Upadacitinib for Treatment of Severe Atopic Dermatitis in a Child

Soraya Regina Abu Jamra, MD; Renata Gomes de Oliveira, MD; Laura Cardoso Brentini, MD; Nathalia Ventura Stefli, MD; Lais Fukuda Cuoghi, MD; Ana Cláudia Rossini Clementino, MD; Fábio André Dias, MD; Patricia Schiavotello Stefanelli, MD; Persio Roxo-Junior, MD, PhD

PRACTICE **POINTS**

- Atopic dermatitis (AD) is one of the most common chronic inflammatory skin diseases in pediatric patients.
- Dupilumab is the first-line treatment for severe AD in children and is approved for use in patients aged 6 months and older. Janus kinase inhibitors are approved only for patients aged 12 years and older.
- Upadacitinib may be a safe treatment option for severe AD in children, even those younger than 12 years.

To the Editor:

Atopic dermatitis (AD) is one of the most common chronic inflammatory skin diseases and is characterized by age-related morphology and distribution of lesions. Although AD can manifest at any age, it often develops during childhood, with an estimated worldwide prevalence of 15% to 25% in children and 1% to 10% in adults.[1] Clinical manifestation includes chronic or recurrent xerosis, pruritic eczematous lesions involving the flexural and extensor areas, and cutaneous infections. Immediate skin test reactivity and elevated total IgE levels can be found in up to 80% of patients.[2]

Although the pathogenesis of AD is complex, multifactorial, and not completely understood, some studies have highlighted the central role of a type 2 immune response, resulting in skin barrier dysfunction, cutaneous inflammation, and neuroimmune dysregulation.[3,4] The primary goals of treatment are to mitigate these factors through improvement of symptoms and long-term disease control. Topical emollients are used to repair the epidermal barrier, and topical anti-inflammatory therapy with corticosteroids or calcineurin inhibitors might be applied during flares; however, systemic treatment is essential for patients with moderate to severe AD that is not controlled with topical treatment or phototherapy.[5]

Until recently, systemic immunosuppressant agents such as corticosteroids, cyclosporine, and methotrexate were the only systemic treatment options for severe AD; however, their effectiveness is limited and they may cause serious long-term adverse events, limiting their regular usage, especially in children.[6]

Therapies that target type 2 immune responses include anti–IL-4/IL-13, anti–IL-13, and anti–IL-31 biologics. Dupilumab is a fully human monoclonal antibody targeting the type 2 immune response. This biologic directly binds to IL-4Rα, which prevents signaling by both the IL-4 and IL-13 pathways. Dupilumab was the first biologic approved by the US Food and Drug Administration (FDA) for the treatment of moderate to severe AD, with demonstrated efficacy and a favorable safety profile.[5]

In addition to biologics, Janus kinase (JAK) inhibitors belong to the small-molecule class. These drugs block the JAK/STAT intracellular signaling pathway, leading to inhibition of downstream effects triggered by several cytokines related to AD pathogenesis. Upadacitinib is an oral JAK inhibitor that was approved by the FDA in 2022 for treatment of severe AD in adults and children aged 12 years and older. This drug promotes a selective and reversible JAK-1 inhibition and has demonstrated rapid onset of action and a sustained reduction in the signs and symptoms of AD.[7] We report the case of a child with recalcitrant severe AD that showed significant clinical

From the Department of Pediatrics, Division of Immunology and Allergy, Ribeirão Preto Medical School, University of São Paulo, Brazil.
The authors have no relevant financial disclosures to report.
Correspondence: Persio Roxo-Junior, MD, PhD (persiorj@fmrp.usp.br).
Cutis. 2025 July;116(1):E12-E14. doi:10.12788/cutis.1253

improvement following off-label treatment with upadacitinib after showing a poor clinical response to dupilumab.

A 9-year-old girl presented to our pediatrics department with progressive worsening of severe AD over the previous 2 years. The patient had been diagnosed with AD at 6 months old, at which time she was treated with several prescribed moisturizers, topical and systemic corticosteroids, and calcineurin inhibitors with no clinical improvement.

The patient initially presented to us for evaluation of severe pruritus and associated sleep loss at age 7 years; physical examination revealed severe xerosis and disseminated pruritic eczematous lesions. Her SCORAD (SCORing Atopic Dermatitis) score was 70 (range, 0-103), and laboratory testing showed a high eosinophil count (1.5×10^3/μL [range, 0-0.6×10^3], 13%) and IgE level (1686 κU/L [range, 0-90]); a skin prick test on the forearm was positive for *Blomia tropicalis*.

Following her presentation with severe AD at 7 years old, the patient was prescribed systemic treatments including methotrexate and cyclosporine. During treatment with these agents, she presented to our department with several bacterial skin infections that required oral and intravenous antibiotics for treatment. These agents ultimately were discontinued after 12 months due to the adverse effects and poor clinical improvement. At age 8 years, the patient received an initial 600-mg dose of dupilumab followed by 300 mg subcutaneously every 4 weeks for 6 months along with topical corticosteroids and emollients. During treatment with dupilumab, the patient showed no clinical improvement (SCORAD score, 62). Therefore, we decided to change the dose to 200 mg every 2 weeks. The patient still showed no improvement and presented at age 9 years with moderate conjunctivitis and oculocutaneous infection caused by herpes simplex virus, which required treatment with oral acyclovir (Figure 1).

Considering the severe and refractory clinical course and the poor response to the recommended treatments for the patient's age, oral upadacitinib was administered off label at a dose of 15 mg once daily after informed consent was obtained from her parents. She returned for follow-up once weekly for 1 month. Three days after starting treatment with upadacitinib, she showed considerable improvement in itch, and her SCORAD score decreased from 62 to 31 after 15 days. After 2 months of treatment, she reported no pruritus or sleep loss, and her SCORAD score was 4.5 (Figure 2). The results of a complete blood count, coagulation function test, and liver and kidney function tests were normal at 6-month and 12-month follow-up during upadacitinib therapy. No adverse effects were observed. The patient currently has completed 18 months of treatment, and the disease remains in complete remission.

Atopic dermatitis is highly prevalent in children. According to the International Study of Asthma and Allergies in Childhood, the prevalence of eczema in 2009 was 8.2% among children aged 6 to 7 years and 5% among adolescents aged between 13 and 14 years in Brazil; severe AD was present in 1.5% of children in both age groups.[8]

The main systemic therapies currently available for patients with severe AD are immunosuppressants, biologics, and small-molecule drugs. The considerable adverse effects of immunosuppressants limit their application. Dupilumab is considered the first-line treatment for children with severe AD. Clinical trials and case reports have demonstrated that dupilumab is effective in patients with AD, promoting notable improvement of pruritic eczematous lesions and quality-of-life scores.[9] Dupilumab has been approved by the FDA for children older than 6 months, and some studies have shown up to a 49% reduction of pruritus in this age group.[9] The main reported adverse effects were mild conjunctivitis and oral herpes simplex virus infection.[9,10]

Upadacitinib is a reversible and selective JAK-1 inhibitor approved by the FDA for treatment of severe AD in patients aged 12 years and older. A multicenter, randomized, double-blind, placebo-controlled trial evaluated adolescents (12-17 years) and adults (18-75 years) with moderate to severe AD who were randomly assigned (1:1:1) to receive upadacitinib 15 mg, upadacitinib 30 mg, or placebo once daily for 16 weeks.[11] A higher proportion of patients achieved an Eczema Area and Severity Index score of 75 at week 16 with both upadacitinib 15 mg daily (70%) and 30 mg daily (80%) compared to placebo. Improvements also were observed in both

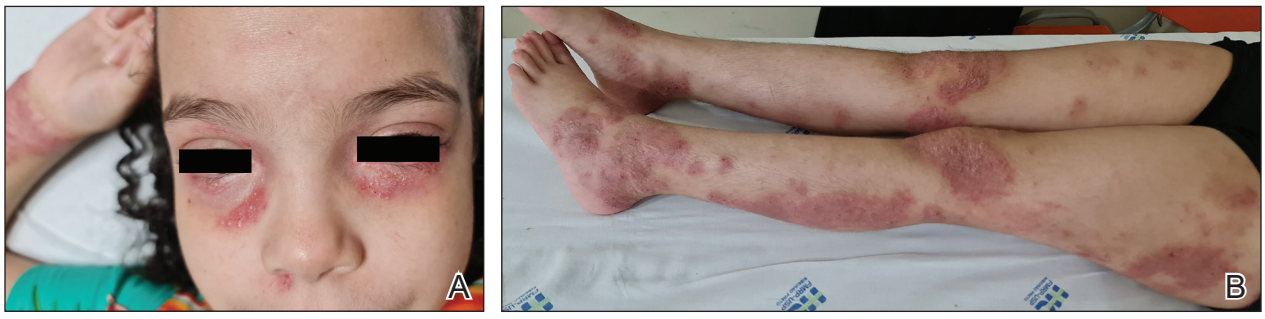

FIGURE 1. Before upadacitinib therapy (SCORAD score, 62), the patient experienced A, culocutaneous infection caused by herpes simplex virus and B, pruritic eczematous skin lesions affecting the legs.

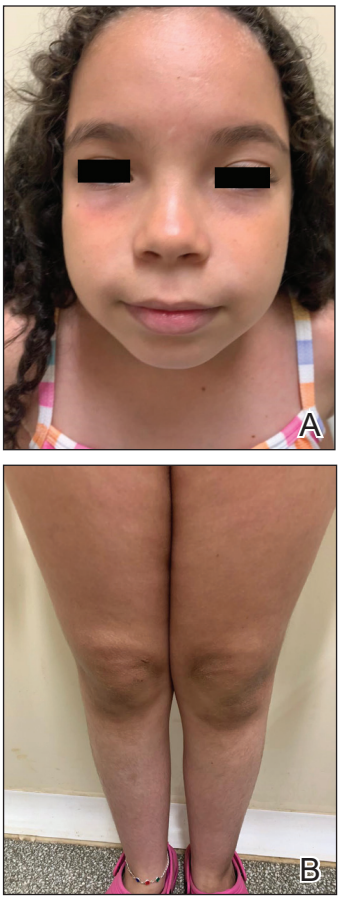

FIGURE 2. A and B, After 2 months of upadacitinib therapy (SCORAD score, 4.5), the patient experienced complete clearance of eczematous lesions.

SCORAD and pruritus scores. The most commonly reported adverse events were acne, lipid profile abnormalities, and herpes zoster infection.[11]

Our patient was a child with severe refractory AD that demonstrated a poor treatment response to dupilumab. When switched to off-label upadacitinib, her disease was effectively controlled; the treatment also was well tolerated with no adverse effects. Reports of upadacitinib used to treat AD in patients younger than 12 years are limited in the literature. One case report described a 9-year-old child with concurrent alopecia areata and severe AD who was successfully treated off label with upadacitinib.[12] A clinical trial also has evaluated the pharmacokinetics, safety, and tolerability of upadacitinib in children aged 2 to 12 years with severe AD (ClinicalTrials.gov Identifier: NCT03646604); although the trial was completed in 2024, at the time of this review (July 2025), the results have not been published.

Interestingly, there have been a few reports of adults with severe AD that failed to respond to treatment with immunosuppressants and dupilumab but showed notable clinical improvement when therapy was switched to upadacitinib,[13,14] as we noticed with our patient. These findings suggest that the JAK-STAT intracellular signaling pathway plays an important role in the pathogenesis of AD.

Continued development of safe and efficient targeted treatment for children with severe AD is critical. Upadacitinib was a safe and effective option for treatment of refractory and severe AD in our patient; however, further studies are needed to confirm both the efficacy and safety of JAK inhibitors in this age group.

REFERENCES

1. Weidinger S, Novak N. Atopic dermatitis. *Lancet*. 2016;387:1109-1122.
2. Wollenberg A, Christen-Zäch S, Taieb A, et al. ETFAD/EADV Eczema Task Force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. *J Eur Acad Dermatol Venereol*. 2020;34 :2717-2744.
3. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venererol*. 1980;92:44-47.
4. Nakahara T, Kido-Nakahara M, Tsuji G, et al. Basics and recent advances in the pathophysiology of atopic dermatitis. *J Dermatol*. 2021;48:130-139.
5. Wollenberg A, Kinberger M, Arents B, et al. European guideline (EuroGuiDerm) on atopic eczema: part I—systemic therapy. *J Eur Acad Dermatol Venereol*. 2022;36:1409-1431.
6. Chu DK, Schneider L, Asiniwasis RN, et al. Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters GRADE– and Institute of Medicine–based recommendations. *Ann Allergy Asthma Immunol*. 2024;132:274-312.
7. Rick JW, Lio P, Atluri S, et al. Atopic dermatitis: a guide to transitioning to janus kinase inhibitors. *Dermatitis*. 2023;34:297-300.
8. Prado E, Pastorino AC, Harari DK, et al. Severe atopic dermatitis: a practical treatment guide from the Brazilian Association of Allergy and Immunology and the Brazilian Society of Pediatrics. *Arq Asma Alerg Imunol*. 2022;6:432-467.
9. Paller AS, Simpson EL, Siegfried EC, et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: a randomized, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2022;400:908-919.
10. Blauvelt A, de Bruin-Weller M, Gooderham M, et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. *Lancet*. 2017;389:2287-2303.
11. Guttman-Yassky E, Teixeira HD, Simpson EL, 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.
12. Yu D, Ren Y. Upadacitinib for successful treatment of alopecia universalis in a child: a case report and literature review. *Acta Derm Venererol*. 2023;103:adv5578.
13. Cantelli M, Martora F, Patruno C, et al. Upadacitinib improved alopecia areata in a patient with atopic dermatitis: a case report. *Dermatol Ther*. 2022;35:E15346.
14. Gambardella A, Licata G, Calabrese G, et al. Dual efficacy of upadacitinib in 2 patients with concomitant severe atopic dermatitis and alopecia areata. *Dermatitis*. 2021;32:E85-E86.