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COMMENTARY

Challenges in the Use of the Treat-to-Target Strategy in Atopic Dermatitis in Latin America: A Case Series Review

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ABSTRACT

Introduction: Atopic dermatitis (AD) is a chronic, relapsing–remitting illness. In moderate-to-severe instances, recommendations urge patient-centered systemic therapy. Existing standards lack long-term treatment success requirements. A treat-to-target methodology was proposed for systemic therapy patients that requires global improvements to prompt decisions about treatment.

Methods: We conducted an observational study between May 2021 and June 2022 in three Ecuadorian patients with severe AD who were treated with dupilumab to assess the clinical evolution and behavior of the subdomains evaluated by clinimetric tools.

Results: Patients A and C satisfied disease-domain response criteria to dupilumab at 12 and 24 weeks, but B did not complete the algorithm objectives. Nonetheless, patient A improved AD severity, itching, bleeding, desquamation, sleep, daily activities, mood, emotions, sexual troubles,

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clothing, and sports subdomains. Patient B experienced reduced symptomatology, AD aggravation, daily activities impact, and work/study impairment. Patient C improved from severe to mild desquamation, itching, exudate, lichenification, and rough/dry skin. Sleep, shame, and study subdomains improved the most.
Conclusion: We provide a new operational construct for analyzing current patient-reported outcome measures (PROMs) and clinician-reported outcome measures (CROMs) based on subdomains to widen our understanding of the state of disease activity and make clinical decisions when the treat-to-target strategy is not attained.

Keywords: Dupilumab; Severe atopic dermatitis; Patient-reported outcome; Treat-to-target; Subdomains

Key Summary Points

1. De Bruin Weller's treat-to-target approach in AD during dupilumab treatment has not been assessed in real-life scenarios

2. We provide the treat-to-target management of three Ecuadorian patients treated with dupilumab, including a new operational analysis of patient-reported and physician-observed outcomes based on subdomains to assess disease activity and make treatment decisions

3. Patients A and C met at least one criterion for treat-to-target response to dupilumab at 12 and 24 weeks, while patient B did not complete the scores required in the algorithm but improved in some subdomains such as bleeding, exudate, desquamation, the severity of symptoms, itching, exacerbations, the impact on daily activities, and work impairment. Regardless of these findings, the three cases maintained dupilumab dosage

4. An analysis of individual subdomains might provide useful information on which changes are predominant, and can help target therapy accordingly. These findings are intended to precede larger studies in Latin America

INTRODUCTION

Atopic dermatitis (AD) is a chronic, relapsing, and inflammatory skin condition characterized by skin barrier dysfunction, caused by mutations of the *FLG* gene (*filaggrin*) in most patients, and an immune dysfunction involving cytokines that regulate immunoglobulin E (IgE), interleukin-4 (IL-4), IL-5, and IL-13, mainly produced by type 2 T-helper lymphocytes [1]. AD's hallmark symptom is pruritus. Vesicles, weeping, crusting, dry, scaly, and erythematous papules and plaques may be lichenified or thickened due to intense and recurrent scratching in chronic presentations [2, 3].

AD affects around 20% of children [4] and up to 10% of adults in high-income nations [5]. AD prevalence peaks in early childhood, decreases in young adults, then peaks again in middle-aged and older populations [6]. AD prevalence has remained steady worldwide since 2017 [6]. AD is more common in tropical nations, especially Latin America, at a prevalence of 15% [7]. Emollients/skin care, topical or systemic corticosteroids, phototherapy, topical calcineurin inhibitors, crisaborole, Janus kinase inhibitors (JAKi), systemic immunosuppressants, and biological therapies are some of the therapeutic options for AD [8]. Dupilumab, a completely human monoclonal antibody, blocks IL-4Rα, the common receptor component for IL-4 and IL-13, thus reducing IL-4 and IL-13 signaling [9]. It was advised for uncontrolled moderate-to-severe AD in children and adults [9]. Dupilumab performed well in clinical trials and real-life studies [10, 11]. When added to moderate-to-severe AD treatment in adults and adolescents, it reduces symptoms, severity, and rescue drug use and improves the quality of life [9].

Despite its benefits, treating patients with AD with biological medicines is difficult, especially in Latin America [12]. Due to physicians' use of nonstandardized procedures and lack of practicality, technical expertise, and time, these nations might have higher rates of AD [12]. AD's chronic and relapsing–remitting course makes treatment difficult. Latin Americans also struggle to pay for treatment [12]. Most Ecuadorian

patients must pay 1500 USD for dupilumab, which is not subsidized by the government. Most Ecuadorians cannot afford dupilumab because the average monthly salary is 425 USD. These issues necessitate additional treatment methods.

The development of guidelines is essential for clinical practice, as well as shared decision-making between patients and caregivers to lessen the disease burden. However, the ideal, sensitive, unbiased, and patient–physician-correlated clinical scale may not exist. A 2022 meta-analysis found AD clinical practice guidelines are not sufficiently clear, unbiased, trustworthy, or evidence-based and may not apply in all cases [13]. In 2021, De Bruin-Weller et al. presented a treat-to-target strategy for systemic therapy patients, where certain global improvements should be obtained to drive decision-making regarding maintaining, altering, or switching agents [14]. This algorithm requires a Patient Global Assessment (PtGA) reduction of at least 1 point, and at least one disease-domain measure change of Eczema Area and Severity Index (EASI) reduction of 50%, Scoring Atopic Dermatitis (SCORAD) reduction of 50%, peak pruritus numerical rating system (NRS) reduction of at least 3 points, Dermatology Life Quality Index (DLQI) reduction of at least 4 points, and Patient-Oriented Eczema Measure (POEM) reduction of at least 4 points at 24 weeks [14].

In Latin America, where doctors do not commonly employ clinical tools [12], the treat-to-target technique is essential because failure to reach the target could improve decision making in the follow-up of patients with moderate-to-severe AD utilizing systemic agents [14]. Clinicians' real-life behavior in assessing a treat-to-target approach in AD during biological agent use is lacking. To fill this gap, we examined three Ecuadorian patients, treated with dupilumab at 12 and 24 weeks, using the treat-to-target method. We also explain what decisions were made for the patient who did not respond according to the proposed strategy, taking into account the above therapy restrictions, and we present a new operational construct of analysis of the current patient-reported outcome measures (PROMs) and clinician-reported outcome measures (CROMs) based on subdomains to identify disease activity and make clinical decisions.

METHODS

This series of observational cases was conducted between May 2021 and June 2022 at the reference and excellence center for the management of atopic dermatitis in Guayaquil, Ecuador. The data were collected during the three patients' follow-up consultations using clinimetric tools, such as EASI, SCORAD, POEM, NRS, DLQI, and Atopic Dermatitis Control Test (ADCT). To use their information, the patients signed informed consent forms.

RESULTS

Case Presentation

Background

This study has three male patients of different ages. At the start of the study patient A was 53, patient B was 27, and patient C was 12 years old. All had AD since childhood, with unremarkable medical histories and laboratory readings. Based on EASI (Fig. 1), SCORAD (Fig. 1), POEM (Fig. 2), ADCT (Fig. 3), NRS (Fig. 4), and DLQI scores (Fig. 5), the three patients showed very severe AD. All exhibited persistent, severe AD symptoms, including erythematous, edematous, excoriated, and severely pruritic lesions on the trunk, face, and upper and lower extremities.

Each patient's personal life was affected by symptoms' intensity and severity. Patient A had self-described family issues, patient B had ceased working (his daily sun exposure at work worsened his lesions), and patient C was dismissed from school due to chronic absenteeism. Before the consultation, all three patients were receiving high doses of oral, intramuscular, intravenous, and topical corticosteroids of medium to high strength (class III to V), and patient C used Cyclosporine.

Dupilumab

Patients A and B got a 600 mg loading dose of dupilumab, followed by 300 mg subcutaneously

Fig. 1 Eczema Area and Severity Index (EASI) and Scoring Atopic Dermatitis (SCORAD) punctuations in patients **A**, **B**, and **C** followed a treat-to-target approach. The bar graph illustrates the progression of three patients evaluated by EASI and SCORAD over a 24-week period, with the difference in scores observed from the baseline, with a severe category to mild category at the end of treatment

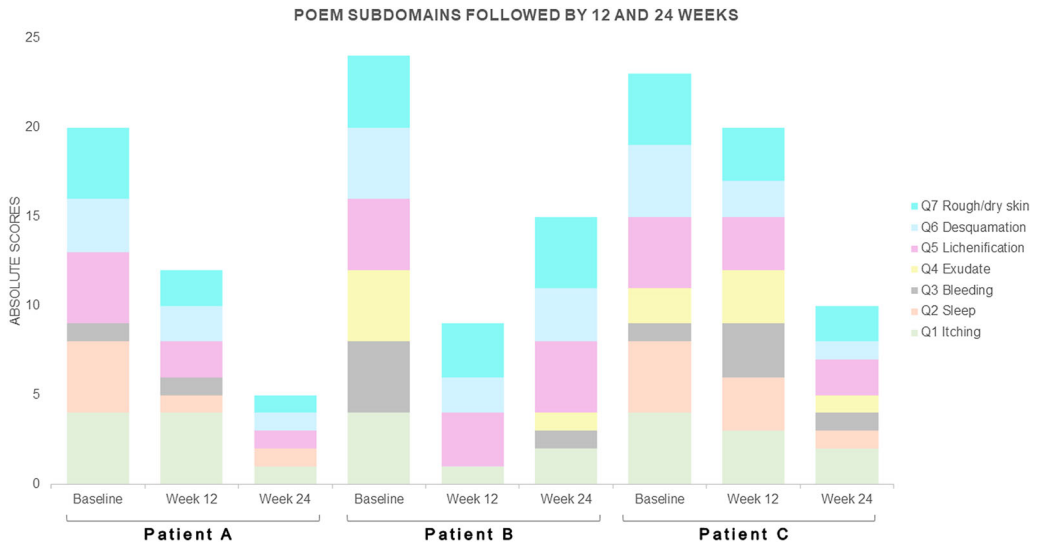

Fig. 2 Patient-Oriented Eczema Measure (POEM) scores in patients A, B, and C were followed using a treat-to-target approach and subdomain analysis. This clustered column chart shows the evolution of the POEM subdomains in three patients at 12 and 24 weeks. It is possible to observe how the domains of itching, sleep, bleeding, exudate, lichenification, desquamation, and rough/dry skin lowered over time

every 2 weeks. Both patients used moisturizers and emollients as needed. Patients aged 6–17 should take 200 mg of dupilumab every 2 weeks. Since Ecuador does not dispense 200 mg, patient C started with 300 mg every 2 weeks, according to weight (67 kg).

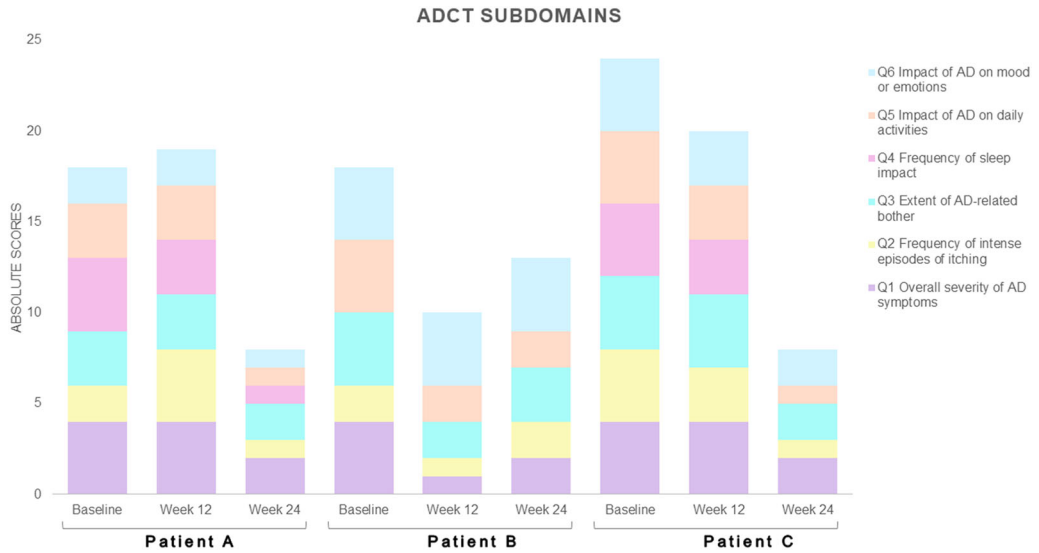

Fig. 3 Atopic Dermatitis Control Test (ADCT) scores in patients A, B, and C were followed using a treat-to-target approach and subdomain analysis. This graph illustrates how the ADCT subdomains evolve, with the impact of AD on overall severity of symptoms, frequency of intense episodes of itching, extent of AD-related bother, frequency of sleep impact, impact on daily activities, and impact on mood or emotions significantly reducing, with the score related to the impact of sleep even being 0 in patients B and C

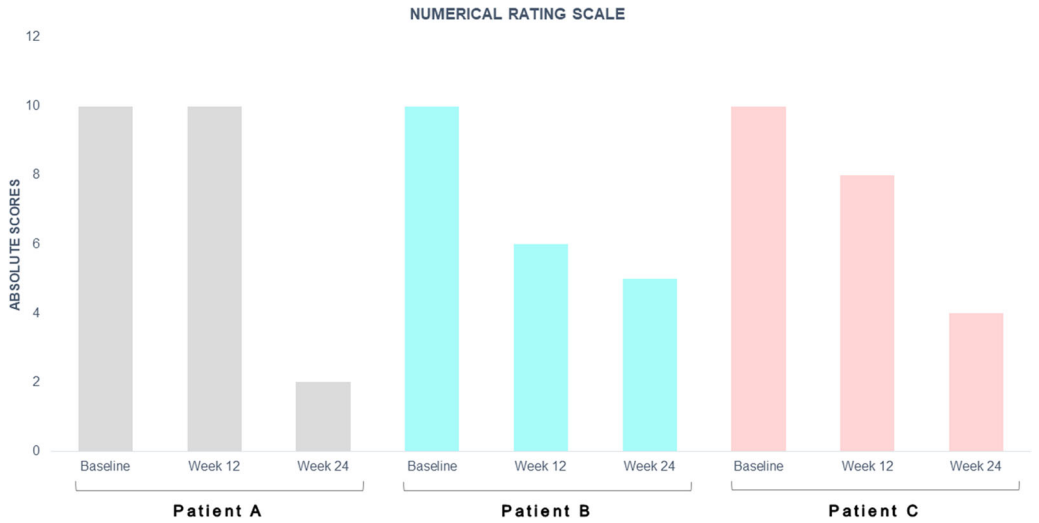

Fig. 4 Peak pruritus numerical rating system (NRS) scores in patients A, B, and C followed using a treat-to-target approach and subdomain analysis. We can see how the NRS scale-measured pruritus behaves at 24 weeks, where it is straightforward that, while the pruritus was severe at the beginning, it ended up being mild at the end of the therapy

Treat-to-Target

To assess patient response, we examined every disease domain at 12 and 24 weeks of treatment. Table 1 contains numerical data and percentage changes. Figures 1, 2, 3, 4, and 5 depict all absolute score differences by subdomain in each patient. During the course of the

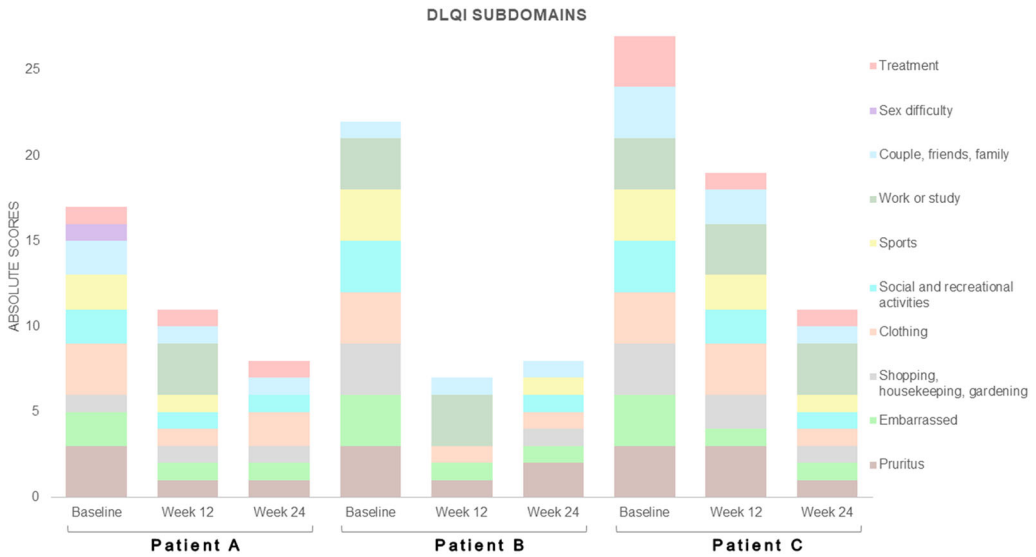

Fig. 5 Dermatology Life Quality Index (DLQI) scores in patients A, B, and C followed using a treat-to-target approach and subdomain analysis. This graph of layered columns illustrates the behavior of the DLQI subdomains, with the greatest improvement seen in "Clothing" in patient A, "Work or study" in patient B, and an improvement seen in all subdomains in patient C at the end of therapy

study, the following events occurred in our three patients:

Patient A improved in all illness domains from severe to mild throughout treatment (Table 1, Figs. 1, 2, 3, 4, and 5). Sexuality, sleep, and itching were the subdomains that changed the most after treatment. At week 24, POEM showed improvements in bleeding (100%), itching, sleep, rough/dry skin, lichenification subdomains (75%), and desquamation (67%). Week 12 was unremarkable in ADCT. At week 24, the subdomains of overall severity of AD, frequency of itching, impact on daily activities, and mood or emotions improved 50%. Sleep improved 75% and NRS improved 80% at week 24.

DLQI scores changed from highly affected to moderately affected quality of life by week 24. Sexual difficulty (100%), pruritus (67%), and clothes (67%) improved at week 12. However, shame, social and recreational activities, sports, couple, friends, and family improved only 50%. At week 24, sports, sexual difficulty, and pruritus improved 100%, 100%, and 67%, respectively. Finally, EASI and SCORAD scores decreased. At 12 weeks, 75% and 48% improved, and at 24 weeks, 86% and 74% improved, respectively.

Patient B improved over the course of treatment. He returned to work after week 24. At week 24, POEM classified patient B as moderate, from severe. Itching and bleeding issues improved 75% and 100%, respectively at week 12. At week 24, itching, bleeding, and exudate subdomains improved 75% and desquamation improved 50% from baseline (Table 1, Figs. 1, 2, 3, 4, and 5).

ADCT was "uncontrolled" after 24 weeks; nevertheless, some subdomains improved. The severity of AD symptoms improved by 75%, followed by the frequency of strong itching, the extent of AD-related bother, and the influence on daily activities, which all improved by 50%. At week 24 NRS improvement was 50%. DLQI was highly impaired at baseline and moderately impaired after 24 weeks. Shopping, gardening, housework, social and leisure activities, and sports improved 100% at 12 weeks. Pruritus, embarrassment, and clothes subdomains improved by 67% each. At 24 weeks, the job or study subdomain improved by 100%, and the patient returned to work, whereas

Table 1 The absolute scores and percentage changes of each subdomain analyzed after 12 and 24 weeks of dupilumab treatment

Subdomains	Patient A					Patient B					Patient C				
	Baseline	Week 12	Δ% at 12 weeks	Week 24	Δ% at 24 weeks	Baseline	Week 12	Δ% at 12 weeks	Week 24	Δ% at 24 weeks	Baseline	Week 12	Δ% at 12 weeks	Week 24	Δ% at 24 weeks
POEM															
Q1 Itching	4	4	0	1	−75[b]	4	1	−75[b]	2	−50[b]	4	3	−25	2	−50[b]
Q2 Sleep	4	1	−75[b]	1	−75[b]	0	0	0	0	0	4	3	−25	1	−75[b]
Q3 Bleeding	1	1	0	0	−100[b]	4	0	−100[b]	1	−75[b]	1	3	+200	1	0
Q4 Exudate	0	0	0	0	0	4	0	−100[b]	1	−75[b]	2	3	+50	1	−50[b]
Q5 Lichenification	4	2	−50[b]	1	−75[b]	4	3	−25	4	0	4	3	−25	2	−50[b]
Q6 Desquamation	3	2	−33	1	−67[b]	4	2	−50[b]	3	−25	4	2	−50[b]	1	−75[b]
Q7 Rough/dry skin	4	2	−50[b]	1	−75[b]	4	3	−25	4	0	4	3	−25	2	−50[b]
Total	20	12[a]	−40[a]	5[a]	−75[a,b]	24	9[a]	−63[a,b]	15	−38	23	20	−13	10	−57[b]
ADCT															
Q1 Overall severity of AD symptoms	4	4	0	2	−50[b]	4	1	−75[b]	2	−50[b]	4	4	0	2	−50[b]
Q2 Frequency of intense episodes of itching	2	4	+100	1	−50[b]	2	1	−50[b]	2	0	4	3	−25	1	−75[b]
Q3 Extent of AD-related bother	3	3	0	2	−33	4	2	−50[b]	3	−25	4	4	0	2	−50[b]
Q4 Frequency of sleep impact	4	3	-25	1	−75[b]	0	0	0	0	0	4	3	−25	0	−100[b]
Q5 Impact of AD on daily activities	3	3	0	1	−67[b]	4	2	−50[b]	2	−50[b]	4	3	−25	1	−75[b]
Q6 Impact of AD on mood or emotions	2	2	0	1	−50[b]	4	4	0	4	0	4	3	−25	2	−50[b]
Total	18	19	+6	8	−56[b]	18	10	−44	13	−28	24	20	−17	8	−67[b]
NRS	10	10	0	2[a]	−80[a,b]	10	6[a]	−40[a]	5	−50[b]	10	8	−20	4[a]	−60[a,b]
DLQI															
Pruritus	3	1	−67[b]	1	−67[b]	3	1	−67[b]	2	−34	3	3	0	1	−67[b]
Embarrassed	2	1	−50[b]	1	−50[b]	3	1	−67[b]	1	−67[b]	3	1	−67[b]	1	−67[b]

Table 1 continued

Subdomains	Patient A					Patient B					Patient C				
	Baseline	Week 12	Δ% at 12 weeks	Week 24	Δ% at 24 weeks	Baseline	Week 12	Δ% at 12 weeks	Week 24	Δ% at 24 weeks	Baseline	Week 12	Δ% at 12 weeks	Week 24	Δ% at 24 weeks
Shopping, housekeeping, gardening	1	1	0	1	0	3	0	−100[b]	1	−67[b]	3	2	−34	1	−67[b]
Clothing	3	1	−67[b]	2	−34	3	1	−67[b]	1	−67[b]	3	3	0	1	−67[b]
Social and recreational activities	2	1	−50[b]	1	−50[b]	3	0	−100[b]	1	−67[b]	3	2	−34	1	−67[b]
Sports	2	1	−50[b]	0	−100[b]	3	0	−100[b]	1	−67[b]	3	2	−34	1	−67[b]
Work or study	0	3	+100	0	0	3	3	0	0	−100[b]	3	3	0	3	0
Couple, friends, family	2	1	−50[b]	1	−50[b]	1	1	0	1	0	3	2	−34	1	−67[b]
Sex difficulty	1	0	−100[b]	0	−100[b]	0	0	0	0	0	0	0	0	0	0
Treatment	1	1	0	1	0	0	0	0	0	0	3	1	−67[b]	1	−67[b]
Total	17	11[a]	−35[a]	8	−53[b]	22	7[a]	−68[a,b]	8	−64[b]	27	19[a]	−30[a]	11	−59[b]
EASI	33.00	8.10	−75.45[a]	4.60[a]	−86.06[a]	51.60	29.60	−42.64	15.80	−69.38[b]	36.41	14.41	−60.42[a]	1.31[a]	−96.40[a]
SCORAD	87.20	45.60	−47.71	23.00[a]	−73.62[b]	73.91	68.10	−7.86	43.52	−41.12	92.00	47.19	−48.71	24.90[a]	−72.93[b]

[a]Achievement of De Bruin-Weller criteria [14]

[b]Improvements in every subdomain of PROMs and CROMs analyzed, expressed in percentage changes at weeks 12 and 24

[c]ADCT control is < 7 points

embarrassment, shopping, gardening and housekeeping, clothing, social and recreational activities, and sports all improved by more than 60%. From baseline to end, EASI scores improved from severe to moderate. EASI scores were 43% improved at 12 weeks, and 69% at 24 weeks. Finally, SCORAD punctuations started severe, and improved to moderate by week 24 (8% by week 12, to 41% decrease by week 24).

In patient C, POEM went from severe to moderate at 24 weeks. Desquamation improved by 50% at week 12. At 24 weeks, sleep and desquamation improved by 75%; itching, exudate, lichenification, and rough/dry skin improved by 50% each. Baseline ADCT was uncontrolled. At week 12, AD symptoms and exacerbations did not improve, nor did the subdomains tested. At week 24, sleep improved by 100%, followed by the improvement of frequency of acute itching (75%), and AD's impact on daily activities (75%). The remaining subdomains improved by 50%.

NRS scores were reduced by 20% at week 12 and by 60% at week 24. DLQI categories only altered from highly to greatly impaired quality of life. At 12 weeks, embarrassment and treatment subdomains improved by 67%. All subdomains improved by 67% at week 24. Finally, EASI and SCORAD ratings improved from severe to mild, with a reduction of 60% and 49% at 12 weeks, respectively, and 96% and 73% by week 24 (Table 1, Figs. 1, 2, 3, 4, 5).

DISCUSSION

The treat-to-target strategy is a therapeutic concept that has been adopted from the study of other chronic diseases (autoimmunity [15], cardiovascular [16], and endocrine [17]). Its main goal is strict disease control to achieve remission or reduced disease activity (according to scores of PROMs and CROMs). Evidence-based guidelines recommend patient-centered care strategies that progress with disease severity in AD. Nevertheless, guidelines are based on randomized controlled trials (RCTs) [18], which are usually conducted on highly selected samples of the population and may not apply to normal care settings. No strategy for patient responses to step-wise therapies exists [8]. A meta-analysis found 40 guidelines < 5 years old from high sociodemographic index nations that were not clear, unbiased, trustworthy, or evidence-based [13]. Despite nonbiological treatment, patients have a "treatment-resistant illness" [8, 19]. De Bruin-Weller et al. provide a decision-making methodology for patients with AD receiving systemic agents at 12 and 24 weeks. If the aim is missed, consider keeping, modifying, or switching systemic agents [14].

We adapted this approach to three male patients with severe AD receiving dupilumab, who were assessed at baseline, 12 weeks, and 24 weeks to assess improvement. Two of our three male patients with severe AD met treat-to-target objectives. When evaluating subdomains, all showed improvements. Patient A improved with AD intensity, itching, bleeding, desquamation, sleep, everyday activities, mood or emotions, sexual trouble, clothes, and sports. EASI and SCORAD improved CROMs from severe to mild. Patient B had less bleeding, exudate, desquamation, AD symptoms, strong itching, AD-related aggravation, and AD's impact on everyday activities. Work/study improved. CROMs became moderate. Patient C improved with desquamation, itching, exudate, lichenification, and rough/dry skin from severe to mild. Sleep, shame, and study improved the most. CROMs showed decreased illness severity. At 12 and 24 weeks, patients A and C met at least one disease-domain response criterion to dupilumab; however, patient B did not complete the algorithm endpoints.

Under medical supervision, AD is hard to treat. Latin America is a region with slow economic growth, poverty, and inequality [20]. Without health insurance and with low monthly salaries, it can be difficult and sometimes impossible to pay for expensive medical treatment. In Colombia, Brazil, and Argentina, the social health system covers dupilumab. Patients B and C paid for their medication. Patient B could not follow the treatment plan because he could not afford it; nevertheless, the patient improved PROM and CROM subdomains at week 24.

These case series analyze clinical assessment scale subdomains. According to some authors, subdomains are reflective of disease impact and can assist target therapy by indicating whether acute (e.g., weeping, bleeding) or chronic (e.g., itching, dryness) changes are predominant [14, 21]. Although each subdomain may not reach the minimal clinical importance differences (MCID) values of significant overall change, the percentage of change, or absolute decrease of an established point value, can indicate that the disease activity is where the patient and dermatologist do not see the need for any therapeutic changes or other interventions [22]. A new construct analysis technique is proposed for the subdomains discussed. The results are evaluated question by question over time, independent of the global values, to determine an improvement or worsening of the disease course and its treatment, rather than a rigid decision based exclusively on the global score [23]. A positive effect that translates into better sleeping, less itchiness, and reactivation of their school and work activities could be observed even though the global score does not show overall improvement.

More than 50% of patients with AD experience a lower quality of life, and 60% say AD limits their daily routine [24]. Stingeni et al. found that patients with AD work less productively (42.6%) [24]. In the past year, 67.8% of AD sufferers felt constrained in job performance, or uncertain about career advancement [24]. A percentage of 39.3% of children were bullied, and 33.9% of workers felt discriminated against due to AD [25]. This is comparable to this study's patients' experiences. Before this study, disease-related side effects forced individuals to quit their careers and studies. After dupilumab treatment, their lesions improved, allowing them to resume their activities, despite not meeting consensus criteria [26].

LIMITATIONS

While the description of three cases in Ecuador is complete, it is not possible to generalize findings due to the small sample size, but it opens the door for additional studies to examine the viability of implementing this new method of analysis by subdomains, in a broader population. Another limitation is that PtGA was not evaluated in our center, because it is not recommended by the Harmonising Outcome Measures for Eczema (HOME) global initiative for follow-up and monitoring of patients with AD [27]. However, we suggest its in-depth study in larger study groups to evaluate its applicability in AD.

CONCLUSIONS

Using De Bruin-Weller's treat-to-target approach, our results help us to understand real-life management of severe AD disease in Latin America. The case studies show that, while patients' clinical signs and symptoms improved when their subdomains were evaluated, they did not achieve the desired treat-to-target score after 24 weeks (6 months). Individualizing treatment modification based on specific patient-reported and physician-observed improvements in both subdomains, as well as patient reintegration into daily activities, is proposed to gain a better understanding of the issues encountered when stepping up treatment in these patients from this geographical region. More research is needed to evaluate this proposed treatment analysis and plan of action during the follow-up of patients with moderate-to-severe AD, who are treated with dupilumab.

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Author Contributions Ivan Cherrez-Ojeda: Conceptualization, Formal Analysis, Resources,

Writing—Original Draft, Writing—Review and Editing, Supervision. Karla Robles-Velasco, Simon Francis Thomsen, German D Ramon, Jorge Sanchez and Benjamin Hidalgo: Writing—Original Draft, Writing—Review and Editing, Supervision, Formal Analysis, Resources. All authors have read and agreed to the published version of the manuscript. Belen Intriago and Maria José Farfán: Data collection.

Disclosures The authors have nothing to disclose.

Compliance with Ethics Guidelines This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors. Our research has been approved by our institutional review board, with number HCK-CEISH-2022-002. Written informed consent was obtained from the patients for publication of this case series and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

REFERENCES

1. Carmela Avena-Woods BP. Overview of Atopic Dermatitis. Suppl Featur Publ. 2017. https://www.ajmc.com/view/overview-of-atopic-dermatitis-article. Accessed 3rd Oct, 2022

2. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. J Am Acad Dermatol. 2014;70(2):338–51. https://doi.org/10.1016/j.jaad.2013.10.010.

3. Böhme M, Svensson A, Kull I, Wahlgren CF. Hanifin's and Rajka's minor criteria for atopic dermatitis: which do 2-year-olds exhibit? J Am Acad Dermatol. 2000;43(5 Pt 1):785–92. https://doi.org/10.1067/mjd.2000.110070.

4. Deckers IAG, McLean S, Linssen S, Mommers M, van Schayck CP, Sheikh A. Investigating international time trends in the incidence and prevalence of atopic eczema 1990–2010: a systematic review of epidemiological studies. PLoS ONE. 2012;7(7):e39803. https://doi.org/10.1371/journal.pone.0039803.

5. Lee HH, Patel KR, Singam V, Rastogi S, Silverberg JI. A systematic review and meta-analysis of the prevalence and phenotype of adult-onset atopic dermatitis. J Am Acad Dermatol. 2019;80(6):1526-1532.e7. https://doi.org/10.1016/j.jaad.2018.05.1241.

6. Laughter MR, Maymone MBC, Mashayekhi S, et al. The global burden of atopic dermatitis: lessons from the Global Burden of Disease Study 1990–2017. Br J Dermatol. 2021;184(2):304–9. https://doi.org/10.1111/bjd.19580.

7. Sánchez J, Sánchez A, Cardona R. Critical review of ISAAC results for atopic dermatitis in tropical cities. Rev Alerg Mex. 2018;65(4):389–99. https://doi.org/10.29262/ram.v65i4.341.

8. Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part II. J Eur Acad Dermatol Venereol. 2018;32(6):850–78. https://doi.org/10.1111/jdv.14888.

9. Agache I, Song Y, Posso M, et al. Efficacy and safety of dupilumab for moderate-to-severe atopic dermatitis: a systematic review for the EAACI

biologicals guidelines. Allergy. 2021;76(1):45–58. https://doi.org/10.1111/all.14510.

10. Blauvelt A, de Bruin-Weller M, Gooderham M, et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. Lancet. 2017;389(10086):2287–303. https://doi.org/10.1016/S0140-6736(17)31191-1.

11. Silverberg JI, Yosipovitch G, Simpson EL, et al. Dupilumab treatment results in early and sustained improvements in itch in adolescents and adults with moderate to severe atopic dermatitis: analysis of the randomized phase 3 studies SOLO 1 and SOLO 2, AD ADOL, and CHRONOS. J Am Acad Dermatol. 2020;82(6):1328–36. https://doi.org/10.1016/j.jaad.2020.02.060.

12. Sanchez J, Cherrez-Ojeda I, Galvan C, et al. The unmet needs in atopic dermatitis control in Latin America: a multidisciplinary expert perspective. Dermatol Ther. 2021;11(5):1521–40. https://doi.org/10.1007/s13555-021-00595-9.

13. Arents BWM, van Zuuren EJ, Vermeulen S, Schoones JW, Fedorowicz Z. Global guidelines in dermatology mapping project (GUIDEMAP), a systematic review of atopic dermatitis clinical practice guidelines: are they clear, unbiased, trustworthy and evidence based (CUTE)? Br J Dermatol. 2022;186(5):792–802. https://doi.org/10.1111/bjd.20972.

14. de Bruin-Weller M, Thaçi D, Smith CH, et al. Dupilumab with concomitant topical corticosteroid treatment in adults with atopic dermatitis with an inadequate response or intolerance to ciclosporin A or when this treatment is medically inadvisable: a placebo-controlled, randomized phase III clinical trial (LIBERTY AD CAFÉ). Br J Dermatol. 2018;178(5):1083–101. https://doi.org/10.1111/bjd.16156.

15. van Vollenhoven R. Treat-to-target in rheumatoid arthritis—are we there yet? Nat Rev Rheumatol. 2019;15(3):180–6. https://doi.org/10.1038/s41584-019-0170-5.

16. Atar D, Birkeland KI, Uhlig T. "Treat to target": moving targets from hypertension, hyperlipidaemia and diabetes to rheumatoid arthritis. Ann Rheum Dis. 2010;69(4):629–30. https://doi.org/10.1136/ard.2010.128462.

17. Wangnoo SK, Sethi B, Sahay RK, John M, Ghosal S, Sharma SK. Treat-to-target trials in diabetes. Indian J Endocrinol Metab. 2014;18(2):166–74. https://doi.org/10.4103/2230-8210.129106.

18. Wang FP, Tang XJ, Wei CQ, Xu LR, Mao H, Luo FM. Dupilumab treatment in moderate-to-severe atopic dermatitis: a systematic review and meta-analysis. J Dermatol Sci. 2018;90(2):190–8. https://doi.org/10.1016/j.jdermsci.2018.01.016.

19. Johnson BB, Franco AI, Beck LA, Prezzano JC. Treatment-resistant atopic dermatitis: challenges and solutions. Clin Cosmet Investig Dermatol. 2019;12:181–92. https://doi.org/10.2147/CCID.S163814.

20. Caribbean EC for LA and the. Latin America and the Caribbean's Growth Will Slow to 2.1% in 2022 amid Significant Asymmetries between Developed and Emerging Countries. Published January 12. (2022). https://www.cepal.org/en/pressreleases/latin-america-and-caribbeans-growth-will-slow-21-2022-amid-significant-asymmetries. Accessed 3rd Oct, 2022

21. Lloyd-Lavery A, Solman L, Grindlay DJC, Rogers NK, Thomas KS, Harman KE. What's new in atopic eczema? An analysis of systematic reviews published in 2016. Part 2: Epidemiology aetiology and risk factors. Clin Exp Dermatol. 2019;44(4):370–5. https://doi.org/10.1111/ced.13853.

22. Carretero G, Carrascosa J, m., Puig L, et al. Definition of minimal disease activity in psoriasis. J Eur Acad Dermatol Venereol. 2021;35(2):422–30. https://doi.org/10.1111/jdv.16564.

23. Schram ME, Spuls PI, Leeflang MMG, Lindeboom R, Bos JD, Schmitt J. EASI, (objective) SCORAD and POEM for atopic eczema: responsiveness and minimal clinically important difference. Allergy. 2012;67(1):99–106. https://doi.org/10.1111/j.1398-9995.2011.02719.x.

24. Stingeni L, Belloni Fortina A, Baiardini I, Hansel K, Moretti D, Cipriani F. Atopic dermatitis and patient perspectives: insights of bullying at school and career discrimination at work. J Asthma Allergy. 2021;14:919–28. https://doi.org/10.2147/JAA.S317009.

25. Xie QW, Chan CLW, Chan CHY. The wounded self-lonely in a crowd: a qualitative study of the voices of children living with atopic dermatitis in Hong Kong. Health Soc Care Community. 2020;28(3):862–73. https://doi.org/10.1111/hsc.12917.

26. Nørreslet LB, Ebbehøj NE, Ellekilde Bonde JP, Thomsen SF, Agner T. The impact of atopic dermatitis on work life—a systematic review. J Eur Acad Dermatol Venereol. 2018;32(1):23–38. https://doi.org/10.1111/jdv.14523.

27. Welcome. (2022). http://www.homeforeczema.org/. Accessed 3rd Oct, 2022.