Received: 31 August 2023 | Accepted: 25 October 2023

DOI: 10.1111/jdv.19605

JEADV JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

LETTER TO THE EDITOR

Tralokinumab improves clinical scores in adolescents with severe atopic dermatitis: A real-life multicentric observational study

Dear Editor,

Atopic dermatitis (AD) usually develops during early childhood but may continue into adolescence.[1–3] The exact prevalence of AD in adolescents remains unknown but recent longitudinal studies indicate a similar prevalence in childhood and adolescence.[4,5] In western European countries, moderate-to-severe AD represents 3.1%–39.1% of young AD patients (12 to <18 years).[6] Efficacy and safety of several new systemic immunomodulatory agents [biologics and Janus kinase inhibitors (JAKi)] have been recently evaluated for the management of moderate-to-severe AD in adolescents.[7–9] Tralokinumab, a fully human IgG4 monoclonal antibody that binds specifically to interleukin-13, is the second biologic (after dupilumab) approved for the treatment of severe AD in this patient population. Its efficacy and safety in adolescents were demonstrated in the ECZTRA 6 trial[10] but real-world data are lacking.

We retrospectively collected real-life data from November 2022 to August 2023, from a multicentric Belgian patients cohort aged 12–17 years, treated with tralokinumab (600 mg at induction dose, followed by 300 mg every 2 weeks) for severe AD (after failure of at least topical corticosteroids). The primary outcome was evaluated by the percentage of patients with an improvement of at least 75% of the Eczema Area and Severity Index (EASI 75) and/or a reduction of Peak Pruritus Numerical Rating Scale (PP-NRS) of ≥4 points from baseline, between week 12 and 16. All adverse events were reported.

Of the 14 adolescents included, eight were male and the median age ± interquartile range (IQR) was 15.3 ± 2.0 years. Patients' characteristics are detailed in Table 1. All patients had severe disease at baseline, presenting with median ± IQR EASI and PP-NRS scores of 24.3 ± 8.4 and 8.0 ± 2.0, respectively. They had been previously treated with a median of two systemic drugs before tralokinumab initiation; three patients were shifted from upadacitinib (two for ineffectiveness, one due to parents' concerns regarding safety issues with JAKi). Tralokinumab was added for one patient with insufficiently controlled

TABLE 1 Demographics and clinical characteristics of patients included in the study.

Variable	Value
Median age, years (± IQR)	15.3 (2.0)
Sex, male, *n*/*n* total	8/14
Age at onset of atopic dermatitis, *n* (%)	
Infant	11 (78.5)
Child	1 (7.1)
Adolescent	2 (14.3)
Atopic dermatitis phenotype, *n* (%)	
Generalized and flexural (classical)	11 (78.6)
Nummular eczema	1 (7.1)
Head and neck	1 (7.1)
Prurigo-like	1 (7.1)
History of personal atopy, *n* (%)	
Allergic asthma	9 (64.3)
Allergic rhinoconjunctivitis	8 (57.1)
Previous topical treatments for atopic dermatitis, *n* (%)	
Emollients	14 (100.0)
Topical corticosteroids	14 (100.0)
Topical immunomodulators	10 (71.4)
Previous systemic treatments for atopic dermatitis, *n* (%)	
Corticosteroids	3 (21.4)
Cyclosporine	7 (50.0)
Phototherapy	4 (28.6)
Methotrexate	2 (14.3)
Dupilumab	0 (0.0)
Nemolizumab	1 (7.1)
Upadacitinib	3 (24.4)
Clinical scores at baseline, median (± IQR)	
EASI	24.3 (8.4)
PP-NRS	8.0 (2.0)

Abbreviations: EASI, Eczema Area and Severity Index; IQR, interquartile range; PP-NRS, Peak Pruritus Numerical Rating Scale.

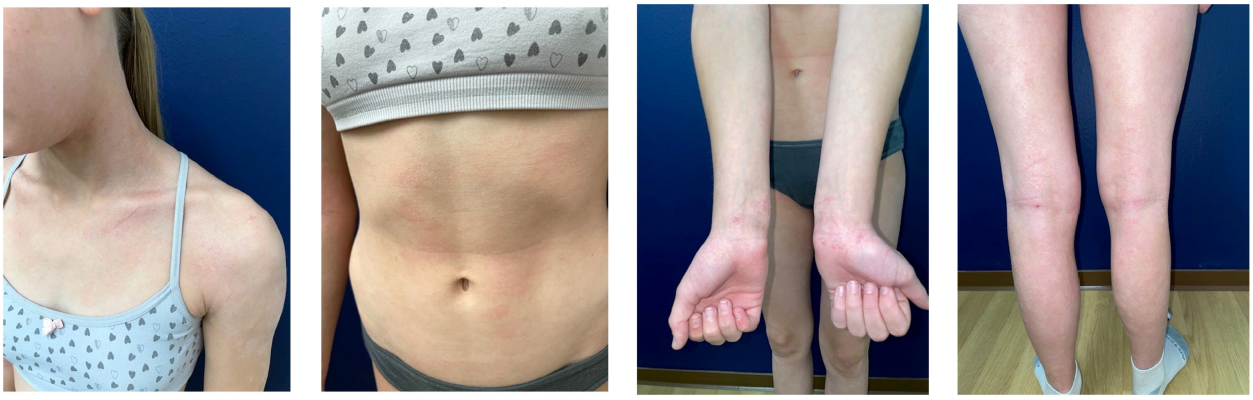

FIGURE 1 Baseline clinical severity and characteristics of the patient with uncontrolled atopic dermatitis (AD) after 9 months of upadacitinib alone. Girl, 15 years, infant-onset AD; allergic asthma and rhinoconjunctivitis; previous systemic treatments for AD included corticosteroids, cyclosporine and nemolizumab, with poor/uncomplete response; Eczema Area and Severity Index (EASI) 22, Peak Pruritus Numerical Rating Scale (PP-NRS) 5.

AD after 9 months of upadacitinib alone (Figure 1). At the follow-up visit between 12 and 16 weeks, four patients (28.6%) achieved an EASI 75 and six patients (42.8%) a four-point or higher reduction in PP-NRS compared to baseline. An EASI 50 was obtained for 10 patients (71.4%). Improvement of EASI and PP-NRS was significant (p value < 0.005, using a pairwise Wilcoxon signed-rank test) compared with baseline values. The two adolescents who had shifted from upadacitinib treatment for ineffectiveness did not reach the endpoint, neither did the patients with prurigo-like, head and neck and nummular lesions. The patient with combined treatment with tralokinumab and upadacitinib reached EASI 90 and the association was well tolerated.

The most frequent adverse events were flare of AD (7/14, 50.0%), followed by injection-site reaction (2/14, 14.3%). No conjunctivitis or upper respiratory tract infection were reported. One adolescent discontinued the treatment at week 8 due to lack of effectiveness and one at week 9 for invalidating injection-site reactions, despite reaching both endpoints.

This real-life study confirmed the effectiveness of tralokinumab in adolescents with severe AD who failed treatment with conventional topical and/or systemic agents, as demonstrated by the improvement of EASI and/or PP-NRS scores in most patients. The rate of patients who reached EASI 75 in the present study (28.6% between 12 and 16 weeks) was similar to that of ECZTRA 6 trial (27.8% at week 16). However, tralokinumab seemed less effective in very severe AD or difficult-to-treat phenotypes. A combination with a JAKi in one patient seemed promising. The high rate of AD flares during the first weeks of treatment in real life (50.0% vs 7.2% in trial), already observed in adults,[11] must be balanced with the progressive improvement expected beyond 16 weeks.[10,12] As with adults, no tralokinumab-induced conjunctivitis were observed but injection-site reactions were more frequent than in trial (14.3% vs 2.1%).[11]

In conclusion, tralokinumab seems effective and well tolerated in adolescents with severe AD. Longer-term real-life studies are warranted.

ACKNOWLEDGEMENTS

We thank Dr. Mariana Andrade, M.D., who provided editorial assistance.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

Axel De Greef, Pierre-Dominique Ghislain, Marleen Goeteyn and Marie Baeck disclose their past participation on the tralokinumab advisory boards organized by LEO Pharma but declare that the present study was conducted in an independent manner. Pierre-Dominique Ghislain received consultancy fees for expert work in clinical trials with other drugs from LEO Pharma. All other authors disclose no conflict of interest. All the authors declare that the present study was conducted in an independent manner.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available upon request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The patients in this manuscript have given written informed consent to the publication of their case details.

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REFERENCES

1. Langan SM, Irvine AD, Weidinger S. Atopic dermatitis. Lancet. 2020;396(10247):345–60.
2. Slattery MJ, Essex MJ, Paletz EM, Vanness ER, Infante M, Rogers GM, et al. Depression, anxiety, and dermatologic quality of life in adolescents with atopic dermatitis. J Allergy Clin Immunol. 2011;128(3):668–71.
3. Hadi HA, Tarmizi AI, Khalid KA, Gajdács M, Aslam A, Jamshed S. The epidemiology and global burden of atopic dermatitis: a narrative review. Life. 2021;11(9):936.
4. von Kobyletzki LB, Bornehag CG, Breeze E, Larsson M, Lindström CB, Svensson Å. Factors associated with remission of eczema in children: a population-based follow-up study. Acta Derm Venereol. 2014;94(2):179–84.
5. Abuabara K, Yu AM, Okhovat JP, Allen IE, Langan SM. The prevalence of atopic dermatitis beyond childhood: a systematic review and meta-analysis of longitudinal studies. Allergy. 2018;73(3):696–704.
6. Silverberg JI, Barbarot S, Gadkari A, Simpson EL, Weidinger S, Mina-Osorio P, et al. Atopic dermatitis in the pediatric population: a cross-sectional, international epidemiologic study. Ann Allergy Asthma Immunol. 2021;126(4):417–428.e2.
7. Simpson EL, Paller AS, Siegfried EC, Boguniewicz M, Sher L, Gooderham MJ, et al. Efficacy and safety of Dupilumab in adolescents with uncontrolled moderate to severe atopic dermatitis: a phase 3 randomized clinical trial. JAMA Dermatol. 2020;156(1):44–56.
8. Guttman-Yassky E, Teixeira HD, Simpson EL, Papp KA, Pangan AL, Blauvelt A, 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 [published correction appears in *Lancet*. 2021;397(10290):2150]. Lancet. 2021;397(10290):2151–68.
9. Simpson EL, Sinclair R, Forman S, Wollenberg A, Aschoff R, Cork M, 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 trial. Lancet. 2020;396(10246):255–66.
10. Paller AS, Flohr C, Cork M, Bewley A, Blauvelt A, Hong HCH, et al. Efficacy and safety of tralokinumab in adolescents with moderate to severe atopic dermatitis: the phase 3 ECZTRA 6 randomized clinical trial. JAMA Dermatol. 2023;159(6):596–605. https://doi.org/10.1001/jamadermatol.2023.0627
11. De Greef A, Ghislain PD, Bulinckx A, Coster A, de Halleux C, Damsin T, et al. Real-life experience of Tralokinumab for the treatment of adult patients with severe atopic dermatitis: a multicentric prospective study. Clin Drug Investig. 2023;43(4):299–306. https://doi.org/10.1007/s40261-023-01258-7
12. Blauvelt A, Langley RG, Lacour JP, Toth D, Laquer V, Beissert S, et al. Long-term 2-year safety and efficacy of tralokinumab in adults with moderate-to-severe atopic dermatitis: interim analysis of the ECZTEND open-label extension trial. J Am Acad Dermatol. 2022;87(4):815–24. https://doi.org/10.1016/j.jaad.2022.07.019