Revista de la Facultad de Medicina Humana

Volume 23 | Issue 3 Article 24

2023

Systemic immunomodulatory therapy in the management of atopic dermatitis: the value of Tralokinumab

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Recommended Citation

Muñoz Ordóñez, Sara; Alexandra Layos, Jessika; Garcia Lozano, Maria Paula; and Picón Jaimes, Yelson Alejandro (2023) "Systemic immunomodulatory therapy in the management of atopic dermatitis: the value of Tralokinumab," *Revista de la Facultad de Medicina Humana*: Vol. 23: Iss. 3, Article 24.
DOI: https://doi.org/10.25176/RFMH.v23i3.5593
Available at: https://inicib.urp.edu.pe/rfmh/vol23/iss3/24

Rev. Fac. Med. Hum. 2023; 23(3):176-178.
DOI: 10.25176/RFMH.v23i3.5593
ISSN Versión Online: 2308-0531
Facultad de Medicina Humana URP
RFMH
LETTERS TO THE EDITOR

SYSTEMIC IMMUNOMODULATORY THERAPY IN THE MANAGEMENT OF ATOPIC DERMATITIS: THE VALUE OF TRALOKINUMAB

TERAPIA INMUNOMODULADORA SISTÉMICA EN EL TRATAMIENTO DE LA DERMATITIS ATÓPICA: EL VALOR DE TRALOKINUMAB

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LETTERS TO THE EDITOR

Mr. Editor:

Atopic dermatitis is a chronic inflammatory skin disease that substantially impacts the quality of life and functional capacity of those who suffer from it [1,2]. In the midst of describing the pathogenesis and pathophysiology of this condition, the aberrant activity of interleukins (ILs) stands out, mainly IL-13 type 2. Currently, there is no definitive and safe treatment to address this disease [2]. Traditionally, antibiotic therapy and corticosteroids have been indicated, but given the adverse effects commonly reported with these drugs, it is not reproducible or safe to continue with these regimens [3]. Over the last few years, some agents with immunomodulatory potential have been proposed, which could change the course of atopic dermatitis. Within the global health objectives stipulated for the year 2030, there is the need to develop drugs that allow control of the burden of diseases that generate pathological entities that considerably affect both the quality of life and the catastrophic expense of the global population. with main emphasis on low- and middle-income countries, where difficulties prevail for timely and effective access to health services and targeted treatments [4]. Therefore, the effort to find an agent that regulates chronicity or solves this disease is a priority both for dermatology and for global health.

Tralokinumab is a complete IgG4 monoclonal antibody targeting IL-13 whose pharmacokinetics, effectiveness, efficacy, and safety are still being studied. Compared to other therapies, some studies such as Drucker et al.[3], where they recently systematized evidence on systemic immunomodulatory treatments, including 60 clinical trials with a total of 16,579 patients. Among the drugs studied are Abrocitinib (Janus kinase [JAK] inhibitor), Upadacitinib (selective and reversible JAK inhibitor), Baricitinib (JAK1 and JAK2 inhibitor), Dupilumab (IL-4 inhibitor and IL-13) and Tralokinumab. The authors showed that, at 16 weeks of treatment, Abrocitinib (200 mg daily doses) and Upadacitinib (30 mg daily doses) reduced the Eczema Area and Severity Index (EASI) to a greater extent, compared to Dupilumab (at doses of 600 and 300 mg every two weeks). Likewise, Abrocitinib (in daily doses of 100 mg), Baricitinib (in daily doses of 2 and 4 mg) and Tralokinumab (in doses of 600 and 300 mg every two weeks), slightly decreased the EASI, compared to Dupilumab, which had better performance [3].

These results were similar for the other indices also evaluated, Patient Oriented Eczema Measure (POEM), Dermatology Life Quality Index (DLQI), y Peak Pruritus Numeric Rating Scales (PP-NRS). This allowed us to conclude that Abrocitinib and Upadacitinib are the most effective agents in controlling atopic dermatitis [3].

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Cite as: Muñoz Ordóñez S, Layos JA, García Lozano MP, Picón Jaimes YA. Systemic immunomodulatory therapy in the management of atopic dermatitis: the value of Tralokinumab. Rev Fac Med Hum. 2023;23(2):176-178. doi 10.25176/RFMH.v23i3.5593

Journal home page: http://revistas.urp.edu.pe/index.php/RFMH

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Nevertheless, it is necessary to highlight that the studies that included Tralokinumab were particularly trials up to phase II, of which many results were not clearly known. At the beginning of 2021, the results of the ECZTRA 3 study (double-blind randomized controlled trial) were published, which evaluated Tralokinumab (300 mg dose every two weeks or four weeks) plus topical corticosteroids in the management of moderate to severe atopic dermatitis, in 369, distributed at a ratio of 2:1 in favor of the intervention group[5]. As primary outcomes, an Investigator's Global Assessment (IGA) score of 0/1 and 75% EASI improvement (EASI 75) were determined. It was evidenced that at week 16, the intervention group had a higher proportion of patients who achieved IGA 1/0 (38.9% vs. 26.2%, p= 0.015) and EASI 75 (56.0% vs. 35.7%, P <0.001). These results were similar with the two and four week doses (with evaluation at week 32), and the incidence of adverse events was similar in both groups. This allowed us to conclude that Tralokinumab was effective and well-tolerated in the management of moderate-severe atopic dermatitis[5].

In March 2022, the results of the ECZTRA 7 study were published[6], with a design similar to the ECZTRA 3 study, which evaluated Tralokinumab plus topical corticosteroids in moderate to severe dermatitis with inadequate response or intolerance to cyclosporine A. Two hundred seventy-seven individuals were randomized 1:1; The intervention group was administered Tralokinumab at a dose of 300 mg every two weeks plus topical corticosteroid as needed. To evaluate the outcome, the improvement of the EASI 75 was analyzed. It was observed that at week 16, the intervention group obtained a significant improvement in the EASI 75 in a superior way, compared to the control group (64.2% vs. 50.5%, p= 0.018), whose effect persisted until week 26[6]. This effect was more significant in those with prior therapeutic failure compared to placebo plus corticosteroid (57% vs. 41%). As in the ECZTRA 3 study, the incidence of adverse events was similar in both groups. This allowed us to conclude that Tralokinumab is effective and safe in the management of uncontrolled atopic dermatitis or with a contraindication to cyclosporine A[6]. Compared to other immunomodulatory therapies, Tralokinumab does not have black box warnings, and its mechanism of action is directly involved with immunological lines associated with the most up-to-date pathogenesis described[2]. Compared to other therapies, an advantage is the dosage of Tralokinumab in a wide time window (every 2 or 4 weeks), which may favor treatment adherence. Within the studies on this agent, specifically on its pharmacokinetics, it is still debated whether the distribution is really affected in overweight or obese patients, but it seems that this factor is not significant[7]. Among the adverse events to consider, which have been reported in the literature, are, for example, the one reported by Lai et a.l[8], on vernal keratoconjunctivitis; although the published case reports are counted.

To date, studies that are elucidating and expanding the therapeutic potential of Tralokinumab continue appearing[1,9]. However, the results of the trials show that it is a good therapeutic option that needs to be studied in greater depth in more populations with different epigenetic characteristics that could influence performance[10]. This goes added to the statement made by Adikusuma et al.[11] regarding the need to promote genetic networks and genomic information in regions where there are no massive databases that allow the extrapolation capacity to be analyzed and integrated with greater complexity of this drug. Unfortunately, in Latin America and the Caribbean, very few centers or researchers have studied this condition or contributed to the development of international multicenter studies, to favor the production of knowledge about the behavior and management of diseases with a low research rate[10,11]. It is necessary to keep abreast of studies that perform subgroup analyzes that determine what other factors may influence the efficiency, efficacy, and safety of Tralokinumab. Meanwhile, the value of Tralokinumab in the approach to this disease and its potential use in healthcare practice must be recognized.

Authorship contributions: All the authors participated in the research through the elaboration of the project, collection and analysis of the information, as well as in the preparation of the manuscript of the present investigation.

Financing: Self-financed.

Conflicts of interest: None of the authors has a conflict of interest, in accordance with their declaration.

Received: March 31, 2023.
Approved: April 14, 2023.

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