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Topical tofacitinib for the treatment of alopecia areata affecting facial hair

Dear Editor,

Alopecia areata (AA) is a common autoimmune condition which can affect any hair-bearing site. Recent studies have demonstrated the effectiveness of Janus kinase inhibitors (JAKis) in the treatment of AA. Most studies documenting response of AA affecting facial hair to JAKi therapy involve oral administration due to extensive concomitant scalp involvement.[1-2] However, oral JAKis are associated with adverse effects, e.g. infections, in 2-6% of patients.[3] Topical JAKis may offer a safer alternative for limited disease, or in cases where systemic therapy is contraindicated or not desired.[3-5] To our knowledge, published reports on the use of topical JAKis in eyebrow and eyelash AA are limited to a small number of cases,[3-5] and none have investigated their effectiveness for beard AA. Our objective was to evaluate the response of AA affecting facial hair to topical tofacitinib.

We retrospectively reviewed the records of all patients with eyebrow, eyelash and/or beard AA who were treated with topical tofacitinib between October 2014 and January 2021. Patients treated with topical tofacitinib (2% gel b.i.d for eyebrow and beard AA, or 0.005% eye drops o.d for eyelash AA) for $\geq$ 3 months were included. Tofacitinib was compounded into a 2% Pluronic gel or a 0.005% aqueous solution by a local pharmacy. Patients who received concomitant topical or intralesional therapies, such as corticosteroids, were excluded. Of the patients also receiving systemic therapies, only those without treatment changes in the previous 6 months were included. Clinical involvement and response were evaluated at baseline and post-treatment using standardised photographs. Eyebrow/eyelash alopecia was graded using the 4-

point clinician-reported outcome (ClinRO) measure,[6] and beard regrowth was documented as none, partial or complete.

Of 26 patients (17 male; 9 female) with a mean age of 30.2 (range 6-54) years, 18 had eyebrow AA, 4 had eyelash AA and 9 had beard AA (Table 1). The mean duration of facial hair loss was 54.4 (range 2-300) months, while the mean length of topical tofacitinib treatment was 7 (range 3-22) months. Partial and complete regrowth were observed in 4 and 8 patients with eyebrow AA respectively. All 4 patients with eyelash involvement treated with topical ophthalmic tofacitinib experienced complete regrowth. Of those with beard AA, 5 experienced partial regrowth whereas 2 experienced complete regrowth. Five patients had AA affecting 2 facial hair-bearing sites (2 with eyebrow/beard; 3 with eyebrow/eyelash). Of those, complete regrowth in both areas was achieved in 80% (4/5) and partial regrowth in 20% (1/5). No adverse events were reported.

Eyebrows, eyelashes and beard play important aesthetic and functional roles. Consequently, loss of facial hair can result in significant psychological impairment. Topical treatments for AA affecting facial hair are currently lacking, given that potent/super-potent topical corticosteroids are contraindicated for prolonged durations and calcineurin inhibitors have failed to demonstrate efficacy.[7] On the other hand, intralesional corticosteroid injections can cause atrophy and may not be tolerated in some cohorts e.g. children. Our study showed that patients with partial eyebrow involvement were more likely to achieve complete regrowth with topical tofacitinib than those with total eyebrow loss. Similarly, complete regrowth was observed in our patients with eyelash alopecia, all of whom had minimal, evenly distributed gaps. However, no such trend was observed in patients with beard AA. In patients with AA affecting >1 facial area, individual hair-bearing sites responded similarly to topical tofacitinib. A similar phenomenon has been described in patients with scalp and beard AA treated with oral tofacitinib.[2] In contrast, scalp and eyebrow/eyelash AA responded differently to oral tofacitinib.[1] A higher proportion of our patients treated with topical tofacitinib achieved complete hair regrowth (eyebrows 44.4%; eyelashes 100.0%; beard 28.6%) than those treated with oral tofacitinib (eyebrows 34.5%;[1] eyelashes 38.7%;[1] beard 22.2%)[2]. Furthermore, our results suggest a better response to topical tofacitinib of AA affecting facial hair than scalp AA.[3-4] However, it needs to be acknowledged that most of our patients who achieved complete regrowth had relatively limited disease, in contrast to studies of oral tofacitinib for the treatment of severe AA or topical tofacitinib for the treatment of scalp AA in which the majority of patients had extensive hair loss, including alopecia universalis, and consequently had a poor prognosis from the outset. Additionally, facial hair bulbs are more superficial than their scalp

counterparts and may therefore be more accessible to topical therapies.[8] Only 4 patients (2 with eyebrow AA and 2 with beard AA) had been on concomitant systemic treatments for moderate-to-severe scalp AA for >6 months with failure of any facial hair regrowth. Three (75%) of those patients experienced regrowth of eyebrow or beard hair with the introduction of topical tofacitinib. Although we cannot fully exclude regrowth induced by systemic treatments, it is likely that topical tofacitinib was responsible for facial hair regrowth in these 3 patients. Finally, we acknowledge the possibility of spontaneous improvement. However, it is noteworthy that our patients had failed to achieve any spontaneous regrowth for 54.4 (range 2-396) months prior to the initiation of topical tofacitinib treatment, suggesting that the latter likely accounted for the improvement.

Limitations of our study include the small sample size and retrospective design. Furthermore, we cannot ascertain whether the effect of topical tofacitinib was long-lasting as most patients who achieved cosmetically significant regrowth were discharged or lost to follow-up. Our findings suggest that topical tofacitinib may be an effective and safe treatment for AA affecting the eyebrows, eyelashes and beard.

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Table 1 Response to topical tofacitinib of 26 patients with alopecia areata affecting facial hair.

	Value, N = 26	**ClinRO measure for hair loss post-treatment, n (%)**			
		0	1	2	3
ClinRO Measure for Eyebrow Loss pre-treatment, n (%)					
0 (full coverage)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1 (minimal gaps in hair, evenly distributed)	6 (23.1)	5 (83.3)	1 (16.7)	0 (0.0)	0 (0.0)
2 (significant gaps in hair or uneven distribution)	7 (26.9)	2 (28.6)	2 (28.6)	2 (28.6)	1 (14.2)
3 (no notable hair)	5 (19.2)	1 (20.0)	0 (0.0)	2 (40.0)	2 (40.0)
ClinRO Measure for Eyelash Loss pre-treatment, n (%)					
0 (full coverage)	0 (0.0)	0 (0.0)			
1 (minimal gaps in hair, evenly distributed)	4 (15.4)	4 (100.0)			
2 (significant gaps in hair or uneven distribution	0 (0.0)	0 (0.0)			
3 (no notable hair)	0 (0.0)	0 (0.0)			
		Degree of beard regrowth			

		Complete	Partial	None
Pattern of beard loss, n (%)				
Solitary patch	1 (3.8)	0 (0.0)	0 (0.)	1 (100.0)
Multiple patches	7 (26.9)	2 (28.6)	4 (57.1)	1 (14.3)
Total beard loss	1 (3.8)	0 (0.0)	1 (100.0)	0 (0.0)