

Improvements in Quality of Life and Itch Symptoms with Dupilumab in Patients with Atopic Dermatitis: A Targeted Literature Review and Meta-Analysis of Real-World Studies

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SYNOPSIS

- Dupilumab, an interleukin-4 receptor alpha antagonist, was approved for the treatment of moderate-to-severe atopic dermatitis (AD) in patients aged ≥6 months based on data from clinical trials.¹
- Subsequent real-world studies further confirmed the effectiveness of dupilumab in patients with moderate-to-severe AD^{2,3}; however, a comprehensive review with a summary effect estimate controlling for potential confounders across different studies has not been reported.

OBJECTIVE

- This targeted literature review (TLR) and meta-analysis (MA) aimed to provide a comprehensive overview of the available real-world studies on dupilumab and estimate a summary effect of its effectiveness in patients with moderate-to-severe AD.

METHODS

- This targeted literature search was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline (Figure 1).
- PubMed and Embase were searched to identify real-world studies between April 01, 2017 and November 18, 2021 evaluating the results of dupilumab in patients with moderate-to-severe AD.
- Screening for study inclusion and exclusion was performed according to PICOS-T (Population, Intervention, Comparators, Outcomes, Study design, and Time horizon) criteria (Table 1).

Table 1. Study eligibility criteria

Elements	Inclusion criteria	Exclusion criteria
Population	Individuals with moderate-to-severe AD aged ≥6 years	Studies not including individuals with moderate-to-severe AD or aged <6 years
Intervention	Dupilumab (monotherapy or add-on therapy)	Studies not including dupilumab as intervention
Comparators	No limitation ^a	No exclusion criteria
Outcomes	Studies reporting at least one effectiveness or patient-reported outcome	Studies without effectiveness or patient-reported outcome
Study design	Observational and real-world studies (e.g., prospective, and retrospective studies, registries, or case reports)	Clinical trials, commentaries, letters, recommendations, guidelines, method articles, protocols, evaluation studies or basic sciences articles, animal, or cell studies
Time horizon	Studies published from April 01, 2017 ^b to November 18, 2021	Studies published before April 01, 2017 and after November 18, 2021
Other	Abstract in English language	Abstract not in English language ^c

^aFor studies with comparators, data were extracted for the dupilumab treatment arm. ^bMonth after the first dupilumab US FDA approval for AD. ^cPublications in non-English language but with an English abstract were screened and included if outcome data was included in the abstract. AD, atopic dermatitis; US FDA, United States Food and Drug Administration.

Data extractions and outcomes

- Data on study characteristics, patient characteristics, quality of life (Dermatology Life Quality Index [DLQI]), and Itch Numeric Rating Scale [NRS]) were extracted.
- Meta-regression models were estimated to assess DLQI and Itch-NRS outcomes.

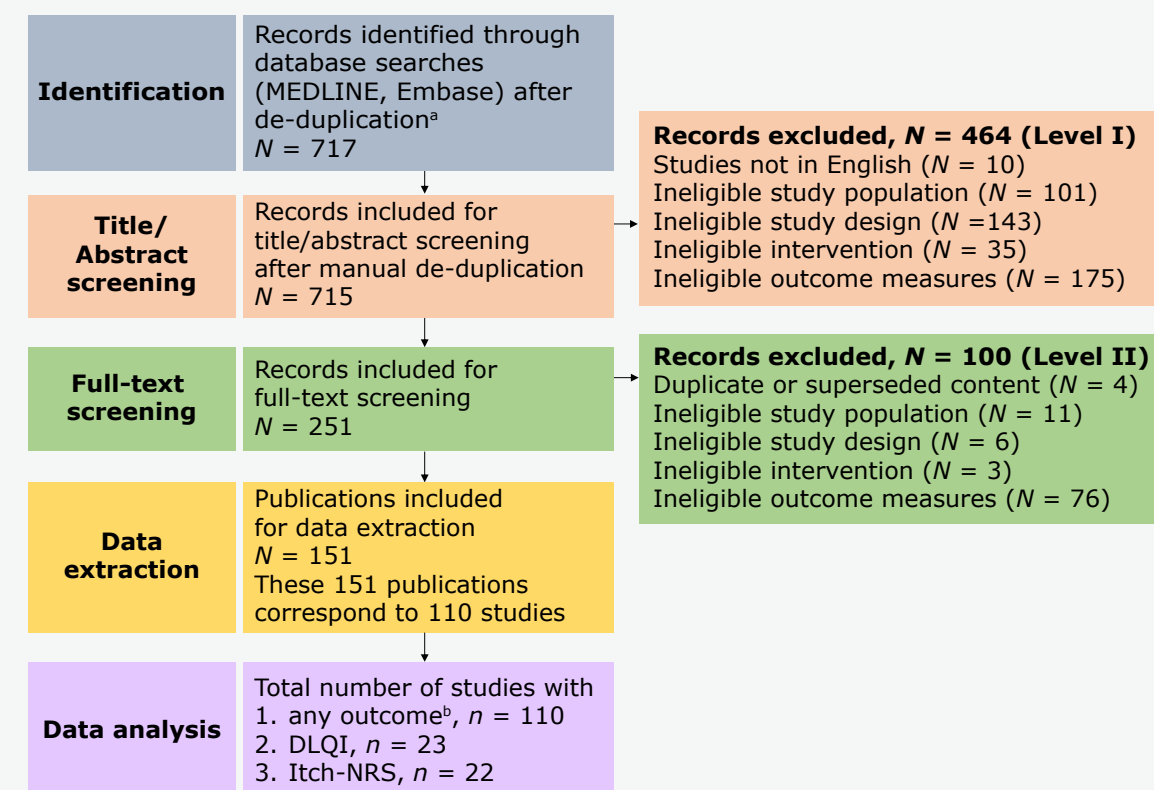
Statistical analysis

- Meta-regressions were estimated as mixed-effects models. Study-level characteristics (age, gender, region, and disease severity) and follow-up duration were included as covariates in meta-regression models of DLQI and Itch-NRS outcomes.
- Results were reported at different follow-up intervals (1–4 weeks, 5–26 weeks, and over 26 weeks) with baseline used as the reference group.
- The “metafor” R package was used for meta-regression.
- A sensitivity analysis was conducted to assess the influence of study sample size (largest [2,428 patients] and small [<10 patients]) on the overall results.

RESULTS

- Overall, 151 publications (110 studies), consisting of 10,187 patients (mean [standard deviation] age, 40.9 [10.6] years; males, 58.5%) were included in the TLR ($n = 49$, case series/reports; $n = 10$, registries; $n = 92$, other longitudinal studies) (Figure 1).
- Of them, 23 and 22 studies, comprising of 3,484 and 3,389 patients, were included in the meta regressions for DLQI and Itch-NRS, respectively.

Figure 1. PRISMA flowchart for the selection of studies



^aAll searches were conducted through Ovid. ^bOutcomes included in the TLR and MA were ADCT, BSA, DLQI, Drug survival, EASI, IGA, Itch-NRS, POEM, PGA, SCORAD, and WPAl-AD. The current analysis included only DLQI and Itch-NRS. ADCT, Atopic Dermatitis Control Tool; BSA, Body Surface Area; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; Itch-NRS, Itch – Numerical Rating Scale; MA, meta-analysis; POEM, Patient Oriented Eczema Measure; PGA, Patient Global Assessment; SCORAD, Scoring Atopic Dermatitis; TLR, targeted literature review; WPAl-AD, Work Productivity and Activity Impairment Questionnaire – Atopic Dermatitis.

- The demographic and clinical characteristics of included studies are presented in Table 2.

Table 2. Demographic and clinical characteristics of study samples

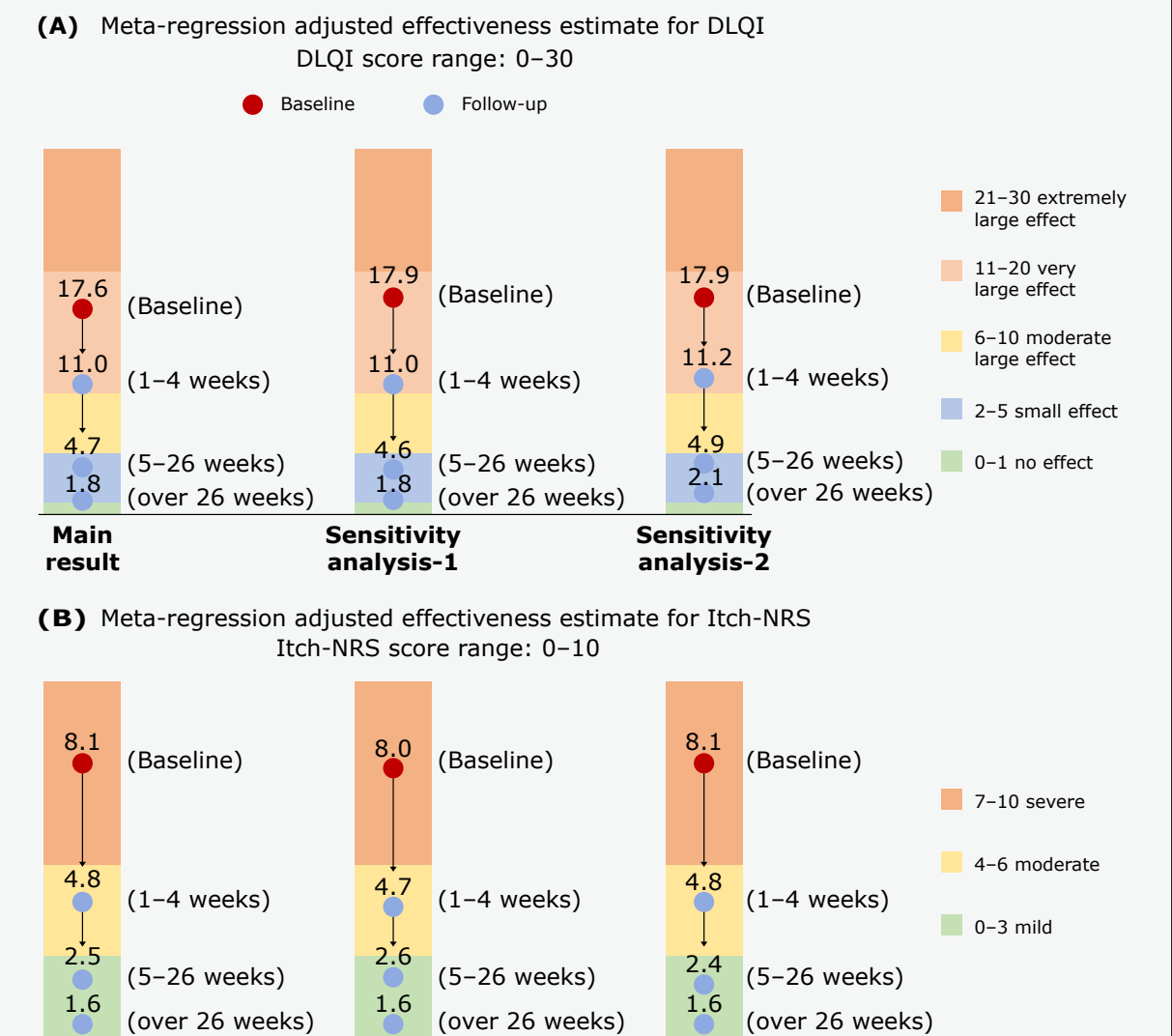
Characteristics	All studies
Publications included in the TLR, N	151
Patients included in the TLR, N	10,187
Studies reporting DLQI data, n	23
Number of patients, n	3,484
Studies reporting Itch-NRS data, n	22
Number of patients, n	3,389
Population, n (%)	
Adults	7,816 (86.6)
Adolescents + adults	785 (8.7)
Children + adolescents + adults	212 (2.3)
Children + adolescents	177 (2.0)
Adolescents	31 (0.3)
Children	5 (0.1)
Region, n (%)	
Europe	7,598 (75.5)
North America	1,672 (16.6)
Asia	392 (3.9)
Others	407 (4.0)
Disease severity, n (%)	
Moderate-to-severe	4,247 (51.1)
Severe	3,661 (44.1)
Mild-to-severe	400 (4.8)
Moderate	1 (0)
Age, years, mean (SD)	40.9 (10.6)
Male, n (%)	5,240 (58.5)

DLQI, Dermatology Life Quality Index; Itch-NRS, Itch – Numeric Rating Scale; n , numbers included in a specified subgroup; N , total count; SD, standard deviation; TLR, targeted literature review.

Effectiveness of dupilumab in reducing DLQI and Itch-NRS scores

- Mean (95% confidence interval) DLQI and Itch-NRS scores were 17.6 (16.0–19.3) and 8.1 (7.5–8.8) at baseline, 11.0 (9.6–12.4) and 4.8 (4.3–5.3) within the first 4 weeks, and 1.8 (0.4–3.2) and 1.6 (1.1–2.1) beyond 26 weeks, respectively (all $P < 0.001$) (Figure 2).
- Dupilumab treatment was associated with significant reductions from baseline in both DLQI and Itch-NRS scores as early as Week 4 (DLQI: 37.5%; Itch-NRS: 40.7%) and beyond 26 weeks (DLQI: 89.8%; Itch-NRS: 80.2%) in patients with moderate-to-severe AD (all $P < 0.001$).
- Heterogeneity between the studies remained substantial after inclusion of all covariates (I^2 , 92%).
- The sensitivity analysis suggested that the results for both outcomes were not influenced by studies with very large or small samples (Figure 2).

Figure 2. Meta-regression adjusted effectiveness estimate for (A) DLQI and (B) Itch-NRS scores



$P < 0.001$ at different follow-up intervals for all comparisons (main results, sensitivity analysis-1, and sensitivity analysis-2) for both DLQI and Itch-NRS outcomes. Model covariates are follow-up time, age, sex, region, and disease severity. Sensitivity analysis-1: outcomes estimated after removing study with largest sample size ($N = 2,428$); sensitivity analysis-2: outcomes estimated after excluding studies with sample size <10 . Total DLQI scores range from 0–30, Itch-NRS scores range from 0–10; higher score indicates more impairment to quality of life (for DLQI) or worse pain (Itch-NRS).^{4,5} Colored bands show severity categories. DLQI, Dermatology Life Quality Index; Itch-NRS, Itch – Numeric Rating Scale.

CONCLUSION

- Meta-regression estimates show that use of dupilumab in the real-world is associated with rapid and sustained improvements in quality of life and itch intensity, as measured by DLQI and Itch-NRS scores, in patients with moderate-to severe AD.
- However, these findings are limited by the information reported in the literature (publication bias, incomplete reporting, and high heterogeneity between studies).

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CONFLICTS OF INTEREST

MB-W is co-principal investigator at Dutch BioDay Registry; has attended advisory boards and educational events at Sanofi-Genzyme, Regeneron, AbbVie, and Galderma; has received institutional research grants from Sanofi Genzyme; and has had consultancy roles, at Sanofi-Genzyme, Regeneron, Leo Pharma, Eli Lilly, AbbVie, Pfizer, Galderma, and UCB, outside the submitted work. **JS** has received consulting fees from AbbVie, Aldena, Amgen, AdBiome, Arcutis, Arena, Asana, Aslan, Attovia, BiomX, Biosion, Bodewell, Boehringer-Ingelheim, Bristol-Myers Squibb, Cara, Castle Biosciences, Celgene, Connect Biopharma, CoreVitas, Dermavant, DermTech, Eli Lilly, Galderma, GlaxoSmithKline, Incyte, Kiniksa, Leo Pharma, My-Or Diagnostics, Nektar, Novartis, Optum, Pfizer, RAPT, Recludix, Regeneron, Sanofi-Genzyme, Shaperon, TARGET-RWE, Union, and UpToDate; grants or contracts from Galderma, Incyte, and Pfizer; and payments or honoraria for lectures, presentations, and speakers bureaus from AbbVie, Eli Lilly, Leo Pharma, Pfizer, Regeneron, and Sanofi-Genzyme. He has on Data Safety Monitoring Board or Advisory Board of Kymab and Biosion and has stocks or stock options at Connect and Verdant. **BM, MY, and MF** are employees of Analysis Group and have received research funding from Sanofi to perform this study. **JZW** is an employee of Regeneron Pharmaceuticals and may hold stocks and/or stock options in the company. **DS, PG, KN, and GB** are employees of Sanofi and may hold stocks and/or stock options in the company.