Treatment of recalcitrant atopic dermatitis with the oral Janus kinase inhibitor tofacitinib citrate

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Background: Treatment of moderate to severe atopic dermatitis (AD) is often inadequate.

Objective: We sought to evaluate the efficacy of the oral Janus kinase inhibitor tofacitinib citrate in the treatment of moderate to severe AD.

Methods: Six consecutive patients with moderate to severe AD who had failed standard treatment were treated with tofacitinib citrate. Response to treatment was assessed using the Scoring of AD index.

Results: Decreased body surface area involvement of dermatitis and decreased erythema, edema/papulation, lichenification, and excoriation were observed in all patients. The Scoring of AD index decreased by 66.6% from 36.5 to 12.2 ($P < .05$) during 8 to 29 weeks of treatment. There were no adverse events.

Limitations: Small sample size, lack of placebo control group, and the possibility of bias are limitations.

Conclusion: The oral Janus kinase inhibitor tofacitinib citrate may be beneficial in the treatment of moderate to severe AD. (J Am Acad Dermatol 2015;73:395-9.)

Key words: atopic dermatitis; Janus kinase inhibitor; tofacitinib.

Atopic dermatitis (AD), a chronic, pruritic inflammatory skin disease, affects 10% to 30% of the pediatric population and 1% to 3% of the adult population.[1,2] Notably, quality of life (QoL) is significantly diminished in AD.[3,4] Pruritus, a prominent feature of AD, is often severe and gives rise to QoL measurements similar to those seen in chronic pain.[5]

In contrast to the significant advances in targeted and biologic therapies for another inflammatory skin disease, psoriasis, the mainstay of treatment for AD includes nonpharmacologic emollients, topical corticosteroids and calcineurin inhibitors, phototherapy, and, for refractory disease, immunomodulatory agents (eg, cyclosporine, methotrexate, azathioprine).[6,7] These therapies are often inadequate for moderate to severe disease.[8-10]

Abbreviations used:

AD:	atopic dermatitis
IL:	interleukin
JAK:	Janus kinase
QoL:	quality of life
SCORAD:	Scoring of Atopic Dermatitis
STAT:	signal transducer and activator of transcription
Th2:	type 2 helper T-cell

Recent advances in our understanding of the pathogenesis of AD have led to the possibility of new, targeted treatments. An exaggerated type 2 helper T-cell (Th2) immune response is well established in the pathogenesis of AD, and dupilumab, a monoclonal antibody that inhibits signaling by interleukin (IL)-4 and IL-13, 2 cytokines

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that are required for Th2 immune responses, has demonstrated reductions in eczema severity when compared with topical corticosteroids in phase I and II clinical trials.[11] Emerging data supports the role of the Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathway in Th2 immunity, activating eosinophils, and suppressing regulatory T cells.[12] Tofacitinib citrate, an oral JAK 1/3 inhibitor approved for the treatment of moderate to severe rheumatoid arthritis, has recently been shown to reverse alopecia areata,[13] which is often associated with AD,[14] and is being evaluated as a topical agent in AD.[15] Here we report the use of oral tofacitinib for patients with refractory moderate to severe AD.

CAPSULE SUMMARY

- Moderate to severe atopic dermatitis is often recalcitrant to treatment.
- We report marked clinical improvement in 6 patients with moderate to severe atopic dermatitis treated with tofacitinib citrate, an oral Janus kinase inhibitor.
- Tofacitinib and other Janus kinase inhibitors are promising agents for the treatment of atopic dermatitis.

METHODS

Patients

Six consecutive patients with moderate to severe AD (defined as >10% body surface area involvement and Scoring of AD [SCORAD] index >20) who had failed standard therapy were treated with tofacitinib at a tertiary care referral center between September 2014 and May 2015.

Treatment with tofacitinib

The dose of tofacitinib was 5 mg twice daily in 5 patients (the rheumatoid arthritis dose) and 5 mg once daily in 1 patient (patient 3 experienced near remission of her symptoms with a lower dose of 5 mg once daily and therefore did not increase to twice daily dosing). All other immunomodulatory agents were discontinued at least 2 weeks before starting tofacitinib except in 1 patient (patient 4) who required prednisone 5 mg twice daily at the initiation of tofacitinib treatment because of severe pruritus. Treatment with topical corticosteroids and topical calcineurin inhibitors could be continued during treatment with tofacitinib at the patient's discretion.

Baseline laboratory evaluation was performed before starting tofacitinib and included complete blood cell count, basic metabolic panel, hepatic function panel, lipid panel, purified protein derivative or QuantiFERON-TB Gold (Cellestis Limited, Melbourne, Australia), and HIV and hepatitis B and C serologies. Complete blood cell count, basic metabolic panel, hepatic function panel, and lipid panel were repeated every 4 weeks during treatment with tofacitinib.

Response to treatment with tofacitinib

Response to treatment was measured using the SCORAD index, a validated scoring system that incorporates both objective physician assessment of the extent and severity of dermatitis and pruritus and the subjective patient-reported assessment of pruritus and sleep loss.[16] The SCORAD index was measured before starting tofacitinib and at 2 follow-up visits after starting the medication to assess for changes over time (the timing of the follow-up visits varied between patients). Treatment was neither held nor withdrawn at any time. The same clinician (B. A. K.) completed the objective clinical evaluation of the SCORAD index at every patient visit.

RESULTS

Patients

Among the 6 patients, 4 were female and 2 were male; the age range was 18 to 55 years old. All but 1 patient had previously failed at least 2 immunomodulatory agents (Table I).

Response to treatment

After initiation of treatment, the SCORAD index was assessed at 4 to 14 weeks and again at 8 to 29 weeks. In all 6 patients, treatment with tofacitinib resulted in decreased body surface area of dermatitis and improvement in erythema, edema/papulation, excoriation, and lichenification (Fig 1). In addition, all 6 patients reported improvement in pruritus and decreased sleep loss after starting tofacitinib. Reflecting these changes, the composite SCORAD index decreased after starting tofacitinib for all of the patients (Fig 2), and this improvement was maintained during follow-up. The average SCORAD index decreased by 54.8% from 36.5 to 16.5 ($P < .05$) during the initial 4 to 14 weeks of treatment (the time to the first follow-up assessment), and this improvement was maintained subsequently with a reduction in the SCORAD index of 66.6% from 36.5 to 12.2 ($P < .05$) observed during 8 to 29 weeks of treatment (the time to the second follow-up