Dupilumab therapy in children aged 6 months to 12 years with uncontrolled moderate-to-severe atopic dermatitis: a Chinese real-world study

Jie Li[1], Bingjing Zhou[1], cong peng[1], Qiaozhi Cao[1], Jiayi Wang[1], and Xiang Chen[1]

[1]Xiangya Hospital Central South University Department of Dermatology

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Body of manuscript:

To the Editor:

Dupilumab is a monoclonal antibody approved for moderate-to-severe atopic dermatitis (AD) in patients aged >6 years in China[1-3]. Recently, a phase 3 clinical trial of dupilumab in children aged 6 months to 6 years with AD demonstrated significant efficacy and safety profiles[4], real-world data are scarce, especially in Asian populations. We conducted a retrospective, real-world, "off-label" observational study to evaluate the efficacy and safety of dupilumab in patients with AD aged < 6 years and compared the data with those aged 6-12 years.

A total of 120 pediatric patients with moderate-to-severe AD treated with dupilumab in China were included and divided into two groups by age: <6 years (n=50) and 6-12 years (n=70) (inclusion criteria and exclusion criteria can be found in Supporting Information). Informed consent was signed by the parents or legal guardians. This study was approved by the Ethics Review Committee of Xiangya Hospital (ethical approval number:2021030471).

The demographic and clinical characteristics of the two groups are shown in Table 1. There was no statistical difference in sex or baseline disease severity between the two groups ($p>0.05$). From baseline to week-16, increasing improvements were observed in the IGA, EASI, SCORAD, and CDLQI (IDQoL) (Fig. 1A and B, Fig. S1, Table S1). Patients aged <6 years responded to dupilumab earlier and better than those aged 6-12 years ($p<0.05$) at week-4, with higher EASI-50 and EASI-75 scores (78.79% vs. 44.00% and 45.45% vs. 16.00%, respectively) (Fig. 1B). However, with continuous dupilumab treatment till week-16, however, the therapeutic efficacy was comparable between the two groups, with similar EASI-75, EASI-90, and IGA0/1 (75.00% vs. 75.51%, 46.88% vs. 48.98%, 78.13% vs. 79.59%, respectively) (Fig. 1A and B). Representative photos of pediatric AD patients in the <6 and 6-12 years old groups after treatment with dupilumab are shown in Fig. 1 C and D.

Erythemato-desquamative and head and neck dermatitis were the most frequent clinical phenotypes in both groups (36.00% vs. 30.00%; 32.86 vs. 28.57%, respectively) (Table 1). patients aged <6 years with head and neck dermatitis as the main clinical phenotype had a higher EASI-50 (90.91%) than those aged 6-12 years (50.00%) at week-4 after dupilumab treatment ($p<0.05$) (Table S2). There was a statistical difference

in blood eosinophil counts between the two groups at week-4 ($0.38\pm0.25\times10^{\hat{}}9$/L vs $0.93\pm0.80\times10^{\hat{}}9$/L, $p<0.05$) (Fig. S1).

No adverse events (AE) were observed in the <6 years group. Two patients (2.86%) in the 6-12 years group developed conjunctivitis during treatment (Table S3), which may be associated with their previous history of conjunctivitis[5,6].

In conclusion, our real-life cohort data demonstrated that dupilumab has a significant efficacy and tolerable safety profile in patients aged < 6 years with uncontrolled moderate-to-severe AD. The efficacy of dupilumab was better in the first 4 weeks in patients aged <6 years when compared with those in patients aged 6-12 years, but comparable therapeutic efficacy at week -16. Compared to the efficacy in phase III clinical trials aged 6 months to younger than 6 years[4], higher EASI-75 and EASI-90 on week-16 were showed in our study (75% vs. 53% and 47% vs. 25%, respectively), which may be related to differences in race, prior medication history, sample size, etc. The first limitation of this study was that it was a single-center study, the second was the lack of patients aged 6 months to 2 years, and the third was the short follow-up period. Therefore, further studies with multi-centers and large samples are needed to provide more data and evidence for a more rational application of dupilumab in pediatric patients with AD.

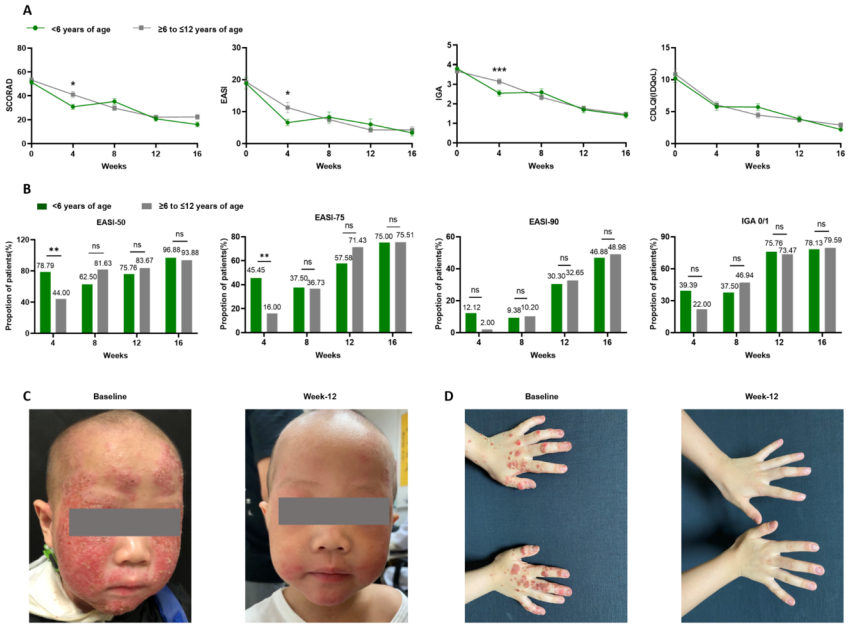

Figure 1. Comparative efficacy and representative photos of AD patients in <6 and 6-12 years old groups after treatment with dupilumab. (A) Efficacy outcomes compared with the respective baseline values over time. Patients treated with dupilumab from T0. Differences of data were assessed by Kruskal–Wallis signed-rank test. (B) Proportion of patients achieving EASI-50, 75, 90, IGA 0/1 at week-4, 8, 12 and 16 after treatment with dupilumab. Differences of data were assessed by Chi-squared test. (C) Skin lesions of a 2-year-old patient and (D) another 8-year-old patient at baseline (left panel) and at week-12 after treatment with dupilumab (right panel). Ns, no significance, *P<0.05, **P<0.01, ***P<0.001, compared between <6 and [?]6 years.

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Authors: Bingjing Zhou[1,2,3+], Cong Peng[1,2,3+], Qiaozhi Cao[1,2,3], Jiayi Wang[1,2,3], Xiang Chen[1,2,3*], Jie Li[1,2,3*]

Affiliations:

[1] Department of Dermatology, Xiangya Hospital, Central South University, Changsha, China, 410008;

[2] Allergy subspecialty direction, Hunan Key Laboratory of Skin Cancer and Psoriasis, Xiangya Hospital, Central South University, Changsha, China, 410008;

[3] National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Central South University, Changsha, Hunan, China, 410008.

Corresponding Authors: Jie Li, Department of Dermatology, Xiangya Hospital, Central South University, Changsha, Hunan, China. Fax: +86 073184327332. E-mail: xylijie@csu.edu.cn

[+] BJ. Zhou and C. Peng contributed equally to this work; *J. Li and X. Chen contributed equally to this work.

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Table legend

Table 1. Baseline demographics and clinical characteristics.

Abbreviations: AD, atopic dermatitis; IgE, immunoglobulin E; IGA, Investigator's Global Assessment; SCORAD, SCORing Atopic Dermatitis Index; EASI, Eczema Area and Severity Index; CDLQI, Children Dermatology Life Quality Index; IDQoL, Infants' Dermatitis Quality of Life. *CDLQI in pediatric patients aged 4 years to < 18 years and IDQoL in patients aged less than 4 years. P-values were calculated using the chi-squared test or Kruskal–Wallis signed-rank test and compared between <6 and [?]6 years. ns, no significance.

Table 1 Baseline demographics and clinical characteristics

Characteristics	**-<6 years of age (N=50)**	**6 to 12 years of age**
Sex, male, n (%)	22(44.00%)	36(51.43%)
Age (y), mean ± SD	4.35±3.20 (2-5 years)	9.07±1.67 (6-12 years)
Weight (kg), range	18.01(12.00-25.00)	35.00(20.00-67.00)
BMI (kg/m^2), mean ± SD	16.22(±2.45)	17.98(±3.27)
Duration of AD (y), mean ± SD	3.20(±1.52)	5.83(±2.95)
Extrinsic status, n (%)	43(86.00%)	66(94.29%)
Phenotypes, n (%)		
Erythemato-desquamative	18(36.00%)	23(32.86%)
Head and neck dermatitis	15(30.00%)	20(28,57%)
Lichenification	7(14.00%)	13(18.57%)
Exudative eczema	7(14.00%)	10(14.29%)
Prurigo nodularis-like	3(6.00%)	4(5.71%)
Family History of Allergy, n (%)	17(34.00%)	20(28.57%)
Atopic/allergic diseases concomitant, n (%)	28(56.00%)	42(60.00%)
Allergic rhinitis	14(28.00%)	20(28.57%)
Asthma	5(10.00%)	7(10.00%)
Allergic conjunctivitis	0	3(4.29%)
Urticaria	2(4.00%)	1(1.43%)
History of systemic medication for AD, n (%)	50(100.00%)	70(100.00%)
Systemic corticosteroids	0	4(5.71%)
Antihistamines	50(100.00%)	70(100%)
Non-steroidal immunosuppressants	0	0
Traditional Chinese medicine	10(20.00%)	19(27.14%)
History of topical medication for AD, n (%)	50(100%)	70(100%)
Topical corticosteroids	50(100%)	70(100%)
Topical calcineurin inhibitors	35(70.00%)	50(71.43%)
Phosphodiesterase 4 (PDE4) inhibitors	9(18.00%)	9(12.86%)
Concomitant topical medications, n (%)	27(54.00%)	39(55.71%)
Topical corticosteroids	16(32.00%)	2840.00%)
Topical calcineurin inhibitors	12(24.00%)	20(28.57%)
Phosphodiesterase 4 (PDE4) inhibitors	4(8.00%)	4(5.71%)
Comorbidities, n (%)	2(4.00%)	3(4.29%)
Chronic hepatitis B	0	1(1.43%)
Alopecia areata	0	1(1.43%)
Epilepsy	0	1(1.43%)
Eosinophilic esophagitis	1(2.00%)	0
Vitiligo	1(2.00%)	0
Total IgE level (IU/ml) at baseline, mean ± SD	1663.32(±2353.16)	1698.90(±2711.52)
Number of circulating eosinophils (×10^9/L), mean ± SD	0.67(±0.49)	0.69(±0.56)
Clinical scores at baseline, mean ± SD		

Characteristics	**-<6 years of age (N=50)**	**6 to 12 years of age**
IGA	3.80(±0.40)	3.67(±0.47)
SCORAD	51.33(±13.95)	53.18(±18.21)
EASI	18.81(±12.39)	19.27(±14.84)
CDLQI (IDQoL)*	10.20(±4.62)	10.86(±6.90)