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RESEARCH LETTER

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A real-world study in Brazilian patients with atopic dermatitis treated with dupilumab who previously received methotrexate and cyclosporine

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Abstract
Introduction: Atopic Dermatitis (AD) is a chronic inflammatory skin disease that significantly impacts patients´ quality of life. Dupilumab was Brazil´s first biologic approved to treat moderate-to-severe AD. We aimed to assess the effectiveness and safety of dupilumab in a real-life setting for 16 weeks.
Methods: Fourteen patients were evaluated at weeks 0, 4, and 16 after the first dupilumab shot. At each visit, disease activity and severity, itching intensity, and impact on quality of life were measured using the EASI (Eczema Area and Severity Index), IGA (Investigator's Global Assessment), SCORAD (Scoring Atopic Dermatitis), NRS (Numeric Rating Scale for itching), and DLQI (Dermatology Life Quality Index).
Results: Clinical improvement observed was significant, with variation in all scores used in the study sample during the first 16 weeks of treatment ($p < 0.0001$).
Conclusion: Dupilumab was effective and safe in our patients with moderate-to-severe AD.

Introduction

Dupilumab, a fully human monoclonal antibody targeting interleukin (IL)-4 and IL-13, was Brazil's first biologic approved to treat moderate-to-severe atopic dermatitis (AD). In a real-life setting at the atopic dermatitis outpatient clinic of the Immunology Service at the Clementino Fraga Filho University Hospital (Universidade Federal do Rio de Janeiro [UFRJ]), we observed and evaluated the clinical improvement and safety of this treatment in adult patients (who had already been using cyclosporine and methotrexate) with a history of uncontrolled disease for over 3 years.

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The evaluations were conducted using validated scales at three different time points. Access to this high-cost biologic therapy was obtained through legal action.

Methods

Following the approval by Clementino Fraga Filho (HUCFF - UFRJ) University Hospital - Rio de Janeiro Medical Ethics Committee (CAAE 31523520.8.00005257), patients under follow-up in the service were included. The inclusion criteria were AD patients at HUCFF aged over 18 years, EASI >16, SCORAD > 25, NRS > 4, IGA > 3, DLQI >10 or EASI <16, DLQI < 10 before therapy with 2 immunosuppressants, and more than 3 years of follow-up.

They were examined at weeks 0, 4, and 16 after the first Dupilumab injection. At each visit, disease activity and severity, itching intensity, and impact on quality of life were measured using the EASI (Eczema Area and Severity Index), IGA (Investigator's Global Assessment), SCORAD (Scoring Atopic Dermatitis), NRS (Numeric Rating Scale for itching), and DLQI (Dermatology Life Quality Index).

The numerical variables did not present normal distribution according to the Shapiro-Wilk test and/or graphical analysis of the histogram; therefore, summarized in median and interquartile range. We also calculate relative delta, which corresponds in percentage to the post-treatment variation according to the pre-treatment moment. The inferential analysis was composed of Friedman's ANOVA to compare the 3 moments. Nemenyi multiple comparison test was applied to identify pairs of moments that differed significantly.

Results

Six (42.9%) women and eight (57.1%) men have initiated treatment with dupilumab 300 mg every second week following a loading dose of 600 mg at treatment initiation and were included in the study. The mean age at enrolment was 25 years, ranging from 18 to 54 years from different ethnic groups, the majority being white (42.9%). Family history of AD in 20%. Regarding personal history, 55,7% had allergic rhinitis and 44,3% presented with asthma, 30% of patients had a history of hospitalization due to AD. The first objective was to characterize the sample to outline the profile of the treated patients. All patients had a history of treatment with at least two traditional systemic immunosuppressive therapies, such as methotrexate dose of 10 - 15 mg/ week and cyclosporin 3 - 5 mg/ kg/day, which were discontinued due to insufficient disease control or side effects. All patients used moisturizers. Given the severity of their chronic disease, they self-administered topical corticosteroids at start-up and in the study period during flares. The total population in this tertiary referral center consisted of 70 patients. Among them, 32 patients were diagnosed with moderate AD, and even after treatment with immunosuppressive drugs, 14 continued to have moderate disease. Out of the 31 patients with severe AD, after immunosuppressives, 20 had moderate disease, and 4 continued to have severe AD. It was observed that 45 improved and 25 did not change the severity. Of these 25, 16 had some exclusion criteria such as autoimmune disease, pregnancy, lactation, psoriasis, inflammatory bowel disease, neoplasia, demyelinating disease, active or latent tuberculosis, use of other biologics for any other disease, or did not meet the inclusion criteria and mainly due to difficulty in accessing high-cost medication, the biologic was obtained through legal proceedings. To date, in 2025, there is no immunobiological available liberally through the Unified Health System.

The second objective verified that there was significant variation in the scores over the 3 moments. Significant variation ($p<0.0001$) was observed over the treatment time for all scores in the study sample. It was identified that the 3 moments differ significantly from each other for EASI, IGA and DLQI, meaning that there was a significant progressive drop in these scores and that between weeks 4 and 16 it was significantly lower than the baseline week for SCORAD and NRS (Table 1).

Third objective to verify whether there is a correlation between the relative deltas of the scores. Significant correlation was observed according to Spearman's coefficient between pairs of variables whose descriptive level was less than or equal to 5%. Observed that the EASI score had a variation, reduced in median values of 71% from the baseline moment (week 0) to the post moment (week 16) (Table 2).

Adverse events were observed as facial erythema in 28.5% of our patients who used dupilumab. We point out that 78.6% of patients previously had periorbital dark

Table 1 Analysis of the evolution of scores of the total sample.

Variable	0 Baseline/week		Week 4		Week 16		p-value*	Significant differences
	Median	IQR	Median	IQR	Median	IQR		
EASI	28,5	12–46	12,9	4–26	9,4	4–15	$p < 0,0001$	Week 0 ≠ 4 ≠ 16
SCORAD	58,9	39–74	33,8	22–48	27,5	19–36	$p < 0,0001$	Week 0 ≠ 4, 0 ≠ 16
IGA	3,0	3–4	2,5	2–3	2,0	2–2,3	$p < 0,0001$	Week 0 ≠ 4 ≠ 16
NRS	7,0	5–9	4,5	2–6	3,5	2–5,3	$p < 0,0001$	Week 0 ≠ 4, 0 ≠ 16
DLQI	11,5	9–21	9,5	6–16	4,5	1,8–10	$p < 0,0001$	Week 0 ≠ 4[a] ≠ 16

IQR: Interquartile Range (Q1–Q3)—Friedman ANOVA *Nemenyi post hoc test at a 5% significance level.

Table 2 Descriptive of the relative deltas of the scores in the total sample.

Relative Delta (%)	n	mean	DP	Median	IQR		min	Max
Baseline - 4ª week								
EASI	14	−47,6	24,9	−46,2	−68	−35	−85	0
SCORAD	14	−33,3	18,4	−35,3	−45	−20	−74,3	−2,6
IGA	14	−19	20,0	−25,0	−33	−0	−33,3	33,3
NRS	14	−32,8	24,5	−28,6	− 51	−14	−83,3	0
DLQI	14	−21,1	30,1	−20,0	−42	−0	−81,8	42,9
Baseline - 4ª week								
EASI	14	−46,3	62,8	**−71,0**	−73	−34	−97,7	151,8
SCORAD	14	−37,6	51,8	−50,5	−62	−30	−89,8	128,2
IGA	14	−33,3	22,9	−33,3	−50	−19	−75	0
NRS	14	−37,1	30,3	−35,4	−57	−25	−83,3	33,3
DLQI	14	−58,0	24,4	−66,1	−76	−32	−95,2	−18,2
4ª week - 16ª week				−43,1			−90	605
EASI	14	20,5	180,6		−55	−9		
SCORAD	14	−10,9	56,6	−28,1	−44	7	−62,5	150,9
IGA	14	−17,3	22,8	0,0	−33	0	−66,7	0,0
NRS	14	−2,9	40,8	−7,2	−33	0	−50	100
DLQI	14	−24,4	110,4	−54,0	−74	−19	−90,9	350

DP: standard deviation; IQR interquartile range (Q1–Q3).

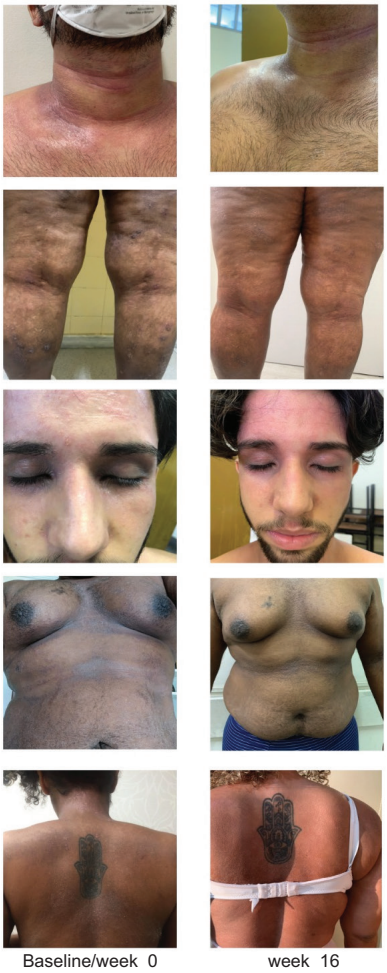

Figure 1 Patients of different phenotypes at week 0 and week 16.

circles. Mild conjunctivitis did not lead to discontinuation of treatment in 21.42% of patients. Three of which patients previously had keratoconus.

Our study also highlights the importance of reporting isolated events. An unexpected event occurred with our only Asian patient (Figure 1 - photos 1 e 2), a 34- 34-year-old doctor with atopic dermatitis since the age of 21, who died used systemic corticosteroid prednisone at a dose between 0.5-1mg/kg/day indiscriminately years during crises for about 10 years, used methotrexate for 5 years, altered liver function, azathioprine for 4 years without efficacy and cyclosporine for an average of 2 years and presented arterial hypertension with use which was discontinued weeks before starting Dupilumab. At week 0, SCORAD was 41.8, which decreased to 32.9 in week 4 and to 27.2 in week 16.

After approximately one year on the medication, he suffered a sudden event and passed away. His family had chosen not to perform an autopsy, and the body was cremated.

Discussion

We highlight the importance of reporting isolated events. An unexpected event occurred with our only Asian patient, a 34-year-old doctor with atopic dermatitis since the age of 21, who had used corticotherapy for years, azathioprine, and cyclosporine, which was discontinued weeks before starting dupilumab. At week 0, the SCORAD was 41.8, which decreased to 32.9 in week 4 and 27.2 in week 16. Already on medication for about a year, he suffered a sudden attack and passed away at his residence. The family chose not to perform an autopsy, and the body was cremated.

Several recent publications have described the efficacy of dupilumab with a reported 75% reduction in EASI scores; we found six recent similar studies. According to a

retrospective study from a single center of adult patients with moderate-to-severe atopic dermatitis treated with dupilumab in China, our patients had more severe disease at an earlier age, with a baseline EASI of 28.5, whereas in the Chinese patients, the baseline EASI was 19.47. However, SCORAD, NRS, and DLQI values were very close to ours. The EASI reduction was similar to the published data in other real-world studies.

Our study may contribute to the accumulation of real-world data for specific therapies in the practice of precision medicine for immune-mediated dermatological diseases, confirming dupilumab was effective and safe in our patients with moderate-to-severe AD.

Competing Interests

None.

Author Contributions

All authors contributed equally to this article.

Conflicts of Interest

Cinthia Dinis has no conflict of interest; Sergio Dortas declares he received fees to dolectures for Sanofi Brazil; and Omar Lupi declares he received fees to do lectures for Sanofi Brazil.

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