nor NP lesions. Topical pimecrolimus was added with modest effect. Despite an increase in tofacitinib dose to 5mg daily severe pruritus ensued and following a significant impact on quality of life the patient decided to withdraw treatment after 32 months of treatment. He did not experience any side effects throughout treatment.

Case 2:

A 16-year old boy with a 10-year history of patchy alopecia areata (AA; SALT 27), AD, NP, allergic rhinitis and asthma, was started on tofacitinib 2.5mg daily, while continuing on cyclosporine (5mg/kg) to manage both his AA and severe AD with NP. No improvement in NP was noted at 2 month review, despite an improvement in AD severity. Tofacitinib was subsequently increased to 5mg daily, ciclosporin weaned and NP lesions treated with intralesional triamcinolone. After 12 months of treatment with tofacitinib, full resolution of AA was seen (SALT 0), however, no improvement in AD or NP severity was noted, prompting a dose increase of tofacitinib to 7.5mg and addition of topical tacrolimus. A severe AD flare requiring treatment with systemic corticosteroids, after 19 months of treatment with tofacitinib, prompted its cessation. He did not experience any side effects throughout treatment.

Case 3:

A 25-year old female with AA (SALT 30), AD, NP and asthma, had been on methotrexate (25mg weekly) with modest improvement in her eczema control. Tofacitinib 2.5mg was added to methotrexate. Prior therapy included ciclosporin (2.5mg/kg) and narrowband UVB

phototherapy (Table 1). Following one month of treatment, NP severity was unchanged whilst minimal improvement in AD severity and partial resolution of AA was observed. Topical corticosteroids and antihistamines were added. Methotrexate was reduced (to 15mg weekly) and then stopped after 5 months of combination with tofacitinib whilst the latter was titrated to a maximum dose of 16mg daily over 10 months. No improvement in NP lesions prompted tofacitinib discontinuation after a total of 15 months of therapy. She experienced no side effects.

We anticipated that tofacitinib would benefit our patients with refractory NP and atopy based on its presumed mechanism of action, and were disappointed with our patient's treatment outcomes. Notably, the dose received by Molloy *et al.*'s patient (10mg daily) was higher than in two of our patients but we also acknowledge that the optimal therapeutic dose of tofacitinib in various dermatological conditions is yet to be established. The varied response to tofacitinib may reflect heterogeneity in NP pathogenesis, as NP features in a number of conditions.[2] With multifactorial evolution of the itch-scratch cycle and neuronal sensitisation leading to pruriginous lesions, we suggest that tofacitinib might only benefit a sub-group of NP patients. More studies are needed to confirm this.

REFERENCES

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Table 1: Clinical and treatment details of three patients with nodular prurigo not responsive to tofacitinib

Case	Disease duration, y	Previous therapies	Average daily tofacitinib dose, mg	Total duration of treatment, mo	Concurrent therapies*
1	>10	TCS, anti-histamines	3.3	32	TCS
2	10	TCS, ciclosporin (5mg/kg)	5.8	20	Ciclosporin (2 months), topical tacrolimus, TCS, intralesional steroids, systemic steroids
3	>10	Methotrexate (25mg weekly), ciclosporin (2.5mg/kg), NB-UVB	8.6	15	Methotrexate (5 months), TCS, anti-histamines

Abbreviations: mo, months; NB-UVB, narrow-band UVB; TCS, topical corticosteroids; y, years

* Concurrent therapies were continued throughout whole treatment duration unless otherwise specified