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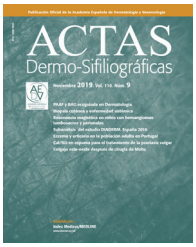

CASE AND RESEARCH LETTER

Mid-Term Efficacy of Dupilumab in Children Aged ≥ 36 Months to <12 Years With Atopic Dermatitis: A Case Series

Eficacia a medio plazo de dupilumab en niños de ≥ 36 meses a < 12 años con dermatitis atópica: serie de casos

To the Editor,

Atopic dermatitis (AD) has a significant negative impact on the patients' quality of life, including pruritus, sleep disturbances, and potential stress among family members.[1,2] Currently, over 20% of the children from first world countries have AD, and in most cases the disease starts within the first 2 years of life.[2] Severe cases of AD in children account for <10%.[3] Increasing knowledge on the pathogenesis of AD results in novel therapeutic targets and pathways.[4] New targeted therapies such as janus quinase (JAK) inhibitors and interleukin 4/13 (IL-4/13) or IL-13 blockers have been recently approved to treat AD in the adult population.[5] However, drugs with a favorable benefit–risk ratio are still limited in children.[3] Long-term treatment with systemic corticosteroids is strongly ill-advised in children. Systemic immunosuppressors are used off-label in pediatric patients whose AD is inadequately controlled by topical therapies without strong evidence to support their use in children.[3,6] Dupilumab—a monoclonal antibody that inhibits the interleukin IL-4/IL-13 signaling pathway—has been approved by both the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) in children aged ≥6 to <12 years with moderate-to-severe AD requiring systemic treatments.[3,6] In addition to this group (6–12 years), dupilumab vs uncontrolled severe AD has been recently approved in children aged 6 months to 5 years[7] by the FDA, but not yet by the EMA, which means that real-life experience series are scarce in children aged ≥6 months to <12 years.[8–10]

This was a single-center case series study of children aged ≥6 months to <12 years with moderate-to-severe AD who were treated with monthly dupilumab 200 mg or 300 mg from June through December 2022 in the dermatology unit of a Spanish tertiary referral center. Study variables measured included the patients' demographics, classical atopic comorbidities (asthma, rhinitis, conjunctivitis, food or environmental allergy, and eosinophilic esophagitis), and dupilumab dose (Table 1). Disease severity was measured using the Eczema Area and Severity Index (EASI), Body Surface Area (BSA), validated investigator global assessment (IGA) for AD, and the sleep quality improvement was assessed by the parents at the baseline visit and on weeks 4, 16 and 24. The primary endpoint was to evaluate dupilumab efficacy assessed by reaching a global EASI < 3 and IGA 0 or 1 at the 4-, 16-, and 24-week follow-up. The secondary endpoint was to assess dupilumab safety at the follow-up. Quantitative variables were expressed as median values (± standard deviation and/or ranges), and the qualitative ones as frequencies.

A total of 7 patients (4 girls, 57.1%) were included. The mean age was 6.8 (3–10) years old, and 3 patients were younger than 6 years. None of them were Caucasian. The median IgE level when AD was diagnosed was 5313 ± 4712.9 kU/L. Four patients (57.1%) had classical flexural and generalized AD, 3 patients (42.8%) had prurigo-like AD, and 4 children (57.1%) had facial involvement at baseline. All participants with prurigo-like AD were Asian. Patient demographics, coexisting AD related comorbidities, dupilumab dose, previous and transition immunosuppressors are shown in Table 1. Five participants (71.4%) had previously received off-label systemic immunosuppressors and 2 (29.6%) had received dupilumab as first systemic therapy (naïve). At baseline, the mean EASI and BSA were 23.7 ± 3.3 and 44.2 ± 10.9% respectively. All patients had an IGA of >3 and sleep disturbances. The efficacy data assessed using the mean global EASI, BSA, IGA and sleep quality improvement reported by parents on weeks 4, 12, 16, and 24 are shown in Table 2. Several dupilumab-induced adverse events, ocular adverse events, or facial dermatitis exacerbation were not reported. Only 2/7 patients (29.6%) experienced dupilumab related pain to an autoinjector device and were changed to prefilled syringe.

The clinical safety and efficacy of dupilumab of our cohort is similar to that seen in clinical trials,[3,6,7] and real-life series published.[8–12] Most of our patients achieved a global EASI < 3 or IGA 0–1 very early on, and improved sleep quality significantly, regardless of weight, clinical phenotype, administration device, age and ethnicity. The Dermatology Life Quality Index (DLQI) was not evaluated due to age related limitations. We also wanted to mention

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Table 1 Patients' demographics, comorbidities, previous systemic treatments, dupilumab dose, and administration device.

	Age (years)	Gender	Race or ethnicity	Weight (kg)	Atopic comorbidities	Other comorbidities	Family history of AD	DA phenotype	Facial involvement	IgE level at the baseline (kU/L)	Previous systemic treatments	Dupilumab dose (mg/days) after induction	Administration device	Basal EASI	Concomitant systemic immunosuppressor
1	10	Male	South American	55	Rhinitis, food allergy	Cow's milk protein allergy	Yes	Generalized and flexural	Yes	3417	None	300/28	Prefilled syringe	22	None
2	3	Male	Asian	19	None	None	No	Generalized and flexural	Yes	13,940	Azathioprine	300/28	Prefilled syringe	24	Decreasing Azathioprine 4 weeks
3	3	Female	South American	15	None	None	Yes	Generalized and flexural	Yes	7200	Cyclosporine, azathioprine	200/28	Autoinjector	23	Decreasing cyclosporine 6 weeks
4	8	Female	South American	30	Rhinitis	None	Yes	Generalized and flexural	Yes	Not available	Cyclosporine	300/28	Prefilled syringe	24	Decreasing cyclosporine 6 weeks
5	9	Male	Asian	24	None	None	No	Prurigo-like and flexural	No	2200	None	300/28	Prefilled syringe	27	None
6	5	Female	Asian	15	Rhinitis, food allergy	None	No	Prurigo-like and flexural	No	1038	Cyclosporine, methotrexate	300/28	Prefilled syringe	28	None
7	10	Female	Asian	34	Rhinitis, food allergy	None	No	Prurigo-like and flexural	No	4084	Azathioprine	300/28	Autoinjector	18	None

Table 2 Dupilumab efficacy assessed by mean EASI, BSA, IGA and improvement in sleep quality on weeks 4, 16, and 24.

	Basal	W-4	W-16	W-24
EASI	23.7 ± 3.3	7.2 ± 2.9	1 ± 0	0.9 ± 0.7
BSA (%)	44.3 ± 10.9	10.4 ± 5.2	1.3 ± 0.5	1.4 ± 1.1
IGA (median)	4 (3–4)	3 (3–4)	1 (0–1)	1 (0–1)
Sleep disturbance improvement (% of patients)		Yes (85.7%)	Yes (100%)	Yes (100%)

the promising dupilumab effectiveness and safeness in children aged 6 months to 5 years with prurigo-like AD. Based on our results, the prefilled syringe device is better tolerated vs the autoinjector device and preferred by children. This study has some limitations such as the small sample size, the short follow-up, the lack of a control group, and its retrospective nature. In conclusion, we want to highlight dupilumab efficacy in children aged ≥6 months to <12 years with moderate to-severe AD, whether naïve or refractory to systemic therapies.

Conflict of interests

The authors declare that they have no conflict of interest.

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