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Research Letter

Sustained Efficacy of a Short Course of Upadacitinib in Atopic Dermatitis

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To the Editor,

Atopic dermatitis (AD) is a heterogeneous disease, both in its clinical presentation and in its natural course. The classic diagnostic criteria of Hanifin and Rajka[1] already referred to its chronic and recurrent nature. Knowledge of the disease has increased substantially in recent years; however, several aspects regarding its natural course and persistence remain unclear. Genetic and pathophysiological data support the concept of AD as a lifelong condition. Therefore, current treatments are generally considered long-term strategies.

Disease symptoms typically follow a variable course. Some patients experience persistent, mild signs; others present with moderate-to-severe disease, with fluctuations and even remission periods.[2] To date, there are few studies addressing the factors associated with long-term remission.[3]

This is the case of a 24-year-old man with a history of asthma, allergic rhinoconjunctivitis, and sensitization to profilin, animal dander, and molds diagnosed with AD at 2 years of age. Since then, he had been on multiple treatments—including oral and topical corticosteroids, oral H1 antihistamines, UVB phototherapy, methotrexate, cyclosporine, azathioprine, and mycophenolate mofetil—with only partial responses. He had even required several hospital admissions. In recent years, he discontinued clinical follow-up and self-medicated almost continuously with oral corticosteroids and H1 antihistamines at variable doses, never achieving complete clearance.

In May 2022, he presented to the dermatology emergency department with a severe AD flare (EASI 22, SCORAD 43.06, BSA 15%, IGA 3, itch-NRS 8/10, sleep-NRS 5/10, ADCT 12). Treatment with upadacitinib 30 mg/day was initiated (Fig. 1). Within a few days, after complete disappearance of pruritus, the patient discontinued all other oral and topical drugs. Two weeks later, the skin lesions had resolved (EASI 0, SCORAD 3, BSA 0%, IGA 0, itch-NRS 0/10, sleep-NRS 0/10, ADCT 2). In August 2022, after 2 months without symptoms, the patient independently decided to discontinue upadacitinib (Fig. 2). Since then—and after a year and a half of follow-up—he has remained practically asymptomatic without treatment, using only emollients.

Current AD management guidelines stratify available treatments according to disease severity but provide no clear recommendations regarding treatment duration.[4] The frequency, intensity, and duration of flares, as well as the presence of flare-free intervals, should be considered when choosing and determining the duration of therapy. However, these factors are rarely added to clinical trials or daily clinical practice. In fact, there is no uniform definition of "flare." The term is generally used to describe disease worsening or exacerbation. Different

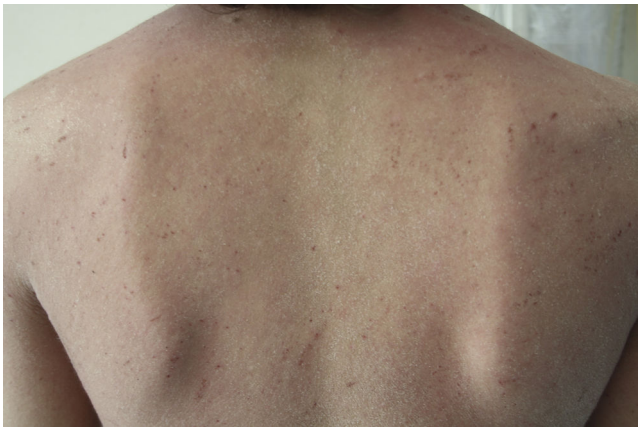

Fig. 1. Before initiating treatment with upadacitinib.

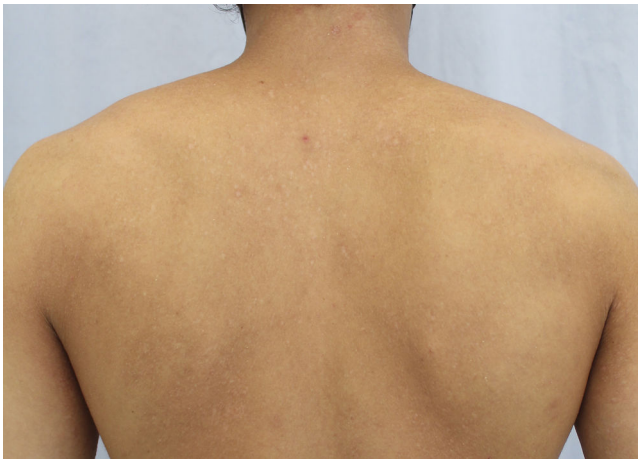

Fig. 2. Twelve weeks into upadacitinib, 4 weeks after treatment discontinuation.

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studies define flares variably, using objective scales, composite sign-and-symptom measures, or patient-reported data.[3]

Individuals who experience frequent flares or persistent signs require a proactive approach, with topical or systemic therapies depending on severity.[2] Conversely, patients with limited, episodic flares and long symptom-free intervals may not require continuous treatment.[5] In such patients—those with intermittent or seasonal disease who may benefit from short treatment cycles—JAK inhibitors are ideal candidates due to their rapid onset of action and short elimination half-life.[6]

Data from a phase 2b trial of upadacitinib show that although many patients lose therapeutic response after treatment discontinuation, a proportion remain asymptomatic > 20 weeks (14.3% with upadacitinib 15 mg/day; 24.6% with upadacitinib 30 mg/day), possibly reflecting the naturally fluctuating course of AD.[5] Among those who relapse after discontinuation, re-treatment restores the initial therapeutic response at the same dose.[5] Similar suspension–reinitiation responses have been observed with other JAK inhibitors.[7] Treatment interruptions due to various circumstances (pregnancy, intercurrent illness, surgery, or travel) do not appear to compromise future efficacy.[5,7]

In recent years, major advances have been achieved in AD treatment. Advanced therapies targeting increasingly specific pathways can achieve complete symptom resolution and sustained responses, as observed in this case. We describe a clinical observation in which assuming definitive AD remission due to treatment would be risky, given the disease's episodic nature—some patients may experience recurrences even decades later.[3]

Additional real-world studies—including large series and diverse treatment scenarios such as prolonged continuous therapy or short intermittent regimens—are needed to identify which patients may benefit from treatment optimization or even discontinuation, ultimately enabling individualized AD management.

Conflict of interest

The authors declare that they have no conflict of interest. Q3

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