Received: 14 May 2024 | Revised: 26 July 2024 | Accepted: 28 July 2024

DOI: 10.1111/cod.14671

CONTACT POINT

CONTACT DERMATITIS | WILEY

# Tralokinumab-induced injection-site reactions

Axel De Greef[1,2] | Marie Baeck[1,2]

[1]Department of Dermatology, Cliniques universitaires Saint-Luc, Université catholique de Louvain (UCLouvain), Brussels, Belgium

[2]Institute of Experimental and Clinical Research (IREC), Pneumology, ENT and Dermatology Pole (LUNS), Université catholique de Louvain (UCLouvain), Brussels, Belgium

**Correspondence**
Axel De Greef, Department of Dermatology, Cliniques universitaires Saint-Luc (UCLouvain), Avenue Hippocrate 10, B-1200 Brussels, Belgium.
Email: axel.degreef@saintluc.uclouvain.be

**Funding information**
Fonds De La Recherche Scientifique - FNRS

**KEYWORDS:** adverse drug reaction, atopic dermatitis, injection site reaction, skin test, tralokinumab

## INTRODUCTION

Injection-site reactions (ISR) have been reported with the subcutaneous injection of tralokinumab, a human monoclonal antibody that binds specifically to interleukin 13, indicated in adults and adolescents for moderate-to-severe atopic dermatitis (AD).[1,2] The pathophysiology of these ISR remains unclear.

## CASE REPORT

Tralokinumab was initiated in a 17-year-old male with severe AD since childhood, insufficiently controlled with topical steroids and several courses of cyclosporine (baseline Eczema Area and Severity Index [EASI] 23, peak pruritus numeric rating scale [PP NRS] 9/10). Tralokinumab treatment led to remarkable improvement of signs and symptoms of AD (EASI 2, PP NRS 3/10 after 7 months of treatment). However, the patient reported pruritic and painful ISR lasting generally less than 24 h after the initial self-injections at home. He had no fever nor systemic symptoms. At the 16-week follow-up visit, swelling and erythema (i.e., symptoms of ISR) were observed at the site of the last injections made by the patient the previous day (Figure 1A). Biologic work-up was unremarkable, except for a mild increase in peripheral blood eosinophil count (845/μL, normal value: 30–600/μL). A skin biopsy was taken and showed a superficial and deep dermal perivascular, perisudoral and slightly perifollicular inflammatory infiltrate, composed of lymphohistiocytic cells with neutrophils and numerous eosinophils (Figure 1B). Immediate (at 30 min) and late readings (on days 2 and 4) of skin tests (patch, prick '*as is*', and intradermal test 1:10 ratio) with tralokinumab were negative (Figure 2A,B). Provocation test with subcutaneous injection of the complete dose of tralokinumab was then carried out and no immediate nor delayed reactions at the injection site were observed. Re-educating the patient about the correct procedure (abdominal fold, needle fully inserted in the subcutaneous tissue, slow injection, etc.) was provided, resulting in a decrease in the frequency and intensity of ISR over time. No recurrences of ISR were reported at the last follow-up visit at 7 months.

## DISCUSSION

The prevalence of ISR with tralokinumab observed in real-life studies[3–5] (14.3%–60%) was notably higher than in clinical trials[1,2] (6.7% in ECZTRA 3 and 2.1% in ECZTRA 6). In a prospective multicentric study, we reported a prevalence of 19% of ISR with tralokinumab,[3] which led to treatment discontinuation in two cases. To better understand the pathophysiology of these tralokinumab-induced ISR and to differentiate between irritative and allergic reactions, skin biopsy and skin testing were performed in our patient. The skin biopsy demonstrated the presence of numerous eosinophils, which was associated with mild circulating eosinophilia, reported as potential side effect of tralokinumab treatment.[1] The negativity of skin tests with immediate and delayed readings, as well as the spontaneous resolution of ISR over time, ruled out the hypothesis of an allergic hypersensitivity reaction to the drug itself

  

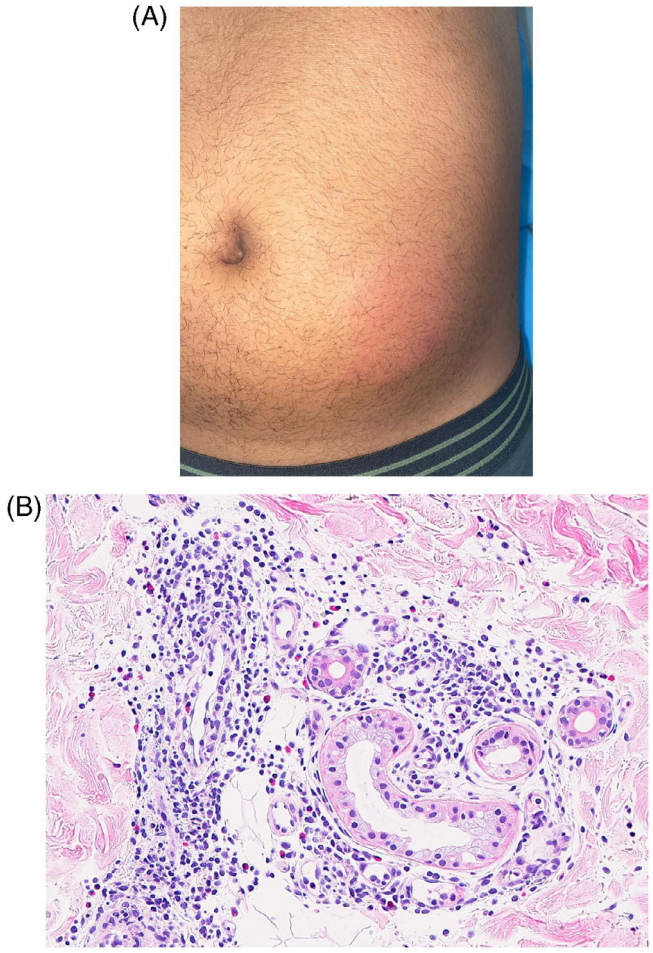


**FIGURE 1** Injection-site reaction observed at week 16 (A). Histopathological features showing perivascular and perisudoral dermal inflammatory infiltrate, composed of lymphohistiocytic cells with neutrophils and numerous eosinophils (haematoxylin and eosin, magnification ×200) (B).

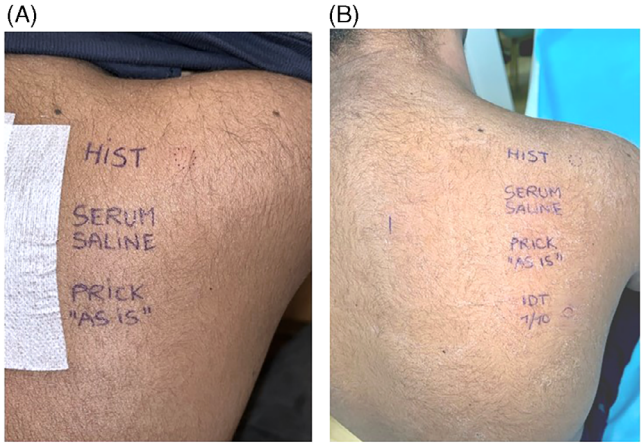


**FIGURE 2** Negative immediate (A) and late readings (day 4) (B) of skin tests (patch, prick '*as is*', and intradermal test 1:10 ratio) with tralokinumab.

or its excipients. Irritation due to incorrect injection procedure could also be one explanation, since education of the patient seems to have resolved ISR.

## AUTHOR CONTRIBUTIONS

**Axel De Greef:** Conceptualization; investigation; writing – original draft. **Marie Baeck:** Conceptualization; investigation; writing – review and editing; supervision.

## ACKNOWLEDGEMENTS

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

## FUNDING INFORMATION

Axel De Greef has a Ph.D. fellowship from the Fund for Scientific Research (F.R.S)—FNRS. The funders had no role in study design, data collection and analysis, interpretation or writing of the manuscript.

## CONFLICT OF INTEREST STATEMENT

Axel De Greef and Marie Baeck disclose their past participation on the tralokinumab advisory boards organised by LEO Pharma. Axel De Greef and Marie have participated as speakers in events sponsored by LEO Pharma.

## DATA AVAILABILITY STATEMENT

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

## INFORMED CONSENT

The patient in this manuscript has given written informed consent to publication of his case details.

## ORCID

*Axel De Greef* https://orcid.org/0000-0003-0713-8283

## REFERENCES

1. Paller AS, Flohr C, Cork M, 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.
2. Silverberg JI, Toth D, Bieber T, et al. Tralokinumab plus topical corticosteroids for the treatment of moderate-to-severe atopic dermatitis: results from the double-blind, randomized, multicentre, placebo-controlled phase III ECZTRA 3 trial. *Br J Dermatol*. 2021;184(3):450-463.
3. De Greef A, Ghislain PD, Bulinckx A, 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.
4. De Greef A, Ghislain PD, de Montjoye L, et al. Tralokinumab improves clinical scores in adolescents with severe atopic dermatitis: a real-life multicentric observational study. *J Eur Acad Dermatol Venereol*. 2024;38(3):e288-e290.
5. Martora F, Patruno C, D'Ascenzo S, Napolitano M. Injection site reactions after dupilumab or tralokinumab for atopic dermatitis. *J Dermatolog Treat*. 2024;35(1):2304027.

**How to cite this article:** De Greef A, Baeck M. Tralokinumab-induced injection-site reactions. *Contact Dermatitis*. 2024;1-2. doi:10.1111/cod.14671