RESEARCH LETTER

Strategies for Managing Suboptimal Response to JAK Inhibitors in Alopecia Areata

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To the Editor,

Significant advancements in the treatment of alopecia areata (AA) have been achieved with Janus kinase (JAK) inhibitors, including baricitinib (JAK1/2 inhibitor) and ritlecitinib (JAK3/TEC family kinase inhibitor), both of which have been approved for this indication. While these agents have demonstrated robust efficacy in many patients, some experience suboptimal outcomes ranging from primary non-response to just partial, cosmetically not significant regrowth or deterioration after initial improvement. Addressing these therapeutic challenges requires individualized, evidence-based strategies that take into account disease severity, comorbid conditions, and emerging clinical data.

In hair clinics that manage complex cases, including referrals from general dermatologists, it is not uncommon for treatment outcomes to deviate from expectations. To assist clinicians encountering such challenges, we propose four pragmatic clinical strategies – *patience, add-on, switching, and dose optimization* – grounded in both current literature and our own clinical experience. Nonetheless, validation through future clinical trials remains essential.

For patients who after 6 months demonstrate a partial but positive response, it may be beneficial to extend the treatment period for another 6 months, and if then considerable regrowth is experienced, another year is justified. JAK inhibitors can produce slow but steady improvements in hair regrowth for responsive individuals. This "watch-and-wait" strategy relies on clinical judgement and shared decision-making, recognizing that regrowth may occur over many months (1). A significant proportion of patients with AA demonstrate gradual (SALT30 at weeks 12–36) or late (SALT30 after 36 weeks) response to JAK inhibitors, highlighting the need for extended treatment durations before deeming therapy ineffective (2, 3).

For those with an insufficient response, combination therapy may enhance efficacy. Treatment with JAK inhibitors can be supplemented with topical, intralesional, or short-term systemic corticosteroids, or a combination of these. Topical minoxidil may also be considered as part of a combined therapy regimen (4). Furthermore, combining low-dose oral minoxidil with a JAK inhibitor appears to be more effective in treating AA than JAK inhibitors monotherapy, suggesting a potential synergistic effect (5, 6). Additionally, contributing factors need to be addressed, such as stress or deficiencies in micronutrients (7).

Preliminary reports suggest that switching between JAK inhibitors, i.e., from broad range to more specific agents and vice versa, may offer benefits in select patients with AA who exhibit a partial response or relapse after an initial favourable response (8). This approach is supported by emerging evidence indicating differential responses to different JAK inhibitors, which may be due to variations in JAK selectivity, pharmacokinetics, or patient-specific immune profiles.

In certain refractory or severe cases of AA, some clinicians have explored increasing the dosage of JAK inhibitors – such as escalating baricitinib to 6 mg or even 8 mg per day – in an effort to enhance therapeutic response. While this dose-escalation strategy may theoretically improve efficacy and is supported by the dose-finding initial studies, it remains highly controversial due to the absence of robust clinical trial data supporting its safety or superior effectiveness. Moreover, JAK inhibitors are associated with a well-documented, dose-dependent risk profile, including serious adverse events such as thromboembolic complications, opportunistic infections, and potential malignancy. Until more data are available, this approach should be used cautiously and off-label and should only be considered under rigorous monitoring.

The management of suboptimal response to JAK inhibitors in AA remains an evolving challenge. Management of inadequate response to JAK inhibitors in AA should be individualized. Clinicians must weigh the risks and benefits of continued therapy, combination regimens, switching agents, or off-label dose escalation. Future randomized controlled trials are essential to define evidence-based pathways for treatment optimization.

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REFERENCES

1. Kwon O, Senna MM, Sinclair R, Ito T, Dutronc Y, Lin CY, et al. Efficacy and safety of baricitinib in patients with severe alopecia areata over 52 weeks of continuous therapy in two phase III trials (BRAVE-AA1 and BRAVE-AA2). Am J Clin Dermatol 2023; 24: 443–451. https://doi.org/10.1007/s40257-023-00764-w
2. King B, Shapiro J, Ohyama M, Egeberg A, Piraccini BM, Craiglow B, et al. When to expect scalp hair regrowth during treatment of severe alopecia areata with baricitinib: insights from trajectories analyses of patients enrolled in two phase III trials. Br J Dermatol 2023; 189: 666–673. https://doi.org/10.1093/bjd/ljad253
3. Senna M, Mostaghimi A, Ohyama M, Sinclair R, Dutronc Y,

Wu WS, et al. Long-term efficacy and safety of baricitinib in patients with severe alopecia areata: 104-week results from BRAVE-AA1 and BRAVE-AA2. J Eur Acad Dermatol Venereol 2024; 38: 583–593. https://doi.org/10.1111/jdv.19665
4. Majewski M, Gardaś K, Waśkiel-Burnat A, Ordak M, Rudnicka L. The role of minoxidil in treatment of alopecia areata: a systematic review and meta-analysis. J Clin Med 2024;13: 7712. https://doi.org/10.3390/jcm13247712
5. Rudnicka L, Arenbergerova M, Grimalt R, Ioannides D, Katoulis AC, Lazaridou E, et al. European expert consensus statement on the systemic treatment of alopecia areata. J Eur Acad Dermatol Venereol 2024; 38: 687–694. https://doi.org/10.1111/jdv.19768
6. Valido K, Kalil L, Peterson D, King B. Combination oral minoxidil and baricitinib treatment of alopecia areata. J Am Acad Dermatol 2025; May 16 [Online ahead of print]. https://doi.org/10.1016/j.jaad.2025.05.1393
7. Thompson JM, Mirza MA, Park MK, Qureshi AA, Cho E. The role of micronutrients in alopecia areata: a review. Am J Clin Dermatol 2017; 18: 663–679. https://doi.org/10.1007/s40257-017-0285-x
8. Kazmi A, Moussa A, Bokhari L, Bhoyrul B, Joseph S, Chitreddy V, et al. Switching between tofacitinib and baricitinib in alopecia areata: a review of clinical response. J Am Acad Dermatol 2023; 89: 1248–1250. https://doi.org/10.1016/j.jaad.2023.03.041