

Real-World Assessment of Dupilumab in Chinese Atopic Dermatitis Patients: Efficacy, Safety, and Impact of Comorbidities

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Background: Atopic dermatitis (AD) is a chronic inflammatory skin disease often accompanied by comorbidities such as allergic rhinitis (AR) and asthma. Dupilumab, a monoclonal antibody targeting IL-4R α , has demonstrated significant efficacy and safety in the treatment of AD. However, its effectiveness in patients with comorbidities remains underexplored. We aimed to evaluate the impact of Dupilumab on the severity of dermatitis, comorbidity control, medication safety, and treatment adherence in Chinese AD patients in real-world settings.

Methods: This is a single-center retrospective-prospective real-world cohort study that included 376 patients with AD who received Dupilumab treatment from February 2021 to February 2024. Among them, 270 patients had AD, and 106 had AD with comorbidities, including 106 cases of AR and 20 cases of asthma. Baseline clinical data and laboratory parameters were collected. The severity of AD, quality of life, and comorbidity control were assessed at week 0, 4, 8, 12, and 16. Efficacy indicators and related predictive factors were evaluated, and drug continuation rates at week 52 were assessed.

Results: After 16 weeks of Dupilumab treatment, the median improvement in EASI score was 95.3% (from 8.5 to 0.40), with an EASI75 response rate of 78.9%. AD efficacy-related scores and comorbidity-related scores showed significant improvement compared to baseline (all $P < 0.05$). There was no statistical difference in efficacy between the AD group and AD with comorbidities group. Drug survival analysis showed similar drug continuation rates at 52 weeks for both groups ($P > 0.05$). Adverse events were mainly eye-related events (8.51%, 32/376), followed by localized symptom worsening (2.13%), hair loss (1.60%), and facial erythema (1.33%). Patients with higher baseline EASI scores were more likely to achieve 90–100% improvement ($P = 0.024$).

Conclusion: Dupilumab effectively improves AD symptoms and comorbidities, with consistent efficacy across comorbid status and good safety profile. Higher baseline disease severity associates with better treatment response.

Keywords: atopic dermatitis, Dupilumab, allergic rhinitis, asthma, real-world study

Introduction

Atopic dermatitis (AD) is a common chronic relapsing inflammatory skin disease mediated by type 2 inflammation, characterized by intense itching and recurrent eczematous lesions, significantly impacting patients' quality of life. Epidemiological studies have shown a significant global increase in the prevalence of AD in recent years, with approximately 13% in children and 5% in adults.¹ The prevalence varies significantly by region, with typically higher rates in industrialized countries.² The pathogenesis of AD is complex, involving interactions of genetic, environmental, skin barrier defects, and immune response abnormalities.^{2–8} Notably, AD often serves as the starting point for the “atopic march,” with over 50% of severe AD children progressing to asthma, 75% developing allergic rhinitis (AR),^{9,10} and also potentially experiencing comorbidities such as food allergies and eosinophilic esophagitis,^{11,12} highlighting the systemic

nature of AD. Traditional AD treatments have relied on topical corticosteroids, calcineurin inhibitors, oral antihistamines, immunosuppressants, and phototherapy.^{7,13–16} However, these conventional therapies have limited efficacy and may lead to adverse reactions such as skin atrophy, telangiectasia, rebound reactions upon discontinuation, and systemic immunosuppression.^{7,13–16} Consequently, treatment strategies are shifting towards precise targeted therapies against the type 2 inflammatory pathway, with biologics emerging as a current research focus.

Dupilumab is a fully humanized monoclonal antibody that specifically binds to the IL-4 receptor alpha subunit (IL-4R α), blocking the signaling of IL-4 and IL-13.^{17,18} These cytokines are central drivers of Th2 immune responses, contributing to the skin inflammation, barrier disruption, and itching in AD.⁷ Dupilumab has demonstrated significant efficacy in multiple randomized controlled trials, rapidly improving the severity of skin lesions, relieving itching, and enhancing patients' quality of life.^{19–21} It is currently approved for moderate-to-severe AD patients aged six months and older.^{4,22} Given that atopic comorbidities and AD share type 2 inflammatory reactions as a common cascading feature,¹¹ Dupilumab's mechanism of action may also have a broad impact on AD-related comorbidities.^{17,23} Clinical studies have confirmed Dupilumab's efficacy to reduce asthma attacks, improve lung function and overall systemic corticosteroid prescriptions;²⁴ alleviate clinical symptoms in nodular prurigo patients;²⁵ reduce the size of nasal polyps in chronic rhinosinusitis with nasal polyps patients, alleviate sinus opacification, and improve their symptoms.²⁶ Clinical trials have shown that AD patients receiving Dupilumab treatment may experience improvements not only in skin symptoms but also in associated conditions such as asthma and sinusitis, potentially reducing the use of related medications.²⁷

While real-world studies have extensively validated Dupilumab's effectiveness for individual type 2 inflammatory diseases,^{28–30} systematic evidence of its efficacy in AD patients with multiple type 2 inflammatory comorbidities remains relatively limited. There may be bidirectional pathological interactions between AD and comorbidities: does the burden of comorbidities weaken Dupilumab's response efficiency to the core symptoms of AD? Conversely, can the relief of AD indirectly improve comorbidities by inhibiting systemic Th2 inflammation? Therefore, our study aims to investigate the systemic immunoregulatory characteristics and safety data of Dupilumab in a complex comorbid group through real-world data, guiding personalized treatment decisions for AD.

Methods

Study Design and Population

This study utilized a retrospective-prospective real-world cohort design, including AD patients who received Dupilumab treatment at Tongji Hospital between February 2021 and February 2024, from the age of 6 months onward, encompassing all ages. All patients were required to meet the Hanifin and Rajka diagnostic criteria,³¹ regardless of whether they had comorbidities such as asthma or AR associated with type 2 inflammation. Exclusion criteria included pregnancy or lactating women, concurrent skin conditions like psoriasis or chronic urticaria that could interfere with assessments, severe cardiovascular, hepatic, or renal diseases, allergy to Dupilumab or its excipients, participation in other clinical trials, active autoimmune diseases, or receiving systemic immunosuppressive therapy. The diagnosis of allergic rhinitis (AR) and asthma were clinically confirmed by physicians according to the ARIA and GINA guidelines, respectively.^{32,33} The study protocol was approved by the Tongji Hospital Ethics Committee (No. TJ-IRB20231112), which waived the requirement for written informed consent for this research.

Follow-Up and Assessment

Research data were collected through standardized case report forms. Baseline information included demographic characteristics (gender, age, BMI), clinical features (disease duration, past medication history, allergic diseases, and family history), and laboratory parameters (serum total IgE, peripheral blood eosinophil count). Efficacy assessments were conducted at treatment weeks 0, 4, 8, 12, and 16, encompassing indicators of AD severity: Eczema Area and Severity Index (EASI), Scoring Atopic Dermatitis (SCORAD), Numeric Rating Scale for itch (NRS), Dermatology Life Quality Index (DLQI), Atopic Dermatitis Control Tool (ADCT), and Patient-Oriented Eczema Measure (POEM), with calculation of EASI 50/75/90 response rates. Comorbidity assessments included Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), and Asthma Quality of Life Questionnaire (AQLQ) for asthma patients; Total Nasal

Symptom Score (TNSS), Visual Analog Scale (VAS), Allergic Rhinitis Control Test (ARCT), and Rhinosinusitis Quality of Life Questionnaire (RQLQ) for rhinitis patients. Safety monitoring recorded all adverse events during treatment. Compliance analysis tracked discontinuation times and reasons within 52 weeks post-Dupilumab treatment, evaluating drug treatment duration through survival analysis. Data were collected using standardized paper-based case report forms completed by physicians and patients during each clinical visit. All efficacy and comorbidity assessment scores were obtained exclusively during these in-person visits. Missing baseline demographic data (eg, family history), reasons for treatment discontinuation, and post-injection adverse events not recorded in outpatient settings were supplemented through telephone follow-ups.

Statistical Analyses

All statistical analyses in this study were performed using SPSS software (version 27.0) with a significance level set at $\alpha=0.05$. Continuous variables were assessed for normality using the Shapiro–Wilk test: normally distributed variables were presented as mean \pm standard deviation and analyzed using t-tests (two groups) or ANOVA (multiple groups); non-normally distributed variables were presented as median (interquartile range) and analyzed using Mann–Whitney *U*-tests (two groups) or Kruskal–Wallis *H*-tests (multiple groups). Categorical variables were presented as frequencies (percentages) and compared using chi-square tests or Fisher’s exact tests. For repeated measures of efficacy indicators (such as EASI, SCORAD), Friedman tests were initially used to analyze time effects. If significant, Wilcoxon signed-rank tests were further employed for pairwise comparisons, with Bonferroni correction for multiple comparisons (adjusted $\alpha=0.005$). For repeated measures of categorical variables (like EASI75 response rate), Cochran’s Q test was used to analyze overall trends over time. Cross-sectional comparisons at different time points among different subgroups were conducted using Mann–Whitney *U*-tests, with Bonferroni correction applied (adjusted $\alpha=0.01$). Drug treatment duration was analyzed using Kaplan–Meier analysis, with intergroup differences compared using the Log rank test. To explore factors related to efficacy, patients were categorized into four response groups based on the improvement rate in EASI at week 16. Differences in baseline characteristics among groups were compared using the aforementioned methods, with pairwise comparisons and Bonferroni correction for statistically significant variables.

Results

Demographic Characteristics

This study ultimately included 376 AD patients receiving Dupilumab treatment, comprising 204 males (54.3%) and 166 females (45.7%). They were categorized based on comorbidity status into the AD group (n=270, 71.8%) and AD with comorbidities group (n=106, 28.2%), with 86 patients having AD and AR (22.9%) and 20 patients having AD, AR, and asthma (5.3%). Group comparisons revealed (see Table 1) that the AD with comorbidities group had a lower BMI compared to the AD group (17.27 vs 18.97 kg/m², $P=0.014$), longer disease duration (5.0 vs 4.0 years, $P=0.030$), higher rates of family history of atopy (63.2% vs 45.6%, $P=0.002$), and higher allergen sensitization rates (90.6% vs 63.3%, $P<0.001$). Regarding inflammatory markers, the AD with comorbidities group exhibited significantly elevated serum total IgE levels (581.00 vs 292.00 KUA/L, $P<0.01$), while there was no difference in eosinophil counts ($P>0.05$). Notably,

Table 1 Baseline Demographic and Clinical Characteristics for AD Patients

	Patients (n=376)	AD (n=270)	AD with Comorbidities (n=106)	Statistical Value	P
Sex (male), n (%)	204(54.3)	144(53.3)	60(56.6)	$\chi^2 = 0.328$	0.567
Age (y)	10.0(5.0–32.8)	12.0(5.0–37.0)	8.0(6.0–19.0)	U=12773.0	0.105
Duration (y)	4.0(2.0–8.0)	4.0(2.0–8.0)	5.0(3.0–8.0)	U=12257.5	0.030
BMI (kg/m ²)	18.65(15.38–22.62)	18.97(15.60–23.14)	17.27(15.03–20.07)	U=12773	0.014

(Continued)

Table 1 (Continued).

	Patients (n=376)	AD (n=270)	AD with Comorbidities (n=106)	Statistical Value	P
Diagnosis, n (%)					
AD	270(71.8)	270(100)			
AD&AR	86(22.9)		86(81.1)		
AD&AR&AS	20(5.3)		20(18.9)		
Atopic family history, n (%)	190(50.5)	123(45.6)	67(63.2)	$\chi^2 = 9.488$	0.002
Allergen, n (%)	267(71.0)	171(63.3)	96(90.6)	$\chi^2 = 27.422$	0.001
HDM	220(58.5)	131(48.5)	89(84.0)	$\chi^2 = 39.39$	0.001
Pollen	73(19.4)	41(15.2)	32(30.2)	$\chi^2 = 10.952$	0.001
Animal fur	41(10.9)	19(7.0)	21(19.8)	$\chi^2 = 14.743$	0.001
Mold	51(13.6)	25(9.3)	26(24.5)	$\chi^2 = 15.137$	0.001
Milk	63(16.8)	41(15.2)	22(20.8)	$\chi^2 = 1.693$	0.194
Egg	77(20.5)	52(19.3)	25(23.6)	$\chi^2 = 0.875$	0.350
Cereals	19(5.1)	13(4.8)	6(5.7)	$\chi^2 = 0.113$	0.736
Tree nuts	48(12.8)	36(13.3)	12(11.3)	$\chi^2 = 0.277$	0.599
Legumes	16(4.3)	11(4.1)	5(4.7)	$\chi^2 = 0.077$	0.781
Fish	23(6.1)	16(5.9)	7(6.6)	$\chi^2 = 0.061$	0.805
Crustaceans	33(8.8)	21(7.8)	12(11.3)	$\chi^2 = 1.193$	0.275
Meats	10(2.7)	6(2.2)	4(3.8)	$\chi^2 = 0.708$	0.477
Others	50(13.3)	43(15.9)	7(6.6)	$\chi^2 = 5.737$	0.017
TlgE (KUA/L)	400.00(111.00–1265.50)	292.00(75.45–1136.00)	581.00(217.75–1627.50)	U=7805	0.004
EOS count (*10 ⁹ /L)	0.43(0.17–0.70)	0.43(0.16–0.70)	0.41(0.23–0.69)	U=2343.5	0.827
AD severity Scores					
ADCT	16.00(11.00–19.00)	16.00(11.00–20.00)	14.00(12.00–18.00)	U=12829.5	0.118
SCORAD	56.75(41.35–67.50)	57.80(43.35–68.53)	55.35(33.95–63.30)	U=12056.5	0.017
POEM	17.00(12.00–22.00)	17.00(12.00–22.00)	17.00(12.00–22.00)	U=13756	0.558
DLQI	9.00(5.00–14.75)	9.00(5.00–15.00)	8.00(5.00–14.25)	U=13534.5	0.413
NRS	8.00(6.00–9.00)	8.00(6.00–9.00)	7.00(6.00–8.00)	U=12390.5	0.040
EASI	8.50(4.30–17.45)	8.90(4.68–18.08)	8.00(2.70–14.25)	U=12834	0.120

Notes: Data are presented as median with interquartile range (IQR) for continuous variables and as number (percentage) for categorical variables; continuous variables compared by Mann–Whitney U-test, categorical by χ^2 /Fisher exact test (expected frequency <5); two-sided tests with P<0.05 considered significant (bold values). Bold values indicate statistical significance (P < 0.05).

Abbreviations: AD, atopic dermatitis; AR, allergic rhinitis; AS, asthma; BMI, body mass index; EASI, Eczema Area and Severity Index; SCORAD, Scoring Atopic Dermatitis; NRS, Numerical Rating Scale; TlgE, Total Immunoglobulin E; EOS, eosinophil.

the AD with comorbidities group had significantly lower baseline SCORAD scores (55.35 vs 57.80, P=0.017) and itch NRS scores (7.00 vs 8.00, P=0.040), while other indicators of AD severity (EASI, DLQI, etc.) as well as gender and age distribution showed no statistically significant differences between the groups (all P>0.05).

Efficacy of Dupilumab on Atopic Dermatitis

The patients in the cohort showed significant improvements in ADCT, SCORAD, POEM, DLQI, NRS, and EASI at the 4th week (all P<0.001), with efficacy continuing to improve up to the 16th week. By the 16th week, the improvement rates were as follows: EASI 95.3% (median 8.5 vs 0.40), SCORAD 83.7% (56.75 vs 9.25), DLQI 88.9% (9.00 vs 1.00), POEM 88.2% (17.00 vs 2.00), NRS 87.5% (8.00 vs 1.00), and a significant increase in the proportion of patients achieving control with ADCT (84.5% vs 9.5%). Group analysis revealed significant clinical improvements over time in both the AD and AD with comorbidities groups (all P < 0.001).

It is noteworthy that despite higher baseline levels of type 2 inflammatory biomarkers in the AD with comorbidities group (total IgE 581 vs 292 kU/L, $P < 0.001$), and statistically significant differences in SCORAD (55.4 vs 57.8, $P=0.017$) and NRS (7.00 vs 8.00, $P=0.040$) scores compared to the AD group, there were no statistically significant differences in efficacy between the two groups at various timepoints during treatment (eg, 16-week EASI: 0.60 vs 0.40, $P=0.205$; SCORAD: 9.05 vs 9.80, $P=0.977$). Furthermore, the EASI75 response rate significantly increased over time ($P < 0.001$), reaching 78.9% (AD group) and 78.3% (AD with comorbidities group) at 16 weeks, with no difference between the two groups ($P=0.900$). Similar trends were observed for EASI50 and EASI90 response rates, with EASI50 response rates at 16 weeks being 88.5% vs 87.7% for the two groups ($P = 0.832$), and EASI90 response rates being 61.1% vs 67.9% ($P = 0.218$), indicating that Dupilumab's improvement in AD symptoms is not influenced by comorbidity status (Figure 1).

Medication Usage

To assess the impact of Dupilumab treatment on the topical medication usage of patients, we analyzed the monthly prescription amounts of topical corticosteroids (TCS) and calcineurin inhibitors (TCI) per person before and within the first four months of Dupilumab treatment. There were significant differences in TCS usage among the overall patients at five timepoints ($P < 0.0001$). There was no significant difference in TCS usage between the month before treatment and the first month of treatment ($P > 0.05$); however, a significant decrease in TCS usage was observed from the second month of treatment onwards compared to both the month before treatment and the first month of treatment (all $P < 0.05$), and this decreasing trend continued until the fourth month (Figure 2A). In contrast, TCI usage showed an overall trend over time ($P < 0.001$), but no significant differences were observed in comparisons between any two specific months. Additionally, there were no statistically significant differences in the monthly prescription amounts of topical medications between the AD group and the AD with comorbidities group (all $P > 0.05$), indicating that the observed overall trends were not driven by drastic changes between specific months (Figure 2B).

Laboratory Parameters

We evaluated the dynamic changes in total IgE (TIgE) and eosinophil count (EoS), two type 2 inflammatory biomarkers, before and after 16 weeks of Dupilumab treatment in the cohort. Prior to treatment, all groups exhibited elevated serum

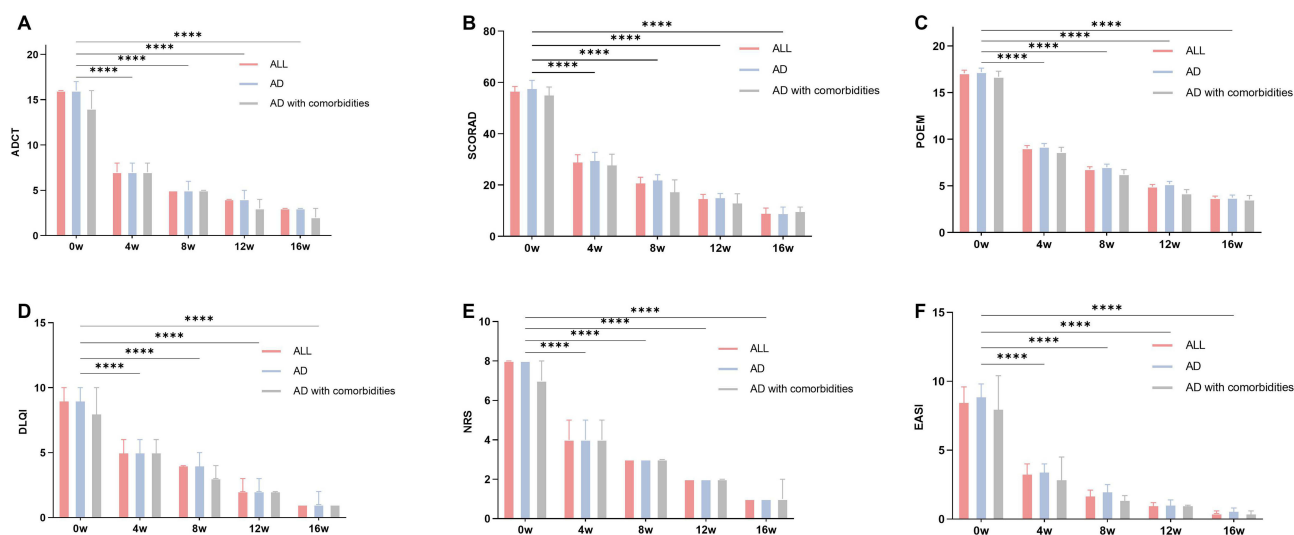


Figure 1 Longitudinal changes in efficacy outcomes in AD patients treated with Dupilumab. (A) ADCT scores, (B) SCORAD index, (C) POEM scores, (D) DLQI scores, (E) NRS itch scores, (F) EASI scores over 16 weeks of treatment in the Overall cohort, AD-only group, and AD with comorbidities group. Data are presented as median with interquartile range. The overall effect of time was assessed by the Friedman test (all $P < 0.001$). Within-group comparisons were analyzed using the Wilcoxon signed-rank test with Bonferroni correction ($\alpha = 0.005$). Between-group comparisons (AD-only vs Comorbidity group) at each time point were performed using the Mann-Whitney U -test with Bonferroni correction for multiple comparisons (significance set at $\alpha = 0.01$). No statistically significant differences were found between the AD-only and comorbidity groups at any time point after correction. **** $P < 0.0001$.

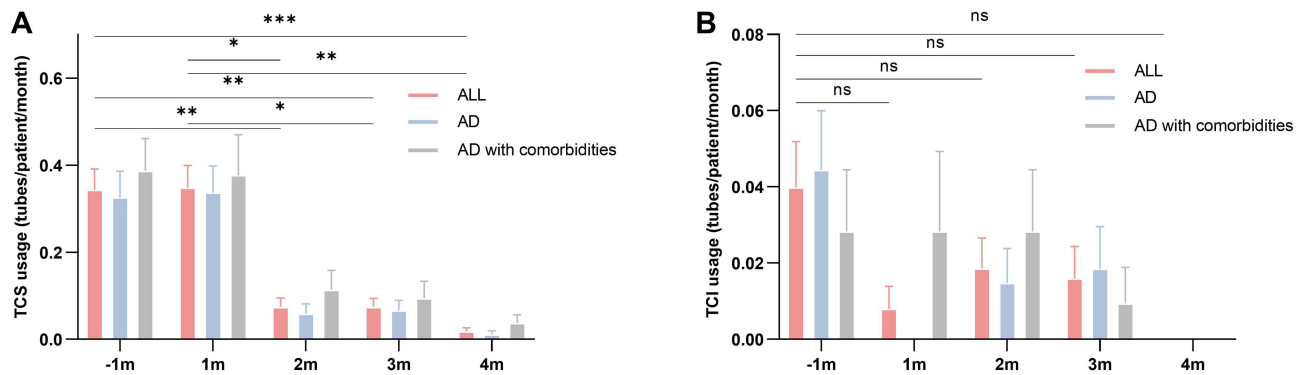


Figure 2 Changes in topical medication prescription patterns following Dupilumab initiation. **(A)** Monthly prescription rate of topical corticosteroids (TCS) and **(B)** topical calcineurin inhibitors (TCI) per patient for one month before (-1m) and for the first four months after (1m-4m) starting Dupilumab therapy in the overall population. Data are presented as median with interquartile range. The overall effect of time was analyzed by the Friedman test. Pairwise comparisons between time points were performed using Wilcoxon signed-rank test with Bonferroni correction for multiple comparisons ($\alpha = 0.005$). Significant differences between specific time points are indicated in the graph. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Abbreviations: ns, not significant; TCS, topical corticosteroids; TCI, topical calcineurin inhibitors.

TiGE levels. The median baseline TiGE for the overall population was 400.00 kUA/L. Subgroup analysis revealed that the baseline TiGE level in AD with comorbidities group was significantly higher than in the AD group (581.00 kUA/L vs 292.00 kUA/L, $P = 0.004$; **Figure 3A**).

After 16 weeks of treatment, TiGE levels significantly decreased in both groups. The median TiGE value for the cohort significantly decreased to 123.00 kUA/L ($P < 0.001$; **Figure 3A**). This decreasing trend reached statistical significance in both the AD group (110.00 kUA/L, $P < 0.001$) and the AD with comorbidities group (130.00 kUA/L; $P < 0.001$). Interestingly, the significant difference in TiGE levels between the two groups at baseline disappeared after treatment ($P = 0.067$).

In contrast, the response of EoS to treatment was weaker and inconsistent (**Figure 3B**). In the cohort, EoS count decreased from $0.43 \times 10^9/L$ at baseline to $0.28 \times 10^9/L$ at week 16, with a statistically significant difference ($P = 0.028$). However, when analyzed separately for the AD group and the AD with comorbidities group, the changes in EoS before and after treatment did not reach statistical significance in either group (both $P > 0.05$). There were no significant differences in EoS count between the two groups, both at baseline and at week 16 (both $P > 0.05$).

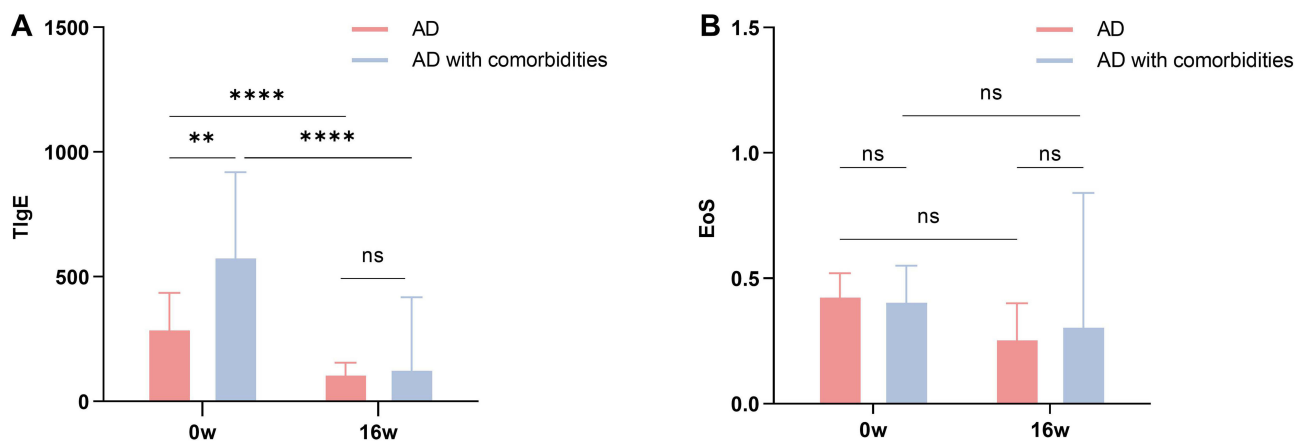


Figure 3 Changes in laboratory parameters following Dupilumab treatment **(A)** The levels of serum total immunoglobulin E (TiGE) in the overall population, non-comorbidity AD group, and comorbidity group at baseline (week 0) and after 16 weeks of treatment. **(B)** The blood eosinophil count (EoS) at baseline and week 16 for the respective groups. The data are presented as median and interquartile range (IQR). Intra-group comparisons (week 16 vs week 0) were analyzed using the Wilcoxon signed-rank test. Inter-group comparisons (the AD group vs AD with comorbidities group at each time point) were analyzed using the Mann-Whitney *U*-test. ** $P < 0.01$, **** $P < 0.0001$.

Abbreviations: ns, not statistically significant; AD, atopic dermatitis.

Effectiveness of Dupilumab on AD-Related Comorbidities

The study included 86 AD combined AR patients and 20 AD with AR and asthma patients, with repeated measurements of AR-related indicators (TNSS, VAS, ARCT, RQLQ) and Asthma-related indicators (ACQ, TRACK, ACT, AQLQ) at baseline (week 0) and at weeks 4, 8, 12, and 16 post-treatments (Figures 3 and 4).

Allergic Rhinitis

Patients in both the AD combined AR group and the AR combined with asthma group showed significant changes in all AR-related scores over the course of treatment (all $P < 0.001$, Figure 4). In the AD combined AR group, TNSS scores significantly decreased from week 4 onwards compared to baseline ($P < 0.01$), while VAS, ARCT, and RQLQ scores also significantly improved from week 4 onwards (all $P < 0.05$). The AD combined AR and asthma group exhibited a similar but slightly delayed improvement trend, with TNSS, VAS, and ARCT scores significantly improving from week 12 compared to baseline (all $P < 0.05$), and RQLQ scores significantly improving from week 8 onwards ($P < 0.05$). Despite differences in the timing of improvement, there were no statistically significant differences in any of the scores between the two groups at all time points (all $P > 0.05$), indicating that Dupilumab had comparable efficacy in improving nasal symptoms in both patient groups.

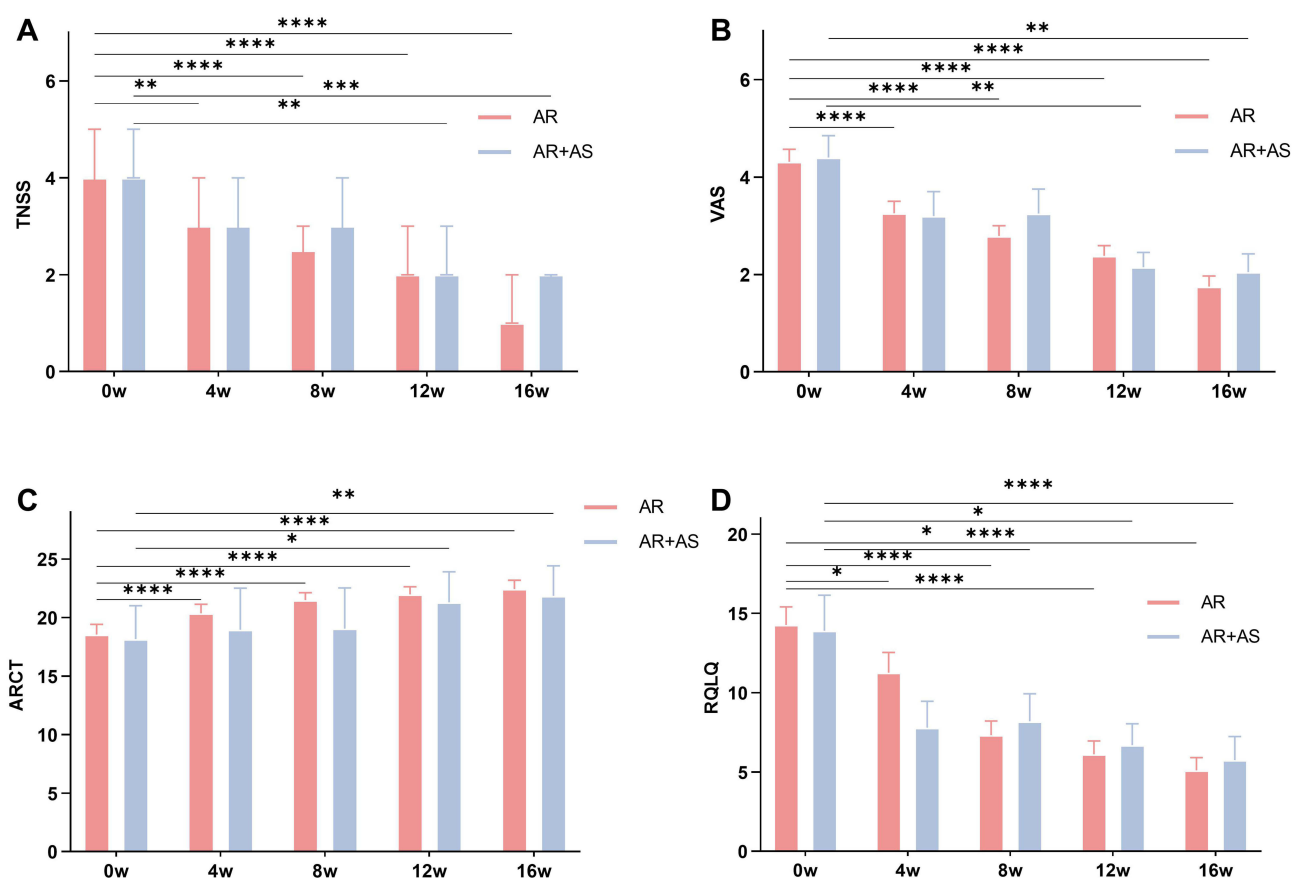


Figure 4 Changes in AR-related outcomes following Dupilumab treatment. **(A)** Total Nasal Symptom Score (TNSS), **(B)** Visual Analogue Scale (VAS) for nasal symptoms, **(C)** Allergic Rhinitis Control Test (ARCT) score, and **(D)** Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) score in patients with atopic dermatitis (AD) and AR ($n=86$) and those with AD, AR, and asthma (AS) ($n=20$) over 16 weeks of treatment. Data are presented as median with interquartile range. The overall effect of time within each group was analyzed by the Friedman test. Pairwise comparisons between each time points (10 comparisons) were performed using the Wilcoxon signed-rank test with Bonferroni correction (significance set at $\alpha = 0.005$). Between-group comparisons at each time point (5 comparisons) were analyzed using the Mann-Whitney *U*-test with Bonferroni correction (significance set at $\alpha = 0.01$). No significant differences were found between groups at any time point after correction. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$.

Abbreviations: AR, allergic rhinitis; AS, asthma.

Asthma Control

Regarding asthma-related indicators, ACQ, TRACK, ACT, and AQLQ scores all demonstrated significant improvement over the course of treatment (all $P < 0.001$) (Figure 5). Specifically, ACQ, TRACK, and ACT scores significantly improved from week 12 compared to baseline (all $P < 0.05$), while AQLQ scores significantly improved from week 8 onwards ($P < 0.01$). AS scores showed no significant changes at any time point ($P = 0.2881$).

Treatment Adherence

To assess treatment adherence, we plotted a 52-week medication persistence survival curve (Figure 6). The results indicate that there was no significant difference in medication survival rates between the AD group and the AD with comorbidities group ($P = 0.685$) (Figure 6). The median treatment duration was similar in both groups (AD group: 45.0 weeks vs AD with comorbidities group: 44.2 weeks). By week 52, both groups maintained comparable treatment persistence rates, with the AD group at 43.3% (117/270) and the AD with comorbidities group at 44.3% (47/106).

During the 52-week observation period, 117 patients (43.3%) in the AD group continued medication use; 122 patients (45.2%) discontinued due to disease improvement, 25 patients (9.3%) stopped due to inadequate efficacy, 3 patients (1.1%) ceased due to adverse drug reactions, and 3 patients (1.1%) stopped due to special events (economic reasons, planned pregnancy, vaccination). In the AD with comorbidities group of 106 patients, 47 patients (44.3%) continued medication use; 47 patients (44.3%) discontinued due to disease improvement, 11 patients (10.4%) stopped due to inadequate efficacy, 1 patient (0.9%) ceased due to a special event, and no cases of discontinuation due to economic reasons or adverse drug reactions were observed (Figure 7). There was no statistically significant difference in the overall reasons for discontinuation between the two groups ($P = 0.902$).

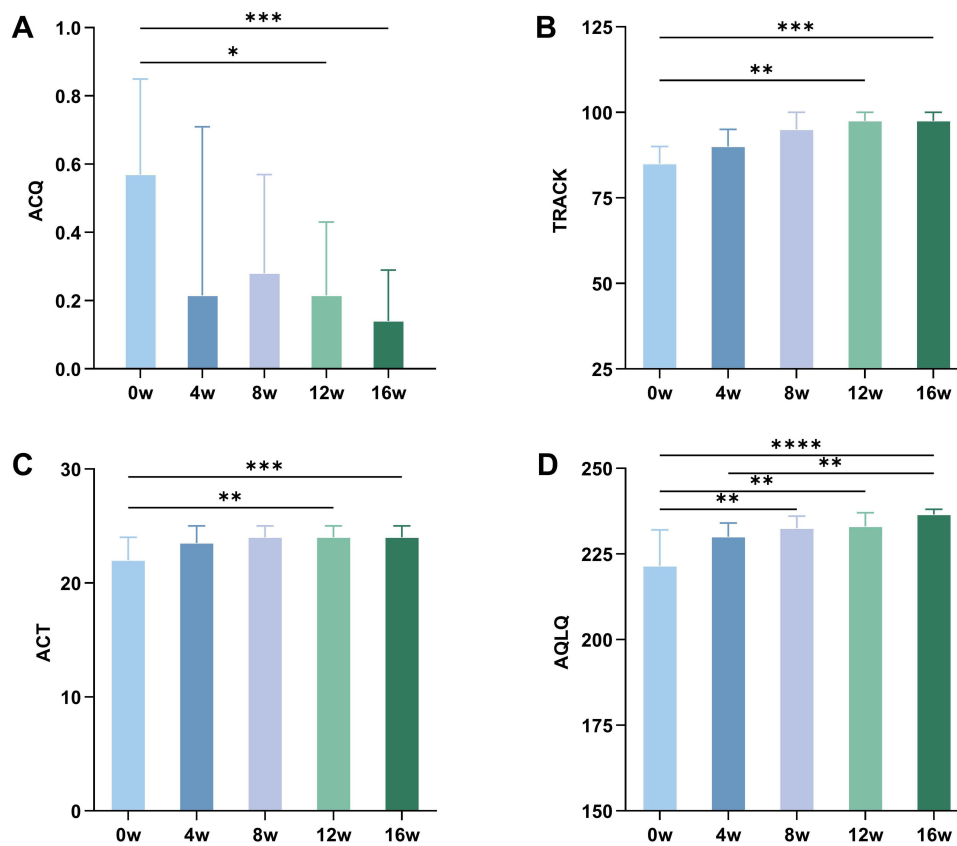


Figure 5 Changes in asthma-related outcomes following Dupilumab treatment. (A) Asthma Control Questionnaire (ACQ), (B) Test for Respiratory and Asthma Control in Kids (TRACK), (C) Asthma Control Test (ACT), and (D) Asthma Quality of Life Questionnaire (AQLQ) scores in patients with AD and AS over 16 weeks of treatment. Data are presented as median with interquartile range. The overall effect of time was analyzed by the Friedman test. Pairwise comparisons between each time points were performed using the Wilcoxon signed-rank test with Bonferroni correction for multiple comparisons. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$.

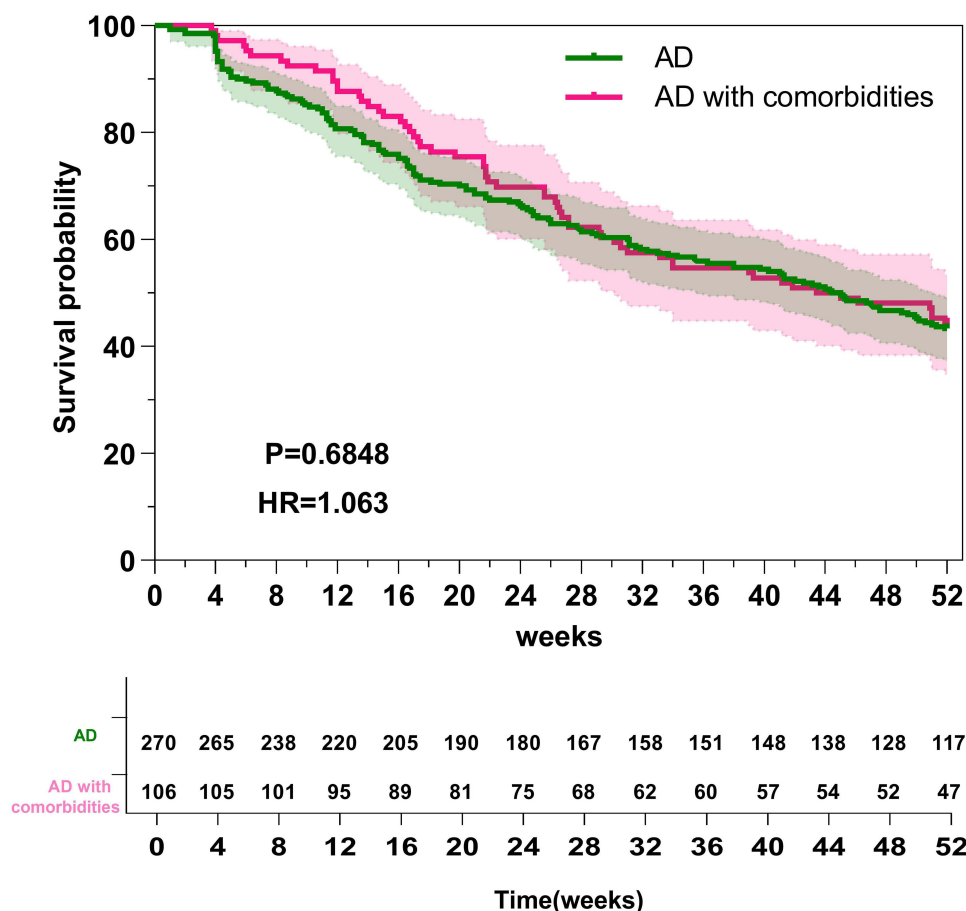


Figure 6 Drug survival analysis of Dupilumab in AD-only and AD with comorbidities groups over 52 weeks. Kaplan-Meier curves show the probability of treatment persistence. The median survival time was 45.0 weeks for the AD-only group and 44.2 weeks for the AD with comorbidities group. The number of patients at risk at each predefined time point (0, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52 weeks) is shown in the table below the graph. The difference between the two groups was not statistically significant by the Log rank test ($\chi^2 = 0.165$, $P = 0.685$).

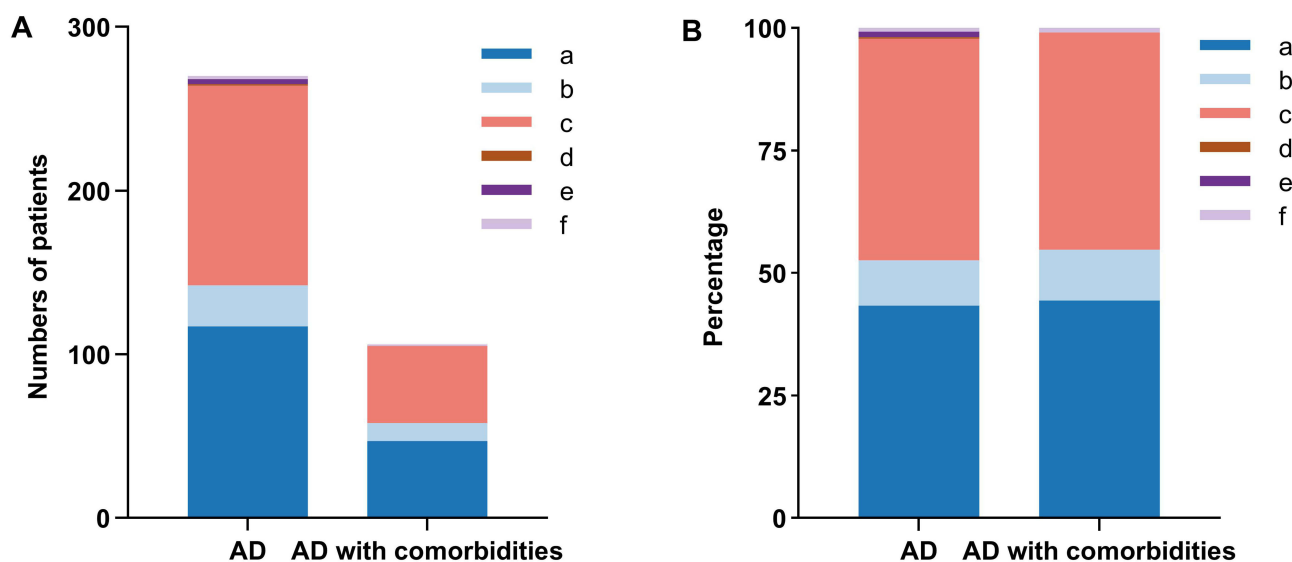


Figure 7 Treatment Status and Reasons for Drug Discontinuation at Week 52. **(A)** Bar graph showing the number of patients in the AD group (n=270) and the AD with comorbidities group (n=106) who continued treatment or discontinued due to various reasons. The stacked bars represent the actual counts of patients in each category. **(B)** Percentage stacked bar graph illustrating the proportional distribution of treatment status and reasons for discontinuation within each group. Data are presented as counts (n) in **(A)** and percentages (%) of the respective group total in **(B)**. The overall distribution of reasons for discontinuation between the two groups was compared using Fisher's exact test ($P = 0.902$), as more than 20% of cells in the contingency table had an expected count of less than 5. No statistically significant difference was found. a, continued use; b, lack of efficacy; c, disease remission; d, financial burden; e, adverse events; f, special circumstances.

Safety

Overall, Dupilumab demonstrates good tolerability. Among the total of 376 patients, 74 patients (19.68%) reported 80 adverse events, the majority of which were mild to moderate. The most common adverse events were concentrated in the eye and skin areas, with the highest occurrence rate related to eye-related events (8.51%, 32/376), followed by skin and subcutaneous tissue disorders (6.91%, 26/376), mainly presenting as worsening of local symptoms (2.13%), hair loss (1.60%), and facial erythema (1.33%). Five patients experienced injection site reactions (1.33%), with a low incidence of fever (0.53%). Additionally, sporadic mild reports were noted in areas such as metabolism, the nervous system, and the immune system, including weight gain (0.80%), dizziness (0.27%), and hypersensitivity reactions (0.53%). A single case of cerebral infarction (0.27%) was reported in a 50-year-old female with a pre-existing history of hypertension, approximately 13.5 months after treatment initiation. Notably, dupilumab treatment was continued for a further six months following the event. Despite a certain proportion of adverse event reports, situations leading to treatment discontinuation were extremely rare, with only three patients discontinuing treatment due to adverse events, resulting in an overall discontinuation rate of 0.80% (Table 2).

Table 2 Incidence of Adverse Events During Dupilumab Treatment (n=376)

System Organ Class/Preferred Term	Patients with Events (n/N)	Number of Events (n)	Incidence Rate (%)	Discontinuations Due to AE (n)
Eye disorders	32/376	32	8.51	
Skin and subcutaneous tissue disorders	26/376	26	6.91	
Facial erythema	5/376	5	1.33	
Alopecia	6/376	6	1.60	
Hand-foot skin peeling, dryness	2/376	2	0.53	
Skin hyperpigmentation	1/376	1	0.27	
Local symptom aggravation	8/376	8	2.13	
Pruritus	2/376	2	0.53	
General disorders and administration site conditions	8/376	8	2.13	
Injection site reaction	5/376	5	1.33	1
Pyrexia	1/376	1	0.27	
Fatigue	2/376	2	0.53	
Gastrointestinal disorders	1/376	1	0.27	
Decreased appetite	1/376	1	0.27	
Infections and infestations	3/376	3	0.80	1
Fungal infection	1/376	1	0.27	
Decreased immunity	2/376	2	0.53	
Metabolism and nutrition disorders	3/376	3	0.80	
Weight increased	3/376	3	0.80	
Nervous system disorders	2/376	2	0.53	
Dizziness	1/376	1	0.27	
Cerebral infarction	1/376	1	0.27	
Immune system disorders	2/376	2	0.53	
Hypersensitivity	2/376	2	0.53	
Cardiac disorders	2/376	2	0.53	
Chest pain	1/376	1	0.27	
Electrocardiogram abnormal	1/376	1	0.27	1

(Continued)

Table 2 (Continued).

System Organ Class/Preferred Term	Patients with Events (n/N)	Number of Events (n)	Incidence Rate (%)	Discontinuations Due to AE (n)
Reproductive system and breast disorders	1/376	1	0.27	
Increased menstrual frequency	1/376	1	0.27	
Total	74/376	80	19.68	3

Notes: Data are presented as the number of patients with events/total patients (n/N), number of events (n), and incidence rate (%). The total number of events (n=80) exceeds the number of patients with events (n=74) because some patients experienced more than one type of event. Incidence rates are calculated based on the number of patients. Discontinuations due to adverse events (AEs) are also listed. AEs are categorized using System Organ Class (SOC) and Preferred Term (PT). Bold text in the “Number of Events (n)” column indicates the total number of events for the corresponding System Organ Class.

Efficacy Prediction Indicator

To investigate potential predictive factors influencing the efficacy of Dupilumab, we categorized the 376 patients into four groups based on the improvement rate of EASI scores at week 16: <50% improvement group (n=44), 50–75% improvement group (n=36), 75–90% improvement group (n=59), and 90–100% improvement group (n=237) (Table 3). There were differences in baseline disease severity among the four groups ($P = 0.024$). The baseline EASI scores in the 90–100% improvement group were significantly higher than those in the 0–50% improvement group ($P = 0.015$). Furthermore, there were no significant differences among the four groups in terms of age, gender, disease duration, history of other allergic diseases, baseline total IgE levels, and eosinophil counts (all $P > 0.05$).

Discussion

We conducted a large-scale retrospective-prospective real-world cohort study to comprehensively evaluate the efficacy, safety, and overall impact of Dupilumab on moderate-to-severe AD patients in China, including its effect on atopic comorbidities. The main findings of the study confirm that Dupilumab not only rapidly and significantly improves the symptoms of AD and quality of life but also effectively alleviates the symptoms of concurrent AR and asthma, with consistent efficacy across different comorbid statuses and a favorable safety profile.

Our study validates the outstanding efficacy of Dupilumab in real-world clinical practice. After 16 weeks of treatment, patients showed a substantial improvement in EASI scores, with a high EASI75 response rate close to 80%, aligning well with pivotal Phase III clinical trial results like SOLO, CHRONOS, which strongly validate Dupilumab’s effectiveness in the Chinese population.^{19–21} The study results also align with multiple real-world studies in Europe, America, and the Asia-Pacific region. For instance, a study in Spain showed that 79.4% of patients achieved EASI75 at week 16, with 40.5% reaching EASI90,³⁴ studies in Italy reported EASI75 response rates of 64.5%,³⁵ and in Korea, 56.1%.³⁶ Domestically, studies conducted in Chongqing, Shanghai, and Hunan showed EASI75 response rates of 42.74%, 64.5%, and 84.62%, respectively.^{28,37,38} Particularly noteworthy is that our study, based on a large population in central China, confirms that despite comorbid patients showing stronger Type 2 inflammation characteristics at baseline (such as higher serum total IgE levels), their response to Dupilumab treatment is no different from that of AD without comorbidities patients. This finding goes beyond previous studies that mainly focused on validating the efficacy of AD alone and corroborates recent reports on comorbid patients,²⁷ providing crucial real-world evidence for the Chinese population. This finding holds significant clinical guidance implications, suggesting that for complex AD patients with multiple Type 2 inflammation comorbidities, Dupilumab should also be considered a first-line treatment option without concerns about efficacy reduced due to comorbidities.

A key finding of this study is the systemic therapeutic effect of Dupilumab on atopic comorbidities. Dupilumab not only improves skin symptoms but also significantly relieves nasal and bronchial symptom and improve quality of life in AR and asthma patients. This aligns well with the mechanism of action of Dupilumab - by blocking the IL-4R α shared pathway, it inhibits the Th2 inflammatory axis that AD, AR and asthma depend on.^{17,23,39} This provides an important treatment perspective for the “atopic march” - targeting a common upstream pathway for treatment may achieve synergistic control of multiple Type 2 inflammatory diseases.

Table 3 Baseline Characteristics of Patients Stratified by EASI Improvement at Week 16

	Patients (n=376)	Improvement <50% (n=44)	Improvement 50–75% (n=36)	Improvement 75–90% (n=59)	Improvement 90–100% (n=237)	Statistical Value	P
Demographics							
Sex (male), n (%)	204(54.3)	23(52.3)	19(52.8)	38(64.4)	124(52.3)	$\chi^2 = 2.909$	0.567
Age, y	10.0(5.0–32.8)	13.00(6.00–41.75)	11.50(6.00–37.25)	12.00(6.00–41.00)	10.00(5.00–30.50)	H = 2.840	0.417
BMI, kg/m ²	18.65(15.38–22.62)	19.68(17.14–24.28)	19.33(16.06–21.07)	19.20(15.00–24.22)	17.97(15.36–22.44)	H = 2.840	0.080
Atopic family history, n (%)	190(50.5)	21(47.7)	24(66.7)	32(54.2)	113(47.7)	$\chi^2 = 4.983$	0.173
Disease duration, y	4.00(2.00–8.00)	5.00(2.25–9.00)	4.00(2.00–8.00)	4.00(2.00–7.00)	4.00(2.00–7.00)	H = 3.118	0.374
Laboratory Parameters							
TigE, KUA/L	400.00 (111.00–1265.50)	258.50(94.23–1910.25)	580.00 (120.00–1636.00)	2239.00 (77.90–2275.00)	430.00 (112.00–1147.00)	H = 0.469	0.926
EOS count, *10 ⁹ /L	0.43(0.17–0.70)	0.49(0.09–0.84)	0.35(0.16–0.51)	0.31(0.18–0.53)	0.44(0.19–0.72)	H = 1.287	0.732
Comorbidities, n (%)							
	106(28.2)	13(29.5)	10(27.8)	11(18.6)	72(30.4)	$\chi^2 = 3.260$	0.353
Allergen, n (%)							
HDM	220(58.5)	25(56.8)	22(61.6)	33(55.9)	140(59.1)	$\chi^2 = 0.345$	0.951
Pollen	73(19.4)	7(15.9)	9(25.0)	13(22.0)	44(18.6)	$\chi^2 = 1.431$	0.698
Animal fur	41(10.9)	1(2.3)	4(11.1)	7(11.9)	29(12.2)	$\chi^2 = 4.235$	0.229
Mold	51(13.6)	4(9.1)	6(16.7)	9(15.3)	32(13.5)	$\chi^2 = 1.259$	0.741
Milk	63(16.8)	4(9.1)	10(27.8)	12(20.3)	37(15.6)	$\chi^2 = 5.754$	0.124
Egg	77(20.5)	4(9.1)	12(33.3)	15(25.4)	46(19.4)	$\chi^2 = 8.209$	0.042
Cereals	19(5.1)	3(6.8)	1(2.8)	4(6.8)	11(4.6)	$\chi^2 = 1.306$	0.717
Tree nuts	48(12.8)	3(6.8)	5(13.9)	11(18.6)	29(12.2)	$\chi^2 = 3.272$	0.350
Legumes	16(4.3)	0(0.0)	1(2.8)	4(6.8)	11(4.6)	$\chi^2 = 2.815$	0.380
Fish	23(6.1)	1(2.3)	1(2.8)	5(8.5)	16(6.8)	$\chi^2 = 2.062$	0.564
Crustaceans	33(8.8)	3(6.8)	2(5.6)	7(11.9)	21(8.9)	$\chi^2 = 1.186$	0.765
Meats	10(2.7)	0(0.0)	1(2.8)	1(1.7)	8(3.4)	$\chi^2 = 1.243$	0.786
AD severity scores							
ADCT	16.00(11.00–19.00)	16.00(10.25–20.00)	16.00(12.00–20.00)	15.00(11.00–19.00)	15.00(11.00–19.00)	H = 0.848	0.838
SCORAD	56.75(41.35–67.50)	53.25(32.38–60.50)	57.90(48.98–66.30)	56.80(41.30–67.30)	58.10(41.65–68.65)	H = 4.147	0.246
POEM	17.00(12.00–22.00)	17.00(10.00–22.00)	19.00(14.25–25.50)	17.00(14.00–23.00)	16.00(12.00–22.00)	H = 5.207	0.157
DLQI	9.00(5.00–14.75)	8.00(6.00–13.75)	11.00(5.25–15.75)	9.00(5.00–13.00)	9.00(5.00–15.00)	H = 1.146	0.766
NRS	8.00(6.00–9.00)	8.00(5.25–9.00)	8.00(6.00–9.00)	8.00(6.00–8.00)	8.00(6.00–9.00)	H = 1.112	0.772
EASI	8.50(4.30–17.45)	5.80(1.45–12.98)	7.75(3.93–14.65)	8.50(3.60–18.00)	9.00(4.80–18.75)	H = 9.402	0.024

Notes: Data are presented as median (interquartile range) or number (%). Between-group comparisons: Continuous variables were compared using the Kruskal–Wallis *H*-test; Categorical variables were compared using the Chi-square or Fisher's exact test. A significant overall difference was found in baseline EASI score ($P = 0.024$); post hoc pairwise comparisons with the Mann–Whitney *U*-test and Bonferroni correction revealed a significant difference only between the 90–100% improvement group and the 0–50% improvement group (adjusted $P = 0.015$). The overall distribution of egg allergy comorbidity differed among groups ($P = 0.042$), but post hoc pairwise comparisons (Fisher's exact test with Bonferroni correction) did not identify significant differences between any specific pairs. All other baseline characteristics were comparable across groups (all $P > 0.05$). Bold values indicate statistical significance ($P < 0.05$).

Abbreviations: EASI, Eczema Area and Severity Index; HDM, house dust mite.

This study provides robust pharmacological evidence for the above mechanisms through dynamic monitoring of key inflammatory markers. We observed a significant decrease in serum total IgE levels post-treatment, while changes in blood eosinophil were relatively modest. This pattern of difference is consistent with findings from various studies,^{7,20,40} indicating that the biological mechanism behind this lies in the varying roles of the IL-4 and IL-13 signaling pathways in regulating different immune cells and molecules. The class switching and generation of IgE are directly and highly dependent on the IL-4/IL-13 signaling pathway, thus Dupilumab's blockade of IL-4R α can efficiently suppress IgE production. In contrast, the generation, activation, release from the bone marrow, and tissue migration of eosinophils are a more complex process, driven not only by IL-4/13 but also by strong cell factors like IL-5, GM-CSF, where Dupilumab has no direct inhibitory effect on the IL-5 pathway. Therefore, the rapid decrease in serum IgE levels can be seen as a biomarker for Dupilumab to take effect, while the relative stability of eosinophil counts reveals the complexity of the Type 2 inflammatory network and suggests that its regulation of eosinophil may be indirect and incomplete.

Moreover, our study's analysis of baseline characteristics revealed significant heterogeneity among different AD patient groups. AD patients with concurrent AR and/or asthma exhibited higher rates of atopic family history, allergen sensitization, and elevated serum total IgE levels compared to AD patients without these comorbidities. This finding aligns with the concept of the "atopic march," indicating a progression towards developing multiple atopic comorbidities from AD due to genetic susceptibility and systemic Type 2 inflammation.^{11,12} Despite higher systemic inflammation markers in the comorbid group, their baseline SCORAD and pruritus NRS scores were lower than those of the AD-only group. This apparent clinical-laboratory disconnect may be explained by several factors. Elevated IgE levels are recognized to reflect a state of multi-organ allergic sensitization rather than directly correlating with cutaneous disease severity.⁴¹⁻⁴⁴ It is plausible that patients with multi-system comorbidities seek medical attention at an earlier stage of skin involvement due to the burden of their respiratory or ocular symptoms. Furthermore, the systemic inflammatory burden in these patients may be more broadly distributed, particularly toward the respiratory tract, thereby attenuating the cutaneous clinical presentation. Adaptive changes in itch perception over the chronic disease course may also contribute. While reporting bias cannot be entirely excluded, the use of standardized CRFs during clinical visits was designed to minimize this. Collectively, these observations underscore the importance of a comprehensive, multi-system assessment to accurately evaluate the disease burden in patients with multiple atopic comorbidities.

Another interesting finding is that comorbid group patients exhibited lower BMI and longer disease duration. We believe that severe AD in early childhood can impact growth and development through various mechanisms. Sustained systemic inflammation may result in high metabolic consumption. Additionally, severe itching and sleep disturbances can hinder nutrient intake and absorption. The chronic disease burden may have lasting negative effects on childhood growth and development. Consequently, a lower BMI may not directly cause comorbidity but could serve as an indicator of more severe, early-onset AD with longer disease duration. These findings emphasize the importance for clinical practitioners to closely monitor the nutritional status and growth indicators of AD patients with multiple atopic comorbidities, particularly in children and adolescents.

Despite the baseline differences mentioned above, Dupilumab demonstrated equally outstanding efficacy across all groups. This indicates that the core driving pathway of AD skin lesions - the IL-4/IL-13 signaling cascade - is efficiently inhibited regardless of whether patients have comorbidities, varying levels of baseline inflammation, or differing disease durations. Therefore, the presence of comorbidities, higher IgE levels, or longer disease duration should not be a concern for clinicians considering the use of Dupilumab. On the contrary, these characteristics may indeed serve as strong indicators of benefit for patients undergoing Dupilumab treatment.

In terms of predicting treatment efficacy factors, we found that patients with higher baseline disease severity had a greater proportion achieving near-complete improvement of 90–100%. This could stem from the more severe inflammatory state providing a precise intervention target for the medication, resulting in a more significant improvement space. This finding, while similar to some real-world study results, differs from the traditional notion that greater baseline severity leads to poorer efficacy.²⁸ Stingeni and others hold a contrary view, suggesting that patients with lower baseline EASI scores exhibit better efficacy,³⁵ a mechanism worthy of further exploration. Additionally, most studies suggest that treatment outcomes are better in females with good medication adherence, while factors like younger age of onset and low BMI are poorer predictive elements.^{28,35,37} Due to the complexity and heterogeneity of AD treatment responses, we

were unable to establish a multivariate predictive model incorporating demographic characteristics and laboratory indicators (IgE, EoS). Future research should integrate genomics, proteomics, and other multidimensional data to construct more precise predictive tools.

Our study confirms the good overall tolerability of Dupilumab in real-world clinical practice, aligning with findings from previous studies.^{28,35–37,45–47} Among 376 patients, 19.68% reported mild to moderate adverse reactions, with only 0.80% discontinuing treatment due to adverse events, indicating its high long-term safety. Ocular events (8.51%) were the most common adverse reactions, likely linked to the drug's impact on ocular mucosal immunity and goblet cell function through the IL-4/IL-13 pathway,^{48,49} typically managed with eye drops. Skin and subcutaneous tissue events (6.91%), including localized symptom exacerbation, hair loss, and facial erythema, suggest temporary regulatory responses in the skin barrier or hair follicle cycle, often self-limiting and manageable in clinical practice. While this study did not comprehensively evaluate safety in these specific populations, rare adverse events were noted during the observation period, such as one case of cerebral infarction (0.27%). However, it was assessed as unrelated to dupilumab treatment. This conclusion was based on several considerations: first, the event is inconsistent with dupilumab's known pharmacological mechanism, and no such association has been reported in previous large-scale studies or post-marketing surveillance; second, the patient had pre-existing hypertension—a well-established independent risk factor for cerebrovascular events; finally, and most compellingly, the clinical decision to continue dupilumab treatment for six months following the event strongly indicates that the treating physicians did not suspect a drug-related causality. This assessment aligns with the established safety profile of dupilumab. Nevertheless, enhanced monitoring is advised for high-risk patients (eg, with cardiovascular disease history or severe metabolic syndrome). Moreover, existing reports suggest that Dupilumab use does not significantly worsen conditions in patients with hepatitis B, HIV infection, or advanced cancer.^{50–52} Some studies hint at symptom relief in COVID-19 cases with Dupilumab use, reinforcing its favorable safety profile.⁵³ Occasional reports of weight gain, dizziness, and hypersensitivity reactions offer valuable insights for identifying and managing atypical adverse reactions in clinical settings.^{47,54}

The analysis of treatment persistence provides insightful perspectives from clinical practice. Our real-world data revealed a 52-week drug survival rate exceeding 40% in both groups, with a median treatment duration of over 44 weeks. More notably, the conventional Kaplan-Meier analysis, while reflecting overall patterns, unveiled a distinctive finding: the primary reason for discontinuation was “disease improvement” (approximately 45%), rather than poor efficacy or adverse reactions. This high rate of discontinuation due to therapeutic success inherently serves as a powerful indicator of the drug's effectiveness. Furthermore, the sustained median drug survival of 44 weeks, even in the context of this substantial “attrition of success,” provides strong complementary evidence of the drug's favorable overall profile in real-world settings. This pattern reveals that in clinical practice, a considerable number of patients may choose to stop biologic therapy once their symptoms are adequately controlled, providing a realistic basis for exploring personalized treatment strategies in the future, such as treatment de-escalation or intermittent therapy. This higher treatment persistence rate and the predominant reason for discontinuation being “disease improvement” corroborate the long-term efficacy and patient acceptance from a real-world perspective.

This study has several limitations. Firstly, it is a single-center study focused primarily on children and adolescents, which may limit the generalizability of the results to a broader population (different ethnicities, adults and the elderly), requiring further research for validation. Secondly, despite using a retrospective-prospective design, some baseline and follow-up data rely on the completeness of medical records and patient recall, which may introduce information bias. Thirdly, the sample size of comorbid subgroups (especially the asthma group) is relatively small, with insufficient statistical power, potentially impacting the robustness of efficacy assessment in this subgroup. Fourthly, the 16-week observation period may be insufficient for a comprehensive evaluation of the long-term efficacy, development of resistance, and the risk of rare adverse reactions. Additionally, this study did not include a systematic analysis of environmental factors (such as pollutants, temperature, humidity changes), which could serve as important variables affecting the efficacy of AD. Existing evidence suggests a relationship between environmental conditions and the prevalence and severity of AD symptoms.^{55–59} For example, studies found that seasonal changes significantly impact the condition of Chinese AD patients, with a considerable number experiencing symptom exacerbation in summer and/or winter.⁵⁸ Future research directions should include conducting multicenter, large-sample, long-term prospective studies

with comprehensive biomarkers, environmental exposure, and racial factor analyses, utilizing multivariable statistical modeling methods to further optimize personalized treatment strategies.

In conclusion, this real-world study from central China provides strong evidence that Dupilumab is an effective, safe, and systemically beneficial treatment for moderate to severe AD and its atopic comorbidities. It can rapidly control skin inflammation, significantly improve quality of life, and concurrently alleviate respiratory comorbidity symptoms, thereby comprehensively blocking the “atopic march.” This study offers robust evidence for the application of Dupilumab in the Chinese population, especially in the central region, and provides important evidence for its positioning as a foundational treatment for AD and multiple Type 2 inflammatory comorbidities.

Data Sharing Statement

The datasets generated and analyzed during the current study are not publicly available due to patient privacy and confidentiality regulations but are available from the corresponding author upon reasonable request. Requests must meet the criteria for access to confidential data as determined by the Tongji Hospital Ethics Committee.

Ethical Approval

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Tongji Hospital (No. TJ-IRB20231112). The ethics committee waived the requirement for additional written informed consent specifically for this research, as the study posed minimal risk, did not alter clinical management, involved retrospective data collection, and all patient data were anonymized to ensure confidentiality. Furthermore, all patients (adults) and parents/guardians (of minors) had already provided written consent for Dupilumab treatment prior to therapy initiation.

Acknowledgments

The authors would like to express their gratitude to all the patients and their families for participating in this study. We also thank the medical staff and clinical coordinators at Tongji Hospital for their invaluable assistance in data collection and patient care.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Chu DK, Chu DK, Schneider L, et al. AAAAI/ACAAI JTF Atopic Dermatitis Guideline Panel. Atopic dermatitis (eczema) guidelines: 2023 American academy of allergy, asthma and immunology/american college of allergy, asthma and immunology joint task force on practice parameters grade- and institute of medicine-based recommendations. *Ann Allergy Asthma Immunol.* 2024;132(3):274–312. doi:10.1016/j.anai.2023.11.009
2. Nutten S. Atopic dermatitis: global epidemiology and risk factors. *Ann Nutr Metab.* 2015;66(1):8–16. doi:10.1159/000370220
3. Sandilands A, Terron-Kwiatkowski A, Hull PR, et al. Comprehensive analysis of the gene encoding filaggrin uncovers prevalent and rare mutations in ichthyosis vulgaris and atopic eczema. *Nat Genet.* 2007;39(5):650–654. doi:10.1038/ng2020
4. Guttman-Yassky E, Renert-Yuval Y, Brunner PM. Atopic dermatitis. *Lancet.* 2025;405(10478):583–596. doi:10.1016/S0140-6736(24)02519-4
5. Stefanovic N, Irvine AD. Filaggrin and beyond: new insights into the skin barrier in atopic dermatitis and allergic diseases, from genetics to therapeutic perspectives. *Ann Allergy Asthma Immunol.* 2024;132(2):187–195. doi:10.1016/j.anai.2023.09.009
6. Schuler CF, Tsoi LC, Billi AC, Harms PW, Weidinger S, Gudjonsson JE. Genetic and immunological pathogenesis of atopic dermatitis. *J Invest Dermatol.* 2024;144(5):954–968. doi:10.1016/j.jid.2023.10.019
7. Gandhi NA, Bennett BL, Graham NMH, Pirozzi G, Stahl N, Yancopoulos GD. Targeting key proximal drivers of type 2 inflammation in disease. *Nat Rev Drug Discov.* 2016;15(1):35–50. doi:10.1038/nrd4624
8. Akdis CA, Arkwright PD, Brügggen MC, et al. Type 2 immunity in the skin and lungs. *Allergy.* 2020;75(7):1582–1605. doi:10.1111/all.14318
9. Spigel JM. From atopic dermatitis to asthma: the atopic march. *Ann Allergy Asthma Immunol.* 2010;105(2):99–106;quiz107–109,117. doi:10.1016/j.anai.2009.10.002
10. Weidinger S, Beck LA, Bieber T, Kabashima K, Irvine AD. Atopic dermatitis. *Nat Rev Dis Primers.* 2018;4(1):1. doi:10.1038/s41572-018-0001-z
11. Silverberg JI. Comorbidities and the impact of atopic dermatitis. *Ann Allergy Asthma Immunol.* 2019;123(2):144–151. doi:10.1016/j.anai.2019.04.020

12. Paller AS, Spergel JM, Mina-Osorio P, Irvine AD. The atopic march and atopic multimorbidity: many trajectories, many pathways. *J Allergy Clin Immunol.* 2019;143(1):46–55. doi:10.1016/j.jaci.2018.11.006
13. Caffarelli C, Giannetti A, Gianni G, Ricci G. Anti-inflammatory and biologic drugs for atopic dermatitis: a therapeutic approach in children and adolescents. *Front Med.* 2023;10:1214963. doi:10.3389/fmed.2023.1214963
14. Bieber T. Atopic dermatitis: an expanding therapeutic pipeline for a complex disease. *Nat Rev Drug Discov.* 2022;21(1):21–40. doi:10.1038/s41573-021-00266-6
15. Meledathu S, Naidu MP, Brunner PM. Update on atopic dermatitis. *J Allergy Clin Immunol.* 2025;155(4):1124–1132. doi:10.1016/j.jaci.2025.01.013
16. Stölzl D, Weidinger S, Drerup K. A new era has begun: treatment of atopic dermatitis with biologics. *Allergol Select.* 2021;5:265–273. doi:10.5414/ALX02259E
17. Harb H, Chatila TA. Mechanisms of Dupilumab. *Clin Exp Allergy.* 2020;50(1):5–14. doi:10.1111/cea.13491
18. Floc'h A L, Allinne J, Nagashima K, et al. Dual blockade of IL-4 and IL-13 with dupilumab, an IL-4R α antibody, is required to broadly inhibit type 2 inflammation. *Allergy.* 2020;75(5):1188–1204. doi:10.1111/all.14151
19. Simpson EL, Paller AS, Siegfried EC, et al. Efficacy and safety of dupilumab in adolescents with uncontrolled moderate to severe atopic dermatitis: a phase 3 randomized clinical trial. *JAMA Dermatol.* 2020;156(1):44–56. doi:10.1001/jamadermatol.2019.3336
20. Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med.* 2016;375(24):2335–2348. doi:10.1056/NEJMoa1610020
21. 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):2287–2303. doi:10.1016/S0140-6736(17)31191-1
22. David E, Ungar B, Renert-Yuval Y, Facheris P, Del Duca E, Guttman Yassky E. The evolving landscape of biologic therapies for atopic dermatitis: present and future perspective. *Clin Exp Allergy.* 2023;53(2):156–172. doi:10.1111/cea.14263
23. Licari A, Castagnoli R, Marseglia A, et al. Dupilumab to treat type 2 inflammatory diseases in children and adolescents. *Paediatr Drugs.* 2020;22(3):295–310. doi:10.1007/s40272-020-00387-2
24. Blaiss M, Bleecker ER, Jacob-Nara J, et al. Real-world effectiveness of dupilumab in patients with asthma: findings from the US ADVANTAGE study. *Ann Allergy Asthma Immunol.* 2024;132(4):463–468.e1. doi:10.1016/j.anai.2023.11.006
25. Yosipovitch G, Mollanazar N, Ständer S, et al. Dupilumab in patients with prurigo nodularis: two randomized, double-blind, placebo-controlled phase 3 trials. *Nat Med.* 2023;29(5):1180–1190. doi:10.1038/s41591-023-02320-9
26. Bachert C, Han JK, Desrosiers M, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials. *Lancet.* 2019;394(10209):1638–1650. doi:10.1016/S0140-6736(19)31881-1
27. Boguniewicz M, Beck LA, Sher L, et al. Dupilumab improves asthma and sinonasal outcomes in adults with moderate to severe atopic dermatitis. *J Allergy Clin Immunol Pract.* 2021;9(3):1212–1223.e6. doi:10.1016/j.jaip.2020.12.059
28. Wang Y, Jia R, Hu Q, et al. Long-term efficacy and safety of dupilumab for moderate-to-severe atopic dermatitis: a prospective real-world cohort study in China. *Front Immunol.* 2024;15:1419164. doi:10.3389/fimmu.2024.1419164
29. Deng S, Wang H, Chen Q, et al. Long-term, observational, real-world study of dupilumab for the treatment of moderate-to-severe atopic dermatitis: a 52-week single-center retrospective analysis in China. *Arch Dermatol Res.* 2024;316(6):304. doi:10.1007/s00403-024-03029-6
30. Stölzl D, Sander N, Heratizadeh A, et al. Real-world data on the effectiveness, safety and drug survival of dupilumab: an analysis from the TREATgermany registry. *Br J Dermatol.* 2022;187(6):1022–1024. doi:10.1111/bjd.21794
31. Hanifin JM, Rajka G. Diagnostic Features of Atopic Dermatitis. *Acta Dermato-Venereologica.* 1980;60:44–47. doi:10.2340/00015555924447
32. Global Initiative for Asthma. Strategy for Asthma Management and Prevention, 2024. Available from: www.ginasthma.org. Accessed December 13, 2024.
33. Brożek JL, Bousquet J, Agache I, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision. *J Allergy Clin Immunol.* 2017;140(4):950–958. doi:10.1016/j.jaci.2017.03.050
34. Iznardo H, Roé E, Vicente A, et al. Dupilumab treatment in paediatric atopic dermatitis (2-18 years): spanish multicentre retrospective real-world study. *Clin Exp Dermatol.* 2024;50(1):104–112. doi:10.1093/ced/llae300
35. Stingeni L, Bianchi L, Antonelli E, et al. Moderate-to-severe atopic dermatitis in adolescents treated with dupilumab: a multicentre Italian real-world experience. *J Eur Acad Dermatol Venereol.* 2022;36(8):1292–1299. doi:10.1111/jdv.18141
36. Jang DH, Heo SJ, Jung HJ, Park MY, Seo SJ, Ahn J. Retrospective study of dupilumab treatment for moderate to severe atopic dermatitis in Korea: efficacy and safety of dupilumab in real-world practice. *J Clin Med.* 2020;9(6):1982. doi:10.3390/jcm9061982
37. Gu C, Wu Y, Luo Y, et al. Real-world efficacy and safety of dupilumab in Chinese patients with atopic dermatitis: a single-centre, prospective, open-label study. *J Eur Acad Dermatol Venereol.* 2022;36(7):1064–1073. doi:10.1111/jdv.18109
38. Zhou B, Peng C, Li L, et al. Efficacy and safety of dupilumab in Chinese patients with atopic dermatitis: a real-world study. *Front Med.* 2022;9:838030. doi:10.3389/fmed.2022.838030
39. Langan SM, Irvine AD, Weidinger S. Atopic dermatitis. *Lancet.* 2020;396(10247):345–360. doi:10.1016/S0140-6736(20)31286-1
40. Hamilton JD, Suárez-Fariñas M, Dhingra N, et al. Dupilumab improves the molecular signature in skin of patients with moderate-to-severe atopic dermatitis. *J Allergy Clin Immunol.* 2014;134(6):1293–1300. doi:10.1016/j.jaci.2014.10.013
41. Greene D, Moore Fried J, Wang J. IgE in Allergic Diseases. *Immunol Rev.* 2025;334(1):e70057. doi:10.1111/imr.70057
42. Thijs JL, Strickland I, Bruijnzeel-Koomen CAFM, et al. Serum biomarker profiles suggest that atopic dermatitis is a systemic disease. *J Allergy Clin Immunol.* 2018;141(4):1523–1526. doi:10.1016/j.jaci.2017.12.991
43. Bellanti JA, Settignano RA. The allergist and IgE: the realization that allergic diseases are not all IgE mediated. *Allergy Asthma Proc.* 2021;42(3):183–186. doi:10.2500/aap.2021.42.210037
44. Shamji MH, Valenta R, Jardetzky T, et al. The role of allergen-specific IgE, IgG and IgA in allergic disease. *Allergy.* 2021;76(12):3627–3641. doi:10.1111/all.14908

45. Ariëns LFM, van der Schaft J, Spekhorst LS, et al. Dupilumab shows long-term effectiveness in a large cohort of treatment-refractory atopic dermatitis patients in daily practice: 52-Week results from the Dutch BioDay registry. *J Am Acad Dermatol.* 2021;84(4):1000–1009. doi:10.1016/j.jaad.2020.08.127
46. Halling AS, Loft N, Silverberg JI, Guttman-Yassky E, Thyssen JP. Real-world evidence of dupilumab efficacy and risk of adverse events: a systematic review and meta-analysis. *J Am Acad Dermatol.* 2021;84(1):139–147. doi:10.1016/j.jaad.2020.08.051
47. Musters AH, van Lookeren FL, van der Gang LF, et al. Real-world reported adverse events related to systemic immunomodulating therapy in patients with atopic dermatitis: results from the TREAT NL (TREATment of ATopic eczema, the Netherlands) registry. *J Eur Acad Dermatol Venereol.* 2024;38(3):530–542. doi:10.1111/jdv.19643
48. Fachler T, Shreberk-Hassidim R, Molho-Pessach V. Dupilumab-induced ocular surface disease: a systematic review. *J Am Acad Dermatol.* 2022;86(2):486–487. doi:10.1016/j.jaad.2021.09.029
49. Tukler Henriksson J, Coursey TG, Corry DB, De Paiva CS, Pflugfelder SC. IL-13 stimulates proliferation and expression of mucin and immunomodulatory genes in cultured conjunctival goblet cells. *Invest Ophthalmol Vis Sci.* 2015;56(8):4186–4197. doi:10.1167/iovs.14-15496
50. Tanczosova M, Hugo J, Gkalpakiotis S. Treatment of severe atopic dermatitis with dupilumab in patients with advanced cancer. *J Clin Med.* 2023;12(3):1191. doi:10.3390/jcm12031191
51. Ly K, Smith MP, Thibodeaux Q, Beck K, Bhutani T, Liao W. Dupilumab in patients with chronic hepatitis B on concomitant entecavir. *JAAD Case Rep.* 2019;5(7):624–626. doi:10.1016/j.jcdr.2019.05.007
52. Edmonds N, Zhao P, Flowers RH. The use of dupilumab in patients with HIV. *Int J STD AIDS.* 2022;33(14):1165–1173. doi:10.1177/09564624221129406
53. Ungar B, Glickman JW, Golant AK, et al. COVID-19 symptoms are attenuated in moderate-to-severe atopic dermatitis patients treated with dupilumab. *J Allergy Clin Immunol Pract.* 2022;10(1):134–142. doi:10.1016/j.jaip.2021.10.050
54. Kychygina A, Cassagne M, Tauber M, et al. Dupilumab-associated adverse events during treatment of allergic diseases. *Clin Rev Allergy Immunol.* 2022;62(3):519–533. doi:10.1007/s12016-022-08934-0
55. Nguyen GH, Andersen LK, Davis MDP. Climate change and atopic dermatitis: is there a link? *Int J Dermatol.* 2019;58(3):279–282. doi:10.1111/ijd.14016
56. Chu H, Shin JU, Park CO, Lee H, Lee J, Lee KH. Clinical diversity of atopic dermatitis: a review of 5,000 patients at a single institute. *Allergy Asthma Immunol Res.* 2017;9(2):158–168. doi:10.4168/aaair.2017.9.2.158
57. Williams JR, Burr ML, Williams HC. Factors influencing atopic dermatitis—a questionnaire survey of schoolchildren’s perceptions. *Br J Dermatol.* 2004;150(6):1154–1161. doi:10.1111/j.1365-2133.2004.05869.x
58. Li Z, Yin H, Wang Y, et al. Temporal and topographical heterogeneities in clinical manifestations of atopic dermatitis in China. *J Clin Med.* 2025;14(3):840. doi:10.3390/jcm14030840
59. Silverberg JI, Hanifin J, Simpson EL. Climatic factors are associated with childhood eczema prevalence in the United States. *J Invest Dermatol.* 2013;133(7):1752–1759. doi:10.1038/jid.2013.19

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