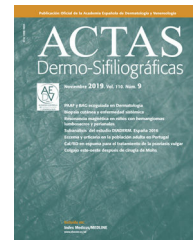




ACTAS Dermo-Sifiliográficas

Full English text available at
www.actasdermo.org



CASE AND RESEARCH LETTER

[Translated article] Dupilumab to Treat Chronic Palmoplantar Eczema: A Retrospective Multicenter Cohort Study

Tratamiento del eccema crónico palmo-plantar con dupilumab: estudio de cohortes retrospectivo multicéntrico

To the Editor,

Chronic hand and/or foot eczema (CHFE) is a chronic skin disease that can have a significant impact on the patients' quality of life.¹ Currently, alitretinoin is the only systemic drug authorized for this indication in the European Union.² In recent years, dupilumab, a human monoclonal antibody targeting interleukin-4 and interleukin-13, has proven its efficacy treating patients with atopic dermatitis (AD), and its various phenotypes or related disorders such as nodular prurigo or CHFE.

This study describes the real-world experience of dupilumab in patients with CHFE. We designed a multicenter, retrospective, observational study with adult patients diagnosed with CHFE on dupilumab, with or without AD lesions in other anatomical regions. Cases of relevant allergic sensitization responsible for the patient's chronic eczema were excluded. Treatment response was assessed objectively (partial improvement if a 75% improvement was achieved or total if lesions were completely gone) and through patient-reported outcomes (PRO) at each clinical visit, using the Visual Analog Scale (VAS) for itch and the Dermatology Life Quality Index (DLQI).

We enrolled a total of 11 patients (9 women [82%] and 2 men [18%]), with a median age of 40 years (range, 28-75). Their clinical-epidemiological characteristics are shown in Table 1. Five patients (45%) had a past medical history of AD onset in childhood (2) or adulthood (3). In 6 patients (54%) only the palms of their hands and/or the soles of their feet were compromised. Lesions in these locations had a mean 4-year history (range, 6 months to



Figure 1 Dyshidrotic eczema on the soles of the feet and toe pulp with complete improvement after 2 months on dupilumab.



Figure 2 Hyperkeratotic eczema on the soles of the feet with improvement after 6 months on dupilumab.

20 years), and 2 patients exhibited the dyshidrotic eczema phenotype vs the remaining 9 who exhibited the hyperkeratotic phenotype. Five patients (45%) had been treated with oral retinoids, 3 of them (27%) with methotrexate, and 2 (18%) with cyclosporine. Two (18%) had received previous treatment with drugs approved for use in psoriasis such as apremilast, brodalumab, or ixekizumab. The median baseline DLQI was 16 (range, 13-28), and the median itch VAS was 9 (range, 8-10). The median follow-up was 68 weeks. All patients reported lesion improvement within the first 4 weeks of treatment, and 8 of them (72%) achieved complete lesion improvement within the first 4 months of therapy (Figures 1 and 2). The median DLQI on week 16 was

DOI of original article:
<https://doi.org/10.1016/j.ad.2023.12.006>

<https://doi.org/10.1016/j.ad.2024.04.010>

0001-7310/© 2024 AEDV. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Please cite this article as: J. Magdaleno-Tapial, A. Torrijos Aguilar, V. González-Delgado et al., [Translated article] Dupilumab to Treat Chronic Palmoplantar Eczema: A Retrospective Multicenter Cohort Study, ACTAS Dermo-Sifiliográficas, <https://doi.org/10.1016/j.ad.2024.04.010>

Table 1 Clinical-epidemiological characteristics of patients with chronic hand and/or foot eczema treated with dupilumab.

Sex, age	Previous atopic history	History of palmar-plantar lesions	Distribution and lesion phenotype	Previous treatments	Baseline PROs	Response to dupilumab
Woman, 40 years	Childhood AD Allergic sensitization to nickel and cobalt	10 years	Hyperkeratotic plantar eczema	Topical corticosteroids and calcineurin inhibitors, Antihistamines Oral corticosteroids Alitretinoin Acitretin	DLQI 28 Itch 10/10	75% improvement at 1 month, at 2 months itch reduced to 2/10 and DLQI to 7/30, escalated every 10 days.
Woman, 28 years	Nickel sensitization	10 years	Hyperkeratotic eczema on 30% of both hands and 40% of both feet	Topical corticosteroids and calcineurin inhibitors, Antihistamines Acitretin Methotrexate Apremilast Brodalumab, Cyclosporine	DLQI 16 Itch 9/10	Whitened after 1 month of treatment
Man, 75 years	Allergic sensitization to fragrance mix I, thiomersal, and balsam of Peru	10 years	Hyperkeratotic eczema on palms and soles	Topical corticosteroids and calcineurin inhibitors, Antihistamines Alitretinoin	DLQI 13 Itch 8/10	Whitened after 2 months of treatment
Woman, 67 years	None	20 years	Hyperkeratotic eczema on palms and soles, dyshidrotic eczema on hands	Topical corticosteroids and calcineurin inhibitors Antihistamines Acitretin	DLQI 23 Itch 9/10	Slight improvement in fissures, discontinued at 16 weeks due to inefficacy
Woman, 33 years	Allergic asthma, sensitization to dust mites and pellitory Perennial rhinitis	6 months	Dyshidrotic eczema on soles of feet and hands	Topical corticosteroids and calcineurin inhibitors Oral corticosteroids	DLQI 19 Itch 10/10	Whitened after 2 months of treatment (figure 1)
Woman, 36 years	Adult AD Nickel sensitization	2 years	Plantar hyperkeratotic eczema, atopic eczema lesions on trunk, legs, and arms	Topical corticosteroids and calcineurin inhibitors, Antihistamines Oral corticosteroids, Methotrexate	DLQI 15 Itch 9/10	50% improvement at 1 month, completely whitened at 6 months, down-titration every 21 days (figure 2)
Woman, 32 years	Childhood AD	2 years	Hyperkeratotic eczema on palms (and dorsum) and flexural	Topical corticosteroids and calcineurin inhibitors Oral corticosteroids Methotrexate	Itch/sleep: 10/10 DLQI 15	DLQI 1 on week 4 DLQI 0 and EASI 0 on weeks 16, 52, and 104

Table 1 (Continued)

Sex, age	Previous atopic history	History of palmar-plantar lesions	Distribution and lesion phenotype	Previous treatments	Baseline PROs	Response to dupilumab
Woman, 56 years	Adult AD ACD to rubber (nurse)	3 years	Palmar hyperkeratotic eczema, Subacute eczema on back and flexures	Topical corticosteroids and calcineurin inhibitors Oral corticosteroids Cyclosporine	EASI 18 BSA 33% DLQI 19, Itch/sleep: 10/8	DLQI 0 and itch 2 on week 4 DLQI 0 and itch 1 on week 16 Whitened since week 16
Man, 71 years	Adult AD ACD to perfumes (isoeugenol, oil of cloves)	7 years	Hyperkeratotic eczema on hands Eczema on trunk and limbs	Topical corticosteroids and calcineurin inhibitors Oral corticosteroids	Itch/sleep: 8/6, DLQI 15 EASI 21, BSA 25%	Itch 0 on week 4 Whitened since week 16 with DLQI 2
Woman, 39 years	None	2 years	Dyshidrotic eczema	Topical corticosteroids and calcineurin inhibitors Oral corticosteroids	DLQI 22 Itch 10/10	Itch 1 on week 4 Whitened from week 16 with DLQI 0
Woman, 53 years	None	4 years	Hyperkeratotic eczema on hands and feet	Topical corticosteroids and calcipotriol, Acitretin Ixekizumab	DLQI 16 Itch 9/10	75% improvement at 1 month, no lesions at 2 months, itch 1/10 and DLQI 2/30

ACD, allergic contact dermatitis; AD, atopic dermatitis; BSA, body surface area; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; PRO, patient reported outcomes.

2 (range, 0–16), representing a 78.3% reduction vs baseline. Treatment was up-titrated every 10 days at the follow-up in 1 patient due to partial response, while another patient had to discontinue treatment on week 16 due to inefficacy. The remaining patients (80%) continued with the drug. One patient down-titrated every 21 days. No adverse events were reported.

The efficacy of dupilumab in palmoplantar involvement has been reported in several case series. Osterhaven et al. presented a prospective, observational study of 47 patients, 74.5% of whom exhibited chronic fissured eczema and 25.5%, vesicular eczema treated with dupilumab, 60% of whom improved—75% compared to baseline—with no differences reported between both clinical subtypes. Additionally, improvement was observed within the first 4 weeks of treatment becoming substantial improvement within the first 16 weeks,³ which are data consistent with those presented in our study. In our patients, the median DLQI reduction was almost 80%, which is similar to what the Dutch series reported (70%). Voorberg et al. published the results of a prospective analysis of 72 patients with CHFE with or without AD treated with dupilumab and a 52-week follow-up, achieving a 75% improvement in the Hand Eczema Severity Index (HECSI-75) and HECSI-90 in 87.1% and 62.9%, respectively, with progressive clinical improvement from week 16 to week 52 and an improved quality of life.⁴ Finally, Lee et al. retrospectively compared the response to dupilumab between patients with AD and hand involvement (38/66) and

those with AD only without hand involvement (28/66), and found no significant differences between both subgroups.⁵ Recently, Olesen et al. reported their experience with 19 patients with chronic hand eczema, and confirmed improvement in 73.7% of them.⁶ Of note in this latter study is the use of biologic drugs approved for psoriasis, as it is the case of 2 of the 11 patients from our series, which reveals the diagnostic challenge posed by hyperkeratotic hand and/or foot eczema without any other suggestive cutaneous lesions of AD or psoriasis.⁷

The experience reported has led to the phase 3 randomized double-blind LIBERTY-AD-HAFT trial NCT04417894 that is evaluating the safety and efficacy profile of dupilumab in adults and adolescents with CHFE. A total of 133 patients were randomized on a 1:1 ratio to receive dupilumab vs placebo, concluding that dupilumab improved the signs, symptoms, and quality of life of patients with hand and foot eczema measured by Investigator Global Assessment (IGA) 0/1, a ≥ 4 point improvement in HECSI, itch VAS, or quality of life scale.⁸

Limitations of our analysis include its small sample size and absence of some data typical of a retrospective study, which would have given greater robustness to the results. On the other hand, The HECSI was not measured, nor were other PROs such as pain, stinging, or specific quality of life scales.

In conclusion, in our experience, patients with CHFE show both clinical and subjective improvement early after

initiating treatment with dupilumab. Longer-term follow-ups of patients and more cases supporting the use of this drug for the treatment of these conditions are necessary.

Conflicts of interest

None declared.

References

1. Thouvenin MD, Bacquey A, Nocera T, Rossi AB. Tolerability and efficacy of a medical device repairing emollient cream in adults with chronic hand dermatitis. *J Cosmet Dermatol*. 2018;17:1158–64.
 2. Thyssen JP, Schuttelaar MLA, Alfonso JH, Andersen KE, Angelova-Fischer I, Arents BWM, et al. Guidelines for diagnosis, prevention, and treatment of hand eczema. *Contact Dermatitis*. 2022;86:357–78.
 3. Oosterhaven JAF, Voorberg AN, Romeijn GLE, de Bruin-Weller MS, Schuttelaar MLA. Effect of dupilumab on hand eczema in patients with atopic dermatitis: An observational study. *J Dermatol*. 2019;46:680–5, <http://dx.doi.org/10.1111/1346-8138.14982>.
 4. Voorberg AN, Romeijn GLE, de Bruin-Weller MS, Schuttelaar MLA. The long-term effect of dupilumab on chronic hand eczema in patients with moderate to severe atopic dermatitis-52 week results from the Dutch BioDay Registry. *Contact Dermatitis*. 2022;87:185–91.
 5. Lee N, Chipalkatti N, Zancanaro P, Kachuk C, Dumont N, Rosmarin D. A Retrospective Review of Dupilumab for Hand Dermatitis. *Dermatology*. 2019;235:187–8.
 6. Olesen CM, Yüksel YT, Zachariae C, Lund TT, Agner T, Petersen TS, et al. Treatment of chronic hand eczema with dupilumab-A retrospective follow-up study. *J Eur Acad Dermatol Venereol*. 2023;37:e557–9, <http://dx.doi.org/10.1111/jdv.18805>.
 7. Al-Janabi A, Foulkes AC, Mason K, Smith CH, Griffiths CEM, Warren RB. Phenotypic switch to eczema in patients receiving biologics for plaque psoriasis: a systematic review. *J Eur Acad Dermatol Venereol*. 2020;34:1440–8.
 8. Simpson EL, Silverberg JI, Worm M, Honari G, Masuda K, Sygula E, et al. 408 Dupilumab Treatment in Patients With Atopic Hand and Foot Dermatitis: Results From a Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial. *Br J Dermatol*. 2023;188, <http://dx.doi.org/10.1093/bjd/ljad162.029>.
- J. Magdaleno-Tapial^{a,*}, A. Torrijos Aguilar^b,
V. González-Delgado^c, P. Hernández-Bel^a
- ^a *Servicio de Dermatología, Hospital General Universitario de Valencia, Valencia, Spain*
^b *Servicio de Dermatología, Hospital Arnau de Vilanova de Valencia, Valencia, Spain*
^c *Servicio de Dermatología, Hospital Clínico Universitario de Valencia, Valencia, Spain*
- * Corresponding author.
E-mail address: jormagta@gmail.com (J. Magdaleno-Tapial).