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Maria Esposito[1], Mario Bruno Guanti[2], Pietro Morrone[3], Maddalena Napolitano[4], Elena Pezzolo[5], Mariateresa Rossi[6]

[1]Department of Applied Clinical and Biotechnological Sciences, University of L'Aquila
[2]Allergology Service, Dermatology Unit, University Hospital of Modena
[3]Dermatology Unit, Cosenza Hospital
[4]Department of Clinical Medicine and Surgery, University of Naples Federico II
[5]Dermatology Unit, San Bortolo Hospital, Vicenza
[6]Department of Experimental and Clinical Sciences, University of Brescia

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Via Gallarate, 106
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redazione@clinicalnetwork.it

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Janus Kinase Inhibitors as first line therapeutic option in atopic dermatitis: a selection of phenotypes to start from

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[5]Dermatology Unit, San Bortolo Hospital, Vicenza
[6]Department of Experimental and Clinical Sciences, University of Brescia

Introduction

Atopic dermatitis (AD) is a chronic, systemic, inflammatory skin disorder associated with a heterogeneous clinical presentation and a significant disease burden affecting multiple aspects of patients' life.[1,2] Conventional systemic therapies, such as cyclosporine A (CsA) and corticosteroids (SCS), present limited efficacy, and long-term toxicity. Hence, long-term control of AD poses a challenge for both clinician and patients.[3] During the last decade, thanks to a deeper insight into the complex pathogenesis of AD, great and rapid advances in drug development have been made.[3,4] Target therapies for the treatment of moderate to severe AD with different mechanisms of action have been developed, such as interleukin (IL)-4 and/or IL-13 inhibitors and the most recent Janus kinase inhibitors (JAKi).[3] While IL-4 and/or IL-13 inhibitors play a crucial role in type 2 driven inflammation of AD,[5] JAKi can reversibly control multiple inflammatory pathways, including Th22 and Th1, which have been shown to be involved in both the acute and the chronic stage of AD, respectively.[6,7]

Currently, three JAKi have been approved by the European Medicine Agency (EMA) for the treatment of moderate to severe AD: baricitinib, upadacitinib and abrocitinib.[8-10] Clinical trials data have shown a favorable benefit-risk profile for the three molecules, characterized by high efficacy and rapid resolution of skin lesions and pruritus.[6] Furthermore, upadacitinib 30 mg and abrocitinib 200 mg showed superior efficacy in resolving AD skin lesions (assessed as a ≥75% or a ≥90% improvement in Eczema Area and Severity Index (EASI75/EASI90) and in reducing significantly itch, compared to dupilumab 300 mg, in adult patients with moderate to severe AD, after 16 weeks of treatment.[11,12] Furthermore, among all available targeted systemic therapies, upadacitinib 30 mg showed the highest efficacy, measured as Investigator Global Assessment (IGA)-AD 0/1 and EASI90, according to a recent network meta-analysis.[12-14] High clinical efficacy, due to deeper and more profound clinical responses, is associated with improvement in multiple domains of the disease such as sleep, overall quality of life (QoL), anxiety, and depression.[15-17] These findings on efficacy make JAKi a promising therapeutic option for patients with moderate-to-severe AD.[18] An EMA review, based on the results from an open-label clinical trial (ORAL Surveillance study) of the JAKi tofacitinib[19] in patients with rheumatoid arthritis and cardiovascular risk factors, confirmed measures to minimize risk of serious side effects, and recommended JAKi for chronic inflammatory disorders only if no suitable treatment alternatives are available in patients with the following conditions:[20]

- 65 years of age and older;
- history of atherosclerotic cardiovascular disease or other cardiovascular risk factors (such as to be current or past long-time smokers);

- malignancy risk factors (e.g. current malignancy or history of malignancy).

However, available safety data about JAKi in dermatology are reassuring,[21-23] as also stated by the Italian Society of Medical, Surgical, Aesthetic Dermatology and Sexually Transmitted Diseases (SIDeMaST).[24]

To date, given the recent approval of JAKi in Italy, there is a need of a therapeutic algorithm that may guide clinicians in the clinical practice,[25] as the AD Group of the Portuguese Society of Dermatology and Venereology has already assessed.[26]

Therefore, the aim of this work is to provide a clinical guidance about patients' selection, based on clinical phenotypes, for identification of moderate-to-severe AD patients' that can benefit from JAKi. Authors' considerations and opinions will be based on the available literature and the authors consolidated clinical experience on JAKi use and management in AD. Our contribution aims to open up a discussion in identifying clinical AD phenotypes, which may gain the maximum benefit in terms of efficacy and safety from a JAKi therapy. However, this represents only a starting point, which can be enriched and periodically updated by the scientific community.

Clinical AD phenotypes to guide patient's selection for treatment with JAKi as first-line therapeutic option

Clinical management of AD should consider clinical, pathogenic, and individual variability; it depends on disease severity, including difficult-to-treat areas.[27] Given the high heterogeneity of AD, as demonstrated by the existence of several well characterized clinical AD phenotypes, the choice of a treatment, based on a specific clinical presentation of the disease, may increase the chances of a therapeutic success.[4]

Both clinical trials[28-30] and real-world studies[31-35] have proven the efficacy of baricitinib, upadacitinib and abrocitinib in the treatment of AD. To finalize this paper, authors have been involved in a Workshop consisting of two meetings, with the aim of identifying AD phenotypes of patients, who are candidates for systemic therapy, in which they would feel confident in prescribing a JAKi as a first-line therapeutic option. This patients' selection has been corroborated by the clinician experience and by the literature evidence, as following.

Lichenified/exudative flexural dermatitis is a typical clinical presentations of AD in adult.[36] In clinical trials[28-30] the patients enrolled typically present this disease phenotype which is the one that can be diagnosed using the Hanifin and Rajka criteria.[37] Therefore, the efficacy data reported for JAKi are primarily related to this AD phenotype. The flexural phenotype is often associated with eczema of the head and neck and/or eczema of the hands.[36]

The *head-and-neck AD* has been significantly associated with deterioration of patients' QoL, greatly than other areas:[38] upadacitinib and baricitinib have shown to be effective in the treatment of this sensitive area.[39,40]

Flares are an integral part of the AD disease course and are generally defined as disease worsening requiring escalation/intensification of treatment. Choice of a systemic treatment for flare management should be based mainly on the rapid onset of action, and JAKi are in general effective fast-acting drugs.[27] The *AD with frequent seasonal flare* could benefit from JAKi therapy: clinical trials showed that the number of flares is reduced with upadacitinib and abrocitinib.[29,41]

Both upadacitinib and baricitinib showed to be effective in the treatment of *psoriasiform AD*.[42,43]

Prurigo-type AD is a morphological variant more common in adults that is especially difficult to treat; only a report is available about efficacy of baricitinib for the treatment of the AD phenotype prurigo-nodularis like.[44]

Over 50% of AD patients, in the clinical population, present *hand involvement*; despite the high prevalence, functional impairment and decreased QoL, treatment options for patients with hand eczema, refractory to topical corticosteroids, are limited.[45] Upadacitinb and abrocitinib have shown to be efficacious in the treatment of *acute and recurrent vescicular hand eczema*.[45,46] Furthermore, two cases of *chronic hand eczema* have been successfully treated with baricitinib.[47]

The severe generalized AD is usually widespread, mainly affecting the face, neck, hands, and flexures, although all body regions can be affected. It is possible to distinguish 2 clinical patterns: inflammatory and lichenoid.[36] The maximum expression of inflammatory pattern is erythroderma. In this patients with generalized AD, the speed of action of JAKi is an important weapon and can influence the therapeutic choice.[36]

Erythrodermic AD, resistant to multiple systemic treatments, has been successfully treated with upadacitinib.[48]

Table 1 summarizes the identified phenotypes of AD for which treatment with JAKi could be advised as first-line optional treatment, based upon data from published literature and authors clinical experience.

Table 1. Clinical AD phenotypes for first-line optional treatment with JAKi

	Phenotype name	Morphology	Distribution of lesions	References
1	Flexural AD	Lichenified or exudative eczematous lesions	Flexural regions, sometimes associated with head-and-neck AD and/or hand eczema	36
2	Head/neck eczema	Erythema, desquamation, exudate, lichenification	Head, neck	39, 40
3	AD with frequent seasonal flares	Active excoriated and essudative/edematous eczema coexistent with signs of chronic lichenification	Flexural and head-neck predominance; eyelid dermatitis and blepharitis	29, 41
4	Overlap AD and psoriasis	Heterogeneous manifestations of erythematous and variably scaling lesions	Typical and atypical psoriatic localizations, including palmoplantar	42, 43
5	Prurigo nodularis-like AD	Extensive eczema with nodular prurigo-like lesions	Upper and lower limbs, back	44
6	AD with coexisting atopic hand eczema	Hyperkeratotic, vescicular, dyshidrotic, nummular lesions and pulpitis	Palmoplantar	45-47
7	Generalized AD	Inflammatory and lichenoid	Diffuse AD affecting mainly face, neck, hands, and flexures, although all regions of the body can be involved	36
8	Erythrodermic AD	Generalized erythemato-pruritic lesions	Widespread, including sensitive areas (face, neck, genitals)	48

According to the Italian Consensus,[25] candidates for systemic therapies in Italy have moderate-to-severe AD, defined by an EASI Score ≥16, or with EASI Score <16, when at least one of the following conditions is present:

- localization on the face, hands, or genitals;
- itch with Numerical Rating Scale (NRS) Score ≥7;
- sleep disturbances with NRS Score ≥7;
- QoL impairment with Dermatitis Life Quality Index (DLQI) ≥10.

Moreover, according to AIFA prescriptions, abrocitinib, baricitinib and upadacitinib are reimbursed for the treatment of severe AD (EASI score ≥24) in adult patients' candidates for systemic therapy:[49]

- in the absence of risk factors indicated by EMA: in case of failure of treatment with cyclosporine.
- in the presence of the risk factors indicated by EMA: solely upon failure of all therapeutic options reimbursed in the indication (CsA and anti-IL) clinically deemed appropriate/possible by the prescribing doctor.

Recently, more attention to the management of the overall AD patients' status was highlighted by the published EDF/EuroGuiDerm Guidelines on Atopic Eczema:[50] candidates for systemic treatment may be either patients with a high composite score such as a SCORAD above 50 (scale definition), or patients clinically failing to respond to an appropriately conducted topical therapy (functional definition), or patients unable to participate in normal daily life activities whilst following an adequate treatment regimen (social definition). [50]

Hence, it is important to address patients' needs and to take accurately into account the presence of comorbidities and the patient's medical history.[51] Comorbidities of AD include atopic disorders (asthma, allergic rhinoconjunctivitis, food allergy, eosinophilic esophagitis), and nonatopic disorders (psychiatric disorders, ichthyosis vulgaris, cutaneous and noncutaneous infections, cardiometabolic disease).[18]

Therefore, we propose here a two-step patients' profile assessment for the selection of candidates for systemic therapy with JAKi. At first the identification of a specific AD phenotype (based on morphology and localization of lesions) as per Table 1.

Then, the analysis of the patients' overall medical history.
As per label, patients need to be 65 years old or younger, without cardiovascular and malignancy risk factors.[8-10,20] Among this category, EMA inserts long-term smokers, based upon the smoking status of patients enrolled in the Oral Surveillance trials with a smoking history.[19] Hence, in case of smoker's patients, the following parameters should be considered: older age, presence of other cardiovascular risk factors for major adverse cardiovascular events (MACE), smoking status – as it is known that risk in smokers is cumulative and that heavy and long-term smokers might be at higher risk with older age.[52] Among CV risk factors for MACE, hypertension and dyslipidemia can be well controlled with pharmacological treatment.[52]
Comorbidities are important, not only for the assessment of the overall patient's profile, but also because sometimes can be also treated with JAKi. For instance, Alopecia Areata (AA) is often associated with AD.[53] While evidence about efficacy of IL-4 and IL-13 blockers for the treatment of AA is controversial,[54] baricitinib recently received approval for the treatment of severe AA in adult patients.[8] Upadacitinib was also shown to be effective for the treatment of AA[55-57] and a phase 3 clinical trial is currently ongoing.[58] Hence, the presence of this condition can also drive the treatment choice. Similarly, even if less frequent, the presence of rheumatoid arthritis or inflammatory bowel diseases (ulcerative colitis and Crohn's disease) would encourage the treatment with a JAKi, as upadacitinb is also approved for these indications.[9]
Regarding atopic comorbidities, clinical trials showed that patients with AD and asthma have been successfully treated with JAKi[28-30] and in this selection of phenotypes, characterized by severe forms of AD, a mild to moderate asthma is not a reason to avoid JAKi prescription.[59] Likewise, when choosing a systemic treatment option for patients with history of severe ocular surface disease (OSD), as conjunctivitis and blefaritis, the treating dermatologist could consider starting with a JAKi, since OSD may be exacerbated by Th2 inhibition with biologics in patients with AD.[60]

Conclusions

The aim of our work is to support goals in the treatment of moderate to severe AD, which consist of:

- an itch-free life to patients, as this is what they strive for;[1]
- a significantly reduced number of flares on a long term prospective;[27]
- an improvement in skin clearance, to a clear/almost clear skin level, as it has been shown that this affects all other disease domain;[1]
- a rapid onset of action, both in skin and itch improvement;[11]
- a multidimensional control of the disease, addressing all QoL parameters.[15-17]

JAKi, with their high efficacy, coupled to a favorable and well-characterized safety profile, can be an important therapeutic option for the above identified patient's AD phenotypes, as well as more data will be needed for supporting the selection of responder patients, based on clinical characteristics and AD phenotypes.

References

1. Augustin M, et al. Real-World Treatment Patterns and Treatment Benefits among Adult Patients with Atopic Dermatitis: Results from the Atopic Dermatitis Patient Satisfaction and Unmet Need Survey. Acta Derm Venereol. 2022; 102:adv00830.
2. Eyeich K, et al. Real-world clinical, psychosocial and economic burden of atopic dermatitis: Results from a multicountry study. JEADV. 2023; doi: 10.1111/jdv.19500. Online ahead of print.
3. Gonçalves F, et al. Selective IL-13 inhibitors for the treatment of atopic dermatitis. Drugs in Context. 2021; 10:2021-1-7.
4. Facheris P, et al. The translational revolution in atopic dermatitis: the paradigm shift from pathogenesis to treatment. Cellular & Molecular Immunology. 2023; 20:448–474.
5. Pappa G, et al. The IL-4/-13 Axis and Its Blocking in the Treatment of Atopic Dermatitis. J. Clin. Med. 2022; 11:5633.
6. Tsuji G, et al. Novel Therapeutic Targets for the Treatment of Atopic Dermatitis. Biomedicines. 2023; 11:1303.
7. Tsiogka A, et al. The JAK/STAT Pathway and Its Selective Inhibition in the Treatment of Atopic Dermatitis: A Systematic Review. Clin. Med. 2022; 11:4431.
8. Baricitinb. EPAR.
9. Upadacitinib. EPAR.

10. Abrocitinib. EPAR.
11. Blauvelt A, et al. Efficacy and Safety of Upadacitinib vs Dupilumab in Adults with Moderate-to-Severe Atopic Dermatitis a Randomized Clinical Trial. JAMA Dermatol. 2021; 157(9):1047-1055.
12. Reich K, et al. Efficacy and safety of abrocitinib versus dupilumab in adults with moderate-to-severe atopic dermatitis: a randomised, double-blind, multicentre phase 3 trial. Lancet. 2022; 400:273-282.
13. Wan H, et al. Comparative efficacy and safety of abrocitinib, baricitinib, and upadacitinib for moderate-to-severe atopic dermatitis: A network meta-analysis. Dermatol Ther. 2022; 35(9):e15636.
14. Silverberg JI, et al. A Mini Review of the Impact of Baseline Disease Severity on Clinical Outcomes: Should We Compare Atopic Dermatitis Clinical Trials?. Dermatol Ther (Heidelb). 2023; 13:3019–3029.
15. Hoy SM. Baricitinib: A Review in Moderate to Severe Atopic Dermatitis. American Journal of Clinical Dermatology. 2022; 23:409–420.
16. Reich K, et al. Higher levels of response on clinical atopic dermatitis severity measures are associated with meaningful improvements in patient-reported symptom and quality of life measures: Integrated analysis of three Upadacitinib phase 3 trials. JEADV. 2023; doi: 10.1111/jdv.18995. Online ahead of print.
17. Cork MJ, et al. Impact of oral abrocitinib on signs, symptoms and quality of life among adolescents with moderate-to-severe atopic dermatitis: an analysis of patient-reported outcomes. JEADV. 2022; 36:422–433.
18. Shih PY, et al. Emerging trends in clinical research on Janus kinase inhibitors for atopic dermatitis treatment. International Immunopharmacology. 2023; 124:111029.
19. Ytterberg SR, et al. Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis. N Engl J Med. 2022; 386(4):316-326.
20. EMA confirms measures to minimise risk of serious side effects with Janus kinase inhibitors for chronic inflammatory disorders. EMA/27681/2023. 27 January 2023. https://www.aifa.gov.it/documents/20142/1804926/2023.01.27_com-EMA_inibitori_Janus_chinasi_EN.pdf Last accessed December 2023.
21. Burmaster GR, et al. Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis. RMD Open. 2023; 9(1):e002735.
22. Bieber T, et al. Safety of baricitinib for the treatment of atopic dermatitis over a median of 1.6 years and up to 3.9 years of treatment: an updated integrated analysis of eight clinical trials. Journal of Dermatological treatment. 2023; 34(1): 2161812.
23. Guttman-Yassky E, et al. Safety of upadacitinib in moderate-to-severe atopic dermatitis: An integrated analysis of phase 3 studies. J Allergy Clin Immunol. 2023; 151(1):172-181.
24. SIDEMAST – Raccomandazioni SIDeMaST per la terapia sistemica con inibitori della Janus Chinasi (JAK) nelle indicazioni dermatologiche. 30 August 2023. https://www.sidemast.org/blog/raccomandazioni-sidemast-per-la-terapia-sistemica-con-inibitori-della-janus-chinasi-jak-nelle-indicazioni-dermatologiche Last accessed December 2023.
25. Costanzo A, et al. Long-term management of moderate-to-severe adult atopic dermatitis: a consensus by the Italian Society of Dermatology and Venereology (SIDeMaST), the Association of Italian Territorial and Hospital Allergists and Immunologists (AAIITO), the Italian Association of Hospital Dermatologists (ADOI), the Italian Society of Allergological, Environmental and Occupational Dermatology (SIDAPA), and the Italian Society of Allergy, Asthma and Clinical Immunology (SIAAIC). Italian Journal of Dermatology and Venereology. 2022; 157(1):1-12.
26. Torres T, et al. Portuguese recommendations for the treatment of atopic dermatitis with biologic therapy and JAK inhibitors in adult patients. Drugs Context. 2021; 10:2021-9-5.
27. Girolomoni G and Busà VM. Flare management in atopic dermatitis: from definition to treatment. Ther Adv Chronic Dis. 2022; 13:20406223211066728.
28. Bieber T, et al. Early improvements in signs and symptoms predict clinical response to baricitinib in patients with moderate-to-severe atopic dermatitis. Clin Exp Dermatol. 2023; 48:881–888.
29. Guttman-Yassky E, et al. Once-daily upadacitinib versus placebo in adolescents and adults with moderate-to-severe atopic dermatitis (Measure Up 1 and Measure Up 2): results from two replicate double-blind, randomised controlled phase 3 trials. Lancet 2021; 397: 2151–2168.
30. Simpson EL, et al. Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomised, placebo-controlled, phase 3 clinical trial. Lancet. 2020; 396(10246):255-266.

31. Boesjes CM, et al. Daily Practice Experience of Baricitinib Treatment for Patients with Difficult-to-Treat Atopic Dermatitis: Results from the BioDay Registry. Acta Derm Venerol. 2022; 102:adv00820.
32. Gargiulo L, et al. Real-Life Effectiveness and Safety of Upadacitinib in Adults and Adolescents with Moderate-to-Severe Atopic Dermatitis: A Single-Center 16-Week Study. Dermatol Ther (Heidelb). 2023; 13:651–660.
33. Olydam JI, et al. Real-world effectiveness of abrocitinib treatment in patients with difficult-to-treat atopic dermatitis JEADV. 2023; 37(12):2537-2542.
34. Chiricozzi A, et al. Effectiveness and Safety of Upadacitinib in the Treatment of Moderate-Severe Atopic Dermatitis: A Multicentric, Prospective, Real-World, Cohort Study. Drugs in R&D. 2022, 22:245–252.
35. Napolitano M, et al. Comparison of Long-Term Effectiveness and Safety of Upadacitinib for Atopic Dermatitis Between Dupilumab-Exposed and Dupilumab-Naïve Patients. Clin Drug Investig. 2024; 44(1):71-77.
36. Silvestre Salvador JF, et al. Atopic Dermatitis in Adults: A Diagnostic Challenge. J Investig Allergol Clin Immunol. 2017; 27(2):78-88.
37. Hanifin JM and Rajka G. Diagnostic features of atopic dermatitis. Acta Dermato-Venereologica. 1980:44-47.
38. Gori N, et al. Head and neck atopic dermatitis: still a challenging manifestation in the biologic era. Expert opinion on Biological Therapy. 2023; 23(7):575-577.
39. Gori N, et al. Successful response to upadacitinib in the treatment of atopic dermatitis lesions involving sensitive and visible areas resistant to dupilumab treatment. Clinical and Experimental Dermatology. 2023; 48(5):558-559.
40. Simpson E, et al. Baricitinib, an oral reversible Janus kinase 1 and 2 inhibitor, for atopic dermatitis: Head and neck response across two phase 3 studies. JAAD. 2020; 83(Suppl 6): ABSTRACT 15059.
41. Flohr C, et al. Efficacy and safety of abrocitinib monotherapy in adolescents and adults: a post hoc analysis of the phase 3 JAK1 atopic dermatitis efficacy and safety (JADE) REGIMEN clinical trial. Journal of Dermatological Treatment. 2023; 34(1):2200866.
42. Patruno C, et al. Psoriasiform dermatitis induced by dupilumab successfully treated with Upadacitinib. Dermatol Ther. 2022; 35(11):e15788.
43. Ali K, et al. Case report: Clinical and histopathological characteristics of psoriasiform erythema and de novo IL-17A cytokines expression on lesioned skin in atopic dermatitis children treated with dupilumab. Front. Med. 2022; 9:932766.
44. He T, et al. Effectiveness of baricitinib in prurigo-type atopic dermatitis: A case report. Dermatol Ther. 2021; 34(2):e14878.
45. Kamphuis E, et al. Experiences from daily practice of upadacitinib treatment on atopic dermatitis with a focus on hand eczema: Results from the BioDay registry. Contact Dermatitis. 2023; 88:351-362.
46. Bissonnette R et al. Efficacy of Abrocitinib and Dupilumab on Chronic Hand Eczema in Patients with Moderate-to-Severe Atopic Dermatitis: Results From the Phase 3 JADE DARE Study. Abstract 1381 presented at EADV Congress 2022; Milan, 7-10 September 2022.
47. Rosenberg FM, et al. Baricitinib treatment of severe chronic hand eczema: Two case reports. Contact Dermatitis. 2022;86(5):419-421.
48. Valente C and Duarte B. Erythrodermic atopic dermatitis resistant to dupilumab and baricitinib successfully treated with Upadacitinib. JEADV. 2022; 37(4): e493-e495.
49. GU N°39 del 16 febbraio 2024.
50. Wollenberg A, et al. European guideline (EuroGuiDerm) on atopic eczema: part I – systemic therapy. JEADV. 2022; 36:1409–1431.
51. Thyssen JP, et al. Upadacitinib for moderate-to-severe atopic dermatitis: Stratified analysis from three randomized phase 3 trials by key baseline characteristics. JEADV 2023; 37:1871-1880.
52. Visseren FLJ and Task Force Members for ESC. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. European Heart Journal. 2021; 42:3227-3337.
53. Freitas E, et al. Baricitinib for the Treatment of Alopecia Areata. Drugs. 2023; 83:761-770.
54. Passeron T, et al. Inhibition of T-cell activity in alopecia areata: recent developments and new directions. Front. Immunol. 2023; 14:1243556.
55. Chiricozzi A, et al. Beneficial effects of upadacitinib on alopecia areata associated with atopic dermatitis: A multicenter retrospective study. JAAD. 2023; 89(6):1251-1253.

56. Cantelli M, et al. Upadacitinib improved alopecia areata in a patient with atopic dermatitis: A case report. Dermatologic Therapy. 2022; 35(4):e15346.
57. Gambardella A, et al. Dual Efficacy of Upadacitinib in 2 Patients with Concomitant Severe Atopic Dermatitis and Alopecia Areata. Dermatitis. 2021; 32(1S1):e85-e86.
58. ClinicalTrials.gov. NCT06012240. A Study to Evaluate the Safety and Effectiveness of Upadacitinib Tablets in Adult and Adolescent Participants with Severe Alopecia Areata (Up-AA). https://classic.clinicaltrials.gov/ct2/show/NCT06012240?term=NCT06012240&rank=1. Last accessed December 2023.
59. Gargiulo L, et al. Upadacitinib improves symptoms of concomitant allergic rhinitis or allergic asthma in patients with severe atopic dermatitis: A 16-week multicentre retrospective study. J Eur Acad Dermatol Venereol. 2024. doi: 10.1111/jdv.19862. Online ahead of print.
60. Adam DN, et al. Expert consensus on the systemic treatment of atopic dermatitis in special populations. J Eur Acad Dermatol Venereol. 2023; 37(6):1135-1148.

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